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Review Article

Extent of liver resection for incidental gallbladder cancer: Anatomic versus nonanatomic approaches in T2–T3 disease

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ABSTRACT

Background: Incidental gallbladder cancer (IGBC) is increasingly diagnosed after cholecystectomy performed for presumed benign disease. For T2 and selected T3 tumors, completion radical re-resection with liver resection and regional lymphadenectomy is recommended, but the optimal hepatic extent—nonanatomic wedge resection versus anatomic segment IVb/V resection—remains debated.

Methods: This narrative review summarizes evidence from IGBC-specific series and registries, international multicenter cohorts, meta-analyses, and contemporary consensus guidelines comparing wedge resection and segment IVb/V resection for T2–T3 gallbladder cancer, with emphasis on oncologic outcomes, perioperative morbidity, and the evolving role of systemic therapy.

Results: Across contemporary cohort studies and meta-analyses, margin-negative wedge resection appears to provide long-term oncologic outcomes comparable to segment IVb/V resection for T2 disease, while segment IVb/V is consistently associated with higher perioperative morbidity. Tumor location (T2a vs T2b) may correlate with prognosis, but does not independently mandate greater liver volume when nodal and margin status are considered. In IGBC, outcomes are driven primarily by nodal involvement, residual disease, and margin status rather than by the specific hepatic volume removed. For T3 and other high-risk presentations, large international datasets suggest limited incremental benefit from escalation to major hepatectomy or routine extrahepatic bile duct resection, although bile duct resection is indicated when the cystic duct margin is positive. Neoadjuvant systemic therapy is increasingly considered in selected borderline-resectable or node-positive disease to enable biologic selection and improve the likelihood of achieving an R0 resection with limited hepatic excision.

Conclusions: For T2 IGBC, a parenchyma-sparing, margin-negative wedge resection of the gallbladder bed combined with high-quality regional lymphadenectomy appears to provide oncologic outcomes comparable to segment IVb/V resection in most patients. Current evidence does not demonstrate a consistent survival advantage for routine segment IVb/V resection. In T3 and high-risk disease, surgical strategy should prioritize biologic selection and integration of systemic therapy, with hepatic extent tailored to margin requirements rather than routine escalation.

1. Introduction

Gallbladder cancer (GBC) is an uncommon but highly lethal biliary tract malignancy with marked geographic variation in incidence. In population-based U.*S. data*, the annual incidence is approximately 1–2 per 100,000, with substantially higher rates in parts of South America and Asia [1–5]. Even among patients who undergo resection, reported 5-year overall survival commonly ranges from 15% to 30% in large contemporary series [6,7].

With the widespread adoption of laparoscopic cholecystectomy and routine histopathologic assessment of resected gallbladders, incidental gallbladder cancer (IGBC)—malignancy diagnosed during or after cholecystectomy performed for presumed benign disease—has become an increasingly common presentation [8,9]. Contemporary series suggest unsuspected carcinoma in approximately 0.7–0.9% of cholecystectomy specimens [10]. Because IGBC is often identified at earlier T stage than primary symptomatic disease, appropriate completion radical re-resection can yield substantially improved long-term outcomes

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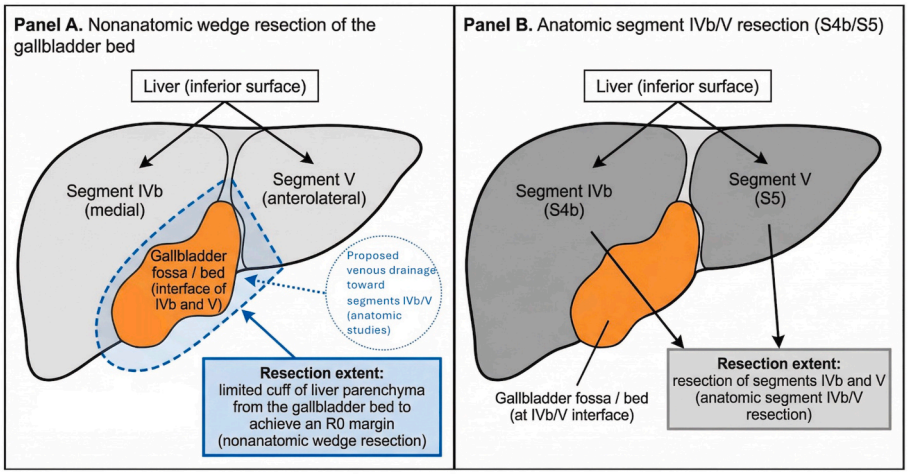

Fig. 1. Hepatic extent in completion radical re-resection for incidental gallbladder cancer: nonanatomic wedge resection versus anatomic segment IVb/V resection.

(A) Nonanatomic wedge resection of the gallbladder bed, illustrating limited excision of a cuff of liver parenchyma adjacent to the gallbladder fossa to achieve a negative hepatic margin (R0). The dotted blue outline indicates a representative wedge-resection extent. The venous drainage callout reflects the historical anatomic rationale for considering larger hepatic resection, based on studies suggesting preferential gallbladder venous drainage toward segments IVb and V.

(B) Anatomic segment IVb/V resection (S4b/S5), illustrating formal resection of the hepatic segments bordering the gallbladder fossa. This approach removes a larger volume of liver parenchyma than wedge resection.

Note: This schematic illustrates the conceptual difference between parenchyma-sparing wedge resection and anatomic segmental resection; terminology and anatomic extent vary across studies (e.g., S4a + S5 vs S4b + S5).

Abbreviations: R0, margin-negative resection; S4a/S4b/S5, Couinaud segments 4a, 4b, and 5.

compared with cholecystectomy alone [11–13].

