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EDITORIAL

- 3074 Changes over time in treatment for obstructive jaundice
Aoki H
- 3078 Single incision laparoscopic surgery for hepatocellular carcinoma
Karabicak I, Yildirim K, Gursel MF, Malazgirt Z
- 3084 Impact of liver metastasis on immunotherapy in gastric carcinoma
Chalkoo M, Bhat MY, Wani YH
- 3087 Urgent need for prognostic markers for hepatocellular carcinoma in the light of genomic instability and non-coding RNA signatures
Velikova T, Gulinac M
- 3091 Advancing perioperative optimization in Crohn's disease surgery with machine learning predictions
Nardone OM, Castiglione F, Maurea S
- 3094 Exploring the landscape of minimally invasive pancreatic surgery: Progress, challenges, and future directions
Donisi G, Zerbi A

ORIGINAL ARTICLE**Case Control Study**

- 3104 Three-dimensional printing for preoperative rehearsal and intraoperative navigation during laparoscopic rectal cancer surgery with left colic artery preservation
Zhao ZX, Hu ZJ, Yao RD, Su XY, Zhu S, Sun J, Yao Y

Retrospective Cohort Study

- 3114 Local excision of early rectal cancer: A multi-centre experience of transanal endoscopic microsurgery from the United Kingdom
Farid A, Tutton M, Thambi P, Gill T, Khan J
- 3123 Clinical significance of peri-appendiceal abscess and phlegmon in acute complicated appendicitis patients undergoing emergency appendectomy
Min LQ, Lu J, He HY
- 3133 Development of a novel difficulty scoring system for laparoscopic liver resection procedure in patients with intrahepatic duct stones
Luo B, Wu SK, Zhang K, Wang PH, Chen WW, Fu N, Yang ZM, Hao JC

Retrospective Study

- 3142** Serum nutritional predictive biomarkers and risk assessment for anastomotic leakage after laparoscopic surgery in rectal cancer patients
Shayimu P, Awula M, Wang CY, Jiapaer R, Pan YP, Wu ZM, Chen Y, Zhao ZL
- 3155** Impact of fast-track surgery on perioperative care in patients undergoing hepatobiliary surgery
Wang XH, Chen FF, Pan J, Jiang YF, Yao MY, Mao JL, Xu YF
- 3163** Follow-up strategy for early detection of delayed pseudoaneurysms in patients with blunt traumatic spleen injury: A single-center retrospective study
Cho SH, Kim GW, Hwang S, Lim KH
- 3171** Adjuvant chemotherapy for isolated resectable colorectal lung metastasis: A retrospective study using inverse probability treatment weighting propensity analysis
Gao Z, Wu SK, Zhang SJ, Wang X, Wu YC, Jin X
- 3185** Recurrence scoring system predicting early recurrence for patients with pancreatic ductal adenocarcinoma undergoing pancreatectomy and portomesenteric vein resection
He H, Zou CF, Jiang YJ, Yang F, Di Y, Li J, Jin C, Fu DL
- 3202** Effects of postoperative treatment with chemotherapy and cellular immunotherapy on patients with colorectal cancer
Ding ZY, Piao Y, Jiang T, Chen J, Wang YN, Yu HY, Zheng ZD
- 3211** Postoperative serum tumor markers-based nomogram predicting early recurrence for patients undergoing radical resections of pancreatic ductal adenocarcinoma
He H, Zou CF, Yang F, Di Y, Jin C, Fu DL
- 3224** Comparison of efficacy and safety of nab-paclitaxel and oxaliplatin + S-1 and standard S-1 and oxaliplatin chemotherapy regimens for treatment of gastric cancer
Wang YC, Feng L, Wang GP, Yu PJ, Guo C, Cai BJ, Song Y, Pan T, Lin BH, Li YD, Xiao JJ
- 3239** Risk factors and survival prediction model establishment for prognosis in patients with radical resection of gallbladder cancer
Li XF, Ma TT, Li T

Observational Study

- 3253** Surgical and non-surgical risk factors affecting the insufficiency of ileocolic anastomosis after first-time surgery in Crohn's disease patients
Cwaliński J, Lorek F, Mazurkiewicz Ł, Mazurkiewicz M, Lizurej W, Paszkowski J, Cholerzyńska H, Zasada W
- 3261** Relationship between intracranial pressure and neurocognitive function among older adults after radical resection of rectal cancer
Song B, Li LP, Wang XL, Guo Y, Li J

