Management of Complex Biliary Cases in A Tertiary Referral Setting: Real World Lessons and Their Role in Shaping Future Clinical Strategies

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ABSTRACT

Background: *In the era of laparoscopic procedure, innovative non-surgical approaches have emerged for managing biliary tract disorders. Techniques such as therapeutic endoscopic retrograde cholangiopancreatography (ERCP) and interventional endoscopic ultrasound (EUS) are increasingly being utilized. However, a clear consensus on a stepwise approach to managing difficult biliary disorders remains elusive. Therefore, this study was performed to evaluate the impact of endoscopic approach management on the outcomes of complex biliary cases.*

Methods: *A retrospective study was conducted using an endoscopy database over two-year period. The characteristics of the study subjects, including demography and clinical data, were presented descriptively. The technical success rate was defined as the completion of the procedure performed on the patients. A bivariate analysis was conducted to evaluate the outcomes of therapy.*

Results: *Sixty-one subjects with similar proportions in malignant (44.3%) and non-malignant (55.7%) etiologies in this retrospective database study were considered as complex biliary cases. Among them, 16.4% underwent a combination of therapeutic ERCP and EUS in one session based on the complexity of the case. Additionally, 8.2% of the subjects underwent ERCP with additional single operator cholangioscopy procedure. One subject (1.6%) underwent a rendezvous ERCP procedure through a percutaneous approach, while 4.9% underwent EUS-guided biliary drainage procedure. This study revealed no significant association between all mortality outcomes and baseline characteristics of the patients. Furthermore, there were no significant associations between mortality and the need for re-intervention, post-procedural pain, or the occurrence of acute pancreatitis.*

Conclusion: *Complex biliary cases require a good clinical approach algorithm to decide which procedure comes first based on a comprehensive evaluation consisting of the patient's factor, expertise, cost, and the risk of complications.*

Keywords: *Biliary tract, endoscopic retrograde cholangiography, endoscopic ultrasound, laparoscopic procedure*

ABSTRAK

Latar Belakang: *Di era prosedur operasi laparoskopi, terdapat inovasi tata laksana non bedah pada kasus penyakit saluran empedu, seperti 'endoscopic retrograde cholangiopancreatography' (ERCP) dan 'endoscopic ultrasound' (EUS). Sampai saat ini belum ada kesepakatan atau panduan jelas mengenai pemilihan tata laksana awal pada kasus penyakit empedu dengan penyulit Oleh karena itu, studi ini dibuat untuk mengetahui dampak dari tatalaksana berbasis endoskopi terhadap luaran kasus-kasus penyakit empedu dengan penyulit.*

Metode: *Studi retrospektif database endoskopi dalam kurun waktu dua tahun dilakukan pada kasus-kasus penyakit empedu yang kompleks. Karakteristik subjek, termasuk data demografi dan klinis, ditampilkan secara deskriptif. Laju keberhasilan teknis didefinisikan sebagai seberapa banyak prosedur yang selesai dilakukan. Penulis juga melakukan analisis bivariat untuk menilai luaran terapi.*

Hasil: *Enam puluh satu subyek dengan proporsi serupa antara etiologi maligna (44.3%) dan non-maligna (55.7%) memenuhi kriteria kasus kompleks empedu pada studi ini. Sebanyak 16,4% pasien menjalani kombinasi tata laksana ERCP dan EUS; dan 8,2% subyek menjalani tindakan ERCP dengan alat tambahan "SpyGlass Cholangioscopy". Satu pasien menjalani tindakan rendezvous ERCP melalui jalur perkutan yang sudah ada. Sebanyak 4,9% subyek menjalani tindakan terapetik EUS untuk drainase sistem bilier. Studi ini tidak menemukan hubungan bermakna antara luaran mortalitas dengan karakteristik dasar pasien. Tidak ditemukan pula hubungan bermakna antara luaran mortalitas dengan prosedur-prosedur re-intervensi atau nyeri pasca prosedur atau pankreatitis akut.*

Kesimpulan: *Kasus penyakit sistem bilier yang kompleks membutuhkan pendekatan yang baik dan keputusan yang tepat terkait metode pertama yang menjadi pilihan berdasarkan kondisi pasien, penilaian keahlian dokter, biaya, dan risiko serta komplikasi yang bisa terjadi.*

Kata kunci: *Sistem bilier, endoscopic retrograde cholangiography, endoscopic ultrasound, prosedur laparoskopi.*

