

# Palliative endoscopic retrograde biliary drainage for malignant biliary obstruction in Korea: A nationwide assessment

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## Abstract

**Background:** Malignant biliary obstruction (MBO) is usually caused by biliary tract cancer or pancreatic cancer. This study was performed to summarize the current situation regarding palliative endoscopic retrograde biliary drainage (ERBD) for MBO in Korea and to determine its clinical significance by analyzing representative nationwide data.

**Methods:** Patients that underwent palliative ERBD for MBO between 2012 and 2015 were identified using the Health Insurance Review and Assessment database, which covers the entire Korean population. We assessed clinical characteristics and complications and compared the clinical impacts of initial metal and plastic stenting in these patients.

**Results:** A total of 9,728 subjects (mean age,  $65 \pm 11.4$  years; male, 61.4%) were identified and analyzed. The most common diagnosis was malignant neoplasm of liver and intrahepatic bile ducts (32.1%) and this was followed by extrahepatic or Ampulla of Vater cancer and pancreatic cancer. Initial plastic stent(s) placement was performed in 52.9% of the study subjects, and metal stent(s) placement was performed in 23.3%. The number of sessions of endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic biliary drainage (PTBD) was significantly higher in patients that underwent initial plastic stenting than in patients that underwent metal stenting ( $2.2 \pm 1.7$  vs  $1.8 \pm 1.4$ ,  $P < 0.0001$ ), but rates of post-ERCP pancreatitis, hospital days, and time to second ERCP or PTBD were not significantly different.

**Conclusion:** This nationwide assessment study suggests that initial metal stenting is associated with fewer sessions of total ERCP or PTBD following the initial procedure, despite the preference for initial plastic stenting in Korea.

**Keywords:** Biliary tract neoplasms, endoscopic retrograde cholangiopancreatography, Korea, obstructive jaundice, pancreatic neoplasms, stents

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**Submitted:** 21-Oct-2020 **Revised:** 03-Jan-2021 **Accepted:** 04-Jan-2021 **Published:** 15-Mar-2021

Access this article online	
Quick Response Code:	Website: www.saudijgastro.com
	DOI: 10.4103/sjg.sjg_589_20

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**How to cite this article:** Jang DK, Kim J, Yoon SB, Yoon WJ, Kim JW, Lee TH, *et al.* Palliative endoscopic retrograde biliary drainage for malignant biliary obstruction in Korea: A nationwide assessment. Saudi J Gastroenterol 2021;27:173-7.

## INTRODUCTION

Malignant biliary obstruction (MBO) is caused by an intrinsic obstruction or extrinsic bile duct compression, which is usually caused by biliary tract cancer or pancreatic cancer.<sup>[1]</sup> MBO location depends on the type of cancer. Distal MBO is caused by periampullary cancers such as pancreatic head cancer (accounts for ~70% of pancreatic cancers) and distal bile duct cancer (20-30% of all cholangiocarcinomas), while proximal MBO is primarily caused by hilar cholangiocarcinoma, which accounts for ~60% of all biliary tract cancers. Treatment strategies depend on whether cancers are operable or metastatic.<sup>[2]</sup>

MBO causes pruritus, weight loss, malaise, and abdominal discomfort or pain, and obstructive jaundice that can be complicated by serious cholangitis, sepsis, or hepatic failure,<sup>[3,4]</sup> which negatively affect patient survival and quality of life. Therefore, various methods must be used to resolve unresectable MBO. Endoscopic retrograde biliary drainage (ERBD) is preferred over percutaneous transhepatic biliary drainage (PTBD) for MBO palliation because of its lower adverse event rate, shorter hospitalization, fewer sessions, and lower cost.<sup>[5]</sup> Recently, endoscopic ultrasound-guided biliary drainage has become a rescue treatment after failed ERBD for MBO.<sup>[6-8]</sup>

A recent European guideline strongly recommends self-expandable metal stents (SEMSs) rather than plastic stents insertion for the palliative drainage of distal MBO because of longer patient survival, a lower risk of stent dysfunction/cholangitis, and fewer reinterventions. The

guideline also recommends uncovered SEMS for the palliative drainage of hilar MBO ensuring drainages of  $\geq 50\%$  of liver volume.<sup>[8]</sup> We performed this study to summarize the current situation in Korea for palliative ERBD for MBO and to determine the clinical impacts of plastic and metal stent use by analyzing representative nationwide data.

