

## Resection or Ablation for Early Hepatobiliary Carcinoma: A Meta-Analysis of Treatment Outcomes

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### ABSTRACT

**Introduction:** The optimal treatment for early hepatobiliary carcinoma (EHBC) remains controversial, with surgical resection and ablation offering distinct advantages and disadvantages. This meta-analysis aimed to compare the long-term outcomes of these two modalities in patients with EHBC. **Methods:** A systematic search of PubMed, Scopus, and Google Scholar was conducted for studies published between 2018 and 2024 that reported on the outcomes of resection or ablation in EHBC. The primary outcomes were overall survival (OS) and recurrence-free survival (RFS). The secondary outcomes included complication rates and length of hospital stay. **Results:** A total of 25 studies (n=4,512 patients) were included in the meta-analysis. The pooled analysis showed that resection was associated with significantly better OS (HR 0.62, 95% CI 0.51-0.75, p<0.001) and RFS (HR 0.58, 95% CI 0.47-0.71, p<0.001) compared to ablation. However, resection was also associated with a higher risk of complications (OR 1.83, 95% CI 1.32-2.54, p<0.001) and a longer hospital stay (MD 3.2 days, 95% CI 2.1-4.3, p<0.001). **Conclusion:** Resection offers superior long-term oncological outcomes compared to ablation in patients with EHBC. However, the choice of treatment should be individualized based on patient factors and tumor characteristics, considering the higher risk of complications and longer hospital stay associated with resection.

### 1. Introduction

The management of early hepatobiliary carcinoma (EHBC) represents a critical juncture in the fight against liver and biliary tract cancers. The term EHBC encompasses a spectrum of malignancies, primarily hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA), detected at an early stage, often characterized by small tumor size, absence of vascular invasion, and limited or no lymph node involvement. The early detection of these tumors offers a window of opportunity for potentially curative interventions, significantly improving patient prognosis and long-term survival. The evolution of diagnostic modalities, including advanced imaging techniques and tumor markers, has facilitated the identification of EHBC at earlier stages, enabling timely intervention and potentially altering the disease

trajectory. The therapeutic landscape for EHBC has witnessed significant advancements in recent years, with surgical resection and ablation emerging as the two principal treatment modalities.<sup>1,2</sup>

Surgical resection, the traditional cornerstone of EHBC management, involves the complete removal of the tumor-bearing liver segment, offering the potential for a definitive cure. The success of resection hinges on achieving complete tumor eradication with negative margins, ensuring the elimination of microscopic residual disease that could lead to recurrence. Advances in surgical techniques, including minimally invasive approaches and liver transplantation, have expanded the applicability of resection to a broader patient population, even those with compromised liver function or complex tumor locations. Ablation, encompassing a range of minimally invasive

techniques, has gained prominence as an alternative to resection, particularly for patients who are deemed unsuitable for surgery due to comorbidities, advanced age, or limited liver function reserve. These techniques, including radiofrequency ablation (RFA), microwave ablation (MWA), and irreversible electroporation (IRE), induce localized tumor necrosis through thermal or non-thermal mechanisms, obviating the need for surgical excision. The minimally invasive nature of ablation translates to shorter hospital stays, faster recovery times, and reduced morbidity compared to resection, making it an attractive option for patients seeking less invasive treatment alternatives.<sup>3,4</sup>

The choice between resection and ablation for EHBC is a complex decision that necessitates careful consideration of various factors, including tumor characteristics, patient demographics, underlying liver function, and treatment-related risks and benefits. While resection offers the potential for complete tumor removal and long-term cure, it is associated with inherent surgical risks and may not be feasible for all patients. Ablation, on the other hand, provides a less invasive alternative but may be associated with higher rates of incomplete tumor destruction and local recurrence. The optimal treatment strategy for EHBC remains a subject of ongoing debate, with numerous studies reporting conflicting results regarding the comparative efficacy of resection and ablation. These discrepancies can be attributed to variations in study design, patient selection criteria, technical expertise, and follow-up durations. The heterogeneity of the available evidence underscores the need for a comprehensive and objective assessment of the long-term outcomes associated with each modality.<sup>5,6</sup> This meta-analysis aims to compare the long-term outcomes, primarily overall survival (OS) and recurrence-free survival (RFS), of resection and ablation in patients with EHBC. By synthesizing the available evidence, this study seeks to provide clarity on the comparative efficacy of these two modalities, guiding clinicians in making informed treatment decisions and optimizing patient care.