INTRODUCTION

Biliary tract disorder has been considered as the most common challenging problem and costly among all gastrointestinal diseases.[1-2]. Since many biliary diseases remain relatively rare, significant geographical variations in their prevalence and incidence can still be found among many regions worldwide. Variable distribution of risk factors also contributes to varied healthcare burdens.[3] Another clinical challenge is advanced biliary malignancies. Biliary malignancies are also known to have non-specific clinical manifestations; therefore, it is mostly found in the late stage of the disease.[5-8]

The management of biliary disorders has undergone many progressive changes in the last three decades. These developments occurred from non-surgical innovation to minimally invasive procedures, notably therapeutic endoscopic retrograde cholangiopancreatography (ERCP) and interventional endoscopic ultrasound (EUS).[9]. Recently, there are two main considerations of attitudes on facing complicated biliary problems. The first approach is the "laparoscopy-first" attitude, which primarily consists of intraoperative cholangiography and laparoscopic exploration of the common bile duct (CBD). For high-risk choledocholithiasis, the success rates of the laparoscopic approach are higher than 90%, with morbidity rates ranging from 8%-15% and a mortality rate of 1%. Common complications include bile leakage, residual stones, surgical site infections, and subhepatic abscesses. Meanwhile, the second approach with "endoscopy-first" attitude yields success rates in stone extraction, ranging from 74.4% to 100%. The most common complications of this approach are acute pancreatitis (1.6%-15.7%), bleeding (1%-3%), perforation (0.1%-0.6%), and infection (<1%)[10,11]. Failure of attempted biliary cannulation also becomes one of the concerns in difficult biliary cases[12,13].

Nevertheless, no definite consensus has clearly stated the most preferrable approach in the management of complicated biliary cases; since it also highly relies on the availability of instruments and skillful personnel. This study aimed to see the impact of endoscopic approach management in complex biliary case series performed in a single referral tertiary healthcare center.

METHODS

Database of ERCP or interventional EUS case series were retrospectively collected within two years period. Complex biliary cases were defined as those

requiring a multi-modality management approach. The study included adult patients (aged 18 years and older) who underwent therapeutic ERCP or EUS procedures due to biliary disorders. Data collection was performed at a private referral tertiary healthcare center in Jakarta, Indonesia (Medistra Hospital) from 2019 to 2021. Inclusion criteria for complex biliary cases required at least one of the following conditions: multi-management approach, biliary obstruction with cholangitis or biliary sepsis, difficult CBD stone, recurrent CBD stone, or advanced progressive malignant biliary obstruction. Diagnostic confirmation of malignant etiologies was established based on EUS biopsy with fine-needle aspiration biopsy (FNAB) or cytology or a combination of imaging studies, tumor markers, and other clinical findings. Only complete datasets meeting the inclusion criteria were selected for final analysis.

All procedures were performed by a senior consultant gastroenterohepatologist with more than a decade of clinical experiences in advanced therapeutic endoscopy procedures. ERCP procedures utilized the Olympus TJF Q 180 V scope, while EUS procedures were conducted using the Olympus GF UCT180 scope, connected to high-end ultrasound equipment (Aloka IPF-1701C, Tokyo, Japan). For EUS-guided biliary access, a 19-G FNA needle (EchoTip, Wilson-Cook) was used to puncture the bile duct, followed by fistula tract creation using a 6-Fr cystotome. A 210-cm, 0.35-inch guidewire (Boston Scientific, USA) was employed for navigation within the bile duct. Clinical observation and laboratory assessments were conducted within seven days post-procedure. Subject characteristics—including demographic and clinical data—were presented descriptively. A bivariate analysis was also performed to evaluate the outcome of the subjects after the procedure. A statistically significant result was considered if the *P*-value was < 0.05. All data were analyzed using IBM SPSS Statistics version 25.

