



KJS
Kosova Journal of Surgery

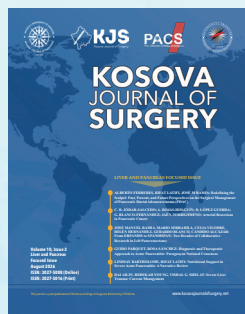


KOSOVA JOURNAL OF SURGERY

LIVER AND PANCREAS FOCUSED ISSUE

Volume 10, Issue 2
Liver and Pancreas
Focused Issue
August 2026
ISSN: 3027-5008 (Online)
ISSN: 3027-5016 (Print)

- ALBERTO FERRERES, RIFAT LATIFI, JOSÉ M RAMIA: Redefining the Scalpel: Past, Present, and Future Perspectives on the Surgical Management of Pancreatic Ductal Adenocarcinoma (PDAC)
- C. R. JÓDAR-SALCEDO; A. ROJAS-HOLGUÍN; D. LÓPEZ GUERRA; G. BLANCO-FERNÁNDEZ; JAÉN-TORREJIMENO: Arterial Resections in Pancreatic Cancer
- JOSÉ MANUEL RAMIA, MARIO SERRADILA, CELIA VILODRE, BELÉN HERNÁNDEZ, GERARDO BLANCO, CÁNDIDO ALCÁZAR: From ERPANDIS to SPANDISPAN: Two Decades of Collaborative Research in Left Pancreatectomy
- GUIDO PARQUET, ROSA SÁNCHEZ: Diagnostic and Therapeutic Approach to Acute Pancreatitis: Paraguayan National Consensus
- LINDSAY BARTHOLOME, RIFAT LATIFI: Nutritional Support in Severe Acute Pancreatitis: A Narrative Review
- DAI AILIN, REBEKAH YOUNG, VISHAL G. SHELAT: Severe Liver Trauma: Current Management



KOSOVA JOURNAL OF SURGERY
Volume 10, Issue 2
Liver and Pancreas Focused Issue
August 2026

ISSN: 3027-5008 (Online)
ISSN: 3027-5016 (Print)
www.kosovajournalofsurgery.net
info@koscs.org • www.koscs.org

EDITOR-IN- CHIEF

Rifat Latifi, MD, USA

DEPUTY EDITORS-IN-CHIEF

Luan Jaha, MD, Kosova
Nexhmi Hyseni, MD, Kosova
Skender Topi, MD, Albania

EDITOR, BIOSTATISTICS

Ilir Hoxha, MD, Kosova

HONORARY EDITORS

Hasan Ahmeti, MD, Kosova
Sadri Bajraktari, MD, Kosova

ASSOCIATE EDITORS

Mentor Ahmeti, MD, USA
Astrit Hamza, MD, Kosova
Lumnije Kqiku Biblekaj, MD, Austria
Mentor Petrela, MD, Albania,
Jose Manuel Ramia, MD, Spain

MANAGING EDITOR

Fatjona Jahaj, Kosova

DESIGN AND LAYOUT

Ardian Veliu, Kosova

© Copyright Kosova Journal of Surgery, Kosova College of Surgeons, University of Prishtina, Pan-Albanian College of Surgeons. All rights reserved. No parts of this Journal may be reproduced or transmitted in any form and by any means without written permission from Kosova Journal of Surgery, Kosova College of Surgeons, University of Prishtina and Pan-Albanian College of Surgeons. Kosova Journal of Surgery, Kosova College of Surgeons, University of Prishtina and Pan-Albanian College of Surgeons reserve the right to reject or accept any advertisement or advertisement material prior to publication.

EDITORIAL BOARD

INTERNATIONAL

Alban Neziri, MD, Switzerland
Alberto R. Ferreres, MD, FACS, Argentina
Arben Baboci, MD, Albania
Arben Beqiri, MD, Albania
Arben Gjata, MD, Albania
Arda Isik, MD, Türkiye
Artur Xhumani, MD, Albania
Carlos Mesquita, MD, Portugal
Charles Doarn, MD, FACS, USA
Demetrius Litwin, MD, FACS, FICS, USA
Dritan Alushani, MD, Albania
Emir Haxhija, MD, Austria
Fatmir Dalladaku MD, Germany
Gentian Kristo, MD, USA
Georgious Tsoulfas, MD, FACS, FICS, Greece
Gezim Dushaj, MD, Switzerland
Girma Tefera, MD FACS, USA
Giuseppe Nigri, MD, FACS, FRCS, Italy
Hayato Kurihara, MD, FACS, Italy
Horacio Rodriguez Rilo, MD, FACS, USA
Hubert Hauser, MD, Austria
Bellal Joseph, MD, FACS, USA
Jörg Tessarek, MD, Germany
Kastriot Haxhirexha, MD, North Macedonia
Kita Sallabanda, MD, Spain
Lars-Peter Kamolz, MD, Austria
Lumnije Kqiku, MDs, PhD, Austria
Manoochehr Ebrahimian, MD, FACS, Iran
Mehmet Eryilmaz, MD, Türkiye
Mentor Ahmeti, MD, FACS, USA
Minir Asani, MD, Germany
Mustafa Ozsoy, MD, Türkiye
Moritz Felsenreich, MD, Austria
Osman Dilek Nuri, MD, Türkiye
Peter Killcomons, MD, USA
Ridvan Alimehmeti, MD, Albania
Russell Andrews, MD, USA
Roberto Bergamaschi, MD, FACS, USA
Salomone Di Saverio MD, FACS, FRCS, England
Selami Sozubir, MD, Türkiye
Selman Uranues, MD, FACS, Austria
Valon Baraliu, MD, Germany
Vishal Shelat, MD, FACS, FRCS, England
Xheladin Draçini, MD, Albania

NATIONAL

Agreta Gashi-Gecaj, MD, Kosova
Antigona Hasani, MD, Kosova
Astrit Hamza, MD, Kosova
Avdyl Krasniqi, MD, Kosova
Bedri Braha, MD, Kosova
Belinda Pustina, MD, Kosova
Cen Bytyqi, MD, Kosova
Dafina Mahmutaj, MD, Kosova
Enver Fekaj, MD, Kosova
Eqrem Shala, MD, Kosova
Fadil Beka, MD, Kosova
Fahredin Veselaj, MD, Kosova
Fatos Sada, MD, Kosova
Ferat Sallahu, MD, Kosova
Gani Çeku, MD, Kosova
Harieta Zherka-Saraqini, MD, Kosova
Hysni Jashari, MD, Kosova
Isa Haxhiu, MD, Kosova
Laura Leci, MD, Kosova
Lulzim Vokri, MD, Kosova
Nazmi Morina, MD, Kosova
Nehat Baftiu, MD, Kosova
Nexhat Rexha, MD, Kosova
Osman Zhuri, MD, Kosova
Raif Cavolli, MD, Kosova
Sadik Llullaku, MD, Kosova
Sami Salihu, MD, Kosova
Sejdi Statovci, MD, Kosova
Syheda Latifi Hoxha, MD, Kosova
Shefqet Lulaj, MD, Kosova
Shqiptar Demaci, MD, Kosova
Shaban Memeti, MD, North Macedonia
Talat Gjnnolli, MD, Kosova
Vjollca Bince, MD, Kosova
Xhevdet Cuni, MD, Kosova
Xhevdet Tahiraj, MD, Kosova
Ylber Zejnullahu, MD, Kosova



Contents

- 5** Editorial: **José Manuel Ramia, Rifat Latifi:** Hepatopancreatobiliary Surgery Today: From Reducing Mortality to Selecting the Right Patient
- 8** **Alberto Ferreres, Rifat Latifi, José M Ramia:** Redefining the Scalpel: Past, Present, and Future Perspectives on the Surgical Management of Pancreatic Ductal Adenocarcinoma (PDAC)
- 12** **C. R. Jódar-Salcedo; A. Rojas-Holguín; D. López Guerra; G. Blanco-Fernández; Jaén-Torrejimenó:** Arterial Resections in Pancreatic Cancer
- 21** **José Manuel Ramia, Mario Serradilla, Celia Vilodre, Belén Hernández, Gerardo Blanco, Cándido Alcázar:** From ERPANDIS to SPANDISPAN: Two Decades of Collaborative Research in Left Pancreatectomy
- 32** **Guido Parquet, Rosa Sánchez:** Diagnostic and Therapeutic Approach to Acute Pancreatitis: Paraguayan National Consensus
- 42** **Rifat Latifi, Lindsay Bartholome:** Surgical and Endoscopic Management of Severe Acute Pancreatitis: The Times Have Changed
- 54** **Lindsay Bartholome, Rifat Latifi:** Nutritional Support in Severe Acute Pancreatitis: A Narrative Review
- 62** **Dai Ailin, Rebekah Young, Vishal G. Shelat:** Severe Liver Trauma: Current Management
- 76** **José M. Ramia, Celia Villodre-Tudela, Paola Melgar – Requena, Juan Jesus Rubio, Mariano Franco – Campello, Cándido F. Alcázar – López:** Surgical Management of Intrahepatic Cholangiocarcinoma: From Technical Resectability to Biological Decision – Making
- 88** **Mario Serradilla Martín, José M. Ramia:** Pushing the Boundaries of Liver Resection in Non-Colorectal Non-Neuroendocrine Metastatic Disease
- 99** **Cándido Alcázar, Celia Villodre, Silvia Carbonell-Morote, José M. Ramia:** Image of the Month: Beaver Tail Liver

Become A MEMBER

of Kosova the College of Surgeons and Receive
Kosova Journal of Surgery Free Editions
online and in-print

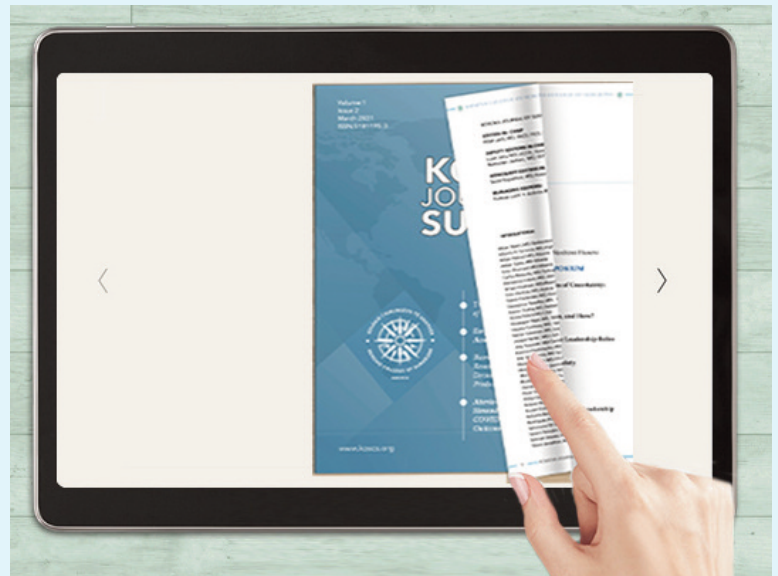
Kosova Journal of Surgery (KJS) is the official scientific publication of the Kosova College of Surgeons (KCS). Kosova Journal of Surgery has the goal of providing its readership the highest quality rapid retrieval of information relevant to surgeons.

KJS is a peer-reviewed journal publishing original contributions on all aspects of surgery. These contributions include original scientific articles, collective reviews, experimental investigations with clear clinical relevance, and a surgeon-at-work section (online and in-print). KJS is a membership benefit for all active KCS Fellows, and Associate and Resident members. Retirees, Medical Students, and Affiliate Members have access to KJS online. Access to KJS online is available to all members of the KCS.

If you are an KCS member who needs to change your address, please visit your Member Profile at our website **www.koscs.org** to make the changes.

To register for KCS Journal please visit our website!

www.kosovajournalofsurgery.net



EDITORIAL

Hepatopancreatobiliary Surgery Today: From Reducing Mortality to Selecting the Right Patient

J.M. Ramia¹, Rifat Latifi²

¹ Editorial, Special Issue on Hepatopancreatobiliary Surgery

² Editor-in-Chief, Kosova Journal Surgery

This special issue brings together a collection of contributions on hepatopancreatobiliary (HPB) surgery, and the Editor-in-Chief's accompanying editorial rightly places those articles in context. This editorial aims to step back and reflect on why HPB surgery matters today, where the field has come from, and where it appears to be heading. HPB surgery is three surgeries under one name — liver, pancreas, and biliary tract — each with its own history, its own technical demands, and, increasingly, its own set of open questions.

For decades, risk defined HPB surgery. Major hepatectomy, pancreatoduodenectomy, and resections of the biliary tree were, and to some extent remain, operations with substantial morbidity and non-negligible mortality. Much of the last thirty years of progress in this field has been spent taming that risk: centralization of complex care, standardization of technique, better anesthesia and critical care, and the emergence of dedicated HPB training and fellowship programs. That effort has largely succeeded. Mortality after major liver and pancreatic resection in high-volume centers is now a fraction of what it was a generation ago, and quality metrics such as “textbook outcome” have become the new benchmark, precisely because survival alone is no longer a sufficiently ambitious goal¹. The question the field faces now is not only “can we make this operation safer?” but “who truly benefits from having it at all?”. That shift — from feasibility to selection — is, to me, the common thread running through liver, pancreatic, and biliary surgery

alike, and it is the lens through which I would like to look briefly at each of the three.

Liver surgery

Diagnostic imaging has transformed how we approach liver disease. Multiphase CT and MRI, contrast-enhanced ultrasound, and increasingly the incorporation of artificial intelligence into image analysis are improving lesion characterization, detection of small or atypical tumors, and preoperative planning². But better imaging is only part of the story. Perhaps the more important conceptual shift has been the move away from thinking primarily about what can be resected and toward thinking about what will be left behind: the future liver remnant now drives operative planning as much as the tumor itself, through volumetric assessment, functional testing, and strategies such as portal vein embolization or staged hepatectomy when the remnant is judged insufficient. In parallel, the field has become more disciplined about measuring what matters — standardized, comparable outcomes rather than isolated case series¹ — and about identifying which patients genuinely benefit from resection, as opposed to those for whom surgery adds risk without meaningful gain. Systemic therapy has been a genuine gamechanger for liver malignancy, with more effective and better-tolerated chemotherapy regimens converting some initially unresectable patients into surgical candidates, and surgical indications have gradually extended to less frequent but increasingly recognized scenarios. Within Europe

specifically, the rising incidence of intrahepatic cholangiocarcinoma deserves particular attention, changing the case mix that liver units now manage and, in many centres, the balance of oncological versus benign indications for resection³. Finally, minimally invasive liver surgery — laparoscopic and, increasingly, robotic — has moved from a niche technique to an accepted, guideline-supported approach for an expanding range of resections, including major and technically demanding cases, with the learning curve and case selection now the main determinants of outcome rather than the approach itself⁴.

Pancreatic surgery

Pancreatic cancer illustrates the same evolution in concentrated form. Diagnostic pathways have improved, though earlier and more accurate detection remains the single greatest unmet need in this disease. Technical refinements in pancreatoduodenectomy and left pancreatectomy, together with better, more standardized definitions of what constitutes a good outcome, have made quality comparison across centres more meaningful¹. Systemic therapy has advanced substantially, and neoadjuvant strategies are now central to management of borderline resectable and some locally advanced tumors, which raises a genuinely difficult question this field is still learning to answer well: which patients actually benefit from proceeding to surgery after neoadjuvant treatment, and which do not, and by what criteria that decision should be made. Minimally invasive distal pancreatectomy has now been validated against open surgery in randomized comparison for resectable pancreatic cancer⁵, and robotic pancreatoduodenectomy is following a similar, if more cautious, trajectory as experience accumulates. Enhanced recovery (ERAS) protocols and, increasingly, structured prehabilitation before surgery — optimizing nutrition, fitness, and physiological reserve in the weeks before the operating room — have become standard components of perioperative care, improving recovery and reducing complications⁶. Beyond cancer, two further areas exemplify the selection challenge directly. Intraductal papillary mucinous neoplasms are now managed through evidence-based guidelines that help distinguish lesions that genuinely warrant resection from those that can be safely observed, sparing many patients an unnecessary operation⁷. And in chronic pancreatitis, recent randomized evidence supports earlier surgery over a prolonged endoscopy-first approach in appropriately selected patients⁸, while nutritional

assessment and support — long underappreciated in this population — is increasingly recognized as integral to both the decision to operate and the outcome once surgery is performed.

Biliary surgery

Biliary surgery remains, in many respects, the most technically demanding branch of the three. Perihilar cholangiocarcinoma (Klatskin tumours) continues to challenge even experienced HPB surgeons because of its anatomical complexity and the need to combine major hepatectomy with biliary and often vascular reconstruction⁹. Minimally invasive approaches, laparoscopic and robotic, are being extended into biliary surgery for both benign and malignant disease, though this remains an area where caution and case selection are essential given the consequences of a biliary complication. What has changed most substantially, however, is the systemic and biological landscape: new chemotherapy and immunotherapy combinations have, for the first time in years, produced a meaningful survival benefit in advanced biliary tract cancer¹⁰, and a deeper understanding of the molecular biology of cholangiocarcinoma is beginning to open the door to targeted treatment in selected patients. As in the liver and pancreas, better systemic options are reshaping the surgical conversation around resectability and timing, and are likely to make patient selection, treatment sequencing, and multidisciplinary discussion as important to outcomes in biliary cancer as the operation itself.

A common thread

Across all three organs, the story is the same. HPB surgery began as a discipline defined by its dangers, and the last generation of surgeons made these operations substantially safer. That achievement should not be understated, but it is no longer the frontier. The questions that now occupy liver, pancreatic, and biliary surgeons are less about whether an operation can be performed and more about whether it should be, in whom, and when — informed by better imaging, better systemic therapy, more rigorous outcome measurement, and a growing willingness to say no to surgery when the evidence suggests another patient will benefit more than this one. Getting that balance right, organ by organ and patient by patient, is, I believe, the real work of HPB surgery for the coming decade, and it is the evolution that this special issue, in its own way, reflects.

References:

1. Pretzsch E, Koliogiannis D, D'Haese JG, et al. Textbook outcome in hepato-pancreato-biliary surgery: systematic review. *BJS Open*. 2022;6(6):zrac149.
2. Chatzipanagiotou OP, et al. Artificial intelligence in hepatocellular carcinoma diagnosis: a comprehensive review of current literature. *J Gastroenterol Hepatol*. 2024. doi:10.1111/jgh.16663.
3. Vithayathil M, Khan SA. Current epidemiology of cholangiocarcinoma in Western countries. *J Hepatol*. 2022. PMID: 35977611.
4. Abu Hilal M, Hoogteijling TJ, Edwin B, et al. The Brescia internationally validated European guidelines on minimally invasive liver surgery. *Br J Surg*. 2025;112(6):znaf113.
5. Korrel M, Jones LR, van Hilst J, et al. Minimally invasive versus open distal pancreatectomy for resectable pancreatic cancer (DIPLOMA): an international randomised non-inferiority trial. *Lancet Reg Health Eur*. 2023. PMID: 37457332.
6. Melloul E, Lassen K, Roulin D, et al. Guidelines for Perioperative Care for Pancreatoduodenectomy: Enhanced Recovery After Surgery (ERAS) Recommendations 2019. *World J Surg*. 2020;44(7):2056-2084.
7. European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. *Gut*. 2018;67(5):789-804.
8. Issa Y, Kempeneers MA, Bruno MJ, et al; Dutch Pancreatitis Study Group. Effect of Early Surgery vs Endoscopy-First Approach on Pain in Patients With Chronic Pancreatitis: The ESCAPE Randomized Clinical Trial. *JAMA*. 2020;323(3):237-247.
9. Fernandes E, Yagi S, Kato K, et al. Changing concepts in perihilar cholangiocarcinoma resections and surgery. *Int J Surg*. 2026;112(6):12579-12587.
10. Oh DY, He AR, Qin S, et al. Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer. *NEJM Evid*. 2022;1(8):EVIDoa2200015.

Redefining the Scalpel: Past, Present, and Future Perspectives on the Surgical Management of Pancreatic Ductal Adenocarcinoma (PDAC)

Alberto R Ferreres MD, PhD¹; Rifat Latifi, MD, PhD²; José M Ramia, MD, PhD³

¹ Professor of Surgery, University of Buenos Aires, Buenos Aires, Argentina
Professor of Surgery and Ethics, University of Washington, Seattle WA, United States

² Professor of Surgery, University of Arizona; Arizona Advanced Surgery and Banner Desert Medical Center, Mesa, Arizona

³ Hospital General Universitario Dr. Balmis
Avda Pinto Baeza 11, 03010 Alicante (Spain)
ORCID 0000-0002-3532-932X

Corresponding Author:

ALBERTO R FERRERES, MD, PHD

¹Professor of Surgery, University of Buenos Aires, Buenos Aires, Argentina
Professor of Surgery and Ethics, University of Washington, Seattle WA, United States
aferres@hospitaldeclinicas.uba.ar
aferre17@uw.edu

Abstract

PDAC is still one of the most lethal cancer challenges, since it is characterized by an aggressive biology, early systemic dissemination, and a historically dismal prognosis. For many years, surgical resection has been considered the only potential treatment modality. However, the role, performance, extent, and opportunity of pancreatectomy (either distal or pancreatoduodenectomy) have undergone a significant paradigm shift. This manuscript traces the evolution of PDAC surgery from its dawn to a highly standardized procedure in high-volume centers.

In the current era, the therapeutic paradigm has predominantly shifted from a “surgery-first” approach to an aggressive multidisciplinary approach, where advanced systemic

neoadjuvant regimens and minimally invasive (laparoscopic/robotic) approaches are systematically used to achieve R0 resection. The future will likely overcome macro- and micro-anatomical boundaries through the full integration of artificial intelligence (AI), radiomics, molecular margin assessment, intraoperative navigation, and personalized immunotherapies. In that fashion, the pancreatic surgeon will need to transition from technician to biological oncologist, and his/her scalpel will transform into a bridge toward systemic disease eradication.

Key Points

- **Question:** How has the role of surgical resection for PDAC evolved through different stages and landscapes?

- **Findings:** The field has shifted from high mortality and few resections to safer, mostly centralized interventions. Neoadjuvant therapy, vascular resections, and minimally invasive (laparoscopic and robotic) platforms characterize the present. The future will integrate artificial intelligence-aided resources, real-time fluorescence-guided molecular margins, and personalized post-operative mRNA vaccines.
- **Meaning:** surgical management of PDAC has shifted from a focus on macro-anatomical technical feasibility to a biology-driven, technologically integrated component of personalized oncologic treatment.

Introduction

Pancreatic adenocarcinoma (PDAC) continues to show a rising incidence worldwide, representing the fourth leading cause of cancer death in Western countries, with a five-year survival rate of 5% to 12%¹. It is the most common histological type, accounting for about 85% to 90% of pancreatic malignancies. Fewer than 15% are considered resectable at the time of diagnosis². The pancreas was first described by Herophilus of Chalcedon (335 BC–280 BC), and the term pancreas (“all flesh”) was coined by Rufus of Ephesus (70–110). Giovanni Battista Morgagni (1682–1771) is credited with the earliest recorded accounts of pancreatic ductal adenocarcinoma (PDAC), as he reported several cases of pancreatic “scirrhus” in his 1761 publication “The seats and causes of diseases”³.

The past

The history and development of pancreatic surgery was characterized by anatomical and physiological hindrances. The gland’s location, its relationship with major visceral vessels, and the corrosive nature of its exocrine secretions made any operative manipulation extremely hazardous. This explains the disastrous outcomes, either due to intraoperative and, most of the time, uncontrollable bleeding or lethal post-operative complications (usually pancreatic fistulas).

The surgical treatment of PDAC underwent several stages: the first one was in the period 1880–1905, represented by bypass operations to alleviate the obstruction and palliate the jaundice. In 1887, almost simultaneously, Otto Kappeler in Munsterlingen, Switzerland, and Nestor Monastyrski in Russia performed the first cholecystojejunostomies for biliary obstruction caused by pancreatic carcinoma^{4,5}. However, Kappeler was the first to report it⁶. In both cases, the patient survived the operation. Swiss surgeon Cesar Roux’s major contribution was describing the Roux-en-Y

anastomosis, which forms the backbone of modern reconstructions after pancreatoduodenectomy (PD)⁷. Ambroise Monprofit (1857–1922) was the first one to perform the Roux-en-Y technique in a cholecystojejunostomy in 1904⁸.

The second stage is focused on the initial resections of the pancreatic tail. Between 1882 and 1905, 21 surgeons performed 24 resections³. Although these patients were not jaundiced, no intestinal resection was needed, and arterial bleeding was easier to control; only half of the patients were able to be discharged from hospitals. The third stage involved developing and achieving peri-ampullary carcinoma resection in two steps: Alessandro Codivilla in Bologna, Italy, and William Halsted in Baltimore, USA, performed the first cases in 1898. Walter Kausch performed a successful partial PD in Berlin. In 1933, at Columbia University in New York, Allen Whipple and his team performed what is considered the modern PD^{9,10}. Whipple’s milestone demonstrated that “en bloc” resection of the pancreatic head, duodenum, distal stomach, and common bile duct was anatomically feasible and compatible with life, although characterized by high morbidity and mortality. Meanwhile, Isaac Trimble from Johns Hopkins also performed pancreatoduodenectomies, apparently earlier than Whipple but published his results later¹¹. Many years later, Traverso proposed the pylorus-preserving pancreatoduodenectomy to prevent delayed gastric emptying¹². Notably, Henrik Dam discovered vitamin K in 1929 (1943 Nobel Prize), and it has been available since 1939, which was crucial because many PDAC patients had clotting disorders.

The burden of a steep mortality kept this procedure dangerous for several decades after its inception. These outcomes and the lack of effective systemic chemotherapy for the treatment of PDAC meant long-term survival was limited. Thus, many questioned the ethical and clinical utility and validity of the Whipple procedure. In more recent times, the PD has been linked to the figure of John L Cameron, from Johns Hopkins, who achieved some of the best surgical outcomes worldwide in the treatment of PDAC¹³.

The turning point that saved pancreatic surgery from dismal results and rejection took place in the late ‘80s and ‘90s with the revolution of clinical centralization, when epidemiological studies revealed an undeniable volume-outcome relationship in pancreatic resections. Centralization shifted complex pancreatic surgery into specialized regional centers hosting multidisciplinary teams of excellence (outstanding pancreatic surgeons, dedicated anesthesia teams, interventional radiologists capable of managing complications percutaneously, intensivists and top nursing

staff). These changes reduced perioperative mortality from over 20% to under 5% in high-volume centers and were associated with better oncological outcomes¹⁴.

The present

Three paradigm shifts characterize the current treatment of PDAC. They are represented by multidisciplinary team synergy, the shift from surgery-first to neoadjuvant therapy, and minimally invasive access with extended vascular resections. As mentioned before, centralization led to the formation of multidisciplinary teams whose achievements improve clinical outcomes (both perioperative and oncological).¹⁵

For decades, the standard clinical approach was upfront surgery for those with PDAC considered resectable, followed by adjuvant chemotherapy. However, this “surgery-first” strategy presented significant limitations: 30% of patients undergoing the procedure were found to have positive microscopic margins (R1), and a substantial proportion of patients presented with early and rapid systemic recurrence within months of surgery, an indication that occult micrometastatic disease was present at the time of operation. Moreover, postoperative complications often delayed or precluded the timely initiation of chemotherapy. The introduction and widespread adoption of neoadjuvant systemic chemotherapy, most notably FOLFIRINOX or Gemcitabine plus Paclitaxel, revolutionized patient care. The neoadjuvant approach presents several advantages: early systemic treatment, tumor biology assessment, tumor downstaging, and improved adjuvant compliance.¹⁶

Early efforts in the ‘90s to introduce laparoscopic techniques for pancreatic surgery were met with skepticism because of the procedure’s inherent technical challenges, including complex anastomoses and extended operative times. These concerns contributed to the delayed adoption of minimally invasive pancreatic resection, which did not gain broader clinical traction until the initial years of this century, with the appraisal of robotic approaches. Currently, Whipple procedures are predominantly performed through an open incision, with minimally invasive PD representing about 10.52% of the cases, 62% robotic and 38% laparoscopic¹⁷. Notably, the resection rate doubled from 8.3% to 16.6%, with improved survival¹⁸.

This era is also characterized by the rise of minimally invasive and robotic platforms, driven by technological innovation in the technical execution of pancreatectomies, both distal and proximal. For tumors located in the pancreatic body and tail, laparoscopic or robotic-assisted distal pancreatectomy with splenectomy has become the standard approach

in many centers, offering equivalent oncological outcomes with significantly reduced postoperative pain, shorter hospital stays, and faster recovery times¹⁹. More recently, robotic platforms have made substantial contributions to performing the Whipple procedure, overcoming the inherent limitations of conventional laparoscopy by providing 3-D vision, wristed instrumentation, tremor filtration, and navigation aids. These features are particularly beneficial during the complex suturing phases of pancreatojejunostomy and hepaticojejunostomy. Robotic platforms have demonstrated equivalent safety and margin clearance when performed by experts, and patients benefit from quicker recovery periods²⁰.

Another aspect of resections is advanced vascular reconstruction, as resectability has evolved from rigid anatomical standards to dynamic, boundary-pushing endeavors. Historically, tumor involvement of major retroperitoneal vessels (superior mesenteric artery, superior mesenteric vein, portal vein or celiac axis) was considered an absolute contraindication. Today, pancreatic surgeons at high-volume centers routinely perform planned, complex vascular reconstructions. After neoadjuvant downstaging, involvement of vascular structures is no longer an impediment to pancreatic resection²¹.

The future

Most probably, the future of pancreatic surgery will lie at the intersection of advanced technology, molecular biology, immunotherapy, and artificial intelligence^{22–23}.

- Total robotic integration will allow autonomous robotic steps under the surgeon’s supervision, assisted by real-time navigation mapping major retroperitoneal vessels and maximizing patient safety.
- Fluorescence-guided surgery: tumor-specific dyes will aid visualization and real-time assessment of tumor margins and positive lymph nodes.
- The concept of “clear margins” will likely shift from metric dimensions (1 mm) to biological dimensions, using intraoperative rapid genetic sequencing.
- Artificial intelligence and radiomics: preoperative machine learning algorithms will predict microvascular involvement and allow improved patient selection for resection. Besides, the operating rooms of the future will offer an immersive, digitally augmented environment.
- Personalized vaccines: postoperative care will include customized mRNA vaccines and/or targeted immunotherapies tailored to the genetic profile of the patient’s tumor²⁴.

Probably the most important conceptual transformation

of the future is that the surgical scalpel will no longer be considered the definitive and standard cure for PDAC. Surgery will probably evolve into a coordinated biological bridge within a personalized immunotherapy framework. The surgical specimen will serve as a valuable biobank, allowing the identification of neo-antigens and the development of specific mRNA vaccines or T-cell therapies²⁵.

In conclusion, the surgical treatment of PDAC has undergone a remarkable evolution since its initial stages. The past established the foundations and principles of the procedure, the present transformed surgery into a multi-modality systemic tapestry, while the future promises a complete departure from pure anatomical surgery. As the field continues to evolve, the modern pancreatic surgical oncologist must look beyond the physical boundaries of the scalpel, embracing technology and tumor biology to finally lead the war against this devastating disease.

We would like to close these reflections with the following quote: “In the world of surgical oncology, Biology is King, selection is queen, technical maneuvers are the Prince and Princess. Occasionally the prince or princess tries to usurp the throne; they almost fail to overcome the powerful forces of the King and Queen”²⁶.

References

1. Sung H, Ferlay J, Siegel RL et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021;71:209-249. doi: 10.3322/caac.21660.
2. Kleeff J, Korc M, Apte M et al. Pancreatic cancer. *Nat Rev Dis Primers* 2016 Apr 21;2:16022. doi: 10.1038/nrdp.2016.22.
3. Howard JM, Hess W. History of the pancreas: mysteries of a hidden organ. Springer-Verlag. New York NY, 2012
4. Kappeler O. Die elinguate Cholecystenterostomies [the one stage cholecystenterostomy.] *Cor Blatt Schwarz Aerate* 1887;17: 98
5. Monastyrski ND. Zur Frage der chirurgischen Behandlung der vollständigen Undurchgängigkeit des Ductus choledochus [On the question of surgical treatment for complete obstruction of the common bile duct]. *Zbl Chir* 1888;15:778
6. Toneto MG, Lopes MHI. Historical evolution of the surgical treatment of pancreatic cancer. *Sci Med* 2014;24(2):193–201
7. Roux C. De la gastroenterostomie [On gastroenterostomy]. *Rev Gynecol Chir Abdom* 1897;1:67
8. Monprofit A. Une nouvelle méthode de cholecystoenterostomos: la cholecystenterostomie en Y. *Arch Provinc Chir* 1904;13:380
9. Chandrakanth A, Dhir M, Ravipati L. History of pancreatoduodenectomy: early misconceptions, initial milestones and the pioneers. *HPB (Oxford)* 2011; 13: 377-384
10. Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. *Ann Surg* 1935
11. Trimble IR, Parsons JW, Sherman CP. A one-stage operation for the cure of carcinoma of the ampulla of Vater and of the head of the pancreas. *Surg Gynecol Obstet* 1941; 73: 711-722
12. Traverso LW, Longmire WP. Preservation of the pylorus in pancreatoduodenectomy. *SGO* 1978; 146: 959-962
13. Cameron JL, Riall TS, Coleman JA et al. One-thousand consecutive pancreatoduodenectomies. *Ann Surg* 2006; 244: 10-15
14. Ahola R, Sand J, Laukkanen J. Centralization of pancreatic surgery improves results: review. *Scand J Surg* 2020;109: 4-10
15. Pawlik TM, Laheru D, Hruban RH. Evaluating the Impact of a Single-Day Multidisciplinary Clinic on the Management of Pancreatic Cancer. *Ann Surg Oncol* 2008; 15: 2081–2088.
16. Conroy T, Hammel P, Hebbar M et al. FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. *New Engl J Med* 2018; 379: 2395-2406.
17. Valukas CS, Zaza NM, Vitello D et al. A Comparative Analysis of Open Versus Minimally Invasive Pancreatoduodenectomies. *J Surg Oncol* 2025 131: 816-826
18. Latenstein AEJ, van der Geest KGM, Bonsing BA et al. Nationwide trends in incidence, treatment and survival of pancreatic ductal adenocarcinoma. *Eur J Cancer* 2020; 125: 83-93
19. Ross SB, Sucandy I, Vasanthakumar P et al. Is the robotic approach the future of distal pancreatectomy with splenectomy? A propensity score matched analysis. *J Robot Surg* 2024; 18: 148 doi: 10.1007/s11701-024-01906-w.
20. Nickel F, Wise PA, Muller PC et al. Short-term outcomes of robotic versus open pancreatoduodenectomy: propensity score-matched analysis. *Ann Surg* 2024; 279: 665-670
21. Cristians KK, Evans DB. Pancreatoduodenectomy and vascular reconstruction: indications and techniques. *Surg Oncol Clin N Am* 2021; 30: 731-746
22. Kotb A, Hafeji Z, Jesry F et al. Intra-operative tumour detection and staging in pancreatic cancer surgery: an integrative review of current standards and future directions. *Cancers (Basel)*. 2024 Nov 12;16(22):3803. doi: 10.3390/cancers16223803.
23. Ducas A, Mangano A, Borgioli L et al. The role of artificial intelligence in pancreatic surgery: current and future perspectives (Editorial). *Ann Hepatobiliary Pancreat Surg* 2024; 29: 1-4
24. Liu Y, Xu H, Bai S et al. Nanomaterial-assisted pancreatic cancer theranostics. *Regen Biomater* 2025; 12: rbaf054. doi: 10.1093/rb/rbaf054
25. Rojas LA, Sethna Z, Soares KC et al. Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. *Nature* 2023;618:144-150.
26. Cady B. Presidential Address: Basic principles in surgical oncology. *Arch Surg* 1997; 132: 338-346.

Arterial Resections in Pancreatic Cancer

Jódar-Salcedo CR¹, Rojas-Holguín A^{1,2}, López Guerra D^{1,2},
Blanco-Fernández G^{1,2}, Jaén-Torrejimenó I¹.

¹Department of HBP and Liver Transplant surgery,
Hospital Universitario de Badajoz, Badajoz, Spain

²University of Extremadura. Departamento de Terapéutica Médico Quirúrgica.
Facultad de Medicina y Ciencias de la Salud, Badajoz, Spain

Jódar-Salcedo CR: cristinarosel.jodar@salud-juntaex.es

Rojas-Holguín A: adela.rojas@salud-juntaex.es ORCID 0000-0002-6467-0658

López-Guerra D: diego.lopezg@salud-juntaex.es ORCID 0000-0001-9763-4402

Blanco-Fernández G: gerardoblanco@unex.es ORCID 0000-0003-4845-5306

Jaén-Torrejimenó I: isabel.jaen@salud-juntaex.es ORCID 0000-0001-6616-4807

Corresponding Author:

GERARDO BLANCO-FERNÁNDEZ, MD, PHD

Hepatobiliary Surgeon of the Department of HBP and Liver Transplant Surgery
Universidad de Extremadura.

Departamento de Terapéutica Médico Quirúrgica.

Facultad de Medicina y Ciencias de la Salud

Avda de Elvas s/n 06006 Badajoz, Spain

Tel. (+34) 9242218022, FAX (+34) 924219838

E-mail: gerardoblanco@unex.es

Abstract

At the time of diagnosis, only about 20% of patients with pancreatic adenocarcinoma are considered resectable. In a large proportion of cases, there is evidence of local vascular invasion, either venous or arterial. Traditionally, arterial resection combined with pancreatic surgery was considered a contraindication. However, with advances in modern chemotherapeutic regimens and increased experience in high-volume referral centers, it has been observed that, in expert hands, arterial resection can improve survival with only a mild increase in postoperative morbidity and mortality. Preoperative radiologic assessment is essential for evaluating arterial involvement and planning the most appropriate surgical approach. Appropriate patient selection is crucial

to identify those who may benefit from this more aggressive oncologic surgical strategy.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive gastrointestinal malignancies, with a particularly poor prognosis. At the time of diagnosis, up to 50% of patients already have overt metastases, and only about 20% of tumors are considered resectable¹. Radical surgical resection with negative margins (R0) remains the only potentially curative option^{1,2}.

In cases of locally advanced pancreatic adenocarcinoma (LA-PDAC), invasion of critical vascular structures is common, with venous involvement being the most

frequent. Historically, this condition precluded curative surgical treatment. However, advances in neoadjuvant chemotherapy, surgical techniques, and perioperative care have led to the emergence of vascular resection as part of aggressive treatment strategies in selected cases³.

Currently, the morbidity and mortality associated with pancreatectomy with venous resection are largely comparable to those of standard pancreatectomy. This has contributed to the acceptance of combined venous resection as a standard technique³.

In contrast, arterial resection remains more controversial due to the highly variable arterial anatomy, the complexity of resection and revascularization procedures, and the risk of arterial occlusion, all of which may negatively impact surgical outcomes⁴.

Indications and Selection Criteria

Traditionally, arterial invasion—particularly involving the superior mesenteric artery (SMA), celiac axis (CA), or common hepatic artery (CHA)—has been considered a contraindication to surgery due to its association with high morbidity and mortality, and poor oncologic outcomes².

With the introduction of neoadjuvant chemotherapy regimens such as FOLFIRINOX and gemcitabine plus nab-paclitaxel, sometimes combined with radiotherapy, patients with locally advanced (LA) or borderline resectable (BR) tumors have shown conversion to resectable disease with curative intent and negative margins (R0) in up to 30% of LA-PDAC cases⁵.

In general, arterial resection should be evaluated within

a multidisciplinary team setting and may be considered for patients with good performance status (ECOG 0–1), no metastatic disease, a favorable radiologic and metabolic response to neoadjuvant therapy, and a reasonable expectation of achieving an R0 resection¹.

A literature review has been performed about the resectability of pancreatic cancer based on the extent of arterial vascular invasion, the selection of candidates for vascular resection, and the evolution of surgical techniques aimed at achieving radical oncologic resection.

Patient Selection based on imaging data

A detailed evaluation using high-resolution imaging techniques is essential to determine resectability in pancreatic cancer with suspected arterial involvement. Imaging allows assessment of the degree of tumor–vessel contact, differentiation between compression and true invasion, and planning of the surgical strategy⁶.

Recommended Imaging Techniques⁷

A) Multidetector computed tomography (CT) angiography (arterial and venous phases; triphasic CT):

This is the standard modality for vascular evaluation. It enables visualization of tumor contact with the SMA, CHA, and CA. Tumor–artery contact is commonly classified as:

- $<180^\circ$ of the arterial circumference: suggestive of contact without invasion
- $\geq 180^\circ$: suggestive of true arterial infiltration (Figure 1).

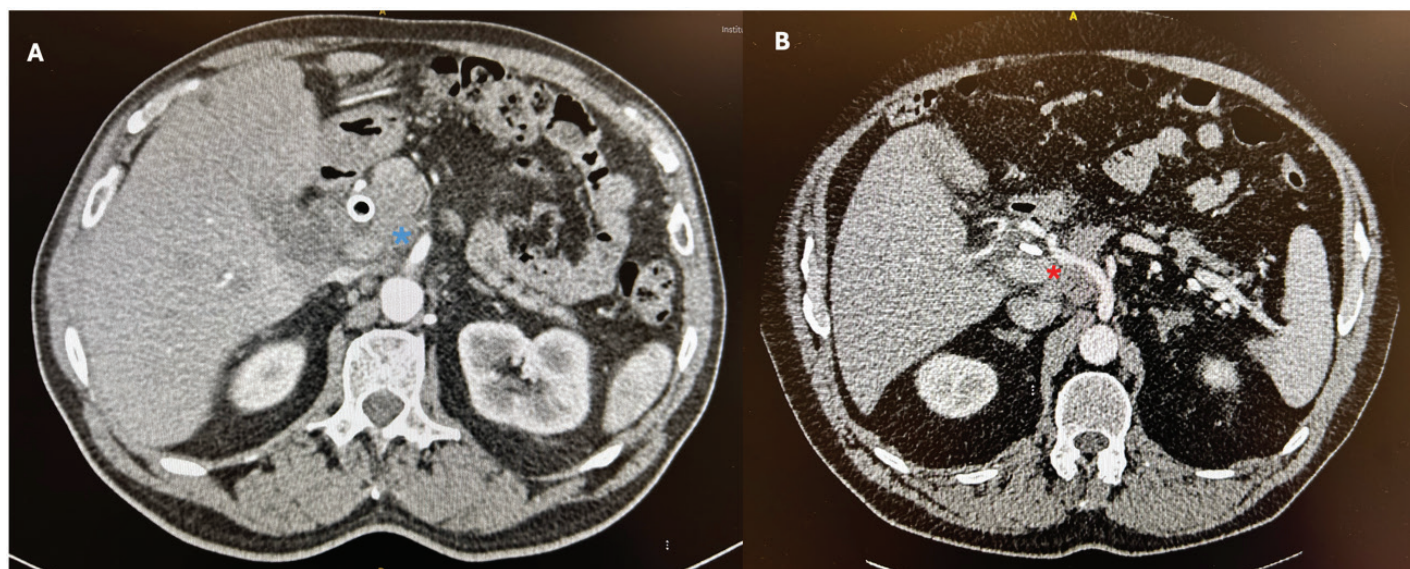


Figure 1: (A) CT scan showing $<180^\circ$ tumor contact with the superior mesenteric artery (SMA) (blue asterisk); (B) CT scan demonstrating involvement of the common hepatic artery (CHA) (red asterisk).

B) Magnetic Resonance Imaging (MRI) with contrast:

Useful in patients with iodine allergy or when CT findings are equivocal. Although it has lower spatial resolution for small vascular structures, it is valuable for assessing perineural spread and treatment response.

C) PET-CT:

It does not replace CT or MRI for anatomical assessment but may help detect occult metastatic disease and evaluate metabolic response after neoadjuvant therapy.

D) Endoscopic ultrasound (EUS):

Provides excellent resolution of peripancreatic structures but is operator-dependent and less useful for evaluating the entire vascular axis.

Radiological Criteria for Unresectability

Given the well-established high lethality of pancreatic ductal adenocarcinoma (PDAC), assessing resectability at the time of diagnosis is a priority to establish an appropriate therapeutic strategy. In fact, up to 50% of patients are considered unresectable at diagnosis despite the absence of distant metastases (8). For this purpose, an adequate imaging work-up using triphasic computed tomography (CT) with thin slices (1–2 mm) is essential to allow a detailed assessment of vascular involvement⁹.

Based on anatomical and radiological criteria, unresectability can be defined in two distinct scenarios: locally advanced disease (LA-PDAC) and metastatic disease (M-PDAC)⁹.

Regarding borderline resectable (BR) disease, this concept was first introduced in 2006 by the National Comprehensive Cancer Network (NCCN). It was defined as patients with PDAC who are at high risk for margin-positive resection and for whom neoadjuvant therapy should be considered. Since then, several groups, including the MD Anderson Cancer Center (MDACC) (10), NCCN, and the Intergroup Alliance¹¹, have proposed different definitions of BR-PDAC.

The concepts of unresectable (UR) and borderline resectable (BR) disease in LA-PDAC have evolved over time due to improvements in surgical techniques and the development and consolidation of neoadjuvant therapies. Consequently, during the 20th meeting of the International Association of Pancreatology (IAP), held in Sendai, Japan, in 2016, an international consensus was established to define resectable, unresectable (UR), and borderline resectable (BR) PDAC. These definitions were based on previously established criteria from the Japan Pancreas Society (JPS, 7th edition), the Intergroup Alliance, and the NCCN (2016 version)⁹ (Table 1). In rare cases involving the origin of the celiac axis (CA), a distal pancreatectomy (body–tail resection) combined with potential celiac axis resection and preservation of the gastroduodenal arcade (modified Appleby procedure) may be considered^{9,12}.

Regarding borderline resectable (BR) disease, a subclassification was established based on the presence of isolated venous involvement (BR-PV) or arterial involvement (BR-A) (Table 2):

Table 1: Anatomical criteria for tumor unresectability established by consensus

LA-PDAC*	M-PDAC
- Tumor-related venous invasion with complete occlusion - Arterial contact/invasion $\geq 180^\circ$ involving the superior mesenteric artery (SMA) or celiac axis (CA) - Extensive involvement of the common hepatic artery (CHA) with extension to the proper hepatic artery (PHA) or celiac axis (CA) - Aortic invasion or tumor contact with the aorta	- Metastatic disease - Distant para-aortic or extra-abdominal lymph node involvement (>10 mm in diameter on CT)

*With the exception of cases with $\geq 180^\circ$ involvement of the origin of the celiac axis (CA) in which a distal pancreatectomy (body–tail resection) with potential celiac axis resection and preservation of the gastroduodenal arcade (modified Appleby procedure) may be feasible.

Table 2: Anatomical criteria for borderline resectability

BR-PV (SMV/PV involvement alone)	BR-A (arterial involvement)
- SMV/PV contact $\geq 180^\circ$ or - bilateral narrowing/occlusion not exceeding the inferior border of the duodenum	- SMA, CA: tumor contact of less than 180° without showing deformity/stenosis - CHA: tumor contact, without showing tumor contact of the proper hepatic artery (PHA) and/or CA.

