Review Article

Investigating the False Positive Rate in Diagnosing Indeterminate Biliary Stenosis

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ABSTRACT

Many bile duct structures are classified as indeterminate biliary strictures (IDBS) due to the low sensitivity of primary diagnostic techniques and the inability to differentiate between malignant and benign. Therefore, since management approaches for malignant and benign cases are different, the increase in false-positive cases has posed a diagnostic challenge for specialists. False-positive cases diagnosed as malignancy can lead to incorrect disease management and result in additional costs, such as surgery, for the patient.

The present study investigated the rate of false-positive cases in the diagnosis of IDBS and the related diagnostic challenges. The results of the evaluations showed that the use of primary techniques for diagnosing IDBS, such as endoscopic retrograde cholangiopancreatography (ERCP) and brushing, and computed tomography (CT) alone, was associated with a high false-positive rate (36.5%-47%). However, when the above techniques were combined with cholangiography, the false-positive rate decreased to 8.1%-15.1%. The results showed that the false positive rates in the diagnosis and evaluation of patiants with IDBS can vary in the range of 0%–47.7%, depending on the techniques used in patient assessment, operator expertise and skill, and patient condition.

Keywords: Indeterminate biliary stenosis, Clinical approach, ERCP, False positive rate

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INTRODUCTION

Biliary strictures that have no overt mass on non-invasive imaging and cannot be differentiated into malignant or benign lesions after endoscopic retrograde cholangiopancreatography (ERCP) fluoroscopic evaluation with standard brush cytology and/or forceps biopsy are classified as indeterminate. Therefore, since the management approaches for malignant and benign cases differ, this issue presents a diagnostic challenge for endoscopists(1).

Evidence suggests that up to 20% of biliary strictures are indeterminate, with approximately one-third of these being benign and two-thirds being malignant (2).

It has also been shown that some types of benign disease, particularly inflammatory strictures such as primary sclerosing cholangitis (PSC) and IgG4-related sclerosing cholangitis, often mimic malignancies, creating diagnostic challenges in this area (3). In addition, PSC and many chronic biliary diseases increase the risk of cholangiocarcinoma, highlighting the importance of their timely diagnosis and management (3).

The most common causes of benign biliary strictures(BBS) are iatrogenic (after liver transplantation or cholecystectomy), chronic pancreatitis, primary sclerosing cholangitis, autoimmune diseases (pancreatitis or cholangitis), and ischemic cholangiopathies (4). Malignant biliary strictures(MBS) are usually due to pancreatic adenocarcinoma and cholangiocarcinoma, and less often due to metastatic pancreatic or liver cancer, growth of ampullary tumors into the bile duct, gallbladder cancer obstructing the bile duct, or malignant lymph nodes around the portal vein. Pancreatic adenocarcinoma has been reported to be the most important cause in patients with distal common bile duct (CBD) strictures (4).Therefore, false positive cases diagnosed as malignancy will lead to incorrect disease management and result in additional costs, such as surgery, for the patient. Wakai and colleagues (5) showed that 3.3% of patients with indeterminate biliary strictures (IDBS) were falsely diagnosed as having a malignancy. This rate reached 8.1% in the study by Wetter and others (6). Currently, the use of imaging methods in identifying the site of stricture is very important. Therefore, the use of endoscopic techniques, including ERCP and endoscopic ultrasonography (EUS), plays a key role in making a correct diagnosis (7). Also, the emergence of new diagnostic methods, such as fluorescence in situ hybridization (FISH), peroral cholangioscopy (POC), intraductal endoscopic ultrasound (IDUS), and confocal laser endomicroscopy (CLE), has increased the quality and accuracy of diagnosis (7). However, it is often necessary to use different techniques simultaneously to ensure and increase the chances of correct diagnosis and reduce false positives. Therefore, in the present study, the rate of false positive cases in the diagnosis of indeterminate biliary strictures and the related diagnostic challenges were investigated.

