

## ORIGINAL ARTICLE

# Perioperative nutritional management of patients undergoing pancreatoduodenectomy: an international survey among surgeons

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## Abstract

**Background:** There is still a lack of good evidence regarding the optimal perioperative nutritional management for patients undergoing pancreatoduodenectomy (PD). The aim of this international survey was to assess the current practice among pancreatic surgeons.

**Methods:** A web survey of 30 questions was sent to the members of the European-African Hepato-Pancreato-Biliary Association (E-AHPBA) and International Hepato-Pancreato-Biliary Association (IHPBA). All members were invited by email to answer the online survey. A reminder was sent after 4 weeks.

**Results:** In total 420 out of 2500 surgeons (17%) answered the survey. Almost half of the surgeons (44%) did not organize a preoperative nutritional consultation for their patients. Seventy-seven percent of the participants did not have specific nutritional thresholds before the operation. A majority (66%) routinely used biological parameters to detect or follow malnutrition. Regarding intraoperative details, 69% of the respondents routinely leaved a nasogastric tube at the end of PD for gastric drainage. Sixty-six percent of the participants reported a postoperative nutritional follow-up consultation during hospitalization, and 58% of them had established local standardized protocols for postoperative nutritional support.

**Conclusion:** Management of perioperative nutrition in patients undergoing PD was very disparate internationally. No specific preoperative nutritional thresholds were used, and postoperative feeding routes and timing were diverse.

Received 17 December 2018; accepted 20 May 2019

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## Introduction

Pancreatic cancer represents an important cause of death from cancer in men and women throughout the world.<sup>1</sup> To date, surgery remains the only potentially curative strategy if complete tumour resection can be achieved. Pancreatoduodenectomy (PD) is therefore performed mainly for oncological reasons and is associated with high morbidity, ranging from 40 to 70%.<sup>2,3</sup> Chronic pancreatitis is the most common indication for non-oncological PD but represents only up to 13% of all pancreatic surgeries.<sup>4</sup>

Many patients undergoing pancreas surgery are frail and in impaired nutritional status, both pre- and postoperatively. Preoperatively, patients often reveal advanced cachexia related to biliary and gastric obstruction, decreased appetite, and cancer itself. Further risk factors additionally impair the nutritional status, e.g. smoking, alcohol consumption, and cardiopulmonary diseases.<sup>5–7</sup> Postoperative complications, such as pancreatic fistula and delayed gastric emptying aggravate nutritional depletion and defer re-alimentation. It is also underestimated that surgery causes disorganization of the digestive absorptive functions that subsequently reduce postoperative absorption.<sup>8</sup> Finally, adjuvant chemotherapy may further impair adequate caloric intake.

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There is still a lack of good evidence concerning the best management of perioperative nutritional assessment and support for patients undergoing PD. A recent systematic review compared the outcomes of different feeding routes after PD and reported no clear supportive evidence for routine enteral and parenteral feeding after PD, therefore an oral diet was recommended.<sup>9</sup> An oral diet is also recommended by the Enhanced Recovery After Surgery (ERAS<sup>®</sup>) guidelines as the preferred routine nutritional strategy after PD.<sup>10</sup> Nevertheless, there is some evidence that postoperative nutritional supports, including early enteral nutrition (EN) and total parenteral nutrition (TPN), improve clinical outcomes after major abdominal surgery.<sup>7</sup>

The aim of the present study was to assess the perioperative nutritional management of PD and to depict current practices. To this end, an international web-based survey was performed among the members of the European-African Hepato-Pancreato-Biliary Association (E-AHPBA) and International Hepato-Pancreato-Biliary Association (IHPBA).

## Methods

### Survey

A survey was developed using an online cloud-based software (SurveyMonkey<sup>®</sup>, Palo Alto, CA, United States). The survey included different items covering four main fields: participant information, preoperative, intraoperative, and postoperative nutritional management of patients undergoing PD. The questions were developed by the authors and tested by surgeons of the Department of Visceral Surgery at Lausanne University Hospital (CHUV), Switzerland, to then be improved. The full survey is provided as [supplementary material](#).

