



Advances in Laparoscopic Surgery for Perihilar Cancer

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Abstract

Perihilar cholangiocarcinoma (PHC) is a malignant tumor originating from the bile duct epithelium, accounting for 50% ~ 60% of all cholangiocarcinoma. In China, both its incidence and mortality rates are on the rise. Currently, radical surgical resection remains the only effective treatment. In recent years, with continuous advancement in minimally invasive surgical techniques, multiple medical centers worldwide have successfully performed laparoscopic radical resection for PHC. The safety and feasibility of this procedure have been well-established. However, due to the complex anatomy of the perihilar region and the intricate surgical workflow, significant variations exist among medical centers regarding the achievement of R0 resection and the incidence of surgical complications. Consequently, laparoscopic radical resection of PHC remains challenging and controversial. Drawing on recent literature and our team's experience, this paper provides a detailed overview of the current status, challenges, and key considerations in laparoscopic radical resection of PHC.

Keywords: Perihilar cholangiocarcinoma; Laparoscopic surgery; R0 resection; Surgical outcomes

Abbreviations: PHC: Perihilar Cholangiocarcinoma; OS: Overall Survival; HR: Hazard Ratio; CI: Confidence Interval

Current Status

Currently, there is no consensus on whether minimally invasive approaches should be routinely recommended for radical resection of PHC. However, laparoscopic techniques for PHC have been widely promoted. Domestic and international guidelines, along with expert opinions, provide detailed descriptions of the key operative points and surgical resection margins for laparoscopic resection of PHC [1,2]. A meta-analysis published by Zhejiang Provincial People's Hospital, incorporating 13 studies, revealed that research interest in laparoscopic radical resection for PHC has significantly increased since 2019. The analysis compared intraoperative outcomes between laparoscopic and open surgical groups for PHC patients, showing that the laparoscopic group achieved an R0 resection rate as high as 95.2% with no statistically significant difference in 1-year overall survival (OS). The in-hospital mortality rate was 0.5%, and the reoperation rate was 1.1% [3]. This indicates that laparoscopic radical resection for PHC is entering a phase of rapid advancement and is gradually gaining recognition among biliary surgeons. A systematic review published by San Camillo-Flanini Hospital in

Rome, Italy, included 18 relevant studies involving 310 patients treated with laparoscopic techniques and 62 patients treated with robotic techniques.

The review evaluated and affirmed the short-term efficacy of minimally invasive techniques in radical resection of PHC, with mortality and complication rates ranging from 5% to 18%. However, most of the included studies were case reports or case-control studies, and over half of the articles lacked long-term outcomes, making it impossible to evaluate patients' oncological prognosis [4]. Similarly, subsequent literature reports have only concluded that laparoscopic techniques do not increase intraoperative or postoperative risks in radical resection for PHC [5,6], can increase the number of lymph nodes removed, and yield comparable clinical outcomes to open surgery [7]. However, they do not suggest that these techniques provide long-term benefits for patients [8]. Until a real-world study confirmed the long-term efficacy of laparoscopic radical resection for PHC, involving 10 domestic centers with 161 laparoscopic cases and 306 open cases. The median overall survival in the laparoscopic

group was longer than that in the open group (NA vs. 22 months; hazard ratio [HR] 1.19, 95% confidence interval [CI] 1.02-1.39, $p = 0.024$). Postoperative complications were comparable between groups, and equivalent long-term survival was achieved across all histological subtypes of PHC [9].

In recent years, our team has completed over 290 laparoscopic radical resections for PHC and spearheaded the development of the Expert Recommendations for the Operational Procedures of Laparoscopic Radical Resection for PHC [2]. A retrospective study by our team included patients with PHC from 2012 to 2022. Survival analysis revealed that overall survival exceeding 2 years and progression-free survival at 3 years were more common in the laparoscopic group [10]. Meanwhile, another multicenter retrospective study conducted by our team, involving 10 domestic centers and enrolling 158 patients, demonstrated that the efficacy of the laparoscopic group was comparable to that of the open surgery group. The R0 resection rate reached 81.6%, with a median survival time of 25.4 months. The 1-year, 3-year, and 5-year survival rates were 67.6%, 28.8%, and 19.2%, respectively [11]. Laparoscopic technology provides a clearer surgical field, enabling more precise dissection and flexible manipulation. Advanced electrosurgical techniques also deliver superior hemostasis. For the highly complex hepatic hilum region, laparoscopy offers distinct advantages during R0 resection. Currently, at relatively mature centers, minimally invasive radical resection for PHC demonstrates confirmed safety, short-term outcomes, and preliminary evidence of long-term prognosis.

