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Biliary drainage prior to pancreatoduodenectomy with Endoscopic Ultrasound-guided choledochoduodenostomy vs conventional Endoscopic Retrograde Cholangiopancreatography: a propensity score matched study and surgeon-survey

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Abstract:

Background

Preoperative endoscopic biliary drainage may lead to complications (16%-24%), potentially hampering surgical exploration. Endoscopic ultrasound-guided choledochoduodenostomy (EUS-CDS) may reduce drainage-related complications, however it is unknown whether EUS-CDS could in itself hamper surgical exploration as series with surgeon reported outcomes are lacking. Aim is to assess the impact of preoperative EUS-CDS on pancreatoduodenectomy.

Method

Consecutive patients who underwent pancreatoduodenectomy after preoperative biliary drainage were included in all eight centers that performed EUS-CDS in the mandatory Dutch Pancreatic Cancer Audit (Jan 2020-Dec 2022). Primary outcome was major postoperative complications. Secondary outcomes included bile leak grade B/C, postoperative pancreatic fistula (POPF) grade B/C, and overall postoperative complications. A propensity score matching (1:3) analysis was performed. Surgeons who performed a pancreatoduodenectomy after EUS-CDS were asked to complete a survey.

Results

Overall, 937 patients with pancreatoduodenectomy after preoperative biliary drainage were included (42 EUS-CDS, 895 ERCP).

Major postoperative complications occurred in eight patients (19%) in the EUS-CDS group and 292 patients (33%) in the ERCP group (RR 0.50; 95%CI, 0.23-1.07). No significant differences were observed in overall complications (RR 0.95; 95%CI, 0.51-1.76), bile leak (RR 1.25; 95%CI, 0.31-4.98) or POPF (RR 0.62; 95%CI, 0.25-1.56). Results were similar after matching. The survey was completed for 29 pancreatoduodenectomies; surgery was not (n=13, 45%), 'slightly' (n=8, 28%), 'clearly' (n=5, 17%) or 'severely' (n=2, 7%) more complex because of the EUS-CDS.

Conclusion
This early experience suggests that preoperative biliary drainage with EUS-CDS does not increase the rate of complications after pancreatoduodenectomy and only infrequently hampers surgical exploration.

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SUPPLEMENTARY MATERIAL

"Biliary drainage prior to pancreatoduodenectomy with EUS-guided choledochoduodenostomy vs conventional ERCP: a nationwide propensity score matched study and surgeon-survey"

Jeska A. Fritzsche, Mike J.P. de Jong, Bert A. Bonsing, Olivier R. Busch, Freek Daams, Foke van Delft, Wouter J.M. Derksen, Lydi M.J.W. van Driel, Joris I. Erdmann, Sebastiaan Festen, Paul Fockens, Erwin M. van Geenen, Bas Groot Koerkamp, Frederik J.H. Hoogwater, Akin Inderson, Geert Kazemier, Sjoerd D. Kuiken, Mike S.L. Liem, Daan J. Lips, Mark Meerdink, Maarten W. Nijkamp, Wouter W. te Riele, Hjalmar C. van Santvoort, Peter D. Siersema, Martijn W.J. Stommel, Niels G. Venneman, Robert C. Verdonk, Frank P. Vleggaar, Roeland F. de Wilde, Marc G. Besselink, Roy L.J van Wanrooij*, Rogier P. Voermans* On behalf of the Dutch Pancreatic Cancer Group and Dutch Pancreatic Cancer Audit.

*These authors share senior authorship.

Table S1. Missing data in baseline and surgical characteristics of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP

	Unmatched cohort		Matched cohort	
	EUS-CDS (n=42)	ERCP (n=895)	EUS-CDS (n=42)	ERCP (n=126)
BMI	0 (0)	5 (0.6)	0 (0)	1 (0.8)
ASA score	0 (0)	8 (0.9)	0 (0)	2 (1.6)
Site of origin	1 (2.4)	13 (1.5)	1 (2.4)	0 (0)
Neoadjuvant therapy	0 (0)	172 (19.2)	0 (0)	25 (19.8)
Time to neoadjuvant therapy[a]	1 (10)	45 (21.4)	1 (10)	12 (44)
Type of stent	NA	83 (9.3)	NA	0 (0)
Time to surgery[b]	0 (0)	25 (5.2)	0 (0)	4 (5.4)
Type of resection	0 (0)	3 (0.3)	0 (0)	1 (0.8)
Minimally invasive	0 (0)	13 (1.5)	0 (0)	0 (0)
Vascular resection	0 (0)	47 (5.3)	0 (0)	3 (2.4)
Additional organ resection	0 (0)	5 (0.6)	0 (0)	0 (0)
Diameter pancreatic duct	3 (7.1)	136 (15.2)	3 (7.1)	21 (16.7)
Pancreatic texture	6 (14.3)	120 (13.4)	6 (14.3)	18 (14.3)
Blood loss	4 (9.5)	43 (4.8)	4 (9.5)	9 (7.1)
Operative time	2 (4.8)	103 (11.5)	2 (4.8)	20 (15.9)
R0-resection	4 (9.5)	97 (10.8)	4 (9.5)	8 (6.3)

Values are n (%). [a]Only in patients in whom biliary drainage was performed prior to the start of neoadjuvant treatment: 10 in EUS-CDS group and 210 in ERCP group in unmatched cohort and 27 in the matched cohort. [b]Only in patients without neoadjuvant therapy: 32 patients in EUS-CDS group and 483 patients in ERCP group in unmatched cohort and 74 patients in matched cohort.
Abbreviations: ASA, American Society Anesthesiologists; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography; EUS-CDS, endoscopic ultrasound guided choledochoduodeostomy.

Table S2. Imputed baseline variables in matched cohort

Variables	Matched cohort		
	EUS-CDS (n=42)	ERCP (n=126)	p-value
BMI (kg/m^2), mean (SD)	24.8 (5.5)	24.7 (3.7)	0.931
ASA score >2	18 (42.9)	55 (43.7)	1.000
Site of origin			0.944[a]
Pancreas	28 (66.7)	88 (69.8)	
Distal bile duct	5 (11.9)	13 (10.3)	
Ampulla of Vater	5 (11.9)	14 (11.1)	
Duodenum or other	4 (9.5)	11 (8.7)	
Neoadjuvant therapy	10 (23.8)	31 (24.6)	1.000

Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Fisher exact test. Abbreviations: ASA, American Society Anesthesiologists; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography; EUS-CDS, endoscopic ultrasound guided choledochoduodeostomy; NA, not applicable; SD, standard deviation.

Table S3. Standardized Mean Differences (SMDs) for Individual Covariates Before and After Matching.

	Unmatched	Matched
Distance	0.620	0.066
Age	0.042	0.092
Geslacht	0.120	0.016
BMI	0.025	0.014
ASA >2	0.129	0.160
Comorbidity		
Liver cirrhosis	0.150	0.000
Chronic pancreatitis	0.222	0.000
Site of origin		
Pancreas	0.040	0.067
Distal bile duct	0.286	0.049
Ampulla of Vater	0.003	0.025
Duodenum or other	0.255	0.027
Neoadjuvant therapy	0.376	0.019
Hospital volume >100 per year	0.436	0.098

Abbreviations: ASA, American Society Anesthesiologists; BMI, body mass index.

