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Current Status of Lymph Node Dissection in Curative Resection for Intrahepatic Cholangiocarcinoma: A Single-Center Retrospective Study Postprint

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Abstract

Background Lymph node metastasis is a crucial factor affecting the prognosis of patients with intrahepatic cholangiocarcinoma, and the extent of lymph node dissection during surgery remains controversial both domestically and internationally.

Objective To investigate the current status of lymph node dissection in radical surgery for intrahepatic cholangiocarcinoma.

Methods We retrospectively analyzed the clinical data of 152 patients with intrahepatic cholangiocarcinoma who underwent radical resection at Zhejiang Cancer Hospital from 2017 to 2022, focusing on the status of lymph node dissection in radical surgery for intrahepatic cholangiocarcinoma, including whether lymph node dissection was performed, the extent of dissection, and the distribution of major positive lymph nodes. Patients were divided into left liver group and right liver group according to tumor location.

Results Of the 152 patients, 83 had tumors in the left liver (left liver group) and 69 in the right liver (right liver group). Eighty-six patients underwent lymph node dissection, with a significantly higher proportion in the left liver group [61 cases (73.5%)] compared to the right liver group [25 cases (36.2%)] ($P<0.05$). The mean number of dissected lymph nodes was (7.6$±$6.1), with no statistically significant difference between the left liver group [7.0 (4.0, 10.5)] and the right liver group [5.0 (1.5, 9.5)] ($P>0.05$). Among the 86 patients who underwent lymph node dissection, 39 (45.3%) had pathologically confirmed lymph node metastasis (positive lymph nodes), with a higher positive rate in the left liver group [34 cases (55.7%)] than in the right liver group [5 cases (20.0%)] ($P<0.05$). Regardless of tumor location in the left or right liver, groups 8,

12, and 13 accounted for a higher proportion of positive lymph nodes in the routinely dissected regional area, with group 12 being the most common, at 79.4% (27/34) and 80.0% (4/5) in the left and right liver groups, respectively.

Conclusion Regardless of whether the tumor is located in the left or right liver, lymph node groups 8, 12, and 13 have higher positive rates and may require routine dissection during surgery.

Full Text

Current Status of Lymphadenectomy During Radical Resection of Intrahepatic Cholangiocarcinoma: A Single-Center Retrospective Study

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Abstract

Background: Lymph node metastasis is a critical factor affecting the prognosis of patients with intrahepatic cholangiocarcinoma (ICC), yet the optimal extent of lymphadenectomy during surgery remains controversial both domestically and internationally.

Objective: To investigate the current clinical practice of lymphadenectomy during radical resection of ICC.

Methods: We conducted a retrospective analysis of clinical data from 152 ICC patients who underwent radical resection at Zhejiang Cancer Hospital between 2017 and 2022. The study examined current lymphadenectomy practices, including the decision to perform lymphadenectomy, the extent of dissection, and the distribution of positive lymph nodes. Patients were stratified into left hemi-liver and right hemi-liver groups based on tumor location.

Results: Among 152 patients, 83 had tumors in the left hemi-liver (left group) and 69 in the right hemi-liver (right group). Lymphadenectomy was performed in 86 patients (56.6%), with a significantly higher proportion in the left group [61 cases (73.5%)] compared to the right group [25 cases (36.2%)] ($P<0.05$). The mean number of dissected lymph nodes was (7.6$±$6.1), with no significant difference between the left group [7.0 (4.0, 10.5)] and right group [5.0 (1.5, 9.5)] ($P>0.05$). Of the 86 patients who underwent lymphadenectomy, 39 (45.3%) had pathologically confirmed lymph node metastasis (positive nodes), with a

significantly higher positive rate in the left group [34 cases (55.7%)] versus the right group [5 cases (20.0%)] (P<0.05). Regardless of tumor location, lymph node stations 8, 12, and 13 accounted for the highest proportion of metastases in routinely dissected areas, with station 12 being the most common (79.4% in the left group and 80.0% in the right group).

Conclusion: Lymph node stations 8, 12, and 13 demonstrate high metastasis rates regardless of whether the tumor is located in the left or right hemi-liver, suggesting these stations should be considered for routine dissection during radical resection.

