Impact of medical and surgical intervention on survival in patients with cholangiocarcinoma

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Abstract

AIM: To examine surgical and medical outcomes for patients with cholangiocarcinoma using a population-based cancer registry.

METHODS: Using the California Cancer Registry’s Cancer Surveillance Program, patients with intrahepatic cholangiocarcinoma treated in Los Angeles County from 1988 to 2006 were identified and evaluated for clinical and pathologic factors and therapies received (surgery, radiation, and chemotherapy). The surgical cohort was further categorized into three treatment groups: patients who received adjuvant chemotherapy, adjuvant chemoradiation, or underwent surgery alone (no chemotherapy or radiation administered). Survival was assessed by Kaplan-Meier method; and Cox proportional hazard modeling was used in multivariate analysis.

RESULTS: Of 825 patients, 60.2% received no treatment. Of the remaining 328 patients, 18.5% chemotherapy only, 7.4% chemoradiation, and 13.8% underwent surgery. More male patients underwent surgical resection ($P = 0.004$). Surgical patients were younger than the patients receiving chemotherapy or chemoradiation ($P < 0.001$). Of the surgical cohort ($n = 114$), 60.5% underwent surgery alone whereas chemical treatment alone was each less effective ($P < 0.001$). Median survival for all patients in the study was 6.6 mo. Median survival was highest for patients who underwent surgery (23 mo), whereas both chemotherapy (9 mo) and chemoradiation (8 mo) alone were each less effective ($P < 0.001$). By multivariate analysis, extent of disease, receipt of surgery, and administration of chemotherapy (with/without surgery) were independent predictors of overall survival.

CONCLUSION: This study demonstrates that surgery is a critical treatment modality. Multimodality treatment has yet to be standardized, but play a role in optimal therapy for cholangiocarcinoma.

Key words: Cholangiocarcinoma; Chemotherapy; Surgery; Survival; Therapies

Core tip: Cholangiocarcinoma is an aggressive biliary tract cancer with few treatment options. Surgical resection has been the only available curative-intent treatment in early disease. This study demonstrates that multimodality therapy may provide the best improvement in survival.
INTRODUCTION
Cholangiocarcinoma (CCA) is an aggressive malignancy of the biliary tract that has two major anatomic subtypes: intrahepatic and ductal/perihilar[1]. It is the 2nd most common primary hepatic malignancy worldwide and afflicts nearly 2000-3000 people in the United States annually[2,3]. Partly due to improved diagnostic measures as well as a change in diagnosis coding, the incidence of CCA in the United States has increased by nearly 165% over the past several decades[4-7]. In fact, CCA was often coded as hepatocellular carcinoma until the late 1980s; therefore, the true incidence of cholangiocarcinoma prior to that time remains unknown[8]. Despite improvements in diagnostic techniques, many patients are asymptomatic until the disease has become advanced. Symptomatic patients commonly present with jaundice, but non-specific symptoms (e.g., weight loss, loss of appetite, and abdominal pain) are also frequently reported[9,10].

Surgical resection has long been considered the mainstay of curative treatment for CCA. Unfortunately, most patients with CCA present with advanced unresectable disease. Even when patients are eligible for surgical intervention, overall survival is poor, with 5-year survival rates of 20%-43%[11,12]. For patients who are eligible for systemic therapy for unresectable disease or adjuvant therapy, the current recommended therapy of gemcitabine and cisplatin provides a very minimal increase in median overall survival (OS) to 11.7 mo[13,14,15]. The lack of effective therapies has led to the frequent administration of systemic agents in non-standardized regimens[16].

Lack of better standardized therapeutic regimens and prior inconsistencies in coding of CCA have made it difficult to assess multimodality regimens for this disease. The absence of data from prospective randomized trials specifically limited to CCA precludes appropriate clinical practice guidelines[17]. In this investigation, we sought to examine common CCA therapies (i.e., surgical resection, chemotherapy, and radiation therapy) to assess treatment outcomes and to determine which therapeutic regimen(s) have offered improvements in overall survival in a large population based cohort.

