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REVIEW ARTICLE

What do surgeons need to know about the mesopancreas

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Abstract

Background Pancreatoduodenectomy is the only treatment with a promise of cure for patients with pancreatic head adenocarcinoma, and a negative resection margin is an important factor related to overall survival. Complete clearance of the medial margin with removal of the so-called mesopancreas may decrease the recurrence rate after pancreatic resection. Here, we present some important information about the mesopancreas, total mesopancreas excision, and technical aspects to achieve negative resection margins. The area named mesopancreas is defined as the tissue located between the head of the pancreas and the superior mesenteric vessels and the celiac axis and consists of the nerve plexus, lymphatic tissue, and connective tissue. The superior mesenteric and celiac arteries define the border of the mesopancreas. En bloc resection of anterior and posterior pancreatoduodenal nodes, hepatoduodenal nodes, along the superior mesenteric artery nodes, pyloric nodes, and nodes along the common hepatic artery is necessary.

Conclusions Improved knowledge of the surgical anatomy of the region and technical refinements of excision of the mesopancreas along with standardized pathological examination are important to increase and to determine radical resection of pancreatic head cancer.

Keywords Mesopancreas · Pancreatic head plexus · Retroportal lamina · Total mesopancreas excision · Negative margins · Survival

Introduction

Pancreatoduodenectomy with adjuvant systemic chemotherapy represents the only curative treatment option for patients with pancreatic ductal adenocarcinoma in the head of the pancreas [1–6]. Surgical resection in resectable pancreatic ductal adenocarcinoma associated with chemotherapy is the most important factor for cure and is related to a significant increase in overall survival compared with any other form of therapy [1, 3, 4, 6]. The prognosis after pancreatoduodenectomy for pancreatic ductal adenocarcinoma is poor, with 5-year and median survival rates of 20–25% and between 12 and 22 months, respectively [6–8]. Survival after resection is significantly higher than that in patients with unresected localized and metastatic disease, and key pathological parameters have an impact on survival after resection of pancreatic ductal adenocarcinoma, including lymph node status, extent of lymph node involvement, tumor grade, and perineural invasion [2, 5, 6, 9, 10].

R status independently predicts overall survival and R0 resection is a key prognostic factor. However, even patients with R0 resection experience retropancreatic recurrence. Moreover, if circumferential margins are thoroughly evaluated using an axial slicing protocol for pathological assessment, high rates of R1 are observed, especially at the retroperitoneal margin [11–16]. Involvement of even a single margin is a predictor of disease recurrence, suggesting that positivity of the pancreatic margin indicates a more aggressive disease [15–17].

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The rates of noncurative resection range from 15 to 40%; however, postmortem investigations in patients with pancreatic ductal adenocarcinoma who underwent pancreatic resection revealed local recurrence rates up to 100% [14–17]. The high rate of noncurative resection in patients with pancreatic ductal adenocarcinoma is mainly related to the close anatomical relationship of the tumor with the SMV and SMA as well as with the celiac trunk (CT). Medial/SMA margins are considered to have a significant impact on recurrence and overall survival rates. This area is by far the most frequent positive site of recurrence after pancreatoduodenectomy associated or not with involvement of the SMV or the pancreatic transection margin. Complete clearance of this region may decrease the recurrence rate after pancreatic resection. [7, 8, 18–20] This retropancreatic perineural and lymphatic tissue, which is also named the "retroportal lamina," "pancreatic head plexus," "P-A ligament," or "mesopancreas," remains poorly known to many surgeons performing pancreatic cancer resections. In pathological assessment, this area is addressed by investigation of the medial and posterior circumferential resection margins. The medial margin is occasionally also described as a retroperitoneal or uncinate margin, defined as the part of the pancreatic head that lies inferior to the transection margin, between the anterior surface and the posterior resection margin including the SMV groove and superior mesenteric artery. [21–35]