For patients with T2 and selected T3 disease without distant metastases, current guidelines and expert consensus recommend completion radical cholecystectomy (re-resection) consisting of hepatic resection of the gallbladder bed and regional lymphadenectomy [14–17]. The principal surgical controversy in the hepatic component of this operation is the necessary extent of liver resection: a parenchyma-sparing, nonanatomic wedge resection of the gallbladder bed (often targeting a limited margin when feasible) versus an anatomic resection of segments IVb/V (S4b/S5) [15,18,19]. The historical rationale for anatomic segment IVb/V resection derives in part from anatomic studies describing preferential venous drainage from the gallbladder into these segments, raising concern for occult micrometastatic spread along this route [20,21]. The anatomic relationship of the gallbladder fossa to hepatic segments IVb and V, and the distinction between wedge and anatomic segment IVb/V resection, are shown in Fig. 1.

Despite this rationale, the optimal hepatic extent—particularly in the incidental setting—remains debated. Earlier registry and single-center experiences, including the German IGBC registry, were often interpreted as supporting at least segment IVb/V resection for T2 tumors [22,23]. However, more contemporary cohort studies, international multicenter series, and meta-analyses have not demonstrated a consistent long-term survival advantage for routine segment IVb/V resection over a margin-negative wedge resection in T2 disease, while repeatedly reporting higher perioperative morbidity associated with the more extensive anatomic approach [24–28]. Reflecting this evolving evidence base, the recent IHPBA–APHPBA international consensus states that a margin-negative wedge resection is an adequate hepatic extent for T2 GBC, whereas evidence remains insufficient to recommend one approach over the other in T3 disease, with emphasis instead on margin requirements and tumor biology [14].

Concurrently, multiple datasets indicate that outcomes after re-resection are driven primarily by biologic and pathologic factors—including lymph node status, residual disease at re-resection, and resection-margin status—rather than the absolute volume of liver removed [7,11,29–31]. In high-risk and locally advanced presentations, escalation to major hepatectomy, hepatopancreatoduodenectomy, or routine extrahepatic bile duct resection (except when required for clearance of the cystic duct margin) has been associated with substantial morbidity and mortality and has not consistently translated into improved survival in large contemporary cohorts [14,32–34]. The increasing integration of systemic therapy—particularly neoadjuvant chemotherapy for borderline-resectable or node-positive disease—further supports a strategy of biologic selection and margin-driven resection rather than routine escalation of operative extent.

Accordingly, this narrative review focuses on incidentally discovered T2–T3 gallbladder cancer and critically evaluates evidence comparing nonanatomic wedge resection with anatomic segment IVb/V resection as the hepatic component of completion radical cholecystectomy. We emphasize oncologic outcomes (R0 resection, residual disease, recurrence patterns, disease-free and overall survival) and perioperative morbidity, and we interpret these data in the context of modern multimodality therapy. Because much of the comparative literature includes mixed primary and incidental cohorts, we highlight IGBC-specific evidence when available and interpret conclusions with appropriate caution.

2. Methods

A structured literature search was conducted to inform this narrative review, covering publications from database inception to January 2026 in PubMed/MEDLINE, Embase, and Scopus. Search terms included combinations of keywords and controlled vocabulary (MeSH/Emtree), including “gallbladder cancer,” “incidental gallbladder cancer,” “IGBC,” “wedge resection,” “segmentectomy,” “segment IVb/V,” and “radical cholecystectomy.”

We prioritized studies directly comparing nonanatomic wedge resection and anatomic segment IVb/V resection in T2–T3 gallbladder cancer, including IGBC-specific cohorts, large international multicenter series, systematic reviews and meta-analyses, and contemporary consensus guidelines. Given the limited number of IGBC-only studies, selected mixed cohorts (incidental and non-incidental cases) were

included when they provided relevant comparative data. Eligible publications included clinical studies, multicenter cohorts, registry analyses, systematic reviews, meta-analyses, and consensus guidelines relevant to hepatic resection extent and outcomes in T2–T3 gallbladder cancer. Case reports, small technical series without oncologic outcomes, and non-relevant studies were excluded.

As this is a narrative (non-systematic) review, formal study selection protocols and quality scoring were not applied. Evidence was synthesized thematically, with emphasis on oncologic outcomes, perioperative morbidity, and key confounders, including margin status, nodal involvement, lymphadenectomy quality, and selection bias (confounding by indication). This review was not conducted as a formal systematic review according to PRISMA guidelines, and no predefined protocol was registered.

3. Incidental gallbladder cancer: why Re-resection matters for the liver-extent debate

3.1. Definition and frequency

Incidental gallbladder cancer (IGBC) refers to malignancy not suspected before or at the start of cholecystectomy and diagnosed intraoperatively (e.g., frozen section) or, more commonly, on final histopathology [8,10,14]. In contemporary series, unsuspected carcinoma is found in approximately 0.7–0.9% of cholecystectomy specimens [8–10]. Because IGBC is frequently detected at an earlier T stage than primary symptomatic disease, timely completion radical re-resection provides an important opportunity for cure when disease remains locoregional [9–13].

3.2. Residual disease at re-resection and prognostic significance

A central rationale for completion radical surgery in IGBC is the high frequency of residual disease at re-exploration, even when preoperative imaging is unremarkable [11,13,35]. In a multicenter IGBC series, Pawlik et al. reported residual or additional tumor in a substantial proportion of re-explored patients, with residual disease increasing sharply with T stage; residual involvement included the liver bed, lymph nodes, and the cystic duct/common bile duct region [11]. Importantly, residual disease—particularly in the liver bed and regional nodes—was strongly associated with inferior long-term survival [11].

Other IGBC series corroborate the dominant prognostic impact of residual disease. Lendoire et al. reported that patients with residual disease at standardized completion resection experienced early recurrence and poor survival compared with those without residual disease [35]. Similarly, Butte et al. confirmed that residual disease predicts outcomes after definitive resection for incidental GBC [36]. Collectively, these studies support completion radical re-resection for fit patients with incidental T2 and selected T3 tumors in the absence of distant metastases [11,35,36].