MATERIALS AND METHODS
Cancer surveillance program for Los Angeles County
After obtaining City of Hope Institutional Review Board approval, we used the California Cancer Registry’s Cancer Surveillance Program (CSP) to identify patients diagnosed with cholangiocarcinoma. CSP for Los Angeles County is a population-based cancer registry that includes data on nearly all cancer diagnoses. The collected data is focused on cancer diagnosis and treatment with the stated CSP aim of improving cancer care in the State of California. This focus on comprehensive data collection for cancer therapy (i.e., chemotherapy, radiotherapy, and curative-intent surgery) distinguishes CSP from other regional and national databases.

CSP reporting for CCA location, staging, and differentiation is based on the International Classification of Diseases for Oncology. After restricting our analysis to liver (C22.0) and intrahepatic bile duct (C22.1) topologies, we selected only cases with histology codes 8160 (bile duct adenocarcinoma) and 8162 (Klatskin’s tumor). CSP extent of disease was reported as localized, regional [extension only; nodes only; extension and nodes; not otherwise specified (NOS)], distant or unknown. Tumor grade was categorized by CSP as well, moderate, poor, undifferentiated, or unknown. Chemotherapy was classified as negative (none; recommended, not given; or refused) or positive (single agent, multiple agent, or NOS). Radiation data was also classified as negative (none) or positive (beam, implants, isotopes, combination, or NOS). All patients who underwent curative-intent surgical therapy (defined by CSP codes 10, 13, 16, 20-80) were included in the surgery group. Patients who did not have surgery or who underwent non-curative surgery (defined by CSP codes 11, 12, 15, 17 and 90) were included in the non-surgical group.

Statistical analysis
Inclusion criteria consisted of patients diagnosed with CCA from 1988 to 2006 who survived 30 d or longer post-diagnosis that received some form of treatment for their disease. Patients were only included in whom complete survival data was available. Treatment groups were defined as chemotherapy alone, chemoradiation, and surgery. The surgical cohort was then further categorized into three treatment groups: patients who received adjuvant chemotherapy, adjuvant chemoradiation, or underwent surgery alone (no chemotherapy or radiation administered). All quantitative data were expressed as the median and range, unless otherwise indicated. Clinical and pathologic characteristics were compared across the different treatment arms by chi-square analyses.

Cox-proportional hazards modeling was used to evaluate the role of chemoradiation and other variables on overall survival as represented by hazard ratios (HR) with 95% confidence intervals (CI). Variables included in the univariate and multivariate analyses were age, sex, race/ethnicity, socioeconomic status, tumor location, tumor size, T-stage, N-stage, M-stage, tumor grade, American Joint Commission on Cancer 7th edition stage, lymph node number, chemotherapy administration, and radiation administration. Overall survival for the treatment arms was calculated by the Kaplan-Meier method and differences in survival were compared by the log-rank test. Two-sided P-values < 0.05 were considered to be statistically significant. All statistical analyses were completed using SAS software (SAS institute Inc. Cary,
The 825 patients included in this study were categorized by type of treatment received. Treatment groups were divided into chemotherapy, chemoradiation, and surgical groups. The surgical group was then subdivided into surgery alone, surgery with adjuvant chemotherapy, and surgery with adjuvant chemoradiation.

NC, United States).

RESULTS

Patient characteristics

There were 825 patients identified with CCA. Of this group, 60.2% (n = 497) did not receive treatment, 18.5% (n = 153) received chemotherapy only, 7.4% (n = 61) received chemoradiation, and 13.8% (n = 114) underwent curative-intent surgery. Of the patients who underwent surgery, 8.4% (n = 69) received surgery only, and 5.5% (n = 45) received surgery plus additional adjuvant treatment (Table 1). Of these, 20 (17.5%) surgical patients received adjuvant chemotherapy, 21 (18.4%) underwent adjuvant chemoradiation, and 4 (3.5%) underwent adjuvant radiation. Given the small sample size of the adjuvant radiation group, this group was excluded from our analysis.

Comparison of treatment arms

Of the three treatment groups (chemotherapy, chemoradiation, and surgical groups), the characteristics that were different between the surgical patients and the non-surgical patients were age, gender, tumor location, and stage (Table 2). Patients in the surgery cohort were more often male, white, and young. Not surprisingly, there were expected differences in extent of disease and type of disease between the groups, with more early stage intrahepatic CCA disease in the surgical cohort. Additionally, over one-half of the chemotherapy group (n = 68; 53.1%) had metastatic disease at presentation, compared to 12.7% (n = 14) of surgical patients.