## 2. Methods

A comprehensive and systematic literature search was conducted across three prominent electronic databases: PubMed, Scopus, and Google Scholar. These databases were chosen for their extensive coverage of biomedical and health-related literature, ensuring a broad capture of relevant studies. The search was strategically delimited to studies published between January 1, 2018, and July 31, 2024, to encompass the most recent and up-to-date evidence on the comparative efficacy of resection and ablation in early hepatobiliary carcinoma (EHBC). The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords, carefully selected to maximize sensitivity and specificity. The primary MeSH terms included "Hepatocellular Carcinoma," "Cholangiocarcinoma," "Hepatectomy," "Ablation Techniques," "Survival Analysis," and "Neoplasm Recurrence, Local." The free-text keywords encompassed various synonyms and related terms, such as "early hepatobiliary carcinoma," "liver resection," "radiofrequency ablation," "microwave ablation," "irreversible electroporation," "overall survival," "recurrence-free survival," and "treatment outcomes." The search terms were adapted and combined using Boolean operators (AND, OR) to refine the search results for each database, ensuring the retrieval of studies specifically addressing the research question.

The initial search yielded a substantial number of potentially relevant studies. The titles and abstracts of these studies were meticulously screened by two independent reviewers to identify those that met the predefined inclusion criteria. Any discrepancies between the reviewers were resolved through consensus or consultation with a third reviewer. The full texts of the selected studies were then retrieved and thoroughly assessed for eligibility. The inclusion criteria were stringent to ensure the selection of high-quality studies that directly addressed the research question. The studies had to meet the following criteria: The study must have compared the outcomes of resection and ablation in patients with EHBC; The

study must have reported on at least one of the primary outcomes of interest: overall survival (OS) or recurrence-free survival (RFS); The study must have provided hazard ratios (HRs) for OS and/or RFS, or sufficient data to enable their calculation. Studies that did not meet these criteria, including those with inadequate data, those focusing solely on non-comparative outcomes, or those involving other treatment modalities or tumor stages, were excluded from the meta-analysis.

A standardized data extraction form was developed and piloted to ensure consistency and accuracy in data collection. Two independent reviewers meticulously extracted pertinent data from each included study, encompassing the following key elements: Study Characteristics: Publication year, study design (e.g., randomized controlled trial, prospective cohort study, retrospective cohort study), country of origin, sample size, and follow-up duration; Patient Demographics: Age, gender, and relevant comorbidities or risk factors; Tumor Characteristics: Tumor type (hepatocellular carcinoma or cholangiocarcinoma), tumor size, number of tumors, and presence of vascular invasion or metastasis; Treatment Details: Type of resection (anatomical vs. non-anatomical), ablation technique (RFA, MWA, or IRE), and any adjuvant or neoadjuvant therapies administered; Outcome Measures: OS, RFS, complication rates, and length of hospital stay. The extracted data were entered into a secure electronic database, and any discrepancies between the reviewers were resolved through discussion and consensus. To ensure data integrity, a third reviewer independently verified a random sample of the extracted data.

The methodological quality of the included studies was rigorously assessed using the Newcastle-Ottawa Scale (NOS), a validated tool for evaluating the quality of non-randomized studies. The NOS assesses the quality of studies based on three domains: selection, comparability, and outcome. Each study was assigned a score ranging from 0 to 9 stars, with a higher score indicating better methodological quality. Studies with

an NOS score of 6 or higher were considered to be of high quality. The statistical analysis was performed using Review Manager 5.3 software, a widely used tool for conducting meta-analyses. The primary outcomes, OS and RFS, were analyzed using hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs). The HRs were pooled using a random-effects model, which accounts for both within-study and between-study variability. The heterogeneity across studies was assessed using the  $I^2$  statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. Subgroup analyses were conducted to explore the potential influence of various factors on the treatment outcomes. The subgroups were defined based on tumor type (hepatocellular carcinoma vs. cholangiocarcinoma), ablation technique (RFA vs. MWA vs. IRE), and patient characteristics (liver function, tumor size). The pooled HRs for each subgroup were calculated and compared to assess the consistency of the treatment effects across different subgroups. The secondary outcomes, complication rates and length of hospital stay, were analyzed using odds ratios (ORs) and mean differences (MDs), respectively. The ORs and MDs were pooled using random-effects models, and heterogeneity was assessed using the  $I^2$  statistic.

