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Diagnosis, differentiation and prevention in pancreatic diseases

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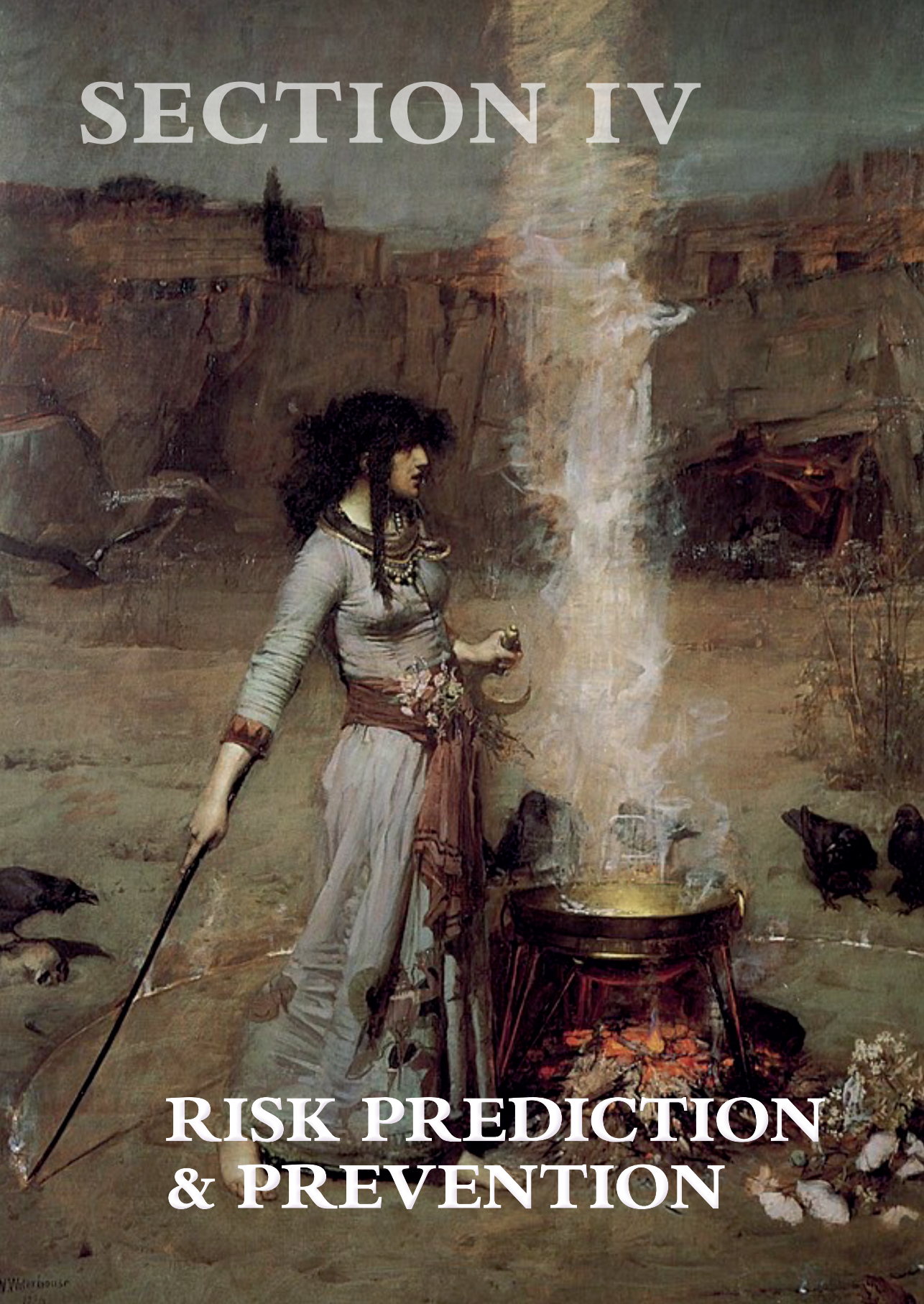
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SECTION IV



RISK PREDICTION
& PREVENTION

ABSTRACT

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs), pancreatic duct stenting, and intensive intravenous hydration have been proven to prevent post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. Trial participation and guideline changes demanded an assessment of the clinical practice of post-ERCP pancreatitis prophylaxis.

Aims: The surveys aim to identify points of improvement to inform and educate ERCPists about current evidence-based practice.

Methods: Two anonymous surveys were conducted among Dutch gastroenterologists in 2013 (n=408) and 2020 (n=575) for longitudinal views and attitudes pertaining to post-ERCP pancreatitis prophylaxis and recognition of post-ERCP pancreatitis risk factors.

Results: In 2013 and 2020, respectively, 121 and 109 ERCPists responded. In the 2013 survey, 98% of them utilized NSAID prophylaxis and 62% pancreatic duct stent prophylaxis in specific cases. In the 2020 survey, the use of NSAIDs (100%), pancreatic duct stents (78%), and intensive intravenous hydration (33%) increased among ERCPists. NSAID prophylaxis was the preferred prophylactic measure for all risk factors in the 2020 survey, except for ampullectomy, pancreatic duct contrast injection, and pancreatic duct cannulation, for which NSAID prophylaxis and pancreatic duct stent combined was equally favored or preferred.

Conclusion: Rectal NSAIDs are the most applied post-ERCP pancreatitis prophylaxis in the Netherlands, followed by pancreatic duct stents and intensive intravenous hydration. Additionally, there is reason to believe that recent guideline updates and active research participation have led to increased prophylaxis implementation.

CHAPTER 7 - INCREASED USE OF PROPHYLACTIC MEASURES IN PREVENTING POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS

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INTRODUCTION

Post-ERCP pancreatitis is the most common complication after an endoscopic retrograde cholangiopancreatography (ERCP) with an incidence range from 2.9 to 14.7% in unselected patient populations resulting in pancreatitis related mortality rate of up to 3%.¹⁻³

There is substantial evidence in favor of a number of effective prophylactic measures for preventing post-ERCP pancreatitis. Rectal nonsteroidal anti-inflammatory drugs (NSAIDs), pancreatic duct (PD) stenting, and intensive intravenous (IV) hydration are commonly accepted interventions that reduce the risk of this complication.⁴⁻⁶ It is unclear whether a combination of these measures offers additive or even synergistic risk reduction beyond the protection conferred by the individual measures.⁷⁻¹⁰

In 2013, we assessed the Dutch clinical practice using a nationwide survey among all ERCPists. This was instigated as a preparatory means to design a nationwide post-ERCP pancreatitis trial under the auspices of the Dutch Pancreatitis Study Group.⁹ There have been multiple developments in the field following this survey. International guidelines have been adapted, particularly when it comes to post-ERCP pancreatitis prophylaxis.¹¹⁻¹³ Since 2010, the guideline of the European Society of Gastrointestinal Endoscopy (ESGE) recommends rectal NSAID administration

for all patients without contraindication, whereas the 2017 guideline of the American Society of Gastrointestinal Endoscopy (ASGE) recommends rectal NSAIDs only for high-risk patients.¹²⁻¹⁴ Both ESGE and ASGE guidelines recommend PD stent placement in high-risk patients. The 2019 ESGE guideline state that intensive IV hydration should be considered in patients with a contraindication to NSAIDs, whereas the ASGE guideline of 2017 suggests the use of intensive IV hydration whenever possible in a moderate to high-risk populations.