(Aortic involvement is categorized as unresectable. Presence of variant arterial anatomy is not taken into consideration)

Following the 2017 international consensus, in addition to the previously described anatomical and radiological criteria, Isaji et al.⁹ also incorporated biological and conditional factors into the definition of BR-PDAC:

- **Biological definition of BR-PDAC (IAP, 2016):** Anatomically potentially resectable tumors with clinical findings suspicious, but not confirmed, for distant metastasis. These include elevated CA 19-9 levels (>500 U/mL) or regional lymph node metastases identified by biopsy or PET-CT.
- **Conditional definition of BR-PDAC (IAP, 2016):** Patients with anatomically resectable PDAC but with a performance status ≥ 2 are classified as BR-PDAC.

NCCN Classification of Resectability¹³

The anatomical classification of pancreatic cancer according to the National Comprehensive Cancer Network (NCCN) guidelines (version 1.2026) defines three categories based on the tumor's relationship to the major vascular structures. This categorization has direct implications for the therapeutic strategy at diagnosis (upfront surgery, neoadjuvant treatment, or palliative care).

1. Resectable

- **Arteries (SMA, CA, CHA):** no tumor contact.
- **Veins (portal vein [PV], superior mesenteric vein [SMV]):** no contact, or $\leq 180^\circ$ contact without contour irregularity.
- **Clinical implication:** candidates for upfront surgery following preoperative evaluation.

2. Borderline Resectable (BRPC)

Arterial involvement:

Pancreatic head/uncinate process:

- **SMA:** tumor contact $\leq 180^\circ$, without deformity or significant stenosis.
- **CA:** tumor contact $\leq 180^\circ$, without involvement of the origin or aortic extension.
- **CHA:** tumor contact without involvement of the segment between the gastroduodenal artery (GDA) and the celiac trunk (CT), and without extension to the bifurcation; reconstruction is feasible.
- **Variant arterial anatomy:** tumor contact with variant arterial anatomy (e.g., accessory right hepatic artery, replaced right hepatic artery, replaced CHA, or the origin of replaced/accessory arteries) should be documented, as it may impact surgical planning.

Pancreatic body/tail:

- Tumor contact with the CA $\leq 180^\circ$.

Venous involvement (SMV or PV):

- Tumor contact $>180^\circ$, or $\leq 180^\circ$ with contour irregularity. Occlusion or thrombosis may or may not be present, but the vessel remains technically resectable and reconstructible.
- Tumor contact with the inferior vena cava (IVC).

Clinical implication: indication for neoadjuvant therapy prior to surgery with curative intent.

3. Locally Advanced / Unresectable

Arterial involvement:

Pancreatic head/uncinate process:

- Solid tumor contact $>180^\circ$ with the SMA or CA.

Pancreatic body/tail:

- Solid tumor contact $>180^\circ$ with the SMA or CA.
- Solid tumor contact with the CA and aortic involvement.

Venous involvement:

- Not amenable to resection and primary reconstruction due to complete occlusion of the SMV/PV.

Clinical implication: indication for systemic therapy (chemotherapy $\pm$ radiotherapy), with the possibility of surgical conversion in cases of favorable response.

Role of Assessment After Neoadjuvant Therapy

This classification should be reassessed after neoadjuvant therapy using a multidisciplinary team approach, as resectability may improve with treatment. Post-neoadjuvant imaging assessment can be challenging because inflammatory changes or chemotherapy-induced fibrosis may mimic persistent tumor¹⁴. In such cases, the concept of "biological resectability" should be considered. This concept, initially introduced by Katz et al.¹¹, refers to regression of vascular involvement or radiological stability, in association with a significant decrease in tumor markers^{15,16}.

According to the latest version of the NCCN guidelines for PDAC (version 1.2026), the criteria for resection include the following surgical principles: en bloc resection of the tumor and "at-risk" tissues to achieve complete tumor excision with negative margins (R0);

reestablishment of end-organ arterial inflow and venous outflow; restoration of gastrointestinal continuity; and adequate biliary drainage. These factors may ultimately be assessed intraoperatively, given the limited accuracy of conventional cross-sectional imaging in differentiating viable tumor tissue from fibrosis or scar tissue. This limitation may justify and support surgical exploration even in the presence of equivocal imaging findings¹³.

Surgical exploration may be indicated in cases demonstrating regression or stability of arterial contact, absence of metastatic progression, and good clinical condition with a favorable metabolic response.

Technical Considerations of Arterial Resection during Pancreatectomy

As previously mentioned, the arteries most frequently involved are the common hepatic artery (CHA), celiac axis (CA), and superior mesenteric artery (SMA). Technical factors that have historically limited the adoption of pancreatic resection with arterial resection (P-AR) include the previously prohibitive mortality rates (up to 45%), mainly due to bleeding or thrombosis of reconstructed vessels, the frequent need for concomitant venous resection, and the requirement for advanced expertise in vascular surgery to perform arterial reconstruction^{3,17}.

However, with advances in surgical techniques and increasing experience, series from high-volume centers specializing in hepatobiliary and pancreatic surgery have demonstrated that P-AR can be performed safely, with acceptable morbidity, mortality, and overall survival rates.

In the series reported by Bachelier et al.³, the rate of P-AR progressively increased over time, reaching approximately 10% of all pancreatic resections in the later study period. Despite the high complexity of the cases treated (>90% involving synchronous arterial and venous resections), the reported 90-day mortality rate (5.1%) was lower than that observed in post-discharge national databases of pancreatic resections in Germany (10.1%) and France (8.1%), as well as lower than rates reported in earlier P-AR series. These findings reflect the progressive evolution and continuous refinement of surgical techniques for combined arterial resection over the past two decades, as well as the impact of institutional policies aimed at reducing failure-to-rescue rates in high-volume pancreatic surgery centers³.

Celiac Axis Resection

The modified Appleby technique allows resection of the celiac axis (CA) in tumors of the pancreatic body and

tail (distal pancreatectomy with celiac axis resection, DP-CAR), taking advantage of retrograde blood flow from the superior mesenteric artery (SMA) through the posterior pancreaticoduodenal artery and the Haller arcade.

Preoperative assessment of collateral hepatic perfusion using CT angiography or Doppler ultrasound is essential. Celiac axis resection requires adequate collateral circulation via the SMA, pancreaticoduodenal arcade (PA), and gastroduodenal artery (GDA) to ensure sufficient hepatic arterial inflow. Therefore, involvement of these arteries during DP-CAR necessitates complex arterial reconstruction to prevent hepatic infarction. Given the morbidity and suboptimal outcomes associated with arterial reconstruction during pancreatic surgery, involvement of the SMA or GDA should be considered a contraindication to DP-CAR¹⁸.

In cases where arterial clamping results in the absence of pulsation at the hepatic hilum, changes in liver color or consistency, or absence of intrahepatic arterial flow (as assessed by intraoperative Doppler ultrasound), reconstruction of the common hepatic artery (CHA) is recommended whenever feasible. Another clear indication for hepatic rearterialization is when a total pancreatectomy is performed for technical or oncological reasons¹⁹.

Regarding reconstruction, after transection of the CA and CHA, extensive mobilization of the proximal and distal arterial ends is performed to allow a tension-free end-to-end anastomosis. If this is not feasible, interposition grafting may be performed using autologous vessels (such as the splenic, middle colic, or gastroepiploic arteries), cadaveric arterial graft (Figure 2) or synthetic grafts¹⁹.

In some cases, preoperative embolization of the GDA is required to induce neovascularization, typically performed at least 10 days before surgery to allow adequate development of collateral circulation^{18–20}.

Hepatic Artery Resection

It may be indicated in cases of focal invasion of the proximal segment, particularly in pancreatic head tumors with extension towards the gastroduodenal artery (GDA).

During preoperative assessment, the presence of an accessory hepatic artery and whether the native hepatic artery is involved should be carefully evaluated. After hepatic artery resection, end-to-end anastomosis is often feasible due to the anatomical proximity to the celiac axis. In cases where primary anastomosis is not possible, graft interposition to the celiac trunk or abdominal

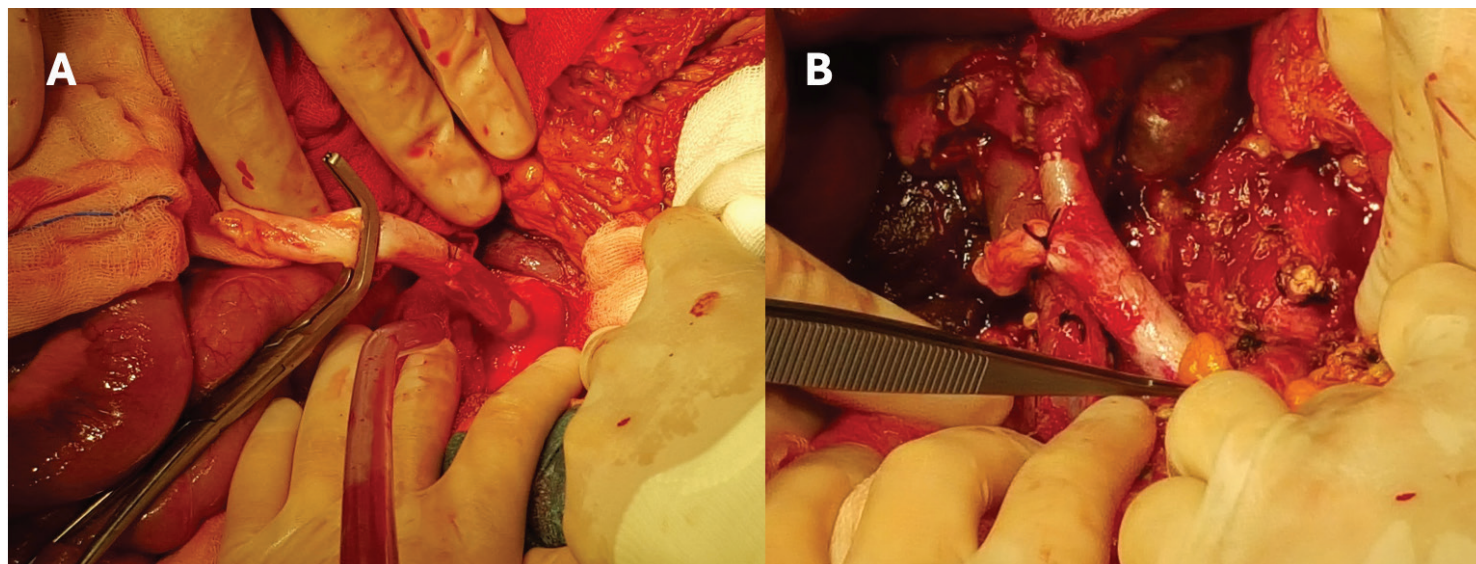


Figure 2: Intraoperative images of a modified Appleby procedure performed for a pancreatic neck–body adenocarcinoma involving the celiac trunk and common hepatic artery. A total splenoduodenopancreatectomy was carried out, and arterial reconstruction was achieved using a cadaveric iliac graft.

aorta is required. Preferred grafts for these anastomoses include the saphenous vein, gastric artery, mesenteric arterial branches, and splenic artery transposition²¹.

Superior Mesenteric Artery Resection

Superior mesenteric artery (SMA) involvement is typically observed in lesions located predominantly in the uncinate process. This involvement is usually limited to the most distal portion of the artery. Proximal SMA involvement, close to its aortic origin, generally occurs in larger tumors in which the superior mesenteric vein (SMV) is also frequently infiltrated¹⁹.

This represents the most technically demanding type of resection. It may be indicated only in highly selected cases with limited vascular invasion and a marked response to neoadjuvant therapy. Complication rates are high (including intestinal ischemia), and early series reported significant mortality, which initially limited its widespread acceptance.

Reconstruction techniques vary and include end-to-end anastomosis, use of prosthetic or biological patches, or en bloc resection with vascular bypass reconstruction²¹.

Oncological and Perioperative Outcomes

Postoperative mortality rates after arterial resections have improved significantly (<5% in expert centers), which is closely associated with surgical experience and perioperative management optimization²². Even in

high-volume pancreatic surgery centers, the perioperative morbidity rate for this high-risk procedure ranges from 25–59%, while postoperative mortality rates range from 10–16%²³.

In the systematic review by Noel et al., 2- and 3-year overall survival rates were 62.2% and 50.1%, respectively, in the arterial resection group compared with 55.7% and 49.8% in the non-arterial resection group²⁴. In some cases, arterial resection does not correspond to histological arterial invasion. In the study by Yang et al., only 64.3% of cases demonstrated microscopic arterial infiltration²⁵.

R0 resection rates range between 60–80%, and median overall survival in patients undergoing resection after neoadjuvant therapy may reach 25–30 months, compared with 11–13 months in unresected patients²⁶. Neoadjuvant chemotherapy has clearly contributed to reducing morbidity and mortality associated with arterial resection, as well as achieving higher R0 resection rates. Although residual tumor and extensive desmoplastic reaction surrounding the artery may complicate surgical dissection after neoadjuvant therapy, higher R0 rates have been achieved even in tumors initially considered locally advanced or unresectable at diagnosis²³.

Furthermore, expertise in vascular surgery and organ transplantation techniques supports the feasibility of the procedure, particularly for primary reconstruction or the use of vascular grafts²².

The main prognostic determinants are the final resection status (R0 vs. R1), nodal status, and response to neoadjuvant

therapy. Patients with borderline resectable or locally advanced tumors exhibit higher rates of positive resection margins, leading to increased recurrence rates. Therefore, the use of more complex surgical techniques, including arterial resection, may enable the achievement of R0 resection, which is a key factor in improving prognosis^{2,26}.

Regarding postoperative complications associated with the surgical procedure, the main concern is clinically significant postoperative hemorrhage, which occurs in approximately 15% of patients.

Ischemic complications represent another inherent limitation of this technique, either due to interruption of arterial continuity when performed without reconstruction or due to thrombosis following arterial reconstruction. These complications have been reported to contribute to postoperative mortality in 45–73% of cases^{27,28}. However, in the systematic review published by Noel et al. (2025), no increased rate of major complications (Clavien–Dindo $\geq$ III) was observed with arterial resection (31.8% in the arterial resection group vs. 34.3% in the standard resection group)²⁴.

Another complication is refractory diarrhea resulting from gastrointestinal denervation following SMA dissection, which may hinder timely administration of adjuvant therapy and negatively impact patient survival²³.

Controversies and Future Perspectives

Arterial resection remains a controversial procedure due to the high rate of complications, particularly in historical series, suboptimal oncologic outcomes related to initial inadequate patient selection, and the technical complexity of the procedures. However, it is emerging as a valid strategy in carefully selected cases, especially with the support of neoadjuvant therapies and targeted treatments.

Recently, arterial preservation procedures have been proposed, employing specific techniques to maintain arterial lumen integrity while achieving oncologic radicality. These include periarterial divestment, periadventitial dissection, subadventitial divestment, and level 3 SMA dissection²⁹. These emerging preservation approaches are based on histopathological evidence suggesting that true arterial wall invasion is relatively uncommon, as well as on the arterial wall's structural resilience, which may remain intact following aggressive periarterial dissection²³.

The incorporation of artificial intelligence, three-dimensional surgical planning, and advances in intraoperative perfusion techniques may further improve procedural safety and long-term outcomes.

Conclusion

Arterial resection in locally advanced pancreatic cancer can be considered no longer an absolute contraindication and represents an advance in aggressive oncologic surgery, reserved for carefully selected patients in highly specialized centers. Although technically demanding and associated with significant risks, it may offer improved survival in a subset of patients historically considered unresectable.

References:

1. Napoli N, Kauffmann E, Cacace C, Menonna F, Caramella D, Cappelli C, et al. Factors predicting survival in patients with locally advanced pancreatic cancer undergoing pancreatectomy with arterial resection. *Updates Surg.* 2021 Feb 1;73(1):233–49. doi:10.1007/s13304-020-00883-7 PubMed PMID: 32978753.
2. Wiltberger G, Bucher JN, Krenzien F, Benzing C, Atanasov G, Schmelzle M, et al. Extended resection in pancreatic metastases: Feasibility, frequency, and long-term outcome: A retrospective analysis. *BMC Surg.* 2015;15(1). doi:10.1186/s12893-015-0114-1 PubMed PMID: 26772176.
3. Bachellier P, Addeo P, Faitot F, Nappo G, Dufour P. Pancreatectomy With Arterial Resection for Pancreatic Adenocarcinoma: How Can It Be Done Safely and With Which Outcomes?: A Single Institution's Experience With 118 Patients. *Ann Surg.* 2020 May 1;271(5):932–40. doi:10.1097/SLA.0000000000003010 PubMed PMID: 30188399.
4. Alva-Ruiz R, Abdelrahman AM, Starlinger PP, Yonkus JA, Moravec DN, Busch JJ, et al. Patency rates of hepatic arterial resection and revascularization in locally advanced pancreatic cancer. *HPB.* 2022 Nov 1;24(11):1957–66. doi:10.1016/j.hpb.2022.06.005 PubMed PMID: 35780039.
5. Noda Y, Pisuchpen N, Mercaldo ND, Sekigami Y, Michalakos T, Parakh A, et al. Arterial involvement and resectability scoring system to predict R0 resection in patients with pancreatic ductal adenocarcinoma treated with neoadjuvant chemoradiation therapy. *Eur Radiol.* 2022 Apr 1;32(4):2470–80. doi:10.1007/s00330-021-08304-y PubMed PMID: 34665317.
6. Ahmed SA, Mourad AF, Hassan RA, Ibrahim MAE, Soliman A, Aboeleun E, et al. Preoperative CT staging of borderline pancreatic cancer patients after neoadjuvant treatment: accuracy in the prediction of vascular invasion and resectability. *Abdominal Radiology.* 2021 Jan 1;46(1):280–9. doi:10.1007/s00261-020-02605-4 PubMed PMID: 32488556.
7. McKinney M, Griffin MO, Tolat PP. Multimodality Imaging for the Staging of Pancreatic Cancer. *Surgical Oncology Clinics of North America.* W.B. Saunders; 2021. p. 621–37. doi:10.1016/j.soc.2021.06.006 PubMed PMID: 34511186.

8. Floortje van Oosten A, Al Efishat M, Habib JR, Kinny-Köster B, Javed AA, He J, et al. Concepts and techniques for revascularization of replaced hepatic arteries in pancreatic head resections. *HPB. Elsevier B.V.*; 2023. p. 1279–87. doi:10.1016/j.hpb.2023.06.002 PubMed PMID: 37419779.
9. Isaji S, Mizuno S, Windsor JA, Bassi C, Fernández-del Castillo C, Hackert T, et al. International consensus on definition and criteria of borderline resectable pancreatic ductal adenocarcinoma 2017. *Pancreatology*. 2018 Jan 1;18(1):2–11. doi:10.1016/j.pan.2017.11.011 PubMed PMID: 29191513.
10. Varadhachary GR, Tamm EP, Abbruzzese JL, Xiong HQ, Crane CH, Wang H, et al. Borderline resectable pancreatic cancer: Definitions, management, and role of preoperative therapy. *Annals of Surgical Oncology*. 2006. p. 1035–46. doi:10.1245/ASO.2006.08.011 PubMed PMID: 16865597.
11. Katz MHG, Marsh R, Herman JM, Shi Q, Collison E, Venook AP, et al. Borderline resectable pancreatic cancer: Need for standardization and methods for optimal clinical trial design. *Ann Surg Oncol*. 2013 Aug;20(8):2787–95. doi:10.1245/s10434-013-2886-9 PubMed PMID: 23435609.
12. Haines M, Chua TC, Jamieson NB, Mittal A, Gill AJ, Samra JS. Pancreatoduodenectomy with Arterial Resection for Locally Advanced Pancreatic Cancer of the Head: A Systematic Review. *Pancreas*. Lippincott Williams and Wilkins; 2020. p. 621–8. doi:10.1097/MPA.0000000000001551 PubMed PMID: 32433398.
13. Ko AH, Malafa MP, Chair V, Cardin DB, Gabriela Chiorean E, Hutchinson Cancer Center Jared Christensen FA, et al. NCCN Guidelines Version 1.2026 Pancreatic Adenocarcinoma [Internet]. 2026. Available from: <https://www.nccn.org/home/member->
14. Ferrone CR, Marchegiani G, Hong TS, Ryan DP, Deshpande V, McDonnell EI, et al. Radiological and surgical implications of neoadjuvant treatment with FOLFIRINOX for locally advanced and borderline resectable pancreatic cancer. In: *Annals of Surgery*. Lippincott Williams and Wilkins; 2015. p. 12–7. doi:10.1097/SLA.0000000000000867 PubMed PMID: 25599322.
15. Yamada S, Oshima K, Nomoto K, Sunagawa Y, Oshima Y, Nakao A. Reappraisal of the current resectability criteria and optimal treatment strategies for pancreatic cancer. *J Gastrointest Oncol*. 2024 Jun 30;15(3):1245–54. doi:10.21037/jgo-24-102
16. Fromer MW, Wilson KD, Philips P, Egger ME, Scoggins CR, McMasters KM, et al. Locally advanced pancreatic cancer: a reliable contraindication to resection in the modern era? *HPB*. 2022 Oct 1;24(10):1789–95. doi:10.1016/j.hpb.2021.09.002 PubMed PMID: 35491339.
17. Mollberg N, Rahbari NN, Koch M, Hartwig W, Hoeger Y, Büchler MW, et al. Arterial resection during pancreatotomy for pancreatic cancer: A systematic review and meta-analysis. *Ann Surg*. 2011;254(6):882–93. doi:10.1097/SLA.0b013e31823ac299 PubMed PMID: 22064622.
18. Sindayigaya R, Barat M, Tzedakis S, Dautry R, Dohan A, Belle A, et al. Modified Appleby procedure for locally advanced pancreatic carcinoma: A primer for the radiologist. *Diagnostic and Interventional Imaging*. Elsevier Masson s.r.l.; 2023. p. 455–64. doi:10.1016/j.diii.2023.05.008 PubMed PMID: 37301694.
19. Vicente E, Quijano Y, Ielpo B, Duran H, Diaz E, Fabra I, et al. ¿Sigue representando la infiltración arterial un criterio de irreseccabilidad en el carcinoma de páncreas? *Cir Esp*. 2014;92(5):305–15. doi:https://doi.org/10.1016/j.ciresp.2013.11.001
20. Ramia JM, de Vicente E, Pardo F, Sabater L, Lopez-Ben S, Quijano M Y, et al. Preoperative hepatic artery embolization before distal pancreatectomy plus celiac axis resection does not improve surgical results: A Spanish multicentre study. *Surgeon*. 2021 Oct 1;19(5):e117–24. doi:10.1016/j.surge.2020.08.012 PubMed PMID: 33023848.
21. Kaya K, Mungan U. Multiple vascular reconstructions during pancreatectomy: Surgical techniques and strategies. *Vascular*. 2023 Oct 1;31(5):861–7. doi:10.1177/17085381221091053 PubMed PMID: 35477336.
22. Xue K, Huang X, Zhao P, Zhang Y, Tian B. Perioperative and long-term survival outcomes of pancreatectomy with arterial resection in borderline resectable or locally advanced pancreatic cancer following neoadjuvant therapy: a systematic review and meta-analysis. *Int J Surg*. 2023 Dec 1;109(12):4309–21. doi:10.1097/JS9.0000000000000742 PubMed PMID: 38259002.
23. Miao Y, Cai B, Lu Z. Technical options in surgery for artery-involving pancreatic cancer: Invasion depth matters. *Surg Open Sci*. 2023 Mar 1;12:55–61. doi:10.1016/j.sopen.2023.03.001
24. Noel C, Azeez A, Du Preez A, Noel K. Arterial Resections in Pancreatic Cancer—An Updated Systematic Review and Meta-Analysis. *Cancers*. Multidisciplinary Digital Publishing Institute (MDPI); 2025. doi:10.3390/cancers17091540
25. Yang F, Wang X, Jin C, He H, Fu D. Pancreatectomy with Hepatic Artery Resection for Pancreatic Head Cancer. *World J Surg*. 2019 Nov 1;43(11):2909–19. doi:10.1007/s00268-019-05106-8 PubMed PMID: 31396672.
26. Wiltberger G, den Dulk M, Bednarsch J, Czigany Z, Lang SA, Andert A, et al. Perioperative and long-term outcome of en-bloc arterial resection in pancreatic surgery. *HPB*. 2022 Jul 1;24(7):1119–28. doi:10.1016/j.hpb.2021.12.003 PubMed PMID: 35078714.
27. Klomp maker S, De Rooij T, Korteweg JJ, Van Dieren S, Van Lienden KP, Van Gulik TM, et al. Systematic review of outcomes after distal pancreatectomy with coeliac axis resection for locally advanced pancreatic cancer. *British Journal of Surgery*. 2016;103(8):941–9. doi:10.1002/bjs.10148 PubMed PMID: 27304847.



28. Klompmaker S, Boggi U, Hackert T, Salvia R, Weiss M, Yamaue H, et al. Distal Pancreatectomy with Celiac Axis Resection (DP-CAR) for Pancreatic Cancer. How I do It. *Journal of Gastrointestinal Surgery*. 2018;1–7. doi:10.1007/s11605-018-3894-7

29. Habib JR, Kinny-Köster B, van Oosten F, Javed AA,

Cameron JL, Lafaro KJ, et al. Periadventitial dissection of the superior mesenteric artery for locally advanced pancreatic cancer: Surgical planning with the “halo sign” and “string sign.” *Surgery (United States)*. 2021 May 1;169(5):1026–31. doi:10.1016/j.surg.2020.08.031 PubMed PMID: 33036782.

From ERPANDIS to SPANDISPAN: Two Decades of Collaborative Research in Left Pancreatectomy

José Manuel Ramia, MD, PhD, FACS, FRCS, FRCS(Ed), FKCS, ESA, FEBS-HPB^{1,2,3}; Mario Serradilla, MD, PhD, FACS, FEBS-HPB^{4,5}; Celia Villodre, MD, PhD, FACS^{1,2,3}; Belén Hernández, MD⁶; Gerardo Blanco, MD, PhD^{7,8}; Cándido Alcázar, MD, PhD, FACS^{1,2,3}

¹ Department of Surgery, Hospital General Universitario Dr. Balmis, Alicante, Spain

² Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL), Alicante, Spain

³ Universidad Miguel Hernández, Elche, Spain

⁴ Department of Surgery, Hospital Universitario Virgen de las Nieves, Instituto de Investigación Biosanitaria ibs. GRANADA, , University of Granada, Granada, Spain

⁵ School of Medicine Universidad de Granada, Granada, Spain

⁶ Department of Surgery, Hospital General Universitario de Elda, Alicante, Spain

⁷ Department of Surgery, Complejo Hospitalario Universitario de Badajoz, Badajoz, Spain

⁸ Universidad de Extremadura, Badajoz, Spain

Corresponding Author:

JOSÉ MANUEL RAMIA, MD, PHD, FACS, FRCS, FRCS(ED), FKCS

Head of Department (HGU Dr. Balmis) and Professor of Surgery
(Universidad Miguel Hernández) Alicante (Spain)

E-mail: jose_ramia@hotmail.com

Abstract

The development of collaborative clinical registries has profoundly transformed pancreatic surgery research over the past two decades. While traditional evidence was largely derived from single-center retrospective studies and administrative databases, prospective, clinician-led registries have generated high-quality evidence and facilitated benchmarking, quality assessment, and continuous improvement in surgical care.

The Dutch Pancreatic Cancer Group pioneered this

model by establishing nationwide prospective audits that produced hundreds of scientific publications and fundamentally shaped pancreatic surgery research across Europe. Inspired by this collaborative philosophy, several national and international initiatives subsequently emerged, including the Spanish projects ERPANDIS (Estudio Retrospectivo PANcreatectomía DISTal) and SPANDISPAN (SPANish DISTal PANcreatectomy)

ERPANDIS represented the first multicenter collaborative (8 centers) effort focused specifically on left

pancreatectomy in Spain. The experience gained through this retrospective registry ultimately led to the development of SPANDISPAN, a nationwide prospective project involving 41 centers and representing approximately three-quarters of all left pancreatectomies performed annually in Spain.

Together, ERPANDIS and SPANDISPAN generated evidence on multivisceral resection, mucinous cystic neoplasms, delayed gastric emptying, textbook outcome, splenic vessel involvement, benchmarking, institutional volume, failure-to-rescue, postpancreatectomy hemorrhage, conversion during minimally invasive surgery, and extended left pancreatectomy.

This article reviews the evolution of both projects, summarizes their key scientific contributions, discusses lessons learned from two decades of collaborative research, and explores how similar initiatives may help develop pancreatic surgery networks in Southeastern Europe.

Keywords: left pancreatectomy, pancreas, registry, outcomes, textbook outcome, failure to rescue, surgery

1. Why Surgical Registries Matter

Over the past two decades, surgical research has evolved from isolated institutional experiences to collaborative prospective data collection. Historically, much of the available evidence in surgery came from single-center retrospective series, often limited by small sample sizes, selection bias, and heterogeneous data collection. At the same time, large administrative databases, particularly in the United States, provided important insights into surgical outcomes and healthcare delivery. Resources such as NSQIP, SEER, NCDB, and Medicare-derived datasets substantially improved our understanding of quality assessment and population-level outcomes^{1,2}.

Nevertheless, administrative databases are typically designed for billing, epidemiological surveillance, or healthcare management rather than for answering specific clinical questions. Consequently, they often lack the granularity needed to evaluate procedure-specific outcomes and the technical aspects of complex operations^{1,2}. Variables related to postoperative pancreatic fistula, benchmarking, textbook outcome, failure-to-rescue, or minimally invasive pancreatic surgery are frequently unavailable or incompletely captured.

Clinician-led registries emerged to address these limitations. Unlike administrative datasets, registries are

designed and governed by healthcare professionals who determine which variables to collect, how outcomes should be defined, and which quality indicators to evaluate^{1,2}. This approach enables detailed assessment of clinically relevant endpoints while also creating platforms for quality improvement, benchmarking, and collaborative research.

Perhaps the most influential example in pancreatic surgery is the Dutch Pancreatic Cancer Group (DPCG). Through the Dutch Pancreatic Cancer Audit, this collaborative network demonstrated that nationwide prospective registries could improve patient care, facilitate benchmarking, and generate high-impact scientific research. Under the leadership of Prof. Marc Besselink, the DPCG became one of the most influential collaborative pancreatic surgery networks worldwide³. More importantly, it established a culture of collaboration, transparency, and continuous quality improvement that has become a model for pancreatic surgery research across Europe⁴.

The influence of the Dutch experience rapidly extended beyond the Netherlands. Similar registry-based initiatives subsequently emerged in France, Germany, Sweden, the United Kingdom, and other European countries. International collaborative projects such as the European Consortium on Minimally Invasive Pancreatic Surgery (E-MIPS) further expanded the concept of prospective registry-based research across national borders⁵. These initiatives demonstrated that registries could serve not only as scientific tools but also as mechanisms for auditing clinical practice, monitoring outcomes, promoting standardization, and fostering academic collaboration.

Perhaps the most important lesson derived from these experiences is that meaningful clinical research does not necessarily require large financial investments or sophisticated infrastructures. Instead, it requires motivated clinicians, standardized definitions, reliable data collection, and a shared willingness to learn from collective experience^{6,7}.

It was within this international movement toward collaborative registry-based pancreatic surgery research that the Spanish projects ERPANDIS (Estudio Retrospectivo PANcreatectomia DIStal) and SPANDISPAN (SPANish DIStal PANcreatectomy) were conceived.

2. ERPANDIS: The Foundation of Collaborative Research in Left Pancreatectomy

The intellectual origins of ERPANDIS trace back to a simple observation that remains relevant today: left

pancreatectomy (LP) is often viewed as less demanding than pancreatoduodenectomy, even though it is performed for a remarkably heterogeneous group of diseases. Years before multicenter registries became common in pancreatic surgery; this concept was captured in a Spanish publication that described LP as “one operation for many indications.”⁸

LP is performed for a wide spectrum of pathological entities, including pancreatic ductal adenocarcinoma, neuroendocrine tumors, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms, solid pseudopapillary tumors, metastatic lesions, and benign conditions. Although the technical procedure may appear similar, these diseases differ substantially in biological behavior, prognosis, operative complexity, and expected outcomes.

When ERPANDIS was conceived, Spain lacked a collaborative registry specifically focused on LP. Most of the available evidence came from single-center retrospective series that were often underpowered to address clinically relevant questions. To overcome these limitations, a multicenter initiative involving eight pancreatic surgery units from Spain and Puerto Rico was launched. With the invaluable organizational support of Mario Seradilla, the ERPANDIS registry was created to combine institutional experiences into a sufficiently large cohort capable of addressing questions that could not be adequately explored by individual centers alone.

The scientific productivity of ERPANDIS exceeded initial expectations⁹⁻¹³. Over the following years, the registry produced a series of studies addressing several aspects of LP, including multivisceral resection, mucinous cystic neoplasms, delayed gastric emptying, textbook outcome, and radiologic splenic vessel involvement⁹⁻¹³. Although each project addressed a different clinical question, common themes gradually emerged.

The first studies examined how disease-specific and technical factors influence outcomes. The analysis of multivisceral resection showed that increased operative complexity does not necessarily preclude acceptable outcomes when careful patient selection is applied⁹. Similarly, the study of mucinous cystic neoplasms underscored the importance of pathological heterogeneity and reinforced the concept that LP should not be considered a uniform procedure¹⁰.

Subsequent investigations focused on quality assessment and postoperative recovery. The delayed gastric emptying study showed that this complication is not

limited to pancreatoduodenectomy and may significantly affect recovery after LP, particularly when associated with a postoperative pancreatic fistula¹¹. The textbook outcome analysis further broadened the concept of surgical quality by emphasizing that optimal care cannot be adequately assessed by morbidity and mortality alone¹².

Finally, the study evaluating radiologic splenic vessel involvement examined the relationship between preoperative imaging findings and oncologic outcomes. The results suggested that radiologic data may provide valuable information about disease aggressiveness and contribute to preoperative risk stratification¹³.

Perhaps the most important achievement of ERPANDIS was not any individual publication but rather the demonstration that collaborative research focused exclusively on LP was feasible and scientifically productive. The registry fostered cooperation among pancreatic surgeons, established a national network capable of generating meaningful evidence, and laid the foundation for future prospective initiatives.

As ERPANDIS evolved, pancreatic surgery itself was changing. Minimally invasive LP became increasingly established, laparoscopic approaches were progressively adopted throughout Spain, and robotic surgery began expanding into specialized pancreatic units. Simultaneously, concepts such as benchmarking, textbook outcome, and failure-to-rescue were gaining prominence within the international pancreatic surgery community. These developments highlighted the limitations of retrospective data collection and underscored the need for a prospective nationwide registry to evaluate contemporary practice.

3. SPANDISPAN: The Evolution of Prospective Collaborative Research

The natural consequence of these developments was SPANDISPAN.

The experience gained through ERPANDIS demonstrated that collaborative research focused on LP was both feasible and scientifically productive. However, it also highlighted the inherent limitations of retrospective studies, including incomplete data collection, heterogeneity across participating institutions, and the inability to evaluate emerging concepts prospectively.

At the same time, as we previously mentioned, pancreatic surgery itself was undergoing a profound transformation. Minimally invasive LP was increasingly adopted throughout Spain, laparoscopic approaches were

progressively replacing traditional open surgery, and robotic platforms were beginning to gain acceptance in specialized pancreatic units.

These developments created the ideal environment for a new collaborative initiative. Under the leadership of Cándido Alcázar and with support from pancreatic surgeons nationwide, the SPANDISPAN project was established as a prospective nationwide registry dedicated to LP.

The project ultimately involved 41 participating centers and captured approximately 75% of all LP performed annually in Spain. To our knowledge, SPANDISPAN is one of the largest prospective national registries exclusively focused on LP. Beyond its scientific productivity, the project created a collaborative network capable of evaluating contemporary surgical practice, identifying opportunities for quality improvement, and generating evidence relevant to everyday clinical decision-making.

Unlike ERPANDIS, which primarily sought to demonstrate the feasibility of multicenter collaborative research, SPANDISPAN was conceived as a mature prospective platform designed to address increasingly sophisticated clinical questions. The resulting studies examined not only perioperative outcomes but also benchmarking, institutional performance, complication management, and the impact of biological and technical factors on surgical outcomes.

Taken together, these analyses provide a comprehensive overview of contemporary LP and constitute the most extensive body of evidence from a national prospective registry dedicated to this procedure.

3.1 Understanding Outcomes After Left Pancreatectomy

The first studies generated by SPANDISPAN sought to define contemporary outcomes after LP and identify the factors that influence surgical results. Beyond describing morbidity and mortality, these analyses aimed to establish standards of excellence and to understand how disease-specific characteristics influence perioperative outcomes¹⁴⁻¹⁶.

- Benchmarking Excellence: Defining the Best Achievable Outcomes

Benchmarking has become one of the most important concepts in contemporary surgical quality assessment⁶. Unlike traditional outcome reporting, which describes average performance, benchmarking identifies the best

achievable results under optimal conditions. By establishing reference values from high-performing centers and low-risk patients, benchmarking provides objective standards for institutions to compare their performance⁶.

Using data from the SPANDISPAN registry, the benchmark study evaluated outcomes after LP in a contemporary national cohort¹⁴. The analysis showed that even in ideal circumstances, LP remains associated with substantial morbidity. Clinically relevant postoperative pancreatic fistula, major complications, and prolonged hospital stay could not be eliminated, underscoring the intrinsic complexity of pancreatic surgery.

Perhaps the most important contribution of this study was the establishment of objective benchmark values for LP in a national setting. These values provide realistic expectations for surgeons, institutions, and patients while identifying areas where quality improvement efforts may be directed.

The study also reinforced an important conceptual message. Benchmarking should not be interpreted as a description of average outcomes but rather as a representation of what can reasonably be achieved under optimal conditions. Consequently, benchmark values offer a more meaningful framework for quality assessment than simple comparisons between institutions.

Ultimately, the benchmark analysis demonstrated that excellence in LP is measurable, but also that even the best achievable outcomes remain associated with significant morbidity. This finding serves as a reminder that LP should continue to be regarded as a major pancreatic operation requiring specialized expertise and multidisciplinary care.

- Contemporary Left Pancreatectomy in Spain

While benchmarking defines excellence, understanding contemporary practice requires evaluating outcomes across the entire spectrum of patients and institutions. For this reason, one of the first objectives of SPANDISPAN was to provide a national snapshot of LP in Spain¹⁵. The analysis demonstrated the remarkable evolution since ERPANDIS's early years. Minimally invasive surgery has become the dominant approach.

Despite these technological advances, postoperative morbidity remained substantial. Complications continued to affect a considerable proportion of patients, and postoperative pancreatic fistula remained the most important determinant of adverse outcomes. However, mortality rates were exceptionally low, underscoring the

considerable improvements achieved in perioperative management, complication recognition, and multidisciplinary postoperative care.

Perhaps the most important message of this study was that modern LP has become safer without being simpler. Technological innovation and minimally invasive surgery have improved perioperative outcomes, but they have not eliminated the inherent challenges of pancreatic resection.

Consequently, the study provided a realistic portrait of contemporary LP in Spain: a procedure increasingly performed using minimally invasive approaches, associated with low mortality yet still marked by significant morbidity and substantial postoperative complexity.

- One Operation for Many Diseases Revisited

One of the original concepts underpinning ERPANDIS was that LP is a single operation performed for multiple diseases. The histology analysis from SPANDISPAN revisited this idea using prospective nationwide data.

The study evaluated postoperative outcomes by underlying pathological diagnosis and found significant differences among disease groups. Patients undergoing surgery for pancreatic ductal adenocarcinoma, neuroendocrine tumors, mucinous cystic neoplasms, and other pancreatic lesions showed distinct clinical characteristics, intraoperative findings, and postoperative outcomes¹⁶.

These observations underscored the importance of accounting for pathological heterogeneity when interpreting surgical results. Comparisons across institutions, studies, and surgical approaches may be misleading if underlying disease distributions are not considered. What appears to be a difference in surgical quality may instead reflect differences in patient selection and disease biology.

Perhaps the most important contribution of this study was confirming that LP should not be viewed as a homogeneous procedure. Rather, it is a common technical operation performed across diseases with profoundly different biological behaviors and clinical trajectories.

The findings therefore validated one of the central ideas that had originally inspired ERPANDIS and demonstrated that the concept remains equally relevant in the era of prospective national registries.

3.2 Understanding Quality and Institutional Performance

While the first SPANDISPAN studies focused primarily on patient characteristics and disease-related factors,

subsequent analyses addressed a different question: why do some institutions consistently achieve better outcomes than others?

- Does Volume Matter? The Relationship Between Institutional Experience and Outcomes

The relationship between hospital volume and surgical outcomes has been among the most debated topics in complex gastrointestinal surgery. For pancreatic resections, numerous studies have suggested that higher procedural volumes are associated with improved outcomes, prompting many healthcare systems to promote varying degrees of centralization³. Nevertheless, data specifically focused on LP remain limited.

Using the SPANDISPAN cohort, this study evaluated the influence of institutional volume on perioperative outcomes after LP¹⁷. The analysis demonstrated significant differences among centers by annual procedural volume. Higher-volume institutions were more likely to adopt minimally invasive approaches, accumulate greater experience in managing complex pancreatic disease, and achieve superior perioperative outcomes overall.

Importantly, the study suggested that volume functions not merely as a numerical indicator but as a surrogate for institutional expertise. High-volume centers typically benefit from dedicated multidisciplinary teams, standardized perioperative pathways, experienced interventional radiology services, and greater familiarity with postoperative complication management. These factors collectively contribute to improved patient care and may help explain part of the observed volume-outcome relationship.

The principal contribution of this study was the confirmation that institutional experience remains an important determinant of outcomes after LP. While volume alone cannot guarantee excellence, the findings support the concept that complex pancreatic surgery benefits from concentration of expertise and from organizational structures capable of delivering highly specialized care.

- Failure to Rescue: Beyond the Prevention of Complications

Traditionally, surgical quality has been assessed using complication rates, mortality, and length of hospital stay. However, contemporary quality research increasingly recognizes that complications are not always entirely preventable. Equally important is how effectively institutions manage serious complications once they occur. This concept, known as failure to rescue (FTR),

has emerged as one of the most informative indicators of healthcare quality^{18,19}.

The SPANDISPAN FTR study examined outcomes among patients who developed major postoperative complications after LP²⁰. Rather than focusing exclusively on complication rates, the analysis examined which patients ultimately died after severe adverse events and which factors influenced successful rescue.

The findings showed that mortality after LP is often determined less by the occurrence of complications than by an institution's ability to recognize, escalate, and manage them appropriately. Patient-related factors such as age and disease complexity contributed to risk, but institutional resources and multidisciplinary expertise also appeared to play a crucial role.

These observations reinforce an important concept in modern surgical quality assessment: excellent care is defined not only by avoiding complications but also by responding effectively when they occur. Consequently, FTR complements traditional outcome measures and offers a more comprehensive view of institutional performance.

Perhaps the most important message of this study is that quality in pancreatic surgery extends beyond technical excellence in the operating room. It also depends on the systems, teams, and organizational structures that support patients in the postoperative period.

3.3 Understanding Complexity and Adverse Events

Beyond quality indicators, SPANDISPAN also examined specific complications and complex clinical scenarios linked to increased perioperative risk. These studies addressed some of the most challenging aspects of contemporary LP, including severe postoperative hemorrhage²⁰, conversion during minimally invasive surgery²¹, and extended resections for advanced disease²².

- Postpancreatectomy Hemorrhage: Understanding a Rare but Potentially Devastating Complication

Although postoperative pancreatic fistula remains the most common complication after LP, post-pancreatectomy hemorrhage (PPH) is often considered the most feared. Its incidence is relatively low compared with other postoperative adverse events, yet its consequences are substantial, including reintervention, prolonged hospitalization, increased resource utilization, and significant mortality. Consequently, understanding the mechanisms and risk factors associated with PPH remains an important objective in pancreatic surgery research.

The SPANDISPAN registry provided a unique opportunity to prospectively evaluate this complication in a contemporary national cohort. The analysis confirmed that PPH remains an uncommon event after LP, affecting only a small proportion of patients. Nevertheless, when hemorrhage occurred, it was frequently associated with a more complex postoperative course, marked by higher rates of clinically relevant pancreatic fistula, reinterventions, and prolonged hospital stay.

Several clinical and technical factors were associated with an increased risk of hemorrhage. However, perhaps the most clinically relevant observation was the strong association between PPH and postoperative pancreatic fistula. This finding supports the widely accepted concept that hemorrhage often results from local inflammatory processes and vascular erosion in the setting of pancreatic leakage rather than from an isolated postoperative event.

Importantly, despite the severity traditionally associated with PPH, mortality in the SPANDISPAN cohort remained exceptionally low. This finding likely reflects advances in postoperative surveillance, interventional radiology, endoscopic therapies, and multidisciplinary management.

The principal contribution of this study was twofold. First, it identified factors associated with an increased risk of hemorrhage after LP. Second, and perhaps more importantly, it reinforced the concept that PPH should be understood within the broader context of postoperative pancreatic fistula and overall complication management.

- Conversion During Minimally Invasive Left Pancreatectomy: Failure or Safety Strategy?

The progressive adoption of minimally invasive LP is one of the most important developments in contemporary pancreatic surgery. However, despite increasing experience and technological advances, conversion to open surgery remains necessary in some cases. Historically, conversion has often been viewed as a technical failure or as an indicator of inadequate preoperative planning. More recently, an alternative perspective has emerged, viewing conversion as a safety strategy to prevent more serious intraoperative complications.

Using data from the SPANDISPAN registry, a dedicated analysis evaluated the incidence, causes, and consequences of conversion during minimally invasive LP²¹. The study, currently submitted for publication, is one of the first prospective national assessments of this issue.

The analysis demonstrated that conversion was associated with increased operative complexity, including longer operative times, greater blood loss, and a more demanding postoperative course. Patients requiring conversion experienced higher rates of complications and longer hospital stays than those undergoing completed minimally invasive procedures. However, these findings should not be interpreted as evidence that conversion itself causes adverse outcomes. Rather, conversion frequently reflected the presence of difficult anatomy, unexpected intraoperative findings, vascular involvement, or technical challenges that increased procedural complexity from the outset.

Perhaps the most important contribution of this study was reinforcing a concept increasingly accepted in pancreatic surgery: conversion should not be viewed as a failure. On the contrary, timely conversion may reflect sound surgical judgment and a commitment to patient safety. The willingness to abandon a minimally invasive approach when necessary is often a sign of experience rather than inadequacy.

The findings, therefore, support a more nuanced interpretation of minimally invasive LP. Success should be defined not by completing the operation laparoscopically or robotically, but by achieving the safest possible outcome for the patient.

- *Extended Left Pancreatectomy: When Technical Complexity Meets Tumor Biology*

Extended LP is among the most demanding procedures in pancreatic surgery. These operations frequently require multivisceral or vascular resection to achieve complete oncological clearance and are typically performed in patients with locally advanced disease. Although increasingly accepted in specialized centers, questions remain about their true impact on perioperative outcomes and oncological benefit.

A recent SPANDISPAN analysis, currently under review for publication, evaluated postoperative and short-term oncological outcomes after extended LP in a prospective national cohort²². Among patients undergoing LP, a substantial minority required extended resections according to International Study Group of Pancreatic Surgery criteria, reflecting the growing complexity of contemporary pancreatic surgical practice.

As expected, extended procedures were associated with longer operative times, greater blood loss, reduced use of minimally invasive approaches, and prolonged hospitalization. Nevertheless, rates of major complications and clinically relevant postoperative pancreatic fistula remained comparable to those observed after standard LP, suggesting that extended resections can be performed safely in experienced hepatopancreatobiliary units.