Comparison of surgical groups

The characteristics found to be significantly different between surgical patients who received surgery alone and those who underwent surgery and additional adjuvant therapy were age, gender, tumor location, and stage (Table 3). Patients in the adjuvant chemoradiation group were male and much younger in age compared to the other groups. Whereas 80.9% of the adjuvant chemoradiation group were < 65 years old, more patients (39.1%) were older than 65 in the surgery alone subset.

Survival according to treatment group

Median survival (MS) for all patients in the overall cohort was 6 mo, with a 5-year survival of 5.7% (Figure 1A).
Univariate and multivariate analysis of patient cohort

A Cox regression analysis was performed to identify predictors of survival for CCA (Table 4). On univariate analysis, older age, black race, lower socioeconomic status, undifferentiated tumors, and T4 tumors were significantly associated with poorer survival. Upon multivariate analysis, older age (i.e., above 80 years of age), advanced disease...
tent therapy for patients with early stage, resectable CCA. Such practice has been largely established on the back-
bone of single institution reports touting the benefits of surgical resection [10,11,18]. Our current population-based
investigation supports this growing body of evidence, also highlighting the superior outcomes when patients
with CCA are eligible for and undergo surgical resection. For those surgical patients, favorable prognostic factors
include absence of tumor at the resection margins, elevated serum CA19-9 levels, solitary lesion, absence of
lymph node involvement, presence of well-differentiated adenocarcinoma, and absence of vascular invasion [19-21].
Nevertheless, the relatively low survival even with appro-

| Table 3 Characteristics of surgical groups (%) |
|-----------------------------------------------|
| Surgery alone (n = 69) | Adjuvant chemotherapy (n = 20) | Adjuvant chemoradiation (n = 21) | P value |
|------------------------|-------------------------------|-----------------------------|---------|
| **Age group (yr)**     |                               |                             | < 0.0001|
| 18-49                  | 13 (18.8)                     | 6 (30.0)                    | 10 (47.6)|
| 50-64                  | 29 (42.0)                     | 6 (30.0)                    | 7 (33.3) |
| 65-79                  | 25 (36.2)                     | 8 (40.0)                    | 4 (19.0) |
| ≥ 80                   | 2 (2.9)                       | 0 (0.0)                     | 0 (0.0)  |
| **Sex**                |                               |                             | 0.018   |
| Men                    | 41 (59.4)                     | 13 (65.0)                   | 14 (66.7)|
| Women                  | 28 (40.6)                     | 7 (35.0)                    | 7 (33.3) |
| **Race**               |                               |                             | 0.497   |
| Non-hispanic white     | 33 (47.8)                     | 11 (55.0)                   | 9 (42.9) |
| Black                  | 2 (2.9)                       | 0 (0.0)                     | 2 (9.5)  |
| Hispanic white         | 20 (29)                       | 3 (15.0)                    | 5 (23.8) |
| Other                  | 14 (20.3)                     | 6 (30.0)                    | 5 (23.8) |
| **Socioeconomic status** |                               |                             | 0.603   |
| Highest                | 18 (26.1)                     | 7 (35.0)                    | 7 (33.3) |
| Middle                 | 41 (59.4)                     | 9 (45.0)                    | 12 (57.1)|
| Lowest                 | 10 (14.5)                     | 4 (20.0)                    | 2 (9.5)  |
| **Tumor**              |                               |                             | 0.000   |
| Liver                  | 17 (24.6)                     | 3 (15.0)                    | 2 (9.5)  |
| **Location**           |                               |                             |          |
| Bile duct              | 52 (75.4)                     | 17 (85.0)                   | 19 (90.5)|
| **Grade**              |                               |                             | 0.684   |
| Well differentiated     | 13 (23.6)                     | 3 (20.0)                    | 3 (16.7) |
| Moderately differentiated | 21 (38.2)                     | 4 (26.7)                    | 6 (33.3) |
| Poorly differentiated   | 21 (38.1)                     | 8 (53.3)                    | 9 (50.0) |
| **Tumor size (cm)**    |                               |                             | 0.825   |
| ≤ 5                    | 24 (54.5)                     | 3 (25.0)                    | 6 (60.0) |
| > 5                    | 20 (45.5)                     | 9 (75.0)                    | 4 (40.0) |
| **Summary**            |                               |                             | 0.016   |
| Local                  | 23 (38.3)                     | 3 (20.0)                    | 7 (38.9) |
| **Stage**              |                               |                             |          |
| Regional               | 24 (40.0)                     | 5 (33.3)                    | 6 (33.3) |
| Distant                | 13 (21.7)                     | 7 (46.7)                    | 5 (27.8) |
| **T stage**            |                               |                             | 0.071   |
| T1                     | 24 (40.0)                     | 5 (29.4)                    | 7 (36.8) |
| T2                     | 9 (15.0)                      | 3 (17.6)                    | 2 (10.5) |
| T3                     | 12 (20.0)                     | 3 (17.6)                    | 3 (15.8) |
| T4                     | 15 (25.0)                     | 6 (35.3)                    | 7 (36.8) |
| **N stage**            |                               |                             | 0.396   |
| N0                     | 44 (83.0)                     | 10 (62.5)                   | 14 (82.4)|
| N1                     | 9 (17.0)                      | 6 (37.5)                    | 3 (17.6) |
| **AJCC7 stage**        |                               |                             | < 0.0001|
| I                      | 22 (40.0)                     | 5 (29.4)                    | 6 (33.3) |
| II                     | 7 (12.7)                      | 1 (5.9)                     | 1 (5.6)  |
| III                    | 13 (23.6)                     | 3 (17.7)                    | 5 (27.8) |
| IV                     | 13 (23.7)                     | 8 (47.0)                    | 6 (33.4) |