Information regarding the surgeon focused on personal data (age, gender, experience, country of practice, hospital type). The preoperative management part asked if a preoperative nutritional consultation was routinely performed at their institution, if the nutritional risk score (NRS)<sup>11</sup> was used, if nutritional supplements were used, if a weight threshold was defined before operation, and if biological biomarkers were measured before operation. Regarding the intraoperative part, it was assessed if nasogastric tube (NGT) or jejunostomy (nasal or percutaneous) were used routinely after completion of PD. The postoperative part focused on the route of nutrition after PD (oral, enteral, parenteral), if nutritional follow-up was performed, if a standardized protocol of nutrition was implemented and if prokinetic drugs were used.

### Surgeons

The targeted audience were members of the E-AHPBA and IHPBA. The survey was first submitted to the research committees of the respective societies in December 2017. After acceptance, the survey was diffused to all members via the respective central secretary offices in February 2018.

Members were invited by email to participate, and a reminder was sent after four weeks. The survey was closed on March 31, 2018. Data were then collected and analysed between April and June 2018. All responses were treated anonymously.

High-volume centers (defined as >50 PD/year)<sup>12</sup> were compared to smaller volume centers in terms of use of preoperative nutritional supplements, NGT and route of feeding on postoperative day 1.

### Statistical analysis

Quantitative variables were compared with Student's *t* test or Mann–Whitney *U* test, according to their normality. Qualitative variables were compared with Pearson's chi-square or Fisher's exact test as appropriate. All statistical analyses were two-sided and performed using SPSS 22.0 software (SPSS Inc., Chicago, IL).

### Ethics

This study did not require approval by the local ethics committee as no patients were enrolled. It was approved by the research committees of the E-AHPBA and IHPBA.

## Results

### Demographics of responders

In total, 420 surgeons answered the survey within 3 months. The exact number of members who received the survey was unknown, but it was estimated that 2500 individual surgeons were contacted. Hence, the response rate was at least 16.8%. Demographics of responders are summarized in [Table 1](#). Most of the surgeons practiced in Europe, 66% of them were <50 years old, and 86% were men. Three quarters of surgeons had >10 years of clinical experience and had senior position in a university hospital. Sixty-eight percent followed a formal training in hepato-pancreato-biliary (HPB) surgery. Annual volume of PD according to surgeons and centres varied from <10 cases to >50 cases per year.

### Preoperative nutritional management

Fifty-six percent of participants stated that preoperative nutritional assessment was used. Among them, 39% used systematic screening, against 17% who used screening only when certain criteria were present. These risk factors mentioned were low body-mass index (BMI), severe weight loss, low serum albumin levels (<35 g/l), preoperative biliary stenting, sarcopenia, and risk scores (Subjective Global Assessment, Malnutrition Universal Screening). The remaining 44% of participants did not use any preoperative nutritional consultation. The NRS was used by 24% of the responding surgeons.

Twenty-nine percent of surgeons used routine preoperative nutritional supplements and 58% may use them depending on the consultation. Only 13% of surgeons did not plan nutritional



**Table 1** Demographics of the survey participants

	Overall, <i>n</i> = 420
Region of practice	
Europe	184 (44%)
North America	104 (24%)
South America	48 (11%)
Africa	12 (3%)
Asia	61 (15%)
Oceania	11 (3%)
Mean age (years)	
<30	8 (2%)
30–39	110 (26%)
40–49	159 (38%)
50–59	106 (25%)
>60	37 (9%)
Male gender	364 (86%)
Specialty <sup>a</sup>	
Hepato-Pancreato-Biliary (HPB) surgery	363 (62%)
General surgery	107 (18%)
Organ transplantation	87 (15%)
Other	26 (5%)
Professional experience (years)	
0–5	26 (6%)
5–10	75 (18%)
10–20	138 (33%)
>20	181 (43%)
Annual pancreatoduodenectomies procedures (Center/Surgeon)	
<10 cases	27 (6%)/127 (30%)
10–25 cases	120 (29%)/182 (43%)
25–50 cases	133 (32%)/70 (17%)
>50 cases	140 (33%)/41 (10%)
Training level	
Resident	33 (8%)
Fellow	61 (15%)
Attending	326 (78%)
Formal training in HPB surgery	286 (68%)
Hospital structure <sup>a</sup>	
University hospital	316 (75%)
Community hospital	86 (20%)
Private practice	63 (15%)