Crippa et al. [36], separately analyzing the superior mesenteric vein (SMV) groove and SMA margin (medial margin), observed that positive margin status (R1 direct and R1 ≤ 1 mm) was an important prognostic factor for recurrence and survival ($p<0.0001$). R1 ≤ mm was an independent predictor of overall recurrence. Different prognoses are related to each pancreatic resection margin, and individual margin status should be considered in every case [36]. Tanaka et al. [19], Kalisvaart et al. [7], and Jones et al. [5], observed local recurrence in 20.8%, 27%, and 49.7%, respectively. Simultaneous local and metastatic recurrence occurred in 26% and 10%, respectively [5, 7]. Similar overall survival rates were found in patients with local, metastatic, or simultaneous recurrence [5, 7]. Ghaneh et al. [20], observed that for patients with an R1-direct margin the overall survival was 18.7 months, compared with 24.9 months for patients with an R0 margin [20]. Some publications have focused on the best technical variant of pancreatoduodenectomy to achieve a better oncological outcome, including total mesopancreas excision [37–41].

A recent single-center study by Quero et al. [38], comparing standard versus mesopancreas excision pancreatoduodenectomy, observed a higher rate of mesopancreas positivity in the standard group ($p=0.04$), a higher number of lymph nodes harvested in the mesopancreas excision group ($p= 0.04$), and local recurrence more frequently in the standard group ($p=0.002$), and in the multivariate analysis, mesopancreas positivity was an independent prognostic factor for worse overall survival and disease-free survival. [38] There are no randomized trials comparing outcomes with or without total mesopancreas excision (TME) for pancreatic ductal adenocarcinoma in the head of the pancreas (Table 1).

The history of the mesopancreas

Gockel et al. [42] first introduced the terms mesopancreas and resection of the mesopancreas (RMP) in pancreatic ductal adenocarcinoma as an analogy to the mesorectum and to the technique of total mesorectum excision known to increase local control after resection for rectal cancer. However, the terms "mesopancreas" and "total mesopancreas excision" have been suggested, but this area is not exactly defined [21, 25, 26, 32, 33]. According to Gockel et al. [42], the mesopancreas is a firm and well-vascularized peripancreatic structure composed of fatty tissue with vascular structures, nerve fibers, lymph nodes, and lymphatic vessels on the fusion fascia of Treitz. The perineural lymphatic layer is located in the dorsal area of the pancreatic head between the pancreatic uncinate process and SMA and SMV (Fig. 1a and b). The mesopancreas is delimited laterally by the medial and posterior aspect of the uncinate process and pancreatic head; medially by the right aspect of the SMV and SMA; proximally (cephalic) by the origin of the celiac trunk; and distally (caudal) by the beginning of the mesenteric root and posteriorly by the left renal vein. The perineural tumor invasion rate in pancreatic cancer is up to 75%. The mesopancreas is considered the main site of a positive resection margin, and it was suggested that en bloc resection of this structure during pancreatoduodenectomy would reduce local recurrence [43–47]. This concept started to be recognized, and TME is considered a promising surgical approach for patients with pancreatic ductal adenocarcinoma (Fig. 2a, b, and c). The term mesopancreas has been used by other authors in the literature [21, 23–25, 28, 42]. However, the term mesopancreas is not universally accepted because of the absence of precise anatomic borders [32–35]. Japan Pancreas Society [29] defines this area as the pancreatic head plexus I (PL phI), located behind the pancreatic head and celiac plexus and the pancreatic head plexus II (PL phII), including the area behind the uncinate process, SMA, and inferior pancreatoduodenal artery (IPDA) [29] (Fig. 3).