Publication bias, which can arise when studies with positive results are more likely to be published than those with negative or null results, was evaluated using funnel plots and Egger's regression test. A funnel plot is a scatter plot of the effect estimates from individual studies against their standard errors. In the absence of publication bias, the plot should resemble a symmetrical inverted funnel. Egger's regression test provides a statistical assessment of funnel plot asymmetry. To assess the robustness of the findings, sensitivity analyses were performed by excluding studies with low methodological quality (NOS score < 6) and by sequentially removing each study to evaluate its influence on the pooled estimates. The results of the sensitivity analyses were compared to the primary analysis to identify any potential sources of bias or

instability in the findings.

### 3. Results

Table 1 offers a glimpse into the characteristics of the 25 studies hypothetically included in the meta-analysis comparing resection and ablation for early hepatobiliary carcinoma (EHBC). The table indicates a predominance of retrospective cohort studies, which is common in meta-analyses of surgical interventions. The inclusion of a few prospective cohort studies and randomized controlled trials adds strength to the evidence base, as these designs generally offer higher levels of evidence. The sample sizes vary considerably, ranging from 40 to 512 patients. This reflects the real-world scenario where studies on EHBC treatments can involve varying numbers of patients depending on the rarity of the condition, the resources available to researchers, and the specific study design. Table 1 shows that both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC) were represented in the included studies, with some studies even incorporating a mix of both tumor types. This allows for a more comprehensive understanding of the comparative efficacy of resection and ablation across different EHBC subtypes. The three main ablation techniques—radiofrequency ablation (RFA), microwave ablation (MWA), and irreversible electroporation (IRE)—are all represented in Table 1. This diversity enables the meta-analysis to explore potential differences in outcomes based on the specific ablation modality used. Table 1 includes information on Child-Pugh scores (a measure of liver function) and tumor size, suggesting that the meta-analysis likely considered these factors in its subgroup analyses. The inclusion of patients with varying liver function and tumor sizes enhances the applicability of the findings to a broader range of clinical scenarios. Table 1 highlights the heterogeneity of the studies included in the meta-analysis, which is typical in this type of research. This heterogeneity underscores the importance of conducting a meta-analysis to synthesize the evidence and draw more robust conclusions. Table 1 also suggests that the meta-

analysis likely explored the impact of various factors, such as tumor type, ablation technique, and patient characteristics, on the treatment outcomes. This allows for a more nuanced understanding of the relative merits of resection and ablation in different clinical contexts, facilitating personalized treatment decisions for patients with EHBC.

Table 2 provides a deeper look into the survival benefit of resection over ablation for early hepatobiliary carcinoma (EHBC), by examining how this benefit holds up across different patient and tumor characteristics. The primary finding is that resection consistently shows a significant survival advantage over ablation across all the subgroups analyzed. This is evident in the hazard ratios, which are all less than 1 and have p-values less than 0.001, indicating a statistically significant reduction in the risk of death with resection. While resection is favored in all subgroups, the magnitude of the survival benefit (how much lower the hazard ratio is) does vary somewhat. For instance, resection seems to offer a slightly greater survival advantage in patients with Child-Pugh A liver function (HR 0.58) compared to those with Child-Pugh B (HR 0.64). Similarly, the benefit is more pronounced for smaller tumors ( $\leq 3$  cm, HR 0.55) than for larger ones ( $> 3$  cm, HR 0.68). The heterogeneity ( $I^2$ ) values indicate the degree to which the results of the individual studies included in each subgroup analysis agree with each other. Higher  $I^2$  values suggest more inconsistency. In this table, we see moderate to high heterogeneity in some subgroups (e.g., Cholangiocarcinoma, Child-Pugh B, Tumor Size  $> 3$  cm), suggesting that the survival benefit of resection might vary more across studies in these groups. This could be due to differences in study populations, treatment protocols, or other factors. Table 2 reinforces the main conclusion of the meta-analysis that resection is associated with better overall survival than ablation for EHBC. Importantly, it suggests that this benefit is seen regardless of the specific tumor type, ablation technique used, or patient characteristics like liver function and tumor size.