<sup>a</sup> Participants could give several answers, which explains why the total is not 100%. The percentages are adapted to the total of the answers.

support for their patients. Standard oral nutritional supplements were mostly administered (81%). Surgeons used immunonutrition sparingly (17%, Fig. 1). Duration of use of preoperative nutritional supplements was ≤7 days in 47%, 8–14 days in 39%, and >14 days in 14%.

Most participants, i.e. 77%, did not have specific preoperative nutritional thresholds, e.g. minimal BMI, serum albumin or prealbumin levels. Sixty-six percent of the surgeons routinely used biological parameters to detect or follow malnutrition, which are depicted in Table 2. Another 11% of participants specified other parameters, such as lymphocyte count, serum proteins, selenium and zinc, procalcitonin, magnesium, calcium, vitamins (A–D–E–K), haemoglobin, transferrin and lipid panel, and iron/ferritin.

### Intraoperative details

Regarding intraoperative details, 69% of the respondents routinely leaved a NGT at the end of PD for gastric drainage. The timing for removal of this NGT is shown in Fig. 2, whereby 50% based removal on clinical criteria instead of a predefined postoperative day. A large majority (88%) did not perform feeding jejunostomy at the end of the procedure.

### Postoperative nutritional management

Sixty-six percent of participants reported a postoperative nutritional follow-up consultation during hospitalisation, and 58% of them had established local protocols for postoperative nutritional support. Usual feeding routes after PD on postoperative days 1 and 3 are described in Fig. 3.

Among surgeons who used EN and/or TPN, postoperative peak flow rates and duration of infusion per day are shown in Table 3. Mean flow rates and duration of infusion for TPN were significantly higher than for EN.

One third of surveyed surgeons used prokinetic agents, including metoclopramide (89%), domperidone (17%), erythromycin (13%) and alvimopan (2%).

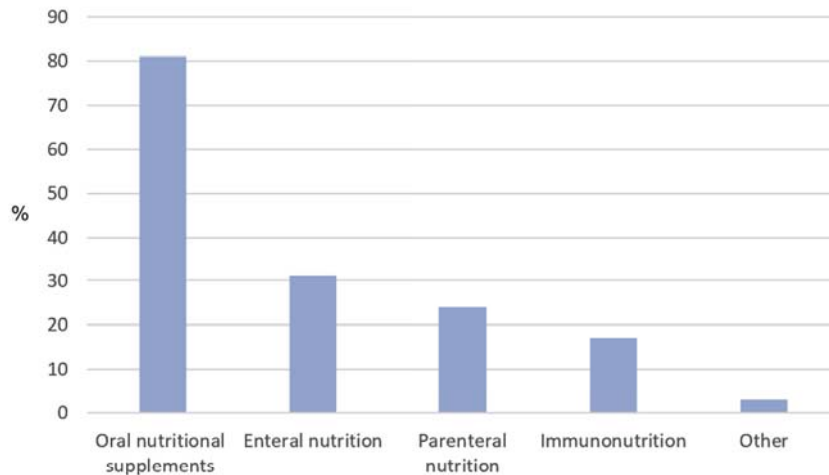
### High-volume vs. low-volume centers

The use and form of preoperative nutritional supplements as well as NGT use were not different between high-volume centers (>50 PD/year) and low-volume centers (Table 4). Use of oral diet only on the first postoperative day was significantly more common in high-volume centers (48% vs. 32% in low-volume centers,  $p < 0.001$ ).

### Discussion

The present snapshot study on current management of perioperative nutrition in patients undergoing PD disclosed important differences. Almost half of the participants responded that patients did not benefit from preoperative nutritional consultation. Any specific nutritional thresholds were not used and feeding routes after PD varied widely. These observations could be related to the fact that whilst many possibilities exist for measuring and managing perioperative nutrition, unfortunately, there is limited data in general, and specifically for PD.