These changes from 2013 onward raise questions on the potential impact of guideline changes on Dutch gastroenterologists' clinical practice. That is why we reassessed the clinical practice of post-ERCP pancreatitis prophylaxis in The Netherlands to identify potential points of improvement to inform and educate ERCPists about current evidence-based practice.

METHODS

The survey was developed following the Declaration of Helsinki and using guidelines in the conduct of survey research.¹⁵ The Medical Ethical Review Committee of the Radboudumc in Nijmegen, the Netherlands, approved this study and waived the need for informed consent. The study was registered in the online Netherlands Trial Registry (NL8493).

STUDY SETTING

In the 2013 and 2020 surveys, the Dutch Society of Gastroenterology (NVGE) was consulted for all affiliated gastroenterologists, respectively, 408 and 575 for these 2 years. These account for 87% (2013) and 90% (2020) of the gastroenterologists registered in the Netherlands.¹⁶ Gastroenterologists were eligible for participation if their current employment was in a community or academic center in the Netherlands and their institutional email address could be attained. For the 2020 survey, all endoscopy departments were separately consulted on whom of their gastroenterologists performed ERCPs (n = 219). Participation was voluntary and no incentives were offered for completion of the survey. The anonymity of participants was guaranteed.

The first survey was distributed as a postal survey from August to November 2013 to all affiliated gastroenterologists of the NVGE, no reminders were sent to non-responders. At that point in time, our research group was exclusively interested in the answers of ERCPists; hence, only their responses were recorded. The online survey was distributed by email between February 6th and March 18th, 2020. Two email reminders were sent with 2 weeks interval for an optimal response rate.

SURVEY DESIGN

The 2013 survey was designed based on the content of the 2010 ESGE and 2012 ASGE guidelines concerning the clinical practice of post-ERCP pancreatitis pro-

phylaxis (**Figure 1**).^{14,17} Three domains were constructed to investigate self-reported use of guideline-recommended prophylactic measures and factors influencing the decision to utilize them. The domains were as follows: respondent characteristics, post-ERCP pancreatitis prophylaxis use, and risk factor recognition (**Supplementary Appendix 1**). The international guidelines recommended rectal NSAIDs and prophylactic PD stenting at that time and thorough details on application and configuration of these prophylactic measures were included. The complete questionnaire consisted of 43 questions and the majority was compulsory and closed-ended formulated and came with a predetermined list of answer choices. Depending on the content of the question, one or multiple answers could be selected. When appropriate, open-ended questions or answer choices were offered for responses not anticipated from the survey design.

For the 2020 survey, the 2013 survey was adopted to an electronic format, containing similar domains and formatted in Google Forms (<https://docs.google.com/forms>). Both the ASGE 2017 and ESGE 2019 guidelines were consulted for additional recommendations relative to the 2013 survey (**Figure 1**).^{12,13} Most notably, intensive IV hydration was introduced as a prophylactic measure. Detailed questions on this prophylactic measure were therefore added to the 2020 survey. Additionally, one risk factor (previous pancreatitis) was removed due to concerns of its unambiguous interpretation caused by similarity to another risk factor. These amendments resulted in an updated survey containing 47 questions (**Supplementary Appendix 2**).

All gastroenterologists in the 2020 survey were required to fill in the respondent characteristics and risk factor recognition domains of each survey. ERCPists answered in-depth questions on the different prophylactic measures only when they indicated that they actually used that particular type of prophylaxis.

The draft versions were piloted by a select group of five expert ERCPists. A consensus was formulated that a risk factor was sufficiently recognized if 85% or more of the respondents considered it as such. Their feedback was further implemented to improve on readability, content validity, and unambiguity of the questions.

STATISTICAL ANALYSIS

Categorical data were listed as frequency and percentage. Numeric data were assessed by mean with standard deviation (SD) or median with interquartile range (IQR). The Chi-squared test was used for comparison with the 2013 survey and subgroup analysis. All statistical analyses were conducted using SPSS, version 24, with statistical significance set at a two-sided alpha level of 5%. The difference in prophylaxis use between ERCPists in 2013 and 2020 was a predefined subgroup analysis.

RESULTS

RESPONSE

Of the 408 gastroenterologists approached by mail in the 2013 survey, 121 (30%) ERCPists responded. The total number of ERCPists among approached gastroenterologists could not be discerned for the 2013 survey. The online survey administered in 2020 reached 548 of the 566 approached gastroenterologists. Of those reached, 161 gastroenterologists responded (29%). The response rate among currently practicing ERCPists was 50% ($n = 109$).

RESPONDENT CHARACTERISTICS

The characteristics of the respondents of the 2013 and the 2020 survey are listed in **Table 1**. Baseline characteristics did not significantly differ between surveys. In the 2020 survey, the mean age of the 161 respondents was 46 year and 116 (72%) were male. Twenty-five (16%) were employed in an academic center. Of the ERCPists, the mean practice time was 13.1 years, with a median lifetime exposure of 750 ERCPs.

PHARMACOLOGICAL PROPHYLAXIS

In the 2013 survey, 98% ($n = 119$) of the ERCPists used NSAID prophylaxis, of which 62% ($n = 73$) in more than 80% of the ERCPs performed (**Table 2, Supplementary Appendix Table S1**). In comparison, all ERCPists in 2020 used NSAIDs prophylaxis. We found no rise in the percentage of ERCPists applying NSAID prophylaxis in comparison to the 2013 survey ($p = 0.18$); however, there was a significant rise in the proportion of ERCPs in which prophylactic NSAIDs were used (respectively, 62% vs. 93%; $p < 0.001$).

Diclofenac was the preferred NSAID of choice and accounting for 95% in the 2020 survey. A dosage of 100 mg was used by 95% ($n = 103$) of the respondents and the drug was administered rectally by 98% ($n = 107$) of respondents. NSAID prophylaxis was administered prior to ERCP by 78% ($n = 85$) of the respondents.

PROPHYLACTIC PD STENTING

Prophylactic PD stenting was used by 62% ($n = 75$) in the 2013 survey versus 78% ($n = 85$) of the ERCPists in the 2020 survey ($p = 0.008$, **Table 2**). Of the 2013 PD stent users, 85% ($n = 62$) used PD stents in less than 20% of the ERCPs they performed versus 80% ($n = 68$) in 2020 ($p = 0.33$).

Table 2 and **Supplementary Appendix Table S2** show the responses with concerning (regularly used) stent configuration, diameter, length, shape, and flanges. In the 2020 survey, the majority (88%, $n = 75$) of the ERCPists checked stent dislocation through radiological imaging, 79% ($n = 67$) between 5 and 14 days. Given, a few (8%) respondents did indicate not checking for stent dislocation in the 2020 survey.

INTENSIVE IV HYDRATION

The 2013 survey did not contain questions regarding intensive IV hydration. In the 2020 survey, intensive IV hydration was used by 33% (n = 36) (**Table 2 and Supplementary Appendix Table S3**). Lactated Ringer's was the IV solution used by 31 respondents (86%). Fluid administration was most frequently in a maintenance dose (72%), and 39% reported bolus administration.

