



Lymph node dissection results, surgical management modalities and oncologic results of intrahepatic cholangiocarcinomas, single center experience

Intrahepatik kolanjiokarsinomların lenf nodu diseksiyon sonuçları, cerrahi tedavi yöntemleri ve onkolojik sonuçları, tek merkez deneyimi

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Background and Aims: Intrahepatic cholangiocarcinoma is a cancer of the biliary tract. The only current curative treatment for intrahepatic cholangiocarcinoma is liver resection. The aim of this study is given the result of the lymph node dissection, surgical management and recurrences ratio of intrahepatic cholangiocarcinomas in our center. **Material and Methods:** The medical record of patients who were treated for intrahepatic cholangiocarcinoma in our clinic were retrospectively evaluated between January 2019 to January 2023. **Results:** Twenty four patients were operated in our clinic. Of the patients, 12 were female, 12 were male, and the mean age was 52.75 ± 10.20 years. The median tumor size was 8.50 cm. Twelve patients had right hepatectomy, 6 patients had left hepatectomy, 2 patients had extended left hepatectomy, 2 patients had central hepatectomy and 2 patients had segment 4 plus 5 resection in the operation. The mean number of lymph node removed was 9.95 ± 3.56 . Malignant lymph node was seen in 5 patients. Postoperative median hospital stay was 13.50 days. Mortality was observed in only 2 patient in the first 3 months postoperatively. The median overall survival of the patients was 318.50 days. **Conclusions:** As a result of our study, in patients with intrahepatic cholangiocarcinoma, patients who will be selected with preoperative correct staging, aggressive surgery by evaluating the comorbidities and conditions of patients with resectable tumors, removal of hepatoduodenal lymph nodes during surgery, and liver volume expansion procedures in patients who may develop remnant liver volume failure, to force to resection, which is the only curative chance of patients is demonstrated that it is necessary.

Key words: Intrahepatic cholangiocarcinoma, surgery, lymph node dissection

Giriş ve Amaç: İntrahepatik kolanjiokarsinom, bir safra yolu kanseridir. İntrahepatik kolanjiokarsinom için mevcut tek küratif tedavi karaciğer rezeksiyonudur. Bu çalışmanın amacı, merkezimizde yapılan intrahepatik kolanjiokarsinomların lenf nodu diseksiyonu, cerrahi yönetimi ve nüks oranlarının sonuçlarını vermektir. **Gereç ve Yöntem:** Ocak 2019 - Ocak 2023 tarihleri arasında kliniğimizde intrahepatik kolanjiokarsinom tedavisi gören hastaların tıbbi kayıtları retrospektif olarak değerlendirildi. **Bulgular:** Kliniğimizde 24 hasta ameliyat edildi. Hastaların 12'si kadın, 12'si erkekti ve yaş ortalaması 52.75 ± 10.20 idi. Ortanca tümör boyutu 8.50 cm idi. Ameliyatta 12 hastaya sağ hepatektomi, 6 hastaya sol hepatektomi, 2 hastaya genişletilmiş sol hepatektomi, 2 hastaya santral hepatektomi ve 2 hastaya segment 4 artı 5 rezeksiyon uygulandı. Ortalama çıkarılan lenf nodu sayısı 9.95 ± 3.56 idi. 5 hastada malign lenf nodu görüldü. Postoperatif ortalama hastanede kalış süresi 13.50 gündü. Postoperatif ilk 3 ayda sadece 2 hastada mortalite gözlemlendi. Hastaların medyan genel sağkalımı 318.50 gündü. **Sonuç:** Çalışmamızın sonucunda preoperatif doğru evreleme ile seçilecek intrahepatik kolanjiokarsinom hastalarında, rezekte edilebilir tümörü olan hastaların komorbiditeleri ve durumları değerlendirilerek agresif cerrahi, cerrahi sırasında hepatoduodenal lenf nodlarının çıkarılması ve hastalarda karaciğer hacim genişletme işlemleri Remnant karaciğer hacim yetmezliği gelişebilecek hastalarda, küratif tek şans olan hastaların rezeksiyona zorlanmasının gerekli olduğu gösterilmiştir.

Anahtar kelimeler: İntrahepatik kolanjiokarsinoma, cerrahi, lenf nodu diseksiyonu

INTRODUCTION

Cholangiocarcinoma (CCA) is a cancer of the biliary tract. It constitutes exactly 10% of hepatobiliary tumors and accounts for 3% of all newly diagnosed malignancies worldwide (1,2). These rare tumors can develop anywhere in the biliary tract. Based on location in the American Joint Committee on Cancer (AJCC) staging systems, CCA is generally classified as intrahepatic, perihilar, and extrahepatic CCA. The reason for the classification is that the treatment approach and prognosis of CCA developing from these three regions are different (2,3). In the distribution of CCAs, intrahepatic CCA (i-CCA) accounts for 10% of all cases (4). The only current curative treatment for iCCA is liver resection (LR). But, the possibility of being cured of the disease by liver resection is exactly 10% (5,6). Despite current progress in surgical technique and developments in treatment, most patients died within 3 years of diagnosis.

