



Recent advances in endoscopic retrograde cholangiopancreatography in Billroth II gastrectomy patients: A systematic review

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Abstract

BACKGROUND

Endoscopic retrograde cholangiopancreatography (ERCP) in patients with Billroth II gastrectomy has been considered a challenging procedure due to the surgically altered gastrointestinal anatomy. However, there has been a paucity of comparative studies regarding ERCP in Billroth II gastrectomy cases because of procedure-related morbidity and mortality and practical and ethical limitations. This systematic and comprehensive review was performed to obtain a recent perspective on ERCP in Billroth II gastrectomy patients.

AIM

To systematically review the literature regarding ERCP in Billroth II gastrectomy patients.

METHODS

A systematic review was performed on the literature published between May 1975 and January 2019. The following electronic databases were searched: PubMed, EMBASE, and Cochrane Library. The outcomes of successful afferent loop intubation and successful selective cannulation and occurrence of adverse events were assessed.

RESULTS

A total of 43 studies involving 2669 patients were included. The study designs were 36 (83.7%) retrospective cohort studies, 4 (9.3%) retrospective comparative studies, 2 (4.7%) prospective comparative studies, and 1 (2.3%) prospective cohort study. Of a total of 2669 patients, there were 1432 cases (55.6%) of side-viewing endoscopy, 664 (25.8%) cases of forward-viewing endoscopy, 171 (6.6%)

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cases of balloon-assisted enteroscopy, 169 (6.6%) cases of anterior oblique-viewing endoscopy, 64 (2.5%) cases of dual-lumen endoscopy, 31 (1.2%) cases of colonoscopy, and 14 (0.5%) cases of multiple bending endoscopy. The overall success rate of afferent loop intubation was 91.3% (2437/2669), and the overall success rate of selective cannulation was 87.9% (2346/2437). A total of 195 cases (7.3%) of adverse events occurred. The success rates of afferent loop intubation and the selective cannulation rate for each type of endoscopy were as follows: side-viewing endoscopy 98.2% and 95.3%; forward-viewing endoscopy 97.4% and 95.2%; balloon-assisted enteroscopy 95.4% and 97.5%; oblique-viewing endoscopy 94.1% and 97.5%; and dual-lumen endoscopy 82.8% and 100%, respectively. The rate of bowel perforation was slightly higher in side-viewing endoscopy (3.6%) and balloon-assisted enteroscopy (4.1%) compared with forward-viewing endoscopy (1.7%) and anterior oblique-viewing endoscopy (1.2%). Mortality only occurred in side-viewing endoscopy ($n = 9$, 0.6%).

CONCLUSION

The performance of ERCP in the Billroth II gastrectomy population has been improving with choice of various type of endoscope and sphincter management. More comparative studies are needed to determine the optimal strategy to perform safe and effective ERCP in Billroth II gastrectomy patients.

Key words: Endoscopic retrograde; Cholangiopancreatography; Therapeutic; Endoscopy; Billroth II operation; Adverse event; Systematic review

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Core tip: Endoscopic retrograde cholangiopancreatography (ERCP) in Billroth II gastrectomy anatomy has been considered a difficult procedure due to the surgical alteration. To date, there has been a paucity of comparative studies regarding ERCP in Billroth II gastrectomy patients. In current study, we systematically and comprehensively reviewed the literatures regarding ERCP in Billroth II gastrectomy cases. The performance of ERCP in the Billroth II gastrectomy has been improving with choice of various type of endoscope and sphincter therapy. More comparative studies are required to perform effective and safe ERCP in Billroth II gastrectomy population.

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INTRODUCTION

Billroth II gastrectomy commonly encounters a challenging surgically altered anatomy when performing endoscopic retrograde cholangiopancreatography (ERCP). The difficulties in performing ERCP in patients with Billroth II gastrectomy include the identification and intubation of the afferent loop, visualization of the papilla, selective cannulation of the desired biliary or pancreatic duct, and sphincter therapy due to the reverse direction of the papilla^[1,2]. As a result, the safety and failure of ERCP have always been a major concern in Billroth II gastrectomy patients.

For successful and safe ERCP in Billroth II gastrectomy patients, there have been many choices for the selection of endoscopy other than conventional side-viewing endoscopy, such as forward-viewing endoscopy (with or without cap-fitting)^[3,4], balloon-assisted enteroscopy (single-balloon or double-balloon)^[5,6], anterior oblique-viewing endoscopy (with or without overtube-assisted)^[7,8], dual-lumen endoscopy^[9], and multiple bending endoscopy^[10]; choices for sphincter therapy, such as endoscopic sphincterotomy (EST), endoscopic papillary balloon dilation (EPBD), and endoscopic papillary large balloon dilation (EPLBD)^[11-13]; and choices for accessories, such as a needle knife (NK) and rotatable or dedicated inverted papillotome^[14,15].

To date, there has been a paucity of comparative studies regarding ERCP in Billroth

II gastrectomy cases because of procedure-related morbidity and mortality and practical and ethical limitations. To obtain a more recent perspective on ERCP in Billroth II gastrectomy, we systematically and comprehensively reviewed the literature regarding ERCP in Billroth II gastrectomy patients. In detail, the aims of our study were: (1) To assess the success rate of afferent loop intubation, the success rate of selective cannulation, and rate of adverse events in ERCP in Billroth II gastrectomy patients; (2) To assess these outcomes according to each type of endoscopy; (3) To assess clinical efficacy according to each type of sphincter management methods.

MATERIALS AND METHODS

Search strategy and study selection

This systematic review was conducted according to the PRISMA guidelines^[16]. Electronic databases, including MEDLINE (PubMed), EMBASE, and Cochrane Library, were searched for all studies published from May 1975 to January 2019. The search terms included “Billroth II gastrectomy” or “Billroth II operation,” or “gastrectomy” and “endoscopic retrograde cholangiopancreatography” or “endoscopic retrograde” combined with “cholangiopancreatography,” or “ERCP.” Two investigators (T.Y.P. and T.J.S.) independently performed the search of the electronic databases and assessed the eligibility of all the studies searched from the databases according to the predetermined selection criteria. Disagreements between evaluators were resolved through discussion.

Studies were included in the systematic review if they met all of the following criteria: (1) Relevant clinical studies of ERCP in patients with prior Billroth II gastrectomy; (2) Studies that enrolled at least 10 Billroth II gastrectomy patients; (3) Studies with full text available; (4) Studies with available information on the patient number, indications for the ERCP, type of endoscopy, type of sphincter therapy, success rate of afferent loop intubation, success rate of selective cannulation, occurrence of adverse events including bowel perforation, post-ERCP pancreatitis, bleeding, cardiopulmonary events and mortality; and (5) Studies written in English. Studies were excluded from the current review if they met any of the following criteria: (1) Irrelevancy to ERCP in Billroth II gastrectomy patients; (2) Fewer than ten patients; (3) Review, abstract only article, commentary, and letter; (4) Non-human study; and (5) Languages other than English.