Table S3. Baseline and surgical characteristics by primary drainage attempt

Variables	Primary EUS-CDS (n=17)	Primary ERCP (n=920)	p-value
Age (years), median (IQR)	65 (55-73)	68 (61-74)	0.409
Sex ratio M:F	9:8	509:411	1.000
BMI (kg/m^2), median (IQR)	24 (22-27)	24 (22-27)	0.682
Missing	-	-	
ASA score >2	5 (29.4)	324 (35.5)	0.799[h]
Missing	-	*8*	
Comorbidity			
Liver cirrhosis	0 (0)	19 (2.1)	1.000[h]
Chronic pancreatitis	0 (0)	46 (5.0)	1.000[h]
Site of origin			0.756[h]
Pancreas	12 (70.6)	520 (57.4)	
Distal bile duct	2 (11.8)	209 (23.1)	
Ampulla of Vater	3 (17.6)	148 (16.3)	
Duodenum or other	0 (0)	29 (3.2)	
Missing	-	*14*	
Neoadjuvant therapy	4 (23.5)	246 (32.9)	0.602[h]
Chemoradiotherapy	1 (5.9)	87 (9.5)	
Chemotherapy	3 (17.6)	155 (16.8)	
Radiotherapy	0 (0)	1 (0.2)	
Other	0 (0)	3 (0.3)	
Missing	*0*	*172*	
Time to neoadjuvant therapy (days)[a], median (IQR)	22.5 (18.75-25.25)	30 (20-42)	0.144
Missing	*0*	*76*	
Hospital volume >100 per year[b]	15 (88.2)	361 (39.2)	**<0.001**
Time to surgery (days)[c], median (IQR)	22 (20-36)	41 (28-54)	**0.014**
Missing	-	*25*	
Type of resection			0.400[h]
PRPD	11 (64.7)	602 (65.6)	
PPPD	5 (29.4)	295 (32.2)	
Other	1 (5.9)	20 (2.2)	
Missing	-	*3*	
Minimally invasive[d]	2 (11.8)	203 (22.4)	0.389[h]
Missing	-	*13*	
Vascular resection[e]	5 (29.4)	167 (19.1)	0.347[h]
Arterial resection	0 (0)	32 (3.5)	
Venous resection	5 (29.4)	143 (16.3)	
Missing	0	47	
Additional organ resection[f]	2 (11.8)	89 (9.7)	0.678[h]
Missing	-	*5*	
Dilated pancreatic duct	7 (43.8)	254 (32.5)	0.495
	1	*138*	
Pancreatic texture			0.404[h]
Normal/soft	5 (38.5)	421 (52.8)	
Fibrotic/hard	8 (61.5)	377 (47.2)	

Missing	*4*	*122*	
Blood loss (mL), median (IQR)	400 (290-450)	500 (200-900)	0.442
Missing	*2*	*45*	
Operative time (min), median (IQR)	306.5 (211-341.5)	347.5 (281-425)	**0.006**
Missing	*1*	*104*	
R0-resection[g]	7 (41.2)	451 (55.1)	0.372
Missing	-	*101*	

Values are n (%) unless otherwise indicated. Bold numbers indicate statistical significance at a 5% level. [a]Only in patients in whom drainage was performed prior to the start of neoadjuvant treatment: 4 in EUS-CDS group and 170 in ERCP group. [b]Hospital volume was based on the mean total annual volume of pancreatoduodenectomy performed during the study period. [c]Only in patients without neoadjuvant therapy: 13 patients in EUS-CDS group and 502 patients in ERCP group. [d]Laparoscopic or robot, including patients with conversion to open surgery. [e]Vascular resection was reported according to the International Study Group for Pancreatic Surgery (ISGPS) classification.(1) [f]Including spleen (intentional or non-intentional), mesocolon transversum, colon segment, hemicolectomy, gastric resection, or other. [g]Resection margin status was classified as microscopically radical (>1 mm; R0) or microscopically irradical (≤1 mm; R1).(2) [h]Fisher exact test. Abbreviations: ASA, American Society Anesthesiologists; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography; EUS-CDS, endoscopic ultrasound guided choledochoduodeostomy; IQR, interquartile range (P25-P75); PPPD, pylorus-preservering pancreatoduodenectomy; PRPD, pylorus-resecting pancreatoduodenectomy.

Table S4. Postoperative outcome by primary drainage attempt

	Primary EUS-CDS (n=17)	Primary ERCP (n=920)	Relative Risk (95% CI) or p-value[a]
Major postoperative complication	1 (5.9)	299 (32.5)	**0.13 (0.02-0.996)**
Any postoperative complication	10 (58.8)	603 (65.5)	0.76 (0.29-1.97)
Postoperative pancreatic fistula, grade B/C	0 (0)	167 (18.2)	0.054[b]
Delayed gastric emptying, grade B/C	2 (11.8)	169 (18.4)	0.60 (0.14-2.59)
Post pancreatectomy hemorrhage, grade B/C	0 (0)	66 (7.2)	0.625[b]
Bile leakage, grade B/C	0 (0)	36 (3.9)	1.000[b]
Chyle leak, grade B/C	2 (11.8)	57 (6.2)	1.98 (0.46-8.47)
Pneumonia	0 (0)	32 (3.5)	1.000[b]
Surgical site infection	1 (5.9)	72 (7.8)	0.74 (0.10-5.50)
Intensive care unit admission	0 (0)	66 (7.2)	0.625[b]
Re-intervention	1 (5.9)	286 (31.1)	0.14 (0.02-1.06)
Endoscopic	0 (0)	61 (6.6)	0.620[b]
Radiological	1 (5.9)	227 (24.7)	0.19 (0.03-1.46)
Reoperation	0 (0)	60 (6.5)	0.619[b]
In-hospital mortality	0 (0)	21 (2.3)	1.000[b]
Length of hospital stay[a], median (IQR)	8 (5-9)	10 (7-16.75)	**0.012**[c]
Readmission within 30 days after discharge	2 (11.8)	148 (16.2)	0.70 (0.16-3.03)

Values are n (%) unless otherwise indicated. Bold values denote statistical significance at a 5% level. [a]Missing in 34 patients in ERCP group. [b]In case of zero events in one of the groups, a p-value was derived by Fishers exact test. [c]P-value derived by Wilcoxon rank sum test with continuity correction. Abbreviations: ERCP, endoscopic retrograde cholangiopancreatography; EUS-CDS, endoscopic ultrasound guided choledochoduodeostomy; IQR, interquartile range (P25-P75).

Table S5. Surgeon survey following pancreatoduodenectomy in patients with prior EUS-CDS (sensitivity analysis in surveys which completed within 14 days after the resection)

Survey questions	N=11 EUS-CDS
Did you visualize the stent during the resection?	
Yes	2 (18)
No	9 (82)
Did you notice the presence of the stent during the resection?	
Yes	5 (45)
No	6 (55)
To what extent was the surgery complicated by the stent?	Median 2 (IQR 1-2)
1 - not complicated	5 (45)
2 - slightly complicated	6 (55)
3 - clearly complicated	0 (0)
4 - severely complicated	0 (0)
5 - impossible	0 (0)
Was there enough space between the hilum and the stent for the establishment of the hepaticojejunostomy?	
Yes	11 (100)
No	0 (0)
Did you have to adapt the surgical plan due to the presence of the stent?	
Yes	0 (0)
No	11 (100)

Values are n (%) unless otherwise indicated. Abbreviations: EUS-CDS, endoscopic ultrasound guided choledochoduodenostomy.

Table S6. Overview of previous studies reporting post-operative outcome of pancreatoduodenectomy in patients with prior EUS-CDS

	Study	Design, geographic area	Period	Number of patients		Outcomes (EUS-CDS vs ERCP)							
				EUS-CDS	ERCP	Serious AEs	Overall AEs	POPF	HBL	Mortality	Hospital stay	Operative time	Time to surgery
1	Fabbri et al. 2019 (3)	Retrospective, single-centre, Europe	NR	5	NA	NR	NR	2 (40%)[a]	0 (0%)[a]	1 (20%)	NR	NR	NR
2	Gaujoux et al. 2021 (4)	Retrospective, multicentre, Europe	2016-2019	21 (7 primary)	NA	3 (14%)	17 (81%)[a]	2 (10%)[b]	0 (0%)[a]	0 (0%)	20 days [9-50]	355 min [180-650]	45 days [31-214][c]
3	Janet et al. 2023 (5)	Retrospective, multicentre, Europe	2015-2022	44 (28 primary)	112 (plastic/ SEMS)	NR	34 (77%)	12 (27%) vs 34 (30%)., p=0.85[a]	2 (5%) vs 5 (5%), p=1.00[a]	4 (9%) vs 3 (3%), p=0.09	17 days [13-22.5] vs 20 days [16-28.2], p=0.01	NR	28 days [17-38] vs 43 days [27.2-63], p=0.03[c]
4	Chen et al. 2023 (6)	RCT, multicentre, Canada and Europe	2019-2022	6 (all primary)	4	NR	NR	NR	NR	NR	7.4 days (1.5)	7.29h (2.22)	NR

[a]Grade unknown, [b]Only grade B/C, [c]Only in patients without neoadjuvant therapy. Abbreviations: AE, adverse event; ERCP, endoscopic retrograde cholangiopancreatography; EUS-CDS, endoscopic ultrasound guided choledochoduodenostomy; LAMS, lumen-apposing metal stent; NA, not applicable; NR, not reported; RCT, randomised controlled trial; SEMS, self-expanding metal stent.