COMBINATION OF PROPHYLAXIS

In 2020, the combination of rectal NSAID and PD stent prophylaxis was used more often compared to 2013, 69% (n = 75) versus 48% (n = 58) (p = 0.002, **Table 2 and Supplementary Appendix Table S4**). The percentage of procedures in which a combination of rectal NSAID and PD stent prophylaxis was used did not differ, 88% (n = 50) versus 79% (n = 59), respectively, in less than 20% of the procedures (p = 0.24). The most cited motivation for this combination was the routine use of NSAID prophylaxis and PD stent placement in the case of repeated or deep guidewire insertion/contrast injection occurred during the ERCP.

The combination of rectal NSAIDs and intensive IV hydration was used by 34% (n = 37) of the 2020 ERCPists, of which 54% (n = 20) in less than 20% of the ERCPs performed and 27% (n = 10) in more than 80% of the ERCPs performed. The most cited reasons favoring the combination were maximal risk reduction for post-ERCP pancreatitis and utilization in high-risk patients and/or procedures.

RISK FACTOR RECOGNITION AND PROPHYLAXIS USE

In the 2013 survey, 11 of the 18 scientifically well-established and recognized risk factors were identified by more than 85% of the ERCPists (**Figure 2, Supplementary Appendix Table S5**). In 2020, eleven of the seventeen risk factors were identified as such. There were a few differences in risk factors identified by the ERCPists in 2013 compared to 2020: balloon dilatation of the papilla was identified by more than 85% and non-dilated extrahepatic bile duct system by less than 85% of the 2020 ERCPists. Three of the risk factors (earlier post-ERCP pancreatitis, non-dilated extrahepatic bile duct system, and normal bilirubin) were categorized as risk factors less frequent by the 2020 respondents in comparison to the 2013 respondents (p = 0.048, p = 0.002, p = 0.001, respectively). Absence of chronic pancreatitis, PD cannulation, and difficult cannulation were categorized as risk factors more often by the 2020 respondents p = 0.005, p = 0.001 and p = 0.004, respectively.

In the 2013 survey, ampullectomy was seen as the only risk factor that warranted a combination of rectal NSAID and PD stent in more than a third (n = 33) of respondents (34%, **Supplementary Appendix Table S6**). The ERCPists stated in 2020 that NSAID prophylaxis was the preferred prophylaxis for 14 of the risk factors (83%). In the case of ampullectomy or PD contrast injection, a similar proportion

of ERCPists elected NSAID prophylaxis or combination of NSAID and PD stent prophylaxis (respectively, 38% and 39%). If the PD was cannulated, some 50% chose the combination, while 34% relied on NSAID prophylaxis.

Eighty-three percent of the 2013 ERCPists indicated the presence of a post-ERCP pancreatitis prophylaxis protocol in their center compared to 84% (n = 92) in 2020 (**Supplementary Appendix Table S7**). Of the respondents in 2020 who indicated that a protocol was present, NSAID prophylaxis was included in nearly 100%, PD stent prophylaxis in 31% in the 2013 survey, and 24%. Intensive IV hydration was present in 38% of the protocols in 2020.

DISCUSSION

Rectal NSAID is the most frequently used prophylaxis to prevent post-ERCP pancreatitis in the Netherlands and is applied by all ERCPists that responded to the 2020 survey. A steep rise in NSAID prophylaxis was observed from 2013 to 2020, exemplified by an increase from 62 to 93% of the respondents in more than 80% of ERCPs. Prophylactic PD stent placement was used in selected cases by 78% of ERCPists in 2020, significantly more than in 2013. One-third of the surveyed ERCPists in 2020 acknowledged the use of intensive IV hydration. Currently, exclusive use of NSAIDs was the preferred prophylactic measure, except for ampullectomy, PD contrast injection, and PD cannulation, in which the combination of NSAID prophylaxis and PD stent was equally favored or preferred.

In 2010 and 2012, two European surveys targeting ERCPists reported 16% and 35% use of rectal NSAID, respectively [18, 19]. The results of a landmark trial published months after the 2012 survey was conducted, demonstrating a significant decrease in post-ERCP pancreatitis due to the use of rectal NSAIDs. Their use as post-ERCP pancreatitis prophylaxis became more common practice, as demonstrated by our already high 98% NSAID use rate among ERCPists in 2013. The high percentage might be attributed to ease of use and negligible costs in certain countries.²⁰ The favored timing (before ERCP), route (rectal), and dosage (100 mg) were answered more frequently by the 2020 respondents. The shift in answers toward these recommended administration methods in the 2020 survey could be explained by our first survey, predating more recent administration recommendations (Table 3).

It is unclear why only 78% of the ERCPists in 2020 agree with the indication of PD stent placement, as it is regarded as an evidence-based prophylactic strategy.^{5,21} Several surveys have reported considerable practice variation in prophylactic PD stent use ranging from 53 to 96%.^{18,19,22} Given that extra manipulation of the PD increases the likelihood of post-ERCP pancreatitis, PD stent placement is not without risk,²³ and the risk rises further if placement fails.²⁴ A 2011 survey among US gastroenterologists showed low-volume ERCPists (< 50 ERCPs/year) feel less comfortable

with pancreatic duct stenting, providing a potential explanation for this discrepancy.²⁵ With respect to stent configuration, the best consensus in the 2020 survey was reached for diameter, with 92% using 5Fr. The flange options “internal” or “external and internal” were given by 14/89 times by 2020 respondents, despite current guidelines arguing internal flanges can impede spontaneous dislodgement.^{13,26} While each prophylactic measure confers protection on its own, their combined effect has not been confirmed by current literature. ERCPists in our 2020 survey did demonstrate consensus on applying NSAID and PD stent prophylaxis in high-risk patients with (inadvertent) PD cannulation. The additional benefit of this combination in high-risk patients is expected to follow from a multicenter randomized controlled trial.¹⁰ Considering intensive IV hydration, a relatively small percentage of ERCPists reported using this prophylactic measure in our 2020 survey compared to 83% in a 2018 North American survey.²⁷ Intensive IV hydration may perhaps be the preferred prophylactic measure in North America given the elevated price of the composite rectal indomethacin in certain countries.^{28,29} Despite a network meta-analysis suggesting this combination yields the lowest post-ERCP pancreatitis incidence,³⁰ the future results of another multicenter randomized controlled trial will provide additional clarification.⁹

The risk factor recognition of surveyed endoscopists must be interpreted with caution. The most recent international guidelines are not consistent on the contribution of each individual patient- or procedure-related risk factor for the development of post-ERCP pancreatitis, such as a non-dilated extrahepatic bile duct system.^{12,13} Each risk factor’s weight has been determined by a limited number of studies with varying quality of evidence, often predating the implementation of routine NSAID prophylaxis.^{29,31}

The promising results from initial pilot studies on post-ERCP pancreatitis prophylactic measures prompted multiple large-scale trials to verify their effectiveness (**Figure 1**). The results have led to guidelines becoming more specific on which patients benefit most from the various prophylactic measures.^{12,13} In the Netherlands, multicenter trials of the Dutch Pancreatitis Study Group have been designed with the input of ERCPists. These trials contribute to their knowledge base and the implementation of evidence-based practice. Additionally, the implementation of a national endoscopic complication registry in 2009 has led to more awareness for post-ERCP pancreatitis and usages of potential prophylactic methods. The mandatory complication meetings, discussing individual cases of post-ERCP pancreatitis with quality improvement goals, have contributed to an increased interest in novel prophylactic measures.^{32,33}

A strength of this study is its high response rate among ERCPists, which is concurrent with other surveys among gastroenterologists.^{18,19,27} This attributed to a valu-

able insight into the opinions and attitudes of ERCPists with regard to the use of post-ERCP prophylaxis in the Netherlands over time. Secondly, this has been the first survey conducted since the publication of the current ESGE guideline 1 year ago.¹³ The questions on the various prophylactic methods were detailed, which resulted not only in an indication of the frequency of use, but also in which manner and with what motivation these methods were applied. The process of survey design was meticulous, with questions based on the most recent guidelines. Lastly, although the prophylaxis use and risk factor recognition captured by this survey may differ for other regions of the world, we can cautiously extrapolate our results to the European clinical practice given the use of the same guidelines. Thereby, our survey can shed insight into where there are differences, and we hopefully ignite international debate on best practices for preventing post-ERCP pancreatitis.