Epidemiology and etiology

The clinical presentation in patients with biliary strictures is often variable. They may be detected incidentally on imaging in asymptomatic patients undergoing testing for other reasons or in patients presenting with abdominal pain or symptomatic jaundice. However, the clinical presentation can range from asymptomatic to fulminant cholangitis or sepsis. A careful history can help to some extent in determining the underlying cause, as painless jaundice and rapid weight loss raise suspicion of underlying malignancy. In contrast, a more progressive course is observed in those with benign strictures (2). Biliary strictures can be benign or malignant in origin and can be caused by intraductal pathology or external compression. BBS is one of the most important pathologies of the biliary system. Still, its definitive diagnosis is a challenge in clinical practice due to the difficulties of differentiating it from malignant strictures. BBS typically presents with asymptomatic elevation of liver enzymes and obstructive jaundice, with or without cholangitis (8). The most common causes of benign biliary strictures are postoperative strictures and those associated with chronic pancreatitis. Postoperative strictures can occur after cholecystectomy, biliary surgery, or liver transplantation and can result from ischemic injury, mechanical injury, anastomotic leakage, and postoperative infections caused by inflammation, underlying autoimmune disease, or malignancy. Chronic inflammation and fibrosis of the pancreatic ducts (PDs) in chronic pancreatitis can cause ulceration and narrowing of the adjacent bile ducts, leading to biliary strictures (2). In some cases, chronic inflammation may lead to extrinsic compression of the bile ducts due to the formation of adhesions and fibrosis. Other benign causes include a wide range of iatrogenic, inflammatory, infectious, and autoimmune conditions, such as choledocholithiasis, sclerosing cholangitis, choledochal cyst, chronic pancreatitis, post-cholecystectomy strictures, IgG4-mediated cholangitis, sarcoidosis, and extrinsic compression by pancreatic fluid collections (9).

However, biliary stricture in malignant conditions occurs due to tumor growth and invasion of the bile ducts or surrounding structures, inflammation, scarring, or metastasis, and is usually associated with pancreatic cancer, cholangiocarcinoma (CCA), gallbladder cancer, and metastatic cancer (2). The most common causes associated with MBS include pancreatic head carcinoma, gallbladder carcinoma, lymphoma, ampullary carcinoma, cholangiocarcinoma, hepatocellular carcinoma, and metastatic cases (9).

Diagnosis

Given that a significant proportion of biliary strictures are classified as IDBS due to the low sensitivity of primary diagnostic methods, the use of standard ERCP methods, including fluoroscopy-guided biopsies with or without brush cytology, plays a crucial role in the initial evaluation of IDBS, as they are readily available and widely familiar. However, when standard ERCP techniques are ineffective, additional endoscopic imaging modalities are employed to enhance diagnostic accuracy and minimize false positives.
Today, it has been shown that the use of new biomarkers and endoscopic techniques significantly improves diagnostic yield and plays a useful role in reducing unnecessary surgeries for benign strictures. However, evidence has shown that a single diagnostic method alone is insufficient to ensure a correct diagnosis, and the use of different techniques is necessary and reasonable to increase diagnostic accuracy.

ERCP with biliary brush cytology and intraductal biopsy

ERCP with brush cytology and intraductal biopsies is commonly used to evaluate biliary strictures suspected of being malignant. A recent meta-analysis found that brush cytology had a sensitivity of 45% and intraductal biopsies had a sensitivity of 48%, but the combination of these two methods increased the average diagnostic sensitivity to 59.4%. However, despite the low sensitivity, the specificity of 100% for confirming the diagnosis of malignancy is a positive and noteworthy point (10).
One study showed that the accuracy of detecting malignancy at the first ERCP with brushings was 54%, with brushings and biopsy 51%, and with cholangioscopy 56% (11). In general, the sensitivity of ERCP-based diagnostic methods, such as brush cytology, is relatively low and typically does not exceed 60%. However, the use of auxiliary methods, as well as the combination of different techniques, increases sensitivity and diagnostic accuracy.