Population-level registry data further reinforce the benefit of re-resection over cholecystectomy alone. In the German IGBC registry, radical re-resection was associated with improved survival for incidental T2 and T3 disease compared with simple cholecystectomy [22,23].

3.3. Key implication for hepatic extent

Across IGBC datasets, outcomes after re-resection appear to be driven primarily by tumor biology and adequacy of oncologic clearance—particularly residual disease status, nodal involvement, and margin status—rather than by escalation of the hepatic volume removed. In Pawlik et al., more extensive hepatic resection and bile duct resection were not independently associated with improved disease-specific survival after adjustment, whereas residual carcinoma and advanced stage were strongly prognostic [11]. This supports a margin-driven approach to liver resection extent rather than routine escalation.

Table 1
IGBC-specific rationale for completion radical re-resection (residual disease and timing).

Domain	Key evidence (study)	Main findings (as reported)	Why it matters for liver-extent decisions
Residual disease is common at re-resection	Pawlik et al. [11]	Substantial rates of residual/additional disease at re-exploration; frequency increases with T stage; residual sites include liver bed, lymph nodes, and cystic duct/common bile duct region.	Justifies completion radical re-resection (liver + nodes). Shifts emphasis from "how much liver" to achieving R0 resection and clearing residual disease.
Residual disease strongly predicts poor outcomes	Pawlik et al. [11]; Lendoire et al. [35]; Butte et al. [36]	Residual disease is associated with markedly worse survival and early recurrence compared with no residual disease.	Supports biology-driven counseling and reinforces that prognosis is driven by residual disease, nodal status, and margin status rather than routine escalation of liver volume.
Re-resection improves survival vs cholecystectomy alone	German IGBC registry: Goetze and Paolucci [22,23]	Improved survival for incidental T2 and T3 after radical re-resection compared with simple cholecystectomy.	Reinforces guideline-concordant completion radical surgery in appropriate candidates.
Timing of re-resection: no rigid threshold	Ethun et al. [37]; Selvakumar et al. [38]; IHPBA–APHPBA [14]	Ethun: best OS signal at 4–8 weeks. Selvakumar IPD meta-analysis: no clear survival difference with ≤4 vs > 4 weeks; timing definitions heterogeneous. Consensus: individualize timing.	Timing should prioritize recovery and completion staging and does not change the wedge vs segment IVb/V conclusion.

Abbreviations: IGBC, incidental gallbladder cancer; OS, overall survival; R0, margin-negative resection; IPD, individual patient data.

3.4. Timing of completion radical re-resection

The optimal timing of re-resection remains uncertain. In a multi-institutional U.S. cohort, Ethun et al. reported the longest median overall survival among patients re-resected 4–8 weeks after index cholecystectomy, with worse survival associated with very early (<4 weeks) or delayed (>8 weeks) reoperation on multivariable analysis [37]. However, an individual patient data meta-analysis by Selvakumar et al. found no clear survival difference using a ≤4-week versus >4-week threshold and highlighted the lack of standardized timing definitions across retrospective series [38]. Current consensus acknowledges the importance of interval selection but does not mandate a rigid cutoff [14]. Practically, re-resection is commonly pursued after adequate recovery and completion staging, often within a roughly 4–8-week window when feasible [14,37,38].

Table 2
Comparative evidence for hepatic extent in T2–T3 gallbladder cancer (wedge resection vs segment IVb/V resection).

Study (Ref)	Design/setting	Cohort type	Population	Comparison	Key oncologic outcomes	Morbidity/operative outcomes	Key takeaway for the review
Kwon et al. [24]	International multicenter retrospective cohort	Mixed (incidental + non-incidental)	pT2 GBC	Extended vs simple; within extended: wedge vs segment IVb/V	Extended improved DFS vs simple. Within extended resections, wedge and segment IVb/V had similar long-term outcomes after adjustment; location not independent after adjustment for nodal and margin status.	Not primary endpoint.	For T2, benefit is radical resection + LND; routine segment IVb/V not proven superior to wedge when R0 achievable.
Chen et al. [26]	Propensity-score matched cohort	Mixed	T2 GBC	Segment IVb/V vs wedge	No significant OS/DFS difference after matching.	Operative time/blood loss higher with segment IVb/V.	Matched evidence supports oncologic equivalence with lower operative burden for wedge.
Nag et al. [27]	Matched case–control	Mixed	T2/T3 GBC	Segment IVb/V vs wedge	No clear oncologic superiority of segment IVb/V.	Complications higher with segment IVb/V.	Supports parenchyma-sparing approach when margins are achievable.
Horiguchi et al. [28]	Registry analysis	Mixed	pT2 GBC	Gallbladder-bed (wedge) vs S4a + S5 hepatectomy	No significant survival difference when R0 and adequate nodal dissection achieved.	Registry heterogeneity.	Early registry signal supports adequacy of limited hepatic resection in pT2 disease with appropriate nodal surgery.
Araida et al. [40]	Multicenter Japanese survey	Mixed	R0 pT2–pT3	Varying hepatectomy extents	No clear advantage for more extensive hepatectomy over minor resection.	Survey design.	Suggests escalation in liver volume does not clearly translate to survival benefit.
Matsui et al. [25]	Systematic review & meta-analysis	Mixed	T2–T3 GBC	Wedge vs segment IVb/V	No significant differences in 5-year DFS/OS or liver metastasis.	Fewer complications with wedge; no increase in bile leak.	Wedge resection appears to offer similar long-term oncologic outcomes with lower morbidity.
Chen Z et al. [39]	Systematic review & meta-analysis	Mixed	T2 GBC	Segment IVb/V vs wedge	Segment IVb/V: modest short-term DFS benefit; no 3-/5-year DFS advantage; OS HR favored wedge.	Complications higher with segment IVb/V.	No durable survival advantage for routine segment IVb/V; morbidity consistently higher.
OMEGA cohort [32]	International multicenter cohort	Mixed	All stages (includes T3)	No liver resection vs wedge resection vs segment IVb/V resection vs major hepatectomy	After adjustment for T stage, nodal status, and margin status, wedge and segment IVb/V were not consistently independently associated with improved survival; major hepatectomy associated with worse outcomes.	Major hepatectomy: higher serious morbidity/90-day mortality; EBDR/ multivisceral increased complications.	Escalation beyond what is needed for R0 (especially major hepatectomy) is not justified routinely.