## METHODS

### Data source

This study was performed using data extracted from the Health Insurance Review and Assessment Service (HIRA) database, which includes all National Health Insurance Service (NHIS) and National Medical Aid claims data. This database covers the entire Korean population and includes information on diagnoses, drug prescriptions, procedures or operations, and medical costs. Individual medical records are anonymized. This study protocol was approved by the Institutional Review Board of Dongguk University Ilsan Hospital (No. DUIH-IRB 2019-01-003), which waived the requirement for informed consent.

### Study subjects

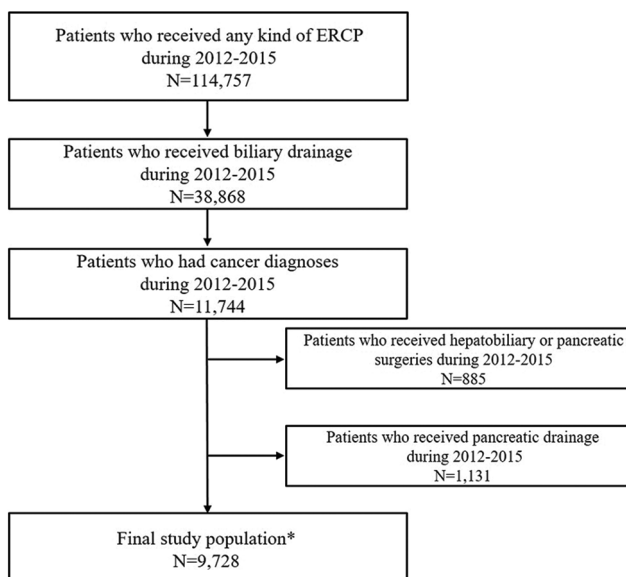
Patients that underwent any type of endoscopic retrograde cholangiopancreatography (ERCP) on an inpatient basis between January 2012 and December 2015 were identified in the HIRA database. After selecting patients with a cancer diagnosis that received biliary drainage, patients that received hepatobiliary or pancreatic surgery or pancreatic drainage were excluded. Thus, the subjects of the present study underwent palliative biliary drainage for MBO presumptively.

### Operational definition

Stenting-related complications (perforation, hemorrhage, and pancreatitis) were determined using International Classification of Diseases (ICD-10) codes. More specifically, we recognized ICD-10 codes for perforation (K63.1 or K83.2, and T81.2), hemorrhage (K92.2 and T81.0 to T81.1), and pancreatitis (K85 and K86.3), which were newly diagnosed within a week from the day ERCP was performed. Receipt of a blood transfusion immediately following ERCP was also recorded as hemorrhage. Severity of post-ERCP pancreatitis (PEP) was graded by length of hospital stay.<sup>[9]</sup> Time to second procedure was defined as duration of stent patency from initial placement.

### Statistical analysis

Continuous variables are presented as means  $\pm$  standard deviations and categorical variables as numbers (%). Continuous variables were analyzed using the Student's *t*-test or the Mann-Whitney *U*-test, as appropriate, and



**Figure 1:** Selection of study subjects. \*Subjects that underwent palliative biliary drainage for malignant biliary obstruction presumptively

**Table 1: Baseline characteristics (n=9,728)**

Characteristic	Value
Age (yr), mean±SD	65±11.4
Male, n (%)	5,969 (61.4)
Diagnosis, n (%)	
Malignant neoplasm of liver and intrahepatic bile ducts	3,122 (32.1)
Malignant neoplasm of gallbladder	784 (8.1)
Malignant neoplasm of extrahepatic bile duct or Ampulla of Vater	2,543 (26.1)
Malignant neoplasm of pancreas	2,150 (22.1)
Others	1,155 (11.9)
Initial procedures, n (%)	
Plastic stent (s) placement	5,147 (52.9)
Metal stent (s) placement	2,264 (23.3)
Nasobiliary catheter placement*	4,081 (42.0)
Hospital days, mean±SD	13±10.2

\*Nasobiliary catheter + plastic stent(s) placement, 1,084; nasobiliary catheter + metal stent(s) placement, 808

categorical variables using Pearson's  $\chi^2$  test or Fisher's exact test. The analysis was conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA), and statistical significance was accepted for  $P$  values <0.05.