The TME concept includes the resection of the peripancreatic lymphatic structures along the neuronal plexus posterior to the pancreatic head and on the right side of the SMA. Providing clearance of the peripancreatic retroperitoneal tissue may improve the prognosis with R0 resection in patients with pancreatic head adenocarcinoma. This area represents an important location of perineural tumor cell infiltration in patients

Table 1 Studies comparing total mesopancreas excision versus standard pancreatoduodenectomy

Author	Results	TME	SPD	p	Ref
Kawabata et al. (2012)	R0 resection (%)	92.8	60	0.019	39
	R1 resection (%)	7.2	40		
	Recurrence (%)	14.2	64	0.036	
Aimoto et al. (2013)	R0 resection (%)	74	68	NS	41
	R1 resection (%)	26	30	NS	
	Local recurrence (%)	0	37	<0.01	
Xu et al. (2017)	Median DFS (Months)	16.9	13.4	0.044	37
	Median OS (Months)	19.9	22.5	0.176	
	1-year total recurrence rate (%)	31.8	55.3	0.054	
	1-year local recurrence rate (%)	18.2	39.5	0.018	
Quero et al. (2021)	Disease-free survival (%)	22.3	14.8	0.04	38
	R1 Mesopancreas margin (%)	5.0	16.7	0.04	
	Local tumor recurrence (%)	26.8	55.5	0.002	

Legends: *TME*, total mesopancreas excision; *SPD*, standard pancreatoduodenectomy; *DFS*, disease-free survival; *OS*, overall survival; *NS*, no significant

with pancreatic head adenocarcinoma. Modern imaging techniques may estimate the extension of the disease and the possibility of vascular invasion preoperatively, suggesting that pancreatic surgeons should be trained for venous resection and reconstruction of the portal mesenteric confluence to achieve R0 margins [22, 37–39, 41, 47–52].

The mesopancreatoduodenum is the term used by Kawabata et al. [39, 48, 49] to define a common mesentery located at the back of the SMA, including the mesentery of the third and fourth portions of the duodenum and proximal jejunum, supplied by the IPDA and first jejunal artery. The mesentery consists of a cluster of loose connective tissue along the IPDA and the first jejunal artery. The mesopancreatoduodenum extends beyond the limits of the mesopancreas, including the lymph nodes at the left side of the SMA. Total mesopancreatoduodenum excision is defined as an important procedure to achieve successful control of the tumor and to reduce locoregional recurrence. The authors considered that mesopancreas resection and circumferential lymphadenectomy around the SMA are necessary to achieve locoregional tumor control successfully for pancreatic ductal adenocarcinoma. [39, 48, 49] Bouassida et al. [33] used the term retroportal lamina as a definite anatomical entity, and the limit was the SMA, despite some controversies about its existence that are due to the absence of fibrous sheath or fascia. Complete removal of this lamina might improve clearance and R0 resection [33]. The authors did not find a fibrous sheath or fascia, and total retroportal lamina resection is possible by subadventitial dissection of the SMA (Table 2). Based on anatomical findings of the region, Muro et al. recently suggested the term P-A ligament for the area previously described as the mesopancreas [30].

Components of the mesopancreas

Treitz's fusion fascia consists of several parallel layers of collagen fibers located between the dorsal aspect of the head of the pancreas and the aortocaval plane [22, 48].

For posterior lateral mesopancreas, the fascia is located between the lateral margin of the duodenum and the left margin of the aorta, extending continuously from the posterior surface of the pancreatic head and the third portion of the duodenum to the posterior aspect of the mesenteric vessels [22, 30, 48, 49].

For mesopancreatic root, the tissue denser than the fusion fascia is located between the neck of the pancreas and the pancreatic uncinate process on one side and the superior mesenteric vessels and CT on the other side. In this area, the nerve plexus, adipose tissue, capillaries, and lymphatics are also observed microscopically. The SMA and CT are surrounded by vessels, nerves, and lymph tissues and are considered the root and core of intramesopancreatic structures [22, 30, 48, 49].

