Improving outcomes of pancreatic surgery

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CHAPTER 4

Pain management, fluid therapy and thromboprophylaxis after pancreatoduodenectomy: a worldwide survey among surgeons

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ABSTRACT

Background: The aim of this survey was to assess practices regarding pain management, fluid therapy and thromboprophylaxis in patients undergoing pancreatoduodenectomy on a global basis.

Methods: This survey study among surgeons from eight (inter)national scientific societies was performed according to the CHERRIES guideline.

Results: Overall, 236 surgeons completed the survey. ERAS protocols are used by 61% of surgeons and respectively 82%, 93%, 57% believed there is a relationship between pain management, fluid therapy, and thromboprophylaxis and clinical outcomes. Epidural analgesia (50%) was most popular followed by intravenous morphine (24%). A restrictive fluid therapy was used by 58% of surgeons. Chemical thromboprophylaxis was used by 88% of surgeons. Variations were observed between continents, most interesting being the choice for analgesic technique (transversus abdominis plane block was popular in North America), restrictive fluid therapy (little use in Asia and Oceania) and duration of chemical thromboprophylaxis (large variation).

Conclusion: The results of this international survey showed that only 61% of surgeons practice ERAS protocols. Although the majority of surgeons presume a relationship between pain management, fluid therapy and thromboprophylaxis and clinical outcomes, variations in practices were observed. Additional studies are needed to further optimize, standardize and implement ERAS protocols after pancreatic surgery.

INTRODUCTION

There is increasing interest in Enhanced Recovery After Surgery (ERAS) protocols as a means of improving clinical outcomes, although to date there is limited data on pancreatoduodenectomy (PD).(1-3) Pain management, fluid therapy and thromboprophylaxis are among key elements in all ERAS protocols and are believed to be equally important following PD. Recent studies have shown an association between low compliance to ERAS protocols and decreased clinical outcomes such as more overall, respiratory, infectious, and major complications (Clavien-Dindo ≥III), longer length of hospital stay and more readmissions following PD.(4, 5)

Although epidural analgesia is recommended over intravenous morphine in the recent ERAS Society guideline for PD(1), the optimal pain management remains controversial, and the reported use of epidural analgesia varies from 11-85%.(6) There are only a few well-conducted randomized controlled pain management trials reporting on patients undergoing PD(7-9) and to date the role of transversus abdominis plane blocks has not been assessed for these patients.

Avoidance of fluid overload and a goal-directed fluid therapy algorithm using intra- and postoperative non-invasive monitoring are recommended in the ERAS Society guidelines for PD.(1) Recent randomized trials on liberal or restrictive fluid therapy have brought conflicting evidence and have not led to a consensus.(10-12) A recent meta-analysis revealed an association between restrictive fluid therapy and lower mortality, although no association with morbidity was observed. It was concluded that more research is needed, ideally by collaboration of surgeons, anaesthesiologists and critical care physicians.(13)

The ERAS Society guidelines for PD recommends mechanical and chemical thromboprophylaxis (low molecular weight or unfractionated heparin) until hospital discharge and extended thromboprophylaxis (four weeks) in patients with cancer.(1) Although many (inter)national thromboprophylaxis guidelines are available, there is still debate about the choice and duration of the appropriate thromboprophylaxis.(14) Despite all guidelines recommend extended thromboprophylaxis in patients with cancer, there is no specific definition.(15)

The aim of this study was to obtain a global assessment of current perioperative practices regarding pain management, fluid therapy and thromboprophylaxis in patients undergoing PD among surgeons.

METHODS

Study design and participants

This survey study was performed and reported according to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES).(16) Institutional Review Board approval was not requested since no patients were involved and informed consent was implied when participants completed the survey.

An online survey (LimeSurvey; https://www.limesurvey.org) was designed in collaboration within an international research team. The survey was tested for usability and technical functionality. An invitation e-mail for the closed-survey (i.e. only accessible through invitation) was sent out from November 2019 through July 2020 to members of six international societies (International Hepato-Pancreato and Biliary Association (HPBA), Americas-HPBA, Asian-Pacific-HPBA, Australia-New Zealand-HPBA, Enhanced Recovery After Surgery Society and American Society for Enhanced Recovery) and two national societies (Association de chirurgie hépato-bilio-pancréatique et transplantation, Society of American Gastrointestinal and Endoscopic Surgeons). The link to the survey also appeared on several social media channels.

In the invitation e-mail, participants were informed about the topic, research team and aim of the survey, the duration (~five minutes) and the fact that all answers were being collected anonymously. Participants received up to three reminders. The survey was closed end of July 2020. The total number of invited participants and response rates was not calculated, since there is overlap between memberships of the international and national associations. IP addresses or cookies were used to prevent multiple responses by the same individual and were deleted after the survey was closed.

