

Review

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Review

Pancreatic Neuroendocrine Tumors: What Is the Best Surgical Option?

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Abstract: Background: Pancreatic neuroendocrine tumors (pNETs) represents a rare subset of pancreatic cancer. Functional tumors caused hormonal changes and clinical syndromes, while non-functional ones are often diagnosed late. Surgical management need a multidisciplinary planning, involving enucleation, distal pancreatectomy with or without spleen preserving, central pancreatectomy, pancreaticoduodectomy or total pancreatectomy. Minimally invasive approach increased in the last decade compared to the open technique. The aim of this study is to analyze current diagnostic and surgical trends for pNETs, to identify better interventions and their outcomes. **Methods:** The study adhered to PRISMA guidelines, conducting a systematic review of literature from May 2008 to March 2022 across multiple databases. Several combinations of keywords was used ("NET", "pancreatic", "surgery", "laparoscopic", "minimally invasive", "robotic", "enucleation", "parenchima sparing") and relevant article references was manually checked. Manuscript quality was evaluated. **Results:** The study screened 3867 manuscripts, twelve studies were selected, primarily from Italy, the United States, and China. A total of 7767 surgical treated patients was collected from 160 included centers. The mean age was 56,3 y.o. Enucleations (EN) and distal pancreatectomy (DP) was the most common performed surgery and represents 43.4% and 38.6% of the total interventions, respectively. Pancreatic fistula, post operative bleeding, re-operation and follow up was recorded and analyzed. **Conclusions:** Enucleation show better postoperative outcomes and lower mortality rates compared to pancreaticoduodenectomy (PD) or distal pancreatectomy (DP), despite similar risks of postoperative pancreatic fistula (POPF). DP was preferred over enucleation for pancreas body-tail, while laparoscopic enucleation is better for head pNETs.

Keywords: pNET; neuroendocrine tumors; pancreas tumor; pancreatic cancer; enucleation; Pancreatectomy

1. Introduction

Pancreatic neuroendocrine tumors (pNETs) are first described in 1869 as a rare subset of neuroendocrine neoplasm (NENs) [1] with a prevalence among Caucasian people (84%), male population and Its incidence increases with age [2]. Tumors can be defined as functional if they overproduce hormones that result in a distinct clinical syndrome; other are non-functional for non or minimal secretion of hormones, without resolve in a manifest syndrome, so 90% of them are silent and diagnosed in late stage [3,4]. Rarely tumors can be included in hereditary syndromes such as multiple endocrine neoplasia type 1 (MEN-1), Von Hippel-Lindau (VHL) disease and

Neurofibromatosis type 1 (NF-1), while they generally occur in a sporadic form [5]. The development of diagnostic tools and the whole genome landscape has related to the significant grow up of impact of NF-pNETs in the last 20 years [6].

Surgical management of pNETs should be planned in a multidisciplinary staff meeting, including accurate preoperative staging (localization and grading) [7]. Parenchyma-sparing surgery should be performed for asymptomatic NF-pNETs > 2 cm and all functional sporadic pNETs except those with unresectable distant metastasis [8]. On the contrary, according to AIOM guideline of NENs, a clinical and radiological follow-up is recommended in case of non-functioning pNET < 2cm [9]. Open or minimally invasive surgical treatment involves enucleation, distal pancreatectomy with or without spleen preserving, central pancreatectomy; pancreaticoduodenectomy (PD) or total pancreatectomy may be indicated in specific case [10]. In the last two decades, the surprising diffusion of minimally invasive surgery introduced a new scenario modifying surgical approach, reducing the number of enucleation procedures in favor of distal pancreatectomy, considered safer and easier from a technical point of view.

Due to this wide variability of surgical options, Authors analyzed current trends in terms of diagnosis and surgical approach in the treatment of pNETs with the aim to identify the preferred intervention and medium-long term results.

2. Material and Methods

The present study was accomplished in accordance with the preferred reporting Items for systematic reviews and meta-analyses (PRISMA) guidelines [11]. A systematic review of the studies published in the literature from May 2008 to March 2022, was independently performed by two authors (F.M.M., G. COZ.) in 4 databases (PubMed, Scopus, Google Scholar, and Medline), based on criteria predetermined by the investigators. The obtained results were discussed with the senior authors (R.P. and G.CON). The research included not only original articles, meta-analyses and reviews, but also the Cochrane database and textbooks, which citations were further cross-checked. Discrepancy in data collection, classification and analysis were solved by consensus of all the authors. A several combinations of the keywords and MeSH (Medical Subject Headings) search terms used including "NET", "pancreatic", "surgery", "laparoscopic", "minimally invasive", "robotic", "enucleation", "parenchyma-sparing". The various terms were included consecutively during the search. References of the more relevant articles were manually searched.