Table 1. Principal Scientific Contributions of ERPANDIS and SPANDISPAN

Registry	Study	Main Topic	Principal Message
ERPANDIS	Multivisceral resection	Extended surgery	Increased complexity does not preclude acceptable outcomes
ERPANDIS	Mucinous cystic neoplasms	Histology	LP is performed for biologically distinct diseases
ERPANDIS	Delayed gastric emptying	Morbidity	DGE remains relevant after LP and is linked to POPF
ERPANDIS	Textbook outcome	Quality assessment	Composite metrics better reflect surgical quality
ERPANDIS	Splenic vessel involvement	Oncology	Radiologic findings may predict tumour aggressiveness
SPANDISPAN	Benchmarking	Surgical excellence	Defines the best achievable outcomes after LP
SPANDISPAN	Contemporary outcomes	National practice	LP is safer but not simpler
SPANDISPAN	Histology	Disease heterogeneity	One operation for many diseases remains valid
SPANDISPAN	Volume	Centralization	Institutional expertise influences outcomes
SPANDISPAN	FTR	Quality systems	Rescue capacity is as important as complication prevention
SPANDISPAN	Postpancreatectomy hemorrhage	Severe complications	PPH is strongly associated with POPF
SPANDISPAN	Conversion	Minimally invasive surgery	Conversion is often a safety strategy rather than a failure
SPANDISPAN	Extended LP	Advanced disease	Tumour biology outweighs technical complexity

The most important observations emerged from the oncological analysis. Patients undergoing extended resections presented more advanced disease, higher rates of lymph node involvement, and a significantly greater risk of early recurrence. These findings indicate that outcomes following extended LP are determined not only by technical complexity but also, and perhaps more importantly, by the biological aggressiveness of the underlying tumor.

The principal message of this study extends beyond the technical aspects of surgery. Extended LP should not be viewed simply as a larger operation, but rather as part of a multidisciplinary strategy for the treatment of biologically advanced disease. Ultimately, surgical expertise remains essential, but tumor biology continues to be the dominant determinant of long-term oncological outcomes.

4. What Have We Learned from Twenty Years of Research in Left Pancreatectomy?

The combined experience of ERPANDIS and SPANDISPAN extends beyond the individual findings of their respective studies. Together, the registries provide a unique perspective on the evolution of LP over the past two decades and offer important lessons on surgical quality, patient selection, institutional performance, and oncologic outcomes^{23,24}.

Left Pancreatectomy Is Not a Minor Pancreatic Operation

Historically, LP has often been viewed as technically less demanding than pancreatoduodenectomy. While this may be true from a reconstructive standpoint, evidence from ERPANDIS and SPANDISPAN shows that LP remains a major pancreatic resection associated with substantial morbidity. Across multiple studies, postoperative complications remained common despite advances in surgical technique, perioperative care, and minimally invasive technology. Benchmark analyses further confirmed that even under optimal circumstances, clinically relevant morbidity cannot be eliminated.

This observation reinforces the need for the same level of expertise, multidisciplinary support, and quality assessment routinely expected for other complex pancreatic procedures.

One Operation for Many Diseases

Perhaps the most enduring concept emerging from this research is that LP is not performed for a single disease

but for a remarkably heterogeneous group of pathological conditions. The histology analysis from SPANDISPAN confirmed that outcomes differ significantly according to underlying pathology. Consequently, comparisons between studies, institutions, and surgical techniques must always consider disease-specific factors. Failure to account for pathological heterogeneity risks oversimplifying a procedure that is fundamentally diverse in its indications and objectives.

Postoperative Pancreatic Fistula Remains the Central Challenge

A recurring lesson concerns the dominant role of postoperative pancreatic fistula. Regardless of study design, patient population, or outcome measure, pancreatic fistula repeatedly emerged as the complication most strongly associated with adverse postoperative events.

The influence of pancreatic fistula extended beyond its direct clinical consequences. It contributed to delayed gastric emptying, PPH, prolonged hospitalization, reinterventions, and FTR. In many respects, the history of LP research can be viewed as a continuing effort to better understand, prevent, and manage the consequences of pancreatic leakage.

Despite substantial advances in surgical techniques and perioperative management, postoperative pancreatic fistula remains the principal unresolved challenge following LP.

Quality Depends on More Than Technical Skill

The volume and FTR analyses highlighted another important principle. Surgical quality is not determined solely by operative performance. Institutional experience, multidisciplinary collaboration, postoperative surveillance, interventional radiology, intensive care support, and the ability to recognize and treat complications all contribute to patient outcomes.

This broader understanding of quality explains why concepts such as benchmarking, textbook outcomes, and FTR have become increasingly important in contemporary pancreatic surgery^{12,18,19,23,24}. Excellent results require not only skilled surgeons but also effective systems of care that support patients throughout the perioperative journey.

Tumor Biology Ultimately Determines Oncological Outcomes

Although technical complexity remains an important determinant of perioperative risk, several studies have

shown that long-term outcomes are more strongly influenced by biological factors than by surgical difficulty alone. Analyses of splenic vessel involvement, pathological subtype, and extended LP consistently show that tumor aggressiveness frequently outweighs technical considerations when recurrence and survival are evaluated.

This observation serves as a reminder that surgery is only one component of modern pancreatic cancer care. Accurate staging, multidisciplinary decision-making, systemic therapies, and patient selection remain fundamental determinants of oncological success.

Collaboration Generates Better Evidence

The final lesson may be the most important. Neither ERPANDIS nor SPANDISPAN would have been possible through the efforts of a single institution alone. The ability to answer increasingly sophisticated clinical questions depended entirely on collaboration among surgeons willing to share data, standardize definitions, and learn from collective experience.

The transition from a retrospective multicenter registry of eight institutions to a prospective nationwide cohort of 41 centers illustrates the remarkable potential of collaborative research networks. More importantly, it shows that meaningful scientific contributions can arise from cooperation rather than competition.

Ultimately, the greatest achievement of ERPANDIS and SPANDISPAN may not be the publications they produced, but the collaborative culture they fostered. By transforming individual institutional experiences into shared knowledge, both registries contributed not only to a better understanding of LP but also to the development of a national community committed to continuous quality improvement and scientific progress.

5. Future Perspectives: Building Collaborative Registries Beyond Spain

The experience gained through ERPANDIS and SPANDISPAN shows that clinical registries can deliver benefits that extend far beyond scientific publications. Although the academic output of both projects has been substantial, their true value lies in their ability to improve quality assessment, facilitate benchmarking, monitor outcomes, and promote collaboration among pancreatic surgeons.

Perhaps the most important lesson from these initiatives is that successful collaborative research does not necessarily require large financial investments or

sophisticated infrastructure. Instead, it depends on motivated clinicians, standardized definitions, reliable data collection, and a shared commitment to improving patient care through collective learning. The Dutch Pancreatic Cancer Group's experience demonstrated that nationwide registries could transform a specialty by generating high-quality scientific evidence while improving clinical practice³. Similar experiences have since emerged throughout Europe, creating networks that integrate research, quality improvement, and professional development.

The Spanish experience, represented by ERPANDIS and SPANDISPAN, shows that these principles can be successfully adapted to diverse healthcare systems and organizational settings. What began as a retrospective collaboration among a small number of institutions evolved into a prospective nationwide registry capable of addressing increasingly complex clinical questions. Equally important, it created a community of surgeons committed to transparency, benchmarking, and continuous quality improvement.

The potential relevance of this model extends across Southeastern Europe. Several centers throughout the region have increasingly contributed to the international pancreatic surgery literature and participate actively in European hepatopancreatobiliary surgical societies. Developing prospective collaborative registries in Kosovo, Albania, North Macedonia, and neighboring countries could offer valuable opportunities to monitor outcomes, benchmark performance, strengthen national surgical networks, and generate evidence that reflects local clinical. Beyond their scientific value, such initiatives may facilitate regional cooperation, promote standardization, and support the development of future collaborative research projects.

Importantly, registries should not be viewed solely as research tools. They also serve as mechanisms for professional development and capacity building. By encouraging participation in multicenter projects, registries create opportunities for younger surgeons to engage in clinical research, develop academic skills, and contribute to generating evidence that directly influences patient care.

Importantly, the story of collaborative LP research in Spain does not end with SPANDISPAN. Building on the experience gained through ERPANDIS and SPANDISPAN, a new nationwide prospective registry, the Spanish Left Pancreatectomy Project (SPANLEPAN), is scheduled to begin on January 1, 2027. The project will

involve 55 hospitals across Spain and is planned for a four-year period. Beyond continuing previous collaborative efforts, this initiative reflects the consolidation of a national research network capable of addressing increasingly complex clinical questions while promoting quality assessment, benchmarking, and continuous improvement in pancreatic surgery.

The launch of SPANLEPAN demonstrates that collaborative research has evolved from an isolated project into a sustainable model for scientific advancement in pancreatic surgery. In this sense, the most important legacy of ERPANDIS and SPANDISPAN may not be the studies they produced, but the collaborative infrastructure they helped build.

The future of pancreatic surgery research will increasingly depend on cooperation among centers, countries, and professional societies. Registries provide one of the most effective mechanisms for achieving this cooperation, enabling collaborative networks that can transform data into knowledge and knowledge into better patient care.

References:

1. Gliklich RE, Leavy MB, Karl J, Campion DM, Levy D, Berliner E. A framework for creating standardized outcome measures for patient registries. *J Comp Eff Res.* 2014 Sep;3(5):473-80. doi: 10.2217/ce.14.38. PMID: 25350799. Black N.
2. Arts DG, Bosman RJ, de Jonge E, Joore JC, de Keizer NF. Training in data definitions improves quality of intensive care data. *Crit Care.* 2003 Apr;7(2):179-84. doi: 10.1186/cc1886. Epub 2003 Feb 18. PMID: 12720565; PMCID: PMC270628.
3. Suurmeijer JA, Henry AC, Bonsing BA, Bosscha K, van Dam RM, van Eijck CH, Dutch Pancreatic Cancer Group. Outcome of Pancreatic Surgery During the First 6 Years of a Mandatory Audit Within the Dutch Pancreatic Cancer Group. *Ann Surg.* 2023 Aug 1;278(2):260-266. doi: 10.1097/SLA.0000000000005628. Epub 2022 Jul 22. PMID: 35866656.
4. van Ramshorst TME, van Hilst J, Boggi U, Dokmak S, Edwin B, Keck T et al. Standardizing definitions and terminology of left-sided pancreatic resections through an international Delphi consensus. *Br J Surg.* 2024 Apr 3;111(4):znae039. doi: 10.1093/bjs/znae039. PMID: 38686655.
5. van der Heijde N, Vissers FL, Boggi U, Dokmak S, Edwin B, Hackert T, Khatkov IE, Keck T, Besselink MG, Abu Hilal M; E-MIPS. Designing the European registry on minimally invasive pancreatic surgery: a pan-European survey. *HPB (Oxford).* 2021;23:566-574.
6. Ramia JM, Soria-Aledo V. Benchmarking in surgery: how to

compare with the best. *Cir Esp (Engl Ed).* 2023 Jun;101(6):445-446. doi:10.1016/j.cireng.2022.12.006. Epub 2022 Dec 26. PMID: 36580996.

7. Domenghino A, Walbert C, Birrer DL, Puhan MA, Clavien PA; Outcome4Medicine consensus group. Consensus recommendations on how to assess the quality of surgical interventions. *Nat Med.* 2023 Apr;29(4):811-822. doi: 10.1038/s41591-023-02237-3. Epub 2023 Apr 17. PMID: 37069361.

8. Ramia JM, Muffak K, Palomeque A, Mansilla A, Villar J, Garrote D, Ferrón JA Pancreatectomía corporocaudal: una misma técnica con variadas indicaciones. *Cir Esp* 2005; 77:22-6.

9. Ramia JM, Del Río-Martín JV, Blanco-Fernández G, Cantalejo-Díaz M, Rotellar- Sastre F, Sabater-Orti L et al Distal pancreatectomy with multivisceral resection: A retrospective multicenter study - Case series. *Int J Surg.* 2020 Oct;82:123-129. doi: 10.1016/j.ijssu.2020.08.024. Epub 2020 Aug 26. PMID: 32860956.

10. Ramia JM, Del Río Martín J, Blanco-Fernández G, Cantalejo-Díaz M, Pardo F, Muñoz-Forner E et al Pancreatic mucinous cystic neoplasms located in the distal pancreas: a multicenter study. *Gland Surg.* 2022 May;11(5):795-804. doi: 10.21037/gs-21-703. PMID: 35694091; PMCID: PMC9177270.

11. Serradilla Martín M, Villodre Tudela C, Rotellar F, Blanco Fernández G, Ramia JM; miembros del Grupo de Trabajo ERPANDIS. Delayed gastric emptying after distal pancreatectomy. *Cir Esp (Engl Ed).* 2023 Aug;101(8):574-576. doi: 10.1016/j.cireng.2023.03.003. Epub 2023 Mar 16. PMID: 36933890.

12. Villodre C, Del Río-Martín J, Blanco-Fernández G, Cantalejo-Díaz M, Pardo F, Carbonell S et al. Textbook outcome in distal pancreatectomy: A multicenter study. *Surgery.* 2024 Apr;175(4):1134-1139. doi: 10.1016/j.surg.2023.11.012. Epub 2023 Dec 9. PMID: 38071134.

13. Blanco-Fernández G, Serradilla-Martín M, Rotellar F, Latorre R, Jaén- Torrejimeno I, Muñoz-Forner E et al Short- and long-term outcomes after distal pancreatectomy with radiologic infiltration of splenic vessels for pancreatic ductal adenocarcinoma. *J Gastrointest Surg.* 2024 Apr;28(4):467-473. doi: 10.1016/j.gassur.2024.01.018. Epub 2024 Jan 23. PMID: 38583897.

14. Ramia JM, Alcázar-López CF, Villodre-Tudela C, Rubio-García JJ, Hernández B, Aparicio-López D, Serradilla-Martín M; SPANDISPAN Collaborative Study Group. Benchmark Outcomes for Distal Pancreatectomy: A Multicenter Prospective Snapshot Study from the Spanish Distal Pancreatectomy Project (SPANDISPAN). *J Am Coll Surg.* 2024 Sep 1;239(3):288-297. doi: 10.1097/XCS.0000000000001086. Epub 2024 Aug 15. PMID: 38533997.

15. Hernández-Roca B, Ramia JM, Busquets J, Secanella L, Peláez N, Alkorta M, et al Surgical approach and postoperative outcomes after left pancreatectomy (Spandispan prospective project). *Cir Esp (Engl Ed).* 2025 Sep;103(9):800197. doi: 10.1016/j.cireng.2025.800197.

16. Belinda Sánchez-Pérez, Cándido F. Alcázar-López, Mario Serradilla-Martin, Celia Villodre-Tudela, Belen Hernández, Julio Santoyo Santoyo, Jose Manuel Ramia, for the SPANDISPAN Collaborative Study Group. Does the type of neoplasm influence the development of postoperative complications following distal pancreatectomy? *Asian Journal of Surgery* 2025; 48: 4137-4143

17. Aparicio-López D, Ramia JM, Villodre C, Rubio-García JJ, Hernández B, Busquets J et al. Effect of Volume on Postoperative Outcomes After Left Pancreatectomy: A Multicenter Prospective Snapshot Study (SPANDISPAN Project). *J Clin Med*. 2025 Aug 25;14(17):6013. doi: 10.3390/jcm14176013. PMID: 40943773;

18. Ramia JM, Villodre C, Vicente Del Río J, Blanco G, Rotellar F, Sabater L, Busquets J, Manuel A, Domingo Del Pozo C, Latorre R, Serradilla-Martín M, Alcázar C; ERPANDIS Collaborative Study Group; SPANDISPAN Collaborative Study Group. Which risk factors are related to failure to rescue in left pancreatectomy? Mixed cohort study (ERPANDIS and SPANDISPAN projects). *Curr Probl Surg*. 2025 Jul;68:101780. doi: 10.1016/j.cpsurg.2025.101780. Epub 2025 May1. PMID: 40500034.

19. Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. *Ann Surg* 2009; 250: 1029.

20. Ruiz de la Cuesta M, Villodre C, Serradilla M, Ruiz de la Cuesta E, Alcazar C, Ramia JM; members of the SPANDISPAN project. Factors related to hemorrhage after distal pancreatectomy (SPANDISPAN project). *Cir Esp (Engl Ed)*. 2025 Jul;103(7):800105. doi: 10.1016/j.cireng.2025.800105. Epub 2025 May 15. PMID: 40381944.

21. Gomez I, Villodre C , Hernández-Roca B, Rubio-García JJ, Juli Busquets, Luis Secanella et al Risk factors for conversion to open surgery during minimally invasive left pancreatectomy: a prospective multicenter study (submitted).

22. Sala S, Villodre C, Hernández-Roca B, Rubio-García JJ, Busquets J, Secanella L et al Extended left pancreatectomy: post-operative and short-term oncologic outcomes. A prospective study (Spandispan Project)

23. Silvia Carbonell-Morote, Celia Villodre, Juan Jesús Rubio, Cándido Alcázar, José M. Ramia Textbook outcome: simple and helpful tool for measuring your surgical results. A narrative review *Kosovo J Surg* 2024

24. Ramia JM, Carbonell-Morote S. Futility, failure to cure, failure to rescue and aborted surgery: New ways to measure the real usefulness of surgery. *Cir Esp (Engl Ed)*. 2025 Feb;103(2):57-59. doi: 10.1016/j.cireng.2024.11.011. Epub 2024 Dec 19. PMID: 39709124.

Diagnostic and Therapeutic Approach to Acute Pancreatitis: Paraguayan National Consensus

Guido Parquet, MD, FICS, FACS^{1,2} — ORCID 0009-0002-1294-5274

Rosa Sánchez, MD, FICS^{1,2,3} — ORCID 0000-0003-1988-7134

¹ 1st Chair of Surgical Clinics, Hospital de Clínicas, Faculty of Medical Sciences, National University of Asunción (UNA). San Lorenzo, Paraguay.

² Paraguayan Chapter of Hepato-Pancreato-Biliary Surgery (HPB), Paraguayan Society of Surgery (SOPACI). Asunción, Paraguay.

³ Minimally Invasive Surgery Service (SCMI), Social Security Institute (IPS), Central Hospital. Asunción, Paraguay.

Corresponding Author:

DR. GUIDO PARQUET

E-mail: gparquet@hotmail.com

** This article is an abbreviated and commented English version of the article “Consenso paraguayo sobre el diagnóstico y tratamiento de la pancreatitis aguda en adultos. Guía para cirujanos – 2025” published in Cirugía Paraguaya in 2025. Authorization was granted by Cirugía Paraguaya.*

Abstract

Background. Acute pancreatitis is a leading cause of hospital admission for inflammatory disease of digestive origin worldwide and in Latin America. Its clinical spectrum ranges from mild, self-limiting episodes to critical illness with multi-organ failure and high mortality. Management in Paraguay remains heterogeneous, and practices persist that may adversely affect outcome.

Methods. The Hepato-Pancreato-Biliary Surgery Chapter of the Paraguayan Society of Surgery convened 24 surgeons in three thematic working groups. Statements were validated by a modified Delphi process with a pre-specified approval threshold of 80% and a final plenary vote.

Results. Thirty-two statements and recommendations were approved, covering diagnosis and severity

classification, initial management and therapeutic support, and the management of local and other surgical complications. Gallstones account for more than 80% of cases nationally. Recommendations include the two-of-three diagnostic rule with serum lipase as the preferred assay, restricted and appropriately timed computed tomography, determinant-based and revised Atlanta severity classification with the modified Marshall score, moderate goal-directed resuscitation with Ringer's lactate, early oral or enteral nutrition, antibiotics only for suspected or confirmed infected necrosis, early cholecystectomy in mild biliary disease, and a step-up approach with intervention deferred beyond four weeks wherever tolerated.

Conclusions. This English-language report presents a national consensus intended to standardize practice across

a health system with uneven access to interventional radiology, therapeutic endoscopy and critical care, and sets out the structural limitations to its implementation.

Key words: Acute pancreatitis; Severity classification; Modified Marshall score; Fluid resuscitation; Step-up approach; Paraguayan consensus.

Introduction

Acute pancreatitis is one of the most challenging gastroenterological conditions in the field of medical-surgical emergencies. In recent decades, a sustained increase in its global incidence has been documented, a phenomenon strongly linked to transitions in sociocultural and demographic habits, such as changes in alcohol consumption patterns, and the rising prevalence of obesity and metabolic syndrome^{1,2}.

Clinically, the disease behaves variably from patient to patient. The vast majority, 80–85% of patients, experience benign interstitial oedema that resolves within a few days with supportive care. A minority, 15–20%, develop pancreatic necrosis, and in these patients the course is characteristically bimodal³. In the first stage, systemic inflammatory response syndrome and multiple organ failure predominate and account for the first peak of mortality^{3,4,5,6}. The second stage occurs in the third and fourth weeks after the onset of the disease due to infection of pancreatic necrosis, which produces a second peak of organ failure and death^{4,5,6}.

Despite growing evidence on the management of acute pancreatitis (AP), in Paraguay there is no uniformity of criteria for managing patients with AP, especially those with severe presentations involving pancreatic necrosis and multiple organ failure. Practices that could potentially lead to an unfavorable prognosis for these patients persist⁷.

With the aim of unifying diagnostic and treatment criteria based on scientific evidence, adapted to the local context, and seeking to improve the quality of healthcare in this area, the Hepatobiliary and Pancreatic Surgery Chapter of the Paraguayan Society of Surgery convened a group of experts to discuss and reach a consensus on different aspects of the epidemiology, diagnosis, classification, and treatment of acute pancreatitis. The objective of this article is to present the results obtained from this consensus in English, in an abbreviated form and with comments, for an international readership; the full consensus has been published in Spanish⁷.

Materials and Methods: Consensus Development

To develop the consensus statement, a panel of 24

leading surgeons was formed, selected through a nationwide survey based on their experience and track record in managing acute pancreatitis. The Board of Directors of the Paraguayan Chapter of Hepato-Pancreato-Biliary (HPB) Surgery entrusted this committee of experts with formulating specific statements and recommendations for each thematic area, based on evidence and personal experience but strictly adapted to the healthcare context of Paraguay.

The work was structured into three thematic sections: Section 1, focused on general information, definitions, and diagnosis; Section 2, centered on initial management; and Section 3, dedicated to addressing complications. Each of these working groups consisted of a panel of eight experts coordinated by two members of the Paraguayan HPB Chapter's Board of Directors.

As a result of the deliberations, a series of statements and recommendations were developed. These were subsequently submitted to a modified Delphi validation process⁸ which was carried out in the following stages: The panel was not blinded, and voting was conducted in plenary rather than anonymously; this is a recognized departure from classical Delphi methodology and is acknowledged as a limitation.

- Discussion and initial voting: a joint plenary session of the panel of 24 experts was held, during which the proposed texts were read, debated, and voted on individually. A minimum approval threshold of 80% was strictly established for the immediate validation of each statement.
- Re-evaluation of discrepancies: the two statements that did not reach the required threshold at first vote were reformulated and submitted to a further cycle of debate and voting until the pre-specified level of agreement was achieved.
- Final plenary approval: after consolidation of the complete document, a final reading was carried out before the plenary. Submitted to a global vote, the final consensus text was approved unanimously (100%).
- Institutional endorsement and dissemination: once completed, the document was submitted to the Paraguayan Society of Surgery (SOPACI) for review and approval. It was also sent to the Ministry of Public Health and Social Welfare (MSPyBS) of the Republic of Paraguay, which has formally recommended its application and adoption as a reference guide in healthcare centers nationwide.

We translated the consensus document into English and prepared an abridged version that highlights the key aspects and recommendations derived from it. Comments were added, particularly regarding the applicability of the guideline in a developing country like Paraguay.

Results

Following the epidemiological and etiological evaluation in Paraguay, the consensus developed 32 statements and recommendations for the management of acute pancreatitis.

In the epidemiological context of the Republic of Paraguay, the reported annual incidence fluctuates between 13 and 45 cases per 100,000 inhabitants⁷. The etiological profile in the Paraguayan population is dominated by gallstones, accounting for over 80% of total diagnoses. This figure significantly exceeds the global averages of other regions of the world, where alcoholism or hypertriglyceridemia are close contenders to gallbladder disease^{9,10}. The second most prevalent etiology nationally is alcohol abuse, representing 10% of cases⁷, with the risk directly proportional to the volume and chronicity of consumption¹¹.

In the specific biliary etiology, which dominates the Paraguayan scenario, three fundamental causal mechanisms are described: direct biliary reflux towards the main pancreatic duct due to obstruction by a stone impacted in the common ampulla; mucosal edema and inflammation of the sphincter of Oddi after the migration and repeated passage of stones towards the duodenum; and the transient incompetence or dysfunction of said sphincter apparatus after the mechanical trauma caused by the same stones^{12,13}.

The statements and recommendations are grouped into the three thematic sections defined for the development of the consensus.

Section 1: Diagnosis and severity classification

1. The diagnosis of acute pancreatitis requires at least two of the following three characteristics: compatible abdominal pain (epigastric, sharp, severe, frequently radiating to the back or hypochondria); serum lipase or amylase greater than or equal to three times the upper limit of normal; or characteristic findings on computed tomography (CT), ultrasound or magnetic resonance imaging (MRI).

2. Serum lipase is the most useful and specific laboratory test for confirmation.

3. Transabdominal ultrasound is established as the

initial study of choice to identify biliary etiology and detect early collections or free fluid.

4. Indications for computed tomography: CT is not routinely recommended for purely diagnostic purposes. Its precise indication is reserved for severity stratification and detection of necrosis between the third and tenth days of evolution (ideally between the third and fifth); diagnostic uncertainty or blunt trauma in the emergency department; and clinical deterioration or suspected complications.

5. Magnetic resonance imaging: indicated in patients with contrast allergy and for assessment of the biliary tree in biliary tract disease, particularly in children.

6. Classification systems: it is recommended to use the determinant-based classification (local determinants and organ failure)¹⁴ or failing that, the revised Atlanta classification (2012)¹⁵, to define severity in four categories: mild (no necrosis or organ failure), moderate (sterile necrosis or transient organ failure), severe (infected necrosis or persistent organ failure) and critical (infected necrosis with persistent organ failure).

7. For the objective assessment of systemic organ dysfunction, the modified Marshall score must be strictly applied^{15, 16}.

Section 2: Initial management and therapeutic support

8. Moderate, goal-directed hydration is prescribed, preferably using Ringer's lactate at 1.5 mL/kg/h, adding a bolus of 10 mL/kg only in case of hypovolaemia¹⁷.

9. The use of colloids is not recommended, and close clinical reassessment is required every 6 hours during the first 24 hours, adjusting volume to the patient's comorbidities.

10. In mild acute pancreatitis, oral intake should be started early as soon as pain and vomiting improve, avoiding prolonged fasting.

11. In moderate and severe cases, the oral route remains the first option if tolerated; otherwise, enteral nutrition by nasogastric or nasojejunal tube should be initiated by the third day.

12. Total parenteral nutrition is reserved exclusively for intolerance of, or failure of, the enteral route to meet minimum caloric needs.

13. Routine antibiotic prophylaxis is not recommended in acute pancreatitis.

14. Broad-spectrum antibiotics with good pancreatic penetration (carbapenems, quinolones, or third-generation

cephalosporins combined with metronidazole) are indicated only on clinical, analytical (CRP or procalcitonin trend) or imaging confirmation of infected necrosis, usually documented after 14 days of evolution.

15. Pain will be addressed under the WHO stepwise approach¹⁸, avoiding NSAIDs if there is renal impairment.

16. Ondansetron is approved for nausea in the intensive care unit.

17. Conventional prokinetics are left to the physician's discretion, with neostigmine suggested only in selected cases of intra-abdominal hypertension in the intensive care unit.

18. In cases of necrosis exceeding 50% of the gland, or exocrine pancreatic insufficiency confirmed by faecal elastase, enzyme replacement therapy (pancreatin) is indicated.

19. In mild acute pancreatitis of biliary etiology, cholecystectomy with intraoperative cholangiography, or pre-operative magnetic resonance cholangiopancreatography (MRCP) should be performed early, during the same hospital admission.

20. In moderate acute pancreatitis, treatment is delayed for at least 4 weeks after discharge, and in severe disease it is postponed for more than 4 weeks after complete resolution of the inflammatory and infectious process.

Section 3: Management of local and other surgical complications

21. Definition of collections (revised Atlanta 2012)¹⁵: collections are divided temporally into those before 4 weeks (acute peripancreatic fluid collection and acute necrotic collection) and those after 4 weeks (pseudocyst and walled-off necrosis), differentiated by the presence of a solid component detectable on contrast-enhanced CT.

22. Asymptomatic collections do not require intervention, regardless of their size.

23. Surgical or interventional treatment is restricted to documented infection (fever, gas on CT, clinical deterioration) or persistent symptoms from mass effect (biliary obstruction or impaired gastric emptying).

24. Routine fine-needle aspiration (FNA) for the diagnosis of infection is not recommended.

25. In infected necrosis or symptomatic walled-off necrosis an initial conservative approach with antibiotics is justified^{19,20,21}. With poor response to antibiotics after 24–48 hours, the step-up approach should be implemented as the standard of care^{22,23}.

26. Endoscopic transmural drainage is the preferred

first step where the collection is adjacent to the stomach or duodenum.

27. Percutaneous drainage is indicated as the first step in collections distant from the upper gastrointestinal tract, using multifenestrated catheters guided by ultrasound or CT, with regulated aseptic lavage. Postponed drainage is preferred over immediate drainage¹⁹.

28. Minimally invasive surgical approach: if there is no clinical improvement or the patient deteriorates after drainage, video-assisted retroperitoneal debridement (VARD) will be performed using the matured tract of the percutaneous drain, strictly avoiding open necrosectomy or routine laparotomy.

29. Controlled delay: any major intervention or pancreatic debridement should ideally be delayed until after the fourth week from onset, since debridement in the first two weeks critically increases morbidity and mortality²⁴.

30. In intestinal perforation, particularly colonic, damage control is required by resection of the affected segment and proximal stoma.

31. In massive haemorrhage, endovascular embolization is prioritized over laparotomy.

32. In abdominal compartment syndrome (sustained intra-abdominal pressure > 20 mmHg with new organ dysfunction)²⁵, if medical measures fail, decompression will be carried out by evacuative paracentesis or decompressive laparotomy, always respecting the pancreatic compartment.

Special clinical scenarios

There are specific subpopulations in which acute pancreatitis carries particular diagnostic and therapeutic considerations:

Acute post-ERCP pancreatitis is the most frequent complication after endoscopic instrumentation of the biliary tract, manifesting as new abdominal pain with elevation of pancreatic enzymes to more than three times the upper limit of normal at 24 hours after the procedure^{4,10}. It requires hospitalization and monitoring for a minimum of 48 hours with intravenous hydration and regulated analgesia.

Acute pancreatitis during pregnancy is infrequent but serious, capable of inducing preterm labor, severe pre-eclampsia, fetal loss and maternal death. It is strongly linked to pro-lithogenic metabolic changes induced by gestational hormones. Early diagnosis requires a high index of suspicion, with ultrasound or magnetic resonance imaging for structural assessment and avoidance of ionizing

radiation unless strictly necessary. Treatment is primarily conservative and supportive^{4,26}.

Acute pancreatitis in the pediatric population is uncommon, and its causes differ substantially from those in adults, with idiopathic factors, congenital anatomical abnormalities of the biliary tree or pancreatic duct (pancreas divisum), systemic disease or trauma predominating. Early diagnosis and timely admission to pediatric referral centers are essential to establish appropriate metabolic support and avoid long-term functional sequelae.

Discussion

Adopting the two-of-three diagnostic rule and prioritizing serum lipase over amylase effectively mitigates underdiagnosis in emergency care. The superior specificity of lipase prevents misinterpretation of hyperamylasemia of non-pancreatic origin²⁷.

One of the greatest challenges of the consensus lies in optimizing the use of computed tomography. The Paraguayan panel agrees with the guidelines of the International Association of Pancreatology and the American Pancreatic Association²⁸ in advising against routine use before 72 hours, since necrosis requires 4 to 7 days to be reliably assessed. Early CT increases hospital costs and radiation exposure without altering the initial therapeutic approach.

Regarding staging, systematic implementation of the determinant-based classification¹⁴ together with the revised Atlanta criteria¹⁵ provides Paraguayan surgeons with a four-category scheme that discriminates prognosis. Integrating the modified Marshall score¹⁶ to define transient or persistent organ failure (> 48 hours) unifies clinical terminology with international intensive care standards and facilitates early identification of severe and critical disease requiring referral to high-complexity centers.

Fluid resuscitation with Ringer's lactate represents a paradigm shift from traditional overhydration with normal saline. Evidence supports that Ringer's lactate reduces hyperchloremic acidosis and modulates the systemic inflammatory response, decreasing intensive care admission²⁹. A moderate regimen with reassessment every 6 hours prevents volume overload, a complication associated with respiratory distress and raised intra-abdominal pressure.

The consensus breaks with the dogma of pancreatic fasting in mild and moderate cases, promoting early oral refeeding to attenuate catabolism and shorten hospital stay. In severe cases, prioritizing enteral over parenteral feeding reduces bacterial translocation across the

intestinal barrier and mitigates the principal cause of superinfection of necrosis³⁰.

The consensus emphasizes that routine antibiotic prophylaxis should be omitted, as it does not prevent infection of necrotic tissue and promotes bacterial and fungal resistance. Restricting antibiotics to suspected or confirmed infected necrosis, typically documented after the second week, preserves the usefulness of carbapenems for true septic conditions.

Performing early cholecystectomy in mild acute pancreatitis during the same admission substantially reduces recurrence³¹.

Modern management of pancreatic fluid collections is governed by two principles endorsed in this document: asymptomatic collections do not require intervention, and early surgical debridement increases mortality. Postponing any major invasive procedure until after the fourth week allows maturation of a fibrotic wall and a safer technical approach^{32,33}.

The consolidation of the step-up approach, validated by the PANTER trial^{22,23}, is reshaping pancreatic surgical practice in the country. The algorithm replaces classic open necrosectomy with minimally invasive options. Endoscopic transmural drainage³⁴ and percutaneous drainage³⁵ are positioned as first-line therapies, limiting surgical trauma in critically ill patients³⁶. The timing of the first drainage has itself been tested: in a randomized trial, immediate catheter drainage was not superior to postponement until walled-off necrosis had developed, and the postponed group required fewer interventions, with a substantial proportion treated with antibiotics alone¹⁹. The evidence supports that patients with signs of infected necrosis should be initially treated with broad-spectrum antibiotics and maximum supportive care^{19,20,21}. VARD is reserved for failure of initial drainage, using the matured tract. Randomized evidence comparing endoscopic and minimally invasive surgical step-up strategies shows equivalent mortality with lower hospital stay and fewer pancreatic fistulae after endoscopic treatment³⁷. This distinction may have relevance where long-term external drainage is difficult to manage in decentralized settings. This sequential strategy optimizes the institutional resources available in the national healthcare system and reduces perioperative morbidity^{38,39,40}.

In Paraguay the health System Network is divided in 18 Regions. In each region the health care facilities are classified in levels of complexity according to the services they can deliver.

Table 1. Integrated and comprehensive health service networks.

Instances	Complexity	Level of Care	Operational Correspondence.
Individual, Family, and Community Care.	Low Complexity	First Level	USF* (ESF) 3 types: USF Satellite, USF Standard, USF Mobile
	Low Complexity	First level	USF Expanded
	Median Complexity	Second Level	District Hospitals
	High Complexity	Third Level	Regional Hospitals
Hospital Care	High Complexity**	Third level	National Hospitals General Hospitals Specialized Hospitals Institutes Other (IPS Central Hospital)

* Family Health Unit

**Highest complexity facilities have national coverage

Extracted from <https://www.mspbs.gov.py>

The applicability of each of the recommendations of this Consensus is different at each level of Health Care Facility. Table two summarizes the applicability of the recommendations at different health care levels.

Table 2. Applicability of the recommendations at different health care levels

Recommendation	First Level	Second level	Third level
1- Diagnosis	YES	YES	YES
2- Lipase	NO	YES	YES
3- Ultrasound	NO	YES	YES
4- CT ¹	NO	YES/NO (not always available)	YES
5- MRI ²	NO	NO	YES
6- Classification	NO	YES/NO (yes where CT is yes)	YES
7- Marshall Score	NO	YES	YES
8, 9- Hydration	YES (Ringer Lactate not available, only saline solution)	YES (Ringer Lactate not always available)	YES
10- Oral intake	YES	YES	YES
11- Enteral nutrition	NO	YES	YES
12- Parenteral nutrition	NO	NO	YES
13- No ATB prophylaxis	YES	YES	YES
14- ATB	NO	YES (usually out of the pocket)	YES
15- Pain relief	YES	YES	YES
16- Ondasentron	YES (out of the pocket)	YES (out of the pocket)	YES
17- Prokinetics	YES	YES	YES
18- Enzyme replacement	NO	NO	YES (out of the pocket)
19- Early cholecystectomy	NO	YES (without IOC ³ or preop MRCPI ⁴)	YES

20-postponed cholecystectomy	NO (Remission to third level)	NO (Remission to third level)	YES
21-Definition of Collections	NO	YES/NO (yes where CT is yes)	YES
22-No intervention in Asymptomatic Collections	YES	YES	YES
23-Dx of Infection	YES	YES	YES
24-no FNA ⁵	YES	YES	YES
25-ATB treatment	NO	YES	YES
26- Endoscopic drainage	NO	NO	YES
27- Percutaneous Drainage	NO	NO	YES
28- VARD ⁶	NO	NO	YES
29- Delay intervention	YES (referral to third level)	YES (referral to third level)	YES
30-Treatment for Surgical Complication	NO	NO	YES
31- Embolization	NO	NO	YES
32-ACS ⁷ treatment	NO	NO	YES

1- Computed Tomography, 2- Magnetic Resonance Imaging, 3- Intraoperative Cholangiography, 4- Magnetic Resonance CholangioPancreatography, 5- Fine Needle Aspiration, 6- Video Assisted Retroperitoneal Debridement, 7- Abdominal Compartmental Syndrome

In the theory of the Paraguayan health system, the categorization of an establishment as a 3rd level (or high complexity) hospital implies the capacity to offer specialized and subspecialized medical care, advanced diagnostic support and intensive care.

However, in clinical and healthcare practice, a marked geosanitary asymmetry is observed: there is a clear gap in problem-solving capacity between the 3rd level centers

located in the Metropolitan Area (Asunción and Central Department) and the so-called regional or general hospitals in the interior of the country.

This fragmentation is evident in the management of WON or infected necrotic collections:

a- In Greater Asunción (Hospital de Clínicas, IPS Hospital Central, Hospital Nacional de Itauguá): The minimally invasive strategy can be systematically applied.

Table 3. Comparison of third level hospitals in the Central Department and the interior of Paraguay

Analytical Dimension	Asunción and Central Department	Regional Hospitals in the Interior
Diagnostic Infrastructure	Contrast-Enhanced Computed Tomography (CECT) with contrast, CT angiography and MRI available 24/7	CT equipment with frequent interruptions due to maintenance or lack of injector/contrast contract.
Critical Care Support	ICU* beds with advanced monitoring, hemodynamic support and pre/continuous hemodialysis.	ICU beds are scarce, overcrowded, and have limitations for dialysis or prolonged multi-organ support.
Minimally Invasive Procedures	Interventional radiology/percutaneous surgery equipment (ultrasound/CT guided drainage).	Shortage or lack of trained specialists, or lack of percutaneous or endoscopic drainage kits 24/7
Advanced Endoscopic Support	Availability of ERCP** and emergency therapeutic endoscopy (stents, endoscopic necrosectomies).	Endoscopy is limited to diagnostic studies or management of basic upper bleeding; ERCP is almost nonexistent in the public network.
Multidisciplinary Management	Active consultation between General Surgery/ HPB, Intensive Care,	Management by isolated general surgeons or intensivists, without a subspecialized support team.

* Intensive Care unit

** Endoscopic Retrograde Colangiopancreatography

This includes serial CT scans, ultrasound- or CT-guided percutaneous drainage as a first-line treatment, the option of endoscopic bypass, and, if necessary, laparoscopic or VARD access.

b- In the interior of the country (e.g., Encarnación, Ciudad del Este, Coronel Oviedo, Concepción): Although they have the designation of high complexity, the lack of technology, equipment, supplies and specialized medical workforce forces the referral of the patient to the Central Department hospitals or to early/inappropriate open laparotomy, increasing morbidity and mortality.

A gap in resolution capacity exists: while regulations assign the role of high complexity care to the main regional centers, the effective implementation of the multidisciplinary approach, such as the step-up approach for local complications of severe acute pancreatitis, is often disrupted in the interior due to a lack of infrastructure, supplies, or specialists.

There are limitations to the application of this consensus. Some recommendations require technology or expertise that is not available in all hospitals in Paraguay, particularly in rural or under-resourced areas; the availability of specialized intensive care or percutaneous drainage may be a limiting factor. Implementation also depends on institutional and individual practice: lack of training, resistance to change, or excessive workload can hinder adoption. Cultural differences and health beliefs can influence adherence to treatment and prevention recommendations⁴¹.

Continuing medical education, support materials such as clinical practice guidelines, and public awareness campaigns are recommended to support successful implementation, together with adaptation to local realities through phased priorities and the creation of collaborative networks.

Conclusion

This consensus establishes a normative framework for standardizing the management of acute pancreatitis in Paraguay, adapted to what the national health system can deliver rather than to the resources of high-volume referral centers. Its formal, interdisciplinary adoption should reduce unwarranted variation in practice, and its principal recommendations — restricted early imaging, moderate resuscitation, early enteral feeding, antibiotics only for infection, early cholecystectomy in mild biliary disease, and deferred, staged intervention for necrosis — are

achievable in the different complexity level institutions in the country. Implementation now depends on regional capacity development, continuing education, phased local adaptation, and prospective audit of outcomes, without which the effect of the consensus on complications and mortality will remain unmeasured.

Declaration of Conflicts of Interest

The authors declare that the preparation, review, and writing of this manuscript were carried out with complete scientific and academic independence. There are no financial, commercial, personal, or institutional relationships with public or private entities that could bias or influence the recommendations or conclusions expressed in this document.

References:

1. Zhou BC, Zhang J, Li GX, Wei Y, Xu S, Xu A, et al. The global, regional, and national burden of pancreatitis from 1990 to 2021: A systematic analysis for the Global Burden of Disease Study 2021. *J Gastroenterol Hepatol*. 2025 May;40(5):1297-1306.
2. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. *Am J Gastroenterol*. 2006 Oct;101(10):2379-2400.
3. de Beaux AC, Palmer KR, Carter DC. Factors influencing morbidity and mortality acute pancreatitis; an analysis of 279 cases. *Gut*. 1995;37:121-126.
4. Suarez Anzorena F, Brahin F. Relato Oficial 91 Congreso Argentino de Cirugía “Estado Actual del Manejo de la Pancreatitis Aguda Biliar”. *Rev Arg Cir*. 2021;113(2):93-198.
5. Pérez F, Arauz Valdes E. Pancreatitis Aguda: Artículo de Revisión. *Rev Méd Cientif*. 2020;33:67-88.
6. Petrov MS, Shanbhag S, Chakraborty M, Phillips AR, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology*. 2010;139: 813-820.
7. Sánchez R, Parquet G, Sánchez ML, Andrada Álvarez J, Heiberger F, Pfingst C, et al. Consenso paraguayo sobre el diagnóstico y tratamiento de la pancreatitis aguda en adultos: Guía para cirujanos 2025. *Cir Parag*. 2025 Apr;49(1):24-38.
8. Broder MS, Gibbs S, Yermilov I. An adaptation of the RAND/UCLA modified Delphi panel method in the time of COVID-19. *J Healthc Ldshp*. 2022 May;14:143-151.
9. Gullo I, Migliori M, Olah A, et al. Acute pancreatitis in five European countries: etiology and mortality. *Pancreas*. 2002; 24: 223 – 7.
10. Wang GJ, Gao CF, Wei D, Wang C, Ding SQ. Acute pancreatitis: etiology and common pathogenesis. *World J Gastroenterol*. 2009;15(12):1427-30.

11. Samokhvalov AV, Rehm J, Roerecke M. Alcohol Consumption as a Risk Factor for Acute and Chronic Pancreatitis: A Systematic Review and a Series of Meta-analyses. *E Bio Medicine*. 2015;2:1996-2002.
12. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. *Gastroenterology*. 2013;144:1252-61.
13. Lowenfels AB, Maisonneuve P, Sullivan T. The changing character of acute pancreatitis: epidemiology, etiology, and prognosis. *Curr Gastroenterol Rep*. 2009;11:97-103.
14. Dellinger EP, Forsmark CE, Layer P, Lévy P, Maraví-Poma E, Petrov MS, et al. Determinant-based classification of acute pancreatitis severity: An international multidisciplinary consultation. *Ann Surg*. 2012;256(6):875-880.
15. Banks PA, Bollen T, Dervenis C, Gooszen H, Johnson, C et al. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;62:102-111.
16. Marshall JC, Cook DJ, Christou NV, et al. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. *Crit Care Med*. 1995;23:1638-52.
17. de-Madaria E, Buxbaum JL, Maisonneuve P, García García de Paredes A, et. al.; ERICA Consortium. Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis. *N Engl J Med*. 2022;387(11):989-1000.
18. Guilabert L, Cárdenas K, de Madaria E. Tratamiento inicial de la pancreatitis aguda. *Gastroenterol Clin North Am*. 2025;54:21-36.
19. Boxhoorn L, van Dijk SM, van Grinsven J, et al. Immediate versus postponed intervention for infected necrotizing pancreatitis. *N Engl J Med*. 2021;385:1372-81.
20. Boumitri C, Brown E, Kahaleh M. Necrotizing Pancreatitis: Current Management and Therapies. *Clin Endosc*. 2017;50:357-365.
21. Hamesch K, Hollenbach M, Guilabert, Lahmer T, Koch A. Practical Management of Sever Acute Pancreatitis. *Eur J Int Med*. 2025;133:1-13.
22. Besselink MG, van Santvoort HC, Nieuwenhuijs VB, Boermeester MA, Bollen TL, et al. Minimally invasive 'step-up approach' versus maximal necrosectomy in patients with acute necrotizing pancreatitis (PANTER trial): design and rationale of a randomised controlled multicenter trial [ISRCTN13975868]. *BMC Surg*. 2006 Apr 11;6:6.
23. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, et. al. for the Dutch Pancreatitis Study Group. A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis. *N Engl J Med*. 2010;362(16):1491-1502.
24. Beij A, Verdonk R, van Santvoort H, de Madaria E, Voermans R. Pancreatitis aguda: una actualización del tratamiento basado en evidencia y tendencias recientes en estrategias de tratamiento. *United European Gastroenterol J*. 2025;00:1-10.
25. Zarnescu NO, Dumitrascu I, Zarnescu EC, Costea R. Abdominal Compartment Syndrome in Acute Pancreatitis: A Narrative Review. *Diagnostics (Basel)*. 2022;13(1):1.
26. International Association of Pancreatology Revised Guidelines on Acute Pancreatitis 2025: Supported and Endorsed by the American Pancreatic Association, European Pancreatic Club, Indian Pancreas Club, and Japan Pancreas Society. *Pancreatology*. 2025;25(6):770-814.
27. Rompianesi G, Hann A, Komolafe O, Pereira S, Davidson B, Gurusamy K. Serum amylase and lipase and urinary trypsinogen and amylase for diagnosis of acute pancreatitis. *Cochrane Database Syst Rev*. 2017;4(4):CD012010.
28. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence based guidelines for the management of acute pancreatitis. *Pancreatology*. 2013;13(4 Suppl 2):e1-15.
29. A. Dawson, M. Karunakaran, Z.D. Sharma, S. Ullah, S.G. Barreto. Fluid resuscitation in the early management of acute pancreatitis - evidence from a systematic review and meta-analysis. *HPB*. 2023;25(12):1451-1465.
30. Bakker OJ, Brunschot S, Farre A. Timing of enteral nutrition in acute pancreatitis: meta-analysis of individuals using a single-arm of randomized trials. *Pancreatology*. 2014;14(5):340-6.
31. da Costa DW, Bouwense SA, Schepers NJ, Besselink MG, van Santvoort HC, van Bunschot S, Bakker OJ, Bollen TL, Dejong CH, van Goor H, Boermeester MA, Boerma D. Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. *The Lancet*. 2015;386: 1261-1268.
32. Purschke B, Bolm L, Meyer MN, Sato H. Interventional strategies in infected necrotizing pancreatitis: Indications, timing, and outcomes. *World J Gastroenterol*. 2022;28(27):3383-3397.
33. Mowery NT, Bruns BR, MacNew HG, Agarwal S, Enniss TM, Khan M, et al. Surgical management of pancreatic necrosis. *J Trauma Acute Care Surg*. 2017;83:316-27.
34. J.Y. Bang, J.P. Arnoletti, B.A. Holt, B. Sutton, M.K. Hasan, U. Navaneethan, et al. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. *Gastroenterology*. 2019;156(4):1027-1040.e3.
35. M.C. van Baal, H.C. van Santvoort, T.L. Bollen, O.J. Bakker, M.G. Besselink, H.G. Gooszen, et al. Systematic review of percutaneous catheter drainage as primary treatment for necrotizing pancreatitis. *Br J Surg*. 2011;98(1):18-27.
36. M.G. Keane, S.F. Sze, N. Cieplik, S. Murray, G.J. Johnson, G.J. Webster, et al. Endoscopic versus percutaneous drainage of symptomatic pancreatic fluid collections: a 14-year experience from a tertiary hepatobiliary centre. *Surg Endosc*. 2016;30(9):3730-3740.

37. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. *Lancet*. 2018;391:51–58.

38. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. *World J Emerg Surg*. 2019;14:27.

39. Párnitzky A, Mikó A, Uc A, Singh A, Elhence A, Saluja A, et

al. Revised International Association of Pancreatology guidelines on acute pancreatitis 2025. *Pancreatology*. 2025;25(5):540-555.

40. Tenner S, Vege SS, Sheth SG, Sauer BG, Yang AL, Conwell D, et al. American College of Gastroenterology guidelines: Management of acute pancreatitis. *Am J Gastroenterol*. 2024;119(3):419-437.

35. Wang Z, Norris S, Bero L. Advantages and limitations of guideline adaptation frameworks. *Implement Sci*. 2018;13(1):74.

A STATE-OF-THE-ART NARRATIVE REVIEW

Surgical and Endoscopic Management of Severe Acute Pancreatitis: The Times Have Changed

Rifat Latifi, MD, FACS, FICS, FKCS¹, Lindsay Bartholome, MD, FACS²

¹ Professor of Surgery, Department of Surgery, University of Arizona, Tucson, AZ, USA; Trauma and Acute Care Surgery Division, Arizona Advanced Surgery, Mesa, Arizona

² Trauma Medical Director, Banner Desert Medical Center, Mesa, Arizona

Corresponding Author:

RIFAT LATIFI, MD, FACS, FICS, FKCS

Professor of Surgery, University of Arizona; Arizona Advanced Surgery and Banner Desert Medical Center, Mesa, Arizona.

E-mail: rlatifi@arizona.edu

Abstract

Background. Necrosis of the pancreas or peripancreatic tissue develops in approximately 20–30% of patients with acute pancreatitis; of those with necrosis, 20–40% develop infection, and mortality among patients with infected necrosis is reported at 15–20% despite intervention. Management has moved from early open necrosectomy toward a staged, minimally invasive strategy.

Methods. Narrative, non-systematic review. PubMed/MEDLINE was searched, supplemented by the reference lists of retrieved articles and of current society guidelines. Randomized trials, meta-analyses of randomized trials, international society guidelines and large cohort studies were selected by the author for relevance rather than by predefined protocol.

Results. Randomized evidence, from trials that are individually small and were conducted in specialized

centres, supports delaying intervention until necrosis is walled off where the patient tolerates delay; drainage before necrosectomy; and a step-up approach in preference to primary open necrosectomy. Endoscopic and minimally invasive surgical step-up strategies have shown no mortality difference, with fewer fistulae and shorter stay after endoscopic treatment. For uncomplicated pseudocysts, endoscopic and surgical cystgastrostomy were equally effective in a small randomized trial.

Conclusions. Where interventional radiology and therapeutic endoscopy are available, open necrosectomy has become a rescue procedure rather than a default.

Key words: necrotizing pancreatitis; step-up approach; endoscopic necrosectomy; cystgastrostomy; cystjejunostomy; walled-off necrosis; open abdomen; video-assisted retroperitoneal debridement (VARD)

Introduction

Acute pancreatitis is among the most common gastrointestinal causes of hospital admission. Necrosis of the pancreas or peripancreatic tissue develops in approximately 20–30% of patients with acute pancreatitis; among patients with necrosis, 20–40% develop infection of the necrotic tissue, and mortality among patients with infected necrosis is reported at 15–20% despite intervention.¹ These are ranges reported across cohorts rather than fixed rates, and they vary with case mix and with the threshold for cross-sectional imaging. The history of treatment is, to an unusual degree, a history of repeated laparotomy: prolonged intensive care, multiple organ failure, the open abdomen, enteric fistula and tracheostomy, with the single definitive operation progressively abandoned.

For most of the twentieth century the surgeon had no alternative to laparotomy, and the debate concerned not whether to operate but how to enter the abdomen, and how to manage the open abdominal cavity afterwards. Three techniques emerged, and each still has descendants in current practice. Open drainage, or open packing, unroofed the superior retroperitoneum, removed necrosum by blunt sequestrectomy, packed the lesser sac with laparotomy pads and returned every two to three days for scheduled re-exploration, allowing the wound to heal by secondary intention; in the original 28-patient series mortality was 11%, but pancreatic fistula occurred in ten patients and incisional hernia in eight.² Closed continuous lavage debrided the cavity once and then irrigated the lesser sac through large-bore inflow and outflow catheters, washing out residual debris over days without further operation.³ Closed packing filled the cavity with stuffed Penrose and closed suction drains and closed the abdomen, achieving a mortality of 6.2% in 64 consecutive patients and, in a later 167-patient experience, a re-operation rate of 12.6%.^{4,5} These were not poor results. They were the best obtainable when the only instrument was a laparotomy and they were achieved in specialist units by surgeons who did little else.

That operation once had a name of its own. Altemeier and Alexander's 1963 analysis of 32 pancreatic abscesses established drainage of the septic retroperitoneal bed as the governing principle,⁶ and Davidson and Bradley named the technique in 1981, reporting no deaths among six patients treated by debridement with open packing against 55% mortality in eleven treated by debridement and sump drainage.⁷ Marsupialization describes a specific construction: the stomach is retracted and stitched

cephalad and the transverse colon displaced caudally, so that an open window into the lesser sac is created and held open. The cavity is packed through that window and re-entered on a schedule. Formalized through the 1980s as laparostomy with preplanned revisions⁸ and reproduced in smaller institutional series,⁹ the term has fallen out of use, but the window and the scheduled return remain the anatomy of every open necrosectomy performed today.

A parallel history belongs to the pseudocyst. Ombrédanne performed the first internal anastomosis — a cystoduodenostomy — in 1911; the patient died on the eleventh postoperative day, but the principle survived.¹⁰ Jedlicka reported the first cystogastrostomy in 1923, and Jurasz gave it the transgastric form still used today: an anterior gastrotomy, puncture and evacuation of the cyst through the posterior wall, and a wide anastomosis between cyst and stomach.^{10,11} Henle performed the first cystjejunostomy in 1923, and in 1946 König added the Roux-en-Y configuration that prevents reflux of intestinal content into the cavity.^{10,11} Comparative data have never been strong; the largest series found equivalent mortality, with more bleeding and more recurrence after cystgastrostomy and a preference for cystjejunostomy where the collection does not abut the stomach.¹² These operations were durable and are still performed; what changed was not their efficacy but the arrival of an endoscopic route that achieves the same internal fistula without a laparotomy.

The cost of the open era was not confined to the admission, and much of it fell on the abdominal wall and the intestine. Repeated re-entry, planned relaparotomy and the physiological need to leave the abdomen open produced a population of survivors with giant incisional hernias, enteroatmospheric fistulae and prolonged reconstruction.¹³ Recognition of intra-abdominal hypertension and abdominal compartment syndrome as distinct, measurable and lethal entities gave the open abdomen a rational indication rather than a reflexive one,¹⁴ while the development of component separation and, later, posterior component release with transversus abdominis release made delayed definitive closure of the resulting defect achievable rather than aspirational.^{15,16}

The step-up approach displaced all of this within a decade. Its central finding — that the first intervention should be a drain, that a third to a half of patients need nothing more, and that the harm of primary open necrosectomy persists for years — has been confirmed in randomized and long-term data.¹⁷ This review summarizes the current

evidence for the surgical and endoscopic management of severe acute pancreatitis and describes how each of the relevant procedures is performed, with attention to the questions a general or acute care surgeon must answer at the bedside: when to intervene, by what route, with what device, through which incision, and when to abandon a minimally invasive strategy for an operation.

Methods

This is a narrative, non-systematic review. The literature was identified by searching PubMed/MEDLINE, supplemented by hand-searching the reference lists of retrieved articles and of current society guidelines. No date limit was applied; the earliest source cited was published in 1963 and the most recent in 2025. Search terms combined the concepts of necrotizing or severe acute pancreatitis, infected pancreatic necrosis, walled-off necrosis and pancreatic pseudocyst with terms for intervention: necrosectomy, step-up approach, percutaneous catheter drainage, endoscopic transmural drainage, direct endoscopic necrosectomy, video-assisted retroperitoneal debridement, transgastric necrosectomy, cystgastrostomy, cystjejunostomy, open abdomen and abdominal compartment syndrome. Eligible sources were English-language randomized controlled trials, meta-analyses of randomized trials, international society guidelines^{1,18–21} and multicentre or large single-centre cohort studies. Case reports, editorials and series of fewer than 20 patients were not cited unless they described a technique of historical importance or supplied the only available data on a question. Where several reports addressed the same question, priority was given to randomized evidence, to multicentre data and to the most recent publication. Studies were selected by the author for relevance to the clinical questions above rather than by predefined protocol; no formal risk-of-bias assessment was undertaken and no PRISMA flow diagram is presented, neither being required of a narrative review. Terminology follows the 2012 revision of the Atlanta classification.²²

Results

Terminology and classification

The revised Atlanta classification distinguishes interstitial oedematous from necrotizing pancreatitis and defines four collection types: acute peripancreatic fluid collection and pseudocyst (no necrosis, before and after four weeks), and acute necrotic collection and walled-off necrosis (containing necrosis, before and after four

weeks).²² The distinction is not academic. A pseudocyst is a fluid-filled cavity that can be drained through a small conduit; walled-off necrosis contains solid debris that will obstruct any small drain and frequently requires necrosectomy. Any surgeon who has evacuated a handful of necrotic debris will recognize the question of whether such a cavity can be drained at all through a catheter or an endoscope; much of the answer lies in timing. Treating the second as though it were the first is one of the commonest errors in this disease, and much of the older literature reporting poor results of “pseudocyst drainage” describes exactly that mistake. Contrast-enhanced computed tomography is the reference investigation; magnetic resonance imaging or endoscopic ultrasound better characterize solid content when the decision between a drain and a necrosectomy depends on it.²⁰

Indications and timing of intervention

For many decades, multiple organ system failure (MOSF) development, and particularly persistent MOSF, was in itself an indication for operation and source control. That principle has not been abandoned: the deteriorating patient with an undrained infected collection needs it decompressed emergently, and the modern dispute is only whether the first move is a catheter or a wide laparotomy. Operation therefore remains indicated for the patient who continues to manifest MOSF despite adequate resuscitation and maximal critical care, even where infected necrosis has not been documented — undrained necrosis is the commonest occult source in these patients, and both culture and early imaging lack the sensitivity to exclude it. It is indicated for infected necrosis that has failed a properly executed step-up strategy — adequate drainage, upsized and irrigated, with no improvement or continuing deterioration — and for the surgical emergencies arising within the disease, where the indication is the complication rather than the pancreatitis: abdominal compartment syndrome failing medical management, bowel ischaemia or perforation, and uncontrolled haemorrhage. Less common indications are persistent gastric or biliary obstruction and disconnected duct syndrome.^{1,19} Sterile necrosis, however extensive, is managed nonoperatively in most patients, and even infection is not automatically an indication: meta-analysis of conservative treatment shows that a substantial proportion of patients with infected necrosis can be treated with antibiotics alone.²³ Persistent organ failure is thus a marker of severity and a trigger to search for a controllable source; it is

not itself anatomical evidence of one, and the decision to operate rests on imaging, the response to drainage, and serial clinical assessment.

Delaying operation is the most consistent finding in this literature to be associated with improved outcome. In a single-centre randomized comparison of necrosectomy within 48–72 hours with necrosectomy after at least 12 days, 41 patients entered the study and 36 were analysed (25 early, 11 late); mortality was 58% against 27%, a difference that did not reach statistical significance but corresponded to an odds ratio for death 3.4 times higher after early operation and led the investigators to terminate the trial,²⁴ and cohort series have repeatedly confirmed that mortality falls as the interval from onset to operation lengthens.^{25,26} European Society of Gastrointestinal Endoscopy (ESGE) therefore suggests that the first intervention be delayed for four weeks where the patient tolerates it, allowing demarcation and encapsulation.¹⁹ The POINTER trial tested whether modern catheter drainage had abolished this requirement: 104 patients with infected necrosis were randomized to drainage within 24 hours or to postponement until walled-off necrosis developed. Immediate drainage conferred no advantage on the Comprehensive Complication Index (CCI), and the postponed group required fewer interventions (mean 2.6 vs 4.4; mean difference 1.8, 95% CI 0.6–3.0), with 39% treated with antibiotics alone and no drainage at all; mortality was 13% and 10% respectively (relative risk 1.25, 95% CI 0.42–3.68).²⁷ Long-term follow-up confirmed no difference in mortality or major morbidity.²⁸ Cohort data suggest that earlier endoscopically centred intervention may be feasible in selected patients, but this remains a deviation from the standard rather than a replacement for it.²⁹ The practical conclusion is that antibiotics and physiological support, not an early drain, are the initial treatment of infected necrosis in the stable patient.

The step-up approach

The PANTER trial randomized 88 patients with infected necrosis to primary open necrosectomy or to a step-up approach of percutaneous drainage followed, if necessary, by video-assisted retroperitoneal debridement. The composite endpoint of major complications or death occurred in 69% after open necrosectomy and 40% after step-up (risk ratio 0.57, 95% CI 0.38–0.87), driven by a reduction in new-onset multiple-organ failure (12% vs 40%). Mortality did not differ, but 35% of step-up patients were cured by drainage alone and never underwent

necrosectomy.¹⁷ Long-term follow-up at a mean of 86 months confirmed the superiority of step-up without an excess of reinterventions, and showed lower rates of incisional hernia, new-onset diabetes and pancreatic enzyme use.³⁰ This is the finding that changed practice: the harm of open necrosectomy is not confined to the admission.

Percutaneous catheter drainage

Percutaneous drainage is the first step in the surgical arm of the step-up approach and the most widely available intervention in this disease. The catheter is placed under computed tomographic or ultrasound guidance, and the route matters as much as the puncture: wherever the anatomy allows, a left retroperitoneal approach is chosen, passing between the descending colon and the lower pole of the left kidney into the collection, because that tract can later be dilated and used for video-assisted debridement. A guidewire is coiled within the cavity, the tract dilated, and a large-bore multi-fenestrated catheter of at least 12 to 14 French positioned with its side-holes in the dependent part of the collection. Fluid is sent for Gram stain and culture. The catheter is flushed with saline several times daily to prevent obstruction by debris, and upsized progressively over a guidewire — commonly to 20 French or beyond — at intervals of a few days, with repeat imaging to confirm that the cavity is collapsing rather than merely being decompressed at one point.³¹

Failure to improve within 72 hours of an adequately positioned and adequately sized drain should prompt escalation, not repeated repositioning. Systematic review of percutaneous drainage as primary treatment found that more than half of patients required no subsequent necrosectomy,³² a proportion consistent with the PANTER experience and with the observation that a conservative, drainage-first strategy improves outcome at institutional level.^{17,33} Where a collection is both retrogastric and extends laterally into the paracolic gutter, percutaneous and endoscopic routes may be combined: a transmural stent decompresses the collection internally while the percutaneous catheter irrigates it, and the external drain is removed once the internal route is patent. This dual-modality technique was designed specifically to avoid the pancreaticocutaneous fistula that follows prolonged external drainage, and in a long-term series it did so.³⁴

Endoscopic transmural drainage and necrosectomy

Endoscopic drainage creates an internal fistula between the collection and the stomach or duodenum. Under

endoscopic ultrasound the collection is identified where it abuts the gastric or duodenal wall, interposed vessels are excluded with Doppler, and the wall is punctured with a 19-gauge needle. A guidewire is coiled within the cavity, the tract is dilated with a balloon or cystotome, and one or more stents are deployed. With double-pigtail plastic stents, two or three 7 to 10 French stents are placed side by side to keep the fistula open; with a lumen-apposing metal stent, a single cautery-tipped device creates and stents the tract in one step, producing an immediate 15 to 20 mm channel through which an endoscope can pass.¹⁹ Outcomes differ sharply between fluid and necrosis: in an early comparative series, endoscopic drainage succeeded in the great majority of pseudocysts but in far fewer patients with necrosis, precisely because solid debris does not pass through a stent.³⁵

Where the collection contains solid necrosis, drainage is followed by direct endoscopic necrosectomy. The endoscope is advanced through the matured tract into the cavity, which is irrigated and inspected, and devitalized tissue is removed piecemeal with a retrieval net, snare, basket or forceps. Only loose, demarcated necrosus is taken; adherent tissue is left, since it is the plane of adherence that bleeds. Sessions are repeated every few days until the cavity is clean, and a series of three to five procedures is typical.³⁶ Direct necrosectomy achieves resolution in a higher proportion of patients than transmural drainage alone, at the cost of more procedures.³⁷ For extensive collections that cannot be cleared through a single window, additional transmural gateways can be created and linked with nasocystic irrigation, an approach that improves resolution in large multiloculated necrosis.³⁸

The randomized comparisons are consistent in direction. The PENGUIN trial randomized 22 patients and showed that endoscopic transgastric necrosectomy reduced the pro-inflammatory response and the composite endpoint of major complications or death compared with surgical necrosectomy.³⁹ The TENSION trial randomized 98 patients to endoscopic or surgical step-up and found no difference in mortality or major complications, but significantly fewer pancreatic fistulae and shorter hospital stay in the endoscopic arm.⁴⁰ The single-centre MISER trial randomized 66 patients and reported a larger advantage for endoscopy — the composite endpoint occurred in 11.8% versus 40.6% (risk ratio 0.29, 95% CI 0.11–0.80) — a difference attributable in part to the inclusion of fistula in the composite endpoint, which the Dutch trial did not count.⁴¹ Meta-analysis of the randomized trials

favours endoscopic intervention for major complications and fistula, without a mortality difference,⁴² and long-term follow-up of the TENSION cohort (ExTENSION) found no divergence between the strategies.⁴³

On stent choice, enthusiasm has outrun evidence. A randomized trial in 60 patients (31 metal, 29 plastic) comparing lumen-apposing metal stents with double-pigtail plastic stents for walled-off necrosis found no superiority for the metal stent in the total number of procedures required to achieve treatment success, nor in treatment success, adverse events, length of stay or cost, and identified delayed adverse events — bleeding, buried stent, biliary obstruction — that led the investigators to recommend imaging and stent removal at three weeks once the collection has resolved.⁴⁴ The metal stent is easier to place and permits necrosectomy through a wide tract; it is not a better outcome.

Minimally invasive surgical necrosectomy

Video-assisted retroperitoneal debridement is performed through a 5 cm incision in the left flank, placed along the track of the percutaneous drain that was sited for this purpose. The drain is followed as a guide into the retroperitoneum, the cavity entered without opening the peritoneum, and the first debridement performed under direct vision with long grasping forceps. A laparoscope is then introduced through the same incision to illuminate and inspect the cavity, without insufflation, and further loose necrosus is removed. Only tissue that separates without traction is taken; adherent necrosus is left for a subsequent session, because it is precisely that plane which lies against the splenic and portal vessels. Two large drains are placed for postoperative continuous lavage, and the wound is closed around them. In a multicentre prospective phase 2 study, this technique was feasible in the majority of patients requiring surgery and produced low mortality and complication rates by comparison with historical open series,⁴⁵ and case-matched comparison of the retroperitoneal approach with laparotomy showed fewer complications for the minimal-access route.⁴⁶ Both the WSES and EAST guidelines endorse minimally invasive necrosectomy in preference to laparotomy where expertise exists.^{1,21}

Where the collection is central and adherent to the posterior gastric wall, a transgastric approach may be preferable. Through a laparotomy or laparoscopically, an anterior gastrotomy is made, the posterior gastric wall is opened into the underlying cavity after needle

localization, and the necrosum is evacuated under direct vision; the posterior opening is then matured as a wide cystgastrostomy so that any residual debris drains internally, and the anterior gastrotomy is closed. In a three-centre series of selected patients this single-stage operation avoided the repeated procedures characteristic of endoscopic and percutaneous routes.⁴⁷ Blunt debridement of adherent necrosum is the mechanism by which necrosectomy causes catastrophic haemorrhage.

Open necrosectomy: incision, cavity and the remaining indications

When laparotomy is unavoidable, the first decision is the incision, and it is a genuine dilemma rather than a matter of preference. A vertical midline incision is fast, gives access to both paracolic gutters and to the pelvis, permits full exploration when bowel ischaemia or perforation is suspected, and can be reopened repeatedly — which is precisely its disadvantage, since repeated re-entry and prolonged retraction produce fascial loss, dehiscence and giant incisional hernia. A transverse or modified Chevron incision, a bilateral subcostal with or without a short upper midline extension, gives markedly better exposure of the lesser sac, the head and body of the gland and both retroperitoneal gutters, tolerates repeated re-entry better mechanically, and is less prone to dehiscence; it takes longer to make and to close, divides more muscle, and forfeits access to the pelvis. In a patient in extremis the midline is the correct answer; in a stable patient in whom several planned debridements are anticipated, the transverse or Chevron approach is usually the better one. No comparative study has addressed the choice of incision in this setting; this paragraph reflects operative principle and expert practice rather than trial evidence.

Access to the cavity is then created deliberately and maintained. The lesser sac is entered through the gastrocolic ligament, the necrotic cavity opened, and devitalized tissue removed by blunt digital and forceps debridement, sharp dissection being avoided. Where repeated necrosectomy is required, the transverse colon is packed inferiorly and the stomach superiorly, as described above, so that the lesser sac remains a walled corridor that can be re-entered at each return without disturbing or adhering to viscera; omentum or a non-adherent layer is interposed to protect the colon and the duodenum, and drains are positioned to define the route. This is what converts a series of relaparotomies into a series of visits to the same cavity, and it is the maneuver that determines whether

the next several operations are straightforward or dangerous. The abdomen is then either closed loosely over packs or left open, according to the physiology, and the packs removed progressively as the cavity granulates.² The construction described here derives from the historical open-packing literature and from operative experience; it has not been compared prospectively with any alternative.

The historical results set out above show that open necrosectomy performed late and by experienced surgeons is not the catastrophe that the step-up literature can imply.^{2,4,5} Its indications are nonetheless now narrow. It remains the operation of necessity in hospitals without interventional radiology or advanced endoscopy.¹ The surgeon who has never performed a necrosectomy may nonetheless one day need to.

The open abdomen and delayed closure

The open abdomen has two legitimate indications in this disease: abdominal compartment syndrome that has failed medical management, and a planned programme of repeated necrosectomy in which closure between operations would be futile or harmful. It should not be a default. Intra-abdominal pressure is measured rather than estimated, and sustained pressure above 20 mmHg with new organ dysfunction defines the syndrome and the indication for decompression.¹⁴ Temporary abdominal closure is achieved with a negative-pressure dressing incorporating a visceral protective layer that separates bowel from the abdominal wall and from the necrotic cavity; the fascial edges are protected and, where possible, held under gentle continuous traction so that they do not retract laterally. Enteral feeding is maintained wherever the bowel allows, since it protects the mucosa and reduces the risk of fistula.¹³

Delayed primary fascial closure is the objective, and the probability of achieving it falls with every day the abdomen remains open. Closure is attempted as soon as resuscitation is complete, edema has resolved and source control is achieved, in practice usually within seven to ten days; beyond that the fascia will not come together and the choice becomes a planned ventral hernia, managed with skin grafting over granulating bowel and definitive reconstruction six to twelve months later.¹³ That reconstruction rests on techniques developed for exactly this population: anterior component separation, which advances the rectus complex some 10 cm at the waistline by dividing the external oblique aponeurosis in a relatively avascular plane,¹⁵

and posterior component separation with transversus abdominis release, which allows large midline defects to be closed with retromuscular mesh in a plane away from the viscera.¹⁶ The enteroatmospheric fistula remains the worst outcome of this pathway and the principal argument for closing early, for interposing a protective layer at every dressing change, and — most of all — for not opening the abdomen unless it is genuinely required.¹³

Pseudocyst: cystgastrostomy and cystjejunostomy

A pseudocyst requires drainage when it is symptomatic, infected, enlarging, or causing gastric or biliary obstruction; size alone is not an indication. Internal drainage — into the stomach or into a Roux limb of jejunum — is preferred to external drainage, which risks a persistent pancreaticocutaneous fistula.

Surgical cystgastrostomy is performed through an anterior gastrotomy. The posterior gastric wall is palpated where the cyst is adherent, aspirated with a needle to confirm position, and opened for 4 to 5 cm — a stoma smaller than this closes prematurely and the collection recurs. A full-thickness ellipse of the cyst wall is excised and sent for histology, which is the step that identifies a mucinous neoplasm masquerading as a pseudocyst. The cavity is evacuated and inspected, the cut edge of the cystgastrostomy is oversewn with a running absorbable suture for haemostasis, and the anterior gastrotomy is closed. Where the cyst does not abut the stomach, a Roux-en-Y cystjejunostomy is constructed: a jejunal limb is divided some 20 cm beyond the ligament of Treitz, brought retrocolically to the most dependent part of the cyst, and anastomosed side-to-side to the cyst wall over 4 to 5 cm in a single or double layer, with jejunojejunostomy restored 50 to 60 cm distally to prevent reflux of enteric content into the cavity. Dependency of the anastomosis, not its size alone, determines whether the cavity stays empty. These technical descriptions reflect established practice rather than comparative data.

A randomized trial of endoscopic against surgical cystgastrostomy in 40 patients found equal efficacy, with no recurrence in the endoscopic arm at 24 months, shorter post-procedure stay, better physical and mental health scores, and lower cost after endoscopy.⁴⁸ An earlier case-controlled comparison reported similar treatment success with shorter stay and lower cost for the EUS-guided approach.⁴⁹ Endoscopic cystgastrostomy is therefore the first-line treatment for an accessible pseudocyst adjacent to the stomach or duodenum where the necessary expertise exists.

Surgical drainage retains defined indications: a collection remote from the stomach or duodenum, giant or multiloculated pseudocysts, pseudocysts in the pancreatic tail better served by distal pancreatectomy, associated gastric outlet or biliary obstruction requiring simultaneous bypass, suspicion of cystic neoplasm requiring tissue, failed endoscopic therapy, and the disconnected pancreatic duct with a viable distal remnant. Disconnected duct syndrome deserves specific mention: where the duct is transected and a viable tail continues to secrete, removing a transmural stent reliably reproduces the collection, and the alternatives are long-term indwelling transgastric stents or definitive surgical internal drainage.²⁰

IAP, intra-abdominal pressure; LAMS, lumen-apposing metal stent; MIS, minimally invasive surgery; RCT, randomized controlled trial; VARD, video-assisted retroperitoneal debridement; WON, walled-off necrosis. Numbers in the final column are reference numbers. Effect estimates and confidence intervals are reported as published in the source; where none is shown, none was reported. The table summarizes the studies selected for this narrative review and is not a systematic synthesis of the literature.

Discussion

Four propositions now rest on randomized evidence and can be stated with reasonable confidence, with the caveat that the supporting trials are individually small and were conducted in specialist centres. Intervention should be postponed until necrosis is encapsulated wherever the patient tolerates the delay. Drainage should precede necrosectomy, and in a third to a half of patients will replace it. The step-up approach reduces major complications compared with primary open necrosectomy. And the route of that drainage — percutaneous with subsequent retroperitoneal debridement, or transmural endoscopic with subsequent direct necrosectomy — matters less for survival than the decision to step up rather than to operate primarily.^{17,27,40}

The divergence between TENSION and MISER is instructive rather than contradictory, and what separates them is fistula.^{40,41} Fistula is precisely the complication that external drainage produces and internal drainage avoids, so the disagreement is really about how much weight to give a morbidity that is real, prolonged and rarely fatal. Surgeons and endoscopists may reasonably weigh it differently; patients, who live with the drain, tend not to.

Table 1. Principal studies cited in this review on the surgical and endoscopic management of severe acute pancreatitis.

Question	Best available evidence	Design	Study (reference)
Timing of first intervention	Immediate drainage not superior to postponement until walled-off necrosis; postponed group needed fewer interventions and 39% required no drainage; mortality 13% vs 10% (RR 1.25, 95% CI 0.42–3.68)	RCT (n=104)	Boxhoorn 2021; van Veldhuisen 2024 (27, 28)
Early vs late necrosectomy	Mortality 58% (<72 h) vs 27% (>12 days), not statistically significant; odds ratio for death 3.4 after early operation; trial terminated early	RCT (n=36 analysed of 41 entered); supporting cohorts	Mier 1997; Besselink 2007; Hartwig 2002 (24–26)
Infection without drainage	A substantial proportion of infected necrosis resolves with antibiotics alone	Systematic review and meta-analysis	Mouli 2013 (23)
Step-up vs open necrosectomy	Major complications or death 40% vs 69% (RR 0.57, 95% CI 0.38–0.87); new-onset multiple-organ failure 12% vs 40%; 35% cured by drainage alone	RCT (n=88)	van Santvoort 2010 (17)
Step-up, long term	Superiority maintained at mean 86 months; fewer incisional hernias, less new-onset diabetes and enzyme use	Long-term follow-up of RCT	Hollemans 2019 (30)
Percutaneous drainage alone	More than half of patients (55.7%) require no subsequent necrosectomy	Systematic review	van Baal 2011 (32)
Dual-modality drainage	Combined percutaneous and transmural drainage avoids pancreaticocutaneous fistula	Long-term cohort	Gluck 2014 (34)
Direct endoscopic necrosectomy	Higher resolution than transmural drainage alone; multiple sessions required	Comparative cohorts	Papachristou 2007; Gardner 2009 (36, 37)
Endoscopic vs surgical necrosectomy	Reduced pro-inflammatory response and composite endpoint with endoscopic transgastric necrosectomy	RCT (n=22)	Bakker 2012 (39)
Endoscopic vs surgical step-up	No difference in mortality or major complications; fewer pancreatic fistulae and shorter stay with endoscopy	RCT (n=98)	van Brunschot 2018; Onnekink 2022 (40, 43)
Endoscopic vs MIS (single centre)	Composite endpoint 11.8% vs 40.6% (RR 0.29, 95% CI 0.11–0.80); fistulae only in surgical arm; lower cost	RCT (n=66)	Bang 2019 (41)
Pooled randomized evidence	Endoscopy superior for major complications and fistula; no mortality difference	Meta-analysis of RCTs	Bang 2020 (42)
LAMS vs plastic stents for WON	No superiority of lumen-apposing metal stents; delayed adverse events prompt removal at 3 weeks	RCT (n=60; 31 LAMS, 29 plastic)	Bang 2019 (44)
VARD	Feasible in the majority of surgical candidates; low mortality vs historical open series	Prospective multicentre phase 2	Horvath 2010; van Santvoort 2007 (45, 46)
Surgical transgastric necrosectomy	Single-stage clearance in selected patients with retrogastric walled-off necrosis	Multicentre cohort	Driedger 2020 (47)
Open necrosectomy technique	Open packing 11% mortality (n=28); closed packing 6.2% (n=64), reoperation 12.6% (n=167); closed lavage the alternative	Cohort series	Bradley 1987; Beger 1988; Fernández-del Castillo 1998; Rodríguez 2008 (2–5)
Abdominal compartment syndrome	Sustained IAP >20 mmHg with new organ dysfunction defines the syndrome and the indication to decompress	Consensus guideline	Kirkpatrick 2013 (14)
Open abdomen and closure	Early fascial closure once resuscitation and source control complete; fistula and hernia the principal late burdens	Guideline	Coccolini 2018 (13)
Delayed abdominal wall reconstruction	Anterior component separation advances the rectus complex ~10 cm; transversus abdominis release enables retromuscular mesh repair of large defects	Anatomic and clinical studies	Ramirez 1990; Novitsky 2012 (15, 16)
Endoscopic vs surgical cystgastrostomy	Equal efficacy; no recurrence at 24 months after endoscopy; shorter stay, lower cost	RCT (n=40)	Varadarajulu 2013; Varadarajulu 2008 (48, 49)
Antibiotic prophylaxis	Recommended against in acute necrotizing pancreatitis	Guideline (strong, high quality)	Arvanitakis 2018 (19)

A second observation follows from the technical descriptions above. Every one of these procedures is defined less by what it removes than by what it leaves. The retroperitoneal, transgastric and endoscopic routes all instruct the operator to take only loose necrosum and to return another day, because the adherent plane contains the splenic and portal vessels. The same logic governs the open operation, where the value of packing the colon inferiorly and the stomach superiorly is that it preserves a corridor for the next visit. The step-up approach is therefore not merely a sequence of escalating interventions; it is an expression of a single surgical principle applied repeatedly, and a surgeon who understands that principle can apply it with whatever instrument the institution possesses. This is an argument from operative principle and from the technical descriptions above; it has not been tested comparatively and should be read as such.

It is also worth recording what the abandonment of open necrosectomy has cost. The long-term benefit of step-up is measured largely in incisional hernia, diabetes and enzyme replacement,³⁰ which is to say in abdominal wall and endocrine morbidity created by the operation rather than by the disease. Where laparotomy and the open abdomen remain unavoidable, that morbidity has not disappeared and must be planned for from the first operation: the choice of incision, the protection of the fascial edges, the interposition of a visceral layer, and a definite intention to close early or to reconstruct later.¹³

Several questions remain open. The optimal management of the disconnected pancreatic duct is unresolved, and the choice between permanent transmural stents and surgical internal drainage rests on cohort data. Whether selected patients benefit from intervention earlier than four weeks is being actively tested and currently rests on observational data.²⁹ The place of open necrosectomy in hospitals without interventional radiology or advanced endoscopy has been almost entirely neglected by a literature generated in high-resource, high-volume centres — a gap of real consequence, since the majority of the world's patients with infected necrosis are treated in such hospitals.¹

Two implications follow for surgical training. First, the surgeon's principal contribution to this disease is now judgement rather than technique: selecting the moment, the route and the least destructive intervention, and recognising the point at which a minimally invasive strategy has failed. Second, the technical skill required for open necrosectomy is being lost precisely as its indica-

tions narrow to the most difficult patients. A trainee who has performed no open necrosectomy will one day face abdominal compartment syndrome, bowel infarction or uncontrolled haemorrhage in a patient with necrotizing pancreatitis, and neither a drain nor an endoscope will answer.

One technical point deserves emphasis, because it is so often left until the patient is already back in the intensive care unit. Whenever the abdomen is opened in severe acute pancreatitis — for necrosectomy, for decompression of the abdominal compartment, for internal drainage, or for an exploration that proves nontherapeutic — the operation should not be concluded without securing enteral access distal to the ligament of Treitz. This is part of the operation, not an afterthought. These patients are profoundly catabolic, they will not eat for weeks, and many of them will return to the operating room more than once; gastric feeding is frequently defeated by ileus, gastroparesis, and extrinsic compression of the stomach and duodenum by the inflammatory phlegmon, which is precisely the circumstance in which the guidelines direct feeding beyond the pylorus.^{18,50} A needle-catheter or Witzel jejunostomy placed some 20 to 30 cm beyond the ligament of Treitz adds only a few minutes to the procedure and, in the surgical series in which it has been examined, was accomplished without major tube- or feeding-related complications.⁵¹ This recommendation rests on guideline direction regarding the route of feeding, on a single small surgical series and on operative experience rather than on comparative trial data. Where the abdomen is to be left open, a nasojejun tube can be advanced manually past the ligament under direct palpation before the temporary closure is applied. Either way, the surgeon leaves the operating room with a feeding route that survives reoperation, gastroparesis, and the loss of the endoscopic option — the practical expression of the principle that the gut, and not merely the patient, is what is being fed.¹ The same practice should apply to reoperative surgery after damage control: an ability to feed the gut distal to the ligament of Treitz should be established whenever the abdomen is open. The metabolic content of that support — timing, formula, caloric and protein targets, and the place of supplemental parenteral nutrition — is addressed in a companion review appearing in this issue.⁵²

Limitations

This is a narrative and not a systematic review; studies were selected for relevance rather than by predefined

protocol, and no formal risk-of-bias assessment was performed. The randomized trials underpinning current practice are individually small, several are single-centre, and their composite endpoints are not identical. The technical descriptions given here represent commonly described practice rather than validated protocols, and details vary legitimately between units; the discussion of incision choice and of cavity packing in particular reflects operative principle and historical description rather than comparative data. Evidence relating to pseudocyst management is older and less robust than that for necrosis. Finally, all of the pivotal trials were conducted in centres with immediate access to interventional radiology, therapeutic endoscopy and specialist surgical expertise. The review was undertaken by a single author, without a registered protocol or duplicate study selection. Recommendations concerning operative technique, incision choice, cavity packing and enteral access reflect operative principle and expert practice, and are distinguished in the text from the propositions that rest on randomized evidence.

Conclusions

The management of severe acute pancreatitis has shifted from a primarily operative discipline toward a staged, multidisciplinary one. Delay, drain, and escalate only if necessary is now the standard sequence in centres so equipped, supported by randomized evidence and by long-term follow-up showing that the benefit of avoiding open necrosectomy extends for years beyond the admission. Endoscopic and minimally invasive surgical routes appear broadly equivalent in survival in the trials reported to date, with less fistula and shorter stay after endoscopic treatment. For the uncomplicated pseudocyst, endoscopic cystgastrostomy has become the first-line approach where the necessary expertise exists, while surgical internal drainage retains clear indications in disconnected ducts, inaccessible collections and diagnostic uncertainty. Open necrosectomy has become a rescue operation — rarer, later, more difficult, and still indispensable — and when it is performed, the incision, the maintained corridor to the lesser sac and the plan for the abdominal wall matter as much as the debridement itself.

Declarations

Funding. None.

Conflicts of interest. None declared.

References:

1. Leppäniemi A, Tolonen M, Tarasconi A, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. *World J Emerg Surg.* 2019;14:27. <https://doi.org/10.1186/s13017-019-0247-0>
2. Bradley EL 3rd. Management of infected pancreatic necrosis by open drainage. *Ann Surg.* 1987;206(4):542–550. <https://doi.org/10.1097/00000658-198710000-00015>
3. Beger HG, Büchler M, Bittner R, Block S, Nevalainen T, Roscher R. Necrosectomy and postoperative local lavage in necrotizing pancreatitis. *Br J Surg.* 1988;75(3):207–212. <https://doi.org/10.1002/bjs.1800750306>
4. Fernández-del Castillo C, Rattner DW, Makary MA, Mostafavi A, McGrath D, Warshaw AL. Débridement and closed packing for the treatment of necrotizing pancreatitis. *Ann Surg.* 1998;228(5):676–684. <https://doi.org/10.1097/00000658-199811000-00007>
5. Rodriguez JR, Razo AO, Targarona J, et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. *Ann Surg.* 2008;247(2):294–299. <https://doi.org/10.1097/SLA.0b013e31815b6976>
6. Altemeier WA, Alexander JW. Pancreatic abscess: a study of 32 cases. *Arch Surg.* 1963;87:80–89. <https://doi.org/10.1001/archsurg.1963.01310130082011>
7. Davidson ED, Bradley EL 3rd. “Marsupialization” in the treatment of pancreatic abscess. *Surgery.* 1981;89(2):252–256. <https://pubmed.ncbi.nlm.nih.gov/7455911/>
8. Függer R, Schulz F, Rogy M, Herbst F, Mirza D, Fritsch A. Open approach in pancreatic and infected pancreatic necrosis: laparostomies and preplanned revisions. *World J Surg.* 1991;15(4):516–521. <https://doi.org/10.1007/BF01675650>
9. Margulies AG, Akin HE. Marsupialization of the pancreas for infected pancreatic necrosis. *Am Surg.* 1997;63(3):261–265. <https://pubmed.ncbi.nlm.nih.gov/9036896/>
10. Navarro S. The art of pancreatic surgery. Past, present and future. The history of pancreatic surgery. *Gastroenterol Hepatol.* 2017;40(9):648.e1–648.e11. <https://doi.org/10.1016/j.gastrohep.2017.03.010>
11. Kluszczyk P, Tobiasz A, Madej A, Wosiewicz P, Mrowiec S, Jabłońska B. Pancreatic pseudocysts: evolution of treatment approaches. *J Clin Med.* 2025;14(17):6152. <https://doi.org/10.3390/jcm14176152>
12. Newell KA, Liu T, Aranha GV, Prinz RA. Are cystgastrostomy and cystjejunostomy equivalent operations for pancreatic pseudocysts? *Surgery.* 1990;108(4):635–640. <https://pubmed.ncbi.nlm.nih.gov/2218873/>
13. Coccolini F, Roberts D, Ansaloni L, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* 2018;13:7. <https://doi.org/10.1186/s13017-018-0167-4>

14. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med.* 2013;39(7):1190–1206. <https://doi.org/10.1007/s00134-013-2906-z>
15. Ramirez OM, Ruas E, Dellon AL. “Components separation” method for closure of abdominal-wall defects: an anatomic and clinical study. *Plast Reconstr Surg.* 1990;86(3):519–526. <https://doi.org/10.1097/00006534-199009000-00023>
16. Novitsky YW, Elliott HL, Orenstein SB, Rosen MJ. Transversus abdominis muscle release: a novel approach to posterior component separation during complex abdominal wall reconstruction. *Am J Surg.* 2012;204(5):709–716. <https://doi.org/10.1016/j.amjsurg.2012.02.008>
17. van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med.* 2010;362(16):1491–1502. <https://doi.org/10.1056/NEJMoa0908821>
18. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatol.* 2013;13(4 Suppl 2):e1–e15. <https://doi.org/10.1016/j.pan.2013.07.063>
19. Arvanitakis M, Dumonceau JM, Albert J, et al. Endoscopic management of acute necrotizing pancreatitis: ESGE evidence-based multidisciplinary guidelines. *Endoscopy.* 2018;50(5):524–546. <https://doi.org/10.1055/a-0588-5365>
20. Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association clinical practice update: management of pancreatic necrosis. *Gastroenterology.* 2020;158(1):67–75. <https://doi.org/10.1053/j.gastro.2019.07.064>
21. Mowery NT, Bruns BR, MacNew HG, et al. Surgical management of pancreatic necrosis: a practice management guideline from the Eastern Association for the Surgery of Trauma. *J Trauma Acute Care Surg.* 2017;83(2):316–327. <https://doi.org/10.1097/TA.0000000000001510>
22. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut.* 2013;62(1):102–111. <https://doi.org/10.1136/gutjnl-2012-302779>
23. Mouli VP, Sreenivas V, Garg PK. Efficacy of conservative treatment, without necrosectomy, for infected pancreatic necrosis: a systematic review and meta-analysis. *Gastroenterology.* 2013;144(2):333–340.e2. <https://doi.org/10.1053/j.gastro.2012.10.004>
24. Mier J, León EL, Castillo A, Robledo F, Blanco R. Early versus late necrosectomy in severe necrotizing pancreatitis. *Am J Surg.* 1997;173(2):71–75. [https://doi.org/10.1016/S0002-9610\(96\)00425-4](https://doi.org/10.1016/S0002-9610(96)00425-4)
25. Besselink MG, Verwer TJ, Schoenmaeckers EJ, et al. Timing of surgical intervention in necrotizing pancreatitis. *Arch Surg.* 2007;142(12):1194–1201. <https://doi.org/10.1001/archsurg.142.12.1194>
26. Hartwig W, Maksan SM, Foitzik T, Schmidt J, Herfarth C, Klar E. Reduction in mortality with delayed surgical therapy of severe pancreatitis. *J Gastrointest Surg.* 2002;6(3):481–487. [https://doi.org/10.1016/s1091-255x\(02\)00008-2](https://doi.org/10.1016/s1091-255x(02)00008-2)
27. Boxhoorn L, van Dijk SM, van Grinsven J, et al. Immediate versus postponed intervention for infected necrotizing pancreatitis. *N Engl J Med.* 2021;385(15):1372–1381. <https://doi.org/10.1056/NEJMoa2100826>
28. van Veldhuisen CL, Sissinagh NJ, Boxhoorn L, et al. Long-term outcome of immediate versus postponed intervention in patients with infected necrotizing pancreatitis (POINTER): multicenter randomized trial. *Ann Surg.* 2024;279(4):671–678. <https://doi.org/10.1097/SLA.0000000000006001>
29. Trikudanathan G, Tawfik P, Amateau SK, et al. Early (<4 weeks) versus standard (≥4 weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. *Am J Gastroenterol.* 2018;113(10):1550–1558. <https://doi.org/10.1038/s41395-018-0232-3>
30. Hollemans RA, Bakker OJ, Boermeester MA, et al. Superiority of step-up approach vs open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis. *Gastroenterology.* 2019;156(4):1016–1026. <https://doi.org/10.1053/j.gastro.2018.10.045>
31. Freeny PC, Hauptmann E, Althaus SJ, Traverso LW, Sinanan M. Percutaneous CT-guided catheter drainage of infected acute necrotizing pancreatitis: techniques and results. *AJR Am J Roentgenol.* 1998;170(4):969–975. <https://doi.org/10.2214/ajr.170.4.9530046>
32. van Baal MC, van Santvoort HC, Bollen TL, Bakker OJ, Besselink MG, Gooszen HG. Systematic review of percutaneous catheter drainage as primary treatment for necrotizing pancreatitis. *Br J Surg.* 2011;98(1):18–27. <https://doi.org/10.1002/bjs.7304>
33. van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology.* 2011;141(4):1254–1263. <https://doi.org/10.1053/j.gastro.2011.06.073>
34. Gluck M, Ross A, Irani S, et al. Dual-modality drainage of infected and symptomatic walled-off pancreatic necrosis: long-term clinical outcomes. *Gastrointest Endosc.* 2014;79(6):929–935. <https://doi.org/10.1016/j.gie.2013.10.014>
35. Baron TH, Harewood GC, Morgan DE, Yates MR. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. *Gastrointest Endosc.* 2002;56(1):7–17. <https://doi.org/10.1067/mge.2002.125106>

36. Papachristou GI, Takahashi N, Chahal P, Sarr MG, Baron TH. Peroral endoscopic drainage/debridement of walled-off pancreatic necrosis. *Ann Surg.* 2007;245(6):943–951. <https://doi.org/10.1097/01.sla.0000254366.19366.69>
37. Gardner TB, Chahal P, Papachristou GI, et al. A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. *Gastrointest Endosc.* 2009;69(6):1085–1094. <https://doi.org/10.1016/j.gie.2008.06.061>
38. Varadarajulu S, Phadnis MA, Christein JD, Wilcox CM. Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis. *Gastrointest Endosc.* 2011;74(1):74–80. <https://doi.org/10.1016/j.gie.2011.03.1122>
39. Bakker OJ, van Santvoort HC, van Brunschot S, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *JAMA.* 2012;307(10):1053–1061. <https://doi.org/10.1001/jama.2012.276>
40. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. *Lancet.* 2018;391(10115):51–58. [https://doi.org/10.1016/S0140-6736\(17\)32404-2](https://doi.org/10.1016/S0140-6736(17)32404-2)
41. Bang JY, Arnoletti JP, Holt BA, et al. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. *Gastroenterology.* 2019;156(4):1027–1040.e3. <https://doi.org/10.1053/j.gastro.2018.11.031>
42. Bang JY, Wilcox CM, Arnoletti JP, Varadarajulu S. Superiority of endoscopic interventions over minimally invasive surgery for infected necrotizing pancreatitis: meta-analysis of randomized trials. *Dig Endosc.* 2020;32(3):298–308. <https://doi.org/10.1111/den.13470>
43. Onnekink AM, Boxhoorn L, Timmerhuis HC, et al. Endoscopic versus surgical step-up approach for infected necrotizing pancreatitis (ExTENSION): long-term follow-up of a randomized trial. *Gastroenterology.* 2022;163(3):712–722.e14. <https://doi.org/10.1053/j.gastro.2022.05.015>
44. Bang JY, Navaneethan U, Hasan MK, Sutton B, Hawes R, Varadarajulu S. Non-superiority of lumen-apposing metal stents over plastic stents for drainage of walled-off necrosis in a randomised trial. *Gut.* 2019;68(7):1200–1209. <https://doi.org/10.1136/gutjnl-2017-315335>
45. Horvath K, Freeny P, Escallon J, et al. Safety and efficacy of video-assisted retroperitoneal debridement for infected pancreatic collections: a multicenter, prospective, single-arm phase 2 study. *Arch Surg.* 2010;145(9):817–825. <https://doi.org/10.1001/archsurg.2010.178>
46. van Santvoort HC, Besselink MG, Bollen TL, Buskens E, van Ramshorst B, Gooszen HG. Case-matched comparison of the retroperitoneal approach with laparotomy for necrotizing pancreatitis. *World J Surg.* 2007;31(8):1635–1642. <https://doi.org/10.1007/s00268-007-9083-6>
47. Driedger M, Zyromski NJ, Visser BC, et al. Surgical transgastric necrosectomy for necrotizing pancreatitis: a single-stage procedure for walled-off pancreatic necrosis. *Ann Surg.* 2020;271(1):163–168. <https://doi.org/10.1097/SLA.0000000000003048>
48. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. *Gastroenterology.* 2013;145(3):583–590.e1. <https://doi.org/10.1053/j.gastro.2013.05.046>
49. Varadarajulu S, Lopes TL, Wilcox CM, Drelichman ER, Kilgore ML, Christein JD. EUS versus surgical cyst-gastrostomy for management of pancreatic pseudocysts. *Gastrointest Endosc.* 2008;68(4):649–655. <https://doi.org/10.1016/j.gie.2008.02.057>
50. Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. *Clin Nutr.* 2020;39(3):612–631. <https://doi.org/10.1016/j.clnu.2020.01.004>
51. Weimann A, Braunert M, Müller T, Bley T, Wiedemann B. Feasibility and safety of needle catheter jejunostomy for enteral nutrition in surgically treated severe acute pancreatitis. *JPEN J Parenter Enteral Nutr.* 2004;28(5):324–327. <https://doi.org/10.1177/0148607104028005324>
52. Bartholome L, Latifi R. Nutritional support in severe acute pancreatitis: a narrative review. *Kosova J Surg.* In press (this issue).