Survey

The content of the survey is available at request. The first part of the survey consisted of questions regarding characteristics of the participants, for example: scope of practice, experience, and annual volume. The second part of the survey was focused on pain management: analgesic technique, standardized protocols, availability of an acute pain service, most effective analgesic technique, and the presumed relationship between analgesic technique and clinical outcome. The third part of the survey covered issues concerning fluid therapy: standardized protocols, type of fluid therapy, means of monitoring, and presumed relationship between fluid therapy and clinical outcome. The fourth and final part of the survey examined thromboprophylaxis practices: the use of mechanical and chemical thromboprophylaxis, duration of thromboprophylaxis, indications for thromboprophylaxis, and presumed relationship between thromboprophylaxis and clinical outcome.

Survey questions included multiple-choice and open questions and were not randomized or altered. Adaptive questioning was used based on the answers in the survey. The survey consisted of 8 pages and a total of 41 questions. A completeness check was performed before submission of the survey and participants were given the chance to review and change their answers. No time limit was set for filling in the survey. Responders were given the option to include their information (e-mail address) separately to receive the study results. No other incentives were offered.

Statistical analyses

No weighting of items or propensity score matching was used to adjust for a potential non-representative sample. Participants who did not complete the first part of the survey (characteristics) were excluded. Continuous variables were presented as median with interquartile range (IQR). Categorical variables were presented as numbers (percentages) and compared by means of Chi-square or Fisher's Exact tests. Participants were analysed in total and compared by continent. IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) was used for statistical analysis.

RESULTS

Participants

In total, 272 surgeons responded to the survey during its open window between November 2019 and July 2020 (Table 1). Thirty-six responses were excluded since they did not complete page 2 (first part of the survey on characteristics). Most participants were from Europe (42%), North America (21%) and Asia (19%). The median age of participants was 45 years old (IQR 37-54), the majority were male (86%), were employed at an academic hospital (79%) and the scope of practice was hepato-pancreato-biliary surgery (71%). In 20% there were a dedicated pancreatic surgeon and anaesthesiologist, in 60% there was a dedicated pancreatic surgeon and in 21% there was no dedicated team. ERAS protocols after pancreatic surgery were practiced in 61% of the participants' institutes (Figure 1). The highest rates of practising ERAS protocols were reported in North America (73%) and Asia (72%) (Figure 1). ERAS protocols were practiced by 62% of surgeons employed at an academic and 54% of surgeons employed at a non-academic hospital (P=0.425).

Table 1. Baseline characteristics of participants

	Surgeons	
Question	**N**	**%**
What is your scope of practice?		
HPB	168	71.2
Surgical oncology	28	11.9
Transplant surgery	3	1.3
General surgery	29	12.3
Other	8	3.4
What is your sex?		
Male	203	86.4
Female	32	13.6
Missing	1	
What is your age in years?		
Median (IQR)	45	37-54
Missing	2	
How many years of work experience do you have after your residency?		
Median (IQR)	12	5-22
In which continent do you work?		
North America	49	20.8
South America	15	6.4
Europe	100	42.4
Africa	4	1.7
Asia	45	19.1
Oceania	23	9.7
Are you employed at an academic hospital?		
Yes	161	78.5
No	44	21.5
Missing	31	
How many PDs does your institution perform annually?		
Median (IQR)	35	20-60
How many PDs do you perform annually?		
Median (IQR)	15	7-29
Missing	40	
Is there a dedicated team for pancreatic surgery?		
Yes, both a pancreatic surgeon and anaesthesiologists	40	19.5
Yes, a pancreatic surgeon	122	59.5
No, there is no dedicated team	42	20.5
Other	1	0.5
Missing	31	

Abbreviations: HPB: hepatopancreatobiliary; IQR: interquartile range; PD: pancreatoduodenectomy