Abbreviations: DFS, disease-free survival; OS, overall survival; LND, lymph-node dissection; EBDR, extrahepatic bile duct resection; R0, margin-negative resection.
Note: "Cohort type" is listed as mixed where studies include both incidental and non-incidental cases. The anatomic extent termed "segment IVb/V" varies across studies (e.g., S4a + S5 vs S4b + S5), which limits strict cross-study equivalence of segmental terminology.

3.5. Implications for the wedge versus segment IVb/V question

For incidental T2–T3 disease, the high prevalence and prognostic impact of residual disease provide the rationale for completion radical surgery, including liver resection and regional lymphadenectomy [11,22,23,35,36]. However, available evidence suggests that the specific hepatic extent (wedge versus segment IVb/V, or escalation beyond these approaches) has less impact on survival than achieving an R0 resection and addressing nodal disease [11,22–27,35]. These principles frame the subsequent comparison of parenchyma-sparing wedge resection versus anatomic segment IVb/V resection in T2–T3 disease. Key IGBC-specific evidence supporting completion re-resection, including residual disease prevalence and timing considerations, is summarized in Table 1.

4. T2 incidental gallbladder cancer: extent of liver resection (wedge vs segment IVb/V) and tumor location

4.1. Why liver resection is required in T2 disease (extended vs simple cholecystectomy)

For T2 gallbladder cancer, simple cholecystectomy alone is generally inadequate; radical cholecystectomy (liver resection plus regional lymphadenectomy) is associated with improved oncologic outcomes and is recommended in contemporary guidelines for fit patients [14,15,17].

In the large international multicenter study by Kwon et al. including 937 patients with pathologic T2 GBC, extended cholecystectomy (cholecystectomy with liver resection and lymph-node dissection) was associated with improved 5-year disease-free survival compared with simple cholecystectomy (73.0% vs 61.5%; P = 0.012), and this association persisted after excluding Nx cases [24]. These data support completion radical re-resection for incidental T2 tumors when staging excludes metastatic disease [14,24].

4.2. Core question: wedge resection versus anatomic segment IVb/V resection in T2 disease

Once radical resection is indicated, the central debated issue is the hepatic extent required: a nonanatomic wedge resection of the gallbladder bed versus an anatomic resection of segments IVb/V. Contemporary evidence—dominated by retrospective cohorts and meta-analyses—suggests that when an R0 hepatic margin is achieved and lymphadenectomy is adequate, routine escalation to segment IVb/V

resection has not consistently been associated with a survival advantage in T2 disease, while morbidity is higher with the anatomic approach [24–28,39].

4.2.1. Evidence synthesis from meta-analyses

Two recent meta-analyses provide the clearest aggregate comparison. Chen Z et al. analyzed nine retrospective studies (n = 2086; 627 segment IVb/V vs 1459 wedge). Segment IVb/V resection was associated with improved 1-year DFS, but there were no differences in 3- or 5-year DFS or in the pooled DFS hazard ratio. Postoperative complications were more frequent after segment IVb/V resection, including higher rates of overall morbidity and greater perioperative burden, although rates of specific complications such as bile leak were not consistently different across studies [39]. Matsui et al., analyzing seven studies (n = 1795; including T2 and T3), similarly found fewer postoperative complications with wedge resection (OR 0.40; 95% CI 0.26–0.60; $P < 0.001$) without an increase in bile leak, and no significant differences in liver metastasis, 5-year DFS, or 5-year OS between wedge and segment IVb/V resection [25]. Together, these meta-analyses do not support routine segment IVb/V resection for T2 disease when a margin-negative wedge resection is feasible, while consistently identifying higher perioperative morbidity with anatomic resection [25,39].

4.2.2. Supportive cohort and registry data

Registry data from Japan have long suggested that limited hepatic resection can be oncologically adequate in pT2 disease when combined with appropriate nodal dissection. Horiguchi et al., analyzing Japanese registration cases, reported no significant survival difference between gallbladder-bed (wedge) resection and hepatectomy of segments 4a and 5 (S4a + S5) in pT2 carcinoma when R0 resection and adequate nodal dissection were achieved [28]. A Japanese multicenter survey of R0 pT2–pT3 cases likewise did not demonstrate a clear advantage of more extensive hepatectomy over minor liver resection [40].

More recent matched analyses have directly compared wedge and segment IVb/V approaches. In a propensity-score–matched study of T2 GBC, Chen et al. reported no significant differences in overall or disease-free survival between anatomic segment IVb/V hepatectomy and wedge resection after matching for key prognostic variables, although operative time and blood loss tended to be greater with segment IVb/V resection [26]. Nag et al. similarly reported a matched case–control study (T2/T3) in which segment IVb/V bisegmentectomy did not demonstrate clear oncologic superiority over wedge resection, while complications were more frequent in the segmentectomy group [27]. While these datasets are retrospective and subject to selection bias, their results align with the findings of the meta-analyses that margin-negative wedge resection is generally sufficient for T2 disease and is associated with lower perioperative burden [25–27,39]. Across cohorts and meta-analyses, long-term outcomes appear broadly comparable, whereas morbidity is higher with segment IVb/V resection; key studies are summarized in Table 2.

