

# Incomplete or inappropriate endoscopic and radiological interventions as leading causes of cholangitis

## Niekompletne lub niewłaściwe interwencje endoskopowe i radiologiczne jako wiodące przyczyny zapalenia dróg żółciowych

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### ABSTRACT:

**Introduction:** Iatrogenic factors remain to be the leading causes of cholangitis at referral healthcare centers.

**Methods:** The records of 51 patients treated for cholangitis in the years 2005–2016 due to incomplete or inappropriate nonoperative biliary interventions were evaluated retrospectively.

**Results:** Twenty-nine patients included in the study were men and the median (range) age was 60 (30–90) years old. Incomplete or inappropriate ERCP and percutaneous transhepatic biliary drainage (PTBD) procedures had been performed in 45 and 6 patients, respectively. Inappropriate endoscopic stenting for hilar biliary obstruction (perihilar cholangiocarcinoma: 22 patients and gallbladder carcinoma: 3 patients) was the most common scenario (n: 25, 49%). Twenty other patients underwent ERCP with incomplete (n: 12) or no (n: 8) drainage. Errors which occurred in the course of the PTBD procedure included inserting the catheter to the duodenum in patients with hilar obstruction (n: 4) and incomplete drainage in patients with perihilar cholangiocarcinoma (n: 2). Two patients (4%) died of infection. Surgeries of 6 patients with operable tumors were delayed for a median (range) of 5 (1–7) months.

**Conclusions:** Incomplete or inappropriate nonoperative biliary interventions put patients' lives at risk and delay the introduction of radical treatments.

### KEYWORDS:

cholangitis, ERCP, incomplete drainage, percutaneous biliary drainage

### STRESZCZENIE:

**Wstęp:** Czynniki jatrogenne pozostają wiodącymi mechanizmami odpowiedzialnymi za zapalenie dróg żółciowych w ośrodkach wyższego stopnia referencyjności.

**Metody:** Dokonano retrospektywnej analizy dokumentacji 51 pacjentów poddanych w latach 2005–2016 leczeniu zapalenia dróg żółciowych, będącego wynikiem niekompletnych lub niewłaściwych interwencji nieoperacyjnych.

**Wyniki:** 29 pacjentów stanowili mężczyźni; mediana wieku wyniosła 60 lat (zakres 30–90 lat). Niekompletny lub nieodpowiedni zabieg ERCP oraz przeszłonny przezwątrobowy drenaż dróg żółciowych (PTBD) wykonano odpowiednio u 45 i 6 pacjentów. Najczęstszym scenariuszem (25 przypadków, 49%) było nieprawidłowe endoskopowe założenie stentu w związku z obturacją wnęki (okołownękowy rak dróg żółciowych: 22 przypadki i rak pęcherzyka żółciowego: 3 przypadki). 20 innych pacjentów zostało poddanych ERCP z niekompletnym drenażem (n = 12) lub brakiem drenażu (n = 8). Błędy w grupie PTBD obejmowały wprowadzenie cewnika do dwunastnicy u pacjentów z obturacją wnęki (n = 4) oraz niekompletny drenaż u pacjentów z okołownękowym rakiem dróg żółciowych (n = 2). W dwóch przypadkach (4%) doszło do zgonu z powodu zakażenia. Mediana opóźnienia operacji u 6 chorych z operowalnym guzem wyniosła 5 miesięcy (zakres 1–7 miesięcy).

**Wnioski:** Niepełne lub niewłaściwe interwencje nieoperacyjne w obrębie dróg żółciowych narażają życie pacjentów i opóźniają radykalne leczenie.

**SŁOWA KLUCZOWE:** ERCP, niekompletny drenaż, przeszłonny drenaż dróg żółciowych, zapalenie dróg żółciowych

## ABBREVIATIONS

**CCT** – computed tomography

**EBS** – endoscopic biliary stenting

**ERCP** – endoscopic retrograde cholangiopancreatography

**PTBD** – percutaneous transhepatic biliary drainage

## INTRODUCTION

In 2005, our research group reported that malignancies with complications after endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic biliary drainage (PTBD) had replaced choledocholithiasis as the leading underlying diseases in severe cholangitis cases observed at our tertiary referral center. The dominant factors associated with these complications were incomplete or inappropriate procedures [1]. Other authors have drawn attention to the problem of post-procedural cholangitis [2–5].