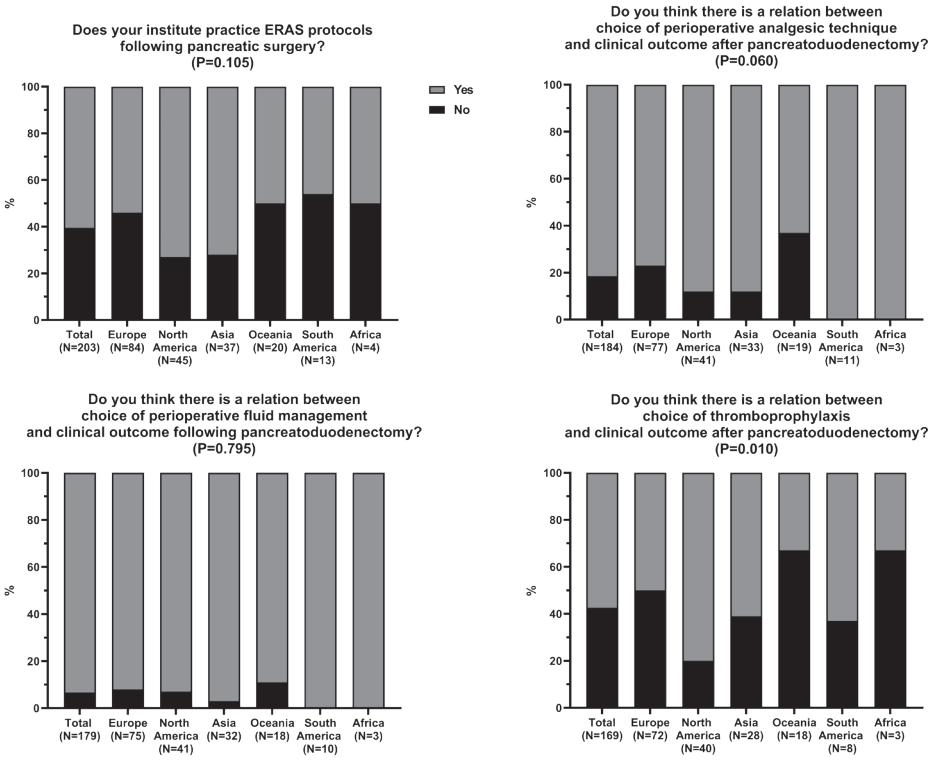

Figure 1. Practice of ERAS protocols following pancreatic surgery and the presumed relationship between perioperative analgesic technique, fluid therapy, thromboprophylaxis, and clinical outcome after PD

Pain management

Overall, the most frequently used analgesic technique for an open PD was epidural analgesia (50%), followed by intravenous morphine (24%), spinal analgesia (10%), transversus abdominis plane block (9%), and continuous wound infiltration (8%) (Figure 2).

In 36% of responses, the surgical staff was responsible for postoperative pain management, in 34% the anaesthesiology staff, and in 26% a dedicated acute pain service team (Table 2). Initial analgesia was stopped before or on postoperative day 3 in 75% of patients and in 25% on postoperative day 4 or later. After discontinuation of the initial analgesic technique, a standardized protocol was used by 65% of participants. In case of minimally invasive (laparoscopic or robot assisted) PD, 51% of participants used a different analgesia technique (Figure 3). An association between the choice of perioperative analgesia technique and clinical outcome after PD was assumed by 82% of participants (Figure 1).

Epidural analgesia and intravenous morphine were the most frequently used analgesic technique in all continents, except for North America, where the transversus abdominis plane block was almost equally popular (Figure 2). The responsibility for postoperative pain management was more clearly distributed in North America, 61% of participants reported that the surgical staff was responsible, and in Oceania, 79% reported that the dedicated acute pain service was responsible (Table S1). The assumed relationship between choice of analgesia technique and clinical outcome varied between the continents; with 88% assuming a relationship in Asia and North America and 63% in Oceania (Table S1).

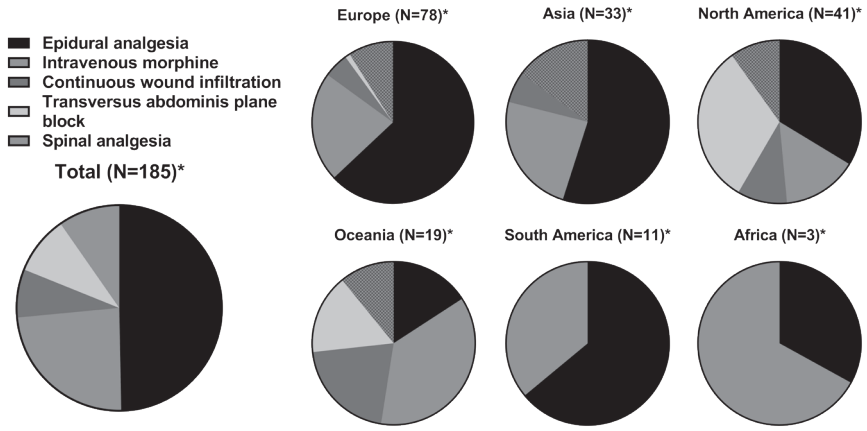

Figure 2. Most popular perioperative analgesic technique in patients undergoing PD

Fluid therapy

A standardized protocol for fluid management was used by 54% of participants for an open PD and 58% reported the use of restrictive fluid therapy in the protocol (Table 2). In case of a minimally invasive procedure 30% of participants used a different protocol (Figure 3). The first night after surgery 94% of participants reported that patients were admitted to a monitored environment. An association between the choice of perioperative fluid management and clinical outcome after PD was assumed by 93% of participants (Figure 1).