Prospective Study

- 3269** Prevention and management of postoperative deep vein thrombosis in lower extremities of patients with gastrointestinal tumor
Shu L, Xia CW, Pang YF

Randomized Controlled Trial

- 3277** Clinical evaluation of sintilimab in conjunction with bevacizumab for advanced colorectal cancer with microsatellite stable-type after failure of first-line therapy
Wang L, Diao YZ, Ma XF, Luo YS, Guo QJ, Chen XQ

Clinical and Translational Research

- 3288** Structured magnetic resonance imaging and endoanal ultrasound anal fistulas reporting template (SMART): An interdisciplinary Delphi consensus
Sudol-Szopińska I, Garg P, Mellgren A, Spinelli A, Breukink S, Iacobellis F, Kołodziejczak M, Ciesielski P, Jenssen C, SMART Collaborative Group, Santoro GA

CASE REPORT

- 3301** Formation and rupture of liver hematomas caused by intrahepatic gallbladder perforation: A case report and review of literature
Huang HW, Wang H, Leng C, Mei B
- 3312** Reassessment of palliative surgery in conversion therapy of previously unresectable hepatocellular carcinoma: Two case reports and review of literature
Zhu YB, Qin JY, Zhang TT, Zhang WJ, Ling Q
- 3321** Lung cancer metastasis-induced distal esophageal segmental spasm confirmed by individualized peroral endoscopic myotomy: A case report
Shi H, Chen SY, Xie ZF, Lin LL, Jiang Y
- 3328** Modified technical protocol for single-port laparoscopic appendectomy using needle-type grasping forceps for acute simple appendicitis: A case report
Chen Y, Fan ZQ, Fu XA, Zhang XX, Yuan JQ, Guo SG
- 3334** Massive simultaneous hepatic and renal perivascular epithelioid cell tumor benefitted from surgery and everolimus treatment: A case report
Yang HT, Wang FR, He N, She YH, Du YY, Shi WG, Yang J, Chen G, Zhang SZ, Cui F, Long B, Yu ZY, Zhu JM, Zhang GY
- 3343** Leukopenia—a rare complication secondary to invasive liver abscess syndrome in a patient with diabetes mellitus: A case report
Niu CY, Yao BT, Tao HY, Peng XG, Zhang QH, Chen Y, Liu L
- 3350** Acute gastric volvulus combined with pneumatosis coli rupture misdiagnosed as gastric volvulus with perforation: A case report
Zhang Q, Xu XJ, Ma J, Huang HY, Zhang YM

LETTER TO THE EDITOR

- 3358** Can serious postoperative complications in patients with Crohn's disease be predicted using machine learning?
Zbar AP
- 3363** Influencing factors and preventive measures of infectious complications after intestinal resection for Crohn's disease
Lv SR, Huang X, Zhou LY, Shi J, Gong CC, Wang MK, Yang JS
- 3371** Evaluation of preoperative blood markers for predicting intra-abdominal infection during colorectal cancer resection: A commentary on recent findings
Zhang SY, Chen J, Cai N
- 3374** Differential diagnosis of gastric submucosal masses and external pressure lesions
Na Y, Liu XD, Xu HM
- 3377** Contributing to the prediction of prognosis for treated hepatocellular carcinoma: Imaging aspects that sculpt the future
Lindner C

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Surgery*, Michele Ammendola, MD, Research Associate, Surgical Oncologist, Science of Health Department, Digestive Surgery Unit, University of "Magna Graecia" Medical School, Catanzaro 88100, Italy. michele.ammendola@unicz.it

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Changes over time in treatment for obstructive jaundice

Hideki Aoki

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Hideki Aoki, Department of Surgery, National Hospital Organization Iwakuni Clinical Center, Iwakuni 740-8510, Yamaguchi, Japan

Corresponding author: Hideki Aoki, PhD, Chief Physician, Department of Surgery, National Hospital Organization Iwakuni Clinical Center, 1-1-1 Atago, Iwakuni 740-8510, Yamaguchi, Japan. xxaoki@gmail.com