RESULTS

Sixty-one subjects in this case series database review study were included. The proportions of malignant and non-malignant etiologies were similar (44.3% *versus* 55.7%, respectively). Among these subjects, the most common etiology was choledocholithiasis (44.3%) and pancreatic cancer (18.0%) (**Table 1**). Of the sixty-one recruited subjects, 59 underwent therapeutic ERCP and/or interventional EUS as the initial procedure. The remaining two subjects underwent cholecystectomy as the initial procedure from another hospital. Peritonitis due to biliary leak complications occurred in the latter subjects **(Figure 1).**

Table 1. Baseline Characteristics of the Study Subjects

	Difficult Biliary Cases (n=61)
Demographic characteristic	
Male, n (%)	35 (57.4)
Female, n (%)	26 (42.6%)
Age, mean ± SD	62 ± 15.74
Body Mass Index (kg/m^2), mean ± SD	24.43 ± 4.35
Etiology, n (%)	
Malignant	27 (44.3)
Non-malignant	34 (55.7)
Primary Disease, n (%)	
Choledocholithiasis	27 (44.3)
Cholelithiasis	2 (3.3)
Cholecystitis	1 (1.6)
Pancreatic cancer	11 (18.0)
Cholangiocarcinoma	8 (13.1)
Bile leakage (post-laparoscopic cholecystectomy)	2 (3.3)
Hepatocellular carcinoma	1 (1.6)
Duodenal tumour	2 (3.3)
Biliary stricture	4 (6.6)
Papilla of Vater tumor	1 (1.6)
Ampullary mass	1 (1.6)
Colorectal tumour	1 (1.6)
Laboratory findings	
Haemoglobin (g/dL), mean ± SD	11.96 ± 2.44
White Blood Cells (10^3/mcL), median (IQR)	8.80 (6.6 – 12.3)
Platelets (10^3/mcL), mean ± SD	319.616 ± 186.25
Total Bilirubin (mg/dL), median (IQR)	5.39 (1.44 – 11.07)
Direct Bilirubin (mg/dL), median (IQR)	4.57 (1.08 – 10.15)
Albumin (g/dL), median (IQR)	3.40 (2.85 – 3.90)
Amylase (U/L), median (IQR)	27.5 (12.5 – 43.0)
AST (U/L), median (IQR)	60.5 (30 – 119)
ALT (U/L), median (IQR)	71.5 (35 – 143.5)
GGT (U/L), median (IQR)	200.5 (93 – 426)
ALP (U/L), median (IQR)	195 (89 – 301)

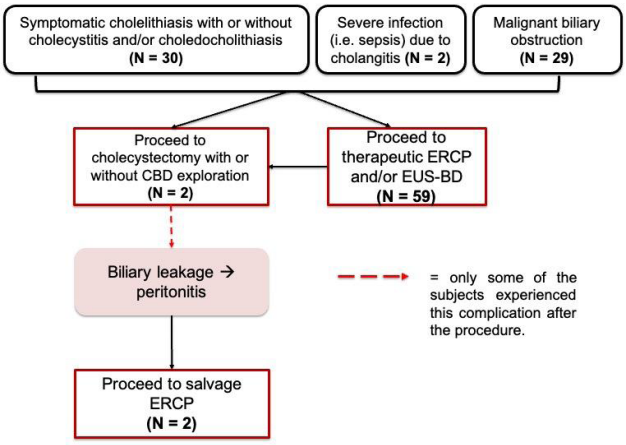

Figure 1. Flow Chart of the Study Subjects' Management, Summarizes the Sequential Events of the Subjects in This Study From Admission Until The Therapeutic Procedures

In this study, forty-two (68.8%) standard therapeutic ERCP procedures were conducted throughout the study period, while ten (16.4%) combination of therapeutic ERCP and EUS in one session procedures were performed based on the complexity of the case. In particular, five (8.2%) therapeutic ERCP with additional single operator cholangioscopy procedures were also performed. One subject underwent the rendezvous ERCP procedure through a percutaneous approach, and three EUS-guided biliary drainage (EUS-BD) procedures were performed due to difficult ERCP cannulation in the previous procedures. The technical success rate of all procedures was 100%. In addition, post-procedural observation within 7-14 days was also noted in all subjects. Re-intervention with ERCP was performed in 6 subjects (9.8%), with clinical indications varied from recurrent biliary obstruction caused by infiltrative malignant process or recurrent CBD stones.

The most commonly adverse event in this study was post-procedural pain (50.8%) (measured by Visual Analog Scale: ≥ 4). Approximately, 14.8% of the subjects also experienced post-procedural acute pancreatitis without any further complications requiring intensive care and/or life-threatening complications. Four subjects (6.6%) died within one month after the procedure. Of these, one patient died due to procedure-related events, while the remaining three were related to the malignant process of the diseases (**Table 2**).

This study also included an analysis of mortality outcomes. No statistically significant associations were found between mortality and patients' baseline characteristics. Additionally, there were no significant correlations between mortality and the need for re-intervention, post-procedural pain, or the occurrence of acute pancreatitis (**Table 3**).