SUPPLEMENTARY REFERENCES

1. Bockhorn M, Uzunoglu FG, Adham M, Imrie C, Milicevic M, Sandberg AA, et al. Borderline resectable pancreatic cancer: A consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2014;155(6):977-88.
2. The Royal College of Pathologists (2013) Standards and datasets for reporting cancers. Dataset for the histopathological reporting of carcinomas of the pancreas, ampulla of vater and common bile duct. The Royal College of Pathologists, London.
3. Fabbri C, Fugazza A, Binda C, Zerbi A, Jovine E, Cennamo V, et al. Beyond palliation: using EUS-guided choledochoduodenostomy with a lumen-apposing metal stent as a bridge to surgery. a case series. J Gastrointestin Liver Dis. 2019;28(1):125-8.
4. Gaujoux S, Jacques J, Bourdariat R, Sulpice L, Lesurtel M, Truant S, et al. Pancreaticoduodenectomy following endoscopic ultrasound-guided choledochoduodenostomy with electrocautery-enhanced lumen-apposing stents an ACHBT - SFED study. HPB (Oxford). 2021;23(1):154-60.
5. Janet J, Albouys J, Napoleon B, Jacques J, Mathonnet M, Magne J, et al. Pancreatoduodenectomy Following Preoperative Biliary Drainage Using Endoscopic Ultrasound-Guided Choledochoduodenostomy Versus a Transpapillary Stent: A Multicenter Comparative Cohort Study of the ACHBT-FRENCH-SFED Intergroup. Ann Surg Oncol. 2023;30(8):5036-46.
6. Chen YI, Sahai A, Donatelli G, Lam E, Forbes N, Mosko J, et al. Endoscopic Ultrasound-Guided Biliary Drainage of First Intent With a Lumen-Apposing Metal Stent vs Endoscopic Retrograde Cholangiopancreatography in Malignant Distal Biliary Obstruction: A Multicenter Randomized Controlled Study (ELEMENT Trial). Gastroenterology. 2023;165(5):1249-61.

Table 1. Baseline characteristics of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP.

Variables	Unmatched cohort			Matched cohort		
	EUS-CDS (n=42)	ERCP (n=895)	p-value	EUS-CDS (n=42)	ERCP (n=126)	p-value
Age (years), mean (SD)	67.7 (8.6)	67.1 (9.9)	0.645	67.7 (8.6)	68.5 (10.0)	0.625
Sex ratio M:F	21:21	497:398	0.585	21:21	64:62	1.000
BMI, mean (SD)	24.8 (5.5)	25.1 (4.1)	0.721	24.8 (5.5)	24.7 (3.7)	0.929
ASA score >2	18 (42.9)	311 (35.1)	0.386	18 (42.9)	54 (43.5)	1.000
Comorbidity						
Liver cirrhosis	0 (0)	19 (2.1)	1.000[c]	0 (0)	0 (0)	NA
Chronic pancreatitis	0 (0)	46 (5.1)	0.260[c]	0 (0)	0 (0)	NA
Site of origin			**0.018**[c]			0.976[c]
Pancreas	28 (68.3)	504 (57.1)		28 (66.7)	88 (69.8)	
Distal bile duct	4 (9.8)	207 (23.5)		4 (9.8)	13 (10.3)	
Ampulla of Vater	5 (12.2)	146 (16.6)		5 (12.2)	14 (11.1)	
Duodenum or other	4 (9.8)	25 (2.8)		4 (9.8)	11 (8.7)	
Neoadjuvant therapy	10 (23.8)	240 (33.2)	0.275	10 (23.8)	27 (26.7)	0.877
Chemoradiotherapy	2 (4.8)	86 (11.9)		2 (4.8)	12 (11.9)	
Chemotherapy	8 (19.0)	150 (20.7)		8 (19.0)	14 (13.9)	
Radiotherapy	0 (0)	1 (0.1)		0 (0)	0 (0)	
Other	0 (0)	3 (0.4)		0 (0)	1 (1.0)	
Time to neoadjuvant therapy (days)[a], median (IQR)	26 (24-31)	30 (20-42)	0.401	26 (24-31)	32 (20-45)	0.296
Type of stent						
Metal	NA	633 (78.0)	NA	NA	126 (100)	NA
Plastic		179 (22.0)			0 (0)	
Hospital volume >100 per year[b]	26 (61.9)	350 (39.1)	**0.005**	26 (61.9)	72 (57.1)	1.000

Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Only in patients in whom biliary drainage was performed prior to the start of neoadjuvant therapy after biliary drainage: 9 in EUS-CDS group, 165 in ERCP group before matching and 15 in ERCP group after matching. [b]Hospital volume was based on the mean total annual volume of pancreatoduodenectomy performed during the study period. [c]Fisher exact test. Abbreviations: BMI, body mass index; ASA, American Society Anesthesiologists; EUS-CDS, endoscopic ultrasound guided choledochoduodenostomy; ERCP, endoscopic retrograde cholangiopancreatography; NA, not applicable

Table 2. Surgical characteristics of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP

	Unmatched cohort			Matched cohort		
	EUS-CDS (n=42)	**ERCP (n=895)**	**p-value**	**EUS-CDS (n=42)**	**ERCP (n=126)**	**p-value**
Time to surgery (days)[a], median (IQR)	32 (22-39.25)	41 (28-54)	**0.010**	32 (22-39.25)	43 (28-54.75)	**0.022**
Type of resection						
PRPD	30 (71.4)	583 (65.4)	0.621[f]	30 (71.4)	86 (68.3)	0.933[f]
PPPD	11 (26.2)	289 (32.4)		11 (26.2)	37 (29.4)	
Other	1 (2.4)	20 (2.2)		1 (2.4)	3 (2.4)	
Minimally invasive surgery[b]	6 (14.3)	199 (22.6)	0.284	6 (14.3)	22 (17.5)	0.811
Vascular resection[c]	12 (28.6)	160 (18.9)	0.176	12 (28.6)	26 (21.1)	0.438
Arterial	1 (2.4)	31 (3.5)		1 (2.4)	6 (4.8)	
Venous	11 (26.2)	137 (16.1)		11 (26.2)	20 (16.0)	
Additional organ resection[d]	5 (11.9)	86 (9.7)	0.594[f]	5 (11.9)	16 (12.7)	1.000[f]
Dilated pancreatic duct (≥5mm)	15 (38.5)	246 (32.4)	0.542	15 (38.5)	33 (31.4)	0.551
Pancreatic texture						
Normal/soft	15 (41.7)	411 (53.0)	0.244	15 (41.7)	53 (49.1)	0.563
Fibrotic/hard	21 (58.3)	364 (47.0)		21 (58.3)	55 (50.9)	
Blood loss (mL), median (IQR)	310 (200-600)	500 (200-900)	0.138	310 (200-600)	500 (250-800)	0.125
Operative time (min), median (IQR)	309 (245.75-353.50)	349 (281-425)	**0.002**	309 (245.75-353)	363 (293-437)	**0.002**
R0-resection[e]	15 (39.5)	443 (55.5)	0.076	15 (39.5)	51 (43.2)	0.828

Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Only in patients without neoadjuvant therapy: 32 patients in EUS-CDS group and 458 patients in ERCP group in unmatched cohort and 70 patients in matched cohort. [b]Laparoscopic or robot, including patients with conversion to open surgery. [c]Vascular resection was reported according to the International Study Group for Pancreatic Surgery (ISGPS) classification.[29] [d]Including spleen (intentional or non-intentional), mesocolon transversum, colon segment, hemicolectomy, gastric resection, or other. [e]Resection margin status was classified as microscopically radical (>1 mm; R0) or microscopically irradical (≤1 mm; R1).[30] [f]Fisher exact test. Abbreviations: IQR, interquartile range (P25-P75); PRPD, pylorus-resecting pancreatoduodenectomy; PPPD, pylorus-preservering pancreatoduodenectomy.