Data of the sample size, study design, indications for the procedure, type of endoscopy (side-viewing endoscopy, forward-viewing endoscopy, double-balloon enteroscopy, single-balloon enteroscopy, anterior oblique-viewing endoscopy, overtube-assisted endoscopy, multi-bending endoscopy, or dual-lumen endoscopy), type of sphincter therapy (EST, EPBD, EPLBD, NK), success rate of afferent loop intubation, success rate of selective cannulation, occurrence of adverse events including bowel perforation, post-ERCP pancreatitis, procedure-related bleeding, cardiopulmonary events, and mortality were extracted from the included studies. Subgroup analysis of successful afferent loop intubation, successful selective cannulation, bowel perforation, post-ERCP pancreatitis, bleeding, and mortality according to the type of endoscopy was performed. And clinical outcomes according to the type of sphincter therapy was also evaluated. Clinical success was defined as the achievement of the planned therapeutic goals including bile duct stone clearance, endobiliary biopsy, biliary stent or nasobiliary catheter insertion. Data extraction was carried out by two independent reviewers (T.Y.P. and T.J.S.) using a standardized table. Discrepancies were resolved by discussion.

Statistical analysis

The primary outcome was to assess the efficacy of ERCP in Billroth II gastrectomy patients by afferent loop intubation and the selective cannulation of the desired duct as well as the safety according to procedure-related adverse events, such as bowel perforation, post-ERCP pancreatitis, bleeding, cardiopulmonary events, and mortality. The secondary outcome was to compare the rate of afferent loop intubation, selective cannulation, and adverse events according each type of endoscope. The categorical variables were reported as the frequency with respective proportions (percentages). The pooled rate of outcome measures was calculated by dividing the percentage of patients or procedures from the included studies.

RESULTS

Literature search and identification of relevant studies

The flow diagram of the study identification, screening, eligibility, and inclusion process is shown in [Figure 1](#). A total of 344 studies were identified through an electronic search of 3 databases and manual search of the relevant bibliographies. Of them, 79 duplicate studies were removed during the initial screening. Then, through a review of the titles and abstracts, 100 studies irrelevant to ERCP in Billroth II gastrectomy patients were excluded. After a thorough review of 265 relevant studies, 222 studies were excluded from the systematic review. The reasons for study exclusion were as follows: Case report ($n = 28$), languages other than English ($n = 26$), fewer than 10 patients ($n = 25$), review ($n = 15$), abstract ($n = 13$), letter ($n = 7$), commentary ($n = 6$), and non-human study ($n = 2$). The remaining 43 studies were included in the final analysis.

Characteristics of the studies included in the final review

The characteristics of the 43 studies are listed in [Table 1](#). The published year ranged from 1984 to 2018. Most of the studies were retrospective single-arm studies, and the most common indications for ERCP were common bile duct (CBD) stones and pancreaticobiliary malignancies. There were six studies that included more than 100 Billroth II gastrectomy patients and, among them, three studies^[17-19] were published in recent years. The detailed characteristics of the recently published studies including more than 100 Billroth II gastrectomy cases are summarized in [Table 2](#).

Results of the systematic review

The results of the current systematic review are shown in [Table 3](#). Of the 43 included studies, there were 36 (83.7%) retrospective cohort studies, 4 (9.3%) retrospective comparative studies, 2 (4.7%) prospective comparative studies, and 1 (2.3%) prospective cohort study. There were 2669 identified patients in total. Conventional side-viewing endoscopy ($n = 1432$, 55.6%) and forward-viewing endoscopy with or without cap-fitting ($n = 664$, 25.8%) were the most frequently used types of endoscopy when performing ERCP in Billroth II gastrectomy patients. The other types of endoscopy that were used were balloon-assisted enteroscopy in 171 cases (6.6%), anterior oblique-viewing endoscopy in 169 cases (6.6%), dual-lumen endoscopy in 64 cases (2.5%), colonoscopy in 31 (1.2%), and multiple bending endoscopy in 14 cases (0.5%). The overall success rate of afferent loop intubation was 91.3% (2437/2669), and the overall success rate of selective cannulation was 87.9% (2346/2437). A total of 195 cases (7.3%) of adverse events occurred. These events were bowel perforations in 74 cases (2.8%), post-ERCP pancreatitis in 65 cases (2.4%), bleeding in 37 cases (1.4%), mortality in 9 cases (0.3%), cholangitis in 7 cases (0.1%), respiratory insufficiency in 1 case (0.04%), aspiration pneumonia in 1 case (0.04%), and cholecystitis in 1 case (0.04%). All the mortality cases ($n = 9$, 0.3%) occurred in procedures using conventional side-viewing endoscopy.

Subgroup analysis

The subgroup analysis according to the type of endoscopy is summarized in [Table 4](#). The success rates of afferent loop intubation by each type of endoscopy ranged from 82.8% to 98.2%. The success rates of selective cannulation ranged from 95.2% to 100%. The occurrence rate of adverse events by each type of endoscopy ranged from 3.6% to 7.9%. The rates of afferent loop intubation, selective cannulation, and adverse events were similar between side-viewing endoscopy and forward-viewing endoscopy, which are the most frequently used types of endoscopy in ERCP in patients with Billroth II gastrectomy. The rates of bowel perforation were slightly higher in side-viewing endoscopy (3.6%) and balloon-assisted enteroscopy (4.1%) compared with forward-viewing endoscopy (1.7%) and anterior oblique-viewing endoscopy (1.2%). Mortality only occurred in side-viewing endoscopy ($n = 9$, 0.6%).

The subgroup analysis by each type of sphincter management summarized in [Table 5](#). The clinical success rates of achievement for the planned therapeutic goals according to the sphincter management ranged from 85.8% to 93.6%. The overall rate of adverse events according to the sphincter therapy ranged from 5.8% to 8.5%. The rate of bowel perforation ranged from 1.3% to 3.5%. The most cases of post-ERCP pancreatitis occurred in patients who underwent EPBD (6.5%). Most of the bleeding occurred in whom EST was used (EST, $n = 25$; EST+EPBD, $n = 8$; EPBD, $n = 3$).