Fluorescence In Situ Hybridization (FISH)

FISH is a molecular cytogenetic technique used to assess aneuploidy and has become a reliable diagnostic marker for malignancy diagnosis in patients with biliary strictures, offering improved sensitivity compared to cytology while maintaining specificity (12). FISH findings in patients with MBS can include polysomy, tetrasomy, trisomy, and a 9p deletion (13). However, a recent meta-analysis study has shown that positive FISH findings, including polysomy or 9p deletion with polysomy, exhibit the best performance characteristics, with moderate sensitivity and high specificity for diagnosing malignancy in patients with biliary stricture. It has also been recommended that, due to the low diagnostic specificity, tetrasomy or trisomy should not be routinely considered as a positive FISH result (12).
Another study also showed that FISH has a low diagnostic sensitivity of 55% and a specificity of 100% in diagnosing MBS. In fact, this study found that although this method plays a significant role in diagnosing biliary system malignancies, its use alone is not recommended due to its low diagnostic sensitivity (14). Studies have confirmed that the combination of cytology and FISH methods can be effective in evaluating proximal and distal biliary strictures, with a sensitivity of 63% and a specificity of 98% (15,16).

Computed tomography (CT)

CT has a sensitivity of 40-77% for diagnosing malignant strictures, and is more sensitive for diagnosing biliary strictures and pancreatic and biliary malignancies. Several studies have shown that CT has a sensitivity of 100% for diagnosing hilar malignancies but a low specificity (60-80%) for evaluating MBS (2). In fact, for patients in whom CT cannot diagnose MBS, the use of peroral cholangioscopy has been recommended as an adjunct (17).

Endoscopic Ultrasonography (EUS) with Fine-Needle Aspiration (FNA) or Biopsy (FNB)

EUS has now been shown to play an important role in the evaluation of IDBS, with a recent meta-analysis of 32 studies including 1123 patients with CCA reporting a diagnostic sensitivity of 73.6% for EUS-FNA compared with 56% for ERCP fluoroscopic biopsies (18). Patients suspected of having malignant biliary stricture are generally evaluated with ERCP and EUS-FNA. In the study by Mathew and others (19), EUS-FNA was more sensitive than ERCP-based tissue sampling. EUS-FNA also had a diagnostic accuracy of 92.63% compared with 71.43% for brush cytology. In fact, this study found that EUS-FNA had better sensitivity and diagnostic accuracy than ERCP-based tissue sampling. Therefore, performing EUS before ERCP in all patients suspected of MBS definitely improves diagnostic accuracy and helps in the management of such cases.
Troncone and colleagues (20) also showed that the use of EUS-FNA/B could make a final diagnosis in 96% of patients with sensitivity, specificity, and diagnostic accuracy of 73.9%, 100%, and 80%, respectively. The results of this study indicated that the combination of EUS and ERCP increased the diagnostic accuracy of IDBS. Performing both methods in one session reduces the time required for diagnostic work and optimizes resources.

Cholangioscopy

In cases of unclear biliary stricture, where initial ERCP with brushing and biopsy is inconclusive, cholangioscopy can play an important role. Cholangioscopy allows for direct visualization and targeted biopsy of the bile ducts. It was first described in 1976 and has since made significant advances (21). Evidence has shown that when cholangioscopy is used, the number of procedures is reduced by more than 30%, and the cost is reduced by 5% (22). Today, in patients with negative ERCP brushings and biopsies, the use of cholangioscopy-guided biopsies has made significant progress in the diagnosis and management of IDBS. As reported in a meta-analysis by Wen and others, the sensitivity and specificity of cholangioscopy-guided biopsies were 74% and 98%, respectively (23). Other evidence has shown that adding cholangioscopy to ERCP increased the diagnostic yield by 27% compared with ERCP alone, with a sensitivity improvement from 49.99% to 74.00% (24,25). A randomized study comparing ERCP and digital single-operator cholangioscopy (DSOC) also demonstrated significant improvements in diagnostic sensitivity. The results of this study showed that the combined approach of these two methods had a sensitivity of 77.27%, which was significantly higher than the 44.4% sensitivity observed with ERCP or DSOC alone. The combined use of the two methods maintained high specificity and positive predictive value, supporting its safety and efficacy for accurately identifying biliary stricture pathology (26). Single-operator cholangioscopy (SOC) is favored due to its availability and ease of use despite lower image quality compared with two-operator systems or reusable scopes. SOC has been recommended due to its better sensitivity and specificity than the traditional primary ERCP with brushing and biopsy (27).