Table 3. Post-operative outcome of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP

	Unmatched cohort			Matched cohort		
	EUS-CDS (n=42)	**ERCP (n=895)**	**Relative Risk or Mean Difference (95% CI)**	**EUS-CDS (n=42)**	**ERCP (n=126)**	**Relative Risk or Mean Difference (95% CI)**
Major postoperative complication	8 (19.0)	292 (32.6)	0.50 (0.23-1.07)	8 (19.0)	40 (31.7)	0.59 (0.29-1.18)
Any postoperative complication	27 (64.3)	586 (65.5)	0.95 (0.51-1.76)	27 (64.3)	85 (67.5)	0.90 (0.52-1.55)
Postoperative pancreatic fistula, grade B/C	5 (11.9)	162 (18.1)	0.62 (0.25-1.56)	5 (11.9)	24 (19.0)	0.77 (0.36-1.65)
Delayed gastric emptying, grade B/C	6 (14.3)	165 (18.4)	0.75 (0.32-1.74)	6 (14.3)	20 (15.9)	0.91 (0.43-1.94)
Post pancreatectomy hemorrhage, grade B/C	1 (2.4)	65 (7.3)	0.32 (0.05-2.31)	1 (2.4)	7 (5.6)	0.49 (0.08-3.11)
Hepatico-jejunostomy biliary leak, grade B/C	2 (4.8)	34 (3.8)	1.25 (0.31-4.98)	2 (4.8)	7 (5.5)	0.88 (0.25-3.09)
Chyle leak, grade B/C	4 (9.5)	55 (6.1)	1.57 (0.58-4.24)	4 (9.5)	11 (8.7)	1.07 (0.44-2.60)
Pneumonia	2 (4.8)	30 (3.4)	1.41 (0.36-5.60)	2 (4.8)	5 (4.0)	1.15 (0.35-3.83)
Surgical site infection	7 (16.7)	141 (15.8)	1.07 (0.48-2.35)	5 (11.9)	6 (4.8)	1.93 (0.95-3.91)
Intensive care unit admission	4 (9.5)	62 (6.9)	1.39 (0.51-3.77)	4 (9.5)	9 (7.1)	1.26 (0.53-2.97)
Re-intervention	6 (14.3)	281 (31.4)	**0.38 (0.16-0.89)**	6 (14.3)	39 (31.0)	0.46 (0.21-1.08)
Endoscopic	1 (2.9)	60 (6.7)	0.35 (0.05-2.50)	1 (2.9)	8 (6.3)	0.43 (0.07-2.79)
Radiological	5 (11.9)	223 (24.9)	0.42 (0.17-1.06)	5 (11.9)	34 (27.0)	0.45 (0.19-1.06)
Reoperation	2 (4.8)	58 (6.5)	0.73 (0.18-2.95)	2 (4.8)	8 (6.3)	0.79 (0.22-2.81)
In-hospital mortality	1 (2.4)	20 (2.2)	1.06 (0.15-7.37)	1 (2.4)	4 (3.2)	0.80 (0.14-4.68)
Length of hospital stay, mean (95%CI) and median (IQR)[a]	13.3 (10.4-18.8)	14.8 (14.0-16.0)	-1.5 (-4.6 – 3.9)	13.3 (10.3-18.7)	15.6 (13.6-18.2)	-2.3 (-6.1 – 3.1)
	8.5 (6-15.25)	10 (7-16)	0.127[b]	8.5 (6-15.25)	11 (7-17.25)	0.078[b]
Readmission within 30 days after discharge	8 (19.0)	142 (15.9)	1.23 (0.58-2.61)	8 (19.0)	17 (13.5)	1.35 (0.71-2.56)

Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Missing in 2 patients in EUS-CDS group and in 32 patients in the ERCP group in the unmatched cohort and in 5 patients in the ERCP group in the matched cohort. [b]p-value derived by Wilcoxon rank sum test with continuity correction. Abbreviations: 95%CI, 95% confidence interval; IQR, interquartile range (P25-P75).

Table 4. Surgeon survey following pancreatoduodenectomy in patients with prior EUS-CDS

Survey questions	N=29 EUS-CDS
Did you visualize the stent during the resection?	
Yes	7 (24)
No	22 (76)
Did you notice the presence of the stent during the resection?	
Yes	20 (69)
No	9 (31)
To what extent was the surgery complicated by the stent?	Median 2 (IQR 1-2)
1 - not complicated	13 (45)
2 - slightly complicated	8 (28)
3 - clearly complicated	5 (17)
4 - severely complicated	2 (7)
5 - impossible	0 (0)
Was there enough space between the hilum and the stent for the establishment of the hepaticojejunostomy?	
Yes	29 (100)
No	0 (0)
Did you have to adapt the surgical plan due to the presence of the stent?	
Yes	3 (10)
No	26 (90)

Values are n (%) unless otherwise indicated. Abbreviations: EUS-CDS, endoscopic ultrasound guided choledochoduodenostomy; IQR, interquartile range (P25-P75).

Figure 1. Flowchart of screening- and inclusion process.
Abbreviations: DPCA, Dutch Pancreatic Cancer Audit; EUS-CDS, Endoscopic ultrasound guided choledochoduodenostomy; ERCP, endoscopic retrograde cholangiopancreatography.

Figure 2. Peroperative image of EUS-CDS.
Green, bile duct; blue, duodenum.

Biliary drainage prior to pancreatoduodenectomy with Endoscopic Ultrasound-guided choledochoduodenostomy vs conventional Endoscopic Retrograde Cholangiopancreatography: a propensity score matched study and surgeon-survey

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Disclosures

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Disclosure

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Data availability

Data will be available upon reasonable request from the authors.

ABSTRACT

Background Preoperative endoscopic biliary drainage may lead to complications (16%-24%), potentially hampering surgical exploration. Endoscopic ultrasound-guided choledochoduodenostomy (EUS-CDS) may reduce drainage-related complications, however it is unknown whether EUS-CDS could in itself hamper surgical exploration as series with surgeon reported outcomes are lacking. Aim is to assess the impact of preoperative EUS-CDS on pancreatoduodenectomy.

Method Consecutive patients who underwent pancreatoduodenectomy after preoperative biliary drainage were included in all eight centers that performed EUS-CDS in the mandatory Dutch Pancreatic Cancer Audit (Jan 2020-Dec 2022). Primary outcome was major postoperative complications. Secondary outcomes included bile leak grade B/C, postoperative pancreatic fistula (POPF) grade B/C, and overall postoperative complications. A propensity score matching (1:3) analysis was performed. Surgeons who performed a pancreatoduodenectomy after EUS-CDS were asked to complete a survey.

Results Overall, 937 patients with pancreatoduodenectomy after preoperative biliary drainage were included (42 EUS-CDS, 895 ERCP). Major postoperative complications occurred in eight patients (19%) in the EUS-CDS group and 292 patients (33%) in the ERCP group (RR 0.50; 95%CI, 0.23-1.07). No significant differences were observed in overall complications (RR 0.95; 95%CI, 0.51-1.76), bile leak (RR 1.25; 95%CI, 0.31-4.98) or POPF (RR 0.62; 95%CI, 0.25-1.56). Results were similar after matching. The survey was completed for 29 pancreatoduodenectomies; surgery was not (n=13, 45%), 'slightly' (n=8, 28%), 'clearly' (n=5, 17%) or 'severely' (n=2, 7%) more complex because of the EUS-CDS.