Despite these findings, interpretation of the comparative literature is limited by important sources of bias. Most available studies are retrospective and subject to confounding by indication, whereby patients with more advanced disease, greater liver involvement, or higher-risk features are more likely to undergo segment IVb/V resection or more extensive hepatectomy. Although several studies employ propensity-score matching, residual confounding remains likely, as key determinants such as tumor biology, nodal burden, and intraoperative assessment of resectability are incompletely captured. In particular, nodal status and margin status strongly influence both treatment allocation and outcomes, which may attenuate or obscure any independent effect of hepatic resection extent. These limitations should be considered when interpreting the observed equivalence between wedge and segment IVb/V resection.

4.3. Tumor location (T2a vs T2b): prognostic information but not a mandate for larger liver volume

The AJCC 8th edition subdivides T2 tumors into T2a (peritoneal-side) and T2b (hepatic-side), based on observations that hepatic-side lesions may have worse outcomes [41,42]. Several institutional series and a meta-analysis have reported inferior survival for T2b compared with T2a tumors, leading some authors to propose more extensive hepatic resection for T2b disease [43–46].

However, the international multicenter analysis by Kwon et al. suggests that the prognostic impact of location is closely intertwined with nodal and margin status rather than indicating a need for routine escalation of hepatic extent. In their cohort, 5-year DFS was lower in T2b than T2a tumors overall (65.5% vs 74.5%; $P = 0.028$), but after stratification by nodal status, DFS differences were not statistically significant in either node-negative or node-positive subgroups, and tumor location was not an independent predictor of recurrence on multivariable analysis, whereas nodal category and margin status were strongly prognostic [24]. Accordingly, tumor location may be useful for risk stratification but does not, by itself, justify routine segment IVb/V resection when a margin-negative wedge resection and adequate lymphadenectomy are achievable [14,24,25,39].

4.4. Practice implications and guideline alignment

Across contemporary data, the benefit in T2 disease appears to derive from performing an oncologically complete radical cholecystectomy rather than from routinely increasing the hepatic volume removed. In the international multicenter cohort by Kwon et al., extended cholecystectomy improved DFS compared with simple cholecystectomy, while within extended resections, wedge resection and segment IVb/V resection were associated with similar long-term outcomes after adjustment [24]. When interpreted alongside meta-analyses demonstrating comparable long-term survival but higher postoperative complication rates with segment IVb/V resection [25,39], these findings support a parenchyma-sparing strategy for most patients with T2 disease.

Consistent with these data, the IHPBA–APHPBA consensus recommends that for T2 gallbladder cancer (including incidental presentations), a margin-negative wedge resection of the gallbladder bed is an adequate hepatic extent when combined with appropriate regional lymphadenectomy; segment IVb/V resection should be reserved for margin-driven indications (e.g., inability to achieve an R0 hepatic margin with wedge resection or gross hepatic extension beyond the gallbladder bed) [14]. Tumor location (T2a vs T2b) may provide prognostic information, but does not independently mandate escalation to segment IVb/V resection when nodal status and margin status are accounted for [24,42,46].

5. T3 and high-risk disease: margin-driven hepatectomy, limits of escalation, and the role of neoadjuvant therapy

5.1. Prognosis and patterns of failure

T3 gallbladder cancer—defined as serosal perforation and/or direct invasion into the liver or adjacent organs—is biologically aggressive and is associated with substantially worse outcomes than T2 disease despite resection [41]. T3 disease, however, represents a heterogeneous group with distinct biological and anatomical patterns of spread. This category includes tumors with limited direct hepatic invasion adjacent to the gallbladder fossa as well as those with more extensive involvement of adjacent organs (e.g., colon, duodenum) or complex local extension. These subgroups differ in resectability, likelihood of achieving an R0 margin, and overall prognosis [47–50]. Consequently, the potential benefit of increasing hepatic resection extent is unlikely to be uniform across all T3 presentations, and surgical strategy should be

individualized based on the pattern and extent of local invasion in addition to overall disease biology.

In large series, 5-year survival after resection for T3 disease is commonly in the 10–20% range, and recurrence is frequent, with distant or multifocal intrahepatic failure predominating over isolated gallbladder-bed relapse [47,48]. These patterns suggest that tumor biology and occult systemic spread frequently determine outcome, limiting the potential incremental benefit of more extensive local resection.

Contemporary multinational data underscore this point. In an international multicenter analysis of advanced GBC (T3–T4), Chirban et al. reported substantial perioperative morbidity, including increased rates of major complications and nontrivial perioperative mortality, as well as significant R1 rates despite extensive resections; after adjustment, major hepatectomy did not confer a survival advantage, whereas nodal metastasis remained strongly prognostic [49]. Similarly, a two-center Korean cohort demonstrated the steep survival decrement from T2 to T3 disease despite high R0 rates and systematic nodal dissection, highlighting the limited capacity of surgical escalation alone to overcome unfavorable biology [50]. Registry-level IGBC data also show that re-resection improves outcomes compared with no further surgery in incidental T3 disease, but long-term survival remains markedly inferior to T2 [23].

5.2. Extent of liver resection in T3 disease: margin-driven strategy rather than routine escalation

Historically, surgeons escalated hepatic extent for selected T3 tumors—formal segment IVb/V resection or major hepatectomy—based on concerns regarding microscopic extension and a desire to maximize margin clearance [18,51,52]. However, contemporary multicenter analyses increasingly question whether increasing liver volume improves long-term outcomes once margin and nodal status are accounted for.

The OMEGA international cohort provides the largest contemporary assessment of surgical extent and outcomes. In this multicenter dataset, wedge resection and segment IVb/V resection were not independently associated with improved recurrence-free or overall survival after adjustment for T stage, nodal status, and margin status, whereas major hepatectomy was associated with worse recurrence-free and overall survival and substantially higher serious morbidity and 90-day mortality [32]. Extrahepatic bile duct resection and multivisceral resections similarly increased complications without clear survival benefit in adjusted analyses [32]. Sensitivity analyses stratified by T stage, including T3 disease, did not demonstrate a consistent survival advantage to segment IVb/V resection or major hepatectomy over limited resections [32].