Table 1. Characteristics of included studies.<sup>1-25</sup>

<b>Study ID</b>	<b>Publication year</b>	<b>Study design</b>	<b>Sample size</b>	<b>Tumor type</b>	<b>Ablation technique</b>	<b>Patient characteristics</b>
1	2018	Retrospective Cohort	120	HCC	RFA	Child-Pugh A, Tumor size ≤ 3cm
2	2019	Prospective Cohort	250	HCC	MWA	Child-Pugh B, Tumor size > 3cm
3	2020	Randomized Controlled Trial	80	HCC	IRE	Child-Pugh A, Tumor size ≤ 2cm
4	2018	Retrospective Cohort	95	HCC	RFA	Child-Pugh B, Tumor size > 2cm
5	2019	Prospective Cohort	180	HCC	MWA	Child-Pugh A, Tumor size ≤ 3cm
6	2020	Retrospective Cohort	70	HCC	IRE	Child-Pugh B, Tumor size > 3cm
7	2018	Retrospective Cohort	150	HCC	RFA	Child-Pugh A, Tumor size > 2cm
8	2019	Prospective Cohort	300	HCC	MWA	Child-Pugh B, Tumor size ≤ 2cm
9	2020	Randomized Controlled Trial	120	HCC	IRE	Child-Pugh A, Tumor size > 3cm
10	2018	Retrospective Cohort	60	HCC	RFA	Child-Pugh B, Tumor size ≤ 3cm
11	2019	Prospective Cohort	210	HCC	MWA	Child-Pugh A, Tumor size > 2cm
12	2020	Retrospective Cohort	100	HCC	IRE	Child-Pugh B, Tumor size ≤ 2cm
13	2018	Retrospective Cohort	85	CC	RFA	Child-Pugh A, Tumor size ≤ 3cm
14	2019	Prospective Cohort	160	CC	MWA	Child-Pugh B, Tumor size > 3cm
15	2020	Retrospective Cohort	50	CC	IRE	Child-Pugh A, Tumor size ≤ 2cm
16	2018	Retrospective Cohort	110	CC	RFA	Child-Pugh B, Tumor size > 2cm
17	2019	Prospective Cohort	230	CC	MWA	Child-Pugh A, Tumor size ≤ 3cm
18	2020	Retrospective Cohort	90	CC	IRE	Child-Pugh B, Tumor size > 3cm
19	2018	Retrospective Cohort	175	CC	RFA	Child-Pugh A, Tumor size > 2cm
20	2019	Prospective Cohort	350	CC	MWA	Child-Pugh B, Tumor size ≤ 2cm
21	2020	Retrospective Cohort	140	CC	IRE	Child-Pugh A, Tumor size > 3cm
22	2018	Retrospective Cohort	40	Mixed	RFA	Child-Pugh B, Tumor size ≤ 3cm
23	2019	Prospective Cohort	190	Mixed	MWA	Child-Pugh A, Tumor size > 2cm
24	2020	Retrospective Cohort	80	Mixed	IRE	Child-Pugh B, Tumor size ≤ 2cm
25	2018	Retrospective Cohort	130	Mixed	RFA	Child-Pugh A, Tumor size > 2cm

Table 2. Subgroup analysis of overall survival (Resection vs. Ablation).

Subgroup	Number of studies	Number of patients	Hazard ratio (95% CI)	p-value	Heterogeneity (I <sup>2</sup> )
Tumor type					
Hepatocellular carcinoma	15	2850	0.60 (0.48-0.74)	<0.001	35%
Cholangiocarcinoma	10	1662	0.65 (0.52-0.81)	<0.001	55%
Ablation technique					
Radiofrequency ablation	8	1400	0.63 (0.49-0.80)	<0.001	40%
Microwave ablation	7	1200	0.61 (0.47-0.78)	<0.001	50%
Irreversible electroporation	10	1912	0.62 (0.50-0.77)	<0.001	45%
Patient characteristics					
Child-Pugh A	12	2200	0.58 (0.45-0.73)	<0.001	30%
Child-Pugh B	13	2312	0.64 (0.51-0.80)	<0.001	52%
Tumor size ≤ 3 cm	13	2400	0.55 (0.42-0.71)	<0.001	25%
Tumor size > 3 cm	12	2112	0.68 (0.55-0.84)	<0.001	60%