A limitation of the current study was the lack of data on actual post-ERCP pancreatitis rates of the surveyed ERCPists. The goal of our study was to capture the nationwide clinical practice and not investigate prophylactic measures set off against risk factors, justifying our methodology. Response bias could be introduced in our survey due to the possibility that ERCPists interested in reducing post-ERCP pancreatitis rates responded more often. Recall bias is an inherent limitation of survey sampling, where responses cannot directly be considered reflective of the general practice, as demonstrated in a recent retrospective review of electronic health databases.³⁴

In conclusion, our most recent survey demonstrated a 100% self-reported use of rectal NSAIDs administration among ERCPists. Significantly more ERCPists place PD stents than in 2013 and intensive IV hydration has come to the stage as a novel prophylactic measure in the clinical practice. In conjunction, this survey reveals the remaining improvements to be made. Recent guideline updates and active research participation have potentially led to this increased prophylaxis implementation.

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TABLES

Table 1 Characteristics of respondents

	ERCPists 2013 (n = 121)	ERCPists 2020 (n = 109)	Total 2020 (n = 161)
Male sex—no. (%)	98 (81)	88 (81)	116 (72)
Age—yr.—median (IQR)	45 (39–53)	46 (39–55)	44 (39–53)
Center—no. (%)			
Community	92 (76)	91 (84)	136 (85)
Academic	28 (23)	18 (17)	25 (16)
Practice time—yr.—median (IQR)	10 (5–16)	12 (7–19)	NA
Total amount of ERCPs—median (IQR)	700 (350–1500)	750 (450–1200)	NA
ERCPs in center per year—median (IQR)	250 (173–350)	260 (220–350)	NA

Table 2 Prophylactic measures

	ERCPists 2013 (n event/ n total)	ERCPists 2020 (n = 109)	p value
Use of NSAID prophylaxis—no. (%)	119 (98)	109 (100)	0.18
Percentage of NSAID prophylaxis ^a —no. (%)			<0.001
<20%	8/116 (7)	0	
20–40%	8/116 (7)	1 (1)	
41–60%	9/116 (8)	1 (1)	
61–80%	18/116 (15)	6 (6)	
>80%	73/116 (62)	101 (93)	
Type NSAID preferred ^a — no. (%)			
Diclofenac	115/119 (98)	103 (95)	
Indomethacin	4/119 (3)	6 (6)	
Dose ^a —no. (%)			
50 mg	10/99 (9)	5 (5)	
80 mg	1/99 (1)	1 (1)	
100 mg	86/99 (74)	103 (95)	
150 mg	1/99 (1)	0	
200 mg	1/99 (1)	0	
Route of administration ^a —no. (%)			
Rectal	117/118 (99.1)	107 (98)	
Oral	0	1 (1)	
Intravenous	0	1 (1)	
S.c./i.m.	1/118 (0.9)	0	
Timing of administration ^a —no. (%)			
Before ERCP	59/119 (50)	85 (78)	
After ERCP	60/119 (50)	16 (15)	
Differs per procedure	NA	8 (7)	
Use of PD stent prophylaxis—no. (%)	75 (62)	85 (78)	0.008
Percentage of ERCPs PD stents are used ^a —no. (%)			0.33
<20%	62/73 (85)	68 (80)	
20–40%	10/73 (14)	17 (20)	
41–60%	1/73 (1)	0	
Stent diameter regularly used ^a —no. (%)			
3Fr	7/75 (9)	11 (13)	
5Fr	67/75 (89)	78 (92)	
7Fr	11/75 (15)	7 (8)	

Table 2 continuation on next page ►

► **Table 2** continuation from next page

Dislocation control ^a —no. (%)			
None	15/74 (20)	8 (9)	
Radiology	54/74 (73)	75 (88)	
Endoscopy	1/74 (1)	0	
Both	2/74 (3)	2 (2)	
Use of intensive IV hydration—no. (%)	NA	36 (33)	
Type of infusion fluid ^a —no. (%)	NA		
Lactated Ringer's		31 (86)	
Normal saline		5 (14)	
Administration as a bolus ^a —no. (%)	NA	14 (39)	
Administration as a maintenance ^a —no. (%)	NA	26 (72)	
Use of NSAID + stent prophylaxis—no. (%)	58/119 (48)	75 (69)	0.002
Use of NSAID + hydration prophylaxis—no. (%)	NA	37 (34)	

ERCP endoscopic retrograde cholangiopancreatography, NSAID nonsteroidal anti-inflammatory drugs, mg milligram, s.c subcutaneously, i.m. intramuscular, PD pancreatic duct, IV intravenous, Fr French, NA not applicable
p values ≤ 0.05 (bold) are statistically significant (Chi-squared test)

^aPercentage of respondents who answered specific question

Table 3 European and American Society of Gastrointestinal Endoscopy guideline overview

Guideline	Rectal NSAID	PD stent	Hydration
2010 ESGE	Diclofenac/indomethacin Rectal 100 mg Before or after ERCP	High-risk patients 5-Fr Short 5–10 days evaluation of stent dislocation, otherwise endoscopic removal of retained stents	NA
2014 ESGE	Diclofenac/indomethacin Rectal 100 mg Before or after ERCP <i>All patients without contraindications</i>	High-risk patients 5-Fr 5–10 days evaluation of stent dislocation, otherwise endoscopic removal of retained stents	NA
2019 ESGE	Diclofenac/indomethacin Rectal 100 mg <i>Immediately before ERCP</i> All patients without contraindications	High-risk patients (<i>defined as inadvertent guidewire insertion/opacification of PD, double guidewire cannulation</i>) 5-Fr Short <i>No internal flanges</i> <i>External flange or pigtail duodenal side</i> 5–10 days evaluation of stent dislocation, otherwise endoscopic removal of retained stents	Aggressive hydration Lactated Ringer's solution In patients with contraindication to NSAIDs, not in patients at risk for fluid overload or if PD stent placement
2012 ASGE	Indomethacin/diclofenac Rectal Before ERCP or upon arrival in recovery room	High-risk patients (defined as SOD, manometry, ampullectomy, pancreatic sphincterotomy, precut sphincterotomy, pancreatic brush cytology, difficult biliary cannulation, and manipulation of the PD with wires)	NA
2017 ASGE	Indomethacin/diclofenac Rectal Before ERCP or upon arrival in recovery room <i>High-risk individuals without contraindication</i> <i>(Suggestion that it may reduce risk and severity in average-risk individuals)</i>	High-risk individuals	Periprocedural Lactated Ringer's solution When feasible