Keywords: Cholangiocarcinoma; Intrahepatic cholangiocarcinoma; Lymph node excision; Retrospective studies

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Intrahepatic cholangiocarcinoma (ICC) is a malignant primary liver tumor second only to hepatocellular carcinoma, accounting for approximately 20% of all liver malignancies [1]. Although clinically relatively rare, with an overall 5-year survival rate of less than 10%, its incidence and mortality have been increasing annually in recent years [2-3]. Surgical resection remains the preferred treatment for ICC, yet early diagnosis is challenging; only 20%-40% of patients are candidates for surgical resection. Moreover, the 5-year survival rate for ICC patients after surgery is only 14%-40%, with high postoperative recurrence rates, while patients who do not undergo resection have a 5-year survival rate of merely 0-5% [4].

Lymph node metastasis is a crucial factor influencing prognosis in ICC patients, with reported rates of 45%-65% [5]. The 5-year survival rate for patients with positive lymph nodes is 0%-20%, compared to 35%-50% for those without lymph node metastasis [6]. Some studies suggest that surgery offers no survival benefit over chemotherapy alone in patients with lymph node metastasis [7], while others have found that R0 resection improves overall survival regardless of the positive lymph node ratio [8]. For patients without lymph node metastasis, lymphadenectomy may simply increase surgical trauma, leading some researchers to propose risk prediction models to guide the decision, as lymphadenectomy does not affect overall survival in low-risk patients [5].

Currently, no international consensus exists regarding the definition of regional lymph nodes for ICC or the appropriate extent of lymphadenectomy for tumors in different liver locations [2]. The relatively low incidence and resectability of ICC have hindered large-scale prospective randomized multicenter studies, resulting in a lack of high-quality evidence on intraoperative lymphadenectomy [5]. Therefore, this study retrospectively analyzed clinical data from 152 ICC patients who underwent radical resection at Zhejiang Cancer Hospital between 2017 and 2022 to examine current lymphadenectomy practices, including the decision to perform dissection, the extent of lymphadenectomy, and the distribution of positive lymph nodes, thereby providing clinical reference.

1.1 Study Subjects

We identified 191 ICC patients who underwent surgical treatment at Zhejiang Cancer Hospital between 2017 and 2022. Inclusion criteria were: (1) pathologically confirmed ICC by two specialized pathologists; (2) no extrahepatic metastasis; (3) radical resection with negative margins. Exclusion criteria were: (1) preoperative or intraoperative detection of extrahepatic metastasis; (2) unresectable primary tumor; (3) positive resection margins; (4) concurrent malignancies in other organs; (5) incomplete medical records. This retrospective study was approved by the Ethics Committee of Zhejiang Cancer Hospital (IRB-2021-227), and all patients provided informed consent (written or telephone).

1.2 Data Collection

Patient data were obtained from the hospital's electronic medical record system, including general patient information, tumor imaging characteristics, and pathological findings.

Statistical Analysis

Normally distributed continuous data were expressed as (x̄±s) and compared between groups using one-way ANOVA. Non-normally distributed continuous data were expressed as M(P25, P75) and compared using rank-sum tests. Categorical data were expressed as frequencies and compared using ^{2} tests. A two-sided P<0.05 was considered statistically significant.

2.1 General Patient Characteristics

A total of 152 patients were included, with a selection flowchart shown in [Figure 1: see original paper]. The cohort comprised 86 males and 66 females, aged 36-85 years with a mean age of (61.6$±10.5)*years.Tumorswerelocatedinthelefthemi−liverin83patientsandrighthemi−liverin69patients.Intheleftgroup,therewere46malesand37femaleswithame*
P=0.752) or age (F=1.092, P=0.298).

2.2 Tumor Characteristics and Lymphadenectomy

Tumor size ranged from 0.6-15.0 cm, with a mean of (5.2$±2.4)*cm.Meantumorsizewas*(5.0±2.5)*cmintheleftgr*
cm in the right group, with no significant difference between groups (F=1.156, P=0.284).

Lymphadenectomy was performed in 86 patients (56.6%). The rate was significantly higher in the left group [61 cases (73.5%)] than the right group [25 cases (36.2%)] (^{2}=21.294, P<0.001). The number of dissected lymph nodes ranged from 1-26, with a mean of (7.6$±$6.1). The median number was 7.0 (4.0, 10.5) in the left group and 5.0 (1.5, 9.5) in the right group, with no significant difference (Z=-1.413, P=0.158).