Conclusion This early experience suggests that preoperative biliary drainage with EUS-CDS does not increase the rate of complications after pancreatoduodenectomy and only infrequently hampers surgical exploration.

INTRODUCTION

Patients with malignant distal biliary obstruction frequently require biliary drainage before undergoing pancreatoduodenectomy.[1] Traditionally, this is performed via endoscopic retrograde cholangiopancreatography (ERCP) with placement of a self-expanding metal stent (SEMS). This procedure is associated with a substantial risk of complications (range 16-24%), especially post-ERCP pancreatitis (9-18%) and re-interventions for stent related problems (4-14%) both potentially delaying and frustrating surgical exploration.[2-7] Moreover, these complications, especially post-ERCP pancreatitis, are associated with postoperative adverse events, prolonged hospital stay [8, 9], and delay of or even cancellation of surgical treatment.[4, 8-10]

In recent years, endoscopic ultrasound guided choledochoduodenostomy (EUS-CDS) with a lumen apposing metal stent (LAMS) has emerged as an alternative to ERCP in malignant distal biliary obstruction.[11] This approach is mostly used if ERCP fails or as primary drainage modality in a trial setting but it has been suggested as a promising alternative for upfront ERCP.[12, 13] Although several studies, including a randomised trial, showed that EUS CDS resulted in promising results, , in terms of technical success and adverse events, experience in resectable patients is still limited.[11-14] Most EUS-CDS series have focused on patients with unresectable or metastatic disease. In patients with resectable disease, endoscopists and surgeons have been reluctant to use EUS-CDS as data on the impact of perforations in both the duodenal and CBD wall on the surgical procedure are lacking and data on the risk of postoperative complications are scarce.[12, 15-19]

The aim of this study was to assess the intraoperative and postoperative outcomes in patients who underwent pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS compared with conventional biliary drainage by ERCP.

METHODS

Study design

This study was a retrospective analysis of prospectively collected data from the Dutch Pancreatic Cancer Audit (DPCA).[20] The DPCA is a mandatory audit for all hospitals performing pancreatic surgery in the Netherlands. Data were collected from all Dutch hospitals in which EUS-CDS was performed in a preoperative setting, five tertiary academic hospitals and three teaching hospitals. From all patients who underwent pancreatoduodenectomy after preoperative endoscopic biliary drainage between January 2020 and December 2022 data of the DPCA were included. Additional data from patients undergoing EUS-CDS and subsequent resection in 2023 were collected to expand the cohort. Patients who underwent percutaneous biliary drainage and patients with missing data in age, sex, and hospital of treatment were excluded for further analyses. The study protocol was approved by the scientific committee of the Dutch Pancreatic Cancer Group (DPCG).[21] Given the observational character of this study, the Medical Ethics Review Committee confirmed that the Dutch Medical Research Act does not apply. In patients where additional data was requested and/or a surgical survey was performed, written informed consent was obtained.

Biliary drainage procedures

Biliary drainage was performed when considered indicated by a multidisciplinary team. In general biliary drainage was performed in patients with cholangitis, severe symptoms such as pruritus (caused by hyperbilirubinemia), severe hyperbilirubinemia (bilirubin concentration ≥250 µmol/L [≥14.6 g/dL]), mild jaundice (>40 µmol/L [≥2.4 g/dL]) before administration of chemotherapy or if the waiting time for surgery exceeded three weeks and it was anticipated that the bilirubin concentration would exceed ≥250 µmol/L [≥14.6 g/dL] at time of surgery. In the ERCP group, preferably a fully-covered self-expanding metal stent (SEMS) was placed, the length of the stent was based on stricture characteristics and preference of the gastroenterologist. EUS-CDS was performed after an unsuccessful ERCP or as primary drainage method in a research setting (SCORPION-p (14) and SCORPION-II-p [NCT05595122]),

or in case biliary cannulation was upfront considered impossible. For EUS-CDS a LAMS was used, in all but one centre Hot-Axios (Boston Scientific) 6x8 or 8x8mm was used, in the other centre Niti-S (Hot-)NAGI (Taewoong Medical) 10x20mm was used. The use of coaxial double pigtail plastic stents (DPS) or fully-covered SEMS (FCSEMS) through the LAMS to prevent stent dysfunction was at the discretion of the endoscopist.

Study outcomes, and definitions

The primary outcome was the incidence of major postoperative complications, defined as Clavien-Dindo score ≥3.[22] Secondary outcomes were overall complications, pancreatic surgery-specific complications grade B/C (i.e., hepatico-jejunostomy biliary leak, postoperative pancreatic fistula (POPF), delayed gastric emptying, post-pancreatectomy hemorrhage, and chyle leakage), pneumonia, surgical site infection, re-interventions, in-hospital mortality, hospital stay, and readmissions. All complications during hospital admission or up to 30 days after resection (in case of earlier discharge) were registered. Pancreatic surgery-specific complications were all defined by the ISPGS or the International Study Group of Liver Surgery.[23-26]

Survey

Surgeons who performed a pancreatoduodenectomy after EUS-CDS were requested to complete a five-question survey about the resection. This questionnaire consisted of questions about intraoperative findings related to the LAMS and potential surgical difficulties. The survey was intended to be send on the same day as the resection, however due to the delayed inclusion of additional centres, in some centres the survey was filled out retrospectively. To assess potential recall bias and the influence of the lack of blinding, a sensitivity analysis was performed in surveys that were filled out within 2 weeks after the resection. The survey was provided in the supplementary material.

Statistical analysis

Normally distributed continuous patient and surgery characteristics data were summarized as means with standard deviations (SD) and compared with an independent t-test. Non-normally distributed data were presented as medians with interquartile ranges (IQR) and compared with a Mann-Whitney U test. The data distribution was evaluated through visual inspection. Categorical data were presented as frequencies with percentages and analyzed using the Chi-square test or Fisher exact test, as appropriate. A p-value below 0.05 was considered statistically significant. Primary and secondary outcomes were presented as relative risk (RR) with corresponding 95% confidence intervals (CI) or as mean differences with 95% CI derived by bootstrapping with 5,000 samples independently of the distribution of the variable.[27]

To minimize the impact of treatment allocation bias, patients from the EUS-CDS group were matched to patients from the ERCP group. Optimal pair matching was performed in a 1:3 ratio to increase power, without replacement. Variables for matching were selected based on baseline discrepancies and expected factors of influence on outcome. Baseline variables sex, age, BMI, ASA-score, liver and pancreas related comorbidities, tumor origin, neoadjuvant therapy, and hospital volume of more than hundred resections per year were identified as variables for the propensity score model. Only patients with a metal stent in the ERCP group were matched. To be able to calculate propensity scores for all patients, missing data in these variables (range 0-19%) were imputed by multiple imputation and reported in Table S1.[28] Only non-imputed data was reported in the manuscript, the imputed data was provided in the supplementary material (Table S2). Covariate balance between treatment and control groups was assessed using the standardized mean difference (SMD) of the propensity score (distance). An SMD below 0.1 was considered indicative of acceptable balance. The overall SMD for the propensity score distance after matching was 0.066, suggesting adequate balance between the groups. Detailed balance diagnostics, consisting of the SMDs for individual covariates before and after matching, are provided in Table S3. Patients who eventually underwent EUS-CDS were included in the EUS-CDS group versus patients who underwent successful ERCP with stent placement in the ERCP group. An exploratory analysis was performed comparing 1. patients who underwent primary drainage

attempt with EUS-CDS (without previous biliary cannulation attempt by ERCP or direct EUS-CDS in a clinical trial setting) and 2. Patients who underwent a primary drainage attempt with ERCP. These results are provided in the supplementary material. Statistical analyses were conducted with R software, version 4.2.1 (R Project for Statistical Computing).