The SpyGlass Direct Visualization System (SDVS)

SDVS is a catheter-based cholangioscopy tool that is highly successful in terms of diagnostic accuracy, and its use in the diagnosis of essential IDBS is recommended, as there is clear evidence that the use of this method can change the clinical outcome in more than 80% of intractable cases (28). According to a study and analysis of SDVS-based interventions in 25 patients over a three-year period, the procedural success rate was 96%, with successful visualization and biopsy in 96% of cases. In this evaluation, the sensitivity, specificity, and accuracy of visual diagnosis were reported to be 100%, 83.3%, and 96%, respectively (28).

Percutaneous transluminal clamp biopsy (PTCB)

Another less invasive method used in evaluating biliary strictures is PTCB. In a study evaluating 194 patients with biliary strictures, this method demonstrated a sensitivity of 81.8% and a specificity of 100%, with a false-negative rate of 18.2%. In fact, this study identified non-cholangiocarcinoma biliary strictures as an independent risk factor for false-negative diagnoses, highlighting the importance of cautious interpretation and the need for further investigations and additional diagnostics (29).

The results of the evaluations showed that the use of primary techniques for the diagnosis of IDBS, such as ERCP and brushing, and CT alone, is associated with a high false positive rate, with one study reporting a rate of 47% (30) and another reporting a rate of 36.5% (31). However, when the above techniques were combined with cholangiography, the false-positive rate decreased to 8.1%-15.1% (6,32-34). Additionally, in the study by Wakai and others (5), which used the PTCB technique to diagnose IDBS patients, the false-positive rate was reported to be 0%.

However, overall, study results show that the false positive rate in the diagnosis and evaluation of IDBS patients can vary from 0% to 47.7% (5, 6, 29-40) (Table 1), which depends on the techniques used in patient evaluation, the expertise and skill of the operator, and the patient's condition. Overall, the results of the evaluations show that, although the gold standard for diagnosis is histopathology of surgical specimens with progression of malignancy in clinical and radiological follow-up (20), standard ERCP with brushing and biopsy appears to be sufficient for the initial evaluation of IDBS. However, cholangioscopy-guided biopsies provide significant diagnostic benefits for IDBS. Also, the use of intraductal imaging methods such as intraductal ultrasound(IDUS) and confocal laser endomicroscopy(CLE) can provide additional specialized assistance, depending on the available facilities and resources and the clinical context. Despite the use of various techniques, IDBS remains a significant challenge in this field due to the inherent limitations of non-invasive imaging methods. Although the use of techniques such as MRI/MRCP can be essential and useful for initial evaluation, they often suffer from false negatives in distinguishing between benign and malignant strictures, especially in cases where operator expertise and patient-specific factors affect the quality of the imaging. Although malignant lesions often appear as nodular, papillary, or infiltrative masses with irregular mucosa and prominent neovascularization, sensitivity varies widely (64% to 95%) depending on the operator's expertise and technique (41,42). However, the use of advanced intraductal imaging tools, although they offer high sensitivity, is less commonly used due to high costs and the specialized training required. Therefore, it is often necessary to repeat and combine different techniques to achieve diagnostic clarity, as well as integrate advanced imaging methods with artificial intelligence-based prediction models, which can play a significant role in this field.

