Factors associated with resectable and unresectable biliary tract cancer using claims and electronic health records

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Objective

- To identify the factors associated with a diagnosis of either resectable or unresectable biliary tract cancer (BTC) in adult patients

Conclusions

- Awareness of factors associated with resectable and unresectable BTC could help clinicians prioritize timely diagnostic investigations for improved long-term outcomes
- Primary tumor site (ampulla of Vater [AoV], gallbladder cancer [GBC], extrahepatic cholangiocarcinoma [eCCA]), primary biliary cholangitis, gallbladder stones, bile duct obstruction / biliary tract disease, and diabetes were associated with a diagnosis of resectable BTC
- These findings suggest that close monitoring with a primary care provider, along with timely outpatient evaluation, may improve the detection of cancers at earlier stages on an individual patient basis

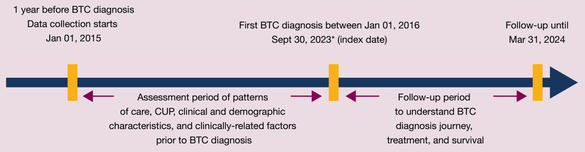
Introduction

- Prognosis of BTC remains poor due to advanced stage presentation and limited therapeutic options[1,2]
- The diverse clinical presentation of BTC, coupled with nonspecific symptoms, is associated with incorrect or delayed diagnosis, limiting timely identification[1,3]
- The aim of this analysis was to delineate distinguishing factors of resectable versus unresectable BTC to inform earlier diagnosis

Methods

- This retrospective, observational study analyzed linked claims and electronic health records data in the US from de-identified Optum® Market Clarity data (Optum® Market Clarity) to identify adult patients diagnosed with resectable or unresectable BTC from January 2016 to September 2023
- Baseline demographics and clinical characteristics were retrieved
- Logistic regression and XGBoost modeling were used to identify factors associated with resectable and unresectable BTC at diagnosis
- Logistic regression incorporated a step-wise approach
- XGBoost is a binary logistic regression model
  - XGBoost model performance was evaluated using receiver operating characteristic area under the curve (AUC)
  - Minority oversampling using SMOTE-NC was used to handle class imbalance in XGBoost model training

Figure 1. Study design



*International Classification of Diseases 10th Revision implementation in 2016. The baseline period was defined as continuous enrollment for 180 days pre-index date.
BTC, biliary tract cancer; CUP, cancer of unknown primary.

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Disclosures

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Results and interpretation

Patient demographics and clinical characteristics (Table 1)

- A total of 4448 patients with BTC were included in this analysis, of which 641 had resectable BTC and 3807 had unresectable BTC
- Median age at diagnosis was 68 years for both resectable and unresectable BTC
- Most patients were female (51.8%) and White (77.2%), with similar proportions in resectable versus unresectable BTC
- A smaller proportion of patients had intrahepatic cholangiocarcinoma (iCCA) among patients with resectable BTC (27.0%) compared with those with unresectable BTC (43.6%)
- AoV and gallbladder cancer (GBC) were more common in those patients with resectable versus unresectable BTC (AoV: 17.0% vs 9.0%; GBC: 28.6% vs 17.0%)