A NARRATIVE REVIEW

Nutritional Support in Severe Acute Pancreatitis

Lindsay Bartholome, MD, FACS¹, Rifat Latifi, MD, FACS, FICS, FKCS²

¹Trauma Medical Director, Banner Desert Medical Center, Mesa, Arizona;

²Professor of Surgery, Department of Surgery,
University of Arizona, Tucson, AZ, USA; Trauma and Acute Care Surgery Division,
Arizona Advanced Surgery, Mesa, Arizona

Corresponding Author:

RIFAT LATIFI, MD, FACS, FICS, FKCS

Professor of Surgery, University of Arizona; Arizona Advanced Surgery and
Banner Desert Medical Center, Mesa, Arizona.

E-mail: rlatifi@arizona.edu

Abstract

Background: Severe acute pancreatitis (SAP) develops in up to 20% of patients with acute pancreatitis and carries a mortality of 15–35%, however, mortality may exceed 40% once infected pancreatic necrosis supervenes. The attendant systemic inflammatory response drives a hypercatabolic, hypermetabolic state (resting energy expenditure rising 20–50% above baseline) and precipitates gut-barrier failure, positioning nutritional therapy as a disease-modifying intervention rather than adjunctive care.

Aims: The primary aim of this review is to synthesize the current evidence and guideline recommendations governing nutritional support in SAP. The secondary aim is to translate that evidence into practical, bedside-applicable guidance for the acute care surgeon and surgical intensivist—covering the timing of initiation, the route and adequacy of enteral access, the recognition and prevention of feeding-related complications, and the safe delivery of parenteral nutrition when enteral feeding fails—and to delineate the areas in which the evidence remains insufficient to direct practice.

Methods: A narrative review of PubMed/MEDLINE and the Cochrane Library (2000–2025) was performed,

integrating randomized controlled trials, meta-analyses, and the guidelines of ESPEN, ASPEN/SCCM, the AGA, the ACG, EAST, and the AAST.

Results: Meta-analytic data demonstrate that enteral nutrition (EN), versus total parenteral nutrition (TPN), reduces mortality (RR 0.50, 95% CI 0.28–0.91), systemic infection (RR 0.39, 95% CI 0.23–0.65), and multi-organ failure (RR 0.55, 95% CI 0.37–0.81). EN initiated within 24–72 h is uniformly recommended; nasogastric and nasojejunal routes are equivalent. TPN retains a defined role when EN is contraindicated, requiring dextrose infusion below 4–5 mg/kg/min and glycemic targets of 140–180 mg/dL. Probiotics are contraindicated (mortality 16% vs 6%).

Conclusion: Early EN is the evidence-based cornerstone of SAP nutritional management, endorsed across all major guidelines. Route, timing, and access independently determine outcome; TPN is reserved for EN failure under strict metabolic control.

Keywords: Severe acute pancreatitis; enteral nutrition; total parenteral nutrition; ASPEN; SCCM; AAST; ESPEN; feeding tube complications; hyperglycemia; nutritional support; critical care surgery

Introduction

Acute pancreatitis is among the most frequently encountered gastrointestinal emergencies in surgical and critical care practice, with an annual global incidence of approximately 34 per 100,000 person-years and a steadily rising trend driven by increasing rates of gallstone disease, obesity, alcohol use, and hypertriglyceridemia.¹ The disease imposes a substantial and growing burden on health systems, pancreatitis being among the most common principal gastrointestinal discharge diagnoses in the United States, where it accounts for approximately 300,000 hospital admissions each year and contributes to aggregate gastrointestinal hospitalization costs measured in the tens of billions of dollars.² While roughly 80% of cases follow a mild, self-limiting course, up to 20% progress to severe acute pancreatitis (SAP), defined by the revised Atlanta Classification (2012) as pancreatitis complicated by persistent single- or multi-organ failure exceeding 48 hours.³ SAP carries a mortality of 15–35%, rising sharply beyond 40% once infected pancreatic necrosis develops, and its clinical course is characteristically prolonged, biphasic, and unpredictable.

From the vantage point of a critical care surgeon whose career has centered on nutritional support of the critically ill and injured, SAP is one of the most instructive and demanding nutritional scenarios in all of surgery. The systemic inflammatory response unleashed by pancreatic autodigestion drives a hypercatabolic, hypermetabolic state physiologically indistinguishable from that following major trauma or major emergency surgery, with resting energy expenditure rising 20–50% above baseline, accelerated proteolysis, negative nitrogen balance, and the potential loss of 20–30% of body protein mass within two to three weeks.^{4,5} Nutritional support of the critically ill has undergone transformative advances in recent decades, evolving from empirical supplementation into a precision, disease- and disorder-based science with measurable impact on morbidity and mortality.⁶ In no disease is this evolution more clearly demonstrated than in SAP, where the metabolic insult is severe, nutritional depletion is rapid, and the consequences of malnutrition—particularly infection—are lethal.

Historically, the principle of “pancreatic rest” drove clinicians to keep SAP patients nil per os (NPO) and to deliver nutrition exclusively through TPN, on the misguided theory that withholding enteral stimulation would quiet pancreatic exocrine secretion and limit autodigestion. Even within that paradigm, as described in a

foundational 1991 analysis,⁷ meticulous attention to both the route and the composition of nutritional support was recognized as essential. What the pancreatic-rest doctrine neglected, however, was the central role of the gut as an immunological and mechanical barrier organ. Loss of enteral stimulation triggers villous atrophy, disrupts epithelial tight junctions, depletes secretory IgA, and enables translocation of luminal bacteria and endotoxin into the portal circulation—seeding inflamed peripancreatic tissue and converting sterile necrosis into infected necrosis, the principal driver of late mortality.⁸ This mechanistic understanding reframed the gut not as an organ to be rested but as one to be protected through early luminal nutrient delivery.

Over the past two decades, high-quality evidence from randomized controlled trials, meta-analyses, and the Cochrane Library—now codified in concordant guidelines from ESPEN,^{9,10} ASPEN/SCCM,¹¹ the AGA,¹² the ACG,¹³ EAST,¹⁴ and the AAST¹⁵—has overturned the pancreatic-rest paradigm completely, establishing early enteral nutrition as the standard of care. In parallel, evolving surgical nutrition research has clarified that the timing of nutritional initiation, the route of delivery, and the adequacy of nutritional access are independent determinants of outcome in surgical patients with acute abdominal pathology, including SAP.^{16,17} As a 2025 editorial in *European Surgery* introducing a special focus on nutritional support across surgical disciplines articulated,¹⁸ effective nutritional intervention enhances immune function, promotes healing, and facilitates recovery, whereas inadequate support heightens the risk of malnutrition, infection, and death. These principles apply with full force to SAP.

Pathophysiology of Nutritional Derangements

SAP triggers sustained hypermetabolism driven by SIRS, with counterregulatory hormone excess (cortisol, glucagon, catecholamines) promoting glycogenolysis, gluconeogenesis, proteolysis, and lipolysis while impairing peripheral glucose uptake.⁴ The result is hyperglycemia, negative nitrogen balance, hypoalbuminemia, and rapid depletion of lean body mass.¹⁹ Concurrently, splanchnic hypoperfusion disrupts epithelial tight junctions and depletes mucosal secretory IgA, producing a “leaky gut” through which bacteria and endotoxin translocate into the portal circulation—the principal mechanism seeding sterile necrosis and converting it to infected necrosis, the event most responsible for late

mortality.⁸ Early enteral nutrition directly counters this vulnerability by maintaining villous height, stimulating mucosal turnover, promoting bile flow, and preserving commensal flora. This strategy has been associated with reduced mortality, fewer infectious complications, and decreased rates of organ failure, largely through preservation of intestinal mucosal integrity and gut-barrier function.^{21,23,24}

The primary aim of this narrative review is to synthesize current evidence and guideline recommendations on optimal nutritional support in SAP. The secondary aim is to translate that evidence into practical, bedside-applicable guidance for the acute care surgeon and the surgical intensivist. To those ends, the review examines the pathophysiologic rationale for early enteral feeding, the comparative evidence for enteral versus parenteral routes, the choice of gastric versus post-pyloric delivery, the complications of both enteral tube feeding and TPN, and the special circumstances of the open abdomen and refractory disease—with particular attention to the metabolic hazards of high-dextrose formulations in metabolically vulnerable patients and the disciplined management that allows parenteral nutrition to be used safely when it is required. It further seeks to make explicit those questions the current evidence base does not answer, so that the residual uncertainty is stated rather than obscured.

Methods

A narrative review of the literature was performed using PubMed/MEDLINE and the Cochrane Library. Individual references were verified against PubMed, publisher and DOI records, and, for Cochrane systematic reviews, the Cochrane Library directly. Search and verification focused on terms relating to severe acute pancreatitis, enteral and parenteral nutrition, route of feeding, feeding-tube and parenteral-nutrition complications, gut-barrier function, and critical care nutrition. Coverage emphasized human studies and English-language publications from 2000 through 2024, with priority given to literature published from 2016 onward. Reporting was guided by the Scale for the Assessment of Narrative Review Articles (SANRA), which addresses justification of the review's importance and aims, description of the literature search, referencing, and the presentation of evidence and data.²⁰

Guideline documents were retrieved and reviewed in full, including the ESPEN Guideline on Clinical Nutrition in Acute and Chronic Pancreatitis (2020)⁹ and the

ESPEN Practical Guideline update (2024);¹⁰ the ASPEN/SCCM Guidelines for the Provision of Nutrition Support Therapy in the Adult Critically Ill Patient (2022);¹¹ the AGA Institute Guideline on Initial Management of Acute Pancreatitis (2018);¹² the ACG Guidelines on Management of Acute Pancreatitis (2024);¹³ the EAST Practice Management Guidelines for Nutritional Support of the Trauma Patient (2004);¹⁴ and the AAST Critical Care and Geriatric Trauma Committees clinical consensus document on geriatric nutrition in the surgical patient (2025).¹⁵ The EAST document (2004) is the only formal trauma-specific nutrition practice management guideline and has not been revised since publication; it therefore predates the revised Atlanta Classification, the major parenteral-nutrition timing trials, and every other guideline cited here. It is included for its acute-care-surgery perspective, and its recommendations remain concordant with the more recent documents, but its age should be borne in mind when it is read alongside them. Two Cochrane systematic reviews were retrieved from the Cochrane Library and reviewed in full as primary evidence sources: enteral versus parenteral nutrition for acute pancreatitis²¹ and nasogastric versus nasojejunal tube feeding for severe acute pancreatitis.²² Relevant peer-reviewed publications by the author and colleagues on nutritional support in critically ill and surgical patients were incorporated where directly applicable.^{16,6,17}

Results

Across converging randomized controlled trials, meta-analyses, and every major society guideline, the evidence favors early enteral nutrition (EN) over total parenteral nutrition (TPN) in SAP. Pooled Cochrane and subsequent meta-analytic data show that EN, compared with TPN, significantly reduces mortality (RR 0.50, 95% CI 0.28–0.91), systemic infection (RR 0.39, 95% CI 0.23–0.65), multi-organ failure (RR 0.55, 95% CI 0.37–0.81), and the need for surgical intervention^{21,23,24} (Table 1). The mechanistic basis is preservation of the intestinal barrier, gut-associated lymphoid tissue, and commensal flora, thereby limiting the bacterial translocation that converts sterile to infected necrosis.⁸

EN initiated within 24–72 hours of admission, once hemodynamic stability is achieved, is recommended by ESPEN, ASPEN/SCCM, the AGA, the ACG, and EAST^{9,10,11,12,13,14} (Table 1). Nasogastric and nasojejunal delivery are equivalent in mortality, aspiration, tolerance, and pain,^{22,25,26} and the technically simpler nasogastric

route is endorsed as first-line. Caloric targets of 25–35 kcal/kg/day and protein of 1.2–1.5 g/kg/day are consistent across guidelines, with higher protein (up to 2.5 g/kg/day) advised in the highest-acuity and open-abdomen patients.¹⁹ Securing and maintaining enteral access is itself independently prognostic, with lower rates of gastrointestinal complications and mortality.¹⁷

TPN retains a defined role when EN is contraindicated—such as refractory shock, high-output fistula, and peritonitis—or simply not tolerated, but early TPN in patients who could receive EN confers no benefit and increases infectious complications, ICU stay, and ventilation.²⁷ When indicated, TPN is delivered safely through disciplined metabolic control—dextrose infusion below 4–5 mg/kg/min, glycemic targets of 140–180 mg/dL, and strict aseptic catheter care.^{28,29,30} Enteral glutamine is no longer recommended, and probiotics are contraindicated, having increased mortality (16% vs 6%) in a landmark trial.^{5,31} The principal studies and guidelines underpinning these findings are summarized in Table 1.

Discussion

We have presented in this review the evidence that early enteral nutrition is the therapeutic cornerstone of nutritional management in SAP.^{9,10,11,12,13,15,14} There is no need for reflexive NPO orders and TPN-first management, in favor of an approach grounded in targeting the specific derangements of pancreatic critical illness: hypercatabolism, gut-barrier failure, insulin resistance, and susceptibility to secondary infection.

Enteral Nutrition: Evidence and Guideline Concordance

The evidence favoring EN over TPN is robust and consistent (Table 1). A Cochrane systematic review, reinforced by subsequent meta-analyses, demonstrated significant reductions in mortality, systemic infection, and multi-organ failure with EN,^{21,23,24} a conclusion echoed in contemporary reviews of nutrition therapy specific to SAP and to current management standards.^{32,33} The question of timing is paramount: early nutrition confers measurable benefit but requires hemodynamic stability as a prerequisite,¹⁶ so EN should commence within 24–72 hours of admission once resuscitation is underway—not after waiting for normalization of amylase, lipase, or inflammatory markers, none of which predict feeding tolerance. All major guidelines are concordant on early EN as first-line therapy, with TPN reserved for EN

failure or contraindication.^{9,10,11,12,13} Securing enteral access is not a secondary concern but a primary therapeutic act; a propensity-matched analysis showed that malnourished elderly patients who received surgical nutritional access had significantly lower gastrointestinal complication rates.¹⁷

Route of Delivery: Nasogastric versus Nasojejunal

The traditional preference for nasojejunal feeding rested on the concern that intragastric nutrients stimulate pancreatic exocrine secretion, but clinical evidence has consistently failed to support this.^{22,25,26} Cochrane and additional systematic reviews found no significant differences between nasogastric and nasojejunal feeding in mortality, aspiration, tolerance, exacerbation, or pain. Because nasogastric placement is a bedside procedure enabling feeding within hours—whereas post-pyloric placement requires fluoroscopy, endoscopy, or electromagnetic guidance and delays initiation—the nasogastric route is endorsed as first-line, with post-pyloric feeding reserved for high aspiration risk or gastric intolerance.^{9,10,11,12}

Complications of Enteral Feeding Tubes

Initiating EN begins rather than ends the clinician's responsibility. Tube malposition (1–3% of insertions) may cause aspiration pneumonitis, pneumothorax, or pulmonary hemorrhage, mandating radiographic confirmation before feeding. Aspiration is the most consequential ongoing complication, elevated in SAP by opioid-induced gastroparesis and impaired airway reflexes; preventive measures include head-of-bed elevation to 30–45 degrees, gastric residual monitoring, prokinetics, and transition to post-pyloric access when residuals persist. Bacterial sinusitis (5–20% with transnasal tubes beyond 5–7 days), diarrhea, tube occlusion, and oropharyngeal discomfort require active surveillance, because delays in diagnosis deprive the patient of a proven therapeutic intervention.

The Open Abdomen and Abdominal Catastrophe

A subset of SAP patients—those with abdominal compartment syndrome, necrosis requiring operative debridement, or enteroatmospheric fistula—present the added challenge of the open abdomen. A comprehensive expert review identified that most failures of primary fascial closure and fistula formation are preventable through effective temporary abdominal closure coupled

with appropriate resuscitation and nutritional support.³⁴ Protein losses through open abdomens are profound (an estimated 1–2 g per 100 mL of peritoneal exudate), so protein targets should be revised upward to 1.5–2.0 g/kg/day, and combined enteral plus supplemental parenteral nutrition is often the most pragmatic approach.

Total Parenteral Nutrition: Role, Timing, and Safe Delivery

When EN is not feasible, TPN retains a major and legitimate role, and its safe delivery depends on disciplined metabolic management rather than avoidance. Absolute indications include bowel obstruction, high-output proximal fistula, mesenteric ischemia, abdominal compartment syndrome, refractory hemodynamic instability, and refractory EN intolerance. The landmark EPaNIC trial established that early TPN in patients who can receive EN provides no benefit and increases infectious complications, ICU duration, and ventilation;²⁷ TPN should therefore not be initiated within the first 7 days if EN is feasible. When TPN is indicated, it remains an essential and effective therapy: the convergence of stress-induced insulin resistance, potential islet-cell dysfunction in necrotizing disease, and glucose-dense formulations makes glycemic control the central determinant of whether TPN helps or harms. The prescribing principles are straightforward—keep the dextrose infusion rate below 4–5 mg/kg/min, balance non-protein calories with lipid, target glucose of 140–180 mg/dL with continuous insulin infusion, and apply strict aseptic catheter care.^{28,29,30} Applied with this rigor, TPN can be delivered safely and prevents the complications historically attributed to it.

Glutamine, Immunonutrition, Probiotics, and Oral Refeeding

A critical review of enteral glutamine noted that two major multicenter RCTs (REDOXS and METAPLUS) not only failed to show benefit but suggested harm in multi-organ failure;⁵ enteral glutamine is therefore no longer recommended, and intravenous glutamine may be considered only when TPN is required and EN is not feasible.¹⁰ Immunonutrition formulas have not shown consistent mortality benefit, and probiotics are contraindicated based on the PROPATRIA trial, which found significantly increased mortality (16% vs 6%).³¹ Early oral refeeding is supported in moderately severe disease once pain is controlled, the patient is alert, and ileus has resolved.

Limitations

Several limitations of the evidence base must be acknowledged. Most RCTs in this field are small, single-center, and methodologically heterogeneous, and many predate the revised Atlanta Classification and the current step-up approach to necrosectomy. The optimal caloric dose in the early acute phase remains incompletely defined, and personalized approaches guided by indirect calorimetry and metabolic phenotyping are promising but not yet integrated into routine guideline recommendations.

Conclusion

Severe acute pancreatitis demands early, evidence-based, and precisely executed nutritional intervention. Early enteral nutrition—initiated within 24–72 hours of admission via the nasogastric route—is the standard of care, endorsed by ESPEN, ASPEN/SCCM, the AGA, the ACG, EAST, and the AAST.^{9,10,11,12,13,15,14} This approach reduces mortality, infectious complications, and organ failure through gut-barrier preservation. The timing of initiation, the route and adequacy of enteral access, and the management of feeding-related complications are independent determinants of clinical outcome.^{16,6,17} TPN retains an important role when EN is not feasible and, delivered with meticulous attention to dextrose load, glycemic control, and catheter care, is safe and effective. In SAP, nutrition is not supportive care—it is, alongside resuscitation and source control, one of the pillars of management upon which patient survival depends.

Conflicts of Interest: The authors have no conflicts of interest.

Author Contributions: Lindsay Bartholome, MD, FACS, and Rifat Latifi, MD, FACS, FICS, FKCS, contributed equally to all aspects of this study — conception and design, literature search and evidence appraisal, interpretation of the data, drafting and critical revision of the manuscript — and both authors read and approved the final version

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgments: The authors thank the guest editor and the reviewers for their thoughtful and constructive contributions, which have improved this manuscript.

Table 1. Evidence Summary of Major References

Ref (Year)	Author / Source	Type of Study	N (patients / trials)	Main Outcome	Clinical Utility
3 (2013)	Banks et al.; Atlanta Working Group	International consensus classification	n/a	Revised Atlanta Classification defining SAP by persistent organ failure >48 h.	Diagnostic framework; defines the SAP population.
8 (2014)	Wu, Sankaran, Plank, Windsor, Petrov	Meta-analysis	AP cohorts	Quantified gut-barrier dysfunction as a driver of infected necrosis.	Mechanistic rationale for early EN.
9,10 (2020/24)	Arvanitakis et al. (ESPEN)	Clinical practice guideline	n/a	EN first-line within 24–72 h; NG acceptable; IV glutamine only if TPN required.	Definitive, most comprehensive guideline reference.
11 (2022)	Compher et al. (ASPEN/SCCM)	GRADE-based guideline	n/a	EN within 24–48 h; avoid TPN in first 7 days if EN feasible.	Most rigorous critical-care nutrition guideline.
12 (2018)	Crockett et al. (AGA)	Clinical practice guideline	n/a	EN over TPN; nasogastric route preferred.	US gastroenterology guideline.
13 (2024)	Tenner et al. (ACG)	Clinical practice guideline	n/a	EN within 48 h when oral intake not tolerated.	Current US ACG guideline.
14 (2004)	Jacobs et al. (EAST)	Practice management guideline	n/a	Early EN within 72 h preferred in the severely injured.	Trauma/acute-care surgery perspective.
15 (2025)	Farrell et al. (AAST)	Clinical consensus document	n/a	Best-practice guidance on nutrition in the surgical/geriatric patient.	Recent multidisciplinary consensus.
17 (2021)	Gogna et al.	Propensity score-matched cohort (NIS)	4,311 pts	Surgical nutritional access reduced GI complications in malnourished elderly.	Shows independent prognostic value of enteral access.
19 (2025)	González-Castillo et al.	Systematic review	n/a	Protein 1.5–2.5 g/kg/day; simplified energy targets when calorimetry unavailable.	Practical targets for the highest-acuity patients.
21 (2010)	Al-Omran et al. (Cochrane)	Systematic review / meta-analysis of RCTs	8 RCTs	EN vs TPN reduced mortality (RR 0.50), systemic infection (RR 0.39), organ failure (RR 0.55).	Foundational Cochrane evidence favoring EN.
22 (2020)	Dutta et al. (Cochrane)	Systematic review / meta-analysis of RCTs	5 RCTs	No difference between NG and NJ feeding in mortality, aspiration, or tolerance.	Supports first-line nasogastric feeding.
23 (2008)	Petrov et al.	Meta-analysis of RCTs	RCTs in SAP	EN reduced mortality and infectious complications vs TPN.	Early confirmatory meta-analysis.
24 (2018)	Wu, Li, Sun	Meta-analysis of RCTs	11 studies / 562 pts	EN reduced mortality and infection vs TPN; no heterogeneity.	Contemporary quantitative confirmation.
25 (2013)	Chang et al.	Meta-analysis of RCTs	6 RCTs	NG feeding equivalent to NJ in safety and tolerance.	Corroborates NG-first approach.
26 (2023)	Carlin-Ronquillo et al.	Systematic review of RCTs	4 RCTs / 192 pts	NG feeding as efficacious and safe as NJ.	Most recent RCT-level synthesis.
27 (2011)	Casaer et al. (EPaNIC)	Large multicenter RCT	4,640 pts	Early TPN increased infection, ICU stay, and ventilation vs late initiation.	Defines timing; supports withholding early TPN when EN feasible.
29 (2001)	Van den Bergh et al.	RCT	1,548 pts	Intensive insulin therapy reduced mortality in the surgical ICU.	Basis for glycemic control during nutrition support.
30 (2009)	NICE-SUGAR Investigators	Large multicenter RCT	6,104 pts	Refined glycemic target to 140–180 mg/dL.	Current standard glucose target under TPN.
31 (2008)	Besselink et al. (PROPATRIA)	Multicenter RCT	296 pts	Probiotics increased mortality (16% vs 6%) in predicted SAP.	Establishes probiotics as contraindicated in SAP.

AP, acute pancreatitis; EN, enteral nutrition; TPN, total parenteral nutrition; NG, nasogastric; NJ, nasojejunal; RR, relative risk; NIS, National Inpatient Sample; RCT, randomized controlled trial.

References:

1. Xiao AY, Tan MLY, Wu LM, Asrani VM, Windsor JA, Yadav D, Petrov MS. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. *Lancet Gastroenterol Hepatol*. 2016;1(1):45–55. doi:10.1016/S2468-1253(16)30004-8. PMID: 28404111
2. Peery AF, Crockett SD, Murphy CC, et al. Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2021. *Gastroenterology*. 2022;162(2):621–644. doi:10.1053/j.gastro.2021.10.017. PMID: 34678215
3. Banks PA, Bollen TL, Dervenis C, et al.; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102–111. doi:10.1136/gut-jnl-2012-302779
4. Joseph B, Wynne JL, Dudrick SJ, Latifi R. Nutrition in trauma and critically ill patients. *Eur J Trauma Emerg Surg*. 2010;36(1):25–30. doi:10.1007/s00068-010-9213-y. PMID: 26815565
5. Stroster JA, Uranues S, Latifi R. Nutritional controversies in critical care: revisiting enteral glutamine during critical illness and injury. *Curr Opin Crit Care*. 2015;21(6):527–530. doi:10.1097/MCC.0000000000000260. PMID: 26539926
6. Latifi R. Nutritional therapy in critically ill and injured patients. *Surg Clin North Am*. 2011;91(3):579–593. doi:10.1016/j.suc.2011.02.002. PMID: 21621697
7. Latifi R, McIntosh JK, Dudrick SJ. Nutritional management of acute and chronic pancreatitis. *Surg Clin North Am*. 1991;71(3):579–595. doi:10.1016/s0039-6109(16)45435-6. PMID: 1904645
8. Wu LM, Sankaran SJ, Plank LD, Windsor JA, Petrov MS. Meta-analysis of gut barrier dysfunction in patients with acute pancreatitis. *Br J Surg*. 2014;101(13):1644–1656. doi:10.1002/bjs.9665
9. Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. *Clin Nutr*. 2020;39(3):612–631. doi:10.1016/j.clnu.2020.01.004
10. Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN practical guideline on clinical nutrition in acute and chronic pancreatitis. *Clin Nutr*. 2024;43(2):395–412. doi:10.1016/j.clnu.2023.12.019
11. Compher C, Bingham AL, McCall M, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr*. 2022;46(1):12–41. doi:10.1002/jpen.2267
12. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology*. 2018;154(4):1096–1101. doi:10.1053/j.gastro.2018.01.032
13. Tenner S, Vege SS, Sheth SG, et al. American College of Gastroenterology Guidelines: Management of Acute Pancreatitis. *Am J Gastroenterol*. 2024;119(3):419–437. doi:10.14309/ajg.00000000000002645
14. Jacobs DG, Jacobs DO, Kudsk KA, et al.; EAST Practice Management Guidelines Work Group. Practice management guidelines for nutritional support of the trauma patient. *J Trauma*. 2004;57(3):660–679. doi:10.1097/01.TA.0000138229.30434.A4. PMID: 15454822
15. Farrell MS, Bongiovanni T, Cuschieri J, Egodage T, Elkbuli A, Gelbard R, Jawa R, Mitha S, Nassar AK, Pathak A, Peralta R, Putnam T, Stein DM. Geriatric nutrition in the surgical patient: an American Association for the Surgery of Trauma Critical Care and Geriatric Trauma Committees clinical consensus document. *Trauma Surg Acute Care Open*. 2025;10(1):e001602. doi:10.1136/tsaco-2024-001602. PMID: 39906299
16. Khan M, Latifi R. Nutrition in surgical patients: how soon is too soon? *Curr Opin Crit Care*. 2019;25(6):701–705. doi:10.1097/MCC.0000000000000672. PMID: 31688164
17. Gogna S, Samson D, Choi J, Con J, Prabhakaran K, Rhee P, Latifi R. The role of nutritional access in malnourished elderly undergoing major surgery for acute abdomen: a propensity score-matched analysis. *Am Surg*. 2021;87(8):1252–1258. doi:10.1177/0003134820973719. PMID: 33345560
18. Latifi R, Gabor S, Hauser H. The critical role of nutritional support in trauma, major operations, re-operative surgery, and cancer care revisited [editorial]. *Eur Surg*. 2025;57:179–180. doi:10.1007/s10353-025-00886-x
19. González-Castillo AM, Picazo L, Manzo E, Marcucci F, Latifi R. Nutritional support in trauma and critically ill patients. *Eur Surg*. 2025;57:181–187. doi:10.1007/s10353-025-00872-3
20. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev*. 2019;4:5. doi:10.1186/s41073-019-0064-8. PMID: 30962953
21. Al-Omran M, AlBalawi ZH, Tashkandi MF, Al-Ansary LA. Enteral versus parenteral nutrition for acute pancreatitis. *Cochrane Database Syst Rev*. 2010;(1):CD002837. doi:10.1002/14651858.CD002837.pub2. PMID: 20091534
22. Dutta AK, Goel A, Kirubakaran R, Chacko A, Tharyan P. Nasogastric versus nasojejunal tube feeding for severe acute pancreatitis. *Cochrane Database Syst Rev*. 2020;3(3):CD010582. doi:10.1002/14651858.CD010582.pub2. PMID: 32216139
23. Petrov MS, van Santvoort HC, Besselink MG, van der Heijden GJ, Windsor JA, Gooszen HG. Enteral nutrition and the risk of mortality and infectious complications in patients with severe acute pancreatitis: a meta-analysis of randomized trials. *Arch Surg*. 2008;143(11):1111–1117. doi:10.1001/archsurg.143.11.1111

24. Wu P, Li L, Sun W. Efficacy comparisons of enteral nutrition and parenteral nutrition in patients with severe acute pancreatitis: a meta-analysis from randomized controlled trials. *Biosci Rep*. 2018;38(6):BSR20181515. doi:10.1042/BSR20181515. PMID: 30333259
25. Chang YS, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a meta-analysis. *Crit Care*. 2013;17(3):R118. doi:10.1186/cc12790
26. Carlin-Ronquillo A, Benites-Goñi H, Diaz-Arocutipa C, Alosilla Sandoval P, Piscoya-Rivera A, Calixto L, Hernández AV. Nasogastric versus nasojejunal tube feeding for severe acute pancreatitis: a systematic review of randomized controlled trials. *Rev Gastroenterol Peru*. 2023;43(3):207–216. doi:10.47892/rgp.2023.433.1542. PMID: 37890845
27. Casaer MP, Mesotten D, Hermans G, et al. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med*. 2011;365(6):506–517. doi:10.1056/NEJMoa1102662
28. Al-Zubeidi D, Stein GY, Stein A, et al. Prevention of complications for hospitalized patients receiving parenteral nutrition: a narrative review. *Nutr Clin Pract*. 2024;39(4):785–800. doi:10.1002/ncp.11201
29. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345(19):1359–1367. doi:10.1056/NEJMoa011300
30. NICE-SUGAR Study Investigators; Finfer S, Chittock DR, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360(13):1283–1297. doi:10.1056/NEJMoa0810625
31. Besselink MG, van Santvoort HC, Buskens E, et al.; Dutch Acute Pancreatitis Study Group. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. *Lancet*. 2008;371(9613):651–659. doi:10.1016/S0140-6736(08)60207-X
32. Jabłońska B, Mrowiec S. Nutritional support in patients with severe acute pancreatitis—current standards. *Nutrients*. 2021;13(5):1498. doi:10.3390/nu13051498
33. Sun JK, Lv C, Gao L, Mao W, Li W, Ke L. Nutrition therapy in critically ill patients with severe acute pancreatitis. *Nutr Clin Pract*. 2024;39(2):271–280. doi:10.1002/ncp.11135. PMID: 38357829
34. Roberts DJ, Leppäniemi A, Tolonen M, Mentula P, Björck M, Kirkpatrick AW, Sugrue M, Pereira BM, Petersson U, Coccolini F, Latifi R. The open abdomen in trauma, acute care, and vascular and endovascular surgery: comprehensive, expert, narrative review. *BJS Open*. 2023;7(5):zrad084. doi:10.1093/bjsopen/zrad084. PMID: 37882630

Severe Liver Trauma: Current Management

Dai Ailin¹, Rebekah Young, [FRACS, MD, MSc, BHealthSci]²,
Vishal G. Shelat, [FRCS, FEBS(HPB Surgery)]³

¹ Lee Kong Chian School of Medicine, Singapore
ORCID: 0009-0009-2449-1477

² Department of General Surgery and Trauma, Tan Tock Seng Hospital, Singapore
Department of General Surgery and Trauma, Royal Brisbane and Women's
Hospital, Brisbane, Australia
ORCID: 0000-0001-6242-5256

³ Department of General Surgery, Tan Tock Seng Hospital, Singapore
ORCID: 0000-0003-3988-8142

Corresponding Author:

DAI AILIN

Lee Kong Chian School of Medicine
Singapore 308232
E-mail: dai.ailin2593@gmail.com
ORCID: 0009-0009-2449-1477

Co-Corresponding Author:

VISHAL G. SHELAT

Tan Tock Seng Hospital
Singapore 308433
E-mail: vgshelat@gmail.com
ORCID: 0000-0003-3988-8142

Abstract

Background: Severe liver trauma requires rapid haemorrhage control while preserving viable liver and anticipating delayed vascular and biliary complications. Modern management is increasingly non-operative, but safe treatment depends on physiology, injury anatomy and institutional rescue capability.

Objective: To review current management of severe adult liver trauma with emphasis on physiology-based

decision-making, liver-specific operative rescue, biliary complications and resource-sensitive pathways.

Findings: Anatomical grade identifies risk but should not determine treatment in isolation. Haemodynamically stable patients with high-grade blunt injury may undergo non-operative management when close monitoring, blood products, urgent surgery and interventional radiology are reliably available. Angioembolization is valuable for selected arterial bleeding but carries risks including hepatic

necrosis, abscess and bile leak. Persistent instability, generalized peritonitis or another indication for laparotomy requires operative management. Damage-control priorities are compression, perihepatic packing and temporary inflow control. Bleeding that persists despite portal triad occlusion should raise concern for major hepatic venous or retrohepatic caval injury; unnecessary liver mobilisation can abolish tamponade, and complex vascular exposure should be reserved for situations in which physiology, expertise and resources permit definitive repair. Major resection is rarely appropriate during uncontrolled shock, whereas staged resectional debridement and, exceptionally, transplantation may be required. Post-traumatic bile leaks are managed stepwise with drainage, endoscopic decompression or stenting, percutaneous techniques and selected reconstruction. Resource availability is itself a treatment variable: high-grade non-operative management without reliable rescue is unsafe, and damage-control packing followed by transfer may be preferable to attempted definitive surgery in a non-specialist centre.

Conclusions and Relevance: Severe liver trauma is best managed through a physiology-first, liver-specific and capability-aware strategy. Outcomes depend on timely haemorrhage control, appropriate selection for non-operative management, expert-led operative rescue and early recognition of complications.

Keywords: Liver/injuries; Embolization, Therapeutic; Damage control resuscitation; Liver trauma; Non-operative management

Introduction

Severe liver trauma remains one of the most demanding problems in emergency surgery. The liver is large and highly vascular, with dual portal venous and hepatic arterial inflow, and lies adjacent to the diaphragm, retrohepatic inferior vena cava, duodenum, pancreas, colon and right kidney. Major hepatic injury can cause haemorrhagic shock and may coexist with significant thoracic, abdominal or vascular injury. The liver also has major roles in coagulation, metabolism, immune regulation, detoxification and bile production. Severe injury may therefore be followed by coagulopathy, bile leak, infected collections, hepatic necrosis and sepsis.

The liver has substantial regenerative capacity, and this supports a parenchymal-preserving philosophy whenever safe. However, regeneration should not be used to justify delayed haemorrhage control or unnecessary complex reconstruction during haemorrhagic shock. In the acute

phase, the priority is damage control, haemostasis, tissue preservation and the management of concomitant injury.

Historically, operative haemorrhage control dominated liver trauma care. Pringle's 1908 paper, "Notes on the Arrest of Hepatic Hemorrhage Due to Trauma," remains a landmark paper and the Pringle manoeuvre is still relevant for inflow occlusion during damage control laparotomy.¹ Over the last four decades, however, the field has moved from mandatory laparotomy to selective non-operative management (NOM), computed tomography (CT) based triage, angioembolization, damage control resuscitation and staged operative care.²⁻⁵ Recent reviews comprehensively describe contemporary assessment and general trauma management of liver injury.⁶ The present review therefore focuses particularly on two areas that are less consistently integrated into general trauma algorithms: liver-specific technical rescue of major vascular, parenchymal and biliary injury, and adaptation of management to institutional capability when interventional radiology, specialist hepatopancreatobiliary surgery or critical-care resources are not continuously available. The practical framework is that physiology determines when intervention is required, hepatic anatomy determines what technical rescue is needed, and institutional capability determines where that rescue can safely be delivered. This review addresses severe liver trauma in adults.

Literature search

A focused literature search was undertaken using PubMed, OpenAlex and Google Scholar for publications from January 1990 to July 2026. Search concepts included liver or hepatic trauma, high-grade liver injury, non-operative management, angioembolization, damage-control surgery, hepatic packing, hepatic vascular injury, vena caval injury, bile leak, biliary injury, hepatic resection and transplantation. English-language adult human studies were considered. Priority was given to clinical guidelines, systematic reviews, multicentre and prospective studies, and landmark reports that materially influenced current management. Reference lists of key guidelines and reviews were also examined for relevant studies. Because this was a narrative review, study selection was purposive and no formal risk-of-bias assessment or quantitative synthesis was undertaken.

Classification and decision-making

Severe liver trauma in this review refers principally to American Association for the Surgery of Trauma (AAST) grade IV–V injury. Grade IV includes disruption of 25%–

75% of a hepatic lobe or active bleeding extending beyond the liver parenchyma, whereas grade V includes disruption of more than 75% of a lobe or juxtahepatic venous injury involving the retrohepatic vena cava or major hepatic veins.⁷ The World Society of Emergency Surgery (WSES) integrates anatomy with physiology: haemodynamically stable AAST IV–V injuries are WSES grade III, whereas haemodynamic instability makes an injury WSES grade IV irrespective of anatomical grade.⁸

The key clinical point is that anatomical grade implies risk but does not dictate management in isolation. A grade IV or V injury identifies a patient at high risk of bleeding, complications and failure of NOM, but it does not automatically mandate laparotomy. Conversely, a lower-grade injury in an unstable patient with peritonitis, bowel injury or major associated trauma may require urgent operation. Modern decision-making should consider five linked questions:

1. Is the patient haemodynamically stable?
2. Is the patient responding to resuscitation?
3. Is there peritonitis or another indication for laparotomy?
4. Does CT show active arterial bleeding or a contained vascular lesion?
5. Can the institution provide close monitoring, transfusion, and interventional radiology?

NOM is appropriate only when serial reassessment, blood products, interventional radiology and urgent operative rescue are reliably available. Associated injuries

are central. Major traumatic brain or spinal injury, thoracic or abdominal trauma, major vascular injury, pelvic or orthopaedic trauma and other injuries requiring urgent intervention may determine treatment priorities more than the liver grade itself. The decision should be based on the whole injury pattern, not the liver injury grade alone. Recent pathway-level evidence further supports physiology-based decision-making. In a protocolized cohort of 350 patients, NOM was initiated in 86.9% and delayed laparotomy was required in 4.9%, most commonly for haemodynamic deterioration, ongoing or delayed haemorrhage, or failed haemostatic control after interventional radiology. Shock index, Injury Severity Score and lactate independently predicted mortality, whereas anatomical grade alone had limited discriminatory value.⁹ This approach is consistent with contemporary guideline frameworks that prioritize physiology, associated injuries and rescue capability over anatomical grade alone.^{8,10} The principal clinical and institutional decision modifiers are summarized in Table 1.

Initial assessment and resuscitation

Initial assessment follows Advanced Trauma Life Support xABCDE priorities, with immediate control of exsanguinating haemorrhage, airway and breathing assessment, circulatory resuscitation, neurological assessment and exposure with prevention of hypothermia.⁵ Extended focused assessment with sonography in trauma (E-FAST) can identify intraperitoneal fluid rapidly, but it does not grade liver injury or reliably exclude hollow viscus injury. A negative

Table 1. Decision modifiers in severe liver trauma

Domain	Key findings	Management implication
Physiology	Stable, transient responder, non-responder, shock, lactate trend, transfusion need	Physiology overrides grade
Anatomy	AAST grade IV–V, devascularization, juxtahepatic venous injury	Identifies risk and need for senior planning
CT vascular findings	Contrast blush, active extravasation, pseudoaneurysm, arteriovenous fistula	Consider angiography/embolization if stable or stabilized
Peritonitis	Abdominal tenderness, guarding, free air, suspected bowel injury	Usually operative exploration
Associated injuries	Hollow viscus, pancreas/duodenum, spleen, kidney, pelvis, thorax, brain, major vessels	May determine pathway more than liver injury
Resources	Blood bank, ICU, operating room, interventional radiology, HPB support, transfer network	Determines safety of NOM and timing of transfer

AAST: American Association for the Surgery of Trauma; CT: computed tomography; HPB: hepatopancreatobiliary; ICU: intensive care unit; NOM: non-operative management.

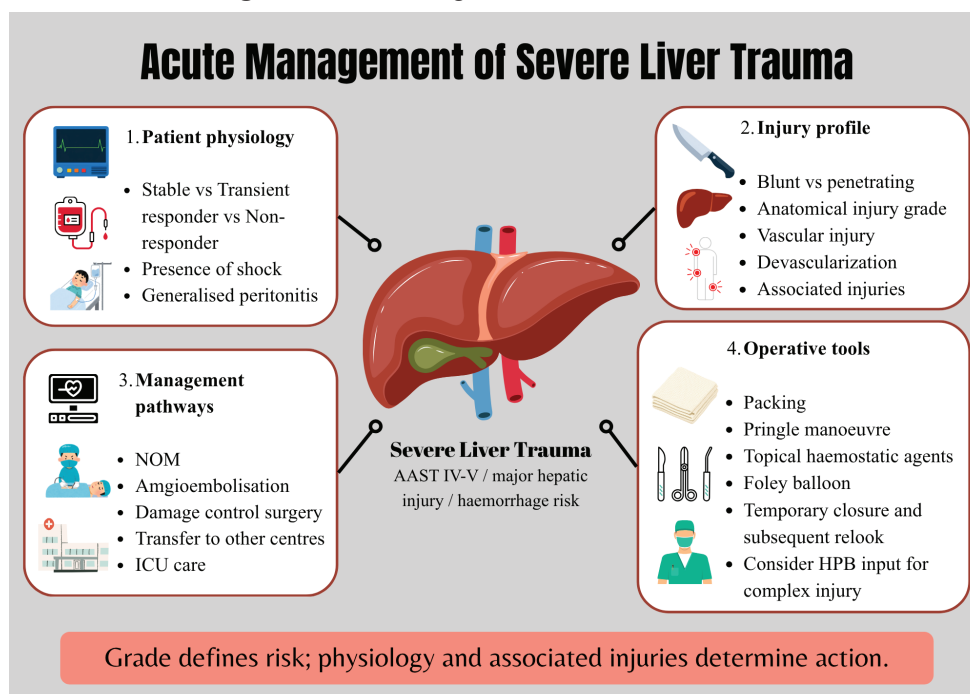
E-FAST examination does not exclude significant hepatic injury and should not override concerning physiology, mechanism or subsequent clinical deterioration.^{8,10} Contrast-enhanced CT is the investigation of choice in haemodynamically stable patients or those who have responded to resuscitation.^{8,10}

The practical decision is whether the patient can safely proceed to CT, angioembolization or observation. Stable patients should undergo contrast-enhanced CT to define the grade of liver injury, presence of vascular injury, presence and extent of haemoperitoneum and associated injuries. Transient responders require individualized assessment; CT is appropriate only after sufficient physiological stabilization and where immediate operative or endovascular rescue remains available. If CT and interventional radiology are immediately available, a hybrid pathway may be appropriate. Persistent non-responders and patients with generalized peritonitis should proceed to operative management.^{8,10}

Resuscitation and haemorrhage control should proceed as a single pathway. Massive-transfusion activation, active

warming, calcium replacement and correction of trauma-associated coagulopathy should accompany definitive haemostasis. Tranexamic acid should be administered as early as possible to patients who are bleeding or at risk of significant bleeding and within three hours of injury; treatment should not await viscoelastic results. Where available, thromboelastography or rotational thromboelastometry can subsequently guide goal-directed haemostatic therapy.¹¹ Whole blood may be incorporated into major-haemorrhage protocols according to local transfusion capability, although the 2026 SWiFT randomized trial did not demonstrate superiority of prehospital whole blood over standard component care for death or massive transfusion.¹² Resuscitative endovascular balloon occlusion of the aorta has been proposed as a temporary bridge in selected exsanguinating torso haemorrhage but is not a liver-specific treatment. The UK-REBOA randomized trial showed no survival benefit and possible harm; REBOA should therefore not delay laparotomy, packing or other definitive haemorrhage control.¹³ The principal acute assessment and treatment domains are illustrated in Figure 1.

