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Unchanged mortality in patients with acute cholangitis despite an increase in malignant etiologies – A 25-year epidemiological study

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Unchanged mortality in patients with acute cholangitis despite an increase in malignant etiologies – A 25-year epidemiological study

Background and Aims: Acute cholangitis (AC) is a rare but serious condition, with an incidence of 7.0 per 10,000 people and mortality rates up to 10%. The aim of this study was to describe changes in obstruction etiology, comorbidities, clinical factors, and mortality among AC patients during a 25-year period.

Methods: Using a database of 11,563 consecutive ERCP-procedures performed from 1990-2015 at Odense University Hospital, we identified all AC cases during that period. Clinical and epidemiological data were collected from the database and the Danish Patient Registry. Association with 30-day mortality was investigated using multiple logistic regression analysis with adjustment for confounding factors.

Results: In total, 775 consecutive and individual cases of AC were included. Among cases, 42% (n = 326) were of malignant etiology, with an increasing incidence over time (regression coefficient [95% CI]: 0.03 [0.01-0.04] per year; p = 0.01). Mean Charlson Comorbidity Index was 1.4, with an increase over time (regression coefficient [95% CI]: 0.04 [0.03-0.05] per year; p<0.01). Malignant obstruction etiology was associated with 30-day mortality (OR [95% CI]: 1.11 [1.04-1.18]; p<0.01). Overall 30-day mortality was 12% (n = 91). After adjustment for confounding factors, no significant changes in 30-day mortality were observed over time (OR [95% CI]: 1 [1-1.00]; p = 0.91 per year).

Conclusion: Significant increases in the incidence of malignant obstruction etiology and severity of comorbidities among AC patients were observed during the study period. Despite those findings, 30-day mortality remained unchanged, potentially reflecting a general improvement in the management of AC.

Keywords: Acute cholangitis (MeSH term); Epidemiology (MeSH term); ERCP (MeSH term); Etiology (MeSH term); Mortality (MeSH term)

Introduction

Acute cholangitis (AC) is a rare but serious condition of bacterial infection in the bile duct. It is associated with high mortality rates of up to 10% despite proper treatment (1, 2), and above 50% without (3, 4). While early ERCP drainage has proven to be the cornerstone in AC treatment regimes (2, 5-9), epidemiological information on clinical presentation, comorbidities and obstruction etiology can be of useful value, as these factors are all shown to have an impact on the outcome in AC patients (2, 5-11).

Given the great diversity in the presentation of AC patients – the trends in obstruction etiologies and other comorbidities should be taken into account when reviewing management guidelines for AC (11-16). A comprehensive study, analyzing eventual changes in disease etiologies and presentation of comorbidities, along with corresponding mortality rates in AC patients would be of great value to provide proper clarification on the effectiveness of AC treatment regimens – both from a historical and current perspective. Unfortunately, epidemiological studies describing these factors in larger populations of AC patients are limited, and no studies have been conducted following their trends and incidence over a longer period of time.

Despite an increasing number of studies that focus on the optimization of AC management strategies, basic epidemiological studies of AC populations are difficult to perform as AC is a relatively rare condition, with an incidence of just 7.0 per 100,000 people (17). Using a large collection of dataset on consecutive ERCP procedures performed at our department over a 25-year period, it was our aim to describe the trends in AC etiologies, comorbidities and other clinical characteristics of AC patients over time.

Methods

Study setting:

This study was conducted as a registry study, at the Department of Medical Gastroenterology S, Odense University Hospital (OUH) – a 1,000 bed hospital and tertiary referral center, with more than 600 ERCP procedures performed annually. Data were collected and stored with the approval and consent from the Danish patient safety agency and the Danish data protection agency.

Study population:

Through an internal ERCP-database, we identified all consecutive AC patients that underwent ERCP at OUH during a period from January 1st 1990 – October 31st 2015. The database contains records of 11,563 consecutive ERCP-procedures performed during the study period, including data on basic patient characteristics, clinical presentation and endoscopic procedures. All patients that received an AC diagnosis – given prospectively, by a highly experienced endoscopist during ERCP, were identified and included in the study. In AC patients receiving multiple ERCP procedures, only the first procedure was included in our analyses. Management procedures were the same for all AC patients – regardless of their obstruction etiology and grade of comorbidities.