Table 2. Summary of result endoscopic approach in patients with difficult biliary cases

Endoscopic Approach in Patients With Difficult Biliary Cases (n=61)	
Primary Procedures, n (%)	
ERCP	42 (68.8)
Rendezvous	1 (1.6)
ERCP + EUS	10 (16.4)
ERCP + Single Operator Cholangioscopy	5 (8.2)
EUS-BD	3 (4.9)
Technical success rate, n (%)	61 (100)
Post-procedure intervention, n (%)	
Re-intervention ERCP	6 (9.8)
Adverse event, n (%)	
Pain (Scale ≥ 4)	31 (50.8)
Acute Pancreatitis	9 (14.8)
Outcome of patient, n %)	
Death	4 (6.6)
Alive	57 (93.4)

Table 3. Comparison of Mortality Outcomes

Variable	Outcome of Patient		
	Death (n = 4)	Alive (n = 63)	P value
Gender, n (%)			
Male	3 (8.8)	31 (91.2)	0.414
Female	1 (3.8)	25 (96.2)	
Age (years), mean ± SD	63.75 ± 12.99	61.16 ± 15.99	0.444
Body Mass Index (kg/m^2), mean ± SD	24.95 ± 5.63	24.46 ± 4.32	0.551
Etiology, n (%)			
Malignant	3 (11.5)	23 (88.5)	0.212
Non-malignant	1 (3)	33 (97)	
Haemoglobin (g/dL), median (IQR)	11.1 (9.4 – 11.7)	12.5 (10.9 – 13.8)	0.123
White Blood Cells (10^3/mcL), median (IQR)	11.4 (7.8 – 23.5)	8.60 (6.5 – 12.3)	0.349
Platelets (10^3/mcL), median (IQR)	230.5 (81 - 405)	288 (217 - 421)	0.483
Total Bilirubin (mg/dL), median (IQR)	6.42 (2.39 – 12.04)	4.78 (1.44 – 11.07)	0.966
Direct Bilirubin (mg/dL), median (IQR)	4.08 (1.26 – 9.76)	3.91 (1.08 – 10.15)	0.742
Albumin (g/dL), median (IQR)	3.30 (2.08 – 3.65)	3.50 (2.85 – 3.90)	0.742
Amylase (U/L), median (IQR)	28 (25 – 49)	26 (10 – 43)	0.577
AST (U/L), median (IQR)	102 (32 – 214)	57 (30 – 106)	0.635
ALT (U/L), median (IQR)	75 (57 – 94)	57 (54 – 152)	0.898

Variable	Outcome of Patient		
	Death (n = 4)	Alive (n = 63)	P value
GGT (U/L), median (IQR)	243 (133 – 416)	184 (91 – 426)	0.989
ALP (U/L), median (IQR)	287 (149 – 503)	156 (87 – 292)	0.413
Re-intervention ERCP, n (%)			
Yes	1 (16.7)	5 (83.3)	0.351
No	3 (5.5)	52 (94.5)	
Pain (Scale ≥ 4), n (%)			
Yes	3 (9.7)	28 (90.3)	0.332
No	1 (3.4)	28 (96.6)	
Acute Pancreatitis, n (%)			
Yes	2 (22.2)	7 (77.78)	0.103
No	3 (5.8)	49 (94.2)	

Several notable cases requiring complex biliary procedures are highlighted in this study (**Figure 1**). **Case 1:** A young male patient, who experienced bile peritonitis and bile leakage after a laparoscopic cholecystectomy procedure at another hospital (two weeks before hospital admission) underwent an ERCP procedure in our hospital due to a migrated plastic CBD stent which had been placed during pre-operative ERCP procedure. After successfully placing a new double pigtail CBD stent, the patient also underwent percutaneous drainage-trans abdominal ultrasound-guided for bile fluid drainage in the abdominal cavity. **Case 2:** A middle-aged male patient was referred to our hospital for an ERCP procedure due to hyperbilirubinemia caused by bile duct obstruction after laparoscopy and conversion to open cholecystectomy with biliodigestive procedures due to extensive adhesions. A very tight biliary stricture was identified near the biliodigestive anastomosis and was managed using a tapered dilator and Soehendra screw prior to stent placement. **Case 3:** A young female patient underwent a salvage ERCP procedure at our hospital for biliary stenting due to bile leakage and bile peritonitis after a laparoscopic cholecystectomy procedure, where surgical abdominal drains were placed during the operative procedure.