A pNET retrospective review analyzing epidemiology data, diagnosis, surgical approach and medium long term results of surgical treatment was performed. The Authors considering the main Literature Collections of pNET patients evaluated current clinical trends in the light of modern knowledge and of diffusion of minimal invasive surgery (MIS).

The following Inclusion and exclusion criteria were applied.

Inclusion criteria

- 1) English language studies including patients with clinical diagnosis of pNET;
- 2) Open surgery vs minimally invasive surgery (laparoscopic or robotic) for surgical treatment of pNET
- 3) Surgical treatment related to the pNET localization reporting, at least, one intraoperative, perioperative and postoperative outcomes.

Exclusion criteria

- 1) Non-English studies;
- 2) Animal studies;
- 3) non-comparative studies;
- 4) Abstracts, expert opinions, editorials and letter to the editors;
- 5) Studies reporting inadequate clinical data;
- 6) Treatment of others pancreatic tumor.

All studies that failed to fulfil the established inclusion criteria were automatically rejected.

The evaluation of manuscript quality was conducted using the Methodological Index for Non-Randomized Studies criteria [12] and the Newcastle-Ottawa Scale [13] to assess the quality of nonrandomized studies in meta-analyses because of the non-randomized nature of selected papers.

3. Results

3.1. Evaluation and Inclusion

We find a total of 3867 manuscripts for initial screening, using a systematic research. 1513 papers were excluded because of were duplicate. Analyzing title, abstract and keywords, Authors selected the full-text version of 43 papers. Main reasons for the exclusion were the absence of patients treated both with MIS and open approach ($n = 478$), no surgical patients ($n = 216$) and the inclusion of other types of pancreatic cancer ($n = 401$). Further causes of exclusion were population treated with palliative intent or case series or absence of specific data on the post-operative outcomes. Other 19 study were excluded during full-text examinations due to inclusion of other benign pancreatic lesions and no systematic post-operative data. Moreover, 9 article were excluded during data extraction because of inadequate clinical data. This led to the final selection of 12 studies which fulfilled the inclusion criteria [10,14–24].

The search strategy flow diagram is shown in Figure 1.