Data collection and management:

Information on therapeutic procedures performed during ERCP, and clinical characteristics of the AC patients – including laboratory values, body temperature and AC etiology, were extracted from the ERCP-database. Diagnosis codes for comorbidities (ICD-8/ICD-10), present in each patient at the time of ERCP, were obtained from the Danish Patient Registry (DPR). Additionally, the date of ERCP for

each patient was extracted from the ERCP-database, and the eventual time of death was obtained from the Danish Civil Registration System (CRS).

Collected information on procedures performed during ERCP included the performance of stone extraction procedures and endoprosthesis insertions. AC etiology was determined by the findings during ERCP and categorized into benign and malignant obstruction etiologies – including common bile duct stone, primary sclerosing cholangitis (PSC), pancreatitis, bile duct cancer (cholangiocarcinoma), pancreatic cancer and liver cancer. Diagnostic codes (in ICD-8, from 1990-1993; and ICD-10, from 1994-2015) for all comorbidities in the Charlson Comorbidity Index (CCI) present at the time of ERCP were extracted from the Danish National Patient Registry (DNPR) for each AC patient. Diagnostic codes for comorbidities in AC patients were applied into the following 17 disease groups – in concordance to CCI: acute myocardial infarction, cancer, cerebral vascular accident, congestive heart failure, connective tissue disorder, dementia, diabetes, diabetes complications, HIV, liver disease, metastatic cancer, paraplegia, peptic ulcer, peripheral vascular disease, pulmonary disease, renal disease, and severe liver disease.

Determination of benign and malignant obstruction etiologies:

AC etiology was determined during ERCP and categorized into either benign or malignant obstruction etiology. Benign obstruction etiology included: common bile duct stone, PSC, pancreatitis, and other benign strictures. Malignant obstruction etiology included: bile duct cancer, pancreatic cancer, liver cancer, and other malignant strictures. Diagnosis of obstruction etiology was performed by an experienced endoscopist based on endoscopic findings and other available clinical information at the time of ERCP (e.g. patient records, radiology findings, and previously biopsy-verified biliary obstructions). In the event of uncertain diagnosis during endoscopy, a brush

and/or forceps biopsy was taken – although the registered obstruction etiologies in our ERCP-database were solely based on information, available at the time of ERCP.

To verify the diagnoses given by the endoscopist during ERCP, each benign and malignant etiology diagnosis from the ERCP-database was matched with diagnostic codes (ICD-8/10) for the most common malignancies associated with biliary obstruction (including: bile duct cancer, gallbladder cancer, pancreatic cancer, liver cancer, colorectal cancer, and malignant neoplasm in ill-defined digestive organs) – assigned to each AC patient, within a period of 2 years before and after the date of ERCP. Any inconsistency between a given benign/malignant obstruction etiology diagnosis in our ERCP-database and ICD-8/10 codes was defined as an incorrect diagnosis by the endoscopist. A Chi-square test was performed to test for potential changes in the proportion of falsely diagnosed benign and malignant obstruction etiologies, respectively, over time.

Statistical analysis:

Proportions of AC patients receiving various clinical procedures or displaying different clinical characteristics were calculated for the whole period, with trend of change over time (continuous variable, years) assessed by fitting a logistic regression model. For continuous clinical variables, the linear regression model was fitted with time as covariate. The Box-Cox transformation was applied if the variable had a skewed distribution. Comorbidities of AC patients were estimated over the whole period. Trend of change in comorbidity over time was analyzed using a logistic regression model with time in 1-year intervals.

The association of each patient variable with 30-day mortality was assessed by fitting logistic regression models that regress 30-day mortality on each variable, with a null hypothesis that the estimated coefficient in the model was not different from zero.

Change in 30-day mortality after ERCP over time was assessed by fitting a multiple logistic regression model regressing the logit of 30-day mortality on time (continuous variable, years) adjusting for all collected patient data as candidate variables in a stepwise regression approach using backward elimination. The order of elimination was based on clinical importance and p-value. Significance of each variable was tested using the Wald test. The p-value cut-off for exclusion of candidate variables during the stepwise regression analysis was 0.1. The goodness of fit was evaluated using the Hosmer-Lemeshow test.

Candidate variables were: gender (categorical variable, male/female), age (continuous variable, years), body temperature (continuous variable, degrees Celsius), Charlson Comorbidity Index (CCI) (continuous variable), P-Alkaline phosphatase (continuous variable, U/L), P-Bilirubin (continuous variable, µmol/L), and malignant AC etiology (categorical variable, yes/no). The appropriateness of the underlying assumptions (collinearity, linearity of independent variables and log odds) was examined statistically.