DISCUSSION

The gastric bypass surgery was first introduced in 1879 by Jules Emile Pean and 1880 by Ludwik Rydygier^[20]. The gastrectomy with gastrojejunal anastomosis (Billroth II gastrectomy) is the most modern form of gastric bypass surgery, which was first performed in 1885 by Theodor Billroth^[21]. Now, Billroth II gastrectomy has been

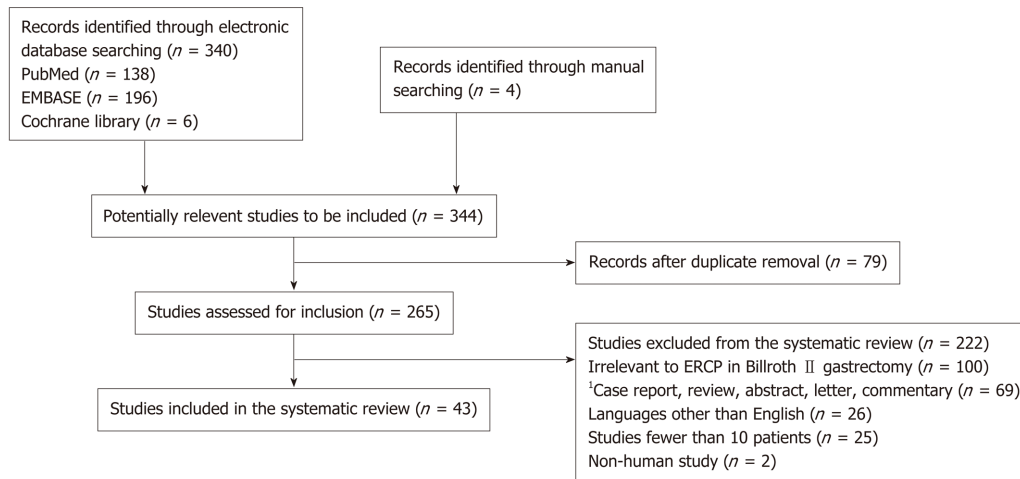


Figure 1 Flow diagram of the study.¹Case report ($n = 28$), review ($n = 15$), abstract ($n = 13$), letter ($n = 7$), and commentary ($n = 6$).

widely used to treat gastric malignancy, refractory peptic ulcer disease with pyloric stenosis, or peptic ulcer perforation^[22]. There are several types of Billroth II anastomosis according to reconstruction following partial gastrectomy such as antecolic or retrocolic, anisoperistaltic or isoperistaltic with or without Roux-en-Y anastomosis.

ERCP in Billroth II gastrectomy patients is a challenging procedure. The difficulties in performing ERCP in Billroth II gastrectomy are selective intubation of the endoscope into the afferent loop due to the acute angulation of the remnant stomach and small bowel, identification of papilla behind the mucosal fold, selective cannulation of the desired pancreaticobiliary duct, and optimal sphincter therapy due to the inverted position^[23]. Particularly, because of procedure-related morbidity and mortality, there has been a paucity of prospective controlled studies in this population, and the treatment strategy or instrument decision, including the choice of endoscope or sphincter therapy, has been determined according to the endoscopists' preference based on their education and experience.

The choice of endoscopy has always been a matter of controversy, and there is no consensus on the issues. Experienced endoscopists usually recommend using a conventional side-viewing endoscope because it has an elevator and a large working channel. However, a side-viewing endoscope has some limitations when used on Billroth II gastrectomy patients because of its limited visibility due to presenting a side view, rigidity and relatively large diameter of the scope. Therefore, in Billroth II gastrectomy patients, ERCP using a side-viewing endoscope may sometimes be difficult, and it may be associated with a risk of small bowel or an anastomosis site perforation, particularly for inexperienced endoscopists. By contrast, insertion of a forward-viewing endoscope may be relatively easy and safe, and various interventions can also be performed safely. Consequently, the use of a forward-viewing endoscope with or without cap-fitting has become more frequent and now is the second most common type of endoscope for ERCP in Billroth II gastrectomy patients despite its disadvantages, such as absence of an elevator, small working channel, and difficulty in obtaining an en face view of the papilla (Figures 2 and 3).

Recently, a meta-analysis^[24] that focused on the efficacy and safety of forward-viewing endoscopy for ERCP in Billroth II gastrectomy compared with conventional side-viewing endoscopy was reported. The meta-analysis showed a higher success rate for afferent loop intubation in forward-viewing endoscopy (with or without cap-fitting) compared to that for conventional side-viewing endoscopy (90.3% *vs* 86.8%). Furthermore, the success rate of selective cannulation in cap-fitting forward-viewing endoscopy has been reported up to 93.7%. This result suggested that forward-viewing endoscopy with or without cap-fitting can be a potential alternative type of endoscopy for ERCP in Billroth II gastrectomy cases, particularly when conventional side-viewing endoscopy fails and balloon-assisted enteroscopy is unavailable. A forward-viewing endoscopy with or without cap-fitting could be the initial choice of endoscopy for an inexperienced endoscopist to minimize the risk of adverse events, such as bowel perforation. However, the studies included in this meta-analysis were non-comparative and had a retrospective design, and therefore, the applicability of their pooled estimate results to general practice might be limited.

Table 1 Characteristics of the 43 studies included in the systematic review

Study	Study design	No.	Indications for ERCP	Type of endoscope	Sphincter therapy	A-loop intubation, No. (%)	Selective cannulation, No. (%)	Adverse events
Forbes and Cotton ^[1] , 1984	Retrospective cohort	53	N/A	S	EST	45/53 (84.9)	35/45 (77.8)	Bowel perforation (<i>n</i> = 1, 1.9%)
Osnes <i>et al</i> ^[2] , 1986	Retrospective cohort	147	N/A	S	EST	134/147 (91.2)	134/134 (100)	Bowel perforation (<i>n</i> = 1, 0.7%) Pancreatitis (<i>n</i> = 1, 0.7%) Bleeding (<i>n</i> = 1, 0.7%) Mortality (<i>n</i> = 2, 1.4%)
Hintze <i>et al</i> ^[31] , 1997	Retrospective cohort	59	CBD stone Papillary stenosis Tumor stenosis Juxtapapillary diverticulum	S	EST	54/59 (91.5)	54/54 (100)	Bowel perforation (<i>n</i> = 1, 1.7%) Mortality (<i>n</i> = 1, 1.7%)
Kim <i>et al</i> ^[3] , 1997	Prospective comparative	45	N/A	F (<i>n</i> = 23) S (<i>n</i> = 22)	EST±NK	44/45 (97.8)	36/44 (80.0)	Bowel perforation (<i>n</i> = 4, 8.9%) Pancreatitis (<i>n</i> = 3, 2.2%)
Lin <i>et al</i> ^[32] , 1999	Retrospective cohort	56	CBD stone CBD dilation RUQ pain with cholestasis	F	EST	43/56 (76.6)	35/43 (81.3)	Bleeding (<i>n</i> = 3, 5.4%)
Faylona <i>et al</i> ^[33] , 1999	Retrospective cohort	110	Cholangitis (<i>n</i> = 58) CBD stone (<i>n</i> = 41) Jaundice (<i>n</i> = 28) CBD dilation (<i>n</i> = 19) Pancreatitis (<i>n</i> = 9) Others (<i>n</i> = 30)	S	EST	² 132/185 (71.4)	² 122/132 (92.4)	Bowel perforation (<i>n</i> = 11, 5.9%) Pancreatitis (<i>n</i> = 1, 0.5%) Bleeding (<i>n</i> = 3, 1.6%) Mortality (<i>n</i> = 2, 1.1%)
Bergman <i>et al</i> ^[11] , 2001	Prospective comparative	34	CBD stone (<i>n</i> = 34)	S	EST/EPBD	N/A	28/34 (82.4)	Bowel perforation (<i>n</i> = 1, 2.9%) Pancreatitis (<i>n</i> = 1, 2.9%) Bleeding (<i>n</i> = 3, 8.8%) Respiratory insufficiency (<i>n</i> = 1, 2.9%)
Swarnkar <i>et al</i> ^[34] , 2005	Retrospective cohort	41	CBD stone (<i>n</i> = 16) CBD dilation (<i>n</i> = 9) Pancreatitis (<i>n</i> = 4) Gastric cancer (<i>n</i> = 3)	S	EST	² 42/48 (87.5)	² 41/42 (97.6)	Bowel perforation (<i>n</i> = 1, 2.1%)