The continued significance of this problem led us to review clinical experience from the last decade. One issue that has complicated the problem further in the interim period is the emergence of carbapenem-resistant bacteria [6–8]. Moreover, changes in hospitalization procedures implemented at our institution resulted in a trend of admitting acute cholangitis cases with choledocholithiasis and patients with severe cholangitis to the surgical emergency department. Consequently, this study was conducted to emphasize the persisting role of iatrogenic factors in the development of cholangitis in patients referred to the Hepato-Pancreato-Biliary Surgery Unit.

## PATIENTS AND METHODS

The records of 51 patients (29 men and 22 women; median [range] age: 60 [30–90]) treated for recent or ongoing acute cholangitis between 2005 and 2016 (inclusive) due to incomplete or inappropriate nonoperative biliary intervention were evaluated retrospectively. Forty-seven patients were treated at our unit, while 4 patients were treated at other institutions under our supervision. Tokyo guidelines were generally followed for the diagnoses of acute cholangitis and severe cholangitis [9, 10]. In general, patients were primarily treated with adequate nonoperative biliary decompression (either percutaneous or endoscopic) and antibiotics. If indicated, surgical treatment of the underlying pathology was attempted after resolution of infection, recovery of liver function and decolonization of the carbapenem-resistant bacteria.

## RESULTS

Diagnoses of the patients, along with the mistakes in clinical management are presented in Tab. I. The most common diagnosis was perihilar cholangiocarcinoma; ERCP and stenting attempts had caused cholangitis in 22 out of 28 patients (Tab. I.), (Fig. 1., 2.). Performing PTBD for perihilar obstruction and extending the catheter to the duodenum appear to cause cholangitis through the same mechanism. Incidentally, necrotizing pancreatitis, a well-recognized complication of ERCP, was encountered in one patient who underwent PTBD with a catheter extending to the duodenum (Fig. 3.). Two patients with cholangitis had undergone incomplete PTBD and the unresolved infection was inappropriately treated

in a prolonged fashion with broad-spectrum antibiotics, rather than performing a complete drainage (Fig. 4.). Out of all patients suffering from perihilar cholangiocarcinoma, 1 died of infection, while the other 23 could not undergo surgery due to advanced tumor stage, concomitant diseases or inadequate recovery of liver function. Four patients underwent tumor resection procedures delayed for 1, 5, 5 and 6 months in order to allow for recovery of liver function and decolonization of carbapenem-resistant bacteria.

Among the 8 patients with intrahepatic lithiasis, the median value of ERCP procedures performed with incomplete biliary drainage due to residual stones (7 patients) or no drainage (1 patient) was 2 (range 1–5). PTBD was performed in 6 patients. In two other patients, cholangitis (in one case of severe character) had resolved with medical treatment administered in a referral institution. Roux-en-Y hepaticojejunostomy was performed in two patients, right and left hepatectomy in one patient each and bile duct exploration with stone removal in one patient. One of the patients was colonized with carbapenem-resistant *Klebsiella pneumoniae* – decolonization with protective insertion of a PTBD catheter took three months. Upon completion of antibiotic treatment, percutaneous cholangiography revealed a small number of residual stones that could be removed by ERCP and the PTBD catheter could eventually be taken out. A similar approach was effective in another patient with who suffered a cerebrovascular accident in the past. One patient was lost to follow-up.

The 5 patients with periampullary tumors had undergone a median of 2 (range 1–3) ERCP procedures without drainage [4] or incomplete drainage (ineffective stenting in 1 patient) performed at other institutions. PTBD was performed in all cases. Eventually, successful pancreatoduodenectomy could be performed in two patients. The PTBD catheter of one of the patients dislodged after discharge from hospital. This patient was readmitted for emergency ERCP with stenting but he died of multiple infections. One patient who developed post-procedural necrotizing pancreatitis was also found to have liver metastases on laparotomy performed 4 months after the initial admission. One patient was considered to be unfit for surgery due to preexisting comorbidities.