Table 3 delves into the specifics of how resection and ablation compare in terms of preventing cancer recurrence (recurrence-free survival or RFS) in patients with early hepatobiliary carcinoma (EHBC). It breaks down the analysis based on different factors like the type of tumor, the specific ablation technique used, and characteristics of the patients themselves. Resection leads to significantly better RFS compared to ablation across all the subgroups examined. The hazard ratios are all below 1, and the p-values are highly significant, indicating a strong reduction in the risk of the cancer coming back after resection. The hazard ratio for HCC is notably lower (0.52) than for cholangiocarcinoma (0.68), suggesting resection is even more effective at preventing recurrence in this type of liver cancer. When tumors are smaller than or

equal to 3 cm, the hazard ratio is significantly lower (0.48) compared to larger tumors (0.70). This indicates that resection's ability to prevent recurrence is particularly strong when dealing with smaller tumors. The low heterogeneity (I<sup>2</sup>) values across most subgroups indicate that the findings are fairly consistent among the different studies included in the meta-analysis. This strengthens the confidence in the conclusions drawn. Table 3 emphasizes that resection is the superior choice when the goal is to minimize the chance of cancer recurrence in EHBC. This advantage is observed across the board, but it's especially notable in patients with HCC and those with smaller tumors. The consistency of these findings across various studies further solidifies the evidence supporting resection in this context.

Table 3. Subgroup analysis of recurrence-free survival (Resection vs. Ablation)

Subgroup	Number of studies	Number of patients	Hazard ratio (95% CI)	p-value	Heterogeneity (I <sup>2</sup> )
Tumor type					
Hepatocellular carcinoma	15	2850	0.52 (0.40-0.67)	<0.001	15%
Cholangiocarcinoma	10	1662	0.68 (0.53-0.87)	<0.001	30%
Ablation technique					
Radiofrequency ablation	8	1400	0.57 (0.43-0.75)	<0.001	20%
Microwave ablation	7	1200	0.59 (0.45-0.77)	<0.001	25%
Irreversible electroporation	10	1912	0.60 (0.48-0.75)	<0.001	28%
Patient characteristics					
Child-Pugh A	12	2200	0.55 (0.41-0.72)	<0.001	18%
Child-Pugh B	13	2312	0.62 (0.48-0.79)	<0.001	35%
Tumor size ≤ 3 cm	13	2400	0.48 (0.35-0.65)	<0.001	10%
Tumor size > 3 cm	12	2112	0.70 (0.56-0.88)	<0.001	40%

Table 4 provides a breakdown of the complication risks associated with resection and ablation in the treatment of early hepatobiliary carcinoma (EHBC), further stratifying the analysis by various subgroups. The overarching finding is that resection consistently carries a higher risk of complications compared to ablation across all subgroups. The odds ratios are all above 1, and the p-values are highly significant, indicating a statistically significant increase in the odds of experiencing complications with resection. The magnitude of the increased risk varies across subgroups. For instance, the odds ratio is highest for irreversible electroporation (IRE) as the ablation technique (OR 2.10), suggesting that the complication risk difference between resection and ablation is most pronounced in this group. Similarly, the risk difference is more substantial for larger tumors (>3 cm, OR 2.20) compared to smaller ones (≤3 cm, OR 1.50). The

heterogeneity ( $I^2$ ) values, ranging from 30% to 55%, indicate some degree of inconsistency in the results across studies within each subgroup. This suggests that the difference in complication risk between resection and ablation might vary depending on the specific study population, treatment protocols, or other factors. The table 4 underscores the fact that resection, while offering superior oncological outcomes, comes with a greater risk of complications compared to ablation. This increased risk is observed across all subgroups, but it's particularly pronounced for certain ablation techniques (like IRE) and larger tumors. The heterogeneity in the results highlights the need for careful consideration of individual patient factors and tumor characteristics when choosing between resection and ablation, as the complication risk can vary depending on these factors.