All statistical analyses were done using the free R package (https://www.r-project.org/).

Results

Baseline characteristics:

In total, 11,563 consecutive ERCP procedures were performed at the Department of Medical Gastroenterology S, OUH, from January 1st 1990 – October 31st 2015. Among

these, 948 cases were prospectively diagnosed with AC during ERCP. When excluding repeat ERCP procedures in the same patients, a total of 775 individual AC patients were identified and included. Among the included AC patients, 47% (n = 361) were male. Changes in gender composition over time were significant with an increasing incidence of male AC patients (regression coefficient [95% CI]: 0.03 [0.01-0.05] per year; p <0.01). Median age of the AC patients was 72 years, with no significant changes in age over time (p = 0.16). The median body temperature among AC patients was 37.1 °C, and median P-Bilirubin was 92 μmol/L [reference range: 5-25 μmol/L]. Baseline characteristics are summarized in **Table 1**.

Comorbidities and Charlson Comorbidity Index:

Diagnosis codes for diseases were classified into one of the 17 disease groups – in concordance to Charlson Comorbidity Index. Among all comorbidity groups, cancer was the most frequent – being present in 53% (n = 409) of all patients. Significant changes in incidences of comorbidities over time included an increased incidence of: metastatic cancers (regression coefficient [95% CI]: 0.04 [0.01-0.07] per year; p <0.01), liver disease (regression coefficient [95% CI]: 0.08 [0.03-0.13] per year; p <0.01), severe liver disease (regression coefficient [95% CI]: 0.09 [0.01-0.16] per year; p = 0.02), and renal disease (regression coefficient [95% CI]: 0.05 [0.00-0.09] per year; p = 0.04), while a decrease in incidence was observed for dementia (regression coefficient [95% CI]: -0.10 [-0.19 to -0.02] per year; p = 0.01).

The mean value for CCI was 1.4, with an increase over time (regression coefficient [95% CI]: 0.04 [0.03-0.05] per year; p <0.01). CCI was higher in male patients (OR [95% CI]: 1.47 [1.20-1.79]; p <0.01). Comorbidities are presented in **Table 1**.

Etiology of obstruction:

The most frequent obstruction etiology among patients was common bile duct stone – accounting for 50% (n = 390) of all AC cases, followed by pancreatic cancer – accounting for 24% (n = 187). Overall, 42% (n = 326) of all AC cases had a malignant obstruction etiology. Malignant obstruction etiologies included: pancreatic cancer (24%, n = 187), bile duct cancer (16%, n = 124), liver cancer (2%, n = 13), and other malignant strictures (1%, n = 10), while benign obstruction etiologies included: common bile duct stone (50%, n = 390), pancreatitis (6%, n = 47), primary sclerosing cholangitis (PSC) (2%, n = 14), and other benign strictures (3%, n = 26). The incidence of PSC has increased over time (regression coefficient [95% CI]: 0.12 [0.04-0.2] per year period; p = 0.01), while the incidence of common bile duct stone has decreased (regression coefficient [95% CI]: -0.04 [-0.06 to -0.02] per year, p <0.01). The overall incidence of cases with malignant obstruction etiology has increased over time (regression coefficient [95% CI]: 0.03 [0.01-0.04] per year; p = 0.01). An overview of obstruction etiologies among AC patients is presented in **Table 2**. Incidence rates of obstruction etiologies and corresponding 30-day mortality over time (from 1990-2015), are illustrated in **Figure 1**. Following analysis for correlation between diagnoses given by the endoscopist and ICD-8/10 codes, there were no differences in the proportion of falsely diagnosed benign (p = 0.18) and malignant obstruction etiologies (p = 0.44) over time.

When adjusting for gender, the incidence of common bile duct stone was lower in men (OR [95% CI]: 0.69 [0.52-0.92]; p = 0.01), while the incidence of pancreatic cancer was higher in male patients (OR [95% CI]: 1.45 [1.04-2.03]; p = 0.03). No difference in the overall incidence of benign and malignant AC etiology was observed when adjusting for gender (p >0.05).