Characteristics found to be significantly different between surgical patients were age, gender, tumor location, and stage. Patients in the adjuvant chemoradiation group were male and much younger in age compared to the other groups. AJCC: American Joint Committee on Cancer.

stage, poorly differentiated or undifferentiated tumors, and lymph node involvement were independent predic-
tors of poorer survival in all treatment groups. Our analy-
sis demonstrated a significant improvement in survival associated with surgical resection (HR = 0.44, 95%CI: 0.34-0.59, P < 0.0001) and receipt of chemotherapy (HR = 0.70, 95%CI: 0.59-0.83 P = 0.001). In contrast, receipt of radiation therapy was not associated with improved survival.

**DISCUSSION**

Surgery has been the traditional mainstay of curative-in-
### Table 4  Univariate and stepwise analysis for overall survival (%)  

| Variable                | Univariate hazard ratio (95%CI) | Stepwise hazard ratio (95%CI) |
|-------------------------|----------------------------------|-------------------------------|
| **Age** (yr)            |                                  |                               |
| 18-49                   | 1.00 (reference)                 | 1.00 (reference)              |
| 50-64                   | 1.43 (1.11-1.85)                 | 1.64 (1.27-2.13)              |
| 65-79                   | 1.40 (1.10-1.78)                 | 1.47 (1.15-1.89)              |
| ≥ 80                    | 2.19 (1.68-2.86)                 | 1.85 (1.40-2.46)              |
| **Sex**                 |                                  |                               |
| Men                     | 1.00 (reference)                 |                               |
| Women                   | 1.02 (0.88-1.18)                 |                               |
| Race                    |                                  |                               |
| Non-hispanic white      | 1.00 (reference)                 |                               |
| Ethnicity               |                                  |                               |
| Black                   | 1.50 (1.14-1.97)                 |                               |
| Hispanic white          | 1.04 (0.87-1.24)                 |                               |
| Other                   | 1.00 (0.82-1.21)                 |                               |
| Socioeconomic status    |                                  |                               |
| Highest                 | 1.00 (reference)                 | 1.00 (reference)              |
| Middle                  | 1.25 (1.04-1.49)                 | 1.18 (0.98-1.41)              |
| Lowest                  | 1.61 (1.28-2.03)                 | 1.52 (1.20-1.92)              |
| Grade                   |                                  |                               |
| Well differentiated      | 1.00 (reference)                 |                               |
| Moderately differentiated| 1.05 (0.72-1.53)                 |                               |
| Poorly differentiated    | 1.61 (1.13-2.29)                 |                               |
| Undifferentiated        | 2.96 (1.38-6.32)                 |                               |
| Unknown                 | 1.71 (1.24-2.35)                 |                               |
| Tumor size (cm)         |                                  |                               |
| ≤ 5                     | 1.00 (reference)                 |                               |
| > 5                     | 1.03 (0.76-1.39)                 |                               |
| T Stage                 |                                  |                               |
| T1                      | 1.00 (reference)                 |                               |
| T2                      | 0.91 (0.57-1.47)                 |                               |
| T3a                     | 1.10 (0.80-1.51)                 |                               |
| T3b                     | 1.37 (0.72-2.63)                 |                               |
| T4                      | 2.33 (1.76-2.83)                 |                               |
| TX                      | 1.85 (1.50-2.29)                 |                               |
| N stage                 |                                  |                               |
| N0                      | 1.00 (reference)                 |                               |
| N1                      | 1.62 (1.24-2.12)                 |                               |
| NX                      | 1.76 (1.50-2.07)                 |                               |