In contrast to the other continents, a minority of participants in Asia (44%) and Oceania (39%) reported the use of restrictive fluid therapy (Table S1). Little variation in the assumed relationship between choice of fluid management and clinical outcome was reported between continents (89-100%) (Figure 1).

Table 2. Perioperative pain management and fluid therapy in patients undergoing PD

	Surgeons	
Question	**N**	**%**
Perioperative pain management		
Who manages the postoperative pain and initial analgesic technique (e.g. epidural analgesia, intravenous analgesia with opioids) when the patient is on the ward?		
Surgical staff	67	36.2
Anaesthesiology staff	63	34.1
Dedicated Acute Pain Service team	48	25.9
Other	7	3.8
Missing	51	
Which method, regardless of analgesic technique, is the most effective following open PD in your opinion (taking into account analgesia, side effects and patient satisfaction)?		
Patient controlled	122	66.3
Continuous	62	33.7
Missing	52	
Is there a set postoperative day for discontinuation of the initial analgesic technique following open PD?		
Yes	91	49.5
No	93	50.5
Missing	52	
Which day is set as postoperative day for discontinuation of the initial analgesic technique following open PD?		
POD 0	2	2.2
POD 1	3	3.3
POD 2	23	25.3
POD 3	40	44.0
POD 4	13	14.3
POD ≥5	10	11.0
Missing	145	
Is there a standardized protocol for pain management after discontinuation of the initial analgesic technique?		
Yes	120	65.2
No	64	34.8
Missing	52	
Is the standardized protocol for pain management after discontinuation of the initial analgesic technique an oral multimodal protocol?		
Yes	100	83.3
No	20	16.7

Table 2. Continued

Perioperative fluid therapy		
Does your institution have a standardized protocol for fluid management during open PD?		
Yes	96	53.6
No	83	46.4
Missing	57	
Does the protocol at your institution describe the use of restrictive fluid therapy (near zero fluid balance) during and following open PD?		
Yes	103	57.5
No	76	42.5
Missing	57	
Do you replace fluid volume according to output of drainage tubes (enteral tube, abdominal drains, biliary/pancreatic drains) following PD?		
Yes	102	57.3
No	76	42.7
Missing	58	
What is the planned destination for patients during the first night following open pancreatoduodenectomy?		
Monitored environment (intensive or medium care unit, post anaesthesia care unit)	137	76.5
Monitored on ward	30	16.8
Unmonitored on ward	12	6.7
Missing	57	

Abbreviations: POD: postoperative day; PD: pancreatoduodenectomy

Thromboprophylaxis

The use of mechanical thromboprophylaxis was reported by 90% of participants (Table 3). The most used mechanical prophylaxis following open PD were early mobilization (77%), TED stockings (66%) and calf compression (61%). The use of chemical thromboprophylaxis was reported by 88% of participants following open PD. Most participants stopped the chemical prophylaxis on discharge (27%) or four weeks after surgery (52%) (Figure 4).

Different thromboprophylaxis protocols were used in 23% for a benign indication and in 7% for a minimally invasive PD (Table 3, Figure 3). Different thromboprophylaxis protocols were also used in 40% in case of an arterial resection and 23% in case of a venous resection (Figure 4). Most participants added a platelet inhibitor for an arterial (68%) or a venous (47%) resection. An association between the choice of thromboprophylaxis and clinical outcome after PD was assumed by 57% of participants (Figure 1).

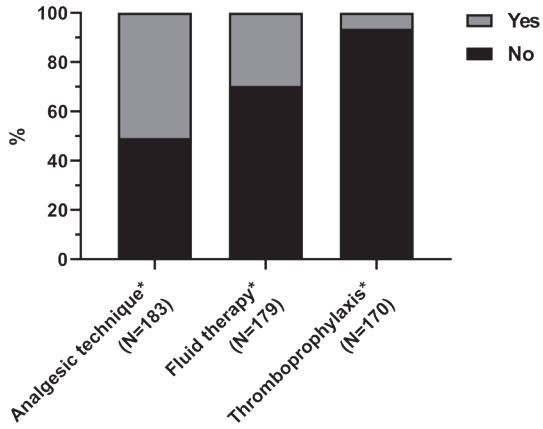

Figure 3. Use of a different protocol of perioperative analgesic technique, fluid therapy, and thromboprophylaxis in minimally invasive compared to open PD