These findings are supported by pooled data including T3 cases. In the meta-analysis by Matsui et al., wedge resection was associated with fewer postoperative complications without significant differences in liver metastasis or long-term survival compared with segment IVb/V resection [25]. Retrospective matched cohorts similarly suggest that the prognostic impact of hepatic extent is generally outweighed by nodal status and margin status [26,27]. Taken together, available evidence supports a margin-driven approach: perform the least hepatic resection required to achieve an R0 margin, rather than routine escalation in liver volume.

5.3. Neoadjuvant therapy as biologic selection in borderline-resectable or high-risk disease

A clinically important subset of patients with T3 or “high-risk” presentations have borderline-resectable or locally advanced disease—such as bulky primary tumors with substantial liver contact, vascular impingement, and/or bulky nodal disease—without overt distant metastasis [14,53,54]. Historically, upfront extended resections requiring major hepatectomy or vascular reconstruction have been associated with high morbidity and poor survival [32,34]. This has motivated surgeons and oncologists to increasingly explore neoadjuvant systemic therapy to (i) treat occult systemic disease early, (ii) test tumor biology over time, and (iii) enrich for surgical candidates likely to achieve an R0 resection with acceptable morbidity. However, current evidence remains limited, largely retrospective, and derived from single-institution experiences, and no standardized neoadjuvant strategy has been established.

In a high-risk cohort treated with neoadjuvant gemcitabine-based chemotherapy, Chaudhari et al. [53] reported that a subset of patients proceeded to exploration and curative-intent resection after demonstrating response or stability; the program deliberately avoided routine major hepatectomy, using parenchyma-sparing resections when feasible, and long-term survival was markedly better among those ultimately resected compared with those unresected. Similarly, in the Memorial Sloan Kettering series [54], systemic chemotherapy enabled a highly selected subset of locally advanced/node-positive patients to undergo resection, and those achieving an R0 resection had substantially improved survival compared with unresectable patients. At the population level, an NCDB analysis [55] suggested that neoadjuvant therapy was associated with improved survival in node-positive resected disease compared with adjuvant therapy or surgery alone.

5.4. Practical implications for hepatic extent in T3/high-risk disease

For T3 and other high-risk presentations, the dominant decision is often whether and when to operate, rather than which standard liver extent should be selected. A practical approach consistent with contemporary consensus includes: (i) comprehensive staging (including diagnostic laparoscopy in appropriate candidates) to exclude occult metastatic disease [56]; (ii) for clearly resectable T3 disease, radical cholecystectomy with wedge resection or segment IVb/V resection as needed to achieve R0 margins plus regional lymphadenectomy; and (iii) for borderline-resectable and/or node-positive disease, neoadjuvant systemic therapy followed by restaging and selective resection when an R0 operation is realistically achievable with acceptable morbidity [14,53–55]. Routine escalation to major hepatectomy or multivisceral resection is not supported by consistent survival benefit and carries substantial morbidity; such procedures should be reserved for exceptional, highly selected circumstances in specialized centers, typically after multidisciplinary review and often after systemic therapy [14,32–34].

Regarding the extrahepatic bile duct, routine extrahepatic bile duct resection (EBDR) is not supported; however, EBDR remains mandatory if the cystic duct margin/stump is positive for malignancy or if bile duct resection is required to facilitate a complete regional lymphadenectomy that might otherwise devascularize the duct [14].

6. Systemic therapy and how it changes the value of more extensive hepatectomy

6.1. Adjuvant therapy after resection

Adjuvant systemic therapy is now an established component of care for resected gallbladder cancer. The phase III BILCAP trial established adjuvant capecitabine as a standard option, demonstrating improved survival in adjusted analyses [57]. Real-world data from the NCDB further support a survival benefit with adjuvant chemotherapy after resection, particularly in node-positive and more advanced disease [55]. Contemporary consensus guidelines therefore support routine consideration of adjuvant chemotherapy for most resected T2/T3 and/or node-positive cases [14,55,57].