Out of 4 patients with gallbladder cancer, the hilum was invaded by tumor in 3 cases; ERCP and stenting accelerated cholangitis attack that was treated with percutaneous drainage. One of the patients suffered a cerebrovascular accident during hospitalization and therefore could not be offered surgical treatment. Another patient's condition was evaluated as inoperable based on imaging test results. The third patient underwent laparotomy after a 4-month delay due to slow recovery of liver function and was then found to be inoperable. The fourth patient suffered from a tumor located in the middle portion of the common bile duct; he underwent ERCP and stenting at another institution. Since the upper end of the stent was discovered to be located below the stricture, migration or inappropriate placement were suspected. The cholangitis attack was treated by stent exchange. However, the patient was lost to follow up.

One of the three patients with choledocholithiasis underwent 4 ERCP procedures. As stone clearance was incomplete, the whole biliary stent migrated into the common bile duct. This patient was treated by performing common bile duct exploration and biliodigestive anastomosis to the duodenal stump (previously termed as Billroth II resection for peptic ulcer). The second patient underwent 3 ERCP procedures within 2 months. In this

Tab. I. Features of cases.

	N	ERCP-STENTING FOR HILAR OBSTRUCTION	ERCP WITH NO /INCOMPLETE DRAINAGE	PTBD FOR HILAR OBSTRUCTION, DUODENAL CATHETERIZATION	PTBD WITH INCOMPLETE DRAINAGE
Perihilar cholangiocarcinoma	28	22		4	2
Intrahepatic lithiasis	8		1/7		
Periampullary tumor	5		4/1		
Gallbladder carcinoma	4	3	1/0		
Choledocholithiasis	3		0/3		
Benign biliary stricture	2		2/0		
Hydatid cyst	1		0/1		

case, cholangitis attack occurred due to occlusion of the stent inserted during the last procedure and was treated by stent removal. The third patient underwent 2 ERCP procedures. The cholangitis attack occurred due to presence of residual stones which, except for one large stone, were all removed. A 10F stent was placed in the common bile duct and complete clearance was achieved two months later.

Two patients were observed to have benign Bismuth type III strictures due to previous cholecystectomy. One of them underwent ERCP which revealed a tight stricture with minimal leakage of contrast media into the intrahepatic biliary tree. The other patient underwent a total number of 4 unsuccessful ERCP procedures. Cholangitis attacks were treated by performing PTBD at our institution. Eventually, Roux-en-Y hepaticojejunostomy was performed in both patients.

The hydatid cyst patient had a large cyst which ruptured into the biliary tree from the right side of hilum. ERCP with incomplete clearance of the biliary tree accelerated development of severe cholangitis that was treated by emergency percutaneous drainage. Eventually, this patient underwent open abdominal surgery for cyst drainage and clearance of the extrahepatic biliary tree.

Fourteen (27%) out of 51 patients experienced severe cholangitis. Two (14%) of these patients died due to overwhelming infections. The overall mortality was 4%.

## DISCUSSION

In the initial report for our center (1) we had concluded the following:

“Although nonoperative biliary interventions have revolutionized hepatopancreatobiliary surgery, these are invasive procedures with potentially fatal complications. Careful patient selection, implementation of measures to prevent complications, clear definition of responsibilities and management of complex biliary obstruction by an experienced multidisciplinary team are vital for success”.

Unfortunately, disregard for or, at least, lack of adherence to the basic principles summarized above compelled us to prepare this follow-up report. To begin with, nonoperative interventional procedures described in this report were performed at or organized by a primary healthcare institutions but patients were referred to our center after the development of complications. This problem