Controversies and Key Points

Radical resection of PHC under laparoscopic guidance remains highly controversial, primarily due to the following issues: 1. There is currently a lack of high-quality, prospective clinical trials, with no detailed long-term prognostic outcomes available and severe deficiencies in follow-up data. 2. Technical limitations persist in laparoscopic procedures, including incomplete lymph node dissection and plexus clearance, significant challenges in laparoscopic vascular resection and reconstruction, and difficulties in assessing the adequacy of longitudinal and radial margins. Beyond refining high-quality clinical trials and enhancing follow-up protocols, ensuring the radicality of minimally invasive surgery and improving long-term outcomes remain critical priorities.

Lymph node dissection and Plexus clearance

Laparoscopic surgery achieves the same standard of lymph node dissection as open surgery and surpasses open procedures in achieving nerve plexus clearance [12]. The author believes that the following considerations should be observed when performing lymph node dissection and plexus clearance during laparoscopic surgery: (1) Adhere to the principle of en-bloc lymph node dissection. While performing lymph node dissection, simultaneously transect the inferior margin of the bile duct and the hepatic artery on the affected side. Depending on lymph node infiltration, transect the gastroduodenal artery or retract the

common hepatic artery and proper hepatic artery to one side to enhance exposure of the laparoscopic surgical field. When lymph nodes are fused together or adherent to vessels, conventional dissection becomes challenging. For such nodes, fully utilize scissors to enter the vascular sheath for dissection, dissect and skeletonize vessels, and consider transecting non-essential vessels along with lymph node tissue (e.g., gastric coronary veins, superior pancreaticoduodenal vein, and gastroduodenal artery) to better expose the lymph node clearance area. (3) Nerve plexus frequently surround the hepatic artery and adhere closely to the portal vein. During nerve plexus dissection, adhere closely to the vascular adventitia for stripping. To avoid damaging the arterial adventitia, minimize use of high-energy surgical instruments such as ultrasonic scalpel or Ligasure device. Alternatively, employ vascular dissection forceps for blunt separation of the arterial adventitia from the nerve fiber tissue space, followed by transection using an electrocoagulation hook or scissors in electrocoagulation mode.

Vascular resection and reconstruction

Vascular resection and reconstruction remains the most contentious technique in current practice. Existing literature predominantly reports portal vein resection and reconstruction, while hepatic artery resection and reconstruction remains in the clinical trial phase. Cases involving simultaneous arterial and venous reconstruction are even rarer. Our team has successfully performed laparoscopic vascular resection and reconstruction procedures, including arterial resection and reconstruction, venous resection and reconstruction, and combined arterial-venous reconstruction, preliminarily validating their feasibility. We believe that with the continuous maturation of biliary surgeons' techniques and the ongoing innovation of laparoscopic instruments, further optimization of vascular resection and reconstruction techniques for laparoscopic radical resection of PHC is anticipated in the future.

Negative margins

Currently, the application of several new technologies has also provided fresh perspectives for laparoscopic radical resection of PHC. These include the SpyGlass DS digital single-operator cholangioscopy system, intraductal ultrasonography, optical coherence tomography, and confocal laser endomicroscopy offer biliary surgeons novel approaches to assessing distal bile duct margins. These techniques facilitate obtaining negative margins and improving R0 resection rates. However, their clinical adoption remains limited. Future prospects include the emergence of more high-quality clinical studies to further validate their feasibility.

Summary

Laparoscopic radical resection for PHC is gradually transitioning from an exploratory phase to a stage of clinical application, with the efficacy and safety of the surgical procedure now preliminarily established. However, certain controversies

and challenges remain. While accumulating surgical experience and improving surgical quality, the therapeutic outcomes of this approach still require further investigation through large-scale, multicenter comparative clinical studies. The author believes that in the near future, as surgeons' technical skills advance, technical challenges will be overcome. The application of new techniques will also contribute to further improving the R0 resection rate and enhancing long-term prognosis.

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