			Pancreatic cancer (<i>n</i> = 2)					
			Others (<i>n</i> = 7)					Bleeding (<i>n</i> = 2, 4.2%)
Kikuyama <i>et al</i> ^[35] , 2005	Retrospective cohort	24	CBD stone (<i>n</i> = 14)	AOE	EST	24/24 (100)	22/24 (91.7)	Bowel perforation (<i>n</i> = 1, 4.2%)
			Pancreaticobiliary malignancy (<i>n</i> = 8)					Pancreatitis (<i>n</i> = 1, 4.2%)
			Others (<i>n</i> = 2)					Bleeding (<i>n</i> = 1, 4.2%)
Çiçek <i>et al</i> ^[36] , 2006	Retrospective cohort	52	CBD stone (<i>n</i> = 27)	S	EST±NK	45/52 (94.2)	43/45 (95.6)	Bowel perforation (<i>n</i> = 6, 11.5%)
			Jaundice (<i>n</i> = 11)					Bleeding (<i>n</i> = 3, 1.6%)
			Pancreaticobiliary malignancy (<i>n</i> = 10)					(<i>n</i> = 2, 3.8%)
			Bile leakage (<i>n</i> = 2)					
			Others (<i>n</i> = 2)					
Park <i>et al</i> ^[37] , 2007	Retrospective cohort	10	CBD stone (<i>n</i> = 9)	¹ F	EST	10/10 (100)	10/10 (100)	None
			CBD stricture (<i>n</i> = 1)					
Dolay and Soyulu ^[38] , 2008	Retrospective cohort	11		S	EST	11/11 (100)	11/11 (100)	None
Nakahara <i>et al</i> ^[39] , 2009	Retrospective comparative	43	CBD stone (<i>n</i> = 43)	AOE	EST/EPBD±NK	38/43 (88.4)	36/38 (94.7)	None
Koo <i>et al</i> ^[10] , 2009	Retrospective cohort	14	CBD stone (<i>n</i> = 8)	Multiple bending endoscope	EST/EPBD	14/14 (100)	13/14 (92.9)	None
			Biliary pancreatitis (<i>n</i> = 2)					
			Pancreaticobiliary malignancy (<i>n</i> = 3)					
			Bile leakage after cholecystectomy (<i>n</i> = 1)					
Shimatani <i>et al</i> ^[40] , 2009	Retrospective cohort	17	N/A	DBE	EST/EPBD	² 22/22 (100)	² 22/22 (100)	None
Kikuyama <i>et al</i> ^[41] , 2009	Retrospective cohort	11	CBD stone (<i>n</i> = 8)	AOE with over tube	EST/EPBD	² 10/15 (66.7)	² 10/10 (100)	None
			Pancreaticobiliary malignancy (<i>n</i> = 3)					
			Chronic pancreatitis (<i>n</i> = 1)					
Lin <i>et al</i> ^[42] , 2010	Retrospective cohort	32	N/A	S (<i>n</i> = 22) DBE (<i>n</i> = 8)	EPBD	30/32 (68.8)	28/30 (93.3)	Bowel perforation (<i>n</i> = 2, 6.3%)
Itoi <i>et al</i> ^[12] , 2010	Retrospective cohort	11	CBD stone (<i>n</i> = 11)	F (<i>n</i> = 8) S (<i>n</i> = 1) AOE (<i>n</i> = 1) SBE (<i>n</i> = 1)	EST+EPLBD	11/11 (100)	11/11 (100)	None
Lee <i>et al</i> ^[30] , 2012	Retrospective cohort	13	CBD stone (<i>n</i> = 13)	¹ F	EPLBD	13/13 (100)	12/13 (92.3)	Bleeding (<i>n</i> = 1, 7.7%)
Byun <i>et al</i> ^[43] , 2012	Retrospective cohort	46	CBD stone (<i>n</i> = 37)	F	EST+EPBD	42/46 (91.3)	42/42 (100)	Bowel perforation (<i>n</i> = 1, 2.2%)