During the salvage ERCP procedure for CBD stent placement, the presence of a large distal CBD stone was noted. s a result, two stents were placed: a 10-Fr straight plastic stent across the leakage site and a 7-Fr double-pigtail stent. One month after the first ERCP procedure, the second ERCP procedure was performed for stone crushing by single operator cholangioscopy procedure due to the narrowing of distal CBD. One subject with advanced pancreatic cancer underwent repeated ERCP procedures due to metal stent blockage caused by biliary stones and sludge. **Case 4:** A salvage ERCP was performed on a critically ill middle-aged female patient in the ICU, who was on ventilator support and suffering from biliary sepsis. The sepsis was caused by a large distal CBD stone and compression of the distal bile duct by a sizable pancreatic pseudocyst. The patient also suffered from cardiovascular problems, hypothyroidism, and type 2 diabetes mellitus. Prior to ERCP, a bedside biliary drainage procedure with percutaneous transhepatic biliary drainage (PTBD) under transabdominal ultrasound guidance (without fluoroscopy) had been performed along with percutaneous cyst aspiration to improve the breathing system. The patient also received wide-spectrum antibiotics and other supportive treatment for her sepsis condition. During the ERCP procedure, salvage biliary drainage was performed by placing a 7-Fr double-pigtail stent inside the CBD. After ERCP, EUS was also conducted to evaluate the large cyst. Once a sufficient fistula tract was established, a 7-Fr double-pigtail stent was inserted into the cyst cavity. The patient showed marked clinical improvement and was eventually discharged from the hospital.

DISCUSSION

This study exhibited the complexity of the management approach in biliary cases with two sides of the story (innovation in surgical and endoscopic approaches). Both malignant and non-malignant complicated biliary cases remain a major challenge for diagnostic approach as well as management, which requires a multidisciplinary approach. The choice of modality, surgical or endoscopic, is typically guided by the complexity of the case, the patient's overall condition, and the invasiveness of the procedure. Two of our cases demonstrated the benefit of ERCP procedure in a patient who experienced bile peritonitis and bile leakage as the post-surgical complications. In one of these cases, ERCP also demonstrated therapeutic

advantages in managing biliary stricture around the biliodigestive anastomotic area.

Although endoscopic procedures are generally considered less invasive compared to intraoperative procedures, several controversies can still arise due to their non-negligible morbidity (4%-15.9%) and mortality (0-1%) rates based on technical difficulties or anatomically challenging situations during the procedures[9,13]. Another common cause of ERCP failure is the history of previous surgical procedures on the stomach, such as Roux-en-Y gastrojejunostomy[13] or gastrectomy with closure of duodenal stump or reconstruction of Billroth II. Other factors, which may influence the failure rate of ERCP, are infiltration of the tumor into the ampulla, obstruction of gastrointestinal passage, or peptic ulcer[14]. In contrast, our study demonstrated a technical success rate reached as high as 100% with less than 10% re-intervention procedures needed afterwards. One anatomically challenging case of biliary stricture around the biliodigestive anastomotic area was managed to be tackled with stent placement and additional tapered dilator and Soehendra screw. In our study, none of the repeated procedures were conducted due to technical failure, and no cases of bile leakage, cholangitis, or stent migration were observed. Four patients passed away within 30 days of the procedure, all due to progression of advanced malignancy, not procedure-related complications. These findings emphasized the critical roles of adequate facilities and clinical experiences of the operators to the outcome of the procedures.

The most common non-malignant etiology found in this study was choledocholithiasis. According to the American Society for Gastrointestinal Endoscopy (ASGE) guidelines, even though the strategies of removing bile duct stones have shifted from major surgery to minimally invasive procedures, the risk of major adverse events associated with ERCP-guided treatment is still ranging from 6-15%. Despite these risks, the ASGE continues to recommend ERCP with the placement of plastic and covered metal stents in patients with difficult choledocholithiasis and signs of infection with planned exchange or removal. To minimize the risk of diagnostic ERCP, ASGE has also established risk stratification criteria to determine whether ERCP should be performed immediately or to choose other modalities for suspected choledocholithiasis[15]. In this study, these criteria were also used to stratify the risk of the subjects with choledocholithiasis to determine the next procedure to be performed.