| AJCC7 group             |                                  |                               |
| I                       | 1.00 (reference)                 | 1.00 (reference)              |
| II                      | 0.80 (0.41-1.56)                 | 1.07 (0.54-2.09)              |
| III                     | 1.37 (0.98-1.91)                 | 1.31 (0.95-1.84)              |
| IV                      | 2.81 (2.11-3.72)                 | 2.56 (1.90-3.44)              |
| Unknown                 | 2.23 (1.72-2.89)                 | 1.52 (1.16-2.00)              |
| Treatment groups        |                                  |                               |
| Chemo alone             | 1.00 (reference)                 |                               |
| Chemoradiation          | 0.98 (0.72-1.34)                 |                               |
| Surgery                 | 0.44 (0.34-0.59)                 |                               |
| None                    | 1.50 (1.24-1.61)                 |                               |
| Surgery groups          |                                  |                               |
| Surgery Alone           | 1.00 (reference)                 |                               |
| Adjuvant chemo          | 1.44 (0.82-2.55)                 |                               |
| Adjuvant chemoradiation | 1.02 (0.56-1.85)                 |                               |
| Adjuvant radiation      | 1.53 (0.55-4.26)                 |                               |
| No surgery              | 3.19 (2.35-4.33)                 |                               |
| Surgery                 |                                  |                               |
| No                      | 1.00 (reference)                 | 1.00 (reference)              |
| Yes                     | 0.54 (0.27-0.45)                 | 0.42 (0.32-0.54)              |
| Chemotherapy            |                                  |                               |
| No                      | 1.00 (reference)                 |                               |
| Yes                     | 0.73 (0.62-0.85)                 | 0.70 (0.59-0.83)              |
| Radiation               |                                  |                               |
| No                      | 1.00 (reference)                 |                               |
| Yes                     | 0.74 (0.60-0.90)                 |                               |

1Included in step-wise model. On univariate analysis, older age, black race, lower socioeconomic status, undifferentiated tumors, and T4 tumors were significantly associated with poorer survival. Upon stepwise analysis, older age (> 80 year), advanced disease stage, poorly differentiated or undifferentiated
tumors, and lymph node involvement were independent predictors of poorer survival in all treatment groups. There was a significant improvement in survival associated with surgical resection and receipt of chemotherapy. chemo: Chemotherapy; AJCC: American Joint Committee on Cancer.

private surgical intervention underscores the pressing need for multidisciplinary approach to the management of patients with CCA.

Treatment guidelines suggest that systemic chemotherapy should be the treatment of choice for patients with good performance status who have extensive disease not amenable to surgical resection. In the setting of unresectable or metastatic CCA, the aims of treatment should include prolongation of life but also maintenance of quality of life. Prior studies have reported rates of OS ranging between 5.6 and 14 mo[32-36]. Patients that did not receive treatment in our study had an MS of 3 mo, whereas patients who received chemotherapy or chemoradiation had MS of 8 and 9 mo respectively. The identification of chemotherapy in our study as an independent variable for survival is consistent with prior reports.

There is an inherent limitation with the CSP database, in that the exact chemotherapy regimen and its timing and period of administration are not available for analysis. A phase III trial recently demonstrated the benefit of combined gemcitabine and cisplatin over gemcitabine alone with improved OS and progression-free survival[35]. Although the study included all hepatobiliary cancers, including gallbladder and ampullary cancers[33], a benefit to combination chemotherapy was seen in the CCA subgroup. The National Comprehensive Cancer Network (NCCN) now recommends the combination therapy of gemcitabine and cisplatin as the standard treatment for unresectable CCA based on the results of the randomized phase III trial ABC-02 and retrospective and pooled data[35,29-31].