			Pancreatico-biliary malignancy (<i>n</i> = 5)					Pancreatitis (<i>n</i> = 1, 2.2%)
			Benign biliary stricture (<i>n</i> = 4)					
Choi <i>et al</i> ^[44] , 2012	Retrospective comparative	26	CBD stone (<i>n</i> = 26)	S (<i>n</i> = 13) F (<i>n</i> = 13)	EST±EPBD	26/26 (100)	26/26 (100)	None
Kianicka <i>et al</i> ^[45] , 2012	Retrospective cohort	120	Cholestasis (<i>n</i> = 100)	F	EST	109/120 (90.8)	109/120 (90.8)	Bowel perforation (<i>n</i> = 1, 0.8%) Pancreatitis (<i>n</i> = 2, 1.7%) Bleeding (<i>n</i> = 2, 1.7%)
			Biliary pancreatitis (<i>n</i> = 12)					
			Acute cholangitis (<i>n</i> = 6)					
			Bile leakage (<i>n</i> = 2)					
Osoegawa <i>et al</i> ^[27] , 2012	Retrospective cohort	15	N/A	DBE	EST/EPBD±NK	² 18/19 (94.7)	² 16/18 (88.9)	Bowel perforation (<i>n</i> = 1, 0.5%)
Sen-Yo <i>et al</i> ^[46] , 2012	Retrospective comparative	65	CBD stone (<i>n</i> = 38)	AOE	EST/EPBD±NK	60/65 (92.3)	60/60 (100)	Bowel perforation (<i>n</i> = 1, 1.5%) Pancreatitis (<i>n</i> = 3, 4.6%) Cholangitis (<i>n</i> = 2, 3.0%)
			Pancreatico-biliary malignancy (<i>n</i> = 17)					
			Other malignancy (<i>n</i> = 2)					
			Chronic pancreatitis (<i>n</i> = 2)					
			Bile leakage (<i>n</i> = 2)					
			Others (<i>n</i> = 4)					
Jang <i>et al</i> ^[47] , 2013	Retrospective cohort	40	CBD stones (<i>n</i> = 40)	S	EPLBD±NK	40/40 (100)	40/40 (100)	Pancreatitis (<i>n</i> = 2, 5.0%)
Yao <i>et al</i> ^[9] , 2013	Retrospective cohort	46	CBD stone (<i>n</i> = 38)	Dual-lumen gastroscop	EST/EPBD	38/46 (82.6)	38/38 (100)	None
			Biliary stricture (<i>n</i> = 3)					
			Pancreatico-biliary malignancy (<i>n</i> = 5)					
Kawamura <i>et al</i> ^[48] , 2013	Retrospective comparative	65	CBD stone (<i>n</i> = 49)	F (<i>n</i> = 56)	N/A	61/65 (93.8)	51/61 (83.6)	Bowel perforation (<i>n</i> = 2, 3.1%) Pancreatitis (<i>n</i> = 4, 6.2%) Bleeding (<i>n</i> = 1, 1.5%)
			Pancreatico-biliary malignancy (<i>n</i> = 26)	S (<i>n</i> = 2) SBE (<i>n</i> = 3) Others (<i>n</i> = 4)				
			Benign biliary stricture (<i>n</i> = 1)					
Kim <i>et al</i> ^[49] , 2014	Retrospective cohort	30	CBD stone (<i>n</i> = 30)	S	EPLBD±EST	30/30 (100)	30/30 (100)	Pancreatitis (<i>n</i> = 2, 6.7%) Bleeding (<i>n</i> = 2, 6.7%)
Iwai <i>et al</i> ^[50] , 2014	Retrospective comparative	19	N/A	SBE	N/A	18/19 (95)	18/18 (100)	None
Cheng <i>et al</i> ^[51] , 2015	Retrospective cohort	77	CBD stone (<i>n</i> = 77)	DBE	EPLBD/EPBD±NK	73/77 (95)	67/73 (92)	Bowel perforation (<i>n</i> = 3, 3.8%)

Jang <i>et al</i> ^[52] , 2015	Retrospective cohort	36	CBD stone (<i>n</i> = 1 ^F 28) Benign biliary stricture (<i>n</i> = 6) Pancreaticobiliary malignancy (<i>n</i> = 1) Post-operative bile leakage (<i>n</i> = 1)	EPBD±EST	36/36 (100)	32/36 (88.9)	Intestinal mucosal tear (<i>n</i> = 2, 2.6%) Bowel perforation (<i>n</i> = 3, 8.3%) Pancreatitis (<i>n</i> = 2, 5.6%)
Ki <i>et al</i> ^[53] , 2015	Retrospective cohort	72	CBD stone (<i>n</i> = 1 ^F 55) Cholangitis (<i>n</i> = 11) CBD stricture (<i>n</i> = 7) Pancreaticobiliary malignancy (<i>n</i> = 3) IHD stone (<i>n</i> = 2)	EST/EPBD	² 125/126 (99.2)	² 125/125 (100)	Bowel perforation (<i>n</i> = 1, 0.7%) Pancreatitis (<i>n</i> = 3, 2.2%) Bleeding (<i>n</i> = 8, 5.9%)
Nakahara <i>et al</i> ^[54] , 2015	Retrospective cohort	25	CBD stone (<i>n</i> = 15) Pancreaticobiliary malignancy (<i>n</i> = 7) Chronic pancreatitis (<i>n</i> = 3)	AOE EST/EPBD	² 26/30 (86.7)	² 26/26 (100)	Pancreatitis (<i>n</i> = 1, 3.3%)
Bove <i>et al</i> ^[17] , 2015	Retrospective cohort	713	CBD stone (<i>n</i> = 365) Obstructive jaundice (<i>n</i> = 177) Acute cholangitis (<i>n</i> = 61) Chronic pancreatitis (<i>n</i> = 55) Biliary pancreatitis (<i>n</i> = 21) Benign biliary stricture (<i>n</i> = 9) Others (<i>n</i> = 5)	S (<i>n</i> = 600) F (<i>n</i> = 18) EST	618/713 (86.7)	580/618 (93.8)	Bowel perforation (<i>n</i> = 22, 3.1%) Pancreatitis (<i>n</i> = 5, 0.7%) Bleeding (<i>n</i> = 11, 1.5%) Mortality (<i>n</i> = 2, 0.3%)
Wu <i>et al</i> ^[18] , 2016	Retrospective cohort	135	CBD stone/cholangitis Benign biliary stricture	S EST+EPBD	120/135 (88.8)	117/135 (86.3)	² Bowel perforation (<i>n</i> = 1, 0.7%) Pancreatitis (<i>n</i> = 9, 4.1%) Bleeding (<i>n</i> = 2, 0.9%)
Park <i>et al</i> ^[19] , 2016	Retrospective cohort	165	CBD stone (<i>n</i> = 1 ^F 133) Benign biliary stricture (<i>n</i> = 21)	EPBD±NK	151/165 (91.5)	144/151 (95.4)	Bowel perforation (<i>n</i> = 3, 1.8%) Pancreatitis (<i>n</i> = 13, 7.9%)

			Pancreaticobiliary malignancy (<i>n</i> = 11)					Hyperamylasemia (<i>n</i> = 22, 13.3%)
Wang <i>et al</i> ^[28] , 2016	Retrospective cohort	18	CBD stone (<i>n</i> = 15)	Dual-lumen gastroscope	EST/EPBD	15/18 (83.3)	15/15 (100)	Pancreatitis (<i>n</i> = 2, 11.1%) Bleeding (<i>n</i> = 1, 5.6%)
			Pancreaticobiliary malignancy (<i>n</i> = 3)					
Wang <i>et al</i> ^[29] , 2016	Retrospective cohort	52	CBD stone (<i>n</i> = 38)	C (<i>n</i> = 31)	EST/EPBD±NK	50/52 (96.2)	50/52 (96.2)	Pancreatitis (<i>n</i> = 2, 3.8%) Hyperamylasemia (<i>n</i> = 2, 3.8%)
			Biliary stricture (<i>n</i> = 9)	F (<i>n</i> = 13)				
			Pancreaticobiliary malignancy (<i>n</i> = 5)	S (<i>n</i> = 11)				
Shimatani <i>et al</i> ^[25] , 2016	Prospective cohort	26	Cholangitis (<i>n</i> = 13)	DBE	EST	25/26 (96.2)	25/25 (100)	Bowel perforation (<i>n</i> = 2, 7.7%) Pancreatitis (<i>n</i> = 5, 19.2%) Cholangitis (<i>n</i> = 1, 3.8%) Aspiration pneumonia (<i>n</i> = 1, 3.8%)
			Hepatobiliary disorder (<i>n</i> = 4)					
			Obstructive jaundice (<i>n</i> = 4)					
			CBD stone (<i>n</i> = 2)					
			Others (<i>n</i> = 3)					
Shimatani <i>et al</i> ^[55] , 2017	Retrospective cohort	11	CBD stone (<i>n</i> = 7)	DBE	EST	11/11 (100)	11/11 (100)	None
			Obstructive jaundice (<i>n</i> = 2)					
			Others (<i>n</i> = 2)					
Yane <i>et al</i> ^[26] , 2017	Retrospective cohort	20	CBD stone	SBE	N/A	20/20 (100)	19/20 (95)	Bowel perforation (<i>n</i> = 2, 1.0%) Pancreatitis (<i>n</i> = 3, 1.5%) Cholangitis (<i>n</i> = 4, 2.0%) Cholecystitis (<i>n</i> = 1, 0.5%)
			Bile duct stricture					
			Anastomosis site stricture					
Li <i>et al</i> ^[56] , 2017	Retrospective cohort	49	CBD stone (<i>n</i> = 49)	S	EPBD	N/A	42/49 (85.7)	Pancreatitis (<i>n</i> = 3, 6.1%)
Han <i>et al</i> ^[57] , 2018	Retrospective cohort	15	CBD stone (<i>n</i> = 15)	¹ F	EST/EPBD±NK	15/15 (100)	15/15 (100)	Pancreatitis (<i>n</i> = 1, 6.7%)