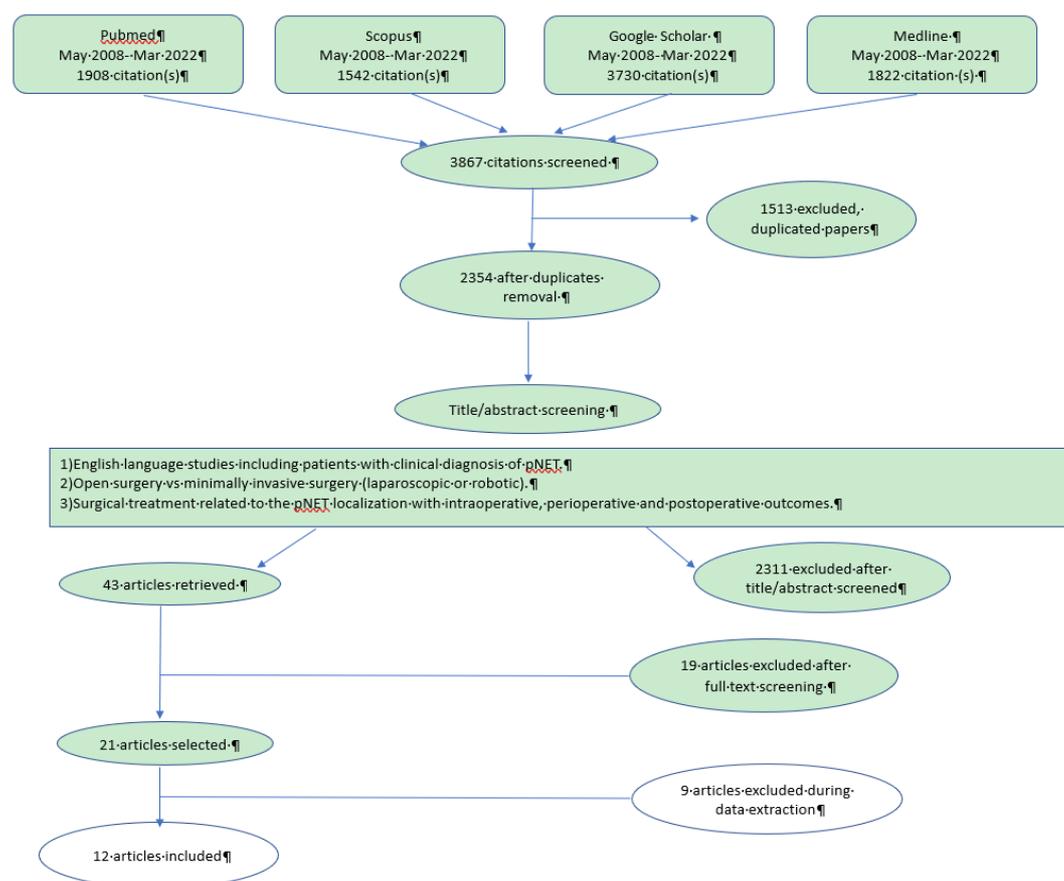


Figure 1. PRISMA flow-chart. Diagram of the systematic review of the literature, performed in 4 databases from May, 2007 up to March, 2022. Search terms included: "NET", "pancreatic", "surgery", "laparoscopic", "minimally invasive", "robotic", "enucleation" "parenchima-sparing". Inclusion criteria are shown in the central box. Major reasons for exclusion were the presence of a clinical diagnosis, localization and grading of pNET ($n = 475$), intraoperative, perioperative and postoperative outcomes of pNET surgery (open or minimally invasive) ($n = 1836$). Further reasons for exclusion were non-comparative studies and these reporting inadequate or partial clinical data. This led to the final selection of 13 studies which fulfilled the inclusion criteria.

No randomized clinical studies was found. All selected papers were retrospective studies and 5 of them were multicenter study [10,15–17,20]. Geographical distribution of the selected papers was as follows: 2 from Italy, United States and China; 1 from Germany (1), Spain, Romania, Netherlands, Korea and Norway.

Characteristics of the included manuscripts are summarized in Table 1.

The process of quality evaluation, followed MINORS and NOS criteria, was reported in Table 2. [12,13]

Table 1. A population's characteristics summary of selected study.

Author	N. Pts	Sex		Ages (years)			N. Center
		M	F	Mean Age	max	min	
Fernandez-Cruz	49	6	43	58	83	22	1
Casadei	44	8	36	60.5	77	42	1
Zerbi	310	166	144	57.6			24
Zhao	328	139	189	42.3	57	27	1
Haugvik	65	27	38	57	87	21	1
Mehrabi	6222	2551	3671	53	72	27	114
Xourafas	171	89	82	61.5	95	20	1
Jilesen	205	93	112	52.6	68	34	2
Han	94	55	39	53.5	75	30	1
Mihalache	18	6	12	53	69	28	1
Zhang	1020	464	556	58	66	48	9
Sutton	282	142	140	59	77	42	4

Table 2. Quality evaluation followed MINORS (Methodological index for non-randomized studies) and NOS (Newcastle-Ottawa Scale) criteria - ProS: Prospective Study; RetS: Retrospective study, SC: Single center, MC: Multi center, DB: Data base.

Year	Author	Country	Type of study	N. Center	NOS			MINORS
					Selection	Comparability	Outcome/Exposure	
2008	Fernandez-Cruz	Spain	ProS - SC	1	**	*	**	15
2010	Casadei	Italy	ProS - SC	1	***	**	***	22
2011	Zerbi	Italy	ProS - MC	24	***	*	**	15
2011	Zhao	China	RetS - SC	1	***	**	**	18
2013	Haugvik	Norway	RetS - SC	1	**	**	**	16
2014	Mehrabi	Germany	RetS - DB	114	***	**	***	20
2015	Xourafas	USA	RetS - SC	1	**	**	***	18
2015	Jilesen	Netherlands	RetS - MC	2	***	**	***	19
2017	Han	Korea	RetS - SC	1	***	**	***	20
2019	Mihalache	Romania	RetS - SC	1	**	*	**	16
2019	Zhang	China	RetS - MC	9	***	**	***	19
2022	Sutton	USA	RetS - MC	4	***	*	***	18

3.2. Baseline Characteristics

A total of 7767 surgical treated patients was collected from 160 included centers. The mean age was 56,3 y.o. (± 2.65 SD) with a prevalence of female sex (57,4%). Table 1

All patients had an histopathological diagnosis of PNETs on surgical specimens.