ERCP characteristics:

During the study period, a total of 775 patients with AC underwent ERCP. The most common endoscopic intervention was endoprosthesis insertion – being performed in 59% (n = 457) of all AC patients, followed by stone extraction and endoprosthesis removal – being performed in 36% (n = 278) and 35% (n = 274) of AC patients, respectively. Endoscopic sphincterotomy was performed in 48% (n = 374) of all patients. Changes in endoscopic procedures performed on AC patients during the 25-year period included a decreasing frequency of stone extractions (regression coefficient [95% CI]: -0.03 [-0.05 to -0.01] per year; $p < 0.01$), and an increasing frequency of endoprosthesis insertions (regression coefficient [95% CI]: 0.04 [0.02-0.05] per year; $p < 0.01$), as well as endoprosthesis removals (regression coefficient [95% CI]: 0.04 [0.02-0.06] per year; $p < 0.01$), respectively. ERCP characteristics are presented in **Table 3**.

30-day mortality and risk factors:

30-day mortality was defined as death occurring in a patient within 30 days from the date of ERCP. Overall 30-day mortality was 12% (n = 91). After adjustment for confounding factors, malignant obstruction etiology (OR [95% CI]: 1.11 [1.04-1.18]; $p <0.01$) and P-Bilirubin (OR [95% CI]: 1.00 [1.00-1.00]; $p <0.01$) were associated with increased 30-day mortality. Time, age and CCI were not associated with increased mortality ($p > 0.1$ for all variables).

A presentation of ’30-day mortality among groups’ is available in **Table 4A**; an overview of ‘Risk factors on 30-day mortality’ is presented in **Table 4B**.

Discussion

Our data indicate that despite an overall increase in malignant obstruction etiologies, and an increase in the severity of comorbidities among AC patients during the study period ($p < 0.01$ for both factors) – 30-day mortality rates remained stable over time ($p = 0.91$). As malignant obstruction etiology is associated with increased 30-day mortality (OR [95% CI]: 1.11 [1.04-1.18]; $p < 0.01$), our results could imply a general improvement in the management of AC patients over time. The present study is the first of its kind, to assess changing patterns of obstruction etiologies, comorbidities and patient characteristics in a large AC population over a longer period of time.

Among a selected few studies with larger AC populations, a German study of 810 AC patients found a malignant cause of obstruction in 51.9% (n = 509) of all cases, with bile duct cancer being the most common malignancy, presented in 21.0% (n = 206) of patients (11). These results correspond with findings from the present study – showing malignant obstruction etiology to be responsible for 42% (n = 326) of all AC cases, with the most frequent malignancies being pancreatic cancer (24%, n = 187), and bile duct cancer (16%, n = 124). Demographical data were also similar in the two studies – with the median age of AC patients being 68 years (compared to 72 years in the present study), and male patients accounting for 56% of all cases (compared to 47% in the present study). Mean age of AC patients in the United States was shown to be 67 years (compared to 70 years in the present study) in a national sample of 23,661 AC patients (18). An Asian study of 6,433 AC cases found malignant obstruction etiology to be present in just 17% (n = 1,035; of 6,072 cases with known etiology) vs. 42% (n = 326) in the present study (15). Conversely, CCI scores were higher amongst patients in that study – with mean CCI score being above 4.5 (mean range between: 4.6-5.8 in different sub-groups), compared to a mean CCI of 1.4 in the present study. These

differences could indicate an epidemiological variation from Western to Asian populations of AC patients.

In general, descriptive data on AC patients do vary in AC populations amongst different studies – with median ages of AC cohorts ranging from 54-71 years, and reported mean CCI scores varying from 1-5; and while benign disease etiology remained the most common cause of AC among studies, the rates of 'common bile duct stone' – the most frequent single cause of obstruction, ranged from between 38.9-72.4% (2, 5, 7-10, 12). Although the variations in reported data among AC studies could be attributed to the use of smaller patient cohorts – they could also reflect actual differences in patient demographics, presentation of comorbidities, and obstruction etiology among AC patients on a geographical scale.