Table 1. Investigating the false positive rates in patients with IDBS

	Sample size	False positive rate	Pre-op investigations	Common location of the stricture	Symptoms	Years included
Alali, et al (30)	151	72 out of 151(47.7%) in patients with indeterminate biliary strictures and atypical biliary cytology	Ultrasound, CT, ERCP, and brushing	CBD	Jaundice, abdominal pain	2011 to 2016
Navaneethan, et al (31)	104	36.5% of patients with indeterminate biliary stricture and atypical cells on brush cytology were subsequently diagnosed with malignancy	Ultrasound, CT, MRI, EUS, ERCP	CBD	Jaundice, Weight loss, Abdominal pain, pruritus, fever	1996 -2012
Fujita T, et al (35)	176	5 of 176 (2.8%)	Percutaneous transhepatic cholangiography, ERCP, MRCP, IgG4		Jaundice	1993 - 2008
Hadjis et al (36)	104	8 (7.7%)		Common hepatic duct		
Erdogan et al (37)	185	32 (17.3%)		Proximal bile ducts		
Are et al. (38)	171	9 (5.2%)	CT, MRCP, Duplex ultrasonography			
Uhlmann et al (39)	49	7 (14.3%)				
Corvera et al (40)	275	22 (8.0%)				
Gerhards et al (32)	132	20 (15.1%)	CT, Cholangiography, Doppler ultrasonography		Jaundice, Weight loss, Abdominal pain, discoloration of stool	
Nakayama et al (33)	99	14 (14.1%)	cholangiography and angiography			
Verbeek et al (34)	82	11 (13.4%)	cholangiography and ultrasonography			
Wetter et al (6)	98	8 (8.1%)	ultrasound and CT, percutaneous transhepatic cholangiography, ERCP			
Wakai T et al (5)	153	5 (3.3%)				1990 -2010
Zhang et al (29)	194	0%	PTCB			2016-2021

Management and Treatments

The evaluation and management of patients with IDBS begins with determining the pathogenesis of the stricture using clinical symptoms, laboratory tests, non-invasive and invasive imaging, and various tissue sampling methods. Once biliary obstruction is identified, an efficient approach to initial diagnostic testing and management is important to reduce complications and guide definitive treatment (43). In the treatment of IDBS, restoration of biliary flow to the duodenum is important. In general, IDBS should be considered malignant unless proven otherwise. In IDBS accompanied by high serum bilirubin levels or with intractable cholangitis or pruritus, adequate biliary drainage is required, and endoscopic treatment, especially ERCP with stent placement, is the first-line treatment in this regard (44). In fact, in the treatment of BBS, the use of stents can be helpful by optimally relieving the stenosis and limiting it. However, it should be noted that one of the main complications of stenting is early duodenal migration of the device, which varies according to the type of stent, the characteristics of the stenosis (malignant or benign), and the patient (45,46). EUS-guided biliary drainage can be a good option in cases of ERCP failure. The percutaneous method can still be an acceptable alternative in all cases of failure or ineffectiveness of the endoscopic method (44).

CONCLUSION

Studies have shown that the false-positive rate in the diagnosis and evaluation of patients with IDBS can vary in the range of 0%-47.7%, depending on the techniques used in patient assessment, operator expertise and skill, and patient condition. Therefore, although standard ERCP with brushing and biopsy appears to be sufficient for the initial evaluation of IDBS, cholangioscopy-guided biopsies provide significant diagnostic advantages for IDBS, and often repetition and combination of different techniques are necessary to achieve diagnostic resolution and reduce false positives. The integration of advanced imaging methods with AI-based predictive models can play a significant role in this field. Therefore, it is recommended that future studies investigate the role of AI and its application alongside conventional techniques in the diagnosis and assessment of IDBS and in minimizing false positives.

