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

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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.

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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 imaging[1].

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 disease[1].

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 (multicenter)	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 (multicenter)	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 / multicenter	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 (multicenter)	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 (multicenter)	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

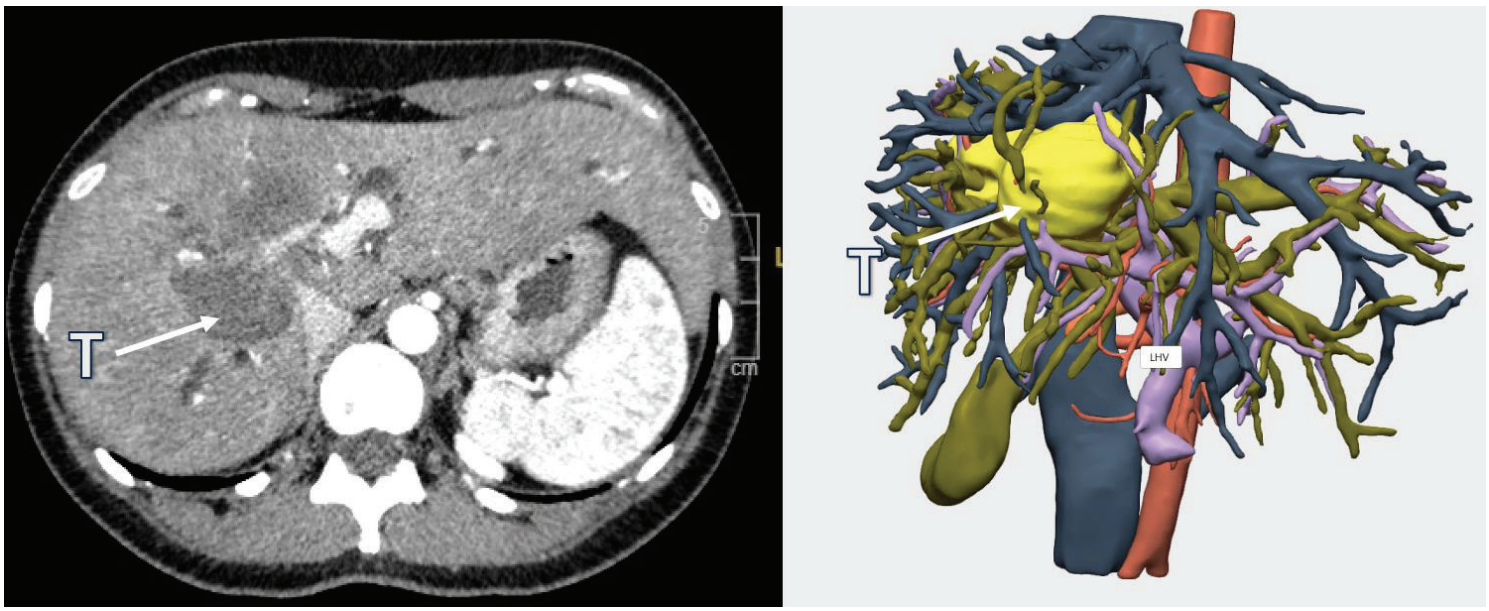


Figure 1: ICC: CT and 3D model. T: tumor

laparotomy in 25–36% of patients considered resectable after imaging[2]. 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 intervention[3].

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 months[7]. 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 outcome[8].

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 intraoperatively[10].

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 resection[9]. 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 disease[13]. 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 survival[14]. In contrast, Lang et al. found no statistically significant survival difference between R0 and R1 resections in their German single-center experience[11], 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 model[8].

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 surgery[9]. 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 staging[14]. Conversely, Lang et al. reported lymphadenectomy in nearly 90% of resections, with a median of 5 lymph nodes retrieved[11].

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 biology[6]. 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 benefit[10].