3.3. Surgical and Post-Operative Results

Enucleations (EN) and distal pancreatectomy (DP) was the most common performed surgery and represents 43.4% and 38.6% of the total interventions, respectively. Other reported surgeries was pancreaticoduodenectomy (PD) 8%, central pancreatectomy (CP) 1,1%, total pancreatectomy (TP) 0,8% and various surgical strategies, multivisceral resection e.g., 7,9%. Table 3

Zhang	7	9	5	\	4	6	4	\	6	\	300	100	\	200	\
Sutton	\	\	\	\	\	\	\	\	\	\	\	\	\	\	\

CR: Conversion Rate; EN: Enucleation; DP: Distalpancreatectomy; PD: Pancreaticoduodenectomy.

4. Discussion

NETs represent a cluster of complex oncological malignancy originate from neuroendocrine cells, with a large spread of clinical presentations and anatomical localizations, especially in the digestive tract, the lung, and the pancreas [1]. Although, PNETs represents 1-2% of all pancreatic neoplasm, their incidence is increasing [25]. The diagnosis is usually complex and requires blood sampling for chromogranin A and synaptophysin [26,27], specific search of hormones, such as serotonin, gastrin, insulin and glucagon, to confirm the diagnosis in patients with clinical symptoms remain the main diagnostic tool useful to obtain an accurate localization, grading, and staging in the pNETs management. In the last years, gallium scintigraphy or PET (positron emission tomography) scan were introduced and sometimes were overutilized for functional pre and postoperative studies; Ga 68 DODATOC PET/TC has better results about sensitivity than Octreoscan (90–100% vs. 50–80%) especially for the identification of liver micrometastases and locoregional lymph nodes [27].

As regard intraoperative localization ecolaparoscopy is recommended in every case with the aim to have a better tumor identification, a better evaluation of healthy pancreatic parenchyma and a better lymph nodes status. This diagnostic tool help the surgeon to made a correct decision for surgical intervention: a precise identification of the relationship between the tumor and the pancreatic duct is crucial to choose the surgical procedure (Enucleation Vs distal pancreatectomy) according to European Neuroendocrine Tumor Society (ENETS) and AIOM guidelines of pNETs [8,9,29].

Table 1 presents a detailed overview of surgical procedures and patient demographics across various international centers about treatment of pNETs. A total of 8,488 patients were included in the analysis, with a predominance of females (53.4%) and an average age of 58.3 years. This demographic profile aligns with Literature characteristics of pNET patients, who are often diagnosed in their fifth to sixth decades of life [28].

Table 2 offers a comprehensive analysis of patient demographics, surgical approaches, and postoperative outcomes in the treatment of pancreatic neuroendocrine tumors (pNETs) across multiple studies and centers worldwide. Demographic data reveals interesting trends in the distribution of patients. While the female-to-male ratio varied slightly across studies, with some showing an higher proportion of female patients, the mean age of patients generally clustered around 58.3 years, indicating that pNETs commonly affect individuals in their late fifties.

In most cases following a multidisciplinary evaluation, a surgical approach was considered. Surgical strategy was related to the volume, the numbers, the localization of the lesions and its distance to the pancreatic duct. All the patients underwent surgical laparotomy or laparoscopy in order to remove pNETs and to analyze them histologically. Open, laparoscopic or robotic surgical choice involves enucleation, distal pancreatectomy (DP) with or without splenectomy, central pancreatectomy, pancreaticoduodenal resection (Whipple's operation) with or without pylorus preservation and total pancreatectomy according to primary tumor location. [30–32].

Patient characteristics, tumor histomorphology, size and location, surgeon preference and the local availability of resources are the preferred decision-making factors [33].

The main focus of survey I-GO-MIPS (mininvasive pancreatic surgery), according to Zerbi et al. is to analyze the volume, type, and surgical indication for mininvasive pancreatic surgery to rate postoperative outcomes and increase the use of MIPS in Italian centers and to contribute to the European registry [34,35]. In the last two decades the rate of pNETs surgery is improved especially mininvasive distal pancreatic surgery on pancreatic body and tail [36,37]. Current preference of **parenchyma-sparing techniques** such as enucleation and middle pancreatectomy (for lesions of the central portion of the gland) arises from the high risk of pancreatic endocrine/exocrine insufficiency following PD and DP [38].