ESGE European Society of Gastrointestinal Endoscopy, ASGE American Society of Gastrointestinal Endoscopy, ERCP endoscopic retrograde cholangiopancreatography, NSAID nonsteroidal anti-inflammatory drugs, PD pancreatic duct, Fr French, NA not applicable

FIGURES

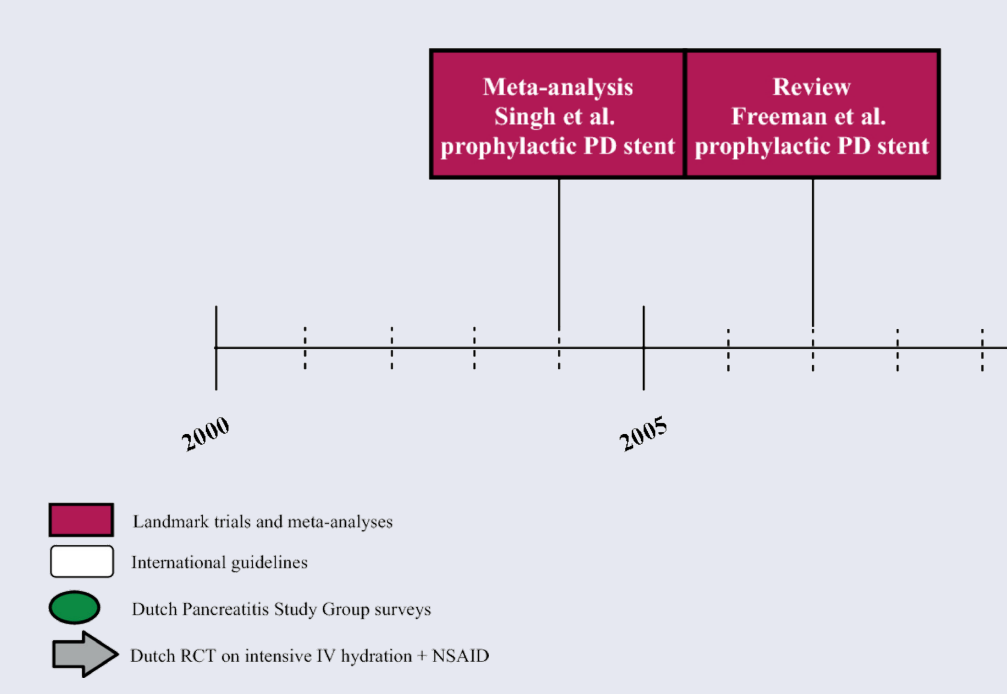
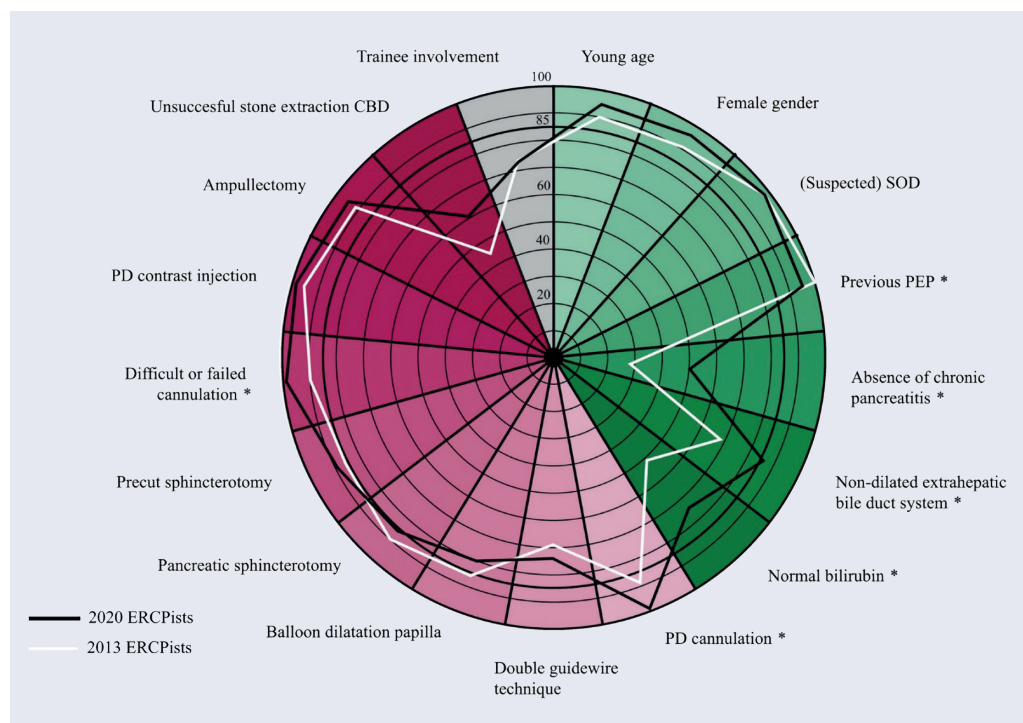
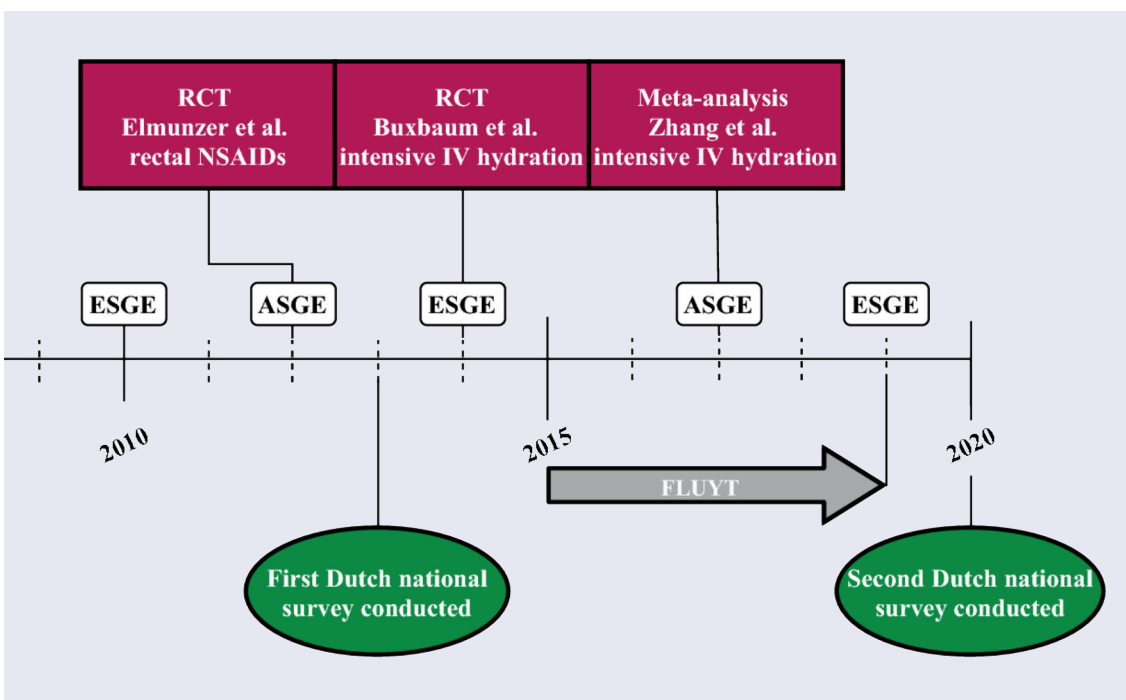


Figure 1. Timeline of landmark trials, guideline publications, and survey administration. RCT randomized clinical trial, PD pancreatic duct, NSAID nonsteroidal anti-inflammatory drug, IV intravenous, ESGE European Society of Gastrointestinal Endoscopy, ASGE American Society of Gastrointestinal Endoscopy

Figure 2. Post-ERCP pancreatitis risk factor recognition by ERCPists in 2013 and 2020. Balloon dilatation papilla is without prior sphincterotomy. PEP post-ERCP pancreatitis, PD pancreatic duct, SOD sphincter of Oddi dysfunction, CBD common bile duct. * $p < 0.05$



SUPPLEMENTAL MATERIAL

SUPPLEMENTARY 1: 2013 SURVEY

I. DEMOGRAPHIC INFORMATION

a. What is your gender?