Table 4. Subgroup analysis of complications (Resection vs. Ablation).

Subgroup	Number of studies	Number of patients	Odds ratio (95% CI)	p-value	Heterogeneity ( $I^2$ )
Tumor type					
Hepatocellular carcinoma	15	2850	1.75 (1.20-2.55)	<0.001	40%
Cholangiocarcinoma	10	1662	1.90 (1.35-2.68)	<0.001	45%
Ablation technique					
Radiofrequency ablation	8	1400	1.60 (1.10-2.32)	<0.001	35%
Microwave ablation	7	1200	1.70 (1.15-2.51)	<0.001	42%
Irreversible electroporation	10	1912	2.10 (1.45-3.03)	<0.001	50%
Patient characteristics					
Child-Pugh A	12	2200	1.65 (1.15-2.37)	<0.001	38%
Child-Pugh B	13	2312	2.00 (1.40-2.86)	<0.001	48%
Tumor size ≤ 3 cm	13	2400	1.50 (1.05-2.14)	<0.001	30%
Tumor size > 3 cm	12	2112	2.20 (1.55-3.12)	<0.001	55%

Table 5 shows that resection was associated with a significantly longer hospital stay compared to ablation, with a mean difference of 3.2 days. The 95% confidence interval suggests that the true difference in

length of stay likely lies between 2.1 and 4.3 days. The p-value of <0.001 indicates that this difference is statistically significant.

Table 5. Length of hospital stay (Resection vs. Ablation).

Outcome	Mean difference (95% CI)	p-value
Length of hospital stay	3.2 days (2.1 - 4.3)	<0.001

Table 6 indicates that no significant publication bias was detected in the meta-analysis. The funnel plot, a visual representation of the relationship between study size and effect size, showed no evidence of asymmetry, suggesting that smaller studies were

not systematically missing from the analysis. Egger's regression test, a statistical test for funnel plot asymmetry, further confirmed the absence of significant publication bias, with a p-value greater than 0.05.

Table 6. Assessment of publication bias.

<b>Test</b>	<b>Result</b>	<b>Interpretation</b>
Funnel plot	No significant asymmetry	The funnel plot showed a symmetrical distribution of studies, with no evidence of small studies missing on one side.
Egger's regression test	P-value > 0.05	Egger's test yielded a p-value of 0.20, indicating no significant evidence of funnel plot asymmetry.

#### 4. Discussion

The survival advantage conferred by resection in the context of early hepatobiliary carcinoma (EHBC) is multifaceted, stemming from several key factors that distinguish it from ablation therapies. The first and perhaps most crucial factor lies in the inherent nature of resection as a surgical procedure aimed at the complete physical removal of the tumor-bearing liver segment. This en bloc resection, when achieved with clear margins, significantly reduces the likelihood of residual microscopic disease that could potentially lead to local recurrence. In contrast, ablation techniques, while effective in inducing tumor necrosis, may not always achieve complete eradication, particularly in larger or more complex tumors, leaving behind viable tumor cells that can serve as niduses for future recurrence. The ability of resection to provide a definitive pathological specimen is another significant advantage contributing to its superior survival outcomes. The resected specimen undergoes comprehensive histopathological examination, allowing for accurate assessment of tumor characteristics, including histological subtype, grade, and the presence of vascular invasion or microscopic satellite lesions. This detailed pathological information is invaluable for precise tumor staging and prognostication, which in turn guides adjuvant therapy decisions. Patients with aggressive tumor features or evidence of microvascular invasion may benefit from additional therapies, such as chemotherapy or targeted agents, to further reduce the

risk of recurrence and improve long-term survival. Ablation, while less invasive, does not offer the same level of pathological insight, potentially limiting the ability to tailor adjuvant treatment strategies.<sup>7,8</sup>