REFRENCES:

1. Oleas R, Alcívar-Vasquez J, Robles-Medranda C. New technologies for indeterminate biliary strictures. *Transl Gastroenterol Hepatol*. 2022;7:22.
2. Yadlapati S, Mulki R, Sánchez-Luna SA, Ahmed AM, Baig KR, Peter S. Clinical approach to indeterminate biliary strictures: Clinical presentation, diagnosis, and workup. *World J Gastroenterol*. 2023; 29 (36): 5198-210.
3. Bowlus CL, Olson KA, Gershwin ME. Evaluation of indeterminate biliary strictures. *Nat Rev Gastroenterol Hepatol*. 2016; 13 (1): 28-37.
4. Singh A, Gelrud A, Agarwal B. Biliary strictures: diagnostic considerations and approach. *Gastroenterol Rep*. 2015; 3 (1): 22-31.
5. Wakai T, Shirai Y, Sakata J, Maruyama T, Ohashi T, Korira PV, et al. Clinicopathological features of benign biliary strictures masquerading as biliary malignancy. *Am Surg*. 2012; 78 (12): 1388-91.
6. Wetter LA, Ring EJ, Pellegrini CA, Way LW. Differential diagnosis of sclerosing cholangiocarcinomas of the common hepatic duct (Klatskin tumors). *Am Surg*. 2012; 78 (12): 1388-91.
7. Xie C, Aloreidi K, Patel B, Ridgway T, Thambi-Pillai T, Timmerman G, et al. Indeterminate biliary strictures: a simplified approach. *Expert Rev Gastroenterol Hepatol*. 2018; 12 (2): 189-99.
8. Sharma P, Arora A. Benign biliary stricture: Causes and management. *Hepatology* 2025;429-44). Academic Press.
9. Raza D, Singh S, Crinò SF, Boskoski I, Spada C, Fuccio L, et al. Diagnostic Approach to Biliary Strictures. *Diagnostics*. 2025; 15 (3): 325.
10. Navaneethan U, Njei B, Lourdusamy V, Konjeti R, Vargo JJ, Parsi MA. Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. *Gastrointestinal Endosc*. 2015; 81(1): 168-76.
11. Coronel M, Kumar D, Bahdi F, Kumar S, Lum P, Nogueras G, et al. The Use of ERCP in the Diagnosis of Indeterminate Biliary Strictures: Experience From a Large Tertiary Care Center. *Official Journal of the American College of Gastroenterology| ACG*. 2021; 116: S1320.
12. Aggarwal M, Simadibrata DM, Kipp BR, Prokop LJ, Barr Fritcher EG, Schneider A, et al. Diagnostic Accuracy Performance of Fluorescence In Situ Hybridization (FISH) for Biliary Strictures: A Systematic Review and Meta-Analysis. *J Clin Med*. 2024; 13 (21): 6457.
13. Adler DG, Witt B. Cytologic diagnosis of biliary strictures: FISH or cut the sensitivity rate?. *Dig Dis Sci*. 2018; 63: 549-50.
14. Singhi AD, Slivka A. Evaluation of indeterminate biliary strictures: Is it time to FISH or cut bait?. *Gastrointest Endosc*. 2016; 83(6):1236-8.
15. Gonda TA, Viterbo D, Gausman V, Kipp C, Sethi A, Poneros JM, et al. Mutation profile and fluorescence in situ hybridization analyses increase detection of malignancies in biliary strictures. *Clin Gastroenterol Hepatol*. 2017; 15(6):913-19. e1.
16. Brooks C, Gausman V, Kokoy-Mondragon C, Munot K, Amin SP, Desai A, et al. Role of fluorescent in situ hybridization, cholangioscopic biopsies, and EUS-FNA in the evaluation of biliary strictures. *Dig Dis Sci*. 2018; 63(3): 636-44.
17. Shima Y, Sugiyama H, Ogasawara S, Kan M, Maruta S, Yamada T, et al. Diagnostic value of peroral cholangioscopy in addition to computed tomography for indeterminate biliary strictures. *Surg Endosc*. 2022; 36 (5): 3408-17.
18. Yoon SB, Moon SH, Ko SW, Lim H, Kang HS, Kim JH. Brush cytology, forceps biopsy, or endoscopic ultrasound-guided sampling for diagnosis of bile duct cancer: a meta-analysis. *Dig Dis Sci*. 2022; 67(7): 3284-97.
19. Mathew P, Kanni P, Gowda M, Devarapu C, Ansari J, Garg A, et al. A comparative study of endoscopic ultrasound fine-needle aspiration (EUS-FNA) and endoscopic retrograde cholangiopancreatography (ERCP)-based brush cytology for tissue diagnosis in malignant biliary obstruction. *Cureus*. 2022; 14 (10): e30291.
20. Troncone E, Gadaleta F, Paoluzi OA, Gesuale CM, Formica V, Morelli C, et al. Endoscopic ultrasound plus endoscopic retrograde cholangiopancreatography based tissue sampling for diagnosis of proximal and distal biliary stenosis due to cholangiocarcinoma: results from a retrospective single-center study. *Cancers*. 2022; 14(7): 1730.
21. Turowski F, Hügle U, Dormann A, Bechtler M, Jakobs R, Gottschalk U, et al. Diagnostic and therapeutic single-operator cholangiopancreatoscopy with SpyGlassDS™: results of a multicenter retrospective cohort study. *Surg Endosc*. 2018;

