

## RESEARCH COMMUNICATION

# Risk Factors for Post-ERCP Cholangitis in Patients with Pancreatic Cancer from a Single Referral Center in Iran

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### Abstract

Cholangitis is relatively uncommon but associated mortality is high due to the predisposition in people with underlying disease. For this recognition of contributing risk factors is necessary. Therefore, the present descriptive-analytical cross-sectional survey was designed to determine contributing risk factors for post-ERCP cholangitis in patients with pancreatic cancer. From 2005 to 2010, 110 consecutive cases of pancreatic cancer attending to a tertiary referral centre (Taleghani Hospital), Tehran, Iran were recruited. The patients all underwent stenting via endoscopic retrograde cholangiopancreatography (ERCP). On univariate analysis, a metallic stent type (95% confidence interval (CI) 1.025-11.34,  $P=0.037$ ), having no jaundice (1.44-2.22,  $P=0.009$ ), having no pain (1.32-1.91,  $P=0.026$ ), a history of prior ERCP (1.16-10.37,  $P=0.020$ ), and having a proximal biliary stone (1.002-5.93,  $P=0.046$ ) were related to cholangitis. However on multivariate analysis, none of these factors were found to be contributing risk factors. Cholangitis is avoidable with adequate biliary drainage. Because success rates are higher and complication rates lower for endoscopists performing large volumes of ERCP, performance of the procedure should be concentrated as much as possible in institutions with endoscopists having adequate experience. Patients with a high risk for complications may be best served by referral to an advanced center.

**Keywords:** Therapeutic-ERCP - cholangitis - risk factors - referral center - Iran

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### Introduction

Cholangitis is relatively uncommon (Boey & Way, 1980). Any condition that leads to stasis or obstruction of bile in the common bile duct (CBD), including benign or malignant stricture, parasitic infection, or extrinsic compression by the pancreas, can result in bacterial infection and cholangitis (Lam et al., 1978; Boey & Way, 1980). Choledocholithiasis is the most common cause of acute cholangitis, followed by endoscopic retrograde cholangiopancreatography [ERCP], and tumors. After ERCP 1-3% of patients develop cholangitis (O'Connor et al., 1982<sup>a</sup>; 1982<sup>b</sup>).

Obstruction of the bile duct by tumor or stones can facilitate bacterial colonization; subsequent instrumentation has resulted in bacteremia rates mean 18.0% (O'Connor et al., 1982<sup>a</sup>; 1982<sup>b</sup>; Gerecht et al., 1989). The highest bacteremia rates are seen in therapeutic ERCP (Gerecht et al., 1989). In purely diagnostic ERCP, the bacteremic rate is lower at 8% (O'Connor et al., 1982<sup>b</sup>; Gerecht et al., 1989). Partial obstruction is associated with a higher rate of infection than complete obstruction (Boey & Way, 1980; Lam et al., 1978). Risk of cholangitis is increased if dye is injected retrograde (Boey & Way, 1980).

Mortality of cholangitis is high due to the predisposition

in people with underlying disease. Historically, the mortality rate was 100% (Gigot et al., 1989; Palazzo et al., 1995; Kama et al., 1999). With the advent of endoscopic retrograde cholangiography, therapeutic endoscopic sphincterotomy, stone extraction, and biliary stenting, the mortality rate has significantly declined to approximately 5-10% (Palazzo et al., 1995; Kama et al., 1999). Nevertheless the prevention of post-ERCP cholangitis is crucial especially in patients with pancreatic cancer that may be result in a decreased burden of disease. For this recognition of contributing risk factors is necessary. Therefore, this study was designed to determine the contributing risk factors for post-ERCP cholangitis in patients with pancreatic cancer to program for reduction of disease by controlling and modifying the risk factors.

### Materials and Methods

This study was performed as a descriptive-analytical cross-sectional survey. From 2005 to 2010, 110 consecutive cases of pancreatic cancer attending to a tertiary referral centre (Taleghani Hospital), Tehran, Iran were recruited. These patients had an initial diagnosis of malignant biliary obstruction that the final diagnosis was pancreatic cancer according to radiology and clinical findings. The staging was performed according to CT Scan and EUS and the

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decision of inability to resection was made according to surgery and anesthesiology consultations. Then the patients underwent stenting via ERCP by metallic or plastic stents in a random manner.