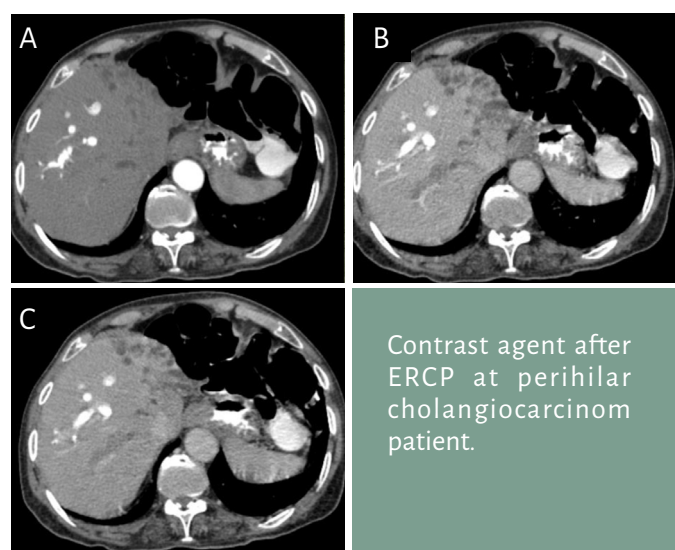
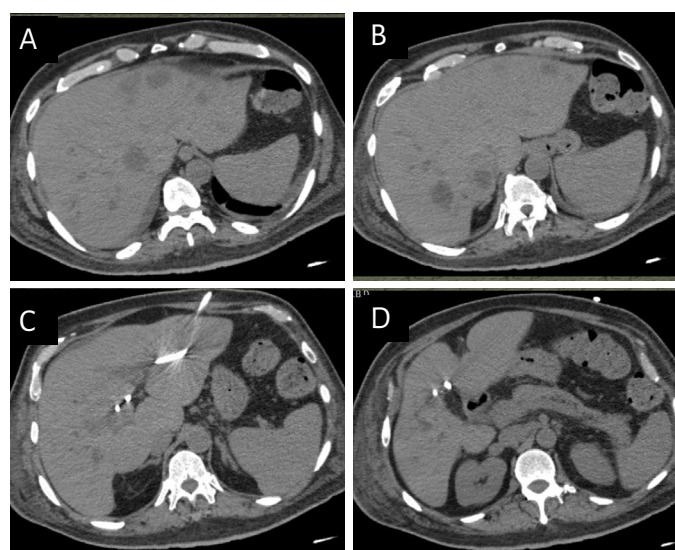
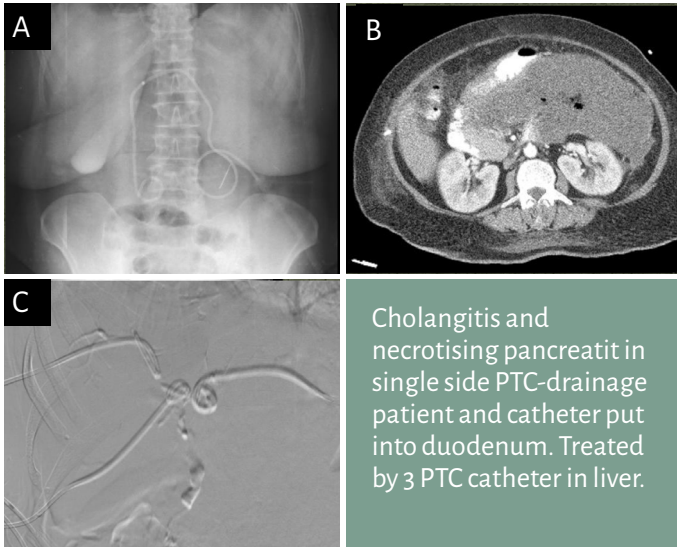


Fig. 1. (A, B, C) CT image of contrast agent residues in the intrahepatic biliary tree after ERCP in a patient with perihilar cholangiocarcinoma.



Severe cholangitis, multiple liver abscess and renal failure due to sepsis after ERCP stenting in perihilar cholangiocarcinoma patient. Treated by PTC drainage.

Fig. 2. (A, B, C, D) CT image of a perihilar cholangiocarcinoma patient who was referred with post-ERCP severe cholangitis, multiple liver abscesses and renal failure. He was treated with PTBD.



Cholangitis and necrotising pancreatitis in single side PTC-drainage patient and catheter put into duodenum. Treated by 3 PTC catheter in liver.

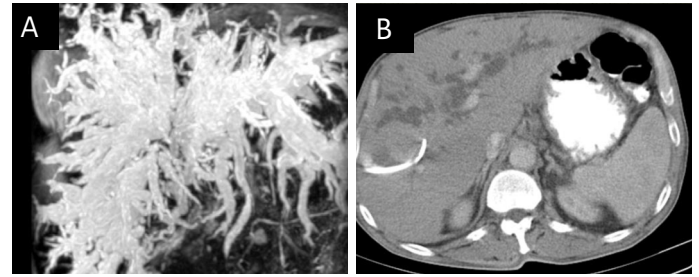
**Fig. 3.** CT image of a perihilar cholangiocarcinoma patient who underwent unilateral PTBD with the catheter extending into the duodenum (A) and was admitted with cholangitis and necrotizing pancreatitis (B). Three PTBD catheters were required for complete drainage of the biliary tree (C). Pancreatic necrosis required percutaneous drainage and eventually limited surgical debridement.

was particularly striking in patients with malignant hilar obstruction. Many eventually harmful procedures were performed at centers with no experience in major hepatobiliary resections. Interventional procedure which, if applied properly, could be a bridge to surgical treatment, lead to severe complications and up to 7-month delays in surgical treatment. In short, we emphasize that:

“Physicians who do not have the expertise and resources to recognize and manage complications of biliary procedures should be very selective in referring patients for these interventions. Instead, they should refer patients to specialized hepato-pancreato-biliary units”.