In the management of CBD stones, nowadays, ERCP with ES remains the most common treatment approach with a reported success rate over 90%[15]. However, as a post-operative procedure, failure of ERCP may lead to another surgical procedure, raising the issues of cost and complications[16]. Meanwhile, since almost three decades ago, laparoscopic CBD exploration has been considered one of the surgical management of biliary cases. Depending on the experiences of the operators, the effectiveness of laparoscopy cholecystectomy is comparable with ERCP for CBD clearance. Nevertheless, longer surgery time (300-358 minutes), expensive instruments, and adequacy of surgical skills remain a hindrance to applying this technique widely[9,17]. A retrospective study involving 141 post-cholecystectomy subjects with choledocholithiasis showed higher success rates for CBD clearance in the ERCP group (97.7%) compared to those who underwent laparoscopic CBD exploration (87%). Additionally, ERCP was associated with shorter procedure times and reduced postoperative hospital stays. Based on our case series, three patients underwent the ERCP procedure due to complications following laparoscopic cholecystectomy procedure. Bile leakage is still considered the most common post-procedural complications after laparoscopic cholecystectomy. In our study, two subjects with bile leakage and one subject with stricture at the site of biliodigestive bypass were referred from another healthcare center, having undergone a second surgery prior to ERCP. Another focus of our results is the malignant biliary cases. Malignant distal biliary obstruction itself is still considered a challenging condition since the diagnosis is often found at an advanced stage due to unspecific early clinical manifestation. In line with the epidemiological data[19,20], the most common malignant distal biliary obstruction cases in our study were pancreatic adenocarcinoma and cholangiocarcinoma.

As demonstrated by our descriptive findings, advances in endoscopic approaches have also been applied to endoscopic biliary malignancies. Approximately 70% of malignant distal biliary obstruction is considered unresectable at the time of diagnosis. Nevertheless, various clinical manifestations, such as nausea, recurrent cholangitis, pruritus, loss of appetite, renal dysfunction, and delayed wound healing, may still cause discomfort for the patients[21]. Therefore, palliative biliary stenting is expected to reduce these symptoms. According to ESGE guidelines, ERCP remains the modality of choice for biliary drainage

compared to surgical bypass due to significantly higher post-operative morbidity and mortality rates with the latter[22]. A meta-analysis further supports this, showing lower 30-day mortality rates following primary biliary stenting compared to surgical bilio-digestive anastomosis.[23]. In case of a failed ERCP procedure, a rendezvous maneuver can be solicited if access to papilla is available. If the papilla is inaccessible (*i.e.,* an anomaly in anatomical structure, gastric outlet syndrome, duodenal obstruction, or history of enteral stents) or if the wire cannot be advanced due to the presence of strictures, EUS-guided biliary drainage (EUS-BD) can be performed by creating non-anatomic direct access with hepaticogastrostomy or choledochoduodenostomy[16]. A recent retrospective study also demonstrated a similar technical success rate between EUS-BD and PTBD (87.5% and 86.7%, respectively)[24]. Moreover, meta-analyses have demonstrated that EUS-BD is associated with higher clinical success, fewer post-procedural adverse events, and reduced need for repeat interventions compared to PTBD. In contrast, PTBD has been linked to higher risks of hemorrhage, cutaneous infections, tumor seeding, and catheter tract recurrence[21,22].

In our study, we also demonstrated the utilization of combination between ERCP and EUS procedure in salvage biliary drainage and the management of large pancreatic pseudocyst. We performed the procedure in a critically-ill patient with distal bile duct compression and a large pancreatic pseudocyst with prominent metabolic comorbidities. With adequate supportive care, the patient showed marked clinical improvement following the combined ERCP-EUS intervention. Similarly, a tertiary single center by de Sousa, et al. also showed excellent technical success rate in EUS-guided transmural drainage for pancreatic pseudocyst using double pigtail plastic stents. While potential complications such as stent migration, occlusion, bleeding, perforation, or false guidewire placement may occur, most can be managed effectively through clinical or endoscopic intervention.[26]

Another common issue with endoscopic biliary palliation is the re-occlusion of stents[27,28]. In our study, 3 out of 8 subjects who underwent repeated ERCP procedures had clogged stents. All of these subjects had advanced malignant biliary obstruction and ERCP procedures were proven to be beneficial in alleviating their symptoms and prolonging their survival. Several approaches have been developed to overcome the patency issue; for instance, by assimilating chemotherapeutic agents, applying anti-reflux covered SEMS design or anti-migration system[21]. While these strategies show promise, further studies are needed to validate their long-term efficacy and safety.