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 surgery[19-21]. 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 surgery[19-21]. 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 studies[19]. 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 difference[22]. 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 invasion[23]. 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 MILS[25]. 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 surgery[26]. 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

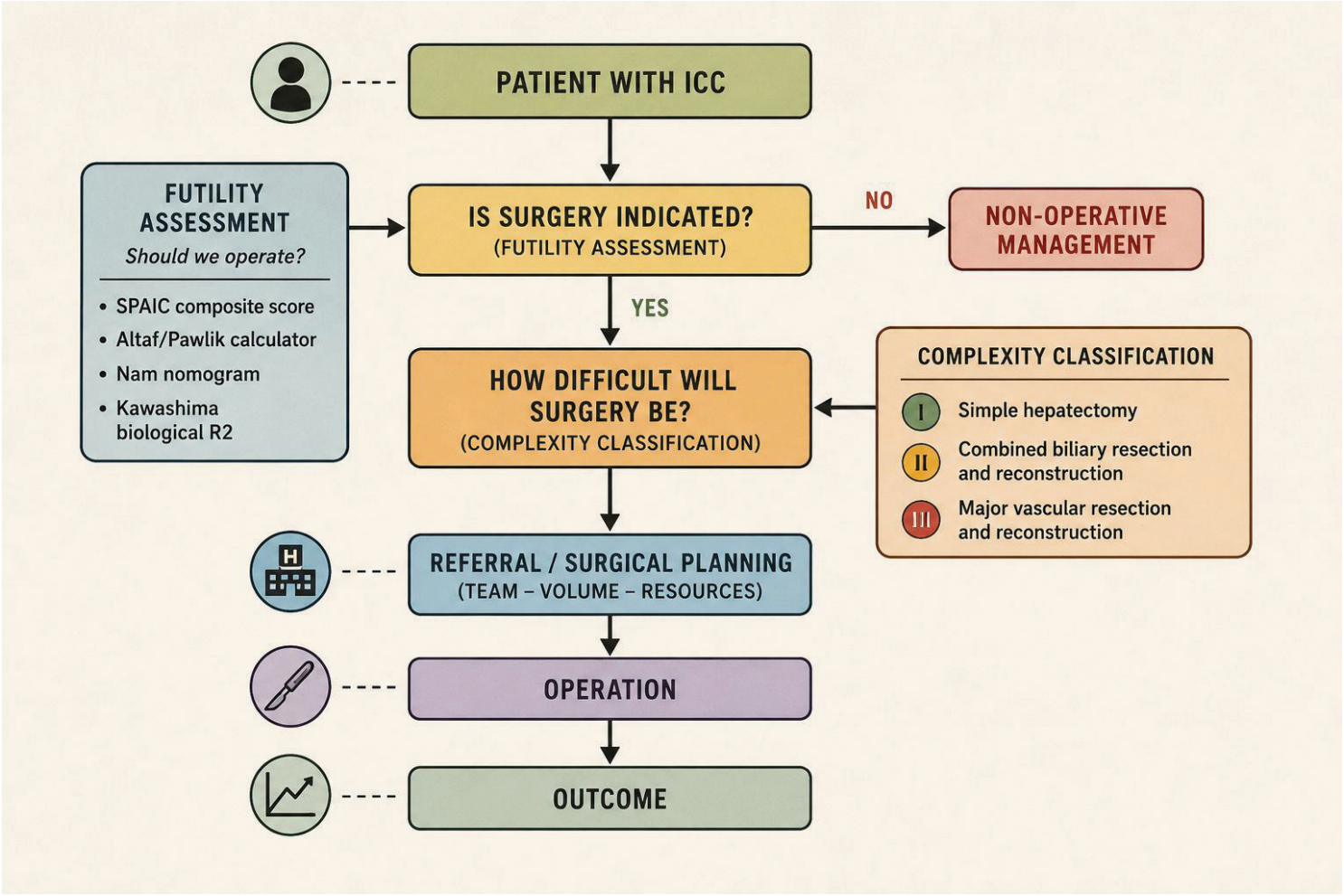


Figure 2. Integrated framework for decision-making in intrahepatic cholangiocarcinoma

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 date[5–9].
- 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 resection[9].
- 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 compromised[19–24].
- 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 disease[5], radiomic prediction[6], a composite perioperative/survival threshold[7], biological R2[8], or the composite endpoint used in our own SPAIC cohort[9] — 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 Torzilli[13] — 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 resection[9], 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 hepatectomy[10]. 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 for[6]. 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 interpretation[24]. 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.

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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 (AFEF). 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.