- Male
- Female

b. What is your age?

c. Are you employed in a community or academic centre?

- Community
- Academic

d. Do you actively perform ERCPs?

- Yes
- No (proceed to section 5)

e. How many years of experience do you have performing ERCP's?

f. How many ERCPs do you estimate to have performed in total?

g. How many ERCPs do you perform per week on average?

h. How many ERCPs does your centre perform each year?

2. PHARMACOLOGICAL PROPHYLAXIS

a. Does your department have a protocol for post-ERCP pancreatitis prophylaxis?

- Yes
- No
- I do not know

b. Does this protocol contain pharmacological and/or PD-stent prophylaxis? (Choose all that apply)

- Pharmacological prophylaxis
- PD-stent prophylaxis

c. Do you use pharmacological prophylaxis?

- Yes
- No (proceed to section 3)

d. In what percentage of all ERCP procedures you perform do you use pharmacological prophylaxis?

- <20%
- 20-40%
- 41-60%
- 61-80%
- >80%

e. When do you use a pharmacological prophylaxis?

- No clear policy
- In high-risk situations
- Always

f. Which medication do you use?

- Diclofenac
- Indomethacin
- Other: ...

g. Which dosage do you use? (in mg)

h. What is the method of administration?

- Rectal
- Oral
- Intravenous
- Subcutaneous/intramuscular

i. When is the medication administered?

- Before the ERCP
- After the ERCP

3. PROPHYLACTIC PD-STENTING

a. Do you ever use PD-stent prophylaxis?

- Yes
- No (proceed to section 4)

b. In what percentage of all ERCP procedures you perform do you use PD-stent prophylaxis?

- <20%
- 20-40%
- 41-60%
- 61-80%
- >80%

c. Which diameters do you use, which do you prefer, and why? (Choose all that apply)

- 3Fr
- 5Fr
- 7Fr
- 8.5Fr
- 10Fr

d. Which lengths do you use, which do you prefer, and why? (Choose all that apply)

- 3cm
- 4cm
- 5cm
- 6cm
- 7cm

e. Which types of stent do you use, which do you prefer, and why? (Choose all that apply)

- Straight
- Pigtail

f. Do you use stents with flanges, which do you prefer, and why? (Choose all that apply)

- No flanges
- Only external flanges
- Only internal flanges
- External and internal flanges

g. How do you check for stent dislocation? (Choose all that apply)

- By endoscopy
- By radiology
- I do not check for stent dislocation

h. When do you check for stent dislocation?

- 1 day
- 2-4 days
- 5-8 days
- 9-14 days
- >15 days

4. COMBINATION PROPHYLAXIS

a. Do you use a combination of pharmacological and PD-stent prophylaxis?

- Yes
- No

i. How often do you use this combination prophylaxis?

- <20%
- 20-40%
- 41-60%
- 61-80%
- >80%

ii. Why do you choose for this combination prophylaxis?

5. PERCEIVED RISK FACTORS AND PROPHYLAXIS PREFERENCE

A list of 18 proposed risk factors, per item the responder was asked prophylaxis preference to indicate if they perceive this item as a risk factor and which form of prophylaxis they preferred for this factor.

SUPPLEMENTARY 2: 2020 SURVEY

I. DEMOGRAPHIC INFORMATION:

a. What is your gender?

- Male
- Female
- Other/ Prefer not to say

b. What is your age?

c. Are you employed in a community or academic centre?

- Community
- Academic

d. Do you actively perform ERCPs?

- Yes
- No (proceed to section 6)

e. How many years of experience do you have performing ERCP's?

f. How many ERCPs do you estimate to have performed in total?

g. How many ERCPs does your centre perform each year?

2. PHARMACOLOGICAL PROPHYLAXIS:

a. Do you use pharmacological prophylaxis?

- Yes
- No (proceed to section 3)

If the answer is no: what is your reason for not using pharmacological prophylaxis?

b. In what percentage of all ERCP procedures you perform do you use pharmacological prophylaxis?

- <20%
- 20-40%
- 41-60%

- 61-80%

- >80%

c. When do you use a pharmacological prophylaxis?

- No clear policy

- Always

d. Which medication do you use?

- Diclofenac

- Indomethacin

- Other: ...

e. Which dosage do you use? (in mg)

f. What is the method of administration?

- Rectal

- Oral

- Intravenous

- Subcutaneous/intramuscular

g. When is the medication administered?

- Before the ERCP

- After the ERCP

- Differs per procedure

h. If a patient has a contra-indication for NSAID's, which policy do you adhere? (Choose all that apply)

- No prophylaxis

- PD stent prophylaxis

- Hydration prophylaxis

- Other: ...

i. Do you ever use one of the following medications as a post-ERCP pancreatitis prophylaxis? (Choose all that apply)

- Sublingual nitrates

- Somatostatin

- Octreotide

- Protease inhibitors

- Local adrenaline (near papilla)

- None of the above

3. PROPHYLACTIC PD-STENTING:

a. Do you ever use PD-stent prophylaxis?

- Yes

- No (proceed to section 4)

b. In what percentage of all ERCP procedures you perform do you use PD-stent prophylaxis?

- <20%

- 20-40%

- 41-60%

- 61-80%

- >80%

c. Which diameters do you use? (Choose all that apply)

- 3Fr

- 5Fr

- 7Fr

- 8.5Fr
- 10Fr

d. Which lengths do you use? (Choose all that apply)

- 3cm
- 5cm
- 7cm
- 8.5cm
- 10cm

e. Which types of stent do you use and which do you prefer? (Choose all that apply)

- Straight
- Pigtail

f. Do you use stents with flanges? (Choose all that apply)

- No flanges
- Only external flanges
- Only internal flanges
- External and internal flanges

g. How do you check for stent dislocation? (Choose all that apply)

- By endoscopy
- By radiology
- I do not check for stent dislocation

h. When do you check for stent dislocation?

- 1 day
- 2-4 days
- 5-8 days
- 9-14 days
- >15 days

4. HYPERHYDRATION PROPHYLAXIS:

a. Do you ever use periprocedural IV hyperhydration?

- Yes
- No (proceed to section 5)

b. What is your motivation for using periprocedural IV hyperhydration?

- Standard procedure
- As post-ERCP pancreatitis prophylaxis
- Other: ...

c. In what percentage of all ERCP procedures you perform do you use periprocedural IV hyperhydration?

- <20%
- 20-40%
- 41-60%
- 61-80%
- >80%

d. Which infusion fluid do you use?