The present study observed an overall increase in malignant obstruction etiology over time in AC patients (regression coefficient [95% CI]: 0.03 [0.01-0.04] per year; $p = 0.01$). The increasing incidence of malignant obstructions etiologies is reflected by an increasing frequency of performed endoprosthesis insertions (regression coefficient [95% CI]: 0.04 [0.02-0.05] per year; $p < 0.01$) and endoprosthesis removals (regression coefficient [95% CI]: 0.04 [0.02-0.06] per year; $p < 0.01$). While epidemiological data on the trends of obstruction etiology in AC are not available from other studies, an overall increase in the incidence of pancreatic cancer in the past decades was reported in Danish, American and other Western populations (19-24). Likewise, an increasing overall incidence in bile duct cancer was observed in Western populations, including in the United States (25-27). In addition to a rise in malignant obstruction etiology, the amount of comorbidities among AC patients was also shown to have increased over time (as reflected by an increase in CCI score). An increasing proportion of male AC patients (regression coefficient [95% CI]: 0.03 [0.01-0.05] per year; $p <0.01$) had a

further impact on the overall morbidity in our population – as male gender was associated with increased CCI score (OR [95% CI]: 1.47 [1.20-1.79]; p <0.01). The reported epidemiological trends in our study are suggestive of a shift towards an increasing morbidity among AC patients – as both malignant obstruction etiology and increasing CCI score are associated with increased mortality and complication rates (8, 11, 28, 29).

Despite the increasing incidence in malignant obstruction etiology and a rise in comorbidities among AC patients, our study did not report an increase in 30-day mortality over time (OR [95% CI]: 1 [1-1.00]; p = 0.91). The absence of an increase in mortality – despite malignant obstruction etiology being associated with increased 30-day mortality (OR [95% CI]: 1.11 [1.04-1.18], p <0.01), is remarkable, and could be attributed to various factors. Firstly, overall long-term survival among patients with malignancies, as well as chronic comorbidities could have improved over time due to improved medical and health care options, as depicted by a reported increase in one- and five-year survivals in Danish patients with liver, bile duct and pancreatic cancers between 1980-2012 (21). Another potential cause for the unchanged mortality could be the optimization of interventional procedures in the treatment regimens of AC. Previous studies have found early ERCP to be associated with improved survival in AC patients – and thus, better timing of ERCP in high risk patients, along with improved procedural techniques and medical management of AC patients could explain a non-increasing mortality rate amongst our study population (5-7, 10, 30). Correlation between diagnoses given by the endoscopist with ICD-8/10 codes was 92% – indicating a high accuracy in the determination of benign and malignant obstruction etiologies by our endoscopists. The increasing incidence of malignant obstruction etiologies could not be explained by advances in diagnostic modalities to detect malignancies – as the

proportion of falsely diagnosed benign obstruction etiologies remained unchanged over time.

The main limitations of this study include its retrospective design, and a reliance on the data quality of various databases. Another limitation is the unavailability of precise time indication (i.e. exact hours and minutes) for the time of admission and time of ERCP, for the majority of patients during the study period – meaning we were not able to adjust for 'timing of ERCP' in our analyses. On the other hand, data quality from the Danish National Patient Registry (DNPR) is reported to be very accurate (31). Data from our own ERCP-database are prospectively registered by experienced endoscopists from our department, and contains information on all consecutive patients receiving ERCP at our department for the past 25 years – thus providing a major point of strength in our study. The large number of consecutive AC patients included in this study is another key factor to its strength and applicability. The centralized function of our institution being the largest tertiary referral center in the Region of Southern Denmark meant that the majority of AC patients requiring ERCP in the region were admitted to our department for endoscopic intervention – including transferred patients from other institutions after failed endoscopy attempts and/or lack of clinical improvement in multi-morbid patients. Thus, patients admitted to our department for ERCP are expected to be representative for the actual population of AC patients in our region.

In conclusion we found significant increases in the incidence of malignant obstruction etiology and severity of comorbidities during a 25-year period – indicating an increasing morbidity among AC patients. Despite those findings 30-day mortality rates remained unchanged, potentially reflecting a general improvement in the management of AC.

Funding

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Tables

Table 1 – Baseline characteristics:

	All patients (n = 775)	Regression coefficient [95% CI], Time (per year)	p-value
Patient characteristics:			
Male gender, n (%)	361 (47%)	0.03 [0.01-0.05]	<0.01
Age, years, Median	72 ± 9	-0.1 [-0.23-0.04]	0.16
Body temperature, Degrees Celsius, Median	37.1 ± 0.5	0.02 [-0.02-0.06]	0.29
Laboratory values:			
Alkaline Phosphatase, U/L, Median	359 ± 172	8.85 [5.27-12.42]	<0.01
Bilirubin, µmol/L, Median	92 ± 57	-0.61 [-1.7-0.47]	0.26
Comorbidities:			
Charlson Comorbidity Index, Mean	1.4 ± 1.4	0.04 [0.03-0.05]	<0.01
Disease groups:			
Acute myocardial infarction	65 (8%)	-0.02 [-0.05-0.02]	0.34