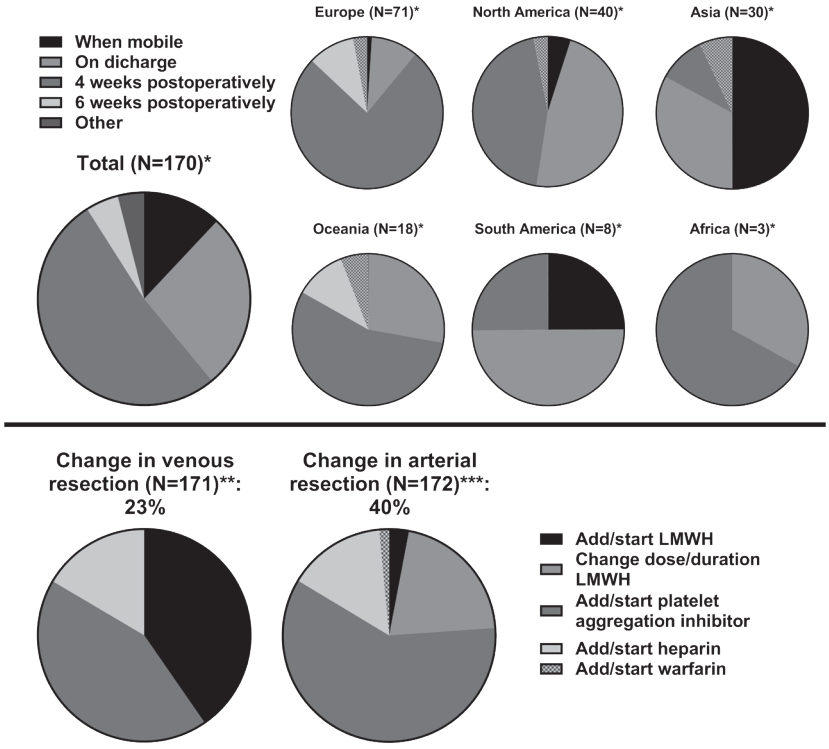

Figure 4. Duration of thromboprophylaxis in open PD and change in protocol in case of venous and arterial resection

In comparison to other continents, participants from Asia reported limited use of chemical thromboprophylaxis (48%) in their protocols (Table S1). The majority in Asia preferred to stop chemical thromboprophylaxis when the patient was mobile (50%), in North America at discharge (48%) and in Europe and Oceania at four weeks postoperatively (76% and 56%) (Figure 4). For an arterial or venous resection, in Oceania a different protocol was used in 11% and 0%, in contrast to 48% and 40% in North America and 55% and 23% in Asia (Table S1). The assumed relationship between choice of prophylaxis and clinical outcome varied between the continents; with 80% in North America assuming a relationship and only 33% in Oceania (Figure 1).

Table 3. Thromboprophylaxis in patients undergoing PD

	Surgeons	
Question	**N**	**%**
Does the protocol at your institution describe the use of mechanical thromboprophylaxis?		
Yes	155	90.1
No	17	9.9
Missing	64	
Which methods of mechanical thromboprophylaxis are used following open PD? *		
TED stockings	102	65.8
Calf compressors	95	61.3
Foot-pump	27	17.4
Early mobilization	120	77.4
Other	1	0.6
Does the protocol describe the use chemical thromboprophylaxis following open PD?		
Yes	151	87.8
No	21	12.2
Missing	64	
Would you use a different protocol of thromboprophylaxis if this was a patient with a benign indication for PD?		
Yes	38	22.5
No	131	77.5
Missing	67	

Abbreviations: TED: Thrombo-embolic deterrent; LMWH: low-molecular weight heparin; PD: pancreatoduodenectomy
*Multiple answers possible

DISCUSSION

This international survey of 236 surgeons gives insight into the current global perioperative practices regarding pain management, fluid therapy and thromboprophylaxis in patients undergoing PD. This survey demonstrates tremendous variation in perioperative practice by pancreatic surgeons around the world. Furthermore, there is limited compliance to the current ERAS Society guideline for PD(1) regarding pain management, fluid therapy and thromboprophylaxis and only 61% of surgeons practice ERAS protocols. Most surgeons assume a relationship between pain management, fluid therapy and thromboprophylaxis and clinical outcome following PD, respectively 82%, 93% and 57%. The preferred method for analgesia was epidural analgesia (50%), followed by intravenous morphine (25%). Restrictive fluid therapy is practiced by 58% of surgeons. Mechanical and chemical thromboprophylaxis are frequently used after PD (90% and 88%), however the duration of chemical prophylaxis varies. In case of minimally invasive surgery most surgeons only changed the analgesia technique (51%), but did not amend fluid therapy (30%) or thromboprophylaxis (7%). Variations between continents exist, mainly related to the choice of analgesia technique, use of restrictive fluid therapy, and duration of chemical thromboprophylaxis.