Figure 1. Acute management of severe liver trauma.



The acute management of severe liver trauma is guided by four interrelated domains: patient physiology, injury profile, available management pathways and operative rescue tools. Anatomical grade identifies injury severity and complication risk but does not independently determine treatment. Haemodynamic response, peritonitis, associated injuries, computed tomography findings and institutional capability determine selection among non-operative management, angioembolization, damage control surgery, definitive surgery or transfer. Operative options include perihepatic packing, temporary inflow occlusion with the Pringle manoeuvre, balloon tamponade of selected deep bleeding tracts, temporary abdominal closure and planned relook surgery.

Abbreviations: AAST, American Association for the Surgery of Trauma; CT, computed tomography; HPB, hepatopancreatobiliary; ICU, intensive care unit; NOM, non-operative management.

Non-operative management of severe liver trauma

NOM is now the preferred approach for haemodynamically stable blunt liver trauma in appropriately selected patients.^{8,10,14} Landmark prospective and multicentre studies established that many adult blunt hepatic injuries can be managed without laparotomy when patients are stable and can be closely monitored. In Croce's prospective study, non-operatively managed patients required fewer transfusions than matched operative controls (1.9 vs 4.0 units) and had fewer abdominal complications (3% vs 11%).² Pachter's 13-centre study reported that 98.5% of 404 selected patients avoided laparotomy, although grade IV–V injuries accounted for two-thirds of those requiring operation.³ Malhotra and colleagues described the paradigm shift from operative to NOM in stable blunt hepatic injury.⁴ Van der Wilden subsequently reported 91.3% successful NOM among selected grade IV–V blunt injuries.¹⁵

This approach extends to carefully selected high-grade injuries. In a UK multicentre cohort of 190 grade IV–V injuries, 64% were initially managed non-operatively and only 7% subsequently required surgery. Liver-specific complications occurred in 18%, predominantly bile leak/biloma (20 patients) and abscess/infection (7 patients).¹⁶ Higher Injury Severity Score, lower admission systolic pressure, grade V injury and penetrating mechanism predicted operative treatment. Across the studies, successful NOM is primarily associated with stable or responding physiology, absence of another indication for laparotomy and reliable rescue capability; failure becomes more likely with physiological deterioration, ongoing bleeding, grade V injury and greater overall injury burden.^{8,14-16}

NOM is an active process which involves close monitoring and serial clinical examination. It requires a monitored setting, repeated clinical examination, serial haemoglobin and lactate assessment, access to blood products, immediate operative capability and a low threshold for repeat imaging or intervention when the clinical course changes. Intensive care or high-dependency monitoring is recommended for

many high-grade injuries, especially when there is large-volume haemoperitoneum, ongoing transfusion requirement, vascular injury, associated injuries or marginal physiology. The role of surveillance imaging remains unsettled. Repeat imaging aims principally to identify treatable vascular and biliary complications. The pooled risk of hepatic pseudoaneurysm rises to 4.6% after grade IV and 10.6% after grade V injury.¹⁷ Although older guidelines favour clinically triggered reimaging, recent prospective multicentre evidence found that scheduled imaging identified complications in 20.6% of grade IV and 34.1% of grade V injuries, with most detected within 36–72 hours.¹⁸ Braschi and colleagues subsequently reported liver-specific complications in 23.1% and reintervention in 19.2% among patients with grade IV–V injury in a two-centre cohort of 229 blunt liver injuries.¹⁹ Together, these findings support consideration of scheduled surveillance imaging after high-grade injury when detection would alter management, although the optimal timing, modality and patient selection remain uncertain. Venous thromboembolism prevention remains important during NOM. Mechanical prophylaxis is appropriate when not contraindicated, and low-molecular-weight heparin should be introduced once haemostatic stability is established.⁸

During NOM, escalation is prompted by haemodynamic deterioration, ongoing transfusion requirement or unexplained haemoglobin fall, rising lactate, new or increasing abdominal pain or peritonism, fever or sepsis, jaundice, or bilious drain output.^{8,14} A point of caution is that success in high-volume trauma centres should not be generalized to all hospitals. NOM is safest when deterioration can be recognized and rescued quickly. Smaller centres with limited capacity for close monitoring and rescue should have a low threshold for transferring to a trauma centre. Practical circumstances in which NOM should not be initiated or should be discontinued are summarized in Table 2.

Angioembolization and hybrid care

Angioembolization is a major adjunct in severe liver

Table 2. When NOM should not be initiated or continued

Situation	Key triggers
Immediate operation	Persistent instability/non-response; generalized peritonitis; associated injury requiring laparotomy
Local NOM unsafe	Inadequate monitoring, blood products, emergency surgery, or timely rescue/transfer
Failure of NOM	New instability; rising transfusion need or unexplained haemoglobin fall; worsening lactate/peritonism; significant delayed bleeding, vascular, biliary or septic complication

Note: High injury grade alone is not a contraindication to NOM in a stable patient with adequate monitoring and rescue capability.

trauma. Its main role is control of arterial bleeding in patients who are stable or stabilized enough to reach the angiography suite. Common indications include contrast blush, active arterial extravasation, pseudoaneurysm, arteriovenous fistula, delayed haemorrhage, haemobilia and persistent arterial bleeding after operative packing. Ciraulo and colleagues helped establish selective hepatic arterial embolization as an extension of resuscitation in grade IV and V blunt hepatic injury.²⁰

Contrast extravasation should not be equated automatically with mandatory embolization. In a 23-centre study of 128 stable patients with blunt liver injury and CT contrast extravasation, observation-first and angioembolization-first strategies had similar adjusted risks of liver-related complications and similar mortality.²¹ The embolization group had more severe anatomical injuries, and the study was not randomized; therefore, the findings support selective rather than reflex embolization but do not establish the superiority of observation.

A national registry analysis of 18,445 severe liver injuries found that the use of angioembolization increased between 2017 and 2022, while overall in-hospital mortality remained 18.7%.²² Integrated operative and endovascular pathways were associated with lower adjusted mortality than laparotomy alone, but registry data are limited in their ability to determine optimal treatment sequence or remove selection and survivor bias.

Angioembolization can support both non-operative and operative pathways. In stable patients with CT blush, it may prevent the failure of NOM. In unstable patients who undergo damage control laparotomy and packing, postoperative angiography may control persistent arterial bleeding that is difficult to control surgically. Hybrid operating rooms may reduce transfer delays, but their availability varies between centres.

Angioembolization should not be portrayed as risk-free. Mohr and colleagues described the combination of low mortality but high morbidity after hepatic embolization.²³ Later work highlighted hepatic necrosis as an important complication, especially after extensive embolization in high-grade injuries.²⁴ A systematic review likewise identified hepatic necrosis, abscess formation and bile leak or biloma as important morbidities after hepatic angioembolization.²⁵ These complications may require radiological drainage, endoscopic treatment or delayed surgery. Super-selective embolization, avoidance of unnecessary non-selective occlusion and close post-procedure surveillance are therefore important. When technically feasible,

segmental rather than main hepatic arterial embolization is preferred to limit ischaemic burden; temporary embolic agents such as Gelfoam may also be used according to bleeding pattern and interventional-radiology strategy.²⁶

Operative management and damage control surgery

Operative management remains essential for unstable non-responders, patients with generalized peritonitis and patients with associated injuries requiring laparotomy. The modern shift toward non-operative care should not create a false impression that operative skill is obsolete. Asensio and colleagues emphasized that trauma surgeons still need to operate for complex grade IV–V hepatic injuries, although angioembolization may help.²⁷

The initial operation should follow damage-control principles: rapid haemorrhage and contamination control, avoidance of prolonged definitive reconstruction, and transfer to intensive care for correction of hypothermia, acidosis and coagulopathy. Complex resections and definitive reconstructions should generally be avoided during index surgery. If resection or debridement is needed for the devascularized liver, this is usually safer if performed as a staged procedure by experienced trauma or hepatopancreatobiliary surgeons.

The Pringle manoeuvre remains useful because it is both therapeutic and diagnostic. Temporary occlusion of the hepatoduodenal ligament reduces hepatic arterial and portal venous inflow. A marked reduction in bleeding suggests a source from hepatic arterial or portal venous branches. If major bleeding persists, hepatic venous, retrohepatic caval or back-bleeding sources should be considered.

Major hepatic venous and retrohepatic caval injury

Persistent major haemorrhage despite effective portal triad occlusion should prompt consideration of a juxtahepatic hepatic venous or retrohepatic caval source, although aberrant arterial inflow should also be excluded. Unnecessary mobilisation of the injured liver may release posterior tamponade and convert partially controlled venous bleeding into exsanguinating haemorrhage. Manual compression and correctly directed perihepatic packing should therefore remain the initial strategy when they control bleeding.⁸

When packing achieves haemostasis in a patient with severely deranged physiology, the appropriate operation may be to stop. Correction of hypothermia, acidosis and coagulopathy takes priority over difficult vascular exposure. Persistent uncontrolled venous haemorrhage requires escalation according to anatomy, physiology and expertise.

Options include direct venorrhaphy after adequate vascular control, repair with selective or total hepatic vascular isolation, and selected lobar resection.⁸ Complete hepatic vascular exclusion may be poorly tolerated in profound shock. Veno-venous bypass and atriocaval shunting have been described but are technically demanding rescue strategies with historically high mortality and should not be regarded as routine next steps after packing.⁸

Useful operative manoeuvres include manual compression, anatomical packing, temporary inflow occlusion, selective vessel ligation, topical haemostatic adjuncts and temporary abdominal closure. Balloon tamponade has been described for selected deep transfixing or non-compressible hepatic tracts when direct compression and packing are insufficient, but it is an uncommon rescue technique rather than a routine component of liver-trauma surgery.^{8,29}

Perihepatic packing remains one of the most important damage control techniques. Packs should reconstitute normal liver anatomy while avoiding unnecessary caval compression or abdominal compartment syndrome (ACS). Persistent arterial bleeding after packing should prompt postoperative or intraoperative angiography when available. Pack removal should be planned after correction of major physiological derangement rather than performed reflexively. In a damage-control pathway, relook laparotomy and pack removal are undertaken after adequate intensive-care resuscitation, generally within approximately 24–72 hours; removal before the first 24 hours may increase rebleeding risk.³⁰ Packs should be removed sequentially in an operating room with immediate access to blood products and haemostatic rescue. Temporary abdominal closure allows correction of physiology, planned relook surgery and staged repair of liver injury. Recent bicentre observational data suggest that open-abdomen management with negative-pressure therapy is feasible in selected patients with major liver trauma.³¹

Hepatic arterial and portal venous injury

Major inflow vascular injury should be approached according to the vessel involved. An identifiable proper hepatic arterial injury should be repaired when feasible. If repair is not possible during damage-control surgery, selective right or left hepatic arterial ligation is preferable to unnecessary proximal arterial sacrifice. If the right or common hepatic artery must be ligated, cholecystectomy should be considered because of the risk of gallbladder ischaemia; hepatic necrosis, abscess and biloma are also recognized consequences of major arterial devascularization.⁸ Main portal

venous injury should preferentially undergo primary repair. Main portal vein ligation is an extreme salvage manoeuvre because hepatic necrosis and severe mesenteric venous congestion may follow, particularly when hepatic arterial inflow is compromised. For lobar or segmental portal venous injuries, packing or resection of unsalvageable parenchyma may be preferable to ligation.⁸

Resection and transplantation

The role of hepatic resection should distinguish limited resectional debridement from formal anatomical hepatectomy. Clearly devitalized or freely disrupted parenchyma may occasionally require limited resectional debridement, but major anatomical resection should rarely be undertaken as the initial haemostatic manoeuvre during uncontrolled shock. Once haemorrhage is controlled and physiology restored, staged segmental or lobar resection may be appropriate for irreversible devascularization, necrosis, uncontrolled sepsis or anatomically unsalvageable liver.⁸ Liver transplantation lies at the extreme end of this pathway. It is exceptionally uncommon but may be considered after otherwise unsalvageable hepatic destruction, extensive irreversible necrosis or post-traumatic hepatic failure when conventional reconstruction is not feasible. Only 72 liver transplants for trauma were identified in the United Network for Organ Sharing database between 1987 and 2022, underscoring the rarity and highly selected nature of this strategy.²⁸ Early discussion with a transplant centre is appropriate when such a trajectory becomes plausible.

Hepatopancreatobiliary input is valuable when there is juxtahepatic venous injury, major devascularization, complex bile duct injury, delayed necrosis, difficult biliary fistula or consideration of staged debridement/resection. However, the first operation in an unstable patient should remain damage-control focused. Specialist input is most valuable after initial damage control, when organ-preserving reconstruction or staged definitive management is considered. A cohort from a centre using a structured trauma–liver surgery partnership provides supportive observational evidence for early hepatobiliary involvement in complex high-grade injury. In a centre with an established active partnership between trauma and liver surgeons, operative 30-day mortality for grade IV–V injury was 23.4% and liver-attributable operative mortality was 15.7%.³² These observational outcomes cannot isolate the effect of specialist collaboration, but the model supports early HPB involvement when complex haemostasis, major devascularization or staged hepatic reconstruction is anticipated. Selected management options,

operative manoeuvres and their limitations are summarized in Table 3.

Penetrating liver trauma

Penetrating liver trauma requires particular attention to wound trajectory and associated hollow-viscus, diaphragmatic and vascular injuries. Haemodynamically unstable patients and those with peritonitis require laparotomy. Stable patients with low-energy penetrating injury may be considered for selective NOM in experienced centres if CT defines the tract, there is no generalized peritonitis and monitoring is reliable. Gunshot wounds, transabdominal trajectories, thoracoabdominal wounds and uncertainty about bowel injury lower the threshold for operative or laparoscopic evaluation. The principles of operative management are similar: control haemorrhage, avoid prolonged complex surgery during shock, manage contamination and plan staged rescue.³⁰ Angioembolization may still be useful when the dominant problem is arterial bleeding and the patient is stable enough for angiography. Recent national data suggest a selective role for angioembolization in penetrating liver trauma. After propensity matching, mortality did not differ significantly between angioembolization and surgery, 2.0% versus 4.8%, although angioembolization was associated with longer hospital, intensive-care and ventilation durations.³³ These findings support integration of endovascular treatment in stable or stabilized patients with a

dominant arterial bleeding source, but not its substitution for laparotomy in uncontrolled shock, peritonitis or suspected hollow-viscus injury.

Complications and delayed rescue

The second phase of severe liver trauma includes delayed haemorrhage, vascular complications, biliary complications, infection and tissue necrosis. High-grade injury carries a substantial risk of liver-related complications.³⁴ Greater injury severity, transfusion requirement, devascularization and associated abdominal injury are associated with increased hepatic morbidity.³⁵ Delayed haemorrhage or pseudoaneurysm is usually treated by angioembolization. Abscess is commonly managed with image-guided drainage and antibiotics, whereas hepatic necrosis requires individualized treatment ranging from drainage and antimicrobial therapy to staged debridement or resection.³⁵

Post-traumatic bile leakage ranges from small peripheral leaks that may resolve with drainage to central duct disruption, disconnected ducts and extrahepatic bile duct injury. Symptomatic bilomas should undergo image-guided drainage, which also helps quantify ongoing bile output.³⁶ In a 10-centre study of 2,225 patients with AAST grade III or higher liver injury, bile leak occurred in 5%, typically around hospital day 6; 30% were managed with drainage alone, while higher-output leaks more often required ERCP, percutaneous transhepatic drainage or surgery.³⁷ Persistent

Table 3. Current management options and operative tools

Situation or tool	Role	Key caution
Non-operative management	Stable blunt injury without peritonitis or other laparotomy indication	Requires monitoring and rescue capacity
Angioembolization	Arterial blush, pseudoaneurysm, delayed haemorrhage, persistent arterial bleeding after packing	Risk of necrosis, abscess, bile leak and re-bleeding
Manual compression	Immediate temporary control during laparotomy	Provides rapid temporary haemorrhage control while packing, vascular control or definitive rescue is prepared
Perihepatic packing	Damage control for major bleeding	Avoid overpacking and monitor for ACS
Pringle manoeuvre	Temporary inflow control; helps distinguish inflow from venous/caval bleeding	Persistent bleeding suggests non-inflow source
Foley balloon tamponade	Deep bleeding tract or cavity not controlled by surface packing	Bridge technique requiring reassessment
Temporary abdominal closure	Allows correction of physiology and planned relook	Requires active closure strategy and ICU care
HPB referral	Complex bile duct injury, devascularization, necrosis, staged resection/debridement	Should not delay initial life-saving damage control

HPB: hepatopancreatobiliary; ICU: intensive care unit; ACS: Abdominal compartment syndrome

or high-output leakage should prompt biliary decompression. ERCP with transpapillary stenting, with selective sphincterotomy, is appropriate when ductal continuity is preserved. An output of approximately 300–400 mL/day has been proposed as a pragmatic threshold for considering ERCP, although this is not absolute.³⁷ Nasobiliary drainage can provide temporary decompression and repeat cholangiographic assessment, while percutaneous transhepatic drainage is useful when endoscopic access is not possible or for selected proximal/disconnected ducts. Extrahepatic bile duct injury is rare and may present late; a systematic review of 66 blunt-trauma injuries reported a mean diagnosis at 11 days in stable patients initially managed non-operatively.³⁸ Persistent jaundice, recurrent bilious collections or bile peritonitis should raise concern for a major bile leak or duct injury and prompt further biliary evaluation.³⁹ Biliothorax, including biliopleural fistula, is uncommon and generally requires pleural drainage with control of the biliary source.⁴⁰ Major duct disruption, uncontrolled sepsis or failure of endoscopic/percutaneous treatment warrants early HPB involvement and consideration of definitive reconstruction after physiological stabilization.

ACS should be anticipated after massive transfusion, visceral oedema, extensive packing, ongoing shock or temporary abdominal closure. ACS should be suspected when increasing abdominal distension or tension is accompanied by new organ dysfunction. Bladder-pressure measurement can confirm the diagnosis when clinically suspected; routine pressure monitoring is unnecessary in patients without relevant risk or clinical features. ACS is defined by sustained

intra-abdominal pressure above 20 mmHg with new organ dysfunction and requires urgent recognition because progressive organ failure may be fatal.⁴¹

Longer-term outcomes after severe trauma include physical function, return to work, psychological health and quality of life. Future liver-trauma studies should therefore complement mortality and procedural outcomes with functional recovery and validated patient-reported outcomes.⁴²

Outcome reporting in liver trauma is also becoming more standardized. A 2026 modified Delphi study involving 20 experts identified 12 core outcomes across operative decision-making, success of non-operative management, hepatic complications and healthcare utilization, with strong inter-rater agreement.⁴³ Future studies should report these core clinical outcomes consistently, while functional recovery, quality of life and patient-reported outcomes should be developed as complementary longer-term endpoints. Landmark evidence shaping current liver-trauma management is summarized in Table 4. The multidisciplinary rescue, recovery and systems-of-care pathway is illustrated in Figure 2.

Resource-sensitive pathway

Severe liver trauma is best managed as a system rather than a single technical problem, with trauma and HPB surgery, interventional radiology, critical care, transfusion medicine and endoscopy contributing at different stages. Safe non-operative management of grade IV–V injury is resource dependent and requires serial reassessment, blood products, emergency operative rescue and access to further haemostatic intervention.^{8,10} Observation without

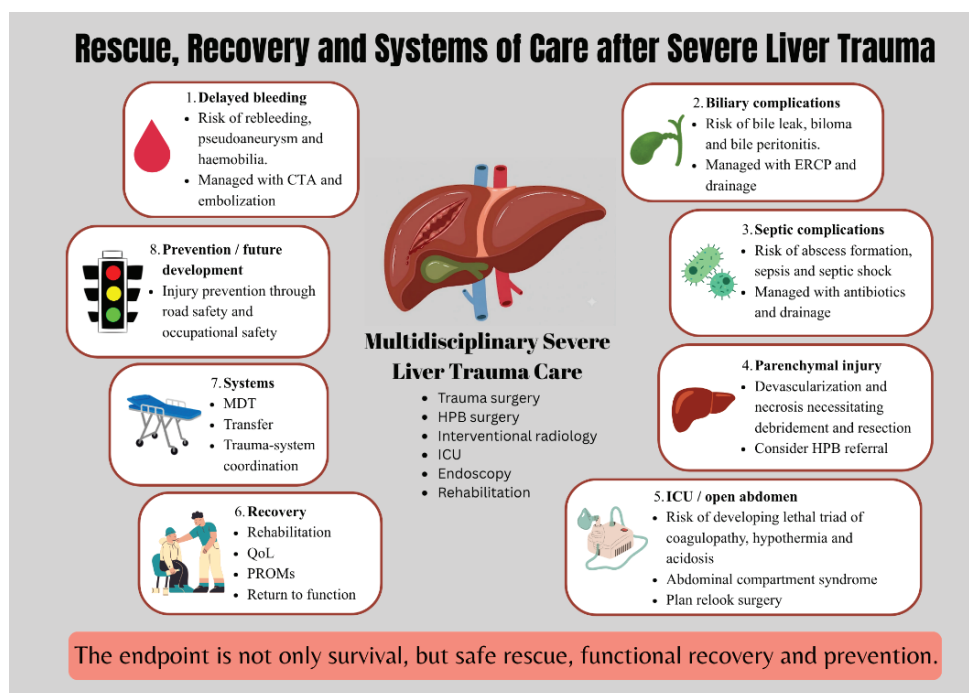
Table 4. Landmark and contemporary evidence in severe liver trauma

Study	Design and population	Key findings	Clinical contribution
Pringle ¹ , 1908	Historical operative description	Temporary occlusion of the hepatoduodenal ligament was described to arrest traumatic hepatic haemorrhage.	Established temporary hepatic inflow control; the manoeuvre remains both therapeutic and diagnostically useful during trauma laparotomy.
Pachter et al. ³ , 1996	Multicentre study of 404 adults managed non-operatively at 13 level I trauma centres	Demonstrated that selected haemodynamically stable blunt liver injuries could be managed without mandatory laparotomy.	Landmark multicentre validation of non-operative management, provided close monitoring and operative rescue are available.
Asensio et al. ²⁷ , 2003	Operative series of 103 AAST grade IV–V injuries	Mean Injury Severity Score was 33, mean estimated blood loss was 9414 mL and overall survival was 43%; 80 injuries were penetrating.	Illustrates the extreme physiological burden of injuries requiring operation and the continuing importance of damage control surgery.
van der Wilden et al. ¹⁵ , 2012	Multicentre cohort of 393 adults with grade IV–V blunt liver injury	NOM was attempted in 262 of 393 patients (66.7%) and succeeded in 91.3%.	Established the feasibility of non-operative management for selected high-grade blunt injuries.

WSES ⁸ , 2020	International evidence-based guideline	Recommended integration of anatomical grade, haemodynamic status and associated injuries; supported non-operative management of stable high-grade injuries in appropriately resourced centres.	Provides the principal multidisciplinary framework for modern management.
Nguyen et al. ²¹ , 2024	WTA multicentre study of 128 stable patients with blunt liver injury and CT contrast extravasation	Observation-first and angioembolization-first strategies had similar mortality, 5.3% versus 5.7%. After adjustment, an embolization-first strategy was not independently associated with more liver-related complications.	Suggests that CT contrast extravasation alone should not mandate reflex angioembolization in every stable patient.
Ramos-Jimenez et al. ³² , 2025	Single-centre cohort of 179 grade IV–V injuries managed through trauma surgery–liver surgery collaboration	Among operatively managed patients, 30-day mortality was 23.4% and liver-attributable mortality was 15.7%; 19.4% of planned non-operative management failed.	Supports early liver-surgery involvement for complex haemorrhage, devascularization, venous injury and staged definitive treatment.
Schaid et al. ²² , 2025	TQIP study of 18,445 severe liver injuries, 2017–2022	Observation was used in 47.0%, laparotomy alone in 42.7%, laparotomy followed by embolization in 5.1% and embolization alone in 4.5%. Overall mortality remained 18.7% despite increasing embolization use.	Shows that severe liver injury mortality remains substantial and supports integrated operative–endovascular pathways rather than reliance on a single modality.
Brooks et al. ¹⁶ , 2026	UK multicentre study of 190 grade IV–V injuries	Initial non-operative management was used in 64%; only 7% subsequently required surgery. Overall mortality was 7% and liver-specific complications occurred in 18%.	Provides contemporary multicentre support for high-grade non-operative management while emphasizing continued complication surveillance.
Cirillo et al. ⁹ , 2026	Protocolized single-centre cohort of 350 blunt and penetrating injuries	Non-operative management was initiated in 86.9%, with conversion to laparotomy in 4.9%. Shock index, Injury Severity Score and lactate predicted mortality, whereas AAST grade alone had limited discrimination.	Reinforces physiology-first decision-making and the limited value of anatomical grade as an isolated treatment trigger.
Braschi et al. ¹⁹ , 2026	Two-centre study of 229 blunt liver injuries	Grade IV–V injuries had liver-specific complications in 23.1% and required re-intervention in 19.2%, compared with 2.0% and 2.6%, respectively, for grade II–III injuries.	Reopens the question of scheduled surveillance imaging after high-grade injury, although optimal timing and patient selection remain uncertain.
Cain et al. ⁴³ , 2026	Modified Delphi consensus involving 20 trauma surgery experts	The expert panel generated 102 initial suggestions, which were consolidated into 41 unique outcomes; 12 outcomes reached final consensus across four domains. Inter-rater agreement was strong (ICC 0.89).	Provides a standardized outcome set for future liver-trauma studies and facilitates comparison across centres and management strategies.
Schellenberg et al. ³⁷ , 2022	Retrospective 10-centre study of 2,225 patients with AAST grade $\geq$ III liver injury	Bile leak occurred in 108 patients (5%); 30% were managed with external drainage alone, while patients requiring ERCP, PTBD or surgery had significantly higher bilious drain output	Defines the burden of post-traumatic bile leak and supports a step-up approach in which external drainage may suffice for selected patients, with persistent or higher-output leaks prompting biliary intervention

Abbreviations: AAST, American Association for the Surgery of Trauma; CT, computed tomography; TQIP, Trauma Quality Improvement Program; WSES, World Society of Emergency Surgery; WTA, Western Trauma Association; ERCP, Endoscopic retrograde cholangiopancreatography; PTBD, Percutaneous transhepatic biliary drainage.

Figure 2. Rescue, recovery and systems of care after severe liver trauma.



Management extends beyond initial haemorrhage control and includes surveillance and rescue for delayed bleeding, pseudoaneurysm, haemobilia, biliary complications, abscess, sepsis, hepatic devascularization or necrosis, and complications related to critical illness or the open abdomen. Treatment may require repeat imaging, angioembolization, percutaneous drainage, endoscopic therapy, antibiotics, reoperation, staged hepatic debridement or resection, and hepatopancreatobiliary referral. Multidisciplinary care incorporates trauma surgery, hepatopancreatobiliary surgery, interventional radiology, intensive care, endoscopy and rehabilitation. Longer-term priorities include functional recovery, quality of life, patient-reported outcomes, trauma-system coordination, and injury prevention.

Abbreviations: ACS, abdominal compartment syndrome; CTA, computed tomography angiography; ERCP, endoscopic retrograde cholangiopancreatography; HPB, hepatopancreatobiliary; ICU, intensive care unit; MDT, multidisciplinary team; PROMs, patient-reported outcome measures; QoL, quality of life.

reliable rescue capability should not be regarded as equivalent to non-operative management in a mature trauma system.

Stable or adequately stabilized patients whose needs exceed local capability should be discussed early with a definitive trauma or HPB centre. Arterial injury requiring embolization, extensive devascularization, suspected juxtahepatic venous injury or complex biliary, vascular or hepatic complications should lower the threshold for transfer; outcomes from specialist centres should be interpreted in the context of the systems that enabled them.^{16,32} Persistent non-responders require local haemorrhage control before transfer. Where interventional radiology is unavailable and the liver is the dominant bleeding source, manual compression and perihepatic packing may be the primary damage-control operation.⁸ Once haemorrhage is controlled, temporary abdominal closure, continued resuscitation and transfer may be safer than unnecessary liver mobilisation, caval exposure

or formal hepatectomy. A practical pack–resuscitate–transfer pathway should communicate the injury pattern, physiological trajectory, transfusion, packs placed, portal triad occlusion, vascular ligation, suspected caval injury and abdominal closure. Local management of grade IV–V injury requires monitored care, blood-product support, contrast-enhanced CT, immediate operative capability and critical care, with interventional radiology, advanced endoscopy, vascular and HPB expertise available locally or through a defined transfer network. Regional systems should support clear referral criteria, shared imaging and direct surgeon-to-surgeon communication.

Conclusion

Current management of severe liver trauma is physiology-first, multidisciplinary and staged. Anatomical grade identifies risk, but haemodynamic response, peritonitis, associated injuries, CT findings and rescue capacity determine treatment. Stable patients with high-grade blunt

liver injury can often be managed non-operatively when monitoring, blood products, urgent surgery and angioembolization are available. Unstable patients still require operative skill, damage control surgery and timely escalation. The best outcomes depend not on choosing operation or observation as an ideology, but on selecting the right intervention at the right time and rescuing complications before they become irreversible.

Author contributions

Dai Ailin: Literature review; clinical interpretation; tables and figures; critical revision and final approval of the manuscript.

Rebekah Young: Literature review; clinical interpretation; critical revision of the manuscript; and final approval of the manuscript.

Vishal G. Shelat: Conceptualization; literature review; interpretation of evidence; development of the clinical framework, tables and figures; writing of the original draft; critical revision and final approval of the manuscript.

All authors meet the International Committee of Medical Journal Editors criteria for authorship, have reviewed and approved the final manuscript, and accept responsibility for the integrity of the work.

Declarations

Funding

No financial support or funding was received for this manuscript.

Conflicts of Interest

The authors declare no potential conflicts of interest concerning the research, authorship, or publication of this article.

Data Availability

Data sharing is not applicable as no data was collected for this study. All referenced sources are cited within the manuscript.

Consent

Not applicable. No individual patient data or human participants were involved in this study.

Ethical Approval

Ethical approval was not required as no data was collected.

Use of generative artificial intelligence

Generative artificial intelligence (ChatGPT, OpenAI) was used during manuscript preparation and revision to assist with language refinement of selected text. All scientific content, clinical recommendations, numerical data and references were reviewed and verified by the authors. The authors take full responsibility for the content of the manuscript.

References:

1. Pringle JH. V. Notes on the Arrest of Hepatic Hemorrhage Due to Trauma. *Ann Surg.* 1908;48(4):541-549. doi:10.1097/00000658-190810000-00005
2. Croce MA, Fabian TC, Menke PG, et al. Nonoperative management of blunt hepatic trauma is the treatment of choice for hemodynamically stable patients. Results of a prospective trial. *Ann Surg.* 1995;221(6):744-755. doi:10.1097/00000658-199506000-00013
3. Pachter HL, Knudson MM, Esrig B, et al. Status of nonoperative management of blunt hepatic injuries in 1995: a multicenter experience with 404 patients. *J Trauma.* 1996;40(1):31-38. doi:10.1097/00005373-199601000-00007
4. Malhotra AK, Fabian TC, Croce MA, et al. Blunt hepatic injury: a paradigm shift from operative to nonoperative management in the 1990s. *Ann Surg.* 2000;231(6):804-813. doi:10.1097/00000658-200006000-00004
5. American College of Surgeons. *Advanced Trauma Life Support (ATLS) Course Manual.* 11th ed. American College of Surgeons; 2025
6. Reed CR, Brown JB, Peitzman AB. Liver injury: What you need to know. *J Trauma Acute Care Surg.* 2026 Jan 1;100(1):1-11. doi: 10.1097/TA.0000000000004684.
7. Kozar RA, Crandall M, Shanmuganathan K, et al. Organ injury scaling 2018 update: Spleen, liver, and kidney. *J Trauma Acute Care Surg.* 2018;85(6):1119-1122. doi:10.1097/TA.0000000000002058
8. Coccolini F, Coimbra R, Ordonez C, et al. Liver trauma: WSES 2020 guidelines. *World J Emerg Surg.* 2020;15(1):24. Published 2020 Mar 30. doi:10.1186/s13017-020-00302-7
9. Cirillo B, Brachini G, Cirocchi R, et al. Contemporary management pathways in liver trauma: predominant and successful use of non-operative strategies at a high-volume tertiary center. *Langenbecks Arch Surg.* 2026;411(1):168. doi:10.1007/s00423-026-04051-0
10. Keric N, Shatz DV, Schellenberg M, et al. Adult blunt hepatic injury: A Western Trauma Association critical decisions algorithm. *J Trauma Acute Care Surg.* 2024;96(1):123-128. doi:10.1097/TA.0000000000004141
11. Rossaint R, Afshari A, Bouillon B, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. *Crit Care.* 2023 Mar 1;27(1):80. doi: 10.1186/s13054-023-04327-7.

12. Smith JE, Cardigan R, Sanderson E, et al. SWiFT Trial Group. Prehospital Whole Blood in Traumatic Hemorrhage - A Randomized Controlled Trial. *N Engl J Med*. 2026 Jun 18;394(23):2305-2316. doi: 10.1056/NEJMoa2516043.
13. Jansen JO, Hudson J, Cochran C, et al. Emergency Department Resuscitative Endovascular Balloon Occlusion of the Aorta in Trauma Patients With Exsanguinating Hemorrhage: The UK-REBOA Randomized Clinical Trial. *JAMA*. 2023 Nov 21;330(19):1862-1871. doi: 10.1001/jama.2023.20850.
14. Stassen NA, Bhullar I, Cheng JD, et al. Nonoperative management of blunt hepatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73(5 Suppl 4):S288-S293. doi:10.1097/TA.0b013e318270160d
15. van der Wilden GM, Velmahos GC, Emhoff T, et al. Successful nonoperative management of the most severe blunt liver injuries: a multicenter study of the research consortium of new England centers for trauma. *Arch Surg*. 2012;147(5):423-428. doi:10.1001/archsurg.2012.147
16. Brooks A, Joyce D, Gouveia S, et al. Outcomes following non-operative management for severe liver trauma: a UK multicentre observational study. *Scand J Trauma Resusc Emerg Med*. 2026;34(1):70. doi:10.1186/s13049-026-01576-7
17. Duncan T, Hajibandeh S, Hajibandeh S, et al. The risk of hepatic pseudoaneurysm after liver trauma in relation to the severity of liver injury: a meta-analysis and meta-regression analysis. *Langenbecks Arch Surg*. 2023;408(1):61. doi:10.1007/s00423-023-02794-8
18. Perea LL, Fletcher KL, Morgan ME, et al. Moderate- to High-grade Blunt Liver and Spleen Injuries Warrant Repeat Imaging to Identify Treatable Complications: Results of the Radiographic Evaluation of Delayed Solid Organ Complications EAST Multicenter Trial. *Ann Surg*. 2025;282(4):580-591. doi:10.1097/SLA.00000000000006831
19. Braschi C, Brosnihan P, Senekjian L, Brennan P, Cyprich J, Keeley JA. Reimaging High-Grade Blunt Hepatic Injuries: Revisiting the Role of Routine Surveillance in Modern Nonoperative Management. *J Surg Res*. 2026 Feb;318:318-322. doi: 10.1016/j.jss.2025.12.016.
20. Ciraulo DL, Luk S, Palter M, et al. Selective hepatic arterial embolization of grade IV and V blunt hepatic injuries: an extension of resuscitation in the nonoperative management of traumatic hepatic injuries. *J Trauma*. 1998;45(2):353-359. doi:10.1097/00005373-199808000-00025
21. Nguyen PD, Nahmias J, Aryan N, et al. Observation-first versus angioembolization-first approach in stable patients with blunt liver trauma: a WTA multicenter study. *J Trauma Acute Care Surg*. 2024;97(5):764-769. doi:10.1097/TA.00000000000004372
22. Schaid TR Jr, Moore EE, Williams R, et al. Severe liver injuries in a contemporary national trauma registry: in-hospital mortality remains high regardless of therapeutic approach. *Surgery*. 2025;184:109457. doi:10.1016/j.surg.2025.109457
23. Mohr AM, Lavery RF, Barone A, et al. Angiographic embolization for liver injuries: low mortality, high morbidity. *J Trauma*. 2003;55(6):1077-1082. doi:10.1097/01.TA.0000100219.02085.AB
24. Dabbs DN, Stein DM, Scalea TM. Major hepatic necrosis: a common complication after angioembolization for treatment of high-grade liver injuries. *J Trauma*. 2009;66(3):621-629. doi:10.1097/TA.0b013e31819919f2
25. Green CS, Bulger EM, Kwan SW. Outcomes and complications of angioembolization for hepatic trauma: A systematic review of the literature. *J Trauma Acute Care Surg*. 2016;80(3):529-537. doi:10.1097/TA.0000000000000942
26. Nguyen PD, Nahmias J, Aryan N, et al. Main versus segmental hepatic artery angioembolization in patients with traumatic liver injuries: a Western Trauma Association multicenter study. *Surgery*. 2025;178:108909. doi:10.1016/j.surg.2024.10.002
27. Asensio JA, Roldán G, Petrone P, et al. Operative management and outcomes in 103 AAST-OIS grades IV and V complex hepatic injuries: trauma surgeons still need to operate, but angioembolization helps. *J Trauma*. 2003;54(4):647-654. doi:10.1097/01.TA.0000054647.59217.BB
28. Orozco G, Gupta M, Ancheta A, Shah MB, Warriner Z, Marti F, Mei X, Desai S, Bernard A, Gedaly R. Liver transplantation for severe hepatic trauma: A multicenter analysis from the UNOS data set. *J Trauma Acute Care Surg*. 2024 May 1;96(5):763-768. doi: 10.1097/TA.00000000000004220.
29. Thomas SV, Dulchavsky SA, Diebel LN. Balloon tamponade for liver injuries: case report. *J Trauma*. 1993;34(3):448-449. doi:10.1097/00005373-199303000-00026
30. Ordoñez CA, Parra MW, Millán M, et al. Damage Control in Penetrating Liver Trauma: Fear of the Unknown. *Colomb Med (Cali)*. 2020;51(4):e4134365. Published 2020 Dec 30. doi:10.25100/cm.v51i4.4422.4365
31. Coppola A, Mottola A, Della Corte M, et al. Safety and feasibility of open abdomen with negative pressure therapy in major liver trauma: a retrospective bicenter study. *Langenbecks Arch Surg*. 2025;410(1):160. doi:10.1007/s00423-025-03729-1
32. Ramos-Jimenez RG, Deeb AP, Truong EI, et al. High-grade liver injury: outcomes with a trauma surgery-liver surgery collaborative approach. *Trauma Surg Acute Care Open*. 2025;10(1). doi:10.1136/tsaco-2024-001611
33. Ku YK, Chen HW, Chan SY, et al. Outcomes of angioembolization in penetrating hepatic trauma: equivalent survival, longer hospitalization. *Surgery*. 2026;197:110393. doi:10.1016/j.surg.2026.110393
34. Kozar RA, Moore JB, Niles SE, et al. Complications of

nonoperative management of high-grade blunt hepatic injuries. *J Trauma*. 2005;59(5):1066-1071. doi:10.1097/01.ta.0000188937.75879.ab

35. Kozar RA, Moore FA, Cothren CC, et al. Risk factors for hepatic morbidity following nonoperative management: multicenter study. *Arch Surg*. 2006;141(5):451-459. doi:10.1001/archsurg.141.5.451

36. Wahl WL, Brandt MM, Hemmila MR, Arbabi S. Diagnosis and management of bile leaks after blunt liver injury. *Surgery*. 2005;138(4):742-748. doi:10.1016/j.surg.2005.07.021

37. Schellenberg M, Ball CG, Owattanapanich N, et al, TAC Bile Leaks Study Group. Diagnosis and management of bile leaks after severe liver injury: A Trauma Association of Canada multicenter study. *J Trauma Acute Care Surg*. 2022 Dec 1;93(6):813-820. doi: 10.1097/TA.0000000000003765.

38. Pereira R, Vo T, Slater K. Extrahepatic bile duct injury in blunt trauma: A systematic review. *J Trauma Acute Care Surg*. 2019 May;86(5):896-901. doi: 10.1097/TA.0000000000002186.

39. Yuan KC, Wong YC, Fu CY, Chang CJ, Kang SC, Hsu YP. Screening and management of major bile leak after blunt liver trauma: a retrospective single center study. *Scand J Trauma Resusc Emerg Med*. 2014 Apr 15;22:26. doi: 10.1186/1757-7241-22-26.

40. Acharya R, Kafle S, Sedhai YR, Shrestha DB, Walsh K, Shamsi WE, Gyawali S, Acharya N, Loschner AL, Rubio ER. Biliothorax: A Case Report and Systematic Literature Review of the Rare Entity. *Pulm Med*. 2024 Jun 21;2024:3973056. doi: 10.1155/2024/3973056.

41. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med*. 2013;39(7):1190-1206. doi:10.1007/s00134-013-2906-z

42. Lotfalla A, Halm J, Schepers T, Giannakópoulos G. Health-related quality of life after severe trauma and available PROMS: an updated review (part I). *Eur J Trauma Emerg Surg*. 2023;49(2):747-761. doi:10.1007/s00068-022-02178-5

43. Cain CD, Byerly S, Stassen NA, et al. Core outcome set for liver trauma: a consensus approach using modified Delphi methodology. *Trauma Surg Acute Care Open*. 2026;11(1). doi:10.1136/tsaco-2025-002164

Surgical Management of Intrahepatic Cholangiocarcinoma: From Technical Resectability to Biological Decision-Making

José M. Ramia ^{1,2,3}, Celia Villodre-Tudela ^{1,2,3}, Paola Melgar-Requena ^{1,2}, Juan Jesus Rubio ^{1,2}, Mariano Franco-Campello ^{1,2}, Cándido F. Alcázar-López ^{1,2,3}

¹ Unidad de Cirugía HPB y Trasplante Hepático, Servicio de Cirugía General y del Aparato Digestivo, Hospital General Universitario Dr. Balmis, Alicante, Spain.

² ISABIAL Alicante, Spain.

³ Universidad Miguel Hernández. Alicante. Spain

Corresponding Author:

JOSÉ MANUEL RAMIA, MD, PHD, FACS, FRCS, FRCS(ED), FKCS

Hospital General Universitario Dr. Balmis
Avda Pinto Baeza 11, 03010 Alicante (Spain)

ORCID 0000-0002-3532-932X

E-mail: jose_ramia@hotmail.com

Abstract

Intrahepatic cholangiocarcinoma (ICC) remains one of the most challenging malignancies in hepatobiliary surgery. Although surgical resection offers the only potential for cure, up to half of patients are unresectable at diagnosis, and long-term survival remains poor. More importantly, contemporary surgical decision-making has evolved beyond technical resectability toward identifying patients most likely to derive meaningful oncological benefit from surgery. This narrative review examines the major clinical decisions that define modern surgical management of ICC, including patient selection, preoperative staging, extent of hepatic resection, lymphadenectomy, resection margins, and minimally invasive surgery. Rather than reviewing these topics independently, the available evidence is interpreted through the emerging concept of futile resection and its relationship with tumor biology.

Current international evidence is integrated with our experience from the Spanish multicenter ICC registry

(SPAIC), including studies on surgical complexity, futility, minimally invasive surgery, and failure to rescue. Across the available literature, biological factors—particularly lymph node metastases, multifocal disease, and advanced T stage—consistently outweigh technical aspects of surgery in determining long-term outcome. Complexity classifications and futility prediction models should therefore be considered complementary tools: the former guiding how surgery should be performed, the latter helping determine whether surgery should be performed at all.

Future progress in ICC surgery will depend on integrating imaging, biomarkers, operative complexity, and tumor biology into individualized multidisciplinary decision-making, allowing surgeons to select not only technically resectable patients, but those most likely to benefit from resection.

Keywords: intrahepatic cholangiocarcinoma; liver resection; futility; lymphadenectomy; minimally invasive surgery; tumor biology.

Introduction

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver malignancy and the most biologically aggressive of the three anatomical subtypes of cholangiocarcinoma. Its incidence has risen steadily over the past two decades in most Western series, a trend attributed only partly to improved diagnostic recognition. Despite advances in imaging and systemic therapy, up to 54% of patients remain unresectable at diagnosis, and five-year survival after resection ranges only from 20% to 39%¹.

Surgery remains the only potentially curative treatment. However, the central question in contemporary ICC surgery has evolved from whether a tumor is technically resectable to whether resection is likely to provide meaningful benefit for an individual patient. The concept of futile resection—an operation that achieves technical success without improving oncological outcome—has therefore emerged as a key consideration in multidisciplinary decision-making.

Rather than reviewing surgical management as a series of isolated technical topics, this narrative review is organized around the major clinical decisions that define the management of ICC: who should undergo surgery, how extensive and radical resection should be, how surgery should be performed, how operative complexity can be anticipated, and ultimately whether resection is likely to benefit the patient. Throughout the review, current international evidence is integrated with our experience from the Spanish multicentre ICC registry (SPAIC), including recent work on surgical complexity, minimally invasive surgery, failure to rescue, and futility after ICC resection.

Search Strategy

For this narrative review, we searched PubMed/MEDLINE and Scopus for articles published in English between January 2015 and August 2026, using combinations of the terms “intrahepatic cholangiocarcinoma”, “liver resection”, “hepatectomy”, “futile resection”, “futility”, “lymphadenectomy”, “resection margin”, “minimally invasive surgery”, “laparoscopic”, “robotic”, and “surgical complexity”. Reference lists of retrieved articles, recent systematic reviews, and current international clinical practice guidelines^{3,12} were manually screened for additional relevant studies. Because this is a narrative rather than a systematic review, no PRISMA-based selection process or formal quality appraisal was applied;

articles were instead selected by the authors according to methodological quality, sample size, and relevance to the clinical questions addressed, with priority given to studies published within the last decade. Findings from our own multicenter Spanish ICC registry (SPAIC) are integrated throughout the review^{9,17,24}. The main studies discussed, together with their design, population, and key findings, are summarized in Table 1.