¹Cap-fitted forward-viewing endoscope;²The data are per procedure, not per patient. A-loop: Afferent loop; ERCP: Endoscopic retrograde cholangiopancreatography; N/A: Not available; RUQ: Right upper quadrant; EST: Endoscopic sphincterotomy; NK: Needle knife; EPBD: Endoscopic papillary balloon dilation; EPLBD: Endoscopic papillary large balloon dilation; CBD: Common bile duct; IHD: Intrahepatic duct; F: Forward-viewing endoscope; S: Side-viewing endoscope; C: Colonoscope; SBE: Single-balloon enteroscope; DBE: Double-balloon enteroscope; AOE: Anterior oblique-viewing endoscope.

As an introduction to balloon-assisted endoscopy, the double-balloon enteroscope or single-balloon enteroscope have been increasingly used to perform ERCP in surgically altered anatomy, including Billroth II gastrectomy^[5,6]. The success rates of ERCP in Billroth II gastrectomy cases by balloon-assisted enteroscopy have been reported from 95.0% to 100%, and seem to be comparable with those of conventional side-viewing endoscopy or forward-viewing endoscopy^[25,26]. Balloon-assisted enteroscope has significant benefit to overcome the sharp curve of the anastomosis site and advance much deeper into the small intestine than conventional side-viewing endoscope or forward-viewing endoscope^[5,27]. However, ERCP by balloon-assisted enteroscopy is technically demanding and requires expertise and specialized equipments. Balloon-assisted enteroscope is also forward-viewing instrument, which has disadvantages of difficulty in obtaining an en face view of the papilla. Therefore, a head to head comparison of outcomes between different types of endoscopy with a randomized controlled trial (RCT) is needed in the future.

Table 2 Detailed characteristics of the most recently published studies with more than 100 patients

	Bove <i>et al</i>^[17], 2015	Wu <i>et al</i>^[18], 2016	Park <i>et al</i>^[19], 2016
	(n = 713)	(n = 135)	(n = 165)
Study design	Retrospective cohort in single center	Retrospective cohort in single center	Retrospective cohort in 5 centers
Male gender, n (%)	567 (79.5)	N/A	116 (70.3)
Age (yr), n (%) or mean $\pm$ SD	> 60 yr, 565 (79.2)	N/A	71.1 $\pm$ 10.0
Type of endoscope	Side-viewing or forward-viewing	Side-viewing	Cap-fitting forward-viewing
Type of sphincter therapy	EST	EST	EPBD $\pm$ NK
Success of afferent loop intubation, n (%)	618/713 (86.7)	120/135 (88.8)	151/165 (91.5)
Success of selective cannulation, n (%)	580/618 (93.8)	117/120 (97.5)	144/151 (95.4)
Bowel perforation, n (%)	22/713 (3.1)	1/135 (0.7)	3/165 (1.8)
Post-ERCP pancreatitis, n (%)	5/713 (0.7)	N/A	13/165 (7.9)
Bleeding, n (%)	11/713 (1.5)	N/A	-
Mortality, n (%)	2/713 (0.3)	-	-

ERCP: Endoscopic retrograde cholangiopancreatography; SD: Standard deviation; EST: Endoscopic sphincterotomy; NK: Needle knife; EPBD: Endoscopic papillary balloon dilation; N/A: Not available.

Recently, the advent of new types of endoscopes, such as a dual lumen or multiple bending endoscope, has allowed successful afferent loop intubation and selective cannulation^[10,28]. The use of dual lumen endoscope has potential advantage that the cooperation of two instruments through different channels can facilitate papillary cannulation in cases with difficult anatomy such as periampullary diverticulum and surgical altered anatomy. Unfortunately, the success rate of these procedures is not significantly higher than that of conventional side-viewing endoscopy, easily available forward-viewing endoscopy or standard colonoscopy (dual lumen endoscope, 82.8%; multiple bending endoscope, 92.9% *vs* conventional side-viewing endoscopy, 93.8%-97.5%; forward-viewing endoscopy, 95.4%; standard colonoscopy, 96.2%)^[9,10,17-19,28,29]. Until now, there has been no large-scale retrospective cohort study or prospective comparative study. Therefore, the new types of endoscopes are practically and economically limited for widespread use.

Another issue, the choice of sphincter therapy, has also been a matter of debate regarding ERCP with Billroth II gastrectomy patients. Traditionally, the performance of sphincterotomy in Billroth II cases is difficult due to its reverse position of the biliary and pancreatic duct. The difficulty of sphincterotomy in optimal direction is associated with the risk of bowel perforation or bleeding. So, there have been continued considerable efforts to perform effective and safe sphincter therapy. Dedicated sphincterotomes for Billroth II anatomy such as inverted sphincterotome or S-shaped sphincterotome have been developed and widely used. Recently, the use of EPBD for sphincter management in Billroth II patients has been on the increase. EPBD is particularly useful in ERCP with a forward-viewing endoscope since sphincterotomy may be difficult with this scope which does not have an elevator. Furthermore, in cases with large CBD stones, application of EPBD can help to efficiently remove these stones in Billroth II gastrectomy cases^[12,30]. Therefore, the increasing use of balloon dilator has been the general trend in sphincter therapy in recent years.