In the present study, 44% of the participants stated that patients did not benefit from any preoperative nutritional



Participants could give several answers, which explains why the total is not 100%. The percentages are adapted to the total of the answers.

**Figure 1** Form of preoperative nutrition supplements

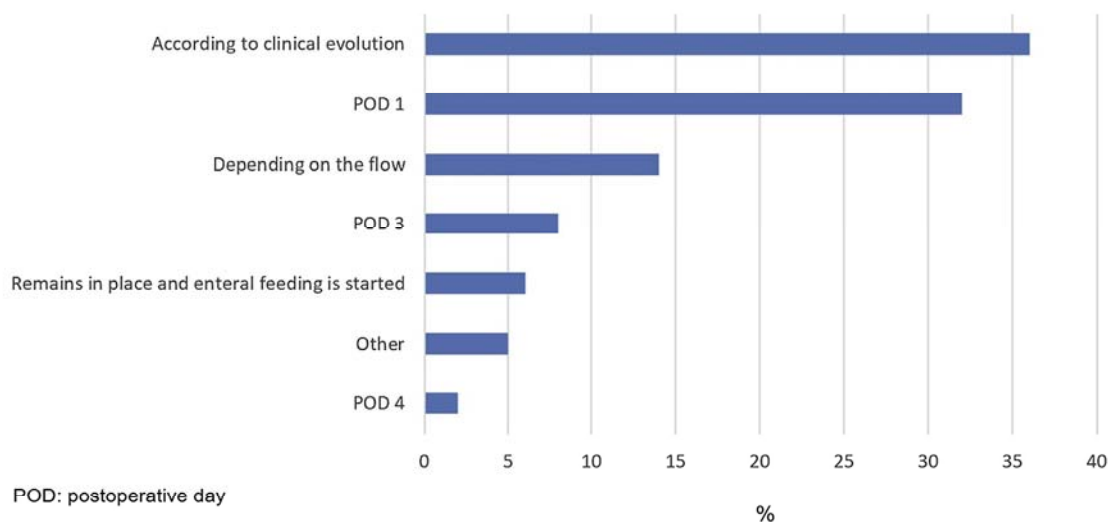
**Table 2** Biological parameters used to detect malnutrition

	Overall, n = 420
Albumin	252 (60%)
Prealbumin	151 (36%)
C-reactive protein (CRP)	89 (21%)
Other	33 (8%)

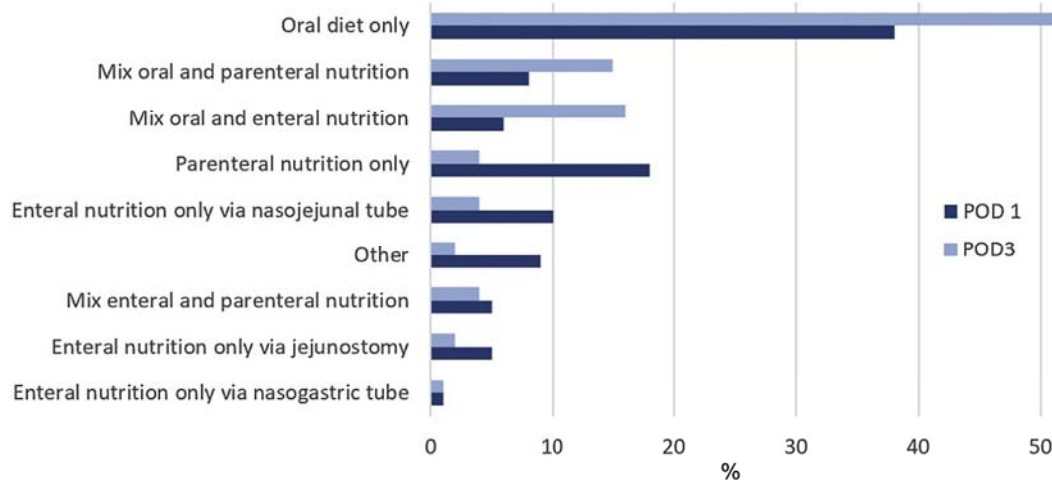
Participants could give several answers, which explains why the total is not 100%.