RESULTS

Patient selection

In total, 2243 patients underwent a pancreatoduodenectomy in the participating centres. Pancreatoduodenectomy following endoscopic biliary drainage was performed in 981 patients, of which 937 were included in the analysis, as shown in the flowchart in Figure 1. EUS-CDS was performed as a rescue strategy after failed ERCP in most patients (n=25, 59.5%), while the other 17 patients (40.5%) underwent primary drainage by EUS-CDS. In twenty patients (47.6%), drainage was performed with LAMS alone, in 17 patients (40.5%) a coaxial DPS was placed through the LAMS and in four patients (9.5%) a FCSEMS was placed through the LAMS. Coaxial stent placement was performed as a prophylactic measure (n=17, 81.0%) or after stent dysfunction (n=4, 19.0%). In one patient, EUS-CDS was performed using a FCSEMS after failed placement of a LAMS. In the ERCP group SEMS were placed in 633 patients (78.0%) and plastic stents in 179 patients (22.0%), in 83 patients (9.3%) the specific type of stent was missing (Table 1). Most placed SEMS were fully covered (n=512, 88.7%).

Patient characteristics

No significant differences were present in baseline characteristics between the EUS-CDS group and ERCP group, except for the site of tumor origin (p=0.018) and hospital volume (p=0.005). After matching, overall balance was obtained in the baseline characteristics (Table 1).

Surgical characteristics

Surgical characteristics were comparable between the two groups, except for time between biliary drainage and surgery in patients without neoadjuvant therapy (median 32 days [IQR 22-39.25] in the EUS-CDS group vs 41 days [IQR 28-54] in the ERCP group, p=0.010) and operative time (median 309 minutes [IQR 245.75-353] in the EUS-CDS group vs 349 minutes [IQR 281-425] in the ERCP group, p=0.002). These differences remained after matching, namely the median time between drainage and surgery in the ERCP group after matching was 43 days (IQR 28-54.75; p=0.022) and median operative

time was 363 minutes (IQR 293-437; p=0.002). Intraoperative variables before and after matching are reported in Table 2.

In the 17 patients who underwent EUS-CDS as primary drainage method, as compared to patients who underwent primary ERCP (n=920), time to surgery was median 22 days (IQR 20-36) versus 41 days (IQR 28-54; p=0.014) and operative time was 306.5 minutes (IQR 211-341.5) versus 347.5 minutes (IQR 281-425; p=0.006) (Table S3).

Complications

Major postoperative complications occurred in eight patients (19.0%) in the EUS-CDS group and 292 patients (32.6%) in the ERCP group (RR 0.50; 95% CI, 0.23-1.07). When including all complications after surgery, 27 patients (64.3%) experienced at least one complication in the EUS-CDS group versus 586 patients (65.5%) in the ERCP group (RR 0.95; 95% CI, 0.51-1.76). A POPF occurred in five patients (11.9%) in the EUS-CDS group and in 162 patients (18.1%) in the ERCP group (RR 0.62; 95% CI 0.25-1.56) (Table 3). In the EUS-CDS group fewer postoperative re-interventions (n=16, 14.3%) were performed compared to the ERCP group (n=281, 31.4%; RR 0.38; 95% CI, 0.16-0.89). This difference remained but was not significant in the matched cohort (RR 0.46; 95% CI, 0.21-1.08). Other secondary outcomes and type of re-interventions were comparable between both groups (Table 3).

In the 17 patients who underwent EUS-CDS as primary drainage method, major postoperative complications occurred in one patient (5.9%), compared with 299 patients (32.5%) after primary ERCP (RR 0.13, 95% CI, 0.02-1.00). Ten patients (58.8%) experienced at least one postoperative complication after primary drainage after EUS-CDS versus 603 (65.5%) after primary ERCP (RR 0.76; 95% CI, 0.29-1.97). None of the 17 patients who underwent primary EUS-CDS developed a grade B/C POPF. Median length of hospital stay was 8 days (IQR 5-9) in the EUS-CDS group versus 10 days (IQR 7-16.75) in the primary ERCP group (p=0.012) (Table S4).

Survey

The survey was sent to surgeons who recently performed 31 pancreatoduodenectomies after EUS-CDS. The survey was completed by 15 surgeons from eight hospitals regarding 29 procedures (response rate 94%). In the majority (n=22, 76%) of procedures, surgeons did not visualize the stent but did notice the presence of the stent (n=20, 69%). In most procedures, surgeons noted some infiltration (n=8, 28%), fibrosis (n=1, 3%) or edema (n=1, 3%). In other patients, surgeons could palpate the stent (n=5, 17%), only noticed the stent when dissecting the bile duct (n=2, 7%), or noticed the adhesion of bile duct to the duodenum (n=3, 10%) (Figure 2). In most cases surgery was not (n=13, 45%) or slightly more complex (n=9, 31%) due to some inflammation (n=4), adhesions (n=3), or fibrosis (n=2). In five patients (17%) the surgery was evidently more complex due to inflammation or infiltration (n=3) or adhesions (n=1) and one surgeon just described a more complex surgery without specifying the possible cause. In one of these five patients a major postoperative complication occurred. In two patients the surgeon described that the surgery was severely hampered. In both cases severe inflammation was present which was presumed to be caused by the stent. In one of these resections there was also unintentional clamping injury of the proper hepatic artery and in the other an aberrant artery was described which hindered the procedure in combination with the inflammation leading to a severe intraoperative bleeding. In all patients the distance between the LAMS and the hilum was sufficient to create a hepaticojejunostomy. The operative plan was altered in three patients due to the presence of the EUS-CDS. One of these patients is described above and in two others a pylorus ring resecting, rather than a pylorus preserving, pancreatoduodenectomy was performed. Surveys were completed a median of 53 days (IQR 1-160 days) after the resection, an exploratory sensitivity analysis in surveys completed within 14 days after the resection was provided in the supplementary material (n=14), in this group surgeons reported a “not” (n=5) or only “slightly” (n=6) complicated surgery due to the presence of the stent (Table S5).

When only patients with EUS-CDS as primary drainage method are included (n=10), two surgeons visualized the stent during a resection (17%) and seven (58%) noticed infiltration, edema or fibrosis presumably caused by the stent. Two surgeons only noticed the stent when dissecting the bile duct or adhesions to the duodenum. Surgery was not (n=5, 42%) or slightly (n=6, 50%) hampered in the vast majority, one surgeon described an evidently hampered surgery due to inflammation.

DISCUSSION

This first propensity-score matched study including a surgeon-survey on EUS-CDS found no increased risk of major complications after pancreatoduodenectomy in patients with EUS-CDS as compared with conventional preoperative biliary drainage by ERCP. In fact, patients undergoing EUS-CDS had a shorter time between biliary drainage and surgery and a shorter operative time. These results remained similar after 1:3 propensity score matching. Only a few surgeons reported that EUS-CDS had a negative impact on surgical exploration.

Two previous studies compared the outcome of patients who underwent pancreatoduodenectomy after EUS-CDS when compared with ERCP. One retrospective French multicentre study assessed the impact of EUS-CDS in 44 patients on the rate of complications after pancreatoduodenectomy compared with ERCP in 112 patients from nine centres. The French study reported that EUS-CDS was associated with fewer post-operative complications (77.3% vs 93.7%) and shorter hospital stay (median 17 vs 20 days) when compared with ERCP.[19] However, both SEMS and plastic stents were included in the ERCP group which may have blurred the study outcomes as previous data showed that postoperative outcome following SEMS is better than plastic stents.[7] In order to neutralize this confounder we additionally performed a matched analysis in which only patients treated with a SEMS were selected for the ERCP group. Moreover, our study is the first to include a surgeon-survey which adds interesting insight on potential difficulties caused by the stent that are not reflected in post-operative complications. We believe that the fact that in the current study the patients were matched, only patients with a SEMS were included in the matched analysis, and the additional surgeon-survey substantially adds to current available data and improves the implications of study outcome.

In a randomised controlled trial (RCT), six patients undergoing pancreatoduodenectomy after EUS-CDS were compared with four patients who underwent preoperative ERCP.[12, 13] A shorter operative time and hospital stay were reported after EUS-CDS but this was not statistically significant given the

very small sample size. Furthermore, two retrospective non-comparative studies have reported the postoperative outcomes of five and 21 patients who underwent preoperative EUS-CDS [16, 17], the latter from the same group as above described later comparative study [19], see Table S6.