Xu et al. [37] proposed that the mesopancreas is an anatomical entity defined by its left boundary located below the middle line along the CT and SMA; its right boundary the second portion of the duodenum; its superior boundary the hepatic artery; its inferior boundaries the lower edge of the third portion of the duodenum; and its anterior edge the surface of the pancreas. The back edge contains two parts: the posterior lateral mesopancreas and the mesopancreatic root. The intramesopancreatic structures are the CT and SMA, including the lymph nodes around the SMA (no. 14). In this definition, the interaortocaval lymph nodes (no. 16) are located outside the posterior lateral mesopancreas and are considered extramesopancreatic structures consistent with the

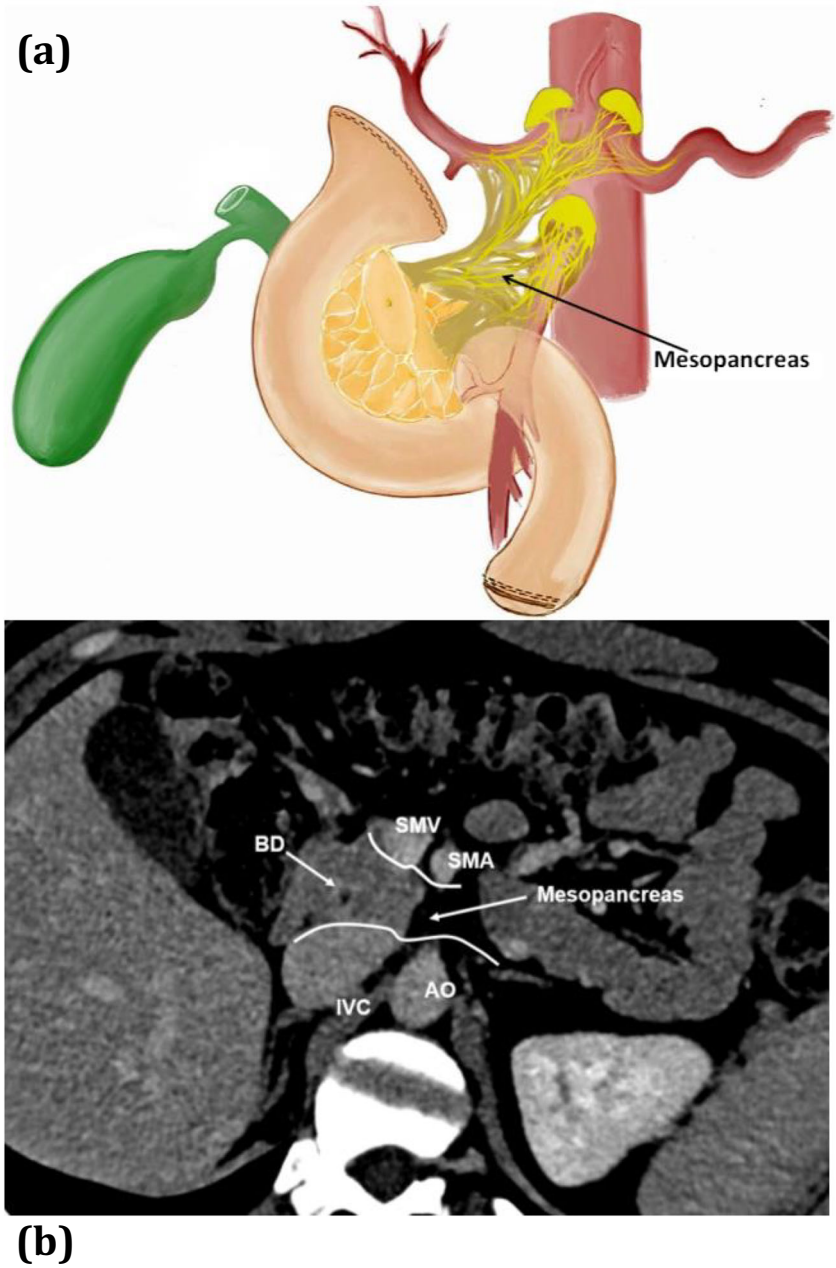

Fig. 1 **a** Anatomic location of the peripancreatic structure defined as the mesopancreas. **b** Computed tomography showing the mesopancreas area including the vascular structures. Legend: BD, common bile duct; IVC, inferior vena cava; AO, aorta; SMA, superior mesenteric artery; SMV, superior mesenteric vein

definition of distant metastatic disease if these lymph nodes are involved in the tumor [22, 30, 39, 48, 49]. Yi et al. [28] morphologically analyzed the relationships among the mesopancreas and the pancreatic head plexus from a clinical perspective and suggested using the term the mesopancreatoduodenum, previously described by Kawabata, instead of the mesopancreas, as the duodenum–pancreas–SMA forms a complex structure related to this region [28, 48, 49].