consultation, and another 17% according to selected criteria only. The level of evidence for nutritional practices in pancreatic surgery is low, and the use of systematic preoperative nutritional

consultation has not been reported as clearly beneficial. However, malnutrition can be detrimental, especially in terms of postoperative outcomes<sup>6,13</sup> and ESPEN guidelines have defined surgical patients at severe nutritional risk by the presence of at least one of the following criteria: weight loss >10–15% within 6 months, BMI <18.5 kg/m<sup>2</sup>, Subjective Global Assessment Grade C or NRS >5, and preoperative serum albumin <30 g/l.<sup>14</sup> Thus, guidelines suggest a preoperative detailed nutritional and medical history that includes body composition assessment and a nutrition intervention plan.<sup>14</sup> A study compared the accuracy of seven validated screening tools in 134 older medical inpatients against two validated nutritional assessment methods (Subjective Global Assessment and Mini-Nutritional Assessment).<sup>15</sup> All



**Figure 2** Timing for removal of nasogastric tube after pancreatoduodenectomy



**Figure 3** Usual feeding routes on postoperative days (POD) 1 and 3

**Table 3** Postoperative peak flow rates and duration of infusion for enteral and parenteral nutrition

	Enteral (n = 104)	Parenteral (n = 83)	p Value
Mean flow rate in ml/h (SD)	59 (32)	74 (23)	<0.001
Mean duration of infusion per day in hours (SD)	19 (6)	21 (5)	0.033

tools were accurate in identifying malnutrition and therefore could be used in elderly hospitalized patients to allow the early identification and prevention of nutritional decline. Another large prospective study on 279 patients found that none of the nutritional scores defined malnutrition relevant to complications after pancreatic surgery.<sup>16</sup> However, it seems that the measurement of nutritional status, nutritional support and therapy are of utmost value in pancreatic surgery for both short- and long-term outcomes.<sup>17</sup> Nevertheless, it seems questionable to postpone or delay an intervention if a patient does not reach any nutritional level. Therefore, preoperative delays (waiting for availability in the operating room, neoadjuvant treatment, etc.) could be used to optimize nutritional status with potential improvement of postoperative outcome.

Preoperative nutritional supplements were used systematically by 29% of surgeons only and according to preoperative nutritional consultation in 58% of cases. The forms of preoperative supplements used were mainly oral nutritional supplements (81%) and artificial enteral or parenteral nutrition (55%). To limit oxidative stress, supplementation of antioxidant amino acids (glutamine, cysteine) and antioxidant micronutrients (zinc, vitamin C, vitamin E,  $\beta$ -carotene, selenium) has been advocated in critically ill patients.<sup>18,19</sup> More particularly in major gastrointestinal surgery such as pancreatic surgery, two randomized prospective trials did not show a reduction of oxidative stress and systemic inflammation markers after short-term preoperative ingestion of oral nutritional supplement with high-dose antioxidants.<sup>20,21</sup>

**Table 4** Comparison of high-volume vs. low-volume centers

	High-volume (n = 139)	Low-volume (n = 281)	p Value
Use of preoperative nutritional supplements			0.842
Always	38 (27%)	74 (26%)	
Never	16 (12%)	38 (14%)	
Depends on preoperative nutritional consultation	85 (61%)	169 (60%)	
Type of nutritional supplements			0.907
Oral	101 (73%)	194 (69%)	
Enteral	12 (9%)	23 (8%)	
Parenteral	4 (3%)	11 (4%)	
Immunonutrition	6 (4%)	16 (6%)	
Postoperative systematic use of nasogastric tube	93 (67%)	204 (73%)	0.138
Use of oral diet only on postoperative day 1	67 (48%)	89 (32%)	<0.001



Thus, any benefits are currently not established. Further studies on the role of oxidative stress in terms of outcomes and the use of antioxidants in patients undergoing PD are needed.