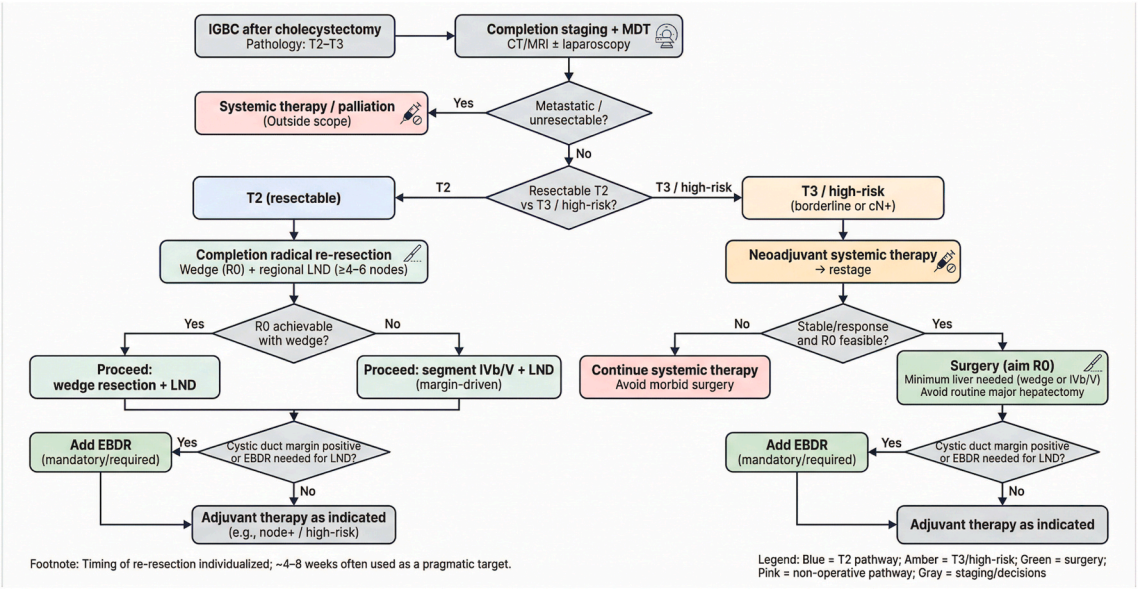

Fig. 2. Clinical decision algorithm for incidental gallbladder cancer (IGBC) after cholecystectomy.
After diagnosis of pathologic T2–T3 IGBC following cholecystectomy, patients undergo completion staging with cross-sectional imaging and multidisciplinary review; diagnostic laparoscopy is considered in selected cases. Patients with metastatic or unresectable disease are directed toward systemic therapy and/or palliation. For resectable T2 disease, completion radical re-resection with regional lymphadenectomy is recommended; wedge resection of the gallbladder bed is preferred when an R0 margin is achievable, whereas segment IVb/V resection is reserved for margin-driven situations. For T3 or other high-risk presentations (e.g., borderline-resectable and/or clinically node-positive disease), neoadjuvant systemic therapy with restaging may be considered to enable biologic selection; surgery is pursued only when stable/responding disease and an R0 resection with acceptable morbidity appear feasible. Extrahepatic bile duct resection (EBDR) is performed only when the cystic duct margin is positive or when required to complete regional lymphadenectomy. Adjuvant therapy is considered according to nodal status and other high-risk features. This algorithm is conceptual and not prescriptive; real-world decisions should be individualized according to patient fitness, disease extent, institutional expertise, and multidisciplinary evaluation.
Abbreviations: EBDR, extrahepatic bile duct resection; IGBC, incidental gallbladder cancer; LND, lymph-node dissection; MDT, multidisciplinary team; R0, margin-negative resection.

6.2. Neoadjuvant therapy as biologic selection in high-risk and borderline-resectable disease

For T3 or otherwise high-risk presentations, neoadjuvant systemic therapy has increasing appeal as a "test of time" that selects candidates most likely to benefit from surgery, although supporting evidence remains non-randomized and evolving. Institutional series and population-level data suggest that gemcitabine–platinum–based chemotherapy can achieve disease control in a subset of locally advanced or node-positive gallbladder cancer, enabling curative-intent resection in selected patients [53–55]. The IHPBA–APHPBA consensus endorses consideration of neoadjuvant systemic therapy for borderline-resectable or biologically aggressive gallbladder cancer, with surgery reserved for patients demonstrating response or durable stability and a realistic path to R0 resection [14].

6.3. How systemic therapy strengthens a margin-driven, parenchyma-sparing liver strategy

The expanding role of adjuvant and neoadjuvant therapy further reduces the rationale for routine escalation of hepatic resection volume. First, systemic therapy targets micrometastatic disease beyond the gallbladder bed—disease that cannot be addressed by increasing local liver excision [55,57]. Second, neoadjuvant approaches identify rapid progressors in whom major operations are unlikely to confer benefit, avoiding futile high-morbidity resections [53–55]. Finally, the principal adverse determinants of outcome in IGBC—nodal positivity, residual disease, R1 margins—are not consistently mitigated by removing more liver once an R0 margin is achievable [11,24,32]. Accordingly, in the modern multimodality era, the most evidence-aligned operative objective is an R0 resection with the minimum hepatic parenchymal sacrifice required, paired with standardized lymphadenectomy and appropriate integration of systemic therapy [14,25,32].

7. Key confounders and quality anchors: nodal status and lymphadenectomy quality

7.1. Nodal status is a dominant prognostic factor

Regional lymph-node metastases are common in T2–T3 gallbladder cancer and remain among the strongest determinants of survival [11,29,58]. Across multiple series, nodal positivity approaches 40–50% in T2 disease and exceeds 50% in T3 disease [11,29]. In IGBC cohorts and registries, nodal involvement markedly reduces long-term survival: in Pawlik et al., 5-year overall survival decreased from approximately 73% in N0 patients to 26.5% in node-positive patients [11]. This has direct implications for the wedge-versus-segment IVb/V debate. Once nodal dissemination is present, variation in hepatic extent (wedge vs segment IVb/V) has not consistently shown an independent survival association once N status and margin status are accounted for [11,25,32].

This further underscores that observed differences in outcomes attributed to hepatic extent may, in part, reflect underlying tumor biology and nodal disease rather than the surgical approach itself.

7.2. Lymphadenectomy quality (node yield and template)

Because nodal status is so prognostic, inadequate lymph-node assessment (Nx) can confound interpretations of liver-extent studies. Importantly, in the multinational OMEGA cohort, Nx patients experienced outcomes comparable to pathologic N1 disease, suggesting that suboptimal nodal assessment can nullify the oncologic value of an otherwise "radical" hepatic procedure [32]. Accordingly, the

IHPBA–APHPBA consensus defines a standard regional (D2) lymphadenectomy template including stations 8, 12a/b/c/p, and 13a, and recommends retrieval of a minimum of 4–6 nodes for accurate staging [14].

7.3. Node yield thresholds and staging implications

Several studies suggest that assessment of at least 4–6 lymph nodes improves staging accuracy and prognostication in gallbladder cancer [31,58]. These principles are incorporated into current consensus recommendations and are particularly important when interpreting comparative studies of hepatic extent, where inadequate nodal evaluation can bias outcomes [14,32].

8. Synthesis and practical conclusions

Cumulative evidence from IGBC cohorts, large international datasets, meta-analyses, and contemporary consensus recommendations supports a margin-driven and biology-informed approach to completion radical re-resection for T2–T3 incidental gallbladder cancer [11,14,24,25,32,36,39]. Because several wedge-versus-segment IVb/V datasets include mixed incidental and non-incidental cohorts, findings should be interpreted accordingly. Interpretation of these findings is further limited by heterogeneity in study populations, including the inclusion of mixed incidental and primary gallbladder cancer cohorts and variation in surgical techniques and reporting standards.