Postoperative pain management is one of the most important pillars of ERAS strategies as adequate pain management leads to shorter hospital stay and less postoperative complications.(17) Epidural analgesia is the most used analgesic technique, in line with the current ERAS Society guideline for PD which strongly recommends epidural analgesia and a multimodal opioid sparing strategy.(1) A previous meta-analysis of non-randomized studies showed a marginal difference with a questionable clinical relevance in mean pain scores between epidural analgesia and intravenous morphine, yet did confirm a reduction in complications, length of stay and mortality in patients receiving epidural analgesia.(6) However, a recent randomized study observed conflicting results with similar gastrointestinal morbidity for both analgesic techniques.(9) The ERAS Society guideline for PD also states the use of continuous wound infiltration as a reasonable alternative to epidural analgesia.(1) In spite of this recommendation, the use of continuous wound infiltration was rarely reported in the survey. Interestingly, in North America the transversus abdominis plane block was highly ranked as the most commonly used technique for analgesia, although this preference was not reported on other continents. This is probably due to personal preferences and experience, since no research has been done on the effectiveness of this analgesic technique in PD. Although it has been shown to be beneficial following other upper gastrointestinal resections including hepatectomy and gastrectomy.(18, 19) In the survey, 66% of surgeons preferred patient controlled analgesia over continuous infusion. Despite evidence of improved effectiveness and higher patient satisfaction within other fields of surgery(20), few studies have investigated this in

pancreatic surgery.(6) More research is needed to determine the optimal analgesic technique for open PD and separately for minimally invasive procedures. Half of the surgeons reported the use of a different analgesic technique in minimally invasive PD, without studies being available which investigated this.

The importance of fluid therapy is affirmed by the high assumed association with clinical outcome (93%). However, the optimal protocol for fluid management is still under debate, due to the use of varying definitions (liberal, restrictive, zero-balance fluid therapy) and low compliance rates.(5, 10-12) This is confirmed in the survey by the large variation in clinical practices. The current ERAS Society guideline for PD strongly recommends avoiding fluid overload to improve outcomes. Despite this recommendation, only 58% of surgeons report the use of restrictive fluid therapy in their institutional protocol. Interestingly, Asia and Oceania reported relatively little use of restrictive fluid therapy and yet do largely assume an association with clinical outcome. A randomized trial in the context of an ERAS protocol found that intraoperative goal directed fluid therapy reduced administration of (intraoperative) fluids, shortened the length of hospital stay and reduced postoperative complications in patients undergoing PD.(21) Additional research is needed to confirm these results and optimize the goal directed fluid therapy protocols, also for minimally invasive procedures.

Thromboprophylaxis protocols are considered one of the highest levels of evidence available in ERAS Society guideline for PD.(1) The recommendation to use extended chemical prophylaxis of four weeks for cancer is only practiced by 52% of surgeons. Especially in Asia and North America, prophylaxis is often discontinued when a patient is mobile or discharged. This poor adherence to the ERAS Society guideline for PD might be explained by differences in health care systems or cultural objections to self-injection of chemical thromboprophylaxis. Few surgeons used a different protocol for a benign indication, possibly exposing these patients to an unnecessary higher risk of four weeks of prophylaxis. In a previous study, we investigated three different thromboprophylaxis regimens and concluded that a high dose of nadroparin (5700IU once daily) for six weeks is associated with an increased risk of post-pancreatectomy haemorrhage. The benefits of (extended) thromboprophylaxis should be carefully reconsidered in case of risk factors for post-pancreatectomy haemorrhage such as postoperative pancreatic fistula.(22) The use of mechanical prophylaxis was widespread in our survey with a weak recommendation in the guideline as an additional measure. However, the compliance to early mobilization has been shown to be difficult, possibly due to the frequent use of epidural analgesia.(5) Standard use of physiotherapists could help stimulate a higher compliance rate. It is questionable if there is enough support to further investigate the optimal thromboprophylaxis protocol due to a relatively low assumed association with clinical outcome (53%). Patients with vascular resections are at high risk of thrombosis.