32 (9): 3981-88.
22. Deprez PH, Duran RG, Moreels T, Furneri G, Demma F, Verbeke L, et al. The economic impact of using single-operator cholangioscopy for the treatment of difficult bile duct stones and diagnosis of indeterminate bile duct strictures. *Endoscopy*. 2018; 50 (02):109-18.
23. Wen LJ, Chen JH, Xu HJ, Yu Q, Liu K. Efficacy and safety of digital single-operator cholangioscopy in the diagnosis of indeterminate biliary strictures by targeted biopsies: a systematic review and meta-analysis. *Diagnostics*. 2020; 10 (9): 666.
24. Gerges C, Beyna T, Tang RS, Bahin F, Lau JY, van Geenen E, et al. Digital single-operator peroral cholangioscopy-guided biopsy sampling versus ERCP-guided brushing for indeterminate biliary strictures: a prospective, randomized, multicenter trial (with video). *Gastrointest Endosc*. 2020; 91 (5): 1105-13.
25. Walter D, Peveling-Oberhag J, Schulze F, Bon D, Zeuzem S, Friedrich-Rust M, et al. Intraductal biopsies in indeterminate biliary stricture: Evaluation of histopathological criteria in fluoroscopy-vs. cholangioscopy guided technique. *Dig Liver Dis*. 2016; 48 (7): 765-70.
26. Kumar D, Dayal VM, Jha SK, Jha AK, Kumar RK. A Randomized Comparative Study of the Use of Individual Modality and Combination of Endoscopic Retrograde Cholangiopancreatography (ERCP) and Digital Single-Operator Cholangioscopy (DSOC) for Diagnosis of Indeterminate Biliary Strictures. *Adv Biomed Res*. 2024: 13:4.
27. Rey Rubiano AM, González-Teshima LY, Arango L, Blanco-Avellaneda C, Carvajal Gutiérrez JJ, Castaño-Llano R, et al. Clinical practice guideline on the use of single-operator cholangioscopy in the diagnosis of indeterminate biliary stricture and the treatment of difficult biliary stones. *Surg Endosc*. 2024; 38(2): 499-510.
28. Pallio S, Sinagra E, Santagati A, D'Amore F, Pompei G, Conoscenti G, et al. Use of catheter-based cholangioscopy in the diagnosis of indeterminate stenosis: a multi-centre experience. *Minerva Gastroenterol (Torino)*. 2024; 70 (1): 29-35.
29. Zhang C, Li Y, Song M, Sun Z, Han X, Ren J, et al. False-negative factors of percutaneous transluminal clamp biopsy for suspected malignant biliary stricture: 194 cases analyzed from a single center. *Insights Imaging*. 2024; 15 (1): 108.
30. Alali A, Moris M, Martel M, Streutker C, Cirocco M, Mosko J, et al. Predictors of malignancy in patients with indeterminate biliary strictures and atypical biliary cytology: Results from retrospective cohort study. J *Can Assoc Gastroenterol*. 2021; 4(5): 222-8.
31. Navaneethan U, Singh T, Gutierrez NG, Jegadeesan R, Venkatesh PG, Brainard J, et al. Predictors for detection of cancer in patients with indeterminate biliary stricture and atypical cells on endoscopic retrograde brush cytology. *J Dig Dis*. 2014; 15 (5): 268-75.
32. Gerhards MF, Vos P, Van Gulik TM, Rauws EA, Bosma A, Gouma DJ. Incidence of benign lesions in patients resected for suspicious hilar obstruction. *Br J Surg*. 2001; 88(1): 48-51.