8.1. T2 disease: hepatic extent

For T2 incidental gallbladder cancer, the preponderance of contemporary evidence indicates that a margin-negative wedge resection of the gallbladder bed, combined with high-quality regional lymphadenectomy, appears to provide long-term oncologic outcomes comparable to those of anatomic segment IVb/V resection, while segment IVb/V resection is associated with consistently higher perioperative morbidity and operative burden [14,24,25,39]. Tumor location (T2a vs T2b) does not independently mandate escalation of hepatic resection volume once nodal status and margin status are considered [24]. Therefore, routine segment IVb/V resection is not supported by consistent evidence for most T2 IGBC cases and should be reserved for margin-driven indications.

8.2. T3 and high-risk disease: selection and systemic therapy integration

In T3 and other high-risk presentations, biologic aggressiveness often dominates prognosis, and attempts to overcome this biology by increasing operative extent are frequently associated with substantial morbidity without a consistent survival benefit once margin and nodal status are accounted for [32–34]. Contemporary international data suggest limited incremental benefit from routine escalation to major hepatectomy, reinforcing a strategy of resection tailored to achieving R0 margins with the minimum necessary liver excision [14,32]. In this setting, neoadjuvant gemcitabine–platinum–based systemic therapy is increasingly considered in selected high-risk or borderline-resectable cases and/or node-positive disease as a means of biologic selection and to improve the likelihood that surgery, when performed, will achieve an R0 resection with acceptable morbidity [14,53–55]. Regarding the extrahepatic bile duct, although routine resection is not supported by the available evidence, extrahepatic bile duct resection remains mandatory when the cystic duct margin is positive for malignancy and may also be required to facilitate complete regional lymphadenectomy that might otherwise devascularize the duct [14]. A practical decision algorithm integrating hepatic extent, lymphadenectomy standards, and systemic therapy selection is provided in Fig. 2. This algorithm is intended as a conceptual framework; real-world decision-making should be individualized and based on multidisciplinary evaluation.

Table 3
Consensus recommendations relevant to hepatic extent and bile duct resection.

Decision domain	Recommendation (practical wording)	Evidence/consensus source
T2 hepatic extent	Margin-negative wedge resection of the gallbladder bed is considered adequate by contemporary consensus and appears comparable to segment IVb/V resection when combined with regional lymphadenectomy; routine segment IVb/V resection has not shown consistent survival benefit.	IHPBA–APHPBA consensus [14]; supported by cohorts/meta-analyses [24,25,39]
T3 hepatic extent	Choose the least hepatic resection required to achieve R0; evidence is insufficient to mandate wedge resection versus segment IVb/V resection; avoid routine escalation to major hepatectomy.	IHPBA–APHPBA [14]; OMEGA cohort [32]
Major hepatectomy	Not routine; consider only in exceptional, highly selected cases in expert centers, typically after multidisciplinary review and often after systemic therapy.	IHPBA–APHPBA [14]; OMEGA and other data [32–34]
Extrahepatic bile duct resection (EBDR)	Routine EBDR is not supported. EBDR is mandatory if the cystic duct margin/stump is positive for malignancy and may be required to complete lymphadenectomy if duct devascularization would otherwise occur.	IHPBA–APHPBA consensus [14]; supportive surgical outcome data [32–34]
Neoadjuvant systemic therapy (high-risk/borderline)	Consider systemic therapy first for borderline-resectable or node-positive/high-risk disease; proceed to surgery only for stable/responding disease with a realistic path to R0 resection with limited hepatic excision.	IHPBA–APHPBA [14]; institutional series + NCDB [53–55]
Lymphadenectomy (quality anchor)	Perform regional lymphadenectomy per template (stations 8, 12a/b/c/p, 13a) and aim for ≥4–6 nodes for accurate staging.	IHPBA–APHPBA [14]; node count studies [31,58]

8.3. Quality anchors

Because nodal status is one of the strongest determinants of recurrence and survival, adequate regional lymphadenectomy and node yield are essential for staging and for valid interpretation of wedge-versus-segment IVb/V comparisons [14,32,58].

8.4. Summary statement

For T2 IGBC, a parenchyma-sparing, margin-negative wedge resection of the gallbladder bed combined with standardized regional lymphadenectomy appears to provide comparable oncologic outcomes in most appropriately selected cases, and routine segment IVb/V resection is not supported by consistent evidence of survival benefit [14,24,25,

39]. For T3/high-risk disease, the priority is appropriate patient selection and systemic therapy integration, with hepatic extent tailored to margin requirements rather than routine escalation [14,32–34,53–55]. Consensus recommendations relevant to hepatic extent and bile duct resection are summarized in Table 3.

9. Future directions and research priorities

Several gaps explain the persistence of the wedge-versus-segment IVb/V controversy. First, most comparative evidence is retrospective and vulnerable to confounding by indication. Prospective multicenter registries should standardize definitions of wedge resection technique, lymphadenectomy template, and complication reporting. Second, future studies should treat nodal evaluation quality as a core analytic variable, as Nx rates can confound interpretations of hepatic extent. Third, there is a need for biology-driven stratification tools; future research should evaluate whether histopathologic risk factors (e.g., lymphovascular invasion) or emerging biomarkers (e.g., ctDNA) can better identify which T2/T3 patients require systemic therapy rather than extensive surgery. Finally, as neoadjuvant strategies expand, research should focus on whether systemic therapy further increases R0 rates and reduces the need for major hepatectomy in high-risk populations, shifting the endpoint from “wedge versus segment IVb/V” toward “R0 resection with minimal morbidity.”

Author contributions

Fazal Saboor: Literature review, data collection, data interpretation, manuscript drafting.

Gao Min: Literature review, data collection, data interpretation, manuscript drafting.

Jiong Lu: Conceptualization, supervision, data interpretation, critical revision of the manuscript, final approval.

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Declarations of interest

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