There are several limitations in this study. First, this is a case series study conducted in a single tertiary referral endoscopic center. Therefore, larger sample size from prospective cohort studies or a randomized clinical trial in a multi-center study are necessary to further validate our findings. However, this study demonstrated the real workflow in daily clinical practice situations, in which, the attitude of "endoscopy-first" does appear to have a significant effect on the clinical outcomes in patients with complicated biliary problems if the procedure is performed by skillful operators in specialized endoscopic centers. The low number of surgical procedures performed after endoscopic management from our data also showed that endoscopic management can still be a single-stage therapeutic option for complicated biliary cases; thus, also decreasing the concern of surgical complications and cost **(Figure 2).** Second, this was not a head-to-head comparison study between endoscopic and surgery approaches. However, this study was not meant to show which one is better as this was based on consecutive real-life clinical problems, where sometimes it could not show the outcome prediction before the procedure. Third, bias selection might occur due to unmasking available data sets. However, the author ensured that all cases in the database were analyzed without depending on their outcome of interest. Mortality as an outcome of interest was set based on death certification.

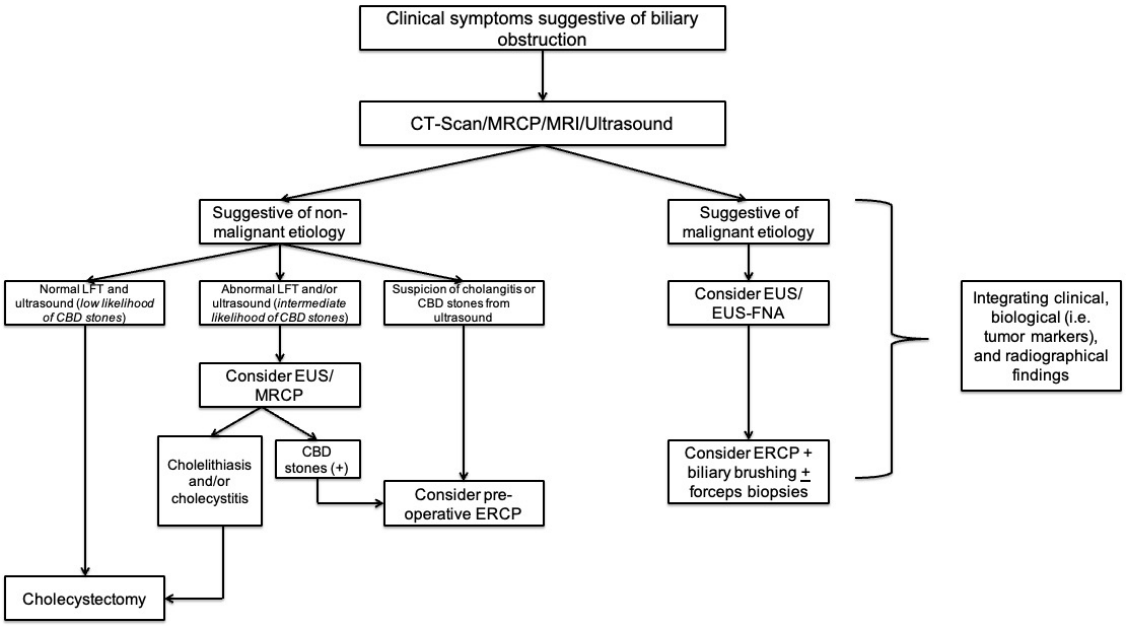

Figure 2. Proposed algorithm for management of complicated biliary cases.

CONCLUSION

In conclusion, complex biliary cases require a good clinical approach algorithm to decide which procedure comes first based on a comprehensive evaluation consisting of the patient's factor, expertise, cost, and the risk of complications. Further studies are still necessary for more detailed patients' stratification with larger sample size to make better recommendations for a clinical-based approach.

Conflict of Interest

The authors confirm that they have no competing interests.

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Author Contribution

All authors contributed to this manuscript.

Data Availability

All datasets are included within this article.

Statement of Ethics

The study was under the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975 (revised in 2008). The patient's informed consent was waived due to a retrospective database study. This study has been approved by the Medistra Hospital Institutional Review Board (Name: Health Research Ethic Committee Medistra Hospital / Ethical Approval No:003/EA/KEPKM/2021).

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