This study has potential limitations that should be discussed. First, in this study, it is not sufficiently and clearly described a recent trend toward a better outcome with novel technologies in ERCP in Billroth II gastrectomy patients. Because most of studies regarding novel technologies were case report, case series, and animal study, they were excluded from current systematic review. This point is major limitation of current study. Second, the studies included in the current systematic review were retrospective, observatory publications from more than 30 years with heterogeneous indications for ERCP. The performance bias of ERCP according to the endoscopist's experience and technique and operative consideration, including the duration and type of Billroth II operation (antecolic or retrocolic, anisoperistaltic or isoperistaltic), were not described. The older studies can lead to bias because there are the difference of the technological advance such as endoscopic instruments and skill, overall knowledge and experience of endoscopists in performing ERCP of Billroth II gastrectomy patients between the past and the present.

In summary, conventional side-viewing endoscopy remains the most commonly used type of endoscopy for ERCP in Billroth II gastrectomy cases. Forward-viewing

Table 3 Results of the systematic review

	No. (%)
Study design, <i>n</i> (%)	
Retrospective cohort	36/43 (83.7)
Retrospective comparative	4/43 (9.3)
Prospective comparative	2/43 (4.7)
Prospective cohort	1/43 (2.3)
Total number of identified patients	2669
¹ Type of endoscope, <i>n</i> (%)	
Side-viewing endoscope	1432/2575 (55.6)
Forward-viewing endoscope	664/2575 (25.8)
Balloon-assisted enteroscope	197/2575 (7.7)
Anterior oblique-viewing endoscope	169/2575 (6.6)
Dual-lumen endoscope	64/2575 (2.5)
Colonoscope	31/2575 (1.2)
Multiple bending endoscope	14/2575 (0.5)
Others	4/2575 (0.2)
Overall success of afferent loop intubation, <i>n</i> (%)	2437/2669 (91.3)
Overall success of selective cannulation, <i>n</i> (%)	2346/2437 (87.9)
Overall adverse events, <i>n</i> (%)	195 (7.3)
Bowel perforation	74 (2.8)
Post-ERCP pancreatitis	65 (2.4)
Bleeding	37 (1.4)
Mortality	9 (0.3)
² Others	10 (0.4)

¹Total number can be changed due to unavailable or incomplete specific data;

²Cholangitis (*n* = 7), respiratory insufficiency (*n* = 1), aspiration pneumonia (*n* = 1), and cholecystitis (*n* = 1). ERCP: Endoscopic retrograde cholangiopancreatography.

endoscopy has been increasingly used to perform ERCP in Billroth II gastrectomy cases because of its advantages, including easy availability and good visual field, as well as the additional advantage of the transparent cap being fitted to the distal end of the endoscope. In recent years, new types of endoscopy, including balloon-assisted enteroscopy, anterior oblique-viewing endoscopy, dual-lumen endoscopy, and multiple bending endoscopy, have been introduced and performed with ERCP safely and effectively. There have also been various types of sphincter therapy applied, including EST, EPBD, and EPLBD, with or without precutting by NK, and the use of diverse types of accessories. As considerable efforts of worldwide investigators have been applied for safe and effective ERCP in this population, the success rate of the procedure and occurrence of adverse events have been improving. In addition, a RCT is required to evaluate the optimal type of endoscopy and sphincter therapy for ERCP in Billroth II gastrectomy patients in the future.

Table 4 Subgroup analysis according to the type of endoscope

	Side-viewing endoscope	Forward-viewing endoscope	Balloon-assisted enteroscope	Oblique-viewing endoscope	Dual-lumen endoscope
	(<i>n</i> = 1432)	(<i>n</i> = 664)	(<i>n</i> = 197)	(<i>n</i> = 169)	(<i>n</i> = 64)
Afferent loop intubation, <i>n</i> (%)	1406 (98.2)	647 (97.4)	188 (95.4)	159 (94.1)	53 (82.8)
Selective cannulation, <i>n</i> (%)	1340 (95.3)	616 (95.2)	179 (97.5)	155 (97.5)	53 (100)
Adverse events, <i>n</i> (%)	113 (7.9)	47 (7.1)	14 (7.1)	6 (3.6)	3 (4.7)
Bowel perforation, <i>n</i> (%)	51 (3.6)	11 (1.7)	8 (4.1)	2 (1.2)	2 (3.1)
Post-ERCP pancreatitis, <i>n</i> (%)	26 (1.8)	27 (4.1)	6 (3.0)	3 (1.8)	1 (1.6)
Bleeding, <i>n</i> (%)	27 (1.9)	9 (1.4)	-	1 (0.6)	-
Mortality, <i>n</i> (%)	9 (0.6)	-	-	-	-

ERCP: Endoscopic retrograde cholangiopancreatography.

Table 5 Subgroup analysis according to the sphincter management methods

	EST	EST+EPBD	EPBD	EPLBD
	(<i>n</i> = 1478)	(<i>n</i> = 598)	(<i>n</i> = 246)	(<i>n</i> = 171)
¹ Clinical success, <i>n</i> (%)	1268 (85.8)	546 (91.3)	214 (87.0)	160 (93.6)
Adverse events, <i>n</i> (%)	103 (7.0)	38 (6.4)	21 (8.5)	10 (5.8)
Bowel perforation, <i>n</i> (%)	51 (3.5)	8 (1.3)	5 (2.0)	3 (1.8)
Post-ERCP pancreatitis, <i>n</i> (%)	18 (1.2)	22 (3.7)	16 (6.5)	4 (2.3)
Bleeding, <i>n</i> (%)	25 (1.7)	8 (1.3)	-	3 (1.8)
Mortality, <i>n</i> (%)	9 (0.6)	-	-	-

¹Clinical success was defined as the achievement of the planned therapeutic goals including bile duct stone clearance, endobiliary biopsy, biliary stent or nasobiliary catheter insertion. The number of patients is much decreased because three studies, unavailable sphincter management information, were excluded from the subgroup analysis. ERCP: Endoscopic retrograde cholangiopancreatography; EST: Endoscopic sphincterotomy; EPBD: Endoscopic papillary balloon dilation; EPLBD: Endoscopic papillary large balloon dilation.