Abstract

This editorial discusses an article by Peng *et al.* This study reviewed the efficacy and safety of a new approach for treating obstructive jaundice. Although the pathophysiology of obstructive jaundice has not yet been fully elucidated, progress has been made in its management. There are two aspects of obstructive jaundice: Cholestatic status and absence of bile in the intestinal lumen. Internal biliary drainage resolved both the conditions. Clinically, endoscopic retrograde biliary drainage (ERBD) has replaced percutaneous transhepatic biliary drainage, and ERBD is transitioning to endoscopic ultrasound guided biliary drainage. This editorial briefly explains the mechanism and treatment of obstructive jaundice and the prospects of this new internal biliary drainage technique.

Key Words: Obstructive jaundice; Intestinal permeability; Biliary drainage; Endoscopic retrograde biliary drainage; Endoscopic ultrasound guided biliary drainage

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Core Tip: Internal drainage is considered ideal for biliary drainage; endoscopic retrograde biliary drainage (ERBD) has replaced percutaneous transhepatic biliary drainage, and ERBD is transitioning to endoscopic ultrasound guided biliary drainage. This editorial describes longitudinal studies on obstructive jaundice and the prospects for new internal biliary drainage.

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INTRODUCTION

Obstructive jaundice is a long-term challenge for surgeons. Jaundice is associated with significant morbidity and mortality due to septic complications and renal dysfunction[1,2]. Many clinical and experimental studies were conducted in the 1990s to investigate pathophysiology of obstructive jaundice[3,4]; these studies revealed that gut-derived endotoxins play an important role. Patients with jaundice are believed to be immunocompromised, and the impairment of reticuloendothelial cells, particularly Kupffer cells, are involved. Cholestatic status may impair Kupffer cell function, and Kupffer cell dysfunction may allow gut-derived endotoxins to enter systemic circulation[5]. However, it is unclear how and by what pathway these endotoxins invade the human body.

TWO ASPECTS OF OBSTRUCTIVE JAUNDICE

There are two aspects of obstructive jaundice: Cholestatic status and absence of bile in the intestinal lumen. The bile contains bile acids, bile salts, and secretory IgA. Bile acids, bilirubin, drugs, and other substances in bile enter the intestine, are absorbed by enterocytes, and are transported back to the liver. The bile acids delivered to the duodenum are recycled approximately 6-10 times per day, constituting a collective total of 95% of all bile acid recycling. When the biliary system is obstructed, there is a deficit in the enterohepatic circulation of bile. Bile salts and secretory IgA play important roles in gut barrier function[6]. Bile acids inhibit the growth of certain bacteria and exert trophic effects on intestinal mucosa. Oral deoxycholate or lactulose is administered to reduce the absorption of endotoxins, and it appears to protect against renal impairment after surgery. Pain *et al*[7] stated that although no significant difference was noted, one patient and none in the control ($n = 35$) and treatment groups ($n = 35$ in lactulose and $n = 32$ in sodium deoxycholate) developed postoperative renal failure[7]. As for secretory IgA, in normal situation, approximately 36% of the gut microbiota is coated with secretory IgA, whereas during inflammation, this number can increase up to 69%. Secretory IgA is involved in maintaining intestinal homeostasis by neutralizing pathogenic microorganisms and regulating the gut microbiota composition[8].

INTESTINAL PERMEABILITY

Increased intestinal permeability was directly observed in jaundiced patients, especially after surgical intervention, by the lactulose-mannitol test[9]. Before internal biliary drainage such as endoscopic retrograde biliary drainage became widespread, percutaneous transhepatic biliary drainage (PTBD) was the main procedure. External biliary drainage resolves the cholestatic status, and liver dysfunction recovers to some extent. However, the drained bile is abandoned, and the deficit of enterohepatic circulation of bile continues. Some experimental studies have demonstrated the superiority of internal biliary drainage[3,10]. Gouma *et al*[10] reported mortality following peritonitis in rats with obstructive jaundice after relief from internal or external biliary drainage. The mortality rate after internal drainage was significantly lower (25%) than after external drainage (63%)[10]. However, internal biliary drainage was not routinely performed in clinical settings at that time. Clinically, bile replacement during external biliary drainage restores the intestinal barrier function in jaundiced patients by repairing physical damage to the intestinal mucosa. Kamiya *et al*[11] reported that the biliary concentrations of bile acids, cholesterol, and phospholipids significantly increased, and the lactulose-mannitol ratio significantly decreased after bile replacement[11].