Cancer	409 (53%)	0.01 [0.00-0.03]	0.15
Cerebral vascular accident	105 (14%)	-0.01 [-0.04-0.01]	0.30
Congestive heart failure	100 (13%)	-0.02 [-0.04-0.01]	0.21
Connective tissue disorder	13 (2%)	-0.02 [-0.09-0.05]	0.55
Dementia	15 (2%)	-0.10 [-0.19 to -0.02]	0.01
Diabetes	176 (23%)	0.01 [-0.01-0.04]	0.21
Diabetes complications	29 (4%)	0.03 [-0.02-0.07]	0.26
HIV	1 (<1%)	3.08 [-2.99-9.15]	0.32
Liver disease	32 (4%)	0.08 [0.03-0.13]	<0.01
Metastatic cancer	87 (11%)	0.04 [0.01-0.07]	<0.01
Paraplegia	2 (<1%)	-0.17 [-0.46-0.12]	0.25
Peptic ulcer	87 (11%)	-0.02 [-0.05-0.01]	0.22
Peripheral vascular disease	27 (3%)	-0.01 [-0.05-0.04]	0.84
Pulmonary disease	86 (11%)	0.02 [-0.01-0.05]	0.16
Renal disease	31 (4%)	0.05 [0.00-0.09]	0.04
Severe liver disease	14 (2%)	0.09 [0.01-0.16]	0.02

Data are presented in number of patients n (%) unless otherwise stated.

Median and mean values are presented in median (SD) or mean (SD).

CI: Confidence interval.

Table 2 – Etiology of obstruction:

	All patients (n = 775)	Regression coefficient [95% CI], Time (per year)	p-value
Benign etiology:			
Common bile duct stone	390 (50%)	-0.04 [-0.06 to -0.02]	<0.01
Primary sclerosing cholangitis	14 (2%)	0.12 [0.04-0.2]	0.01
Pancreatitis	47 (6%)	-0.01 [-0.05-0.03]	0.57
Other benign stricture	26 (3%)	0.05 [0.00-0.1]	0.06
Total cases with benign etiology	449 (58%)	-0.03 [-0.04 to -0.01]	0.01
Malignant etiology:			

Pancreatic cancer	187 (24%)	0.01 [-0.01-0.03]	0.4
Bile duct cancer	124 (16%)	0.01 [-0.02-0.03]	0.53
Liver cancer	13 (2%)	0.02 [-0.05-0.09]	0.53
Other malignant stricture	10 (1%)	0.27 [0.1-0.45]	<0.01
Total cases with malignant etiology	326 (42%)	0.03 [0.01-0.04]	0.01

Data are presented in number of patients n (%) unless otherwise stated.

CI: Confidence interval.

Table 3 – ERCP characteristics:

	All patients (n = 775)	Regression coefficient [95% CI], Time (per year)	p-value
Procedures during ERCP:			
Visualization of common bile duct	758 (98%)	-0.02 [-0.08-0.04]	0.48
Visualization of pancreatic duct	217 (28%)	-0.06 [-0.08 to -0.04]	<0.01
Endoscopic sphincterotomy	374 (48%)	-0.03 [-0.05 to -0.02]	<0.01
Stone extraction	278 (36%)	-0.03 [-0.05 to -0.01]	0.01
Endoprosthesis insertion	457 (59%)	0.04 [0.02-0.05]	<0.01
Endoprosthesis removal	274 (35%)	0.04 [0.02-0.06]	<0.01
Findings during ERCP (non-etiology related)			
Dilated bile ducts	676 (87%)	-0.04 [-0.07 to -0.01]	<0.01
Pancreatic cyst	5 (1%)	-0.09 [-0.22-0.05]	0.2
Duodenal diverticulum	109 (14%)	-0.05 [-0.08 to -0.03]	<0.01

Data are presented in number of patients n (%) unless otherwise stated.

CI: Confidence interval.

Table 4A – 30-mortality among groups:

	All patients (n = 775)	Malignant obstruction etiology	Benign obstruction etiology (n = 449)	p-value

		(n = 326)		
30-day mortality	91 (12%)	60 (18%)	31 (7%)	<0.01

Data are presented in number of patients n (%).