(23) Our survey showed that 40% and 23% used a different protocol for arterial and venous resections and there were large variations in type, dose and duration of the thromboprophylaxis protocols. This could create possibilities for optimizing the thromboprophylaxis in these high-risk patients.

This survey does have some limitations. Firstly, the sample is rather small and heterogeneous (for example the distribution among the different continents). Furthermore, the exact the number of invited participants and the response rate remain unknown. Secondly, the relatively high representation of academic surgeons that could be explained by potential selection bias due to the participation of several (inter)national scientific societies. However, since PD is increasingly being centralized to high-volume centres, the sample could equally be considered representative. Lastly, responses are preferences and perceptions of individuals (response bias) were not confirmed by patient-data.

Overall, the observed variations in perioperative practice have to be considered during interpretation and extrapolation of study results to other hospitals or regions. This study also highlights the issue of surgeons not practicing evidence-based medicine. The exact reasons for the choice of specific perioperative practices were not surveyed in this study. Another survey study among surgeons showed that the most common reasons for not implementing recommended practices are: scepticism regarding the validity of the applied methodology of the available evidence, low clinical relevance and organizational or financial considerations. Clinically relevant and well-designed randomized trials with adequate methodology and external validity and global dissemination of the results (besides conventional methods, visual abstracts and videos have a high potential) are needed to increase the compliance to recommended practices.(24) This will create more uniformity of protocols over the globe and further optimize the perioperative care after PD.

In conclusion, this international survey showed that there is a limited compliance to the current ERAS Society guidelines for PD and only 61% of surgeons practice to ERAS protocols. Although the majority of surgeons presume a relationship between pain management, fluid therapy, thromboprophylaxis, and clinical outcomes, large variations in practices were observed. Additional studies are needed to further optimize, standardize, and implement ERAS protocols after pancreatic surgery into daily practice.

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SUPPLEMENTARY MATERIAL

Table S1. Subgroup analysis by continent

	Europe		North America		Asia		Oceania		South America		Africa		
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**P-value**
	100	42.4	49	20.8	45	19.1	23	9.7	15	6.4	4	1.7	
Baseline													
What is your scope of practice?													0.008
HPB	72	72.0	29	59.2	34	75.6	21	91.3	11	73.3	1	25.0	
Surgical oncology	12	12.0	11	22.4	3	6.7	0	0.0	1	6.7	1	25.0	
Transplant surgery	0	0.0	0	0.0	3	6.7	0	0.0	0	0.0	0	0.0	
General surgery	15	15.0	7	14.3	2	4.4	1	4.3	2	13.3	2	50.0	
Other	1	1.0	2	4.1	3	6.7	1	4.3	1	6.7	0	0.0	
Does your institute practice ERAS protocols following pancreatic surgery?													0.105
Yes	45	53.6	33	73.3	28	71.8	10	50.0	6	46.2	2	50.0	
No	39	46.4	12	26.7	11	28.2	10	50.0	7	53.8	2	50.0	
Missing	16		4		6		3		2		0		
Pain management													
Who manages the postoperative pain and initial analgesic technique (e.g. epidural analgesia, intravenous analgesia with opioids) when the patient is on the ward?													<0.001
Surgical staff	22	28.2	25	61.0	15	45.5	1	5.3	3	27.3	1	33.3	
Anaesthesiology staff	32	41.0	9	22.0	11	33.3	3	15.8	6	54.5	2	33.3	
Dedicated acute pain service team	20	25.6	5	12.2	7	21.2	15	78.9	1	9.1	0	0.0	
Other	4	5.1	2	4.9	0	0.0	0	0.0	1	9.1	0	0.0	
Missing	22		8		12		4		4		1		