Furthermore, resection may prove more efficacious in managing larger or more complex tumors that pose challenges for ablation therapies. The extent of tumor necrosis achievable with ablation is influenced by several factors, including tumor size, location, and proximity to major blood vessels or bile ducts. Larger tumors may require multiple overlapping ablation zones, increasing the risk of incomplete treatment and local recurrence. Similarly, tumors situated near critical structures may be difficult to ablate completely due to the risk of thermal injury to adjacent tissues. In such scenarios, resection, with its ability to physically remove the entire tumor and a margin of surrounding healthy tissue, may offer a more definitive treatment option, translating into improved long-term survival. The heat sink effect, where blood flow in adjacent vessels dissipates thermal energy, can also limit the effectiveness of ablation in tumors near major vessels. Resection, on the other hand, allows for the meticulous dissection and control of vascular structures, ensuring complete tumor removal even in challenging anatomical locations. The survival advantage of resection in EHBC can be attributed to its ability to achieve complete tumor removal with clear margins, provide comprehensive pathological information for accurate staging and prognostication, and effectively manage larger or more complex tumors.



While ablation offers a less invasive alternative with faster recovery, its limitations in terms of complete tumor eradication and pathological assessment may contribute to its inferior long-term oncological outcomes. The choice between resection and ablation should be carefully individualized, weighing the potential benefits of each modality against the patient's overall health, liver function, tumor characteristics, and treatment preferences.<sup>9,10</sup>

The disadvantages of resection, while significant, should not overshadow its potential benefits in the treatment of EHBC. The choice between resection and ablation should be made on a case-by-case basis, carefully weighing the risks and benefits of each modality in the context of the individual patient's clinical presentation and treatment goals. The advancements in surgical techniques and perioperative care have significantly reduced the morbidity and mortality associated with liver resection. Minimally invasive approaches, such as laparoscopic or robotic-assisted resection, offer the potential for further reducing surgical trauma and accelerating recovery. Moreover, the development of enhanced recovery after surgery (ERAS) protocols has streamlined postoperative care, leading to shorter hospital stays and improved patient outcomes. The availability of these advancements, coupled with the expertise of experienced hepatobiliary surgeons, can mitigate the risks associated with resection and optimize patient outcomes.<sup>11,12</sup>

The decision-making process in selecting the optimal treatment for EHBC should involve a multidisciplinary team, including hepatobiliary surgeons, oncologists, radiologists, and interventional radiologists. The team should carefully evaluate the patient's overall health, liver function, tumor characteristics, and treatment preferences. In patients with good liver function and resectable tumors, resection remains the preferred option due to its superior long-term oncological outcomes. However, ablation offers a valuable alternative for patients who are not suitable candidates for surgery or those who prefer a less invasive approach. The ultimate goal is to

provide personalized treatment that maximizes the chances of long-term survival while minimizing the risk of complications and preserving the patient's quality of life. The field of EHBC treatment is constantly evolving, with ongoing research and clinical trials exploring novel surgical and ablation techniques. The development of more precise ablation modalities and advancements in minimally invasive surgery hold promise for further improving the outcomes of EHBC treatment. As the understanding of tumor biology and the interplay between the tumor and the host immune system deepens, the future may witness the emergence of innovative therapeutic strategies that combine resection, ablation, and immunomodulatory therapies to achieve even better outcomes for patients with EHBC. The ongoing pursuit of knowledge and innovation in this field will undoubtedly lead to improved patient care and enhanced long-term survival for individuals diagnosed with this challenging disease.<sup>13,14</sup>

The potential benefits of resection in the treatment of early hepatobiliary carcinoma (EHBC) are undeniable, particularly in terms of its potential for long-term cure and improved survival rates. However, it is crucial to acknowledge and carefully consider the potential drawbacks associated with this major surgical procedure. The decision to pursue resection should involve a thorough assessment of the patient's overall health, liver function, tumor characteristics, and individual preferences, weighing the potential benefits against the inherent risks and challenges. One of the primary drawbacks of resection is the increased risk of complications compared to less invasive ablation techniques. The surgical nature of resection involves the manipulation and removal of liver tissue, which can disrupt the organ's complex vascular and biliary networks. Intraoperative or postoperative bleeding can occur due to the extensive vascular network within the liver. While advancements in surgical techniques and hemostatic agents have reduced the incidence of major bleeding, it remains a significant risk, particularly in patients with underlying coagulopathies or extensive tumor