Patient Selection: Imaging, Biomarkers, and Staging Laparoscopy

Preoperative patient selection relies primarily on high-quality cross-sectional imaging. Contrast-enhanced CT remains the cornerstone for assessing local tumor extent and resectability, with an overall staging accuracy of approximately 70% (sensitivity 78%, specificity 80%) and a negative predictive value for resectability of 85–100% (Figure 1). However, its performance for nodal staging is considerably lower, with an accuracy of only 77%¹. MRI with MRCP provides complementary information, increasing overall staging accuracy to approximately 93%, although sensitivity for lymph node metastases remains limited (74%)¹. PET-CT is particularly useful for detecting occult extrahepatic disease and for identifying unsuspected metastases in 20–30% of patients who appear resectable on conventional imaging¹.

Imaging findings should always be interpreted together with clinical presentation and serum biomarkers, as no single modality is sufficiently accurate to define resectability or biological aggressiveness.

Serum CA19-9 remains a valuable adjunct rather than a stand-alone decision-making tool. However, its interpretation requires caution in patients with biliary obstruction, as cholestasis may cause marked elevations that are unrelated to tumor burden. Whenever possible, CA19-9 should therefore be interpreted after adequate biliary drainage and resolution of jaundice. Values above 100 U/mL support the clinical suspicion of ICC with good specificity and sensitivity, whereas concentrations exceeding 1000 U/mL should raise concern for biologically advanced or metastatic disease¹.

Despite continuous improvements in cross-sectional imaging and serum biomarkers, accurate preoperative staging remains challenging, particularly for lymph node metastases. A lymph node with a short-axis diameter ≥ 10 mm has only about 50% sensitivity for metastatic involvement. Consequently, staging laparoscopy continues to play an important role by avoiding unnecessary

Table 1. Summary of the main studies discussed in this review.

Study (ref.)	Country / data source	Design & population (n)	Focus	Key finding(s)
Nam et al., 2017 ⁵	South Korea (2 centers)	Retrospective, n=718	Preoperative futility nomogram	Futile resection in 13.8%; nodal enlargement, multifocality, IHD stones and NLR ≥ 2.7 independent predictors (C-index 0.85/0.74)
Chu et al., 2021 ⁶	China (2 centers)	Retrospective, n=203	CT-radiomics futility model	Radiomics model AUC 0.80 vs. clinical variables alone AUC 0.59
Altaf et al., 2025 ⁷	International (15 institutions)	Retrospective, n=889	Online futility calculator	Resection discouraged if predicted 90-day mortality >25% or expected survival <18 months
Kawashima et al., 2025 ⁸	International multicenter	Retrospective, n=1,138	“Biological R2” concept	Biological R2 in 9.3%; driven by nodal disease, T stage and cirrhosis; margin width not independently associated
Ramia et al. (SPAIC), 2026 ⁹ (submitted)	Spain (multi-center)	Retrospective, n=282	Composite futility endpoint	Futility 40.1%; T3 stage OR 8.03; minor hepatectomy protective, OR 0.34
Nassar et al., 2022 ¹⁰	France (2 centers)	Retrospective, n=120	Early recurrence / frozen-section nodal assessment	Positive frozen-section nodes predicted early recurrence (OR 3.31) and death <12 months (OR 12.70)
Lang et al., 2021 ¹¹	Germany (single center)	Retrospective, n=286 explored	Long-term outcomes, margins, LN yield	No survival difference R0 vs. R1; lymphadenectomy in ~90% (median 5 nodes)
Torzilli et al., 2020 ¹³	Italy (single center)	Retrospective cohort	Vascular R1 concept	Intentional vascular R1 margin oncologically acceptable vs. gross residual disease
Hammad et al., 2016 ¹⁴	USA (National Cancer Database)	Retrospective, n=2,897	Margins, LN status, adjuvant radiotherapy	Median survival 31.2 vs. 19.5 months (R0 vs. R1/R2); R1 HR 1.47, R2 HR 1.57
Kim et al., 2025 ¹⁵	Multicenter (Asia)	Retrospective validation cohort	Validation of prognostic models	External validation of existing postsurgical prognostic models
Shen et al., 2023 ¹⁶	China	Propensity-matched cohort	Laparoscopic safety/feasibility	Laparoscopic resection safe and feasible, with comparable oncological outcomes
Ramia et al. (SPAIC), 2026 ¹⁷ (submitted)	Spain (multi-center)	Retrospective, external validation	Complexity classification validation	Class II: higher major morbidity (66.7% vs. 18.5%), perineural invasion and LN metastases; no Class III cases
Yoh et al., 2025 ¹⁸	Japan / multi-center	Retrospective, original classification cohort	Surgical complexity classification	Defines Class I–III operative complexity (simple, combined biliary, major vascular)
Aliseda et al., 2023 ¹⁹	International (meta-analysis)	Systematic review/meta-analysis of PSM studies	Laparoscopic vs. open	Modest survival advantage for laparoscopy in pooled PSM analysis
Hu et al., 2023 ²⁰	International (systematic review)	Systematic review of PSM studies	Laparoscopic vs. open	Equivalent OS/DFS; improved perioperative outcomes with laparoscopy
Zhao et al., 2023 ²¹	International (meta-analysis)	Meta-analysis/systematic review	Laparoscopic vs. open	Equivalent oncological outcomes; lower blood loss/length of stay with laparoscopy
Brustia et al., 2022 ²²	International multicenter	Propensity-matched cohort	Laparoscopic vs. open	Survival advantage disappeared once restricted to patients with adequate nodal staging
Yang et al., 2022 ²³	China (multi-center)	Matched database study	Laparoscopic vs. open, learning curve	Improved outcomes only after excluding learning-curve cases and advanced-stage tumors
Ramia et al. (SPAIC), 2025 ²⁴	Spain (multi-center)	Retrospective, n=298 (202 open/96 laparoscopic)	Failure to rescue	Lower Comprehensive Complication Index (8.7 vs. 20.9) and mortality (1.0% vs. 7.9%) with laparoscopy
Du et al. (Wei-DSS), 2024 ²⁵	China	Retrospective, difficulty-score cohort	MILS difficulty scoring	Wei-DSS predicts operative difficulty/complications better than anatomical extent alone
Ratti et al., 2021 ²⁶	Italy (single center)	Propensity-matched cohort	MILS oncological outcomes	Equivalent DFS/OS; earlier initiation of adjuvant chemotherapy after laparoscopy

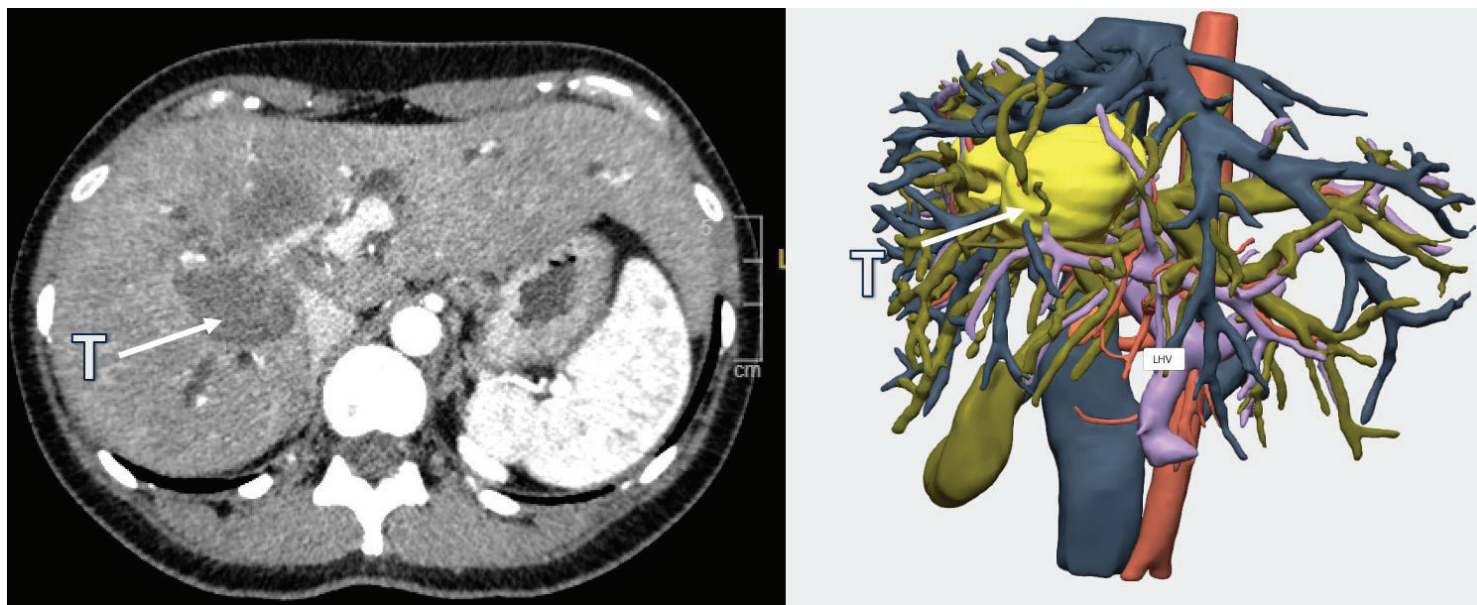


Figure 1: ICC: CT and 3D model. T: tumor

laparotomy in 25–36% of patients considered resectable after imaging². Its greatest value appears to be in patients with a high risk of occult dissemination, including multifocal tumors, suspected vascular or biliary confluence involvement, or markedly elevated CA19-9 levels after exclusion of obstructive jaundice. Accordingly, current international guidelines and most experienced centers advocate a selective rather than routine use of staging laparoscopy, reserving the procedure for patients in whom the likelihood of detecting otherwise unsuspected metastatic disease justifies the additional intervention³.

Clinical pearls:

1. CT defines resectability, while MRI better characterizes tumor extent and biliary anatomy; both are complementary in modern preoperative assessment.
2. Interpret CA19-9 only after relief of obstructive jaundice whenever possible.
3. Use staging laparoscopy selectively in patients at high risk of occult metastatic disease.

Beyond Resectability: Avoiding Futile Surgery

Traditionally, a tumor was considered suitable for surgery if it was technically resectable. Contemporary hepatopancreatobiliary surgery, however, has progressively shifted its focus from technical feasibility to biological benefit. The critical question is no longer whether a tumor can be removed, but whether resection is likely to provide meaningful oncological benefit for an individual patient. Consequently, the concept of futile resection—

an operation that achieves technical success but fails to improve survival or quality of life—has emerged as one of the defining paradigms in modern ICC surgery^{3,4}.

Over the last few years, several groups have proposed complementary definitions and predictive models of futile resection. Although these models differ in methodology and endpoints, they consistently converge on the same biological determinants of poor outcome. Nam et al., in a two-center Korean cohort of 718 patients evaluated for potentially resectable ICC, defined futile resection as gross residual disease (R2), including “open-close” and palliative procedures, and reported a futile rate of 13.8%. Independent predictors included lymph node enlargement ≥ 10 mm (OR 12.66), multiple tumors (OR 5.99), intrahepatic duct stones (OR 3.46), and a neutrophil-to-lymphocyte ratio ≥ 2.7 (OR 1.98), with excellent discrimination (C-index 0.85 in the derivation cohort and 0.74 in external validation)⁵. Using a different approach, Chu et al. developed a CT-radiomics model in 203 patients from two Chinese centers, achieving a validation AUC of 0.80, clearly outperforming conventional clinical variables alone (AUC 0.59)⁶. Altaf et al., analyzing an international cohort of 889 patients across 15 institutions, proposed an online calculator that integrates perioperative mortality and expected survival, suggesting that resection should be discouraged when predicted 90-day mortality exceeds 25% or projected survival is less than 18 months⁷. Kawashima et al. further expanded the concept by introducing biological R2, defined as recurrence within 12 weeks of an apparently curative resection,

regardless of pathological margins. In their international cohort of 1,138 patients, biological R2 occurred in 9.3% of patients and was determined predominantly by tumor biology—including lymph node metastases, advanced T stage and cirrhosis—whereas operative variables such as resection margins, extent of hepatectomy or lymphadenectomy were not independently associated with this outcome⁸.

Despite the diversity of these models, a remarkably consistent message emerges. Regardless of how futility is defined—gross residual disease, early recurrence, composite oncological failure, or biological R2—the same biological variables consistently determine the outcome. Lymph node metastases, multifocal disease, advanced T stage, and markers of aggressive tumor biology consistently outweigh technical aspects of surgery. This evolution represents a fundamental conceptual shift in HPB surgery, shifting the emphasis from achieving technically complete resections to identifying patients most likely to benefit from surgery.

The SPAIC registry provides complementary evidence from routine national practice. In our retrospective STROBE-compliant multicenter study including 282 patients undergoing resection for ICC between 2016 and 2021, futility was defined using a composite endpoint comprising any non-R0 resection (R1, R1 vascular, or R2), 90-day postoperative mortality, and tumor recurrence or tumor-related death within six months. Overall futility reached 40.1%, driven mainly by R2 resection (22%) and early recurrence (16.3%), figures comparable to those reported by Altaf et al.⁷ On multivariable analysis, T3 stage was the strongest independent predictor of futility (OR 8.03), whereas minor hepatectomy independently reduced the likelihood of futile surgery (OR 0.34)⁹. These findings reinforce the concept that the challenge is no longer simply to achieve resectability, but to identify patients in whom surgery is expected to provide durable oncological benefit.

The logical consequence of this evolving concept is that biological information should influence intraoperative decision-making whenever possible. In this regard, Nassar et al. demonstrated that positive frozen-section assessment of regional lymph nodes independently predicted both early recurrence (OR 3.31) and death within 12 months (OR 12.70) in a bicentric French cohort of 120 patients, supporting consideration of abandoning major hepatectomy in favor of neoadjuvant or palliative strategies when adverse biological features are identified intraoperatively¹⁰.

Clinical pearls:

- Technical resectability should not be considered synonymous with meaningful oncological benefit.
- Tumor biology consistently outweighs operative technique as the principal determinant of futile resection.
- Assessment of nodal disease should guide not only prognosis but also intraoperative decision-making.

How Radical Should Surgery Be?

Balancing Oncological Radicality and Functional Preservation

Major hepatectomy is required in a substantial proportion of patients undergoing resection for ICC, accounting for approximately 56–78% of reported series^{5,8,11}. Historically, extensive liver resection has frequently been considered necessary to achieve adequate oncological clearance, with some reviews estimating that nearly 70% of curative resections require major or extended hepatectomy, at the cost of postoperative morbidity exceeding 50% and mortality approaching 7%². However, increasing evidence indicates that the relationship between operative radicality and oncological benefit is far from linear.

The contemporary objective is no longer to perform the largest possible resection, but rather the smallest resection that achieves adequate oncological clearance while preserving functional liver reserve. Consistent with this concept, our SPAIC futility analysis demonstrated that minor hepatectomy independently reduced the risk of futile resection (OR 0.34), whereas futility itself remained predominantly determined by tumor biology rather than by the extent of liver resection⁹. These findings support an increasingly accepted parenchymal-sparing philosophy whenever oncologically feasible.

When major hepatectomy remains necessary, preservation of an adequate future liver remnant becomes paramount. Preoperative portal vein embolization remains the standard strategy to increase remnant liver volume, whereas associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) should be reserved for highly selected patients managed in experienced centers, as ICC-specific evidence remains considerably more limited than for colorectal liver metastases or hepatocellular carcinoma^{3,12}.

This evolution towards parenchymal preservation has also challenged the traditional interpretation of surgical margins. Within this philosophy, Torzilli introduced the concept of vascular R1, describing intentional

microscopic detachment of the tumor from a major vascular structure to preserve functional liver parenchyma while avoiding gross residual disease¹³. Unlike an unintended positive margin, vascular R1 represents a deliberate compromise between oncological radicality and preservation of postoperative liver function.

Accordingly, margin status should no longer be interpreted as a simple binary indicator of surgical success. Although R0 resection remains the intended objective of every ICC operation, its independent prognostic impact appears more complex than traditionally assumed. Hammad et al., analyzing 2,897 patients from the National Cancer Database, reported a median survival of 31.2 months after R0 resection compared with 19.5 months after R1/R2 resection, with both R1 (HR 1.47) and R2 (HR 1.57) remaining independently associated with worse survival¹⁴. In contrast, Lang et al. found no statistically significant survival difference between R0 and R1 resections in their German single-center experience¹¹, while Kawashima et al. demonstrated that margin width, whether analyzed using thresholds of <1 mm, <5 mm or <10 mm, was not independently associated with early biological failure once tumor biology was incorporated into the multivariable model⁸.

Our SPAIC registry deliberately adopted a more patient-centered definition of futility by considering every non-R0 resection—including the vascular R1 category—as one component of futile surgery⁹. This approach does not imply that every microscopic positive margin carries the same biological significance; rather, it reflects the principle that a margin-positive resection should not automatically be considered a successful oncological outcome. Ultimately, technical radicality should always be interpreted in the context of tumor biology, which remains the principal determinant of long-term benefit after surgery.

Lymphadenectomy: Essential for Staging, Uncertain as Therapy

The same balance between surgical radicality and clinical benefit applies to lymphadenectomy. Current staging systems recommend retrieval of at least six lymph nodes, while nodal metastases are identified in approximately 25–50% of resected patients^{2,11,14,15}. Nevertheless, compliance remains inconsistent. Hammad et al. reported that formal lymphadenectomy was not routinely performed in the National Cancer Database, leaving almost half of patients without adequate pathological nodal

staging¹⁴. Conversely, Lang et al. reported lymphadenectomy in nearly 90% of resections, with a median of 5 lymph nodes retrieved¹¹.

The prognostic importance of lymph node involvement is remarkably consistent across contemporary studies. Positive nodal status independently predicts worse survival in large international, European, and Asian cohorts^{11,14,16}. Similarly, within the SPAIC registry, lymph node metastases were significantly more frequent in technically complex resections requiring combined liver and biliary procedures, reflecting the close relationship between operative complexity and tumor biology^{17,18}.

Whether lymphadenectomy itself provides therapeutic benefit, however, remains uncertain. Although some studies suggest improved outcomes after lymph node dissection, these associations largely disappear after adjustment for tumor biology⁶. Consequently, the principal value of lymphadenectomy currently lies in accurate pathological staging, appropriate prognostic stratification, selection for adjuvant treatment, and, potentially, intraoperative decision-making. As proposed by Nassar et al., frozen-section assessment of suspicious regional lymph nodes may help identify patients in whom continuation of major hepatectomy is unlikely to provide meaningful oncological benefit¹⁰.

Clinical pearls:

- Major hepatectomy should be performed only when required to achieve oncological clearance while preserving an adequate future liver remnant.
- Parenchymal preservation and the concept of vascular R1 illustrate the shift from maximal surgery to biologically tailored surgery.
- Regional lymphadenectomy is essential for accurate staging, although its independent therapeutic benefit remains uncertain.
- Modern ICC surgery seeks the optimal—not the maximal—operation.

How Should Surgery Be Performed?

Minimally Invasive Surgery: Better Recovery Without Compromising Oncological Principles

Over the last decade, minimally invasive liver surgery (MILS) has progressively evolved from a highly selected option for minor hepatectomy to an accepted approach for increasingly complex resections in specialized hepatopancreatobiliary centers. For ICC, however, the key question is no longer whether laparoscopic liver

resection is technically feasible, but whether its well-established perioperative advantages translate into equivalent—or even superior—oncological outcomes.

Current evidence consistently demonstrates significant short-term benefits of laparoscopy. Across the largest propensity score-matched studies and meta-analyses, laparoscopic resection is associated with reduced intraoperative blood loss, shorter hospital stays and fewer major postoperative complications compared with open surgery¹⁹⁻²¹. These advantages have been remarkably consistent across different healthcare systems and study designs. Nevertheless, lymphadenectomy remains a recognized limitation of the MILS. Several meta-analyses report lower rates of lymph node dissection and, when performed, a lower lymph node yield than with open surgery¹⁹⁻²¹. Given the prognostic importance of nodal staging in ICC, this limitation should be carefully considered when selecting patients for MILS.

Whether MILS provides a genuine oncological advantage remains considerably more controversial. Most contemporary meta-analyses demonstrate equivalent overall and disease-free survival between laparoscopic and open approaches^{20,21}, whereas Aliseda et al. reported a modest survival advantage favoring laparoscopy in a pooled analysis of propensity score-matched studies¹⁹. However, this apparent benefit appears largely attributable to patient selection. In the international multicenter study by Brustia et al., the survival advantage observed after propensity matching disappeared completely once analysis was restricted to patients with adequate lymph node staging, strongly suggesting that incomplete pathological staging and residual selection bias account for much of the reported difference²². Similarly, Yang et al. observed improved long-term outcomes after laparoscopy only after excluding learning-curve cases and limiting the analysis to highly selected early-stage tumors without vascular invasion²³. Taken together, these findings indicate that appropriate patient selection, rather than the surgical approach itself, remains the principal determinant of oncological outcome.

The SPAIC registry reached a similar conclusion. In our national multicenter comparison including 298 patients (202 open and 96 laparoscopic resections), laparoscopic surgery was associated with a markedly lower Comprehensive Complication Index (8.7 versus 20.9) and lower postoperative mortality (1.0% versus 7.9%)²⁴. Nevertheless, because the proportion of major hepatectomies was comparable between groups, these findings

could not be confidently attributed to the surgical approach alone, and residual selection bias remains the most plausible explanation. This cautious interpretation closely mirrors the conclusions reached by the broader international literature.

Patient selection for MILS is itself evolving. Rather than relying exclusively on the traditional distinction between major and minor hepatectomy, several groups have proposed procedure-specific difficulty scores. The Wei Difficulty Scoring System (Wei-DSS), which incorporates tumor size, segmental location, proximity to major vascular structures, cirrhosis, and CA19-9 level, more accurately predicts operative difficulty and postoperative complications than anatomical extent alone in patients undergoing MILS²⁵. Such tools may provide a more rational framework for selecting the optimal surgical approach in the future.

Robotic liver surgery represents the next stage in the evolution of MILS techniques. Although high-quality comparative data specific to ICC remain limited, the robotic platform may overcome some technical limitations of conventional laparoscopy, particularly during lymphadenectomy, biliary reconstruction, and complex hilar dissection. At present, however, available evidence suggests that the choice of platform is likely less important than careful patient selection, surgeon experience, and adherence to sound oncological principles^{3,4}.

Finally, MILS may provide indirect oncological benefits beyond the operation itself. Ratti et al. demonstrated equivalent disease-free and overall survival after propensity matching, while patients undergoing laparoscopic resection started adjuvant chemotherapy significantly earlier than those treated by open surgery²⁶. Whether this earlier initiation of systemic therapy ultimately translates into improved long-term outcomes remains unknown but represents an important area for future investigation.

Clinical pearls:

- MILS consistently improves short-term postoperative outcomes without compromising established oncological principles.
- Current evidence does not demonstrate a clear intrinsic oncological advantage of MILS over open surgery after adequately addressing selection bias.
- Appropriate patient selection remains the cornerstone of successful minimally invasive surgery for ICC.

- Difficulty scoring systems and increasing surgical experience are likely to guide the future expansion of minimally invasive and robotic liver surgery.

Integrating Complexity and Futility: A New Decision-Making Framework

Modern ICC surgery requires answering two fundamentally different questions before entering the operating room. The first is how difficult the operation will be; the second is whether the patient is likely to benefit from that operation. Although these questions are closely related, they address different dimensions of surgical decision-making and should not be considered interchangeable. (Figure 2)

Surgical complexity classifications and futility prediction models have evolved independently over recent years, yet they should be regarded as complementary rather than competing frameworks. Complexity classifications—such as the system proposed by Yoh et al.—estimate the technical demands of surgery by distinguishing between simple

hepatectomy (Class I), combined biliary resection and reconstruction (Class II), and major vascular resection and reconstruction (Class III). Their principal value lies in operative planning, allocation of resources and identification of patients who may benefit from referral to high-volume hepatopancreatobiliary centers^{17,18}.

In contrast, futility models—including the SPAIC composite score, the Altaf/Pawlik calculator, Nam's nomogram and Kawashima's biological R2 concept—address a fundamentally different question: whether surgery is likely to provide meaningful oncological benefit^{3,5-7}. These models focus predominantly on tumor biology rather than operative complexity and aim to identify patients in whom technically successful surgery is unlikely to improve long-term outcome.

The SPAIC registry provides external validation supporting both concepts. In our Western multicenter validation of the Yoh classification, Class II procedures were associated with substantially higher major morbidity (66.7% versus 18.5%) together with more aggressive

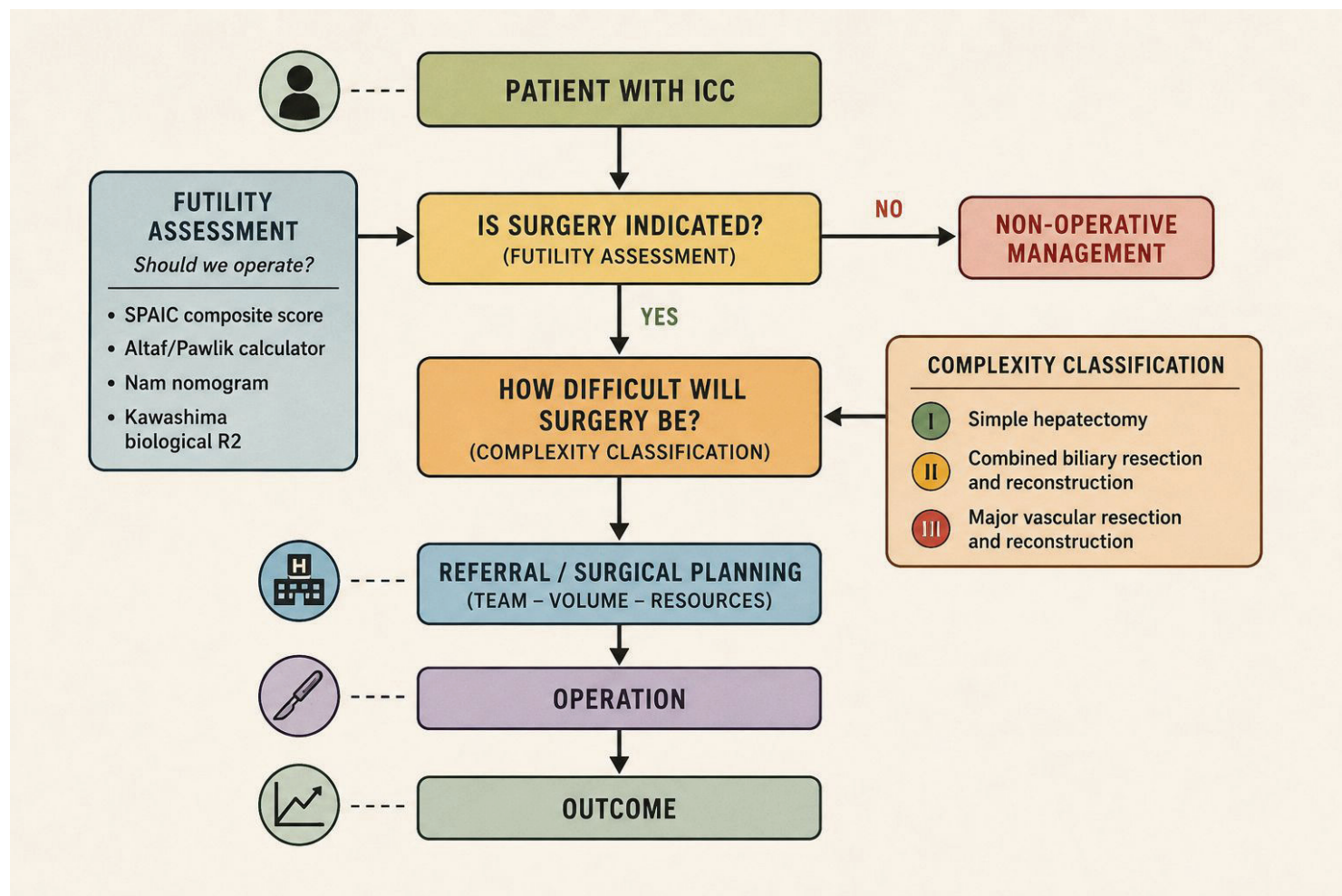


Figure 2. Integrated framework for decision-making in intrahepatic cholangiocarcinoma

tumor biology, including higher rates of perineural invasion (75.8% versus 30.9%) and lymph node metastases (36.4% versus 15.3%) compared with Class I resections^{17,18}. Interestingly, no Class III procedures were identified in our cohort, in contrast with the original Japanese experience, probably reflecting differences in referral patterns and case-mix rather than limitations of the classification itself.

Rather than viewing these systems separately, we believe they should be integrated into routine multidisciplinary decision-making. Complexity classifications answer the question “How should we perform this operation?”, whereas futility models answer the more fundamental question “Should we perform this operation at all?” Used together, these complementary frameworks may help reduce both overtreatment of patients unlikely to benefit from surgery and undertreatment of patients whose anatomy and tumor biology justify an aggressive surgical strategy.

Clinical pearls:

- Surgical complexity and oncological futility measure different dimensions of surgical decision-making and should not be considered competing concepts.
- Complexity classifications guide operative planning and referral, whereas futility models guide patient selection.
- Integrating both frameworks into multidisciplinary discussions may optimize patient selection for ICC surgery.
- The future of ICC surgery lies in combining technical expertise with objective assessment of tumor biology.

Discussion

This narrative review was designed to move beyond a descriptive account of the literature on intrahepatic cholangiocarcinoma (ICC) surgery and to translate the available evidence into explicit, clinically actionable conclusions. The main points arising from the studies summarized in Table 1 are outlined below, together with the limitations of this review.

Key evidence-based conclusions:

- Preoperative staging should combine cross-sectional imaging, CA19-9 interpreted after biliary decompression, and selective staging laparoscopy; no single test is sufficiently accurate in isolation^{1,2}.

- Tumor biology — nodal disease, multifocality, and advanced T stage — rather than operative technique, is the dominant and reproducible determinant of futile resection across every model tested to date⁵⁻⁹.
- Extent of hepatectomy should be dictated by oncological necessity rather than by a default preference for major resection; parenchyma-sparing surgery is independently associated with a lower risk of futile resection⁹.
- Lymphadenectomy is essential for accurate staging and prognostication but has not been shown to be independently therapeutic once tumor biology is accounted for^{6,11,14,16}.
- Minimally invasive surgery improves perioperative outcomes without a demonstrated independent oncological disadvantage, provided nodal staging is not compromised¹⁹⁻²⁴.
- Surgical complexity classification and futility prediction address different questions — how to operate versus whether to operate — and should be used together in multidisciplinary decision-making^{9,17,18}.

Preoperative staging remains imperfect despite continuous technical improvement. No single imaging modality or biomarker is sufficiently accurate in isolation, and nodal staging in particular remains unreliable even with modern cross-sectional imaging^{1,2}. In our view, this limitation justifies a multimodal strategy — contrast-enhanced CT complemented by MRI/MRCP, CA19-9 interpreted after biliary decompression, and selective staging laparoscopy in patients at high risk of occult dissemination — rather than reliance on any single test.

A second, more consistent message emerges from the futility literature summarized in Table 1: irrespective of how futile resection is defined — gross residual disease⁵, radiomic prediction⁶, a composite perioperative/survival threshold⁷, biological R2⁸, or the composite endpoint used in our own SPAIC cohort⁹ — the same biological variables (nodal disease, multifocal tumors, advanced T stage) repeatedly emerge as the dominant predictors, while operative variables carry comparatively little independent weight. The convergence of these findings across geographically and methodologically diverse cohorts — Korean, Chinese, international multicenter, and Spanish — is, in our view, the strongest argument currently available for incorporating formal futility assessment into preoperative decision-making, rather than an argument resting on any single study.

Our perspective: major hepatectomy versus conservative, parenchyma-sparing surgery

On the specific question of major hepatectomy versus conservative, parenchyma-sparing surgery, our position is that the extent of resection should be dictated by oncological necessity rather than by a default preference for the largest possible operation. Major hepatectomy remains indispensable when required to achieve adequate oncological clearance or when tumor location or vascular/biliary confluence involvement precludes a lesser resection, and it should not be withheld from otherwise favorable candidates simply to minimize perioperative risk. However, when a parenchyma-sparing resection — including, where appropriate, an intentional vascular R1 margin as described by Torzilli¹³ — can achieve equivalent oncological clearance, we believe it should be preferred. In the SPAIC registry, minor hepatectomy was independently associated with a lower risk of futile resection (OR 0.34), even though futility itself remained predominantly determined by tumor biology rather than by the extent of resection⁹, and major or complex hepatectomy accounted for a disproportionate share of postoperative morbidity across the reviewed literature^{2,18}. We therefore favor a strategy of the smallest oncologically adequate resection over routine major hepatectomy, reserving extended resections for cases in which anatomy and tumor biology make them unavoidable, and we support integrating intraoperative biological information — such as frozen-section nodal assessment — into the decision to continue or abandon a planned major hepatectomy¹⁰. This is, admittedly, an interpretive position rather than a directly tested hypothesis, since no randomized comparison of major versus conservative hepatectomy exists in ICC; it is based on the consistent association between extended resection, morbidity, and futility observed across the cohorts summarized in Table 1, and it should be tested prospectively.

Regarding lymphadenectomy, the evidence is equally consistent but points in a different direction: nodal status is one of the strongest prognostic markers identified across every cohort reviewed^{11,14,16}, yet no study demonstrated an independent therapeutic survival benefit of the dissection itself once tumor biology was accounted for⁶. We therefore consider adequate lymphadenectomy (≥ 6 nodes) mandatory for staging accuracy and treatment selection, but we do not consider it, by itself, a therapeutic maneuver, and we would caution against extending an operation's morbidity solely to achieve a more extensive dissection once distant nodal disease is evident.

For minimally invasive surgery, the evidence base is now mature enough to support a clear, if qualified, conclusion: laparoscopic resection reduces perioperative morbidity without a demonstrable independent oncological disadvantage, but the survival advantages reported in some series are best explained by patient selection and incomplete nodal staging rather than a true oncological benefit of the approach itself^{19–23}. Our own SPAIC comparison is consistent with this interpretation²⁴. Until lymph node retrieval during MILS reaches parity with open surgery, we recommend that patient selection for a minimally invasive approach continue to prioritize adequate nodal staging over the surgical platform itself.

Limitations of this review

This review has the inherent limitations of a narrative, non-systematic synthesis: study selection was not governed by a PRISMA-type protocol, and formal risk-of-bias or quality appraisal was not performed, so publication bias cannot be excluded. Nearly all primary data, including our own SPAIC series, derive from retrospective cohorts, and several futility definitions have not yet been externally validated outside their derivation populations. Two of the studies discussed were still unpublished (in submission) at the time of writing^{9,17} and should be interpreted with this caveat until they complete peer review. Randomized evidence in this field remains essentially absent and is unlikely to become available given the rarity and heterogeneity of ICC; prospective, harmonized multicenter registries therefore represent the most realistic path toward stronger evidence.

Conclusion

Surgery for intrahepatic cholangiocarcinoma is undergoing a fundamental conceptual evolution. The central question is no longer simply “Can this tumor be resected?”, but rather “Will this resection provide meaningful benefit for this patient?” Throughout this review, a consistent message emerges: although technical expertise remains essential, tumor biology has become the principal determinant of surgical success. Decisions regarding patient selection, the extent of resection, lymphadenectomy, resection margins, and surgical approach should therefore be interpreted within a biological rather than purely technical framework.

This evolution also highlights the complementary roles of the two conceptual models discussed in this review. Complexity classifications help surgeons determine

how an operation should be performed, whereas futility models help determine whether that operation should be performed at all. Rather than competing, these frameworks should be integrated into multidisciplinary decision-making to individualize treatment, avoid unnecessary surgery, and identify those patients most likely to benefit from aggressive surgical management.

Future progress will depend not only on technical innovation but also on better integration of imaging, biomarkers, objective measures of operative complexity, and biological predictors of outcome. Prospective multicenter registries and international collaborative studies will be essential for validating these concepts and translating them into practical decision-support tools. Ultimately, excellence in ICC surgery will be defined not by performing the most complex operation, but by selecting the right patient for the right operation at the right time.

Funding: No funds

Conflict of Interest: No conflict of interest

References:

1. Sauré Maritano A, Mandiola Bunster C, Gaete Letelier D. Actualización del manejo clínico del colangiocarcinoma intrahepático. Parte I: epidemiología, clasificación y diagnóstico. *Rev Cir.* 2025;77(1):79-87.
2. Sauré Maritano A, Mandiola Bunster C, Gaete Letelier D. Actualización del manejo clínico del colangiocarcinoma intrahepático. Parte II: Etapificación y tratamiento. *Rev Cir.* 2025;77(2):177-184.
3. European Association for the Study of the Liver. EASL-ILCA Clinical Practice Guidelines on the management of intrahepatic cholangiocarcinoma. *J Hepatol.* 2023 Jul;79(1):181-208. doi: 10.1016/j.jhep.2023.03.010.
4. Ruff SM, Pawlik TM. Clinical management of intrahepatic cholangiocarcinoma: surgical approaches and systemic therapies. *Front Oncol.* 2024 Jan 24;14:1321683. doi: 10.3389/fonc.2024.1321683.
5. Nam K, Hwang DW, Shim JH, Song TJ, Lee SS, Seo DW, et al. Novel preoperative nomogram for prediction of futile resection in patients undergoing exploration for potentially resectable intrahepatic cholangiocarcinoma. *Sci Rep.* 2017;7:42954.
6. Chu H, Liu Z, Liang W, Zhou Q, Zhang Y, Lei K, et al. Radiomics using CT images for preoperative prediction of futile resection in intrahepatic cholangiocarcinoma. *Eur Radiol.* 2021;31(4):2368-2376.
7. Altaf A, Khalil M, Beliza A, Rashid Z, Kawashima J, Zindani S, et al; Pawlik TM. An easy-to-use online calculator to identify patients least likely to benefit from surgical resection of intrahepatic cholangiocarcinoma. *Surgery.* 2025;186:109545.
8. Kawashima J, Endo Y, Woldesenbet S, et al; Pawlik TM.

“Biological R2” resection for intrahepatic cholangiocarcinoma: identification of patients at risk for poor oncologic outcomes after curative-intent resection. *HPB (Oxford).* 2025;27:619-629.

9. Ramia JM, Villodre C, Alcázar CF, Franco-Campello M, et al, for the SPAIC Collaborative Study Group. Futility in intrahepatic cholangiocarcinoma resection: a Spanish multicenter study (SPAIC project). Submitted 2026.

10. Nassar A, Tzedakis S, Sindayigaya R, Hobeika C, Marchese U, Veziant J, et al. Factors of early recurrence after resection for intrahepatic cholangiocarcinoma. *World J Surg.* 2022;46(10):2459-2467.

11. Lang H, Baumgart J, Heinrich S, Huber T, Heuft LK, Margies R, et al. Liver resection for intrahepatic cholangiocarcinoma—single-center experience with 286 patients undergoing surgical exploration over a thirteen-year period. *J Clin Med.* 2021;10:3559.

12. Neuzillet C, Decraecker M, Larrue H, Ntanda-Nwandji LC, Barbier L, Barge S et al. Management of intrahepatic and perihilar cholangiocarcinomas: Guidelines of the French Association for the Study of the Liver (AFLF). *Liver Int.* 2024 Oct;44(10):2517-2537. doi: 10.1111/liv.15948.

13. Torzilli G, Viganò L, Fontana A, Procopio F, Terrone A, Cimino MM, Donadon M, Del Fabbro D. Oncological outcome of R1 vascular margin for mass-forming cholangiocarcinoma. A single center observational cohort analysis. *HPB (Oxford).* 2020 Apr;22(4):570-577. doi: 10.1016/j.hpb.2019.08.015.

14. Hammad AY, Berger NG, Eastwood D, Tsai S, Turaga KK, Christian KK, et al. Is radiotherapy warranted following intrahepatic cholangiocarcinoma resection? The impact of surgical margins and lymph node status on survival. *Ann Surg Oncol.* 2016;23(Suppl 5):S912-S920.

15. Kim DH, Choi SH, Kim S, Lee W, Kim HD, Rhee H, et al. Validation of prognostic models for predicting postsurgical outcomes in intrahepatic cholangiocarcinoma patients using a multicenter cohort. *Int J Surg.* 2025;111:7032-7040.

16. Shen Z, Tao L, Cai J, Zheng J, Sheng Y, Yang Z, et al. Safety and feasibility of laparoscopic liver resection for intrahepatic cholangiocarcinoma: a propensity score-matched study. *World J Surg Oncol.* 2023;21:126.

17. Ramia JM, Villodre C, Alcázar CF, Franco-Campello M, for the SPAIC Collaborative Study Group. External validation of a surgical complexity classification for intrahepatic cholangiocarcinoma. Submitted 2026.

18. Yoh T, et al. Original surgical complexity classification for intrahepatic cholangiocarcinoma. *HPB (Oxford).* 2025;27(10):1250-1258.

19. Aliseda D, Sapisochin G, Martí-Cruchaga P, Zozaya G, Blanco N, Goh BKP, et al; Rotellar F. Association of laparoscopic surgery with improved perioperative and survival outcomes in patients with

resectable intrahepatic cholangiocarcinoma: a systematic review and meta-analysis from propensity-score matched studies. *Ann Surg Oncol.* 2023;30(8):4888-4901.

20. Hu YF, Hu HJ, Ma WJ, Jin YW, Li FY. Laparoscopic versus open liver resection for intrahepatic cholangiocarcinoma: a systematic review of propensity score-matched studies. *Updates Surg.* 2023;75:2049-2061.

21. Zhao X, Gao FW, Jiang KY, Yang J, Xie QY, Gong J, et al. Laparoscopic or open liver resection for intrahepatic cholangiocarcinoma: a meta-analysis and systematic review. *Front Oncol.* 2023;13:1096714.

22. Brustia R, Laurent A, Goumard C, Langella S, Cherqui D, Kawai T, et al; Scatton O. Laparoscopic versus open liver resection for intrahepatic cholangiocarcinoma: report of an international multicenter cohort study with propensity score matching. *Surgery.* 2022;171(5):1290-1302.

23. Yang J, Wang Y, Zheng Y, Ma D, Chen X, Wang Y, et al; Chen G. Laparoscopic versus open surgery for early-stage intrahepatic cholangiocarcinoma after mastering the learning curve: a multicenter database matched study. *Front Oncol.* 2022;11:742544.

24. Ramia JM, Villodre C, Villota-Tamayo B, Alcázar CF, Franco-Campello M, for the SPAIC Collaborative Study Group. Failure to rescue in patients undergoing surgery for intrahepatic cholangiocarcinoma (SPAIC project). *Cir Esp.* 2025 [article in press]. DOI: 10.1016/j.ciresp.2024.11.001

25. Du C, Cao W, Liu J, Liu J, Jin L, Feng X, et al; Wei F. Utility of a novel scoring system for difficulty of pure laparoscopic hepatectomy for intrahepatic cholangiocarcinoma. *Sci Rep.* 2024;14:31546.

26. Ratti F, Casadei-Gardini A, Cipriani F, Fiorentini G, Pedica F, Burgio V, et al. Laparoscopic surgery for intrahepatic cholangiocarcinoma: a focus on oncological outcomes. *J Clin Med.* 2021;10(13):2828.

Pushing the Boundaries of Liver Resection in Non-Colorectal Non-Neuroendocrine Metastatic Disease

Mario Serradilla Martín¹, José M. Ramia²

¹ Department of Surgery, Hospital Universitario Virgen de las Nieves, Instituto de Investigación Biosanitaria ibs.GRANADA, School of Medicine, University of Granada, Granada, Spain

² Department of Surgery, Hospital General Universitario Dr. Balmis, ISABIAL, Miguel Hernández University, Alicante, Spain

Corresponding Author:

MARIO SERRADILLA MARTÍN

Department of Surgery, Hospital Universitario Virgen de las Nieves
Av. de las Fuerzas Armadas, 2, 18014 Granada, Spain
E-mail: mserradilla@ugr.es

Abstract

Background: The liver, after the lymph nodes, is the most common site of metastatic disease. Liver resection is well established for colorectal and neuroendocrine liver metastases, but its role in metastases from other, non-colorectal non-neuroendocrine primary tumors remains debated because of the rarity of cases, the heterogeneity of the primary tumors involved, and the scarcity of prospective trials.

Objective: To synthesize the available evidence on outcomes after liver resection for non-colorectal non-neuroendocrine liver metastases according to the primary tumor of origin, and to identify the clinical and technical factors most consistently associated with improved survival.

Findings: A narrative review of clinical series, systematic reviews, and meta-analyses indexed in PubMed/MEDLINE was performed, organized by primary tumor of origin. A recent systematic review and meta-analysis of 40 studies and 5,696 patients reported 3- and 5-year overall survival of 40% and 32%, respectively, after

resection, with postoperative morbidity of 28% and 30-day mortality of 2%. Outcomes varied markedly by tumor of origin: 5-year overall survival exceeded 40% for breast cancer, gastrointestinal stromal tumor, and melanoma, but remained below 25% for gastric and pancreatic cancer. Across nearly all tumor types, negative resection margins, limited hepatic disease, a disease-free interval longer than 12 months, and a favorable response to systemic therapy were the factors most consistently associated with better survival.

Conclusions and Relevance: In carefully selected patients with limited hepatic disease, a favorable response to systemic therapy, and no uncontrolled extrahepatic disease, liver resection provides a clear survival benefit over non-surgical treatment and, in some subgroups, particularly breast cancer, gastrointestinal stromal tumor, and uveal melanoma, the possibility of long-term disease control. Because prospectively validated selection criteria are still lacking, the surgical decision should be individualized within a multidisciplinary team.

Keywords

liver metastases; hepatectomy; surgical oncology; gastrointestinal stromal tumor; uveal melanoma

Introduction

Malignant tumors tend to spread, and the liver, after the lymph nodes, is the most common site of metastasis from abdominal tumors, owing to its dual portal and arterial blood supply and its rich lymphatic network. Liver resection with curative intent for the treatment of metastatic disease has been described for more than a century and is now widely accepted. Technical advances, technological innovation, and improved patient selection have markedly increased the safety of liver surgery, pushing the boundaries of resectability even for extensive resections.

For colorectal liver metastases, liver resection is now the reference treatment, with 5-year survival ranging from 40 to 58%.¹ The management of neuroendocrine liver metastases is also well supported in the literature. However, the role of surgery in non-colorectal non-neuroendocrine liver metastases, an enormously heterogeneous group that includes digestive tumors such as gastric cancer or gastrointestinal stromal tumor, and non-digestive tumors such as breast cancer, melanoma, soft tissue sarcoma, germ cell tumors, ovarian cancer, renal cell carcinoma, or differentiated thyroid carcinoma, remains poorly defined. This is due to the relative rarity of cases, the wide variety of biological behaviors depending on the primary tumor, and the near-absence of prospective randomized studies to guide decision-making.²⁻⁴

The aim of this narrative review is to examine the available evidence on the usefulness of liver resection in non-colorectal non-neuroendocrine liver metastases, reviewing the published oncologic outcomes according to the primary tumor of origin, common prognostic factors, patient selection criteria, and relevant surgical technical aspects, including parenchymal-sparing techniques and minimally invasive approaches. Wherever possible, findings from the largest available series are cross-referenced against recently published, tumor-specific systematic reviews and meta-analyses, so that the conclusions of each section are grounded in quantifiable, reproducible evidence rather than in narrative impression alone.