Some authors questioned the existence of a real mesopancreas because of the lack of a surrounding fascia or fibrous sheath clearly defining its anatomical borders [21, 25, 26, 32, 33]. Xu et al. [37] described the standard TME (extent level I) when all the resected tissue was within the mesopancreas as the routine choice for pancreatic head carcinoma. Extended TME (level II) includes the extension of level I, such as the complete circular dissection of the SMA or CT and the dissection of lymph nodes at station 16. In standard TME, lymph node dissection of the left side of the SMA is not included [22, 37–39, 41, 48–52].

Other definitions have been adopted, and Adham and Singhirunnusorn [50] described the triangle of the mesopancreas where the anatomical boundaries are represented by an inverted triangle in the origin of the CT/hepatic artery and SMA, its base at the posterior face of the SMV and the portal vein (PV). Hackert et al. [53] described the triangle

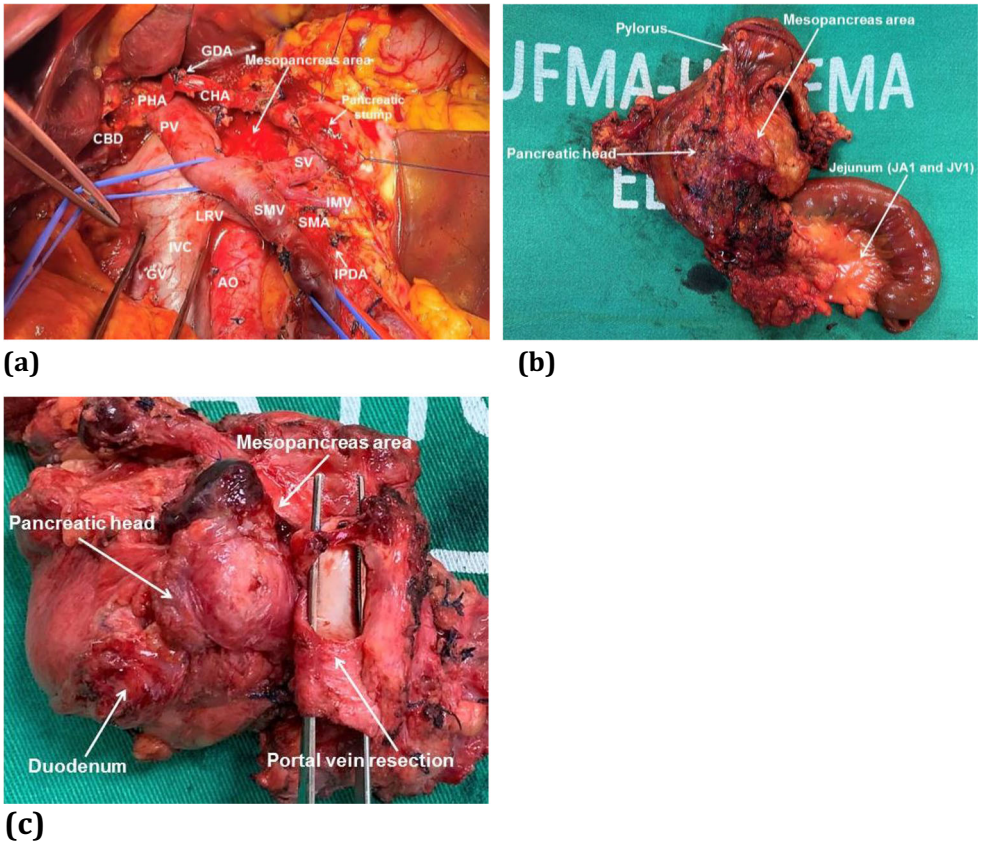

Fig. 2 **a** Anatomy of the region after total mesopancreas excision. **b** Specimen including the mesopancreatic area. **c** Portal vein resection. Legend: GDA, gastroduodenal artery; PHA, proper hepatic artery; CHA, common hepatic artery; BD, common bile duct; PV, portal vein; LRV, left renal vein; IVC, inferior vena cava; GV, gonadal vein; SMV, superior mesenteric vein; SV, splenic vein; IMV, inferior mesenteric vein; SMA, superior mesenteric artery; IPDA, inferior pancreatoduodenal artery; AO, aorta; JA1, first jejunal artery; JV1, first jejunal vein