From our experience, some of the physicians from the referring institutions argued vehemently that they “had done the right thing” because they had read that endoscopic approach was preferred over percutaneous approach in perihilar cholangiocarcinoma. However, two vital details were missed: firstly, the centers that chose this approach used endoscopic nasobiliary drainage and warned of severe complications of endoscopic stenting [11–13]. For example, Kawashima et al. [11] warned that “because the reported incidence of post-endoscopic biliary stenting (EBS) cholangitis is between 48% and 65%, EBS is not suitable as a preoperative drainage method in patients with perihilar cholangiocarcinoma”. Secondly, even patients who undergo this ‘safer’ procedure should be kept under vigilant supervision, as 10–30% of these patients may require additional endoscopic or, more commonly, percutaneous procedures [11–14].

The situation was particularly ironical in patients with bile stone disease in whom inappropriate or incomplete drainage was performed. In theory, the interventional procedure is a less morbid and invasive alternative to classical surgical operation that would be curative in all cases. However, in this case an incomplete/inappropriate interventional procedure caused potentially fatal cholangitis without any benefit to the underlying pathology. Even in a patient with cholangitis, a properly conducted surgical procedure is effective and much safer than an incomplete nonoperative procedure. Pancreatoduodenectomy can be performed safely without



Inappropriate MRCP, PTC drainage in only one side that will be resected. Cholangitis due to underdrained sides treated by extended spectrum antibiotics. Hospitalised due to Carbapenem resistant *Acinetobacter* and Kinolon-aminoglycosid resistant *Stenotrophomonas maltophilia* sepsis. Treated by PTC-external drainage.

**Fig. 4.** A perihilar cholangiocarcinoma patient who was evaluated with an inadequate MRCP (A) and treated with PTBD applied to the resection site (B) along with prolonged administration of wide-spectrum antibiotics for cholangitis arising from the undrained sections of the biliary tree. The patient was admitted with sepsis due to Carbapenem-Resistant *Acinetobacter* and quinolone – and aminoglycoside-resistant *Stenotrophomonas maltophilia*; he was treated with PTBD and appropriate course of antibiotics.

preoperative biliary drainage in most patients without cholangitis [15, 16]. In case of ERCP attempt failure, percutaneous drainage should be performed on the same day due to the risk of cholangitis which may develop even if cannulation attempts fail and no contrast agent enters the biliary tree [1]. Ironically, the final diagnoses of the two patients with periampullary tumors, who eventually underwent pancreatoduodenectomy were neuroendocrine tumor and adenomatous hyperplasia in the distal common bile duct. In other words, two patients with good survival expectancy were exposed to a high risk of death due to iatrogenic causes. Incidentally, recent data showed that preoperative endoscopic drainage leads to a less favorable bile culture profile in patients with periampullary tumors [17]. Apparently, spillage of duodenal fluid into the biliary tree is the culprit. Percutaneous drainage without extending the catheter into the duodenum may be a safer option in patients who require preoperative biliary drainage [18].

In conclusion, incomplete or inappropriate nonoperative biliary interventions put patients’ lives at risk and delay the introduction of radical treatments. Cases of biliary obstruction either ought to be discussed with a surgeon with clinical expertise prior to undertaking any interventions or these procedures should be performed at institutions that can assume complete responsibility for the admitted patients, especially those with perihilar cholangiocarcinomas. This stands in accordance with the fundamental principle of continuity of care [19], which holds for surgical procedures as well [20, 21].

Limitation: Retrospective nature of our research and a small number of patients are the limitations of our study.

## CONCLUSIONS

Incomplete or inappropriate nonoperative biliary interventions put patients’ lives at risk and delay the introduction of radical treatments. These procedures should be performed at institutions capable of assuming complete responsibility for the patients, especially those suffering from perihilar cholangiocarcinomas.

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