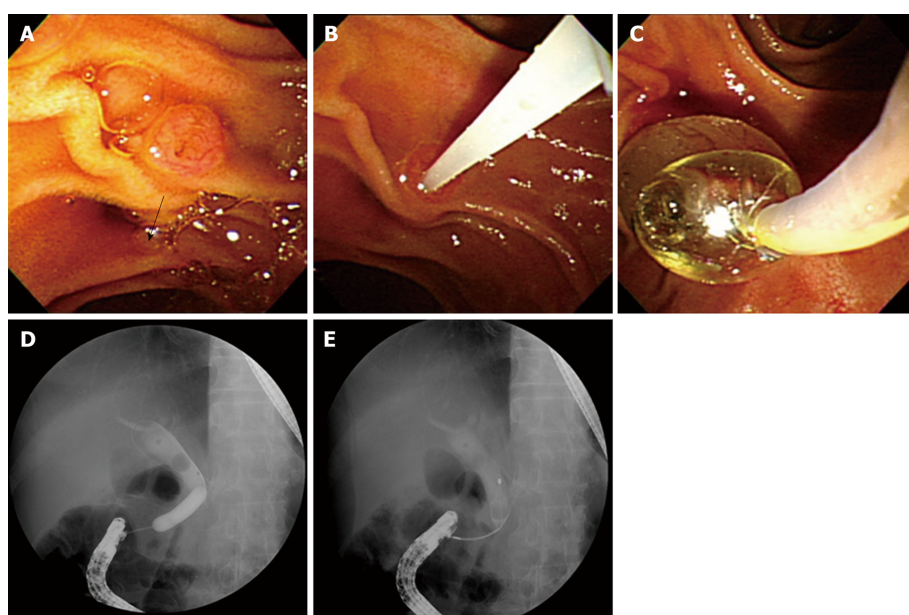


Figure 2 Side-viewing endoscopy. A: Naïve papilla; *En face* view can be obtained with ease. The direction of bile duct is reversed (arrow); B: Selective cannulation can be achieved with assistance of elevator; C: Sphincter management with papillary balloon dilation; endoscopic view; D: Sphincter management with papillary balloon dilation; fluoroscopic view; E: Common bile duct stone was removed by basket.

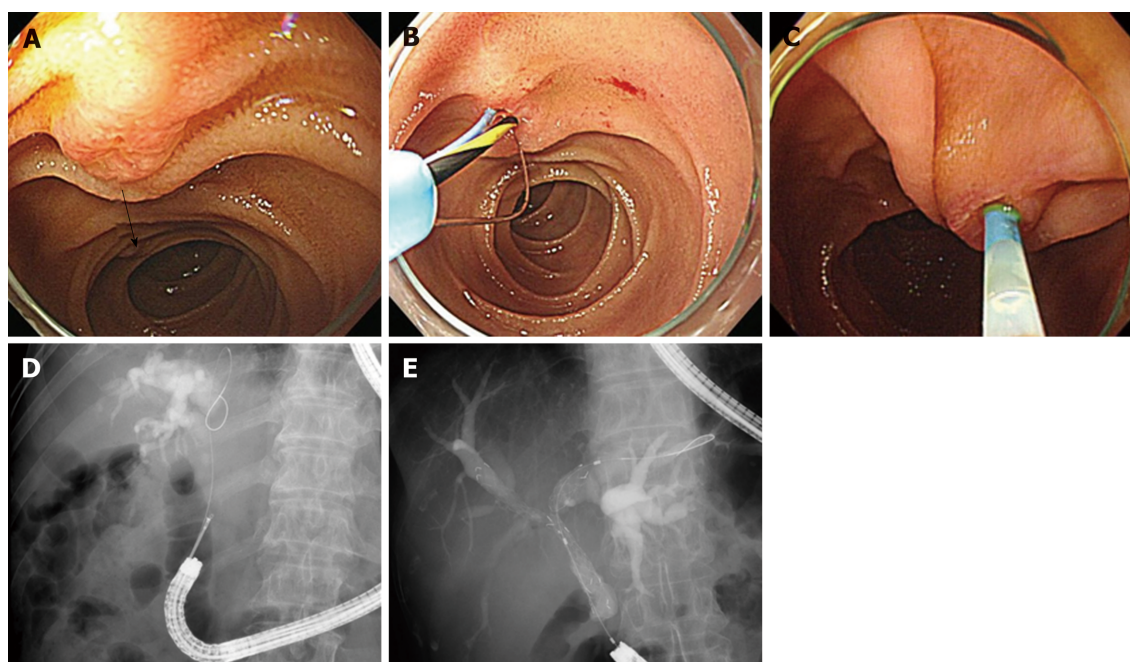


Figure 3 Cap-fitting forward-viewing endoscopy. A: Naïve papilla; It is difficult to obtain *en face* view. The direction of bile duct is reversed (arrow); B: Gastroscop at 7 o'clock position working channel; Sphincter management with inverted sphincterotome; C: Pediatric colonoscope at 5 o'clock position working channel; D: Endobiliary biopsy was performed in distal common bile duct stricture; E: Bilateral uncovered metal stents were inserted in the malignant hilar stricture.

ARTICLE HIGHLIGHTS

Research background

Endoscopic retrograde cholangiopancreatography (ERCP) in patients who have a Billroth II gastrectomy has been considered a difficult procedure due to the surgically altered anatomy. The difficulties of ERCP in patients with Billroth II gastrectomy include the intubation of the afferent loop, visualization of the papilla, selective cannulation of the bile duct, and optimal sphincter management due to the reverse direction of the papilla. To perform safe and effective ERCP in Billroth II gastrectomy cases, considerable efforts have been put in several ways including the choice of endoscope and sphincter management. However, there has been a paucity of comparative studies on the efficacy and safety regarding ERCP in Billroth II gastrectomy.

Research motivation

At present, comparative studies on the efficacy and safety of ERCP in Billroth II gastrectomy cases are lacking because of practical and ethical limitations due to procedure-related morbidity and mortality. This systematic and comprehensive review was performed to obtain a recent perspective on ERCP in Billroth II gastrectomy patients.

Research objectives

The main objective of the study was to assess the efficacy and safety of ERCP in Billroth II gastrectomy patients. In detail, the assessment of success rate of afferent loop intubation and selective cannulation, and rate of adverse events including bowel perforation, post-ERCP pancreatitis, bleeding, cardiopulmonary events, and mortality was performed. In addition, the assessment of these outcomes according to each type of endoscopy and sphincter management methods was performed.

Research methods

A systematic review was performed on the literatures that evaluated the outcomes of ERCP in Billroth II gastrectomy patients. Electronic databases were searched, including PubMed, EMBASE, and Cochrane Library. The outcomes of afferent loop intubation and selective cannulation, and occurrence of adverse events were assessed.

Research results

A total of 43 studies involving 2669 patients were included. The overall success rate of afferent loop intubation was 91.3% (2437/2669), and the overall success rate of selective cannulation was 87.9% (2346/2437). A total of 195 cases (7.3%) of adverse events occurred. Bowel perforations occurred in 74 cases (2.8%), post-ERCP pancreatitis in 65 cases (2.4%), bleeding in 37 cases (1.4%), mortality in 9 cases (0.3%).

Research conclusions

This systematic review showed that the performance of ERCP in the Billroth II gastrectomy

patients has been improving with choice of endoscope and sphincter management. To determine the optimal method to perform safe and effective ERCP in Billroth II gastrectomy patients, more comparative studies are needed in the future.

Research perspectives

The success of ERCP in Billroth II gastrectomy has been improving with technical advance. Future research is needed to explore the optimal approach in performance of ERCP in Billroth II gastrectomy cases.

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