operation for patients with locally advanced PDAC after neoadjuvant chemotherapy and stable disease to increase resection rates even after arterial encasement (Fig. 4) [50, 53]. Neoadjuvant chemotherapy in patients with pancreatic ductal adenocarcinoma (resectable or borderline resectable) is a standard of care in some centers [53].

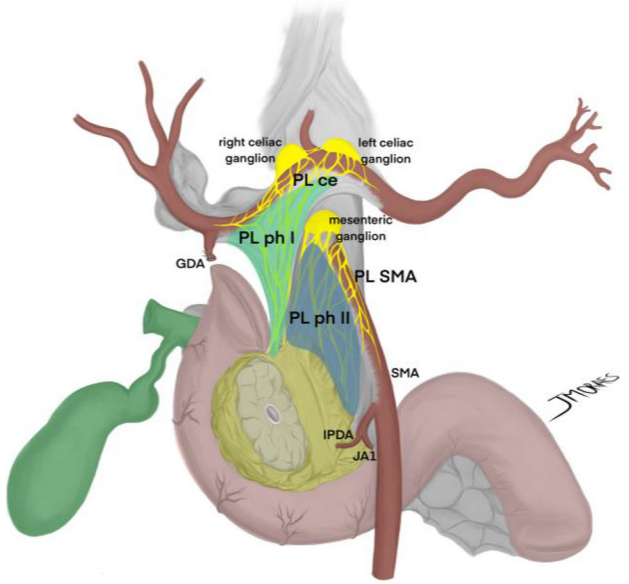

Fig. 3 Anatomic definition of the mesopancreas was performed according to the Japan Cancer Society (pancreatic head plexus) [29]. Legend: PL ph I, pancreatic head plexus 1; PL ph II, pancreatic head plexus 2; PL SMA, superior mesenteric artery plexus; PL ce, celiac plexus; GDA, gastroduodenal artery; SMA, superior mesenteric artery; IPDA, inferior pancreatoduodenal artery; JA1, first jejunal artery

Pathological evaluation

After curative resection for pancreatic ductal adenocarcinoma, negative margin rates are variable, depending on different definitions and techniques for evaluation, mainly related to pathological assessment. The incidence of recurrence after pancreatoduodenectomy ranges from 8.0 to 84% (medial and posterior). The most frequent positive area is the medial/SMA (between 15 and 45%). Incomplete lymphadenectomy and perineural dissection are also considered factors associated with recurrence. The most important cause related to incomplete resection is the inability to clear from the tumor on the left side of the SMA [15–18, 24].

The rate of positive resection margins after pancreatoduodenectomy is high when standardized protocols of pathology are used. The protocol for pathological examination of pancreatoduodenectomy specimens with pancreatic ductal adenocarcinoma should be standardized. The specimen should be reviewed by an experienced surgical pathologist [15–18, 24]. The Royal College of Pathologists specifies that tumor clearance should be given for seven margins designated