- Lactated Ringer's
- Normal Saline

e. Do you administer the fluid in a bolus?

- Yes
- No

i. When is the bolus is administered?

- Before ERCP
- During ERCP
- After ERCP

ii. How much fluid in millilitre is administered?

f. Do you administer the fluid as a maintenance dose?

- Yes
- No

i. How much fluid in millilitre is administered and for how many hours?

5. COMBINATION PROPHYLAXIS:

a. Do you use a combination of pharmacological and PD-stent prophylaxis?

- Yes
- No

i. How often do you use this combination prophylaxis?

- <20%
- 20-40%
- 41-60%
- 61-80%
- >80%

ii. Why do you choose for this combination prophylaxis?

b. Do you use a combination of pharmacological and hyperhydration prophylaxis?

- Yes
- No

i. How often do you use this combination prophylaxis?

- <20%
- 20-40%
- 41-60%
- 61-80%
- >80%

ii. Why do you choose for this combination prophylaxis?

6. POST-ERCP PANCREATITIS PROPHYLAXIS PROTOCOL:

a. Does your department have a protocol for post-ERCP pancreatitis prophylaxis?

- Yes
- No (proceed to section 7)
- I do not know (proceed to section 7)

*b. Does this protocol contain pharmacological, PD-stent and/or intensive IV hydration prophylaxis?
(Choose all that apply)*

- Pharmacological prophylaxis
- PD-stent prophylaxis
- Hyperhydration prophylaxis

7. PERCEIVED RISK FACTORS AND PROPHYLAXIS PREFERENCE:

A list of 17 proposed risk factors, per item the responder was asked to indicate if they perceive this item as a risk factor and which form of prophylaxis they preferred for this factor.

Table S1: NSAID prophylaxis

	ERCPists 2013 (n event/n total)	ERCPists 2020 (n=109)	P Value
Use of NSAID prophylaxis – no. (%)	119 (98)	109 (100)	0.18
Percentage of NSAID prophylaxis ^a – no. (%)			<0.001
• <20%	8/116 (7)	0	
• 20-40%	8/116 (7)	1 (0.9)	
• 41-60%	9/116 (8)	1 (0.9)	
• 61-80%	18/116 (15)	6 (5.5)	
• >80%	73/116 (62)	101 (92.7)	
Situations in which NSAIDs are used ^a – no. (%)			
• No clear policy	8/116 (7)	4 (3.7)	
• In high risk situations	27/116 (23)	NA	
• Always	81/116 (69)	105 (96.3)	
Type NSAID preferred ^a – no. (%)			
• Diclofenac	115/119 (98)	103 (94.5)	
• Indomethacin	4/119 (3)	6 (5.5)	
Dose ^a – no. (%)			
• 50mg	10/99 (9)	5 (4.6)	
• 80mg	1/99 (1)	1 (0.9)	
• 100mg	86/99 (74)	103 (94.5)	
• 150mg	1/99 (1)	0	
• 200mg	1/99 (1)	0	
Route of administration ^a – no. (%)			
• Rectal	117/118 (99.1)	107 (98.2)	
• Oral	0	1 (0.9)	
• Intravenous	0	1 (0.9)	
• S.c. / i.m.	1/118 (0.9)	0	
Timing of administration ^a – no. (%)			
• Before ERCP	59/119 (50)	85 (78)	
• After ERCP	60/119 (50)	16 (14.7)	
• Differs per procedure	NA	8 (7.3)	

^a percentage of respondents who answered specific question

p-values ≤0.05 (bold) are statistically significant (chi-squared test)

ERCP: endoscopic retrograde cholangiopancreatography; NSAID: non-steroidal anti-inflammatory drugs; mg: milligram; s.c.: subcutaneously; i.m.: intramuscular; NA: not applicable

Table S2: Pancreatic duct stent prophylaxis

	ERCPIsts 2013 (N=121)	ERCPIsts 2020 (N=109)	P Value
Use of PD-stent prophylaxis – no. (%)	75 (62)	85 (78)	0.008
Percentage of ERCPIs PD stents are used ^a – no. (%)			0.33
• <20%	62/73 (85)	68 (80)	
• 20-40%	10/73 (14)	17 (20)	
• 41-60%	1/73 (1)	0	
Stent diameter regularly used ^a – no. (%)			
• 3Fr	7/75 (9)	11 (13)	
• 5Fr	67/75 (89)	78 (92)	
• 7Fr	11/75 (15)	7 (8)	
Stent length regularly used ^a – no. (%)			
• 3cm	24/67 (36)	36 (42)	
• 4cm	11/67 (16)	NA	
• 5cm	50/67 (75)	69 (81)	
• 6cm	6/67 (9)	NA	
• 7cm	5/67 (7)	3 (4)	
Stent shape regularly used ^a – no. (%)			
• Straight	44/65 (68)	61 (72)	
• Pigtail	23/63 (37)	33 (39)	
Favourite stent shape ^a – no. (%)			
• Straight	7/11 (64)	42 (50)	
• Pigtail	3/11 (27)	31 (37)	
• No preference	1/11 (9)	12 (14)	
Flange regularly used ^a – no. (%)			
• No flanges	8/57 (14)	23 (27)	
• External	40/57 (70)	52 (61)	
• Internal	2/57 (4)	2 (2)	
• External and internal	5/57 (9)	12 (14)	
Dislocation control ^a – no. (%)			
• None	15/74 (20)	8 (9)	
• Radiology	54/74 (73)	75 (88)	
• Endoscopy	1/74 (1)	0	
• Both	2/74 (3)	2 (2)	
Time to dislocation control ^a – no. (%)			
• 2-4 days	11/62 (18)	5 (6)	
• 5-8 days	39/62 (63)	49 (58)	
• 9-14 days	10/62 (16)	18 (21)	
• >15 days	2/62 (3)	13 (15)	

^a percentage of respondents who answered specific question

p-values ≤ 0.05 are statistically significant (chi-squared test)

PD: pancreatic duct; ERCP: endoscopic retrograde cholangiopancreatography; Fr: French

Table S3: Intensive intravenous hydration prophylaxis

	ERCPists 2020 (N=109)
Use of intensive IV hydration– no. (%)	36 (33)
Motivation for use ^a – no. (%)	
• Standard procedure	4 (11)
• As post-ERCP pancreatitis prophylaxis	24 (67)
• Other ^b	8 (22)
Type of infusion fluid ^a – no. (%)	
• Lactated Ringer's	31 (86)
• Normal saline	5 (14)
Administration as a bolus ^a – no. (%)	14 (39)
Administration as a maintenance ^a – no. (%)	26 (72)

^a percentage of respondents who answered specific question

^b contra-indication NSAID n=6, other n=2

IV: intravenous

Table S4: Combination of prophylaxes

	ERCPists 2013 (N=121)	ERCPists 2020 (N=109)	P value
Use of NSAID + stent prophylaxis – no. (%)	58/119 (48)	75 (69)	0.002
Percentage of ERCPs in which NSAID + stent is used ^a – no. (%)			0.24
• <20%	50/57 (88)	59 (79)	
• 21-40%	6/57 (11)	15 (20)	
• 41-60%	1/57 (2)	0	
• 61-80%	0	0	
• 81-100%	0	1 (1)	
Use of NSAID + hydration prophylaxis– no. (%)	NA	37 (34)	
Percentage of ERCPs in which NSAID + hydration is used ^a – no. (%)	NA		
• <20%		20 (54)	
• 21-40%		4 (11)	
• 41-60%		1 (3)	
• 61-80%		2 (5)	
• 81-100%		10 (27)	