Surgical interventions exhibited notable disparities in the frequency and types of procedures performed across different centers. Enucleation (EN), a procedure aimed at preserving pancreatic tissue, emerged as a prominent choice in several studies, particularly in centers located in Italy and China. This trend may reflect a growing emphasis on preserving pancreatic function and minimizing

surgical invasiveness. Conversely, more extensive procedures such as pancreaticoduodenectomy (PD) and total pancreatectomy (TP) were performed less frequently but were still significant in managing advanced or complex cases.

Enucleations (EN) represents the most common surgical treatment for PNETs (43,4%) and was reported, as surgical treatments, from 9 Authors [10,14–16,18–21] but Zerbi et al not divided in minimal-invasive and open approaches [16]. Surgical interventions varied across centers, with enucleation (EN) being the most common procedure, accounting for 43.4% of cases [Tab 1]. Enucleation is favored for small, well-defined tumors, as it allows for tumor removal while preserving pancreatic parenchyma. Despite of a large diffusion of laparoscopy and, in the last years, of robotic surgery, EN was performed in open surgery in 89.5% and was reported a 7.3% of conversion in MIS approach.

In the series by Haugvik et al, laparoscopic enucleation of PNET of pancreatic head is most supported than major surgery (Whipple's procedure), on the other hand laparoscopic resection of PNET in the pancreatic body and/or tail could be favored than enucleation [19]. This preference could be justified by the lesser invasiveness and potential benefits of laparoscopy, such as reduced blood loss, shorter hospital stays, and quicker postoperative recovery, compared to the Whipple procedure involving more extensive pancreatic and intestinal resection. On the other hand, for PNETs located in the body and/or tail of the pancreas, laparoscopy might be preferred over enucleation. The concept of safety about parenchyma sparing is highlighted by the numbers of post-operative deaths after PD [39]. In summary, the choice between enucleation and laparoscopic resection depends on the tumor's location and specific characteristics, as well as consideration of long-term complications and benefits for the patient.

According to Beane et al, the post-operative outcome comparison between enucleation and resection showed a higher PD or DP mortality rate than enucleation ($p = 0,016$). Instead, serious morbidity, length of stay and surgical site infection have a low rate both DP and enucleation than PD [40]. According to Jilesen et al, postoperative morbidity after enucleation of pNETs was comparable to PD or DP and therefore it must be considered an high-risk operation. In every case pNETs need a pre-operative appropriate size, location, and functional status [20].

The long-term oncologic outcomes are similar between LDP for PNETs and ODP decreasing total morbidity in terms of postoperative complications without compromising survival [41]

Distal pancreatectomy (DP) was the second most frequently performed procedure, representing 38.6% of cases [Table 1]. DP is typically indicated for tumors located in the body or tail of the pancreas and offers a curative option for localized disease. Also in this case, the Laparoscopic approach was reserved only at a small segment of populations with a 21.2%.

Regional variations in surgical practices were evident, with centers in Europe and Asia demonstrating distinct preferences. For instance, Italian centers favored EN, while Norwegian and Dutch centers adopted a more balanced approach between EN and distal pancreatectomy (DP). In contrast, centers in the United States showed a greater utilization of DP, possibly influenced by local surgical expertise and institutional protocols. Temporal trends revealed a gradual shift towards minimally invasive techniques, with laparoscopic and robotic-assisted surgeries gaining traction in recent years. While these approaches offer advantages such as reduced postoperative pain and shorter hospital stays, their adoption varied across regions, reflecting differences in technological infrastructure and surgeon training.