The aim of this study is given the result of the lymph node dissection, surgical management and recurrences ratio of intrahepatic cholangiocarcinomas in our center between January 2019 to January 2023.

MATERIAL and METHODS

After getting local ethical committees approval, the medical record of patients who were treated for i-CCA in our clinic were retrospectively evaluated between January 2019 to January 2023. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Ankara Bilkent City Hospital (Date: 22/03/2023; Session Number and Decision No: E1- 23-3393).

Demographic data of the patients, clinical and radiological findings, preoperative bile drainage procedure, preoperative liver volume augmentation procedure, type of surgical procedure, length of hospital stay, perioperative and postoperative complications, perioperative liver invasion type, postoperative pathological results, mortality and morbidity of the postoperative 90 days and recurrence in follow up were examined.

Statistical Analysis

IBM Statistical Package for Social Sciences (SPSS) ver 20.0 (IBM Corporation, Armonk, NY, USA) was used. According to the distribution of normality, student t-test and Mann-Whitney U test were used to evaluate the numerical data. Chi square test was used for the categorical data. Numerical data were given as mean \pm standard deviation (SD) and median (minimum – maximum values) according to the normality test; categorical values were given as count (n) and percentage (%). A $p > 0.05$ value was statistically significant

RESULTS

Between January 2019 and January 2023, 24 patients with the diagnosis of i-CCA were operated in our clinic. Of the patients, 12 were female, 12 were male, and the mean age was 52.75 ± 10.20 years (range 34 - 70). The median tumor size was 8.50 cm (range: 2 - 17 cm). Preoperative median CA 19-9 level was 36.05 (range 5.20 - 12179). Hepatitis B infection was seen in 4 patients and chronic liver disease was detected in these 4 patients. After preoperative drainage procedures median bilirubin level (the day before the surgery) was 0.95 mg/dl (range 0.3 - 1.40 mg/dl). Comorbid disease was seen in 12 patients and the first two most frequent comorbid diseases were hypertension and chronic obstructive lung disease, respectively. Twelve patients had right hepatectomy, 6 patients had left hepatectomy, 2 patients had extended left hepa-

tectomy, 2 patients had central hepatectomy and 2 patients had segment 4 and 5 resection in the operation (Figure 1 and 2). Preoperative portal vein embolization was performed in 3 of the patients and associating liver partition and portal vein ligation for staged hepatectomy (ALLPS) procedure was performed in 2 patients who underwent right hepatectomy. As a result of histopathological examinations, the final pathology result was reported as iCCA in all patients and 4 of 24 patients were

well differentiated, 15 were moderately differentiated, and 5 were poorly differentiated. The mean number of lymph node removed was 9.95 ± 3.56 . Malignant lymph node was seen in 5 patients. In the postoperative period, hepatic failure was observed in 2 patients, which improved with medical treatment and follow-up, and bile leakage was observed in 6 patients. Of these 6 patients who developed biliary fistula, 2 of them were stented with endoscopic retrograde cholangiopancreatog-