## RESULTS

The process used to select study subjects is described in Figure 1. A total of 114,757 patients that received any kind of ERCP between 2012 and 2015 were identified. After further selection and exclusion, the final study population consisted of 9,728 subjects (mean age, 65 ± 11.4 years; male, 61.4%), who presumptively underwent palliative biliary drainage for MBO [Table 1]. The most common diagnosis was a malignant neoplasm of liver and intrahepatic bile ducts (C22, 32.1%), which mainly included hepatocellular carcinoma and intrahepatic cholangiocarcinoma, and this was followed by malignant neoplasm of extrahepatic bile duct or Ampulla of Vater (C24, 26.1%) and malignant neoplasm of pancreas (C25, 22.1%). Initial plastic stent(s) placement was performed in 52.9% of the 9,728 study subjects, while metal stent(s) placement was performed in 23.3%. Nasobiliary catheter placement, a bridge therapy usually adopted prior to stent placement, was initially selected in 42.0% (4,081/9,728). Among the subjects with nasobiliary catheter placement, 1,084 (26.6%) and 808 (19.8%) underwent subsequent or simultaneous plastic stent(s) and metal stent(s) placement, respectively. Mean hospital stay was 13 ± 10.2 days.

Stenting-related complications are summarized in Table 2. Only a small proportion of the subjects experienced PEP (12/9,728, 0.12%) of usually moderate severity. However, no case of stenting-related perforation or hemorrhage was recorded. Table 3 shows the results of initial plastic and metal stenting in the 6,545 subjects that underwent a stenting procedure. Significantly more metal

stenting than plastic stenting was performed initially in older, female, gallbladder cancer, and pancreatic cancer patients. The total number of ERCP or PTBD sessions was significantly higher in patients that underwent initial plastic stenting than metal stenting ( $2.2 \pm 1.7$  vs  $1.8 \pm 1.4$ ,  $P < 0.0001$ ), while PEP rate, hospital stay, and time to second ERCP or PTBD were not significantly different.

## DISCUSSION

This nationwide assessment study was conducted to summarize the real-world situation of palliative ERBD for MBO and to determine its clinical significance, which has rarely been reported in Korea. The study shows that palliative biliary drainage is performed predominantly in patients with hepatocellular carcinoma or intrahepatic cholangiocarcinoma initially using plastic rather than metal stents. The overall complication rate was extremely low in patients that underwent stenting. Importantly, initial metal stenting was associated with significantly fewer ERCP or PTBD sessions after initial procedures.

Palliative ERBD for MBO is usually performed to alleviate obstructive jaundice in patients not planned to receive surgery. The European guideline recommends the endoscopic placement of SEMS for preoperative or palliative biliary drainage for MBO after confirming a malignant etiology.<sup>[8]</sup> The assessment of resectability is also important during method selection. However, the majority of our study subjects received initial plastic stent(s) or nasobiliary catheter placement for palliative ERBD probably because surgical strategy could not be determined at time of diagnosis. SEMSs are not usually inserted from the beginning when the diagnosis or operability is unclear. The European guideline also recommends against the initial insertion of uncovered SEMS for the drainage of extrahepatic biliary obstruction of unconfirmed etiology.<sup>[8]</sup> It seems that initial metal stenting did not affect hospital stays or time to second procedure but did significantly reduce total sessions. Several high-quality meta-analyses have addressed initial stent selection (SEMS vs plastic)<sup>[10-12]</sup> and shown SEMS placement is associated with a low rate of re-intervention, as was found in our study. Complication rates were reported to be lower for SEMS in two of these studies.<sup>[10,12]</sup> In terms of stent patency, all studies asserted that SEMS placement resulted in longer stent patency, which was not found in the present study. Plastic stents may be occluded more easily due to bacterial biofilm, biliary sludge, and duodenobiliary reflux of dietary fiber.<sup>[13]</sup> It is possible that our results were less than accurate because we used time to second procedure as a surrogate of stent patency. In addition, we believe that selection bias