Nevertheless, MIS approach represented a more frequent surgical options in SDP then EN. These unexpected results, in our opinion, it could be due to better standardization of SDP then EN, that represent a surgical tailored intervention on specific needs of the patients and often required ultrasonography for the correct identifications of the lesions and for a better evaluation of its distance from the main duct. Another possible explication of this result could be that, if the surgeon was not sure to be able to perform an EN, he might prefer the open approach because it would be simpler modify the surgical strategy in way to perform a more complex surgical intervention (TP, CP or DP). In fact, pancreaticoduodenectomy (PD), which accounts for 8% of all surgical procedures, as well as total pancreatectomy (TP) at 1.1% and central pancreatectomy (CP) at 0.8%, exhibited notably low rates of minimally invasive approaches, with only 2.7%, 1.1%, and 1% respectively. This indicates that these complex procedures, which involve extensive resection of pancreatic tissue and intricate anatomical reconstruction, are less frequently performed using minimally invasive techniques such

as laparoscopy or robotics. Therefore, it was obviously related to the high surgical complexity but there was also a specific study limitations: our selected study collect data from papers wrote since 2008 [21]; only 6 papers was published after 2015 [14,15,17,20,22,23] (Table 2).

Five Authors reported other various surgical interventions (e.s. multivisceral resections, atypical pancreatic resection) [10, 16, 18-19, 21; Table 2].

Data from Literature clearly explain that MIS for pancreas cancer has seen rapid development in the past decade and only since 2017 promising outcomes have been reported by early adopters from high-volume centers [15]. Subsequently, multicenter series as well as randomized controlled trials were reported with an increasing scientific publication in this field [42]. This paper was focused on MIS approach of all pancreatic cancers, but our aim was on PNET, a specific and rare disease; for this reason, was not possible to select a most update papers, except Sutton et al. [15]. The safety and efficacy of laparoscopic and open surgical approach is compared in a lot of studies, improving results were reported following lap procedures in terms of cosmetic scars, reduced postoperative pain and hospitalization [43]. Laparoscopic technique speeds up the oral intake after surgery and the recovery of gastrointestinal function [44], it use is greatly increased in several pancreatic disease despite the complexity due to the long operating time and the long learning curve. In the series by Casadei et al, the 14,6% of patients needed distal pancreatectomy particularly with non-malignant pancreatic tumors (90.9%), have undergone laparoscopic distal pancreatectomy associated to splenectomy and rarely with spleen preservation [24].

A particular attention should be reserved for robotic pancreatic resection or enucleation and several advantages are connected to specific functions. Clinical series are few and moreover it derives from referral centres where surgical pancreatic experience is associated to advanced laparoscopic skill. More data are necessary to confirm that robotic surgical approach is safe and viable procedure [45]. In fact, this surgical treatment resolves considerable advantages, as lower conversion rate, parenchyma sparing, reduction of hospitalization, despite high costs and longer operative times. The literature shows a significant lack of data on robotic PNET surgery, so a comparison between other surgical techniques and robotic is limited and not feasible. Perhaps, the oncological and perioperative score between laparoscopic and robotic approach are comparable as the EBM (evidence base medicine) describes [46].

About postoperative outcomes, pancreatic fistula rate, length of hospital stay (LHS) and blood loss were evaluated. About post-surgical results, a post operative bleeding (POB) with a Clavien-Dindo classifications ≥ 2 was reported in 2% of all patients with a median overall length hospital stay (LHS) of 6.75 days [47]. 156 patients need a readmission in surgical room: 45 for pancreatic fistula, 87 for POB and 24 for other reason (perforations, anastomotic leak).

The incidence of pancreatic fistula varied across studies, with some demonstrating higher rates compared to others. The classification of pancreatic fistulas into Grade A, B, and C (following the International Study Group on Pancreatic Fistula - ISGPF - criteria provides) offers crucial insights into the severity and management of postoperative pancreatic complications [48]. According to our analysis, a higher rate of POPF is most related with laparoscopic enucleations of PNET than laparoscopic resections. Fernandez-Cruz et al. reported a pancreatic fistula rate of 8%, while Haugvik et al. observed a lower rate of 7% [19,21]. These differences may be attributed to the variations in patient selection criteria, surgical techniques, and postoperative management protocols. Notably, Zhao et al. and Zhang et al. reported relatively higher rates of pancreatic fistula, suggesting potential challenges or complexities associated with performing pancreatic surgery in those centers [17,18]. Possible explications for these challenges could include variations in surgical techniques, expertise levels among surgical teams, patient populations with more advanced disease or comorbidities, differences in postoperative management protocols, or institutional factors affecting the quality of care. This result underscores the importance of ongoing quality improvement efforts, standardization of surgical protocols, and continued education and training for surgical teams to optimize outcomes and minimize complications in pancreatic surgery.