INTERNAL BILIARY DRAINAGE

Although some mechanisms have become clear in obstructive jaundice, complications occur at a certain frequency among patients with jaundice, especially after hepatectomy. Therefore, it is essential to improve the condition of patients with jaundice before surgery. Internal biliary drainage resolves cholestasis and bile absence. When endoscopic retrograde cholangiopancreatography (ERCP) fails, PTBD or bypass biliary reconstruction are the only treatment options for treating obstructive jaundice thus far. PTBD is associated with a high rate of complications and dislodgement, and bypass surgery is invasive. In unresectable cases, one report indicated that ERCP was associated with significantly reduced mortality compared with PTBD in patients with pancreatic cancer[12].

In contrast, van der Gaag *et al*[13] revealed that routine preoperative biliary drainage in patients undergoing surgery for pancreatic head cancer increased the rate of complications. The problem was cholangitis after biliary drainage[13]. Drainage was performed mainly *via* endoscopic plastic stent placement. Moreover, in their meta-analysis, Tian *et al*[14] concluded that external drainage is better than internal drainage for malignant biliary obstruction in terms of rate of preoperative cholangitis rate, incidence of stent dysfunction, and total morbidity[14]. They also stated that plastic stents were predominantly used by patients involved. Cholangitis is a problem in patients with cancer undergoing chemotherapy or surgery; therefore, an expandable metallic stent (EMS), which can secure a larger caliber, is becoming the device of choice. In a meta-analysis, Lyu *et al*[15] revealed that the use of EMS in patients with pancreatic cancer undergoing neoadjuvant therapy followed by surgery was associated with lower rates of reintervention, delay of neoadjuvant therapy, recurrent biliary obstruction, and cholangitis than the use of plastic stents. Specifically, the rate of postprocedural cholangitis was 15.4% and 32.5% with EMS and plastic stents, respectively[15]. The clinical guidelines of

the American College of Gastroenterology state that EMS provides significantly longer stent patency and reduces cholangitis events than plastic stents and recommend that EMS be applied to patients with extrahepatic biliary stricture attributable to a resectable malignancy who will undergo preoperative neoadjuvant therapy[16]. However, EMS is associated with a significant range of postprocedural complications, including pancreatitis and cholecystitis, when a covered stent is used.

Endoscopic ultrasound-guided biliary drainage (EUS-BD) using electrocautery-enhanced lumen-apposing metal stents (ECE-LAMs) is a suitable treatment option to resolve these issues. Peng *et al*[17] emphasize a high success rate and low incidence of adverse events, even when performed by nonexperts. However, they mentioned that most of the included studies were retrospective, possibly causing a selection bias. But one distinct advantage of EUS-BD is the significantly reduced rate of postprocedural pancreatitis, which is sometimes lethal. EUS-BD with ECE-LAMS is a palliative treatment option. Although this method has adaptation limitations, it has the potential to become the first choice and is widely used. Furthermore, EUS-BD using ECE-LAMS has been recognized as a bridge-to-surgery approach for planned pancreatoduodenectomies. Chen *et al*[18] conducted a multicenter, randomized controlled study comparing EUS-BD with lumen-apposing metal (LAM) ($n = 73$) and EMS ($n = 71$) in patients with malignant biliary obstruction stemming from unresectable, locally advanced, or borderline resectable periampullary cancers. No significant differences were noted in safety, clinical success, or postoperative outcomes; however, EUS-BD with LAM was associated with a significantly shorter procedural time and lower radiation exposure than EMS. EUS-BD is a relatively new technology, and studies on EUS-BD are ongoing. Further investigation, including long-term results, requires large-scale prospective studies.

CONCLUSION

The bile should be returned to the intestine. Internal biliary drainage is ideal both physiologically and cosmetically. This editorial briefly describes these theories.

FOOTNOTES

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Country of origin: Japan

ORCID number: Hideki Aoki [0000-0003-3892-1123](https://orcid.org/0000-0003-3892-1123).

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