Artificial nutrition was recently modified by adding specific substrates (arginine, omega 3 fatty acids, RNA) to modulate immunometabolic response.<sup>22</sup> In the present survey, immunonutrition was only used by a minority of surgeons (17%). There are few reports on the effects of preoperative immunonutrition on outcomes and immune functions in highly stressful surgeries such as PD.<sup>23–25</sup> A Japanese randomized study showed that infectious complication rate and severity of complications were reduced in patients receiving immunonutrition 5 days before PD.<sup>23</sup> A retrospective study suggested that 5 days preoperative oral immunonutrition was effective in patients scheduled for PD, reducing the risk of postoperative infectious complications (22.9% vs. 43.7%,  $p = 0.034$ ) and length of hospital stays ( $18.3 \pm 6.8$  days vs.  $21.7 \pm 8.3$ ,  $p = 0.035$ ).<sup>26</sup> More generally in major abdominal surgery, a total of 83 randomised controlled trials with 7116 patients were included in a recent Meta-analysis.<sup>27</sup> Immunonutrition did not seem to alter mortality but reduced overall complications, infectious complications and shortened hospital stay. However, the existence of bias diminished confidence in the evidence, and non-industry-funded trials reported no positive effects.<sup>27</sup> Thus, evidence for the use of immunonutrition is disparate, but almost 1 in 5 survey participants reported its systematic use.

Biological parameters to evaluate malnutrition are widely used by surgeons (66%), mainly albumin, prealbumin and CRP. Serum albumin and prealbumin concentrations are used mainly to indicate and monitor catabolic activity.<sup>28</sup> Moreover, a consensus of experts stated that indicators of malnutrition included elevated serum CRP concentrations and/or reduced serum concentrations of albumin.<sup>28</sup> Nevertheless, their validity as nutrition indicators was low because of the inflammation-induced perturbation.<sup>29</sup> Biochemical markers rather show the degree of catabolism/inflammation but are less convenient as indicators of nutritional status.<sup>30</sup>

Regarding intraoperative details, 69% of the respondents routinely placed a NGT for gastric drainage, with various postoperative managements. A recent retrospective study compared patients with and without NGT after PD.<sup>31</sup> The length of hospital stay and rate of postoperative complications of grade 2 or higher (Clavien classification) were significantly higher in the NGT group (14 vs. 10 days,  $p = 0.005$  and 82.8 vs. 40%,  $p < 0.001$ , respectively). Incidence and severity of delayed gastric emptying (grade B–C) were also higher in the NGT group. A retrospective study of 228 patients also showed that postoperative gastric decompression could be safely avoided in patients after PD.<sup>32</sup> In addition, a systemic review including 5240 patients concluded that routine nasogastric decompression should be abandoned in favour of selective use, because patients without routine tube had earlier return of bowel function and decreased pulmonary

complications after abdominal surgery.<sup>33</sup> Another meta-analysis showed that routine NGT seemed not to be beneficial, was uncomfortable and may even be harmful after abdominal surgery.<sup>34</sup> Therefore, the authors recommended NGT only as therapeutic approach. Despite these data and despite ERAS Society recommendations, the absence of NGT following PD has not yet been widely adopted by pancreatic surgeons, as confirmed by this present survey.<sup>10</sup> This mistrust has various causes, including the type of pancreatic anastomosis, and, importantly, the frequency of observed delayed gastric emptying.<sup>31</sup> Of note, a recent position paper of the International Study Group on Pancreatic Surgery (ISGPS) ruled that the available data did not show any definitive nutritional advantages for one specific type of gastrointestinal reconstruction technique after PD over the others.<sup>17</sup>