33. Nakayama A, Imamura H, Shimada R, Miyagawa SI, Makuuchi M, Kawasaki S. Proximal bile duct stricture disguised as malignant neoplasm. *Surgery*. 1999; 125(5): 514-21.
34. Verbeek PC, Van Leeuwen DJ, De Wit L, Reeders JW, Smits NJ, Bosma A, et al. Benign fibrosing disease at the hepatic confluence mimicking Klatskin tumors. *Surgery*. 1992; 112(5): 866-71.
35. Fujita T, Kojima M, Gotohda N, Takahashi S, Nakagohri T, Konishi M, et al. Incidence, clinical presentation and pathological features of benign sclerosing cholangitis of unknown origin masquerading as biliary carcinoma. *J Hepatobiliary Pancreat Sci*. 2010; 17(2): 139-46.
36. Hadjis NS, Collier NA, Blumgart LH. Malignant masquerade at the hilum of the liver. *Br J Surg*. 1985; 72: 659–61.
37. Erdogan D, Kloek JJ, Ten Kate FJ, Rauws EA, Busch OR, Gouma DJ, et al. Immunoglobulin G4-related sclerosing cholangitis in patients resected for presumed malignant bile duct strictures. *J British Surg*. 2008; 95(6): 727-34.
38. Are C, Gonen M, D'Angelica M, DeMatteo RP, Fong Y, Blumgart LH, et al. Differential diagnosis of proximal biliary obstruction. *Surgery*. 2006; 140(5): 756-63.
39. Uhlmann D, Wiedmann M, Schmidt F, Kluge R, Tannapfel A, Berr F, et al. Management and outcome in patients with Klatskin-mimicking lesions of the biliary tree. *J Gastrointest Surg*. 2006; 10: 1144-50.
40. Corvera CU, Blumgart LH, Darvishian F, Klimstra DS, DeMatteo R, Fong Y, et al. Clinical and pathologic features of proximal biliary strictures masquerading as hilar cholangiocarcinoma. *J Am Coll Surg*. 2005; 201(6): 862-9.
41. Kahaleh M, Gaidhane M, Shahid HM, Tyberg A, Sarkar A, Ardengh JC, et al. Digital single-operator cholangioscopy interobserver study using a new classification: the Mendoza Classification (with video). *Gastrointest Endosc*. 2022; 95(2): 319-26.
42. Sethi A, Tyberg A, Slivka A, Adler DG, Desai AP, Sejpal DV, et al. Digital single-operator cholangioscopy (DSOC) improves interobserver agreement (IOA) and accuracy for evaluation of indeterminate biliary strictures: the Monaco classification. *J Clin Gastroenterol*. 2022; 56(2):e94-7.
43. Petersen BT. Indeterminate biliary stricture. *InErcp* 2019 (pp. 394-404). Elsevie
44. Impellizzeri G, Grassini MV, Donato G, De Angelis CG, Pagano N. An Approach to and Treatment of Indeterminate Biliary Strictures: A Comprehensive Review of the Literature. *J Clin Med*. 2024; 14(1): 29.
45. Chaput U, Vienne A, Audureau E, Bauret P, Bichard P, Coumaros D, et al. Temporary placement of fully covered self-expandable metal stents for the treatment of benign biliary strictures. *United European Gastroenterol J*. 2016; 4(3): 403-12.
46. Taghavi SA, Ejtehadi F, Niknam R, Sivandzadeh GR, Tahani M, Aminisefat A, et al. Biliary Stent Migration: A Review of the Literature. *GOVARESH*. 2024; 29(1): 23-31.