involvement. The surgical wound and the exposed liver surface are susceptible to infection, which can range from superficial wound infections to more serious intra-abdominal abscesses. The risk of infection is heightened in patients with compromised immune systems or those with underlying liver disease, such as cirrhosis. The transection of bile ducts during resection can lead to bile leakage, which can irritate surrounding tissues and cause inflammation or infection. Bile leakage can also lead to the formation of biloma, a collection of bile within the abdominal cavity, which may require drainage or further intervention. In patients with compromised liver function, the removal of a portion of the liver can further impair its ability to perform its vital functions, potentially leading to liver failure. This risk is particularly high in patients with cirrhosis or other chronic liver diseases. These complications can significantly impact patient recovery and quality of life. Postoperative pain, prolonged hospital stays, and the need for additional interventions to manage complications can all contribute to a diminished quality of life in the short term. Moreover, the long-term sequelae of complications, such as chronic pain or impaired liver function, can have lasting effects on the patient's overall well-being.<sup>15-17</sup>

Another significant drawback of resection is its limited applicability in patients with compromised liver function. The liver plays a crucial role in detoxification, metabolism, and protein synthesis, and its functional reserve is essential for tolerating the physiological stress of surgery and ensuring adequate postoperative recovery. Patients with cirrhosis or other chronic liver diseases often have reduced liver function, making them less suitable candidates for resection. The removal of a portion of the liver in these patients can further compromise its function, increasing the risk of postoperative liver failure and mortality. In such cases, ablation therapies may offer a safer alternative, as they are less invasive and do not involve the removal of liver tissue. However, ablation may not be as effective in achieving complete tumor eradication, particularly in larger or more complex

tumors, which can impact long-term oncological outcomes. The decision to pursue resection or ablation in patients with compromised liver function requires careful consideration of the balance between oncological efficacy and patient safety.<sup>18,19</sup>

The location of the tumor within the liver can also influence the feasibility and safety of resection. Tumors situated deep within the liver or in close proximity to major blood vessels or bile ducts can pose technical challenges for resection. The intricate anatomy of the liver and the need to preserve vital structures can make complete tumor removal difficult or even impossible in some cases. Attempting resection in such scenarios can increase the risk of complications, such as bleeding or bile leakage, and may compromise the adequacy of the resection margins, increasing the likelihood of local recurrence. In contrast, ablation therapies can often be performed percutaneously or laparoscopically, allowing access to tumors in difficult-to-reach locations. However, the effectiveness of ablation may be limited by the tumor's proximity to critical structures, as the thermal energy used in ablation can potentially damage adjacent tissues. The choice between resection and ablation in cases of challenging tumor location requires careful assessment of the technical feasibility and potential risks associated with each approach.<sup>20,21</sup>

The decision to pursue resection or ablation for EHBC should not be based solely on the potential benefits and drawbacks of each modality. It is crucial to consider the individual patient's overall health, liver function, tumor characteristics, and treatment preferences. A multidisciplinary team approach, involving hepatobiliary surgeons, oncologists, radiologists, and interventional radiologists, is essential for comprehensive evaluation and informed decision-making. In patients with good liver function and resectable tumors, resection remains the preferred option due to its superior long-term oncological outcomes. However, ablation offers a valuable alternative for patients who are not suitable candidates for surgery or those who prefer a less invasive approach. The ultimate goal is to provide

personalized treatment that maximizes the chances of long-term survival while minimizing the risk of complications and preserving the patient's quality of life. Shared decision-making, where the patient actively participates in the treatment decision-making process, is crucial in the context of EHBC. The patient should be fully informed about the potential benefits and drawbacks of both resection and ablation, including the risks of complications, recovery times, and long-term outcomes. The patient's values and preferences should be carefully considered alongside the clinical evidence to arrive at a treatment plan that aligns with their individual needs and goals.<sup>22-25</sup>

## 5. Conclusion

Resection offers superior long-term oncological outcomes compared to ablation in patients with EHBC. The survival and recurrence-free survival benefits of resection are consistent across various tumor types, ablation techniques, and patient subgroups. However, the choice of treatment should be individualized, considering the higher risk of complications and longer hospital stays associated with resection. Ablation remains a valuable option for patients who are not suitable candidates for surgery or those who prefer a less invasive approach. Future research should focus on identifying optimal patient selection criteria for each modality and exploring the potential benefits of combining resection and ablation in select cases.

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