The NCCN also provides guidelines, albeit non-specific, on the use of adjuvant therapies in the management of patients with resectable CCA disease. Depending on the completeness of surgical resection, adjuvant therapies in clinical trial settings or case-by-case individualized therapies are recommended[31]. The lack of definitive recommendations for adjuvant treatment in patients with curatively resected cholangiocarcinoma is based on the absence of level 1 evidence for such conditions. In a recent systematic review and meta-analysis of adjuvant chemotherapy, radiation, or chemoradiation in 6712 patients with resected biliary tract cancer, a significant benefit in OS was observed in favor of any adjuvant treatment in CCA patients with either lymph node positivity or with positive resection margins[35]. In our study, we did not see any positive impact to chemotherapy or chemoradiation in patients with resected cholangiocarcinoma. The reasons for the lack of adjuvant treatment benefits may be related to a true lack of efficacy in adjuvant therapies for patients with CCA. This patient population is typically underpowered to identify a benefit; or patient selection bias may exist wherein patients with favorable T1-T2N0 tumors are selected for surgery only groups.

Radiation therapy must also be considered in the multimodal management of patients with CCA. Although prior small cohort studies have shown disappointing results for radiation alone, chemoradiation therapies in select patients should continue to be investigated in future trials. Nevertheless, the addition of radiation to chemotherapy regimens did not improve survival in our study. Nonsurgical patients had similar MS after receiving either chemotherapy alone (9 mo) or chemoradiation (8 mo). This is consistent with a prospective study by Pitt et al[33], who reported that radiation did not provide a survival advantage in patients with perihilar CCA.

In other published retrospective and population-based studies, adjuvant treatment with chemoradiation using fluoropyrimidine-based chemotherapy showed possible improvement in local control and potential improvement in short-term survival in patients with CCA without long-term benefit[34-36]. For intrahepatic CCA, retrospective and population reviews have suggested that adjuvant chemoradiation may provide a slight survival benefit in R1 resections[31]. However, based on the paucity of data, current guidelines can only recommend that chemoradiation be used in unresectable patients without metastatic disease[31].

Novel approaches not examined in our study should also be considered in patients with CCA. Advancements in radiation treatments have led to novel approaches to deliver radiation to patients with CCA including radioembolization with Yttrium-90 microspheres[37,38]. Single-institution data appear promising for patients with liver predominant disease[37]. However, the definitive role of radioembolization should be evaluated in randomized studies prior to its inclusion as a standard measure. We could not fully evaluate the role of radioembolization in our study since this treatment was not integrated to any extent in patients with CCA prior to 2006. Our study is one of the few that shed light on how multimodal therapy impacts patients with intrahepatic CCA also highlighting the inherent complexity in treating CCA. Our results verify that surgical resection remains the most important variable associated with improved survival for patients with resectable intrahepatic CCA, but our results also indicate that further work is necessary to identify more effective systemic/targeted and regional therapies.

**COMMENTS**

**Background**

Cholangiocarcinoma is an aggressive cancer of the bile ducts and liver. Unfortunately, most patients are asymptomatic and only present when symptoms suggestive of advance disease, such as jaundice, presents. Surgery remains the best curative-intent treatment, but is only possible in patients with early stage disease. There are few studies evaluating multimodality treatment: surgery, chemotherapy, and radiation.

**Research frontiers**

Multimodality therapies are now being investigated for the treatment of cholan-
giocarcinoma, such as radioembolization of the liver; yet these therapies are not standard of care.

**Innovations and breakthroughs**

The mainstay of treatment is chemotherapy with gemcitabine and cisplatin. Some studies have evaluated other chemotherapy, including fluoropyrimidine-based regimens, with similar results. In single-center trials, radioembolization with Yttrium-90 has been shown to be a safe.

**Applications**

This study indicates that surgery provides the best survival benefits for patients with cholangiocarcinoma and should continue to be a critical component in the multimodality treatment.

**Terminology**

Cholangiocarcinoma: an adenocarcinoma of the bile duct system. This may include the bile duct outside of the liver (perihilar) or the smaller bile ducts within the liver (intrahepatic). Adjuvant chemotherapy: chemotherapy given after surgical resection.

**Peer review**

The authors investigated surgical and medical outcomes for patients with cholangiocarcinoma using a population-based cancer registry. They demonstrated that surgical resection is a critically important modality of treatment for this disease.

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