The study was approved by medical ethics committee of Shahid-Beheshti University of Medical Sciences, Tehran, Iran. The inclusion criteria were having unresectable pancreatic cancer with a performance status of more than three on the Eastern Cooperative Oncology Group Scale. The patients candidate for surgical resection or any type of chemotherapy or radiation-therapy, those who had undergone laparotomy 30 days before the intervention or those in poor general condition were excluded.

Evaluated variables were age, gender, papilla nature, diverticulum, pancreatitis, cholangitis, stent type, jaundice, pain, fever, cholelithiasis, cholecystectomy, PSC, prior ERCP, sphincterectomy, anemia (hemoglobin less than 10 g/dl), BUN, bilirubin, albumin, location of biliary stones, common bile duct (CBD) diameter, AST, ALT, and amylase. The cholangitis diagnosis was made according to clinical and laboratory findings during 72 hours after ERCP. All the patients were received antibiotic prophylaxis before ERCP.

Data from 110 patients were analyzed using SPSS (version 13.0) software [Statistical Procedures for Social Sciences; Chicago, Illinois, USA]. Differences were tested by Exact Fisher test, Independent-Sample-T test, Chi-Square test, and Logistic Regression analysis and were considered statistically significant at P values less than 0.05.

**Results**

The mean age (±SD) was 51.4±11.4 years. Twenty seven patients (24.5%) were female and 83 subjects (75.5%) were male. In univariate analysis the metallic stent type (95% confidence interval 1.025-11.34, P=0.037), having no jaundice (95% confidence interval 1.44-2.22, P=0.009), having no pain (95% confidence interval 1.32-1.91, P=0.026), history of prior ERCP (95% confidence interval 1.16-10.37, P=0.020), and having proximal biliary stone (95% confidence interval 1.002-5.93, P=0.046) were related to cholangitis. However in multivariate analysis, none of these factors were contributing risk factors for

**Table 1. Contributing Factors for Cholangitis**

		Cholangitis			
		Positive		Negative	
		Count	Percent	Count	Percent
Stent Type:	Metallic	12	21.4%	44	78.6%
	Plastic	4	7.4%	50	92.6%
Jaundice:	Yes	11	11.3%	86	88.7%
	No	5	38.5%	8	61.5%
Pain:	Yes	11	11.6%	84	88.4%
	No	5	33.3%	10	66.7%
Prior ERCP:	Yes	8	27.6%	21	72.4%
	No	8	9.9%	73	90.1%
Location of Biliary Stone:					
	Proximal	8	25.0%	24	75.0%
	Distal	8	10.3%	70	89.7%

**Table 2. Non-Related Numerical Factors for Cholangitis**

	Cholangitis	Mean	Std. Deviation
Age:	Yes	64.1	10.1
	No	62.0	12.8
Length:	Yes	8.6	1.9
	No	8.3	1.8
Duration:	Yes	65.1	63.9
	No	81.4	55.0
AST:	Yes	81.3	48.8
	No	92.1	77.4
ALT:	Yes	124.3	116.7
	No	104.0	116.4
Amylase:	Yes	347.2	711.4
	No	378.3	855.1
CBD Diameter:	Yes	12.4	4.2
	No	12.5	5.1