Table S1. Continued

Organize the analgesia techniques by descending frequency of use following open PD:													
Rank 1: EA / ivM / CWI / TAP / spinal	62.8 / 21.8 / 5.1 / 1.3 / 9.0		34.1 / 14.6 / 9.8 / 31.7 / 9.8		54.5 / 24.4 / 6.1 / 0.0 / 15.2		15.8 / 36.8 / 21.1 / 15.8 / 10.5		63.6 / 36.4 / 0.0 / 0.0 / 0.0		33.3 /66.6 / 0.0 / 0.0 / 0.0		<0.001
Missing	22		8		12		4		4		1		
Rank 2: EA / ivM / CWI / TAP / spinal	14.1 / 47.4 / 19.2 / 11.5 / 5.1		12.2 / 51.2 / 4.9 / 29.3 / 2.4		24.2 / 42.4 / 18.2 / 12.1 / 3.0		31.6 / 15.8 / 15.8 / 10.5 / 26.3		0.0 / 18.2 / 27.3 / 9.1 / 45.5		66.6 / 0.0 / 0.0/ 33.3 / 0.0		<0.001
Missing	22		8		12		4		4		1		
Which method, regardless of analgesic technique, is the most effective following open PD in your opinion (taking into account analgesia, side effects, and patient satisfaction)?													0.547
Patient controlled	55	71.4	27	65.9	21	63.6	12	63.2	7	63.6	0	0.0	
Continuous	22	28.6	14	34.1	12	36.4	7	36.8	4	36.4	3	100.0	
Missing	23		8		12		4		4		1		
Do you think there is a relation between choice of perioperative analgesic technique and clinical outcome after PD?													0.060
Yes	59	76.6	36	87.8	29	87.9	12	63.2	11	100.0	3	100.0	
No	18	23.4	5	12.2	4	12.1	7	36.8	0	0.0	0	0.0	
Missing	23		8		12		4		4		1		
Fluid therapy													
Does your institution have a standardized protocol for fluid management during open PD?													0.804
Yes	40	53.3	24	58.5	18	56.3	7	38.9	5	50.0	2	66.7	
No	35	46.7	17	41.5	14	43.8	11	61.1	5	50.0	1	33.3	
Missing	25		8		13		5		5		1		
Does the protocol at your institution describe the use of restrictive fluid therapy (near zero fluid balance) during and following open PD?													0.161
Yes	45	60.0	28	68.3	14	43.8	7	38.9	7	70.0	2	66.7	
No	30	40.0	13	31.7	18	56.3	11	61.1	3	30.0	1	33.3	
Missing	25		8		13		5		5		1		

Table S1. Continued

Do you think there is a relation between choice of perioperative fluid management and clinical outcome following PD?												0.795
Yes	69	92.0	38	92.7	31	96.9	16	88.9	10	100.0	3	100.0	
No	6	8.0	3	7.3	1	3.1	2	11.1	0	0.0	0	0.0	
Missing	25		8		13		5		5		1		
Thromboprophylaxis												
Does the protocol at your institution describe the use of mechanical thromboprophylaxis?												0.651
Yes	64	88.9	37	92.5	26	83.9	17	94.4	8	100.0	3	100.0	
No	8	11.1	3	7.5	5	16.1	1	5.6	0	0.0	0	0.0	
Missing	28		9		14		5		7		1		
Does the protocol describe the use chemical thromboprophylaxis following open PD?												<0.001
Yes	70	97.2	38	95	15	48.4	17	94.4	8	100.0	3	100.0	
No	2	2.8	2	5	16	51.6	1	5.6	0	0.0	0	0.0	
Missing	28		9		14		5		7		1		
At which time the chemical thromboprophylaxis is discontinued following open PD?												<0.001
When mobile	1	1.4	2	5.0	15	50.0	0	0.0	2	25.0	0	0.0	
On discharged	7	9.9	19	47.5	10	33.3	5	27.8	4	50.0	1	33.3	
4 weeks postoperatively	54	76.1	18	45.0	3	10.0	10	55.6	2	25.0	2	66.6	
6 weeks postoperatively	7	9.9	0	0.0	0	0.0	2	11.1	0	0.0	0	0.0	
Other	2	2.8	1	2.5	2	6.7	1	5.6	0	0.0	0	0.0	
Missing	29		9		15		5		7		1		

Table S1. Continued

Would you use a different protocol of thromboprophylaxis in case of an arterial resection?												0.012
Yes	25	34.7	19	47.5	17	54.8	2	11.1	5	62.5	0	0.0	
No	47	65.3	21	52.5	14	45.2	16	88.9	3	37.5	3	100.0	
Missing	28		9		14		5		7		1		
Would you use a different protocol of thromboprophylaxis in case of a venous resection?												0.025
Yes	15	20.8	16	40.0	7	23.3	0	0.0	2	25.0	0	0.0	
No	57	79.2	24	60.0	23	76.7	18	100.0	6	75.0	3	100.0	
Missing	28		9		15		5		7		1		
Do you think there is a relation between choice of thromboprophylaxis and clinical outcome after PD?												0.010
Yes	36	50.00	32	80.0	17	60.7	6	33.3	5	62.5	1	33.3	
No	36	50.00	8	20.0	11	39.3	12	66.7	3	37.5	2	66.7	
Missing	28		9		17		5		7		1		

Abbreviations: HPB: hepatopancreatobiliary; ERAS: enhanced recovery after surgery; PD: pancreatoduodenectomy; EA: epidural analgesia; ivM: intravenous morphine; CWI: continuous wound infiltration; TAP: transversus abdominis plane block