In contrast to this previous study, we found no difference in (major) post-operative complications and hospital stay between the EUS-CDS and ERCP groups. No differences in individual adverse events could be identified in neither of the studies.[19] When comparing our outcomes to studies on conventional endoscopic biliary drainage, the rate of postoperative major complications in the unmatched cohort (33%) was somewhat higher when compared with a previous nationwide study from the Netherlands (24%) and an RCT from Sweden comparing ERCP with SEMS and plastic stents (21%).[3, 7] However, after excluding plastic stents in the matched cohort, results were comparable with the SEMS groups in both previous studies, showing the potential influence of including plastic stents on the study outcomes. More specifically, no difference was found in the rates of bile leak and POPF between the groups. A previous Dutch nationwide comparison between patients who underwent preoperative ERCP with either a plastic stent or SEMS reported less POPF with SEMS (9.8% vs. 14.8%).[7] The higher risk of POPF is thought to be inversely correlated to fibrosis of the pancreas.[31, 32] It was presumed that SEMS induces more pressure on the pancreatic duct, compared with plastic stents, leading to more pancreatic fibrosis and subsequently fewer POPF. Consequently, one might hypothesize that EUS-CDS could increase the risk of POPF as compared with ERCP with LAMS, given that in EUS-CDS, the LAMS does not cause compression of the pancreatic duct. However, our data do not support this hypothesis, showing no difference in pancreatic texture nor risk of POPF, even after exclusion of patients who underwent plastic stent placement in the matched analysis. Moreover, it is worth mentioning that none of the patients who underwent EUS-CDS as primary drainage method developed POPF.

A potential benefit of EUS-CDS could be a shorter time between drainage and upfront surgery or time to neoadjuvant therapy, which was first reported by Janet et al. and further supported by our findings. [19] The shorter time to surgery after EUS-CDS may reflect less delay due to drainage related complications. Preoperative complications caused by biliary drainage were, however, not part of the outcomes in our study. This was done by intent as it has been clearly shown, even in RCT, that preoperatively EUS-CDS does not increase and possibly even reduces drainage-related complications, and the risk of reporting bias would have been significantly higher in this retrospective study.[12, 13]

The observed similar postoperative outcomes do however, as mentioned, not exclude the possibility that the surgical procedure becomes more technically challenging following EUS-CDS. Therefore, a surgeon-survey was performed which indeed showed that, in a subgroup of patients, EUS-CDS did complicate the procedure, presumably due to inflammation/infiltration or adhesions following the small intentionally made duodenal and biliary perforations. ERCP with SEMS placement may also cause some inflammation/infiltration or adhesions, even in absence of a clinically apparent pancreatitis. Currently, data on surgeon experience after ERCP with stent placement is unavailable so we are unable to compare or even confirm this finding. It is nonetheless reassuring that most resections were not or only slightly hampered by the stent.

This result of this study should be interpreted considering several limitations. First, missing data are unavoidable due to the retrospective nature of this study. By using the prospectively collected data from the DPCA database, which is known for high quality data, we were able to limit the extent of missing data.[20]. Second, only patients who underwent a pancreatoduodenectomy were included, and therefore patients who had severe drainage-related complications who could not undergo surgery were not part of the study. Third, both patients who underwent primary EUS-CDS, as well as patients who first underwent an unsuccessful ERCP were included. This may have introduced bias since the attempted ERCP could have negatively influenced the results of the EUS-CDS group. Therefore, we

performed an additional exploratory analysis including only patients who underwent EUS-CDS without previous biliary cannulation attempt by ERCP. The analysis shows promising results with low (major) postoperative complication rates (Table S3), although no firm conclusion can be drawn due to the small number of patients and the lack of events in this group. Fourth, the fact that part of the surveys was completed retrospectively, potentially after the surgeon was aware of any possible occurred complications, could have influenced the results. In an exploratory sensitivity analysis assessing surveys completed within 2 weeks no surgeons reported a “clearly” complicated resection indicating the potential influence of the lack of blinding. Fifth, the sample size remains relatively small, which means that the fact that no differences were found in the primary and secondary outcomes does not necessarily imply the absence of true differences. This study should therefore be considered an exploratory study, paving the way for larger prospective studies to include patients with a potentially resectable tumor as well. Sixth, we acknowledge that propensity-score matching is vulnerable to residual confounding. In this study, propensity-score matching was used as a sensitivity analysis, and no conclusions were drawn solely from the matched cohort. The consistency of outcome differences before and after matching suggests that baseline differences in observed variables were unlikely to drive these results. However, residual confounding cannot be excluded. The main strength of this study is its relatively large cohort, the first study with propensity-score matching comparing EUS-CDS to ERCP with only SEMS, and the first study with a surgeon-survey to assess intraoperative findings due to EUS-CDS.

In conclusion, this study found that EUS-CDS was not associated with an increased rate of postoperative complications as compared with SEMS placement by ERCP. Surgeons encountered no or minimal technical difficulties possibly related to EUS-CDS during the majority of resections. To confirm these findings and assess whether EUS-CDS may reduce the rate of post-biliary drainage complications, future randomised trials should specifically include patients with resectable tumor and report postoperative outcomes.

REFERENCES

1. Dumonceau JM, Tringali A, Papanikolaou IS et al. Endoscopic biliary stenting: indications, choice of stents, and results: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline - Updated October 2017. Endoscopy 2018; 50: 910-930. doi:10.1055/a-0659-9864
2. Liu P, Lin H, Chen Y et al. Comparison of Metal and Plastic Stents for Preoperative Biliary Drainage in Resectable and Borderline Resectable Periampullary Cancer: A Meta-Analysis and System Review. J Laparoendosc Adv Surg Tech A 2018; 28: 1074-1082. doi:10.1089/lap.2018.0029
3. Olsson G, Frozanpor F, Lundell L et al. Preoperative biliary drainage by plastic or self-expandable metal stents in patients with periampullary tumors: results of a randomized clinical study. Endosc Int Open 2017; 5: E798-e808. doi:10.1055/s-0043-110565
4. Tol JA, van Hooft JE, Timmer R et al. Metal or plastic stents for preoperative biliary drainage in resectable pancreatic cancer. Gut 2016; 65: 1981-1987. doi:10.1136/gutjnl-2014-308762
5. Song TJ, Lee JH, Lee SS et al. Metal versus plastic stents for drainage of malignant biliary obstruction before primary surgical resection. Gastrointest Endosc 2016; 84: 814-821. doi:10.1016/j.gie.2016.04.018
6. van der Gaag NA, Rauws EAJ, van Eijck CHJ et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med 2010; Jan 14;362(2): 129-137. doi:10.1056/NEJMoa0903230
7. Latenstein AEJ, Mackay TM, van Huijgevoort NCM et al. Nationwide practice and outcomes of endoscopic biliary drainage in resectable pancreatic head and periampullary cancer. HPB (Oxford) 2021; 23: 270-278. doi:10.1016/j.hpb.2020.06.009
8. Chen YH, Xie SM, Zhang H et al. Clinical impact of preoperative acute pancreatitis in patients who undergo pancreaticoduodenectomy for periampullary tumors. World J Gastroenterol 2015; 21: 6937-6943. doi:10.3748/wjg.v21.i22.6937

9. Asari S, Matsumoto I, Ajiki T et al. Perioperative management for pancreatoduodenectomy following severe acute pancreatitis in patients with periampullary cancer: our experience with six consecutive cases. Surgery Today 2015; 45: 181-188. doi:10.1007/s00595-014-0900-x

10. Yoon SJ, Lee O, Jung JH et al. Does Preoperative Acute Pancreatitis Inevitably Delay Pancreatoduodenectomy in Patients with Periampullary Tumors? Cancers (Basel) 2021; 13: 6289. doi:10.3390/cancers13246289

11. van der Merwe SW, van Wanrooij RLJ, Bronswijk M et al. Therapeutic endoscopic ultrasound: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2021; 54: 185-205. doi:10.1055/a-1717-1391