Table 1. Patient demographics and clinical characteristics

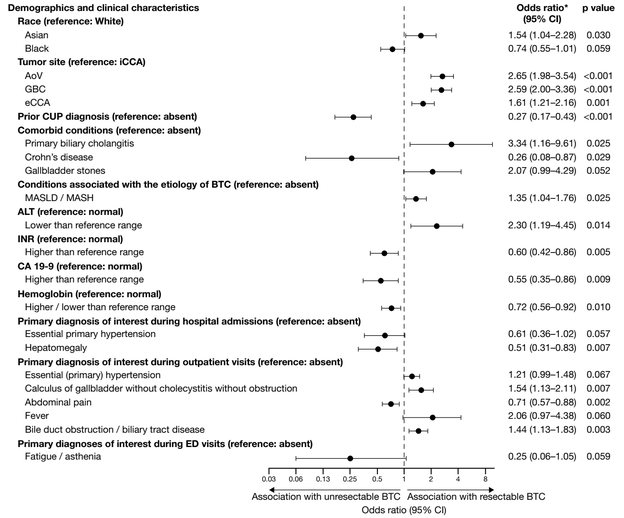
	Patients with resectable BTC (n=641)	Patients with unresectable BTC (n=3807)	Total (N=4448)
Age, years, median (Q1–Q3)	68 (60–76)	68 (60–76)	68 (60–76)
Female, n (%)	331 (51.6)	1971 (51.8)	2302 (51.8)
Race, n (%)			
White	490 (76.4)	2943 (77.3)	3433 (77.2)
Black	58 (9.1)	440 (11.6)	498 (11.2)
Asian	39 (6.1)	152 (4.0)	191 (4.3)
Other / unknown	54 (8.4)	272 (7.1)	326 (7.3)
Site of primary tumor recorded at the earliest BTC diagnosis, n (%)			
iCCA	173 (27.0)	1661 (43.6)	1834 (41.2)
GBC	183 (28.6)	648 (17.0)	831 (18.7)
eCCA	91 (14.2)	471 (12.4)	562 (12.6)
AoV	109 (17.0)	341 (9.0)	450 (10.1)
Other BTC*	85 (13.3)	686 (18.0)	771 (17.3)
Payor close to index, n (%)			
Medicare	337 (52.6)	2030 (53.3)	2367 (53.2)
Commercial	226 (35.3)	1274 (33.5)	1500 (33.7)
Medicaid	37 (5.8)	289 (7.6)	326 (7.3)
Other payor†	34 (5.3)	184 (4.8)	218 (4.9)
Unknown payor	7 (1.1)	30 (0.8)	37 (0.8)
CCI,‡ median (Q1–Q3)	1 (0–3)	2 (0–3)	2 (0–3)
Primary biliary cholangitis, n (%)	6 (0.9)	11 (0.3)	17 (0.4)
Conditions associated with the etiology of BTC observed during baseline (not mutually exclusive), n (%)			
MASLD / MASH	88 (13.7)	392 (10.3)	480 (10.8)
Alcohol-associated liver disease	5 (0.8)	86 (2.3)	91 (2.1)
Signs and symptoms of, and procedures related to, BTC during baseline (not mutually exclusive), n (%)			
Biliary obstruction	176 (27.5)	924 (24.3)	1100 (24.7)
Insertion or exchange of biliary stent	109 (17.0)	487 (12.8)	596 (13.4)
Jaundice	162 (25.3)	890 (23.4)	1052 (23.7)
CUP diagnosis during baseline, n (%)	20 (3.1)	524 (13.8)	544 (12.2)

*Other BTC includes patients with primary tumor at multiple sites and International Classification of Diseases 10th Revision diagnosis codes of C24.8 (Malignant neoplasm of overlapping sites of biliary tract) or C24.9 (Malignant neoplasm of biliary tract, unspecified). †Other payor includes commercial plus Medicare and commercial plus Medicaid. ‡The CCI score includes myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease (stroke / transient ischemic attack), dementia, chronic pulmonary disease, connective tissue / rheumatic disease, peptic ulcer disease, mild to severe liver disease, diabetes (with and without chronic complications), hemiplegia or paraplegia, chronic kidney disease, any solid tumor, leukemia, lymphoma, metastatic solid tumor, and AIDS / HIV.
AoV, ampulla of Vater; BTC, biliary tract cancer; CCI, Charlson Comorbidity Index; CUP, cancer of unknown primary; eCCA, extrahepatic cholangiocarcinoma; GBC, gallbladder cancer; iCCA, intrahepatic cholangiocarcinoma; MASLD / MASH, metabolic dysfunction-associated steatotic liver disease / metabolic dysfunction associated steatohepatitis; Q, quartile.