Studies employing enucleation (EN) as the primary surgical approach reported higher rates of PF compared to more extensive procedures like pancreaticoduodenectomy (PD) and total pancreatectomy (TP). This underscores the inherent challenges associated with preserving pancreatic tissue integrity during surgery. While EN offers advantages in terms of preserving pancreatic function and reducing postoperative morbidity, it also carries a higher risk of PF formation due to

the delicate nature of tissue dissection and manipulation. Conversely, PD and TP, although associated with lower PF rates, entail greater pancreatic resection and may result in exocrine and endocrine insufficiency. The variation in PF rates underscores the importance of tailored surgical decision-making based on tumor characteristics, patient comorbidities, and surgical expertise.

LHS is a critical parameter for assessing the efficiency of surgical management and postoperative recovery. It is considerable the variability in LHS across different centers, reflecting differences in patient populations, surgical techniques, and institutional practices. Notably, in centers with an high minimally invasive approach rate, such as laparoscopic and robotic-assisted surgeries, tended to exhibit shorter LHS compared to traditional open procedures. This result highlights the potential benefits of minimally invasive techniques in facilitating faster postoperative recovery and reducing healthcare resource utilization. Casadei et al. and Mehrabi et al. reported shorter median LHS, indicating efficient postoperative care and patient recovery [10,24]. Conversely, Zhang et al. and Xourafas et al. showed longer LHS, possibly influenced by factors such as postoperative complications and institutional protocols [17,22]. The range of LHS across studies underscores the importance of identifying factors contributing to prolonged hospital stays and implementing strategies to optimize perioperative care and discharge planning. However, it is essential to interpret LHS data in conjunction with other clinical factors, such as complication rates and patient outcomes, to assess the overall quality and safety of surgical care.

Blood loss during pancreatic surgery can impact postoperative outcomes and necessitate transfusions, thereby increasing the risk of complications. The analysis revealed variations in intraoperative blood loss across different procedures and centers. Zhao et al. and Zhang et al. reported varying degrees of blood loss, with median values ranging from 149 mL to 716.7 mL [17,18]. These differences may reflect variations in surgical complexity, tumor characteristics, and intraoperative management. While studies implementing minimally invasive techniques reported lower intraoperative blood loss compared to traditional open procedures, the magnitude of reduction varied depending on the complexity of the surgery and the surgeon's proficiency in minimally invasive approaches. Effective intraoperative hemostasis techniques, meticulous surgical planning, and advanced surgical technologies such as intraoperative blood salvage systems contribute to minimizing blood loss and optimizing patient outcomes.

Postoperative outcomes provided valuable insights into the safety and efficacy of surgical interventions. While EN was associated with shorter hospital stays compared to more extensive procedures like PD and TP, it also exhibited higher rates of pancreatic fistula formation, highlighting the importance of careful patient selection and surgical technique. Additionally, differences in postoperative bleeding rates underscored the need for standardized perioperative management protocols to mitigate complications and optimize patient outcomes.

In summary, the analysis of pancreatic fistula rate, length of hospital stays, and blood loss across different studies provides valuable insights into the variability and determinants of postoperative outcomes in pancreatic surgery. Future research endeavors should focus on elucidating factors contributing to these outcomes and developing standardized protocols to optimize surgical care and enhance patient recovery.

Despite the comprehensive nature of the dataset, several limitations should be acknowledged. The retrospective design of the studies may introduce selection bias, and the heterogeneity in reporting outcomes across centers hinders direct comparisons. Additionally, the absence of randomized controlled trials limits the ability to draw definitive conclusions regarding the optimal surgical approach for pNETs.

5. Conclusions

In our analysis, the enucleation is associated with better rate in terms of postoperative outcomes and mortality despite the same risk of POPF than PD or DP. DP should be favored between the mininvasive procedures as surgery of pancreatic body-tail than enucleation, on the other hand laparoscopic enucleation performed in head pNETs. In conclusion, the comprehensive analysis of demographic characteristics, surgical practices, and postoperative outcomes elucidates the multifaceted nature of pNET management. Moving forward, efforts to standardize surgical protocols, enhance training in minimally invasive techniques, and promote multidisciplinary collaboration are crucial for improving the quality of care and optimizing outcomes for patients with pNETs.

Furthermore, our review shows preoperative multidisciplinary management is necessary to focus the better pancreatic treatment as well as the patient's characteristics, localization, functional state and size are decision making factors for the surgery.

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