Postoperative nutritional management after PD is heterogeneous in the literature. In the present study, 66% of participants reported to perform postoperative nutritional follow-up consultation during hospitalization, and 58% of them had established local standardized protocols for postoperative nutritional support. Feeding routes after PD were varied on postoperative days 1 and 3. Different feeding routes have been used; but controversies remain about the optimal strategy after PD.<sup>35–37</sup> For patients requiring prolonged nutritional support, the enteral route has proven benefits over TPN: improvement of immune function, preservation of gastrointestinal mucosal integrity, and decreased infectious complications (in particular, those linked to central venous catheter).<sup>38</sup> The ISGPS recommends that EN should be preferred whenever possible over TPN if any artificial nutritional support is needed.<sup>17</sup> The choice between EN, TPN and combined enteral–parenteral nutritional after PD remains controversial as well.<sup>9,38–40</sup> A multicentre randomized controlled trial (Nutri-DPC) showed that nasojejunal early EN compared to TPN after PD was associated with increased overall postoperative complication rate.<sup>39</sup> On the contrary, a Korean trial found that EN after PD was associated with preservation of weight and better recovery of digestive function compared with TPN.<sup>41</sup> Furthermore, a literature review showed that early EN after PD, which appeared to be safe and well tolerated, did not show any reduction in delayed gastric emptying, pancreatic fistulas, haemorrhage, infectious complications and length of stay.<sup>38</sup> There is also a variety of possibilities for administration of artificial nutrition. In this present survey, mean flow rates and duration of infusion for TPN were significantly higher than for EN. According to ESPEN guidelines, tube feeding should be initiated within 24 h after surgery, but should be considered in patients in whom early oral nutrition cannot be initiated, with special regard to those with obvious undernutrition at the time of surgery, and in whom oral intake will be inadequate (<60%) for more than 10 days.<sup>14</sup> Moreover, tube feeding should be started with a low flow rate (e.g. 10–20 ml/h) due to limited postoperative intestinal tolerance and it may take 5–7 days to reach the target intake.<sup>42</sup> This could explain why the Nutri-DPC trial showed that TPN was more successful in



covering energy requirements on postoperative day 5.<sup>39</sup> Moreover, the present survey showed that the peak flow rates chosen by surgeons were higher through TPN, possibly to avoid a negative energy balance. Nonetheless, no evidence is available on how to manage flow rates and duration of infusion of TPN and EN after PD.

There is good evidence suggesting that ERAS pathway application reduces hospital stay and hospital costs after pancreatic surgery and may have an impact on delayed gastric emptying as well.<sup>43–45</sup> According to ESPEN and ERAS guidelines, early oral feeding is the preferred route of nutrition for surgical patients.<sup>10,14</sup> In the present survey, high-volume centers were more likely to use oral diet alone on the first postoperative day compared to low-volume centers. One hypothesis to this difference is that high-volume centers are usually academic centres with particular interest in different aspects of pancreas surgery, including nutritional issues. Considering that malnutrition and underfeeding are risk factors for postoperative complications, early EN is particularly relevant for any patient at nutritional risk and should be initiated within 24 h after surgery.<sup>14,28</sup> Finally, nutrition after hospital discharge should be evaluated. A recently published systematic review and meta-analysis evaluated oral nutritional supplement in medical and surgical patients aged over 65 years and suggested positive associations between dietary intake and weight status.<sup>46</sup>

Several limitations of the present study need to be addressed. The aim was not to achieve consensus or develop evidence for nutritional management, but rather to observe and report current practices. As the response rate was around 17%, this could represent a selection of surgeons already interested in nutritional support. In addition, as this survey included rather high-volume centres (>60% performed >25 procedures/year), some findings may not be representative for low-volume centres. There was also a selection bias, as the survey was only available to E-AHPBA and IHPBA members, which usually represent more academic/urban surgeons, and may not be representative of true general practices. Furthermore, characteristics of surgeons associated with specific practice were not analysed and timing of preoperative nutritional support or if there were any specific pathologies where surgeons feel more comfortable opting for an early resection or a preoperative nutritional optimization were not addressed. Biological parameters that were used to detect malnutrition could be a result of what the lab values are commonly accrued at the surgeon's institution, with possibly an accessibility limitation. Finally, enteral and parenteral flow rates and duration of infusion were assessed, but daily caloric intake was not taken into consideration.

In conclusion, the present survey disclosed important disagreements worldwide regarding the perioperative nutritional management in patients undergoing PD. No specific preoperative nutritional threshold was used by most of the respondents, and postoperative feeding routes were varied. More evidence is needed to improve and standardize nutritional management in patients undergoing PD.

#### Conflicts of interest

None declared.

#### Funding source

None.

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#### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpb.2019.05.009>.