

Table S1 Limitations of relevant studies on the risk factors for MS PEP

Study	Sample size	Risk factors for MS PEP	Inadequate factors
Abbas <i>et al.</i> (10)	35,395	Older patients, males, high comorbidities	1. Retrospective study 2. Lack of information about the use of rectal indomethacin 3. Did not include procedure-related variables
Maruyama <i>et al.</i> (13)	168	Pancreatic volume	1. Retrospective study 2. Small sample size 3. Did not include procedure-related variables
Kim <i>et al.</i> (14)	258	Obesity	1. Single-center retrospective study 2. Small sample size 3. Did not include procedure-related variables
Our study	6,944	Prolonged cannulation time	Single-center retrospective study

MS, moderate-to-severe; PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis.

Table S2 The incidence rates of PEP of patients with pancreatic head cancers excluded or included

Variables	All patients		P value
	Excluding patients with pancreatic head cancers (n=6,723)	Including patients with pancreatic head cancers (n=6,944)	
Overall PEP	5.3% (356/6,723)	5.2% (362/6,944)	0.83
Cotton-related MS PEP	1.1% (75/6,723)	1.1% (76/6,944)	0.91
Atlanta-related PEP	0.3% (17/6,723)	0.2% (17/6,944)	0.93

PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; MS, moderate-to-severe.

Table S3 Univariate logistic regression analysis for different severities of PEP according to the 5-5-1 criteria

Variables	Overall PEP	Cotton criteria		Revised Atlanta criteria	
		Mild PEP	MS PEP	Mild PEP	MS PEP
Cutoffs determined by difficult cannulation criteria (5-5-1 criteria)					
Cannulation time >5 min	1.85 (1.49–2.30) ^{####}	1.86 (1.46–2.37) ^{####}	1.72 (1.08–2.73) ^{####}	1.74 (1.40–2.17) ^{####}	8.40 (1.92–36.77) [#]
Cannulation attempts >5 times	1.81 (1.44–2.28) ^{####}	1.69 (1.31–2.19) ^{####}	2.19 (1.35–3.56) ^{#*}	1.71 (1.35–2.16) ^{####}	6.84 (1.88–24.87) ^{###}
Inadvertent PD cannulation >1 time	2.80 (2.17–3.62) ^{####}	2.51 (1.88–3.56) ^{####}	3.57 (2.14–5.97) ^{####}	2.72 (2.10–3.54) ^{####}	4.73 (1.37–16.37) ^{#*}
Cutoffs determined by ROC curve in this study					
Cannulation time >15 min	2.13 (1.67–2.67) ^{####}	1.95 (1.51–2.52) ^{####}	2.79 (1.76–4.42) ^{####}	2.01 (1.59–2.53) ^{####}	5.73 (2.18–15.09) ^{####}
Cannulation attempts ≥8 times	1.61 (1.25–2.01) ^{####}	1.56 (1.18–2.06) ^{####}	1.78 (1.06–2.98) ^{#*}	1.56 (1.21–2.02) ^{####}	3.50 (1.24–9.15) ^{#*}
Inadvertent PD cannulation ≥1 time	3.07 (2.40–3.93) ^{####}	3.03 (2.30–4.01) ^{####}	2.90 (1.73–4.87) ^{####}	3.02 (2.35–3.89) ^{####}	0.86 (0.30–2.49) ^{#*}

The data are presented as the odds ratio (95% CI) or relative risk (95% CI). [#], P<0.1; ^{*}, P<0.05; ^{**}, P<0.01; ^{###}, P<0.001. PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; MS, moderate-to-severe; PD, pancreatic duct; ROC, receiver operating characteristic curve; CI, confidence interval.

Table S4 Multivariate logistic regression analysis for different severities of PEP with defining difficult cannulation by 5-5-1 criteria

Variables	Overall PEP	Cotton criteria		Revised Atlanta criteria	
		Mild	MS	Mild	MS
Female	2.06 (1.30–3.29)**	1.95 (1.18–3.22)**	2.39 (1.36–4.22)**	2.28 (1.41–3.71)**	–
ALT <1× ULN	1.80 (1.15–2.81)*	1.64 (1.02–2.67)*	–	1.77 (1.20–2.79)*	–
Inadvertent PD cannulation	4.93 (3.13–7.76)***	4.45 (2.74–7.25)***	2.93 (1.74–5.00)**	5.07 (3.19–8.08)***	–
Cannulation time >5 min	–	–	–	–	10.1 (1.22–83.97)*

The data are presented as the odds ratio (95% CI) or relative risk (95% CI). *, P<0.05; **, P<0.01; ***, P<0.001. PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; MS, moderate-to-severe; ALT, alanine aminotransferase; PD, pancreatic duct; ULN, upper limit of normal; CI, confidence interval.

Table S5 Overall and MS PEP in patients receiving or not receiving indomethacin at different times

Variables	The use of indomethacin				All pts using indomethacin vs. none	P value	
	None	Pre-procedure	Post-procedure	Unknown time		Pre-procedure vs. none	Post-procedure vs. none
Overall PEP	5.0% (261/5,255)	4.1% (34/828)	7.6% (51/672)	8.5% (16/189)	0.10	0.28	<0.01*
Cotton-related MS PEP	1.1% (58/5,255)	0.7% (6/828)	1.3% (9/672)	1.6% (3/189)	0.89	0.32	0.59
Atlanta-related MS PEP	0.2% (13/5,255)	0.1% (1/828)	0.3% (2/672)	0.5% (1/189)	0.94	0.48	0.81

*, Bonferroni correction was applied for multiple comparisons. MS, moderate-to-severe; PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; pts, patients.

Table S6 Overall and MS PEP in patients receiving or not receiving prophylactic PD stents

Variables	The use of prophylactic PD stents, n (%)		P value
	No (n=6,276)	Yes (n=654)	
Overall PEP	310 (49.4)	52 (8.0)	0.001
Cotton-related MS PEP	65 (1.0)	11 (1.7)	0.13
Atlanta-related MS PEP	11 (0.2)	6 (0.9)	0.001
Difficult cannulation rate	3809 (60.7)	590 (90.2)	<0.001

PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; MS, moderate-to-severe; PD, pancreatic duct.

Table S7 Changes in the preventive methods for PEP over time

Variables	In 2010–2014 (n=2,040), n (%)	In 2014–2022 (n=4,904), n (%)	P value
Indomethacin	59 (2.9)	1,630 (33.2)	<0.001
Prophylactic PD stent	68 (3.3)	586 (11.9)	<0.001
Overall PEP	151 (7.4)	211 (4.3)	0.02
Cotton-related mild PEP	122 (6.0)	164 (3.3)	0.355
Cotton-related MS PEP	29 (1.4)	47 (1.0)	0.865
Atlanta-related mild PEP	145 (7.0)	200 (4.1)	0.658
Atlanta-related MS PEP	6 (0.3)	11 (0.2)	0.592

PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis; MS, moderate-to-severe; PD, pancreatic duct.