12. Chen YI, Sahai A, Donatelli G et al. Endoscopic Ultrasound-Guided Biliary Drainage of First Intent With a Lumen-Apposing Metal Stent vs Endoscopic Retrograde Cholangiopancreatography in Malignant Distal Biliary Obstruction: A Multicenter Randomized Controlled Study (ELEMENT Trial). Gastroenterology 2023; 165: 1249-1261. doi:10.1053/j.gastro.2023.07.024

13. Teoh AYB, Napoleon B, Kunda R et al. EUS - guided choledocho-duodenostomy using lumen apposing stent versus ERCP with covered metallic stents in patients with unresectable malignant distal biliary obstruction. A multi-center randomized controlled trial. (DRA-MBO trial). Gastroenterology 2023; 165: 473. doi:10.1053/j.gastro.2023.04.016

14. Fritzsche JA, Fockens P, Besselink MG et al. Endoscopic ultrasound-guided choledochoduodenostomy using single-step lumen-apposing metal stents for primary drainage of malignant distal biliary obstruction (SCORPION-p): a prospective pilot study. Endoscopy 2024; 56: 47-52. doi:10.1055/a-2134-3537

15. Bang JY, Navaneethan U, Hasan M et al. Stent placement by EUS or ERCP for primary biliary decompression in pancreatic cancer: a randomized trial (with videos). Gastrointest Endosc 2018; 88: 9-17. doi:10.1016/j.gie.2018.03.012

16. Gaujoux S, Jacques J, Bourdariat R et al. Pancreaticoduodenectomy following endoscopic ultrasound-guided choledochoduodenostomy with electrocautery-enhanced lumen-apposing stents an ACHBT - SFED study. HPB (Oxford) 2021; 23: 154-160. doi:10.1016/j.hpb.2020.06.001

17. Fabbri C, Fugazza A, Binda C et al. Beyond palliation: using EUS-guided choledochoduodenostomy with a lumen-apposing metal stent as a bridge to surgery. a case series. J Gastrointestin Liver Dis 2019; 28: 125-128. doi:10.15403/jgld.2014.1121.281.eus

18. Tyberg A, Sarkar A, Shahid HM et al. EUS-Guided Biliary Drainage Versus ERCP in Malignant Biliary Obstruction Before Hepatobiliary Surgery: An International Multicenter Comparative Study. Journal of clinical gastroenterology 2023; 57: 962-966. doi:10.1097/mcg.0000000000001795

19. Janet J, Albouys J, Napoleon B et al. Pancreatoduodenectomy Following Preoperative Biliary Drainage Using Endoscopic Ultrasound-Guided Choledochoduodenostomy Versus a Transpapillary Stent: A Multicenter Comparative Cohort Study of the ACHBT-FRENCH-SFED Intergroup. Ann Surg Oncol 2023; 30: 5036-5046. doi:10.1245/s10434-023-13466-8

20. van Rijssen LB, Koerkamp BG, Zwart MJ et al. Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit. HPB (Oxford) 2017; 19: 919-926. doi:10.1016/j.hpb.2017.06.010

21. Strijker M, Mackay TM, Bonsing BA et al. Establishing and Coordinating a Nationwide Multidisciplinary Study Group: Lessons Learned by the Dutch Pancreatic Cancer Group. Annals of Surgery 2020; 271: e102-e104. doi:10.1097/sla.0000000000003779

22. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205-213. doi:10.1097/01.sla.0000133083.54934.ae

23. Besselink MG, van Rijssen LB, Bassi C et al. Definition and classification of chyle leak after pancreatic operation: A consensus statement by the International Study Group on Pancreatic Surgery. Surgery 2017; 161: 365-372. doi:10.1016/j.surg.2016.06.058

24. Wente MN, Bassi C, Dervenis C et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007; 142: 761-768. doi:10.1016/j.surg.2007.05.005

25. Koch M, Garden OJ, Padbury R et al. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. Surgery 2011; 149: 680-688. doi:10.1016/j.surg.2010.12.002

26. Bassi C, Marchegiani G, Dervenis C et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery 2017; 161: 584-591. doi:10.1016/j.surg.2016.11.014

27. DiCiccio TJ, Efron B. Bootstrap Confidence Intervals. Statistical Science 1996; 11: 189-212.

28. Pishgar F, Greifer N, Leyrat C, Stuart E. MatchThem:: Matching and Weighting after Multiple Imputation. The R Journal 2021; 13: 292-305.

29. Bockhorn M, Uzunoglu FG, Adham M et al. Borderline resectable pancreatic cancer: A consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2014; 155: 977-988. doi:https://doi.org/10.1016/j.surg.2014.02.001

30. [Anonymous]. The Royal College of Pathologists (2013) Standards and datasets for reporting cancers. Dataset for the histopathological reporting of carcinomas of the pancreas, ampulla of vater and common bile duct. The Royal College of Pathologists, London. In:

31. Mathur A, Pitt HA, Marine M et al. Fatty pancreas: a factor in postoperative pancreatic fistula. Ann Surg 2007; 246: 1058-1064. doi:10.1097/SLA.0b013e31814a6906

32. Deng Y, Zhao B, Yang M et al. Association Between the Incidence of Pancreatic Fistula After Pancreaticoduodenectomy and the Degree of Pancreatic Fibrosis. J Gastrointest Surg 2018; 22: 438-443. doi:10.1007/s11605-017-3660-2

FIGURE AND TABLE LEGENDS

Figure 1. Flowchart of screening- and inclusion process. DPCA, Dutch Pancreatic Cancer Audit; EUS-CDS, Endoscopic ultrasound guided choledochoduodenostomy; ERCP, endoscopic retrograde cholangiopancreatography.

Figure 2. Peroperative image of EUS-CDS. Green, bile duct; blue, duodenum.

Table 1. Baseline characteristics of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP. Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Only in patients in whom biliary drainage was performed prior to the start of neoadjuvant therapy after biliary drainage: 9 in EUS-CDS group, 165 in ERCP group before matching and 15 in ERCP group after matching. [b]Hospital volume was based on the mean total annual volume of pancreatoduodenectomy performed during the study period. [c]Fisher exact test. Abbreviations: BMI, body mass index; ASA, American Society Anesthesiologists; EUS-CDS, endoscopic ultrasound guided choledochoduodenostomy; ERCP, endoscopic retrograde cholangiopancreatography; NA, not applicable.

Table 2. Surgical characteristics of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP. Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Only in patients without neoadjuvant therapy: 32 patients in EUS-CDS group and 458 patients in ERCP group in unmatched cohort and 70 patients in matched cohort. [b]Laparoscopic or robot, including patients with conversion to open surgery. [c]Vascular resection was reported according to the International Study Group for Pancreatic Surgery (ISGPS) classification.[29] [d]Including spleen (intentional or non-intentional), mesocolon transversum, colon segment, hemicolectomy, gastric resection, or other. [e]Resection margin status was classified as microscopically radical (>1 mm; R0) or microscopically irradical (≤1 mm; R1).[30] [f]Fisher exact test.

Abbreviations: IQR, interquartile range (P25-P75); PRPD, pylorus-resecting pancreatoduodenectomy; PPPD, pylorus-preservering pancreatoduodenectomy.

Table 3. Post-operative outcome of patients undergoing pancreatoduodenectomy after preoperative biliary drainage by EUS-CDS and ERCP. Values are n (%) unless otherwise indicated. Bold values indicate statistical significance at a 5% level. [a]Missing in 2 patients in EUS-CDS group and in 32 patients in the ERCP group in the unmatched cohort and in 5 patients in the ERCP group in the matched cohort. [b]p-value derived by Wilcoxon rank sum test with continuity correction. Abbreviations: 95%CI, 95% confidence interval; IQR, interquartile range (P25-P75).

Table 4. Surgeon survey following pancreatoduodenectomy in patients with prior EUS-CDS. Values are n (%) unless otherwise indicated. Abbreviations: EUS-CDS, endoscopic ultrasound guided choledochoduodenostomy; IQR, interquartile range (P25-P75).