^a percentage of respondents who answered specific question

p-values≤0.05 are statistically significant (chi-squared test)

ERCP: endoscopic retrograde cholangiopancreatography; NSAID: non-steroidal anti-inflammatory drugs

Table S5: Risk factor recognition

	ERCPists 2013	ERCPists 2020 N=109	Total Respondents 2020 n=161	P value^b
Young age – no. (%)	73/81 (90)	104 (95)	154 (96)	0.15
Female gender – no. (%)	72/79 (91)	105 (96)	154 (96)	0.13
(Suspected) SOD – no. (%)	81/83 (98)	107 (98)	156(97)	0.78
Previous PEP – no. (%)	83/83 (100)	104 (95)	152 (94)	0.048
Previous Pancreatitis – no. (%)	48/77 (62)	NA	NA	NA
Absence of chronic pancreatitis – no. (%)	18/65 (28)	54 (50)	79 (49)	0.005
Non-dilated extrahepatic bile duct system – no. (%)	50/74 (68)	94 (86)	135 (84)	0.002
Normal bilirubin – no. (%)	34/67 (51)	81 (74)	117 (73)	0.001
PD cannulation – no. (%)	69/78 (88)	108 (99)	160 (99)	0.001
Double guidewire technique – no. (%)	51/74 (69)	81 (74)	110 (68)	0.39
PD contrast injection – no. (%)	78/81 (96)	108 (99)	160 (99)	0.18
Balloon dilatation papilla ^a – no. (%)	67/78 (86)	87 (80)	127 (79)	0.36
Pancreatic sphincterotomy – no. (%)	64/71 (90)	94 (86)	132 (82)	0.50
Precut sphincterotomy – no. (%)	64/74 (86)	97 (89)	133 (83)	0.61
Difficult or failed cannulation – no. (%)	71/79 (90)	108 (99)	157 (98)	0.004
Ampullectomy – no. (%)	68/74 (92)	104 (95)	150 (93)	0.27
Unsuccessful stone extraction CBD – no. (%)	30/66 (45)	66 (61)	104 (65)	0.05
Trainee involvement – no. (%)	48/65 (74)	80 (73)	122 (76)	0.76

^a Without prior sphincterotomy

^b Comparing 2013 and 2020 ERCPists

p-values ≤ 0.05 are statistically significant (chi-squared test)

SOD: sphincter of Oddi dysfunction; PEP; post-ERCP pancreatitis; PD: pancreatic duct; CBD: common bile duct

Table S6: Preferred prophylaxis for risk factors

	ERCPists 2013				ERCPists 2020 n=109				Total 2020 n=161			
	NSAID	PD stent	NSAID + PD stent		NSAID	PD stent	Hyd-ration	No prophylaxis				
Young age – no. (%)	99 (94)	1 (1)	5 (5)		109 (100)	8 (7)	22 (20)	0	161 (100)	10 (6)	31 (19)	0
Female gender – no. (%)	95 (91)	1 (1)	8 (8)		108 (99)	8 (7)	20 (18)	0	159 (99)	10 (6)	27 (17)	2 (1)
(Suspected) SOD– no. (%)	70 (63)	10 (9)	30 (27)		105 (96)	29 (27)	24 (22)	1 (1)	157 (98)	32 (20)	31 (19)	1 (1)
Previous PEP– no. (%)	87 (76)	5 (4)	23 (20)		108 (99)	23 (21)	26 (24)	0	160 (99)	30 (19)	9 (6)	0
Previous Pancreatitis– no. (%)	89 (93)	2 (2)	5 (5)		NA	NA	NA	NA	NA	NA	NA	NA
Absence of chronic pancreatitis– no. (%)	76 (97)	1 (1)	1 (1)		104 (95)	2 (2)	12 (11)	5 (5)	153 (95)	2 (1)	18 (11)	8 (5)
Non-dilated extrahepatic bile duct system– no. (%)	89 (98)	1 (1)	1 (1)		107 (98)	2 (2)	14 (13)	2 (2)	157 (98)	4 (2)	22 (14)	4 (2)
Normal bilirubin– no. (%)	83 (100)	0	0		106 (97)	2 (2)	12 (11)	3 (3)	156 (97)	3 (2)	19 (12)	5 (3)
PD cannulation– no. (%)	72 (69)	8 (8)	25 (24)		106 (97)	69 (63)	15 (14)	0	152 (94)	102 (63)	24 (15)	0
Double guidewire technique– no. (%)	69 (70)	9 (9)	20 (20)		106 (97)	52 (48)	15 (14)	1 (1)	154 (96)	63 (39)	21 (13)	3 (2)
PD contrast injection– no. (%)	72 (67)	7 (7)	27 (25)		105 (96)	57 (52)	20 (18)	0	153 (95)	23 (14)	31 (19)	0
Balloon dilatation papilla ^a – no. (%)	90 (90)	1 (1)	6 (6)		108 (99)	5 (5)	13 (12)	1 (1)	159 (99)	9 (6)	21 (13)	2 (1)
Pancreatic sphincterotomy– no. (%)	64 (68)	6 (6)	23 (25)		101 (93)	42 (39)	16 (15)	4 (4)	151 (94)	60 (37)	27 (17)	4 (2)
Precut sphincterotomy– no. (%)	87 (90)	2 (2)	8 (8)		105 (96)	8 (7)	14 (13)	4 (4)	156 (97)	13 (8)	21 (13)	5 (3)
Difficult or failed cannulation– no. (%)	83 (78)	5 (5)	18 (17)		106 (97)	22 (20)	22 (20)	1 (1)	157 (98)	32 (20)	31 (19)	1 (1)
Ampullectomy– no. (%)	44 (46)	17 (18)	33 (34)		100 (92)	57 (52)	19 (17)	3 (3)	148 (92)	80 (50)	27 (17)	3 (2)
Unsuccessful stone extraction CBD– no. (%)	86 (97)	1 (1)	2 (2)		106 (97)	4 (4)	14 (13)	3 (3)	156 (97)	10 (6)	21 (13)	5 (3)
Trainee involvement– no. (%)	79 (96)	0	0		106 (97)	0	11 (10)	3 (3)	157 (98)	0	20 (12)	4 (2)
No risk factor present– no. (%)	NA	NA	NA		105 (96)	0	10 (9)	4 (4)	154 (96)	0	15 (9)	7 (4)

^a Without prior sphincterotomy

SOD: sphincter of Oddi dysfunction; PEP: post-ERCP pancreatitis; PD: pancreatic duct; CBD: common bile duct; NA: not applicable

Table S7: Post-ERCP pancreatitis prophylaxis protocol

	ERCPists 2013	ERCPists 2020
PEP prophylaxis protocol present in centre— no. (%)		
• Yes	100 (83)	92 (84)
• No	21 (17)	10 (9)
• Unknown	0	7 (6)
Includes ^a – no. (%)		
• NSAID prophylaxis	99/100 (99)	90 (98)
• PD-stent prophylaxis	31/100 (31)	22 (24)
• Hydration prophylaxis	NA	35 (38)

^a percentage of respondents who answered specific question

PEP: post-ERCP pancreatitis; PD: pancreatic duct; NA: not applicable