Table 4B – Risk factors on 30-day mortality:

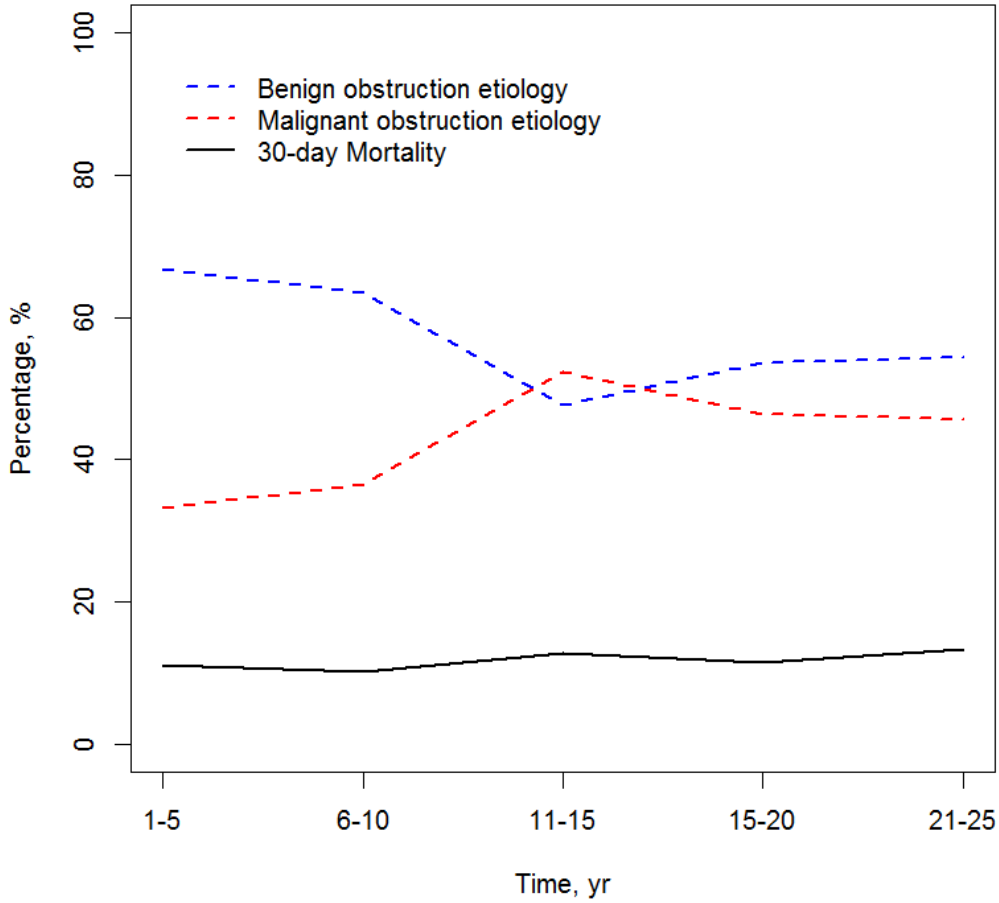
	Univariate, OR [95% CI]	Multivariate, OR [95% CI]	Multivariate, p-value
Patient characteristics:			
Male gender	0.98 [0.92-1.05]	-	-
Age, years	1.00 [1-1.00]	-	-
CCI	1.03 [1.01-1.06]	-	-
Body temperature, Degrees Celsius	1 [0.99-1.01]	-	-
Laboratory values:			
Alkaline Phosphatase, U/L	1.00 [1-1.00]	-	-
Bilirubin, µmol/L	1.00 [1.00-1.00]	1.00 [1.00-1.00]	<0.01
Obstruction etiology:			
Malignant obstruction etiology	1.13 [1.06-1.2]	1.11 [1.04-1.18]	<0.01
Time period:			
Time, years	1.00 [1-1.01]	1 [1-1.00]	0.91

OR: Odds ratio; CI: Confidence interval.

Cells marked with '-' indicate the variable was eliminated during stepwise backwards elimination process (p>0.1).

Figures

Figure 1 – Incidence rates of benign and malignant obstruction etiology and 30-day mortality rates, during the 25-year period:



During a 25-year period (from 1990-2015) a significant increase in the incidence of malignant obstruction etiology was observed among AC patients ($p < 0.01$) – while 30-day mortality remained unchanged ($p = 0.91$).

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