**Table 3. Non-Related Categorical Factors for Cholangitis**

		Cholangitis			
		Positive		Negative	
		Count	Percent	Count	Percent
Sex:	Female	1	3.7%	26	96.3%
	Male	15	18.1%	68	81.9%
Fever:	Yes	10	17.2%	48	82.8%
	No	6	11.5%	46	88.5%
Cholelithiasis:	Yes	4	8.9%	41	91.1%
	No	12	18.5%	53	81.5%
Cholecystectomy:	Yes	4	15.4%	22	84.6%
	No	12	14.3%	72	85.7%
PSC	Yes	2	33.3%	4	66.7%
	No	14	13.5%	90	86.5%
Pancreatitis:	Yes	5	27.8%	13	72.2%
	No	11	12.0%	81	88.0%
Sphincterectomy:	Yes	4	8.2%	45	91.8%
	No	12	19.7%	49	80.3%
Anemia:	No	13	15.3%	72	84.7%
	Yes	3	12.0%	22	88.0%
Bilirubin:	>10	10	17.9%	46	82.1%
	≤10	6	11.1%	48	88.9%
Albumin:	≥2.5	15	15.6%	81	84.4%
	<2.5	1	7.1%	13	92.9%
BUN:	≥20	3	8.6%	32	91.4%
	<20	13	17.3%	62	82.7%
Papilla Nature:	Normal	4	7.1%	52	92.9%
	Buldge	3	11.5%	23	88.5%
	Tumoral	5	31.3%	11	68.8%
	Ulcerated	3	33.3%	6	66.7%
	Diverticula	1	33.3%	2	66.7%
Diverticulum:	Yes	4	26.7%	11	73.3%
	No	12	12.6%	83	87.4%

cholangitis (Table 1).

The age, sex, papilla nature, diverticulum, pancreatitis, fever, cholelithiasis, cholecystectomy, PSC, sphincterectomy, anemia, BUN, bilirubin, albumin, CBD diameter, AST, ALT, and amylase had no statistically significant association with cholangitis (P > 0.05) (Table 2 and 3).

**Discussion**

Endoscopic retrograde cholangiopancreatography

(ERCP) is the preferred technique to achieve biliary decompression with placement of an internal or nasobiliary stent. Infection is one of the most morbid complications of ERCP and among the most common causes of ERCP-related death. Septic complications of ERCP include ascending cholangitis, liver abscess, acute cholecystitis, infected pancreatic pseudocyst, infection following perforation of a viscus, and less commonly, endocarditis/endovasculitis (Gigot et al., 1989).

In a study by Vandervoort et al. (2002) in United States, data were collected prospectively on patient characteristics and endoscopic techniques from 1223 ERCPs performed at a single referral center. Independent risk factors for post-ERCP cholangitis were identified as a history of recurrent pancreatitis, previous ERCP-related pancreatitis, multiple cannulation attempts, pancreatic brush cytology, and pain during the procedure. However, none of these factors were identified as risk factors in our study.

Cheng et al. (2006) performed a similar study in United States on 1115 subjects. They found that female gender, history of recurrent idiopathic pancreatitis, pancreas divisum, SOM, difficult cannulation, and major papilla sphincterotomy (either biliary or pancreatic) were not multivariate risk factors for post-ERCP cholangitis. We found similar results.

Freeman et al. (2001) evaluated 1963 consecutive ERCP procedures. Combinations of patient characteristics including female gender, normal serum bilirubin, recurrent abdominal pain, and previous post-ERCP pancreatitis placed patients at increasingly higher risk of pancreatitis, regardless of whether ERCP was diagnostic, manometric, or therapeutic. However our results were different from them.

Christoforidis et al. (2002) in Greece evaluated 556 consecutive patients under ERCP. Age less than 50 years, history of relapsing pancreatitis, pancreatic duct opacification, and difficulty in obtaining bile duct cannulation all proved to be significant predictive risk factors for the development of either hyperamylasemia or pancreatitis. In contrast, additional procedures and sphincterotomy seemed to reduce the likelihood of both complications. However we found different results (Christoforidis et al., 2002).

Complications and technical failures of ERCP cause significant morbidity and, occasionally, mortality (Palazzo et al., 1995; Kama et al, 1999). An understanding of patient- and procedure-related risks is important for decision making with regard to whether or how ERCP should be performed. Cholangitis is avoidable with adequate biliary drainage. Because success rates are higher and complication rates lower for endoscopists performing large volumes of ERCP, ERCP should be concentrated as much as possible among endoscopists with adequate experience. Patients with a high risk for complications may be best served by referral to an advanced center.

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