Factors associated with diagnosis of resectable or unresectable BTC by multivariable logistic regression (Figure 2)

- Resectable BTC at diagnosis was associated with primary tumor site (AoV, GBC, eCCA), primary biliary cholangitis, metabolic dysfunction-associated steatotic liver disease (MASLD) / metabolic dysfunction-associated steatohepatitis (MASH), and outpatient visits for gallbladder stones or bile duct obstruction / biliary tract disease
- Unresectable BTC at diagnosis was associated with prior cancer of unknown primary, Crohn's disease, inpatient visits for hepatomegaly, and outpatient visits for abdominal pain

Figure 2. Characteristics associated with resectable or unresectable BTC diagnosis

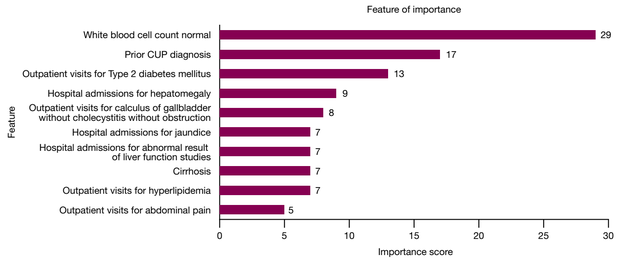


*Odds ratio >1 favors resectable BTC; odds ratio <1 favors unresectable BTC.
ALT, alanine aminotransferase; AoV, ampulla of Vater; CUP, cancer of unknown primary; eCCA, extrahepatic cholangiocarcinoma; ED, emergency department; GBC, gallbladder cancer; iCCA, intrahepatic cholangiocarcinoma; INR, international normalized ratio; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease.

XGBoost modeling (Figure 3)

- The XGBoost binary classification algorithm identified several of the same factors as multivariable logistic regression and thus supported the results of the multivariable logistic regression model
- Additionally, normal white blood cell count, diabetes, jaundice, abnormal results of liver function studies, cirrhosis, and hyperlipidemia were found to be important features that distinguished between unresectable and resectable BTC in the XGBoost model
- Discrimination between resectable and unresectable BTC at diagnosis was achieved, yielding an AUC of 71.7% (95% CI, 70.2–73.4%)

Figure 3. Feature importance ranking with XGBoost: predictors that distinguish between resectable versus unresectable BTC



Feature importance indicates which information the model relied on most to distinguish resectable from unresectable BTC.
BTC, biliary tract cancer; CUP, cancer of unknown primary.

Plain language summary

Background: Why did we perform this research?

- Biliary tract cancers (BTCs) are types of cancer found in the bile ducts or gallbladder and are often diagnosed at advanced stages, when it is too late to offer curative therapy
- People with BTC often have varying symptoms and disease characteristics, which can lead to incorrect diagnosis or delayed detection of BTC
- Resectable BTC is a type of BTC that can be removed via surgery; unresectable BTC cannot be removed by surgery
- The aim of this study was to identify the factors associated with resectable BTC versus those associated with unresectable BTC, to help facilitate earlier diagnosis

Methods: How did we perform this research?

- We used data from the Optum® Market Clarity database to find adult patients in the US who had been diagnosed with resectable or unresectable BTC between 2016 and 2023
- We used statistical modeling and machine learning to identify characteristics associated with the diagnosis of resectable or unresectable BTC in these patients

Results: What were the findings of this research?

- Of all patients with BTC included in this analysis, most had unresectable BTC (3807 patients with unresectable BTC vs 641 patients with resectable BTC)
- We found several characteristics common to people diagnosed with resectable BTC, including cancer that originated in the gallbladder or in the bile ducts outside the liver, inflammation of the bile ducts, metabolic liver diseases, and doctor visits for bile duct disease or gallstones
- Characteristics that were associated with unresectable BTC included cancer that originated in the bile ducts inside the liver, cancer of an unknown origin, Crohn's disease, hospital visits for an enlarged liver (hepatomegaly), and doctor visits for abdominal pain
- In addition, normal white blood cell count, diabetes, jaundice, abnormal results of liver function studies, cirrhosis, and high cholesterol were characteristics that distinguished between resectable and unresectable BTC

Conclusions: What are the implications of this research?

- Close and frequent monitoring by a doctor may improve the detection of cancers at earlier stages for individual patients

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Poster

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