2.3 Distribution of Positive Lymph Nodes

Among the 86 patients who underwent lymphadenectomy, 39 (45.3%) had pathologically confirmed lymph node metastasis. The positive rate was significantly higher in the left group [34 cases (55.7%)] than the right group [5 cases (20.0%)] (^{2}=9.138, P=0.003).

Positive lymph nodes were primarily distributed at stations 1 (right paracardial), 3 (lesser curvature), 7 (left gastric artery), 8 (common hepatic artery), 9 (celiac artery), 12 (hepatoduodenal ligament), 13 (posterior pancreatic head), and 16 (paraaortic). In the left group, the top three stations were 12, 8, and 13, while in the right group they were 12, 16, and 8/13, as detailed in .

Lymph node metastasis represents a major metastatic pathway in ICC, occurring in over 40% of patients [5] and correlating with poor prognosis [6]. Current guidelines, including the NCCN, recommend routine lymphadenectomy for ICC surgery [1,9]. However, some surgeons perform selective lymphadenectomy, partly because its survival benefit remains unproven despite high metastasis rates [2]. While some studies suggest lymphadenectomy reduces local recurrence and improves prognosis—a Korean propensity score-matched study reported disease-free and overall survival of 64 and 90 months in the dissection group versus 20 and 44 months in the non-dissection group [10]—others find no significant survival benefit and increased postoperative complications [11-12]. Some argue lymphadenectomy aids staging and prognosis assessment but does not improve outcomes [13].

Our results show that only 56.6% of patients underwent lymphadenectomy, with 43.4% undergoing tumor resection only. Most lymphadenectomy patients (70.9%) had left hemi-liver tumors. Interviews with our surgeons revealed that lymphadenectomy decisions were often based on preoperative imaging or intraoperative findings of enlarged lymph nodes. Studies show left hemi-liver tumors have higher lymph node metastasis rates (51.4%) than right hemi-liver tumors (39.1%) [14], explaining the higher dissection rate for left-sided lesions.

Consistent with prior literature [14], we found higher positive lymph node rates in the left group, with distinct distribution patterns between groups, similar to findings from Kumamoto University Hospital in 2001 [15]. This likely reflects hepatic lymphatic drainage pathways. Deep lymphatic drainage occurs via portal tracts, with approximately 80% of hepatic lymphatics entering the Glissonian sheath at the hepatoduodenal ligament and porta hepatis. The hepatoduodenal ligament lymph nodes communicate with celiac and cardioesophageal nodes along the lesser curvature (stations 1, 3, 5, 7, 8) and with superior mesenteric nodes via peripancreatic nodes, ultimately draining to paraaortic nodes (station 16) and the cisterna chyli. Superficial drainage from the liver's diaphragmatic surface occurs via coronary, triangular, and falciform ligaments to pericardial and diaphragmatic nodes, while drainage from the inferior surface primarily enters the porta hepatis system, with the caudate lobe and bare area draining via the inferior vena cava to posterior mediastinal nodes [16]. This explains

why left hemi-liver tumors metastasize to stations 1, 3, 5, and 7, whereas right hemi-liver tumors rarely involve these nodes.

Station 16 lymph node metastasis was observed in both groups, though this station is not routinely dissected. These cases typically involved enlarged nodes detected preoperatively or intraoperatively that were resected for more accurate staging rather than therapeutic benefit, as station 16 positivity indicates distant metastasis (M1 disease), guiding prognosis assessment and postoperative systemic therapy decisions.

Our findings suggest that stations 8, 12, and 13 should be considered for routine dissection regardless of tumor location. However, as a single-center retrospective study with limited evidence level, these results provide only preliminary reference. Further multicenter prospective randomized controlled trials are needed to definitively address lymphadenectomy in ICC.

Author Contributions: HU Chao conceived and designed the study, supervised implementation, drafted the manuscript, and takes overall responsibility; CHENG Xi conducted literature search, screening, and patient consent acquisition; JIN Wangxun performed statistical analysis and prepared figures and tables; YAO Hongqing collected patient data; WANG Xinbao revised the manuscript and provided quality control.

Conflict of Interest: The authors declare no conflicts of interest.

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