**Table 2: Stenting-related complications (n=9,728)**

Complication	Perforation	Hemorrhage	Pancreatitis (n=12)			Total
			Mild	Moderate	Severe	
No. (%)	0	0	0	10 (83.3)	2 (16.7)	12 (0.12)

**Table 3: Comparison of the details of patients that underwent initial plastic or metal stenting (n=6,545)**

	Plastic (n=4,717)	Metal (n=1,831)	P
Age (yr), mean±SD	65±11.4	66±11.7	0.0002
Male, n (%)	2,989 (63.4)	1,001 (54.7)	<.0001
Diagnosis, n (%)			
Malignant neoplasm of liver and intrahepatic bile ducts	1,750 (37.1)	382 (20.9)	<.0001
Malignant neoplasm of gallbladder	294 (6.2)	236 (12.9)	<.0001
Malignant neoplasm of extrahepatic bile duct or Ampulla of Vater	1,323 (28.1)	331 (18.1)	<.0001
Malignant neoplasm of pancreas	899 (19.1)	668 (36.5)	<.0001
Others	463 (9.8)	218 (11.9)	0.01
Complications, n (%)			
Pancreatitis	6 (0.1)	0 (0.0)	0.1
Hospital days, mean±SD	13.3±10.5	13.6±3.7	0.4
Total sessions*, mean±SD	2.2±1.7	1.8±1.4	<.0001
Interval to 2 <sup>nd</sup> ERCP or PTBD†, mean±SD	36±80.9	37±91.9	0.6

\*ERCP or PTBD. †A surrogate of stent patency duration. ERCP: Endoscopic retrograde cholangiopancreatography; PTBD: Percutaneous transhepatic biliary drainage

occurred because a maximum of two SEMs per patient were reimbursed according to NHIS policy during the study period (2012-2015). Nevertheless, the study shows that in Korea, initial SEMs placement has an advantage as it reduces number of procedures.

Complication rates related to stenting were extremely low. During patient selection, we found that the number of patients with PEP decreased significantly after selecting patients with cancer diagnoses. This result is consistent with the results of a previous study, in which it was reported that PEP is less likely to develop in patients with obstructive jaundice.<sup>[14]</sup> On the other hand, in terms of difficult cannulation, patients with MBO, who are prone to difficult cannulation,<sup>[15]</sup> may not have been appropriately included in the study, because they were switched to another procedure (e.g., PTBD) after ERCP had failed.

Since the main purpose of this study was to summarize the overall status of endoscopic drainage for inoperable MBO, it is difficult to present clinical guidelines based on our results. However, we were able to isolate diagnostic information and details of complications, hospital stays, and total numbers of procedure sessions by analyzing almost 10,000 subjects with MBO. Actually, in Korea, plastic stent placement is preferred as an initial treatment for patients with MBO, but our results show that SEMs placement reduced additional procedures in the long term, which is in-line with the European guideline.<sup>[8]</sup> Additional study of information from 2015 is required to establish overall trends and outcomes in Korea and the effects of NHIS stent policy changes.

Some limitations of this study warrant consideration. First, survival data was not evaluated due to a lack of availability in the HIRA database.<sup>[16]</sup> Second, it is likely that complications were underestimated as they were counted using only entered diagnosis codes, excluding subjects undergoing surgery for a complication such as perforation. Third, number of stents or levels of MBO were not evaluated, which may have been meaningful, especially in patients with extrahepatic MBO. Finally, since the histological diagnosis is usually made at the first ERCP session, it is natural that more plastic stents are inserted initially when the diagnosis is not certain. This could result in more subsequent sessions eventually. Nonetheless, by analyzing nationally representative data, we were able for the first time to summarize the overall status of the procedures used for MBO.

In conclusion, this nationwide assessment study indicates that initial metal stenting is associated with fewer ERCP or PTBD sessions after initial procedures, which contrasts with the preference for initial plastic stenting in Korea. As mentioned above, since changes were made in stent-related policies after the study period, we recommend that an analysis of data collated after 2015 be conducted.

### Financial support and sponsorship

This study was supported by a grant from the Korean Gastrointestinal Endoscopy Research Foundation.

### Conflicts of interest

There are no conflicts of interest.



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