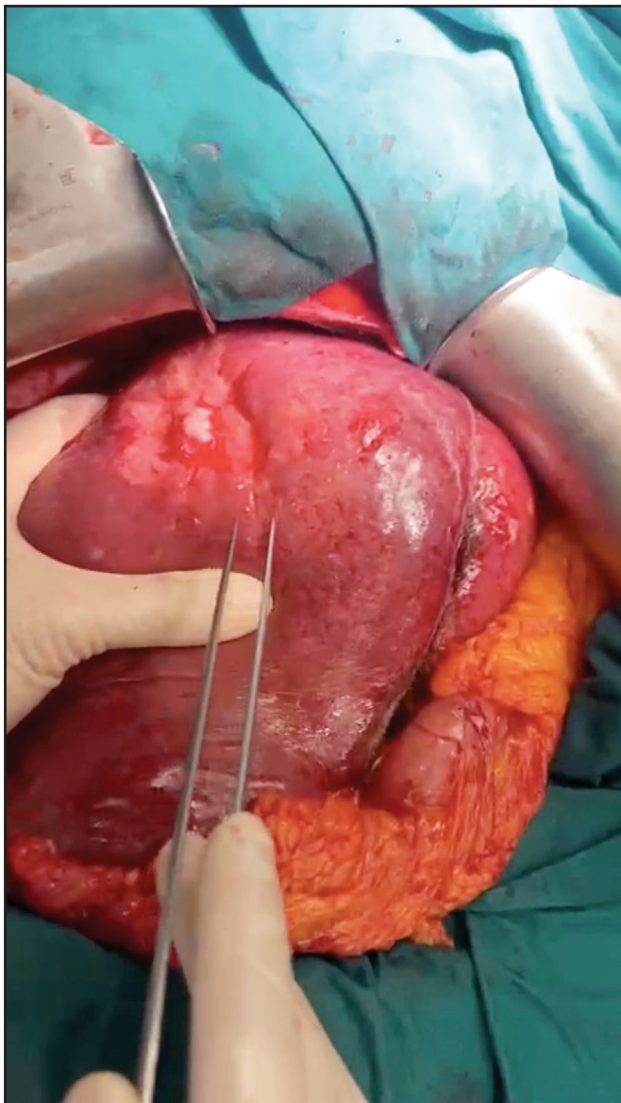


Figure 1 Intraoperative view of an intrahepatic cholangiocarcinoma in right liver



Figure 2 Pathology specimen of an intrahepatic cholangiocarcinoma after resection

raphy (ERCP), 1 patient was stented with percutaneous transhepatic cholangiography (PTC), and the other 3 patients were treated medically. In all patients, the biliary fistula was closed without need for surgery. Postoperative median hospital stay was 13.50 days (range 6 - 62 days). Mortality was observed in only 2 patient in the first 3 months postoperatively. One of these patients died due to Covid-19 infection and the other due to sepsis developing fifth day after surgery. In the postoperative follow-up, 5 patients developed recurrent liver lesion, peritoneal carcinomatosis, and abdominal ascites at 3.,4.,5.,12., and 24. months, respectively. In 3 patients, multiple metastases developed in the lung at the 9th, 10th and 14th months, respectively and in 1 patient, multiple metastases developed in the brain at the 11th month. The median overall survival of the patients was 318.50 days (range 13 - 990 days).

DISCUSSION

We conducted this study for investigated the lymph node dissection results, surgical management modalities, complication rates and survival results of iCCA. Newest procedures for expanding the liver volume were provided an increased resection rates and improved overall survival in selected iCCA patients (6).

Radical surgery is still currently the only curative treatment for iCCA when resection with a tumor-free surgical margin is achieved. An aggressive surgical approach, including major liver resection, has been recommended at many centers to improve outcomes (6). In our study, we found that patients with iCCA had better overall survival after curative resection compared to previous reports, suggesting that complete removal of tumor-containing segments and regional lymph nodes plays an important role in improving survival outcomes. This high rate in our series was the result of well preoperative evaluation of the patients and aggressive

resections with volume-expanding procedures before resection. We follow this aggressive approach as resection offers the only chance for cure.

Many previous studies have reported prognostic factors after radical surgery for ICC, including cirrhosis, tumor size, multiple lesions, number of segments removed, and tumor markers (7-14). Lymph node metastasis is also one of the prognostic factors (15). In our series, we performed lymph node dissection for all our patients and we found that 5 of our patients had lymph node metastases.

Intrahepatic cholangiocarcinoma (i-CCA) is an aggressive biliary cancer arising from the biliary epithelium proximal to the second-degree bile ducts. An aggressive surgical approach, including extended liver resection and vascular reconstruction, and further systemic therapy and application of locoregional therapy leads to increased resection rate and overall survival in selected i-CCA patients (1,16).

Diagnosis of cholangiocarcinoma is made by the combination of clinical/biochemical features and imaging findings with non-specific tumor markers for complementary (17). Of the tumor marker substrates, CA 19-9 has been reported to have the most common diagnostic effects (18,19). In our study, approximately half of the patients had elevated CA 19-9 preoperatively. In the subgroup analysis, we found that patients with higher than normal CA 19-9 levels had one or more of the previously mentioned poor prognostic markers (tumor size, degree of tumor differentiation, lymph node metastasis, vascular invasion..) (19).

This study had several limitations. Firstly, it is a retrospective study and given that only patients undergoing surgical resection were included in this study. In addition, the number of cases was small but the reason of this was iCCA is a rare disease.

As a result of our study, in patients with iCCA patients who will be selected with preoperative cor-

rect staging, aggressive surgery by evaluating the comorbidities and conditions of patients with resectable tumors, removal of hepatoduodenal lymph nodes during surgery, and liver volume expansion procedures in patients who may develop remnant liver volume failure, to force to resection, which is the only curative chance of patients is demonstrated that it is necessary. However, it should be supported by prospective multicenter studies on this subject.

Ethics Committee: *This study protocol was approved by Ethics Committee of Ankara Bilkent City Hospital (Date: 22/03/2023; Session Number and Decision No: E1- 23-3393). The study was complied with The World Medical Association Declaration of Helsinki.*

Conflict of Interest: *There is no conflict of interest with any institution or person.*

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