Methods

A narrative, non-systematic search of the literature indexed in PubMed/MEDLINE was conducted, combining the terms “liver resection,” “hepatectomy,” “liver

metastases,” “non-colorectal,” and “non-neuroendocrine” with the names of the main primary tumors in this group (breast, gastric, gastrointestinal stromal tumor, melanoma, sarcoma, ovarian, testicular/germ cell, renal, and thyroid). Priority was given to large clinical series, systematic reviews, and meta-analyses published in English, without strict date limits given the scarcity of recent series in some subgroups; the search was last updated in September 2026 to add tumor-specific systematic reviews and meta-analyses through 2023, used throughout to corroborate and quantify the older primary series. Selection and synthesis were performed narratively by the authors, without a formal systematic protocol (no PRISMA diagram, dual independent screening, or risk-of-bias assessment); this remains a limitation of the work, addressed further in the Discussion.

Patient selection criteria and prognostic factors

Unlike colorectal liver metastases, no prospectively validated selection criteria exist for non-colorectal non-neuroendocrine liver metastases. The largest multicenter series published to date, including 1,452 patients treated at French centers, reported 5- and 10-year overall survival (OS) of 36 and 23% respectively after resection, with low postoperative mortality, and identified ten independent prognostic factors that allowed the development of a risk model to help guide surgical indication.¹ This has since been corroborated at a population level by a meta-analysis pooling 40 studies and 5,696 patients, reporting 3- and 5-year OS of 40% and 32% after resection, with morbidity of 28% and 30-day mortality of 2%.⁵ Factors consistently associated with worse prognosis include age over 60 years, a primary tumor other than breast, melanoma or squamous histology, a disease-free interval (DFI) under 12 months, extrahepatic disease, inability to achieve negative margins, and the need for a major hepatectomy.^{1,2,6} Other relevant factors include elevated bilirubin, severe complications, multiple or bilobar lesions, and regional lymph node metastases from the primary tumor.

Overall, the best candidates for resection are patients with good performance status, controlled primary tumor, limited hepatic disease, no uncontrolled extrahepatic disease, favorable response or stability after systemic therapy, and a reasonable expectation of negative margins. The decision should be individualized within a multidisciplinary team (hepatobiliary surgery, medical oncology, interventional radiology), since no single criterion has

sufficient predictive capacity alone.^{3,4} Figure 1 summarizes a proposed practical algorithm, derived from these criteria, for guiding patient selection, reflecting a composite, multidisciplinary assessment rather than reliance on any single threshold.

Liver metastases of digestive origin

Gastric cancer

Gastric cancer is among the most frequently diagnosed malignancies worldwide and an important cause of cancer mortality, largely because it is often diagnosed at an advanced stage.⁷ With liver metastases, standard of care remains systemic chemotherapy (median survival about 12 months), but several meta-analyses show a survival

benefit for hepatectomy versus non-surgical treatment at 1, 3, and 5 years in carefully selected patients.⁸ Median survival after resection ranges 5-8 months in older series (1-year survival 15-50%, 5-year survival approximately 19%), with up to 39% 5-year survival for resected metachronous metastases with wide margins.⁹ Lymph node status of the primary tumor is an important independent prognostic factor, with better outcomes in N0/N1 than N2/N3 disease.¹⁰ Metachronous resection appears to outperform synchronous resection, and a single lesion with wide margins is likewise favorable. A larger, more recent meta-analysis of 55 studies and 1,990 patients corroborated these figures, reporting 5-year OS of 24.7% and median OS of 24.5 months after hepatectomy, with

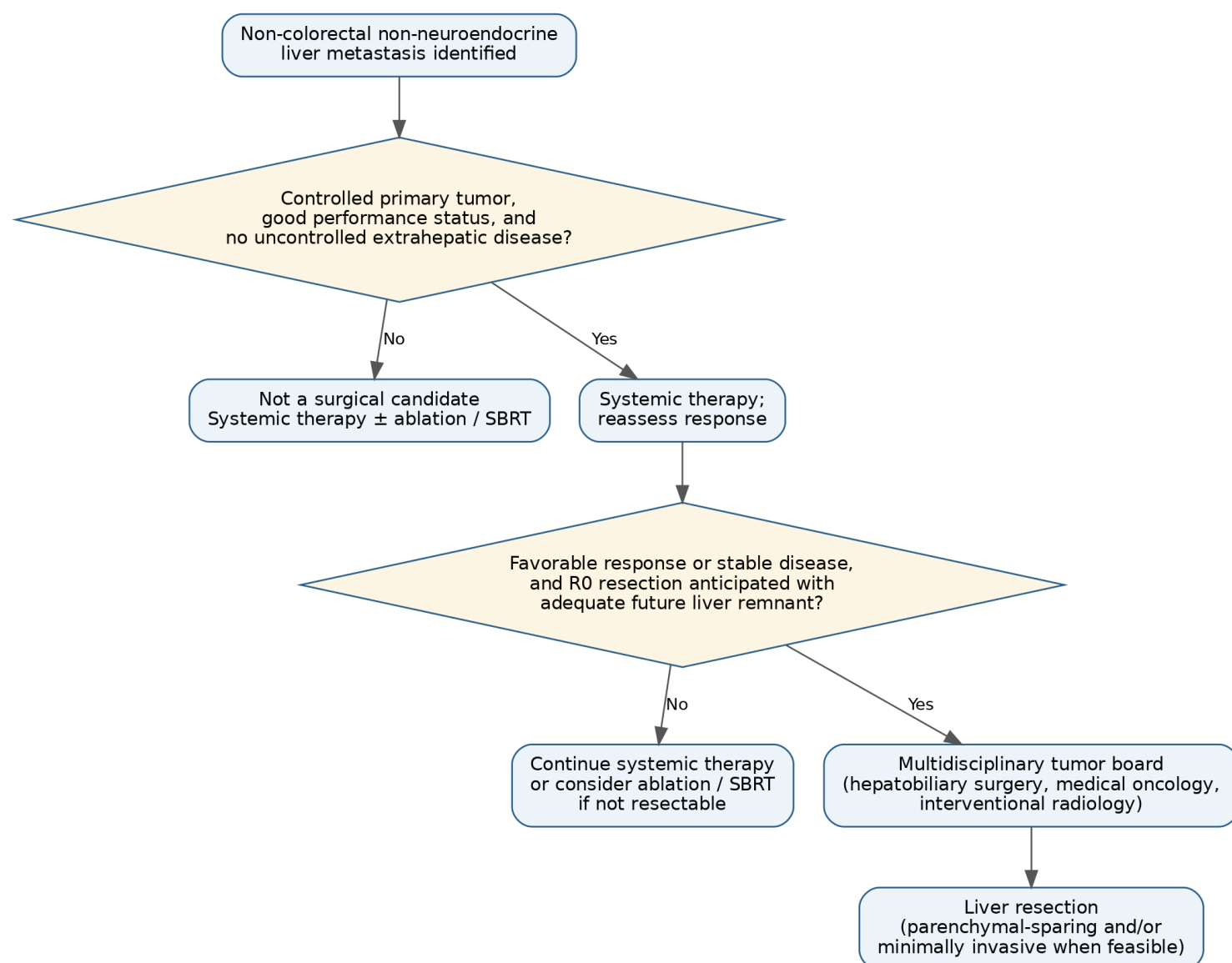


Figure 1. Proposed algorithm for the selection of candidates for liver resection in non-colorectal non-neuroendocrine liver metastases, based on control of the primary tumor, performance status, extrahepatic disease status, response to systemic therapy, and anticipated completeness of resection. SBRT, stereotactic body radiotherapy.

low 30-day mortality (1.4%); metachronous presentation, well- to moderately differentiated histology, small tumor size, early nodal stage, R0 resection, unilobar involvement, and solitary lesions predicted a favorable outcome.¹¹ Hepatectomy is therefore best regarded as a selective option for patients meeting several of these criteria, not as routine care.

Gastrointestinal stromal tumor

Gastrointestinal stromal tumor (GIST) accounts for 1-3% of digestive neoplasms and is the most common mesenchymal tumor of the gastrointestinal tract; the liver and peritoneum are its most frequent metastatic sites.¹² Before tyrosine kinase inhibitors (TKI), resection was the only available treatment, with 5-year survival approximately 30% and median survival 36-47%.¹³ Imatinib radically changed prognosis, with response rates up to 80%, though secondary resistance develops in roughly half of patients around two years into treatment, renewing interest in surgery as an adjunct to systemic therapy; surgical series report 5-year OS approximately 34%, with low morbidity and mortality (about 10% and 2%).¹⁴ Postoperative TKI therapy is associated with the best outcomes, while extrahepatic disease at resection predicts worse survival.^{15,16} Surgery has been proposed mainly for focal, early resistance within the first six months of treatment, to reduce the risk of selecting resistant clones.¹⁷ A meta-analysis of 11 studies and 988 patients has since confirmed this benefit quantitatively: adding surgery to TKI therapy significantly reduced the risk of death compared with pharmacotherapy alone (hazard ratio 2.10, 95% CI 1.58–2.79), supporting a combined surgical and pharmacologic strategy in patients with focal, non-progressive disease.¹⁸

Pancreatic cancer

Pancreatic ductal adenocarcinoma (PDAC) carries a particularly poor prognosis (overall 5-year survival below 8%), and the liver is its most common metastatic site. With synchronous liver metastases, median OS barely reaches 5 months with non-surgical treatment, and surgery has traditionally been contraindicated. Recent series of combined resection of the primary tumor and liver metastases in oligometastatic disease (usually ≤ 3 lesions) report postoperative morbidity around 45-50% and mortality below 5%, with 1-, 3-, and 5-year survival of 41%, 13%, and 7-8% — higher than with systemic treatment alone in selected patients responding to neoadjuvant chemotherapy.^{19,20} These results, although modest, suggest a

very selected subgroup with oligometastatic disease confined to the liver and a favorable response to systemic therapy might benefit from a combined approach; however, the lack of a validated definition of oligometastatic pancreatic disease and the single-center, retrospective nature of the available series preclude firm conclusions at present.

Liver metastases of non-digestive origin

Breast cancer

Breast cancer is the leading cause of cancer death in women worldwide, and the liver is the third most common site of metastasis after bone and lung.²¹ Five-year survival for localized breast cancer exceeds 99%, but the development of untreated liver metastases drastically reduces prognosis, with median survival of 4 to 8 months. Systemic therapy remains the cornerstone of management of metastatic disease, and leading international guidelines recommend that local treatment of the liver, including surgery, be reserved for very selected patients with good performance status, limited hepatic disease, no extrahepatic lesions, and demonstrated disease control after systemic therapy, with no consensus on the optimal local technique among surgery, stereotactic radiotherapy, or intrahepatic chemotherapy.²²

In the largest published series, liver resection was associated with 5-year OS of 41% and disease-free survival (DFS) of 21%, clearly superior to the 3-to-6-month median survival of untreated disease and to the approximately 15 months achieved with systemic therapy alone.²³ Factors associated with a better prognosis after resection include partial response to neoadjuvant chemotherapy, hormone receptor positivity, negative resection margins, a disease-free interval longer than 2 years, HER2 overexpression treated with targeted therapy, smaller tumor size, and unilobar disease, whereas prior failure of systemic therapy and a positive margin predict worse survival.²³⁻²⁵ Careful intraoperative exploration is essential to avoid missing undetected disease, and both open and laparoscopic approaches have proven safe, with favorable results for the minimally invasive approach in selected patients. A 2023 meta-analysis of nine studies and 1,732 patients confirmed and quantified this benefit: 5-year OS was significantly better after resection than with non-surgical treatment (46.0% vs 24.7%; odds ratio 0.46, 95% CI 0.25–0.87), with an overall survival hazard ratio of 0.69 (95% CI 0.59–0.80) favoring surgery — among the most robust evidence for any tumor type in this review.²⁶

Melanoma

Uveal melanoma spreads exclusively via the hematogenous route, since the uveal tract lacks lymphatic vessels, and metastasizes in isolation to the liver in approximately half of patients.^{27,28} Untreated hepatic disease carries a grim prognosis, with median survival of 4 to 6 months. Cutaneous melanoma, although sharing a melanocytic origin, spreads first via lymphatics to regional nodes and only later hematogenously, with the liver as its third most common visceral site; its liver metastases respond better to chemotherapy and checkpoint inhibitors than those of uveal origin, which has generated particular interest in local treatment, including surgery, for the latter.

Reference surgical series have reported complete resection of all measurable disease in approximately 75% of selected patients, with median OS of 27 to 29 months after surgery, compared with 6 months in patients treated non-surgically, and 2- and 5-year survival of 59 and 42% respectively in more recent series.²⁹⁻³¹ No relevant differences in survival have been observed according to the ocular or cutaneous origin of the primary melanoma once liver metastases are resected.³⁰ The prognostic factor most consistently associated with better survival is resection with disease-free margins, together with a lower number of liver lesions, a longer disease-free interval, a lower tumor burden, and the addition of systemic therapy. A pooled analysis of 912 patients with metastatic uveal melanoma from 29 prospective trials found substantially higher 1-year survival with liver-directed therapies, including resection, than with systemic therapy alone (57.2% vs 38.4%); elevated lactate dehydrogenase and alkaline phosphatase were the strongest adverse prognostic factors regardless of treatment.³² Overall, surgical resection of melanoma metastatic to the liver, whether of uveal or cutaneous origin, can meaningfully prolong survival in highly selected patients, although subsequent hepatic recurrence is common.

Soft tissue sarcoma

Liver metastases from soft tissue sarcoma are uncommon outside GIST. Small reference-center series report 5-year OS of approximately 30-31%, median survival of 24-46 months, and actuarial 1-, 3-, and 5-year survival of approximately 88-90%, 48-50%, and 30-32%.^{13,33,34} Complete resection is the key determinant of prognosis, with 5-year survival dropping to single digits when disease is not completely resected.¹³ Ideal candidates have good performance status, disease confined to the liver,

a disease-free interval of at least 12 months, small tumor size, fewer than five resectable lesions, and no progression on prior systemic therapy; extrahepatic disease makes surgical benefit unlikely.³⁴ Comparing histologic subtypes, the best long-term outcomes are seen for GIST, followed by leiomyosarcoma and other sarcomas, although these series remain individually underpowered and heterogeneous, so the magnitude of benefit by subtype cannot be reliably estimated; decisions should rely more on histology-specific discussion than on sarcoma-wide statistics.³³

Germ cell tumors and testicular cancer

Liver metastases from germ cell tumors, particularly non-seminomatous testicular cancer, arise hematogenously and frequently coexist with retroperitoneal disease. Surgery on residual masses after chemotherapy is standard multimodal treatment, since such masses may contain necrotic tissue, mature teratoma, or viable tumor, each with distinct implications.³⁵ Complete resection has been associated with 3-year survival up to 78% in favorable series, though broader-criteria series report more modest 5-year survival of around 45%.^{36,37} Residual mass size and primary histology help identify patients with a better prognosis, with worse outcomes for larger lesions. Evidence on liver metastases of testicular origin specifically remains confined to fewer than 30 patients across all published series combined, so larger studies are needed before surgery's role here is firmly established.

Ovarian cancer

Ovarian cancer is frequently diagnosed at advanced stages and is a major cause of mortality among gynecologic cancers.³⁸ The liver may be affected by superficial peritoneal seeding or by true hematogenous spread; available series suggest somewhat better survival with peritoneal seeding.³⁹ Cytoreductive surgery, typically including hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and resection of all visible disease, is the cornerstone of treatment for advanced disease, with liver resection as part of this procedure when parenchymal involvement is present.⁴⁰ Complete cytoreduction is associated with markedly better survival than suboptimal cytoreduction (median survival up to 65 months vs only a few months with substantial residual disease).⁴¹ Liver resection combined with primary cytoreduction appears to yield better outcomes than when performed as secondary or salvage surgery.³⁹ Morbidity of liver resection within

cytoreductive surgery is acceptable in experienced centers, but because bilobar involvement is generally a contraindication and no data isolate the specific contribution of liver resection from the rest of the cytoreductive procedure, current evidence supports it mainly as a component of complete cytoreduction rather than as an independent intervention.⁴²

Renal cell carcinoma

Renal cell carcinoma comprises several histologic subtypes with distinct metastatic behavior; liver metastases are relatively uncommon compared with pulmonary, bone, or brain sites, and more frequent in the chromophobe subtype.⁴³ They account for approximately 5-8% of non-colorectal non-neuroendocrine liver metastases and carry a traditionally poor prognosis, usually multifocal; because the primary tumor responds only marginally to conventional chemotherapy and radiotherapy, resection has long been the only potentially curative option.⁴⁴ Single-center series report 5-year OS of 26-43% after resection, with median survival exceeding 10 years in the most favorable series; better prognosis is associated with male sex, tumor size under 5 cm, DFI over

24 months, and negative margins.⁴⁵ A meta-analysis of 17 studies of metastasectomy (including hepatic metastasectomy) in metastatic renal cell carcinoma corroborated this benefit, reporting significantly higher mortality without metastasectomy (hazard ratio 2.15, 95% CI 1.59–2.92), with clear-cell histology and prior nephrectomy as additional favorable factors.⁴⁶ Targeted therapy and immunotherapy have substantially changed systemic treatment over the past two decades, making it necessary to reassess surgery's role within a combined approach.⁴⁴

Differentiated thyroid carcinoma

Liver metastases from differentiated thyroid carcinoma are extremely rare, as this tumor behaves indolently and spreads preferentially to cervical nodes, lung, and bone; the literature is limited to very small series and isolated case reports. Distant metastases are the most important negative prognostic factor, with 10-year survival around 50% in disseminated disease.⁴⁷ When liver metastases do not take up radioactive iodine, which further worsens prognosis, surgical resection has been described as offering the best chance of prolonged survival in the isolated published cases, ahead of chemoembolization or

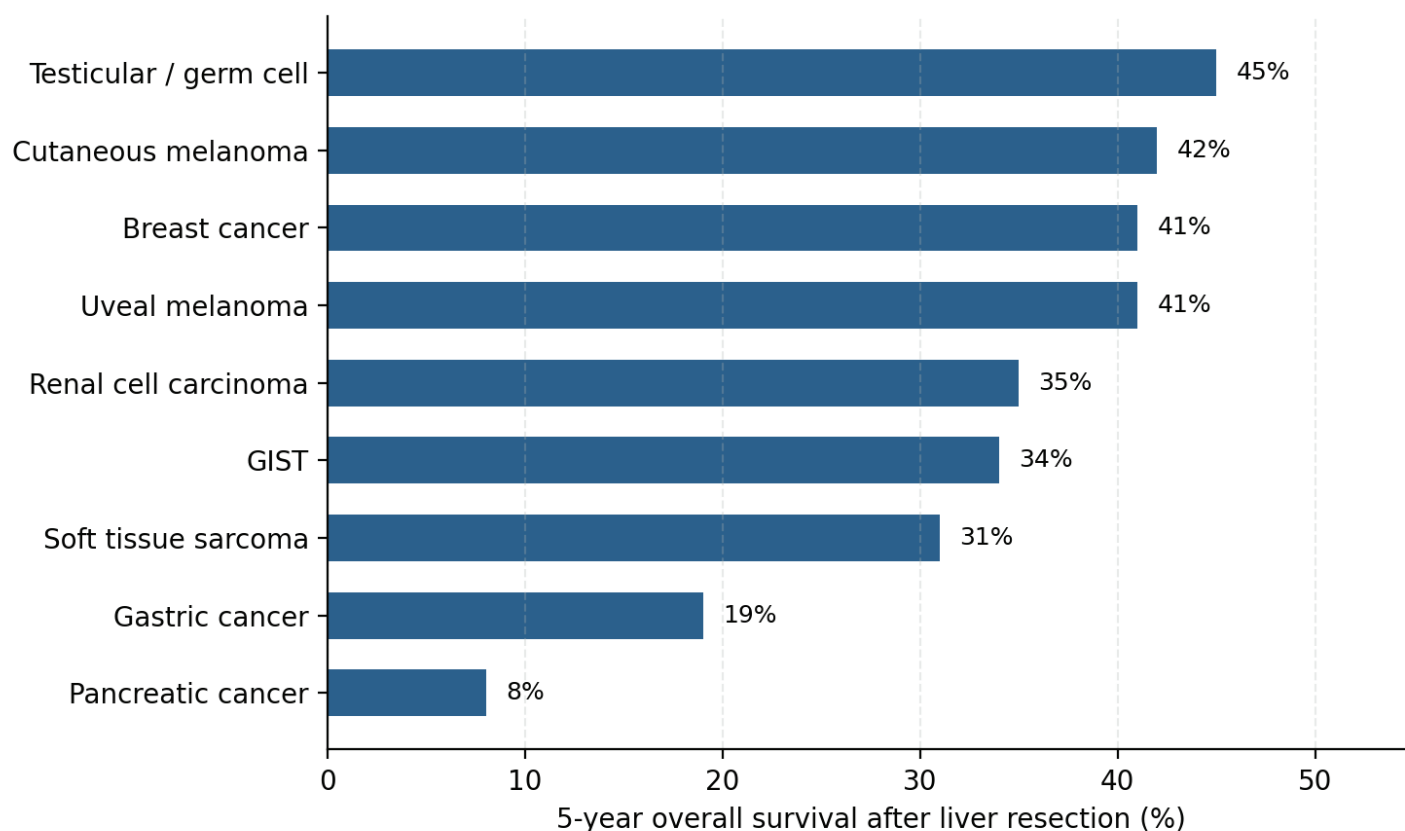


Figure 2. Reported 5-year overall survival (%) after liver resection, by primary tumor of origin. Values correspond to the midpoints or representative figures of the ranges reported in Table 1 and discussed in the text.

Table 1. Summary of reported outcomes after liver resection for non-colorectal non-neuroendocrine liver metastases, by primary tumor of origin.

Primary tumor	5-year OS (%)	Median survival (months)	Key favorable prognostic factors	Ref.
Breast cancer	41	~40	Partial response to neoadjuvant chemotherapy; hormone receptor positivity; R0 resection; DFI >2 years	23,24,26
Gastrointestinal stromal tumor	34	36	Postoperative TKI therapy; no extrahepatic disease at resection	14,15,18
Uveal melanoma	40–42	27–29	R0 resection; low tumor burden; longer DFI; addition of systemic therapy	29-31,32
Cutaneous melanoma	42	27–29	R0 resection; factors similar to uveal melanoma	30
Soft tissue sarcoma	30–31	24–46	Complete resection; DFI ≥12 months; fewer than 5 resectable lesions	13,33,34
Gastric cancer	19–25	5–24	Metachronous disease; N0/N1 nodal status; solitary lesion with wide margins; R0 resection	8-10,11
Renal cell carcinoma	26–43	often >60	Male sex; tumor <5 cm; DFI >24 months; R0 resection	45,46
Ovarian cancer (as part of cytoreduction)	NR	up to 65*	Complete (R0) cytoreduction; primary rather than secondary setting	39,41
Germ cell / testicular tumors	45–78	NR	Small residual mass (<30 mm); favorable histology	36,37
Pancreatic cancer (oligometastatic)	7–8	~12	Oligometastatic disease (≤3 lesions); response to neoadjuvant chemotherapy	19,20

OS, overall survival; DFI, disease-free interval; TKI, tyrosine kinase inhibitor; R0, microscopically negative resection margin; NR, not consistently reported across series. *Median survival reported for complete (R0) cytoreduction including liver resection. Figures are approximate and derived from the heterogeneous retrospective series and meta-analyses discussed in the corresponding sections of the text.

radiofrequency ablation. However, this entire evidence base consists of small retrospective series and case reports, none exceeding a handful of patients, with no comparative or prospective data; no recommendation stronger than individualized, case-by-case decision-making is currently justified for this tumor type.⁴⁸

Summary of reported outcomes

Table 1 summarizes the reported 5-year OS, median survival, and key favorable prognostic factors by primary tumor of origin, corroborated where available by recent tumor-specific meta-analyses. Figure 2 illustrates the corresponding 5-year OS graphically: outcomes are generally most favorable for germ cell tumors, melanoma, and breast cancer, and least favorable for gastric and pancreatic cancer, consistent with the pooled 5-year OS of 32% across all tumor types combined in the largest available meta-analysis.⁵

Technical aspects of liver resection

Technical advances over the past two decades have expanded the indications for liver surgery across the whole spectrum of liver metastases. Parenchymal-sparing surgery, using limited atypical or segmental resections rather than major anatomic hepatectomies, preserves functional parenchyma, reduces the risk of postoperative liver failure, and facilitates a second intervention in case of recurrence, without compromising oncologic outcome when an adequate margin is achieved; this is particularly relevant for breast cancer and GIST, in which recurrence after a first resection is not uncommon and a second hepatectomy can again provide a survival benefit. The laparoscopic and, more recently, robotic approaches have been progressively incorporated into oncologic liver surgery, with favorable perioperative results and no evidence of oncologic harm compared with the open approach in experienced hands, including for breast cancer

and melanoma metastases, although the evidence derives predominantly from retrospective studies.

In extensive bilobar disease that would leave an insufficient liver remnant after a single resection, two-stage hepatectomy and, more recently, associating liver partition and portal vein ligation for staged hepatectomy have been used; the latter achieves much faster hypertrophy of the future remnant (one to two weeks) than conventional portal vein embolization, with resection rates up to 90-100% in colorectal disease. Its role in non-colorectal non-neuroendocrine liver metastases is far less studied and should be considered with particular caution, given its higher perioperative risk and the sometimes more aggressive biology of this group of tumors.

Role of alternative local therapies

In patients not candidates for resection because of technical factors, comorbidity, or lesion location, radiofrequency or microwave ablation and stereotactic body radiotherapy offer alternative local control, alone or combined with surgery, particularly in liver-metastatic uveal melanoma, where iterative treatments combining resection and ablation have achieved prolonged survival.^{31,45} These techniques do not replace resection when it is technically feasible and oncologically reasonable, but they broaden options for non-surgical candidates; their role in this tumor group continues to evolve, with no randomized trials comparing both modalities to date.

Discussion

This review synthesizes the evidence on liver resection across ten non-colorectal non-neuroendocrine primary tumor types. In the largest available meta-analysis, resection achieved 3- and 5-year OS of 40% and 32%, with morbidity of 28% and 30-day mortality of 2%.⁵ Outcomes were most favorable for breast cancer, GIST, and melanoma (5-year OS >40%, and up to 78% for selected germ cell tumor series) and least favorable for gastric and pancreatic cancer (approximately 20-25% and 7-8%). Negative margins, limited hepatic tumor burden, a disease-free interval exceeding 12 months, and a favorable response to systemic therapy were the factors most consistently associated with improved survival across tumor types.

These findings are directly confirmed by recent tumor-specific meta-analyses. For breast cancer, resection nearly doubled 5-year survival versus non-surgical treatment (46.0% vs 24.7%; hazard ratio 0.69, 95% CI

0.59–0.80).²⁶ For GIST, adding surgery to TKI therapy more than halved the risk of death versus pharmacotherapy alone (hazard ratio 2.10, 95% CI 1.58–2.79).¹⁸ A similar effect size was reported for metastasectomy, including hepatic metastasectomy, in renal cell carcinoma (hazard ratio for death without metastasectomy 2.15, 95% CI 1.59–2.92).⁴⁶ Even gastric cancer, traditionally considered a poor surgical candidate, showed 5-year survival of 24.7% after hepatectomy in selected patients, challenging guidelines that discourage surgery in this setting.¹¹ This consistency across independently conducted meta-analyses strengthens confidence that the survival advantage attributed to resection reflects a genuine treatment effect and not only favorable patient selection, although residual confounding by indication cannot be excluded.

The variation in outcomes across tumor types most plausibly reflects differences in underlying biology rather than surgical technique. Breast cancer, GIST, and uveal melanoma tend toward indolent growth, organ-limited (often liver-only) spread, and, for breast cancer and GIST, effective systemic therapy capable of durable disease control around resection. Gastric and pancreatic adenocarcinoma are biologically more aggressive, with early micrometastatic dissemination that is frequently unrecognized at resection, likely explaining their persistently poor outcomes despite apparently complete clearance. The recurring prognostic value of a disease-free interval longer than 12 months across tumor types fits this framework, as it likely marks inherently less aggressive metastatic potential rather than being itself a modifiable target of treatment.

This review's strength is breadth: organizing fragmented, tumor-specific literature within one framework, cross-referenced against recent meta-analyses, provides an updated reference for a disease group individual centers rarely see in numbers sufficient to study alone. Its main limitation is methodological: a narrative, non-systematic review without a registered protocol, PRISMA-compliant search, dual screening, or risk-of-bias assessment, so selection cannot be considered free of the authors' judgment and publication bias cannot be excluded. Nearly all evidence is retrospective, from a few high-volume centers, with inherent selection bias since operated patients are by definition those judged fit for and likely to benefit from surgery; no randomized trial has compared resection with best systemic therapy for any tumor type discussed, and sample sizes for rarer tumors

(thyroid, testicular germ cell) remain in the dozens rather than hundreds of patients.

For practice, these findings support multidisciplinary consideration of resection when the primary tumor is controlled, hepatic disease is limited and resectable, extrahepatic disease is controlled, and systemic therapy has shown response or stability, weighting these criteria by the biology of the primary tumor. For research, the priority is prospective, multicenter or international registries with standardized eligibility and reporting criteria, allowing the comparative effectiveness of resection versus modern systemic therapy to be estimated with far less confounding than in today's retrospective series — of particular value for rarer subtypes unlikely ever to reach adequate single-center power.

Conclusions

Non-colorectal non-neuroendocrine liver metastases are a biologically heterogeneous group of diseases, and the evidence reviewed here indicates that liver resection can provide prolonged survival and, in selected subgroups such as breast cancer, gastrointestinal stromal tumor, and uveal melanoma, the possibility of long-term disease control, in carefully selected patients with limited hepatic disease, a controlled primary tumor, no uncontrolled extrahepatic disease, and a favorable response to systemic therapy. Advances in systemic therapy and in parenchymal-sparing and minimally invasive surgical techniques have progressively broadened these indications while reducing perioperative morbidity. Because prospectively validated selection criteria remain lacking, the decision to proceed with resection should always be individualized within a multidisciplinary team, and further prospective, multicenter studies are needed to define more precisely which patients truly benefit from surgery within this heterogeneous group of diseases.

Acknowledgments

None.

Author contributions

M.S.M. and J.M.R. conceived and designed the review. M.S.M. performed the literature search and drafted the manuscript. J.M.R. critically revised the manuscript for important intellectual content. Both authors read and approved the final version and agree to be accountable for all aspects of the work.

Funding

The authors declare that they received no specific funding for this work.

Conflicts of interest

The authors declare no conflicts of interest related to the content of this manuscript.

Informed consent

Not applicable: this work is a narrative review of the published literature and does not include original patient data.

References:

1. Adam R, Chiche L, Aloia T, Elias D, Salmon R, Rivoire M, et al. Hepatic resection for noncolorectal nonendocrine liver metastases: analysis of 1,452 patients and development of a prognostic model. *Ann Surg.* 2006;244(4):524-535.
2. Harrison LE, Brennan MF, Newman E, Fortner JG, Picardo A, Blumgart LH, et al. Hepatic resection for noncolorectal, nonneuroendocrine metastases: a fifteen-year experience with ninety-six patients. *Surgery.* 1997;121(6):625-632.
3. Takemura N, Saiura A. Role of surgical resection for non-colorectal non-neuroendocrine liver metastases. *World J Hepatol.* 2017;9(5):242-251.
4. Del Basso C, Usai S, Levi Sandri GB. Non-colorectal non-neuroendocrine liver metastasis: a narrative review of surgical treatment. *Chin Clin Oncol.* 2022;11(4):28.
5. Ng KKC, Cheng NMY, Lok HT, et al. Is hepatic resection justified for non-colorectal non-neuroendocrine liver metastases? A systematic review and meta-analysis. *Surgeon.* 2023;21(3):160-172.
6. Elias D, Cavalcanti de Albuquerque A, Eggenspieler P, Plaud B, Ducreux M, Spielmann M, et al. Resection of liver metastases from a noncolorectal primary: indications and results based on 147 monocentric patients. *J Am Coll Surg.* 1998;187(5):487-493.
7. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. *Lancet.* 2020;396(10251):635-648.
8. Cui JK, Liu M, Shang XK. Hepatectomy for liver metastasis of gastric cancer: a meta-analysis. *Surg Innov.* 2019;26(6):692-697.
9. Miyazaki M, Itoh H, Nakagawa K, Ambiru S, Shimizu H, Togawa A, et al. Hepatic resection of liver metastases from gastric carcinoma. *Am J Gastroenterol.* 1997;92(3):490-493.
10. Oki E, Tokunaga S, Emi Y, Kusumoto T, Yamamoto M, Fukuzawa K, et al. Surgical treatment of liver metastasis of gastric cancer: a retrospective multicenter cohort study (KSCC1302). *Gastric Cancer.* 2016;19(3):968-976.
11. Conde Monroy D, Ibáñez-Pinilla M, Sabogal JC, et al. Survival outcomes of hepatectomy in gastric cancer liver metastasis: a systematic review and meta-analysis. *J Clin Med.* 2023;12(2):704.
12. Nishida T, Hirota S. Biological and clinical review of

stromal tumors in the gastrointestinal tract. *Histol Histopathol.* 2000;15(4):1293-1301.

13. DeMatteo RP, Shah A, Fong Y, Jarnagin WR, Blumgart LH, Brennan MF. Results of hepatic resection for sarcoma metastatic to liver. *Ann Surg.* 2001;234(4):540-548.

14. Nunobe S, Sano T, Shimada K, Sakamoto Y, Kosuge T. Surgery including liver resection for metastatic gastrointestinal stromal tumors or gastrointestinal leiomyosarcomas. *Jpn J Clin Oncol.* 2005;35(6):338-341.

15. Xia L, Zhang MM, Ji L, Li X, Wu XT. Resection combined with imatinib therapy for liver metastases of gastrointestinal stromal tumors. *Surg Today.* 2010;40(10):936-942.

16. Cavnar MJ, Seier K, Curtin C, Balachandran VP, Coit DG, Yoon SS, et al. Outcome of 1000 patients with gastrointestinal stromal tumor (GIST) treated by surgery in the pre- and post-imatinib eras. *Ann Surg.* 2021;273(1):128-138.

17. Machairas N, Prodromidou A, Molmenti E, Kostakis ID, Sotiropoulos GC. Management of liver metastases from gastrointestinal stromal tumors: where do we stand? *J Gastrointest Oncol.* 2017;8(6):1100-1108.

18. Rahimi-Ardabili A, Murdande S, Dong M, Gu KW, Zhang B, Miller K, et al. Liver resection for metastatic GIST tumor improves survival in the era of tyrosine kinase inhibitors: a systematic review and meta-analysis. *Langenbecks Arch Surg.* 2023;408:373.

19. Andreou A, Knitter S, Klein F, Malinka T, Schmelzle M, Struecker B, et al. The role of hepatectomy for synchronous liver metastases from pancreatic adenocarcinoma. *Surg Oncol.* 2018;27(4):688-694.

20. Hackert T, Niesen W, Hinz U, Tjaden C, Strobel O, Ulrich A, et al. Radical surgery of oligometastatic pancreatic cancer. *Eur J Surg Oncol.* 2017;43(2):358-363.

21. Hess KR, Varadhachary GR, Taylor SH, Wei W, Raber MN, Lenzi R, et al. Metastatic patterns in adenocarcinoma. *Cancer.* 2006;106(7):1624-1633.

22. Cardoso F, Paluch-Shimon S, Senkus E, Curigliano G, Aapro MS, André F, et al. 5th ESO-ESMO International Consensus Guidelines for advanced breast cancer (ABC 5). *Ann Oncol.* 2020;31(12):1623-1649.

23. Adam R, Aloia T, Krissat J, Bralet MP, Paule B, Giacchetti S, et al. Is liver resection justified for patients with hepatic metastases from breast cancer? *Ann Surg.* 2006;244(6):897-908.

24. He X, Zhang Q, Feng Y, et al. Resection of liver metastases from breast cancer: a multicentre analysis. *Clin Transl Oncol.* 2020;22(4):512-521.

25. Elias D, Maisonneuve F, Druet-Cabanac M, Ouellet JF, Guinebreiere JM, Spielmann M, et al. An attempt to clarify indications for hepatectomy for liver metastases from breast cancer. *Am J Surg.* 2003;185(2):158-164.

26. Calpin GG, Davey MG, Calpin P, Browne F, Lowery AJ, Kerin MJ. The impact of liver resection on survival for patients with metastatic breast cancer: a systematic review and meta-analysis. *Surgeon.* 2023;21(4):242-249.

27. Jager MJ, Shields CL, Cebulla CM, Abdel-Rahman MH, Grossniklaus HE, Stern MH, et al. Uveal melanoma. *Nat Rev Dis Primers.* 2020;6(1):24.

28. Bustamante P, Piquet L, Landreville S, Burnier JV. Uveal melanoma pathobiology: metastasis to the liver. *Semin Cancer Biol.* 2021;71:65-85.

29. Rose DM, Essner R, Hughes TM, Tang PC, Bilchik A, Wanek LA, et al. Surgical resection for metastatic melanoma to the liver: the John Wayne Cancer Institute and Sydney Melanoma Unit experience. *Arch Surg.* 2001;136(8):950-955.

30. Ryu SW, Saw R, Scolyer RA, Crawford M, Thompson JF, Sandroussi C. Liver resection for metastatic melanoma: equivalent survival for cutaneous and ocular primaries. *J Surg Oncol.* 2013;108(2):129-135.

31. Mariani P, Piperno-Neumann S, Servois V, Berry MG, Dorval T, Plancher C, et al. Surgical management of liver metastases from uveal melanoma: 16 years' experience at the Institut Curie. *Eur J Surg Oncol.* 2009;35(9):1192-1197.

32. Khoja L, Atenafu EG, Suci S, et al. Meta-analysis in metastatic uveal melanoma to determine progression free and overall survival benchmarks: an international rare cancers initiative (IRCI) ocular melanoma study. *Ann Oncol.* 2019;30(8):1370-1380.

33. Brudvik KW, Patel SH, Roland CL, Conrad C, Torres KE, Hunt KK, et al. Survival after resection of gastrointestinal stromal tumor and sarcoma liver metastases in 146 patients. *J Gastrointest Surg.* 2015;19(8):1476-1483.

34. Tirotta F, Hodson J, Parente A, Pasquali S, Sutcliffe R, Desai A, et al. Liver resection for sarcoma metastases: a systematic review and experience from two European centres. *Eur J Surg Oncol.* 2020;46(10 Pt A):1807-1813.

35. Rivoire M, Elias D, De Cian F, Kaemmerlen P, Theodore C, Fizazi K, et al. Multimodality treatment of patients with liver metastases from germ cell tumors. *Cancer.* 2001;92(3):578-587.

36. Maluccio M, Einhorn LH, Goulet RJ. Surgical therapy for testicular cancer metastatic to the liver. *HPB (Oxford).* 2007;9(3):199-200.

37. Hahn TL, Jacobson L, Einhorn LH, Foster R, Goulet RJ. Hepatic resection of metastatic testicular carcinoma: a further update. *Ann Surg Oncol.* 1999;6(7):640-644.

38. Nakayama K, Nakayama N, Katagiri H, Miyazaki K. Mechanisms of ovarian cancer metastasis: biochemical pathways. *Int J Mol Sci.* 2012;13(9):11705-11717.

39. Bacalbasa N, Dima S, Brasoveanu V, David L, Balescu I, Bacalbasa I, et al. Liver resection for ovarian cancer liver metastases as

part of cytoreductive surgery is safe and may bring survival benefit. *World J Surg Oncol.* 2015;13:235.

40. Pekmezci S, Saribeyoglu K, Aytac E, Karabork A, Baysal M, Onguru O, et al. Surgery for isolated liver metastasis of ovarian cancer. *Asian J Surg.* 2010;33(2):83-88.

41. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol.* 2002;20(5):1248-1259.

42. Luna-Abanto J, García Ruiz L, Laura Martinez J, Alfredo Bravo Taxa M, Ruiz Figueroa E. Liver resection as part of cytoreductive surgery for ovarian cancer. *J Gynecol Surg.* 2020;36(2):70-75.

43. Dudani S, de Velasco G, Wells JC, Gan CL, Donskov F, Porta C, et al. Evaluation of clear cell, papillary, and chromophobe renal cell carcinoma metastasis sites and association with survival. *JAMA Netw Open.* 2021;4(1):e2021869.

44. Choueiri TK, Motzer RJ. Systemic therapy for metastatic renal-cell carcinoma. *N Engl J Med.* 2017;376(4):354-366.

45. Ruys AT, Tanis PJ, Nagtegaal ID, van Duijvendijk P, Verhoef C, Porte RJ, et al. Surgical treatment of renal cell cancer liver metastases: a population-based study. *Ann Surg Oncol.* 2011;18(7):1932-1938.

46. Hsieh PY, Hung SC, Li JR, et al. The effect of metastasectomy on overall survival in metastatic renal cell carcinoma: a systematic review and meta-analysis. *Urol Oncol.* 2021;39(7):422-430.

47. Elisei R, Molinaro E, Agate L, Bottici V, Masserini L, Ceccarelli C, et al. Are the clinical and pathological features of differentiated thyroid carcinoma really changed over the last 35 years? *J Clin Endocrinol Metab.* 2010;95(4):1516-1527.

48. Niederle B, Roka R, Schemper M, Fritsch A, Weissel M, Ramach W. Surgical treatment of distant metastases in differentiated thyroid cancer: indication and results. *Surgery.* 1986;100(6):1088-1097.

IMAGE OF THE MONTH

Cándido Alcázar MD PhD FACS ^{1,2,3}, Celia Villodre MD PhD FACS ^{1,2,3}, Silvia Carbonell-Morote MD PhD FACS ESA ^{1,2,3}, Jose M. Ramia MD PhD FACS FRCS FRCS Ed FKCS ESA FEBS-HPB ^{1,2,3}

¹ Department of Surgery. Hospital General Universitario Dr. Balmis de Alicante.

² Instituto de Investigación Sanitaria y Biomédica de Alicante (ISABIAL). Alicante (Spain)

³ Universidad Miguel Hernández. Alicante (España)

Corresponding Author:

JOSÉ MANUEL RAMIA, MD, PHD, FACS, FRCS, FRCS(ED), FKCS

Head of Department. Department of Surgery. Hospital General Universitario de Alicante

Professor of Surgery. Universidad Miguel Hernández

Sol Naciente 8, 16D Alicante (Spain), 03016.

E-mail: jose_ramia@hotmail.com

Key words: liver, anatomic variation, surgery, beaver tail liver

- The case report was approved by the Ethics Committee of Hospital General Universitario Dr. Balmis. Alicante (Spain).
- Written consent was obtained from patient.
- This manuscript includes one image. Castor image was done by ChatGPT
- Manuscript word count: 306

Beaver tail liver

A 33-year-old woman underwent magnetic resonance cholangiopancreatography following an episode of acute pancreatitis associated with transient elevation of liver function tests. Axial T2-weighted magnetic resonance imaging demonstrated an unusual elongation of the left hepatic lobe (BTL) extending into the left upper quadrant and wrapping around the spleen (S) (Fig. 1A). This characteristic appearance corresponds to a beaver tail liver, a rare anatomical variant also known as the “sliver of liver”. The spleen is almost surrounded by normal hepatic parenchyma, creating a configuration that resembles the broad, flattened tail of a beaver (Fig. 1B).

BTL results from excessive lateral extension of

segments II and III of the liver. Although this variation is usually asymptomatic and discovered incidentally on imaging studies, awareness of it is clinically important. Because the elongated hepatic tissue may have similar density or echogenicity to the spleen, it can be mistaken for perisplenic fluid, splenic subcapsular hematoma, or splenic injury, particularly in the setting of abdominal trauma. Identification of portal or hepatic venous branches within the tissue helps establish the correct diagnosis.

In addition, failure to recognize this variant may complicate upper abdominal surgery, interventional radiology procedures, or image-guided biopsies. Rarely, patients may report discomfort or pain in the left upper quadrant due to the unusual anatomical relationship between the liver and spleen.

Although no treatment is required, knowledge of this uncommon variant may prevent diagnostic errors and avoid unnecessary interventions. The present image illustrates a classic example of beaver tail liver, a fascinating anatomical curiosity with important implications for surgeons and radiologists.

Learning points: Beaver tail liver is a rare anatomical variant characterized by the lateral extension of the left

hepatic lobe around the spleen. Recognition of this entity is important because it may mimic splenic pathology on imaging studies and may alter surgical planning in the left upper abdomen.

References:

1. Atalar MH, Karakus K. Beaver tail liver. *Abdom Radiol (NY)*. 2018 Jul;43(7):1851-1852. doi: 10.1007/s00261-017-1395-x.

PMID: 29167946.

2. Khanduri S, Malik S, Khan N, Singh H, Rehman M. Beaver Tail Liver: A Hepatic Morphology Variant. *Cureus*. 2021 Jul 12;13(7):e16327. doi: 10.7759/cureus.16327. PMID: 34395114; PMCID: PMC8357019.

3. Covantsev S, Lebedinsky I, Slepukhova D, Kovaleva M, Mulaeva K. Beaver tail liver: an incidental but crucial anatomical variation in case of acute abdomen. *Iberoamerican J Med*. 2023;5:93–95.

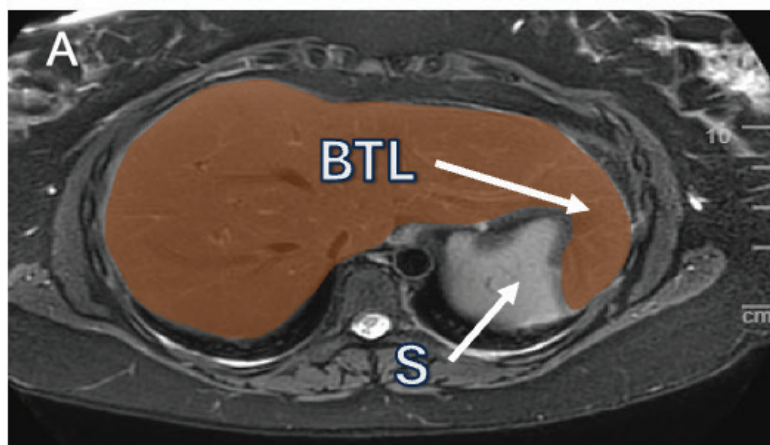


Figure 1:

A: MRI: BTL: beaver tail liver; S: Spleen; **B:** beaver tail explaining the reason of the etymology of the liver anatomical variation name

2nd CLINICAL CONGRESS OF PAN-ALBANIAN COLLEGE OF SURGEONS

Updates in Surgical Sciences

ABOUT

Join us for the 2nd Clinical Congress of Albanian Surgeons, a premier scientific gathering that brings together leading surgeons, clinicians, researchers, and innovators from across the Albanian-speaking world and beyond.

DATE

22-24 October 2026

VENUE

**TIRANA INTERNATIONAL HOTEL
TIRANA, ALBANIA**

EVENT HIGHLIGHTS

KNOWLEDGE EXCHANGE

NETWORKING

STRATEGIC PARTNERS