Table 2 The history of the mesopancreas

Terms for mesopancreas				
	Author	Term	Year	Ref
1	Gockel	Mesopancreas	2007	42
2	Gaedcke	Mesopancreatic resection	2010	23
3	Agrawal	Does not exist	2010	32
4	Japan Pancreas Society	Pancreatic head plexus	2012	29
5	Adham	Mesopancreas triangle	2012	50
6	Bouassida	Retroportal lamina	2013	33
7	Sharma	Pseudomesopancreas	2016	35
8	Wu	Two mesopancreas (ant and post)	2016	51
9	Kawabata	Mesopancreatoduodenum	2016	49
10	Muro	P-A ligament	2021	30

the anterior and posterior pancreatic margins, medial margin (the SMV groove and superior mesenteric artery), pancreatic transection, gastric (or duodenal) transection, and biliary transection (Fig. 5a, b, and c) [17]. According to Esposito et al. [16], the transection margins in all of the specimens as well as the vascular resection margins should be identified and completely embedded. After that, the specimens should be sliced into 3- to 5-mm-thick slices following an axial plane perpendicular to the duodenal axis and identified in the pancreatic head above and below the ampulla. An R1 margin is defined when the tumor is located ≤ 1 mm from the resection margin. There is a positive correlation between R1 status and the frequency of sampling in the circumferential margins of resection as an independent prognostic factor. After resection of pancreatic ductal adenocarcinoma in the head of the pancreas, the use of a standardized protocol to analyze resection margins has shown that the overall survival is significantly different when comparing negative vs. positive (24.9 months vs. 18.7 months, respectively) [15–17, 24].

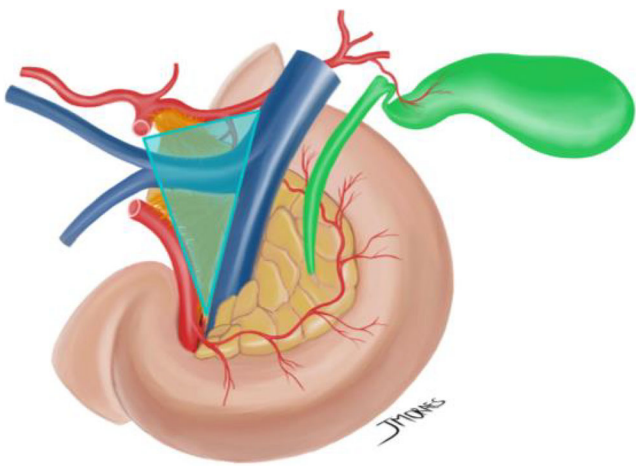

Fig. 4 Posterior view of the "triangle operation" by Hackert et al. [53]

The pancreatoduodenectomy specimens should be sliced serially in a plane perpendicular to the duodenal axis after staining the anterior and posterior circumferential resection margins and the SMV groove surface. The three-dimensional size of the tumor, its relationship to the nearest resection margin, and all principal anatomical structures were recorded (distal bile duct, ampulla, and pancreatic duct). Multiple tissue samples were taken from the tumor deemed closest to the circumferential resection margin. One block each was sampled from the transection margins of the distal bile duct, pancreatic neck, and stomach. R1 resection is defined as a tumor within 1 mm of circumferential or transection, independent of the mode of tumor spread. The origin of the cancer is determined by the site of the tumor bulk and the presence of in situ neoplasia. The SMV groove circumferential resection margin represents the surface of the pancreatic head that faces the SMV and separates the anterior from the posterior circumferential resection. The pancreas is separated from the mesopancreas, and the mesopancreas is prepared for histological and immunohistochemical examinations. [15–17, 24] After pancreatoduodenectomy for pancreatic adenocarcinoma, lymph node involvement is important to predict survival, and the number of lymph nodes required for adequate evaluation according to some studies ranges from 10 to 16, while the UICC suggests a minimum of 12 lymph nodes to provide a full assessment. The median number of examined lymph nodes by Strobel et al. was 24 (range 18–32), and the number of positive lymph nodes was the only independent predictor of survival [2, 9, 13].

Artery first

The concept of mesopancreas and TME led to the increased use of a new approach defined as "artery-first" techniques to ensure "en bloc" resection of lymphatics in the retroperitoneum [54, 55]. The artery-first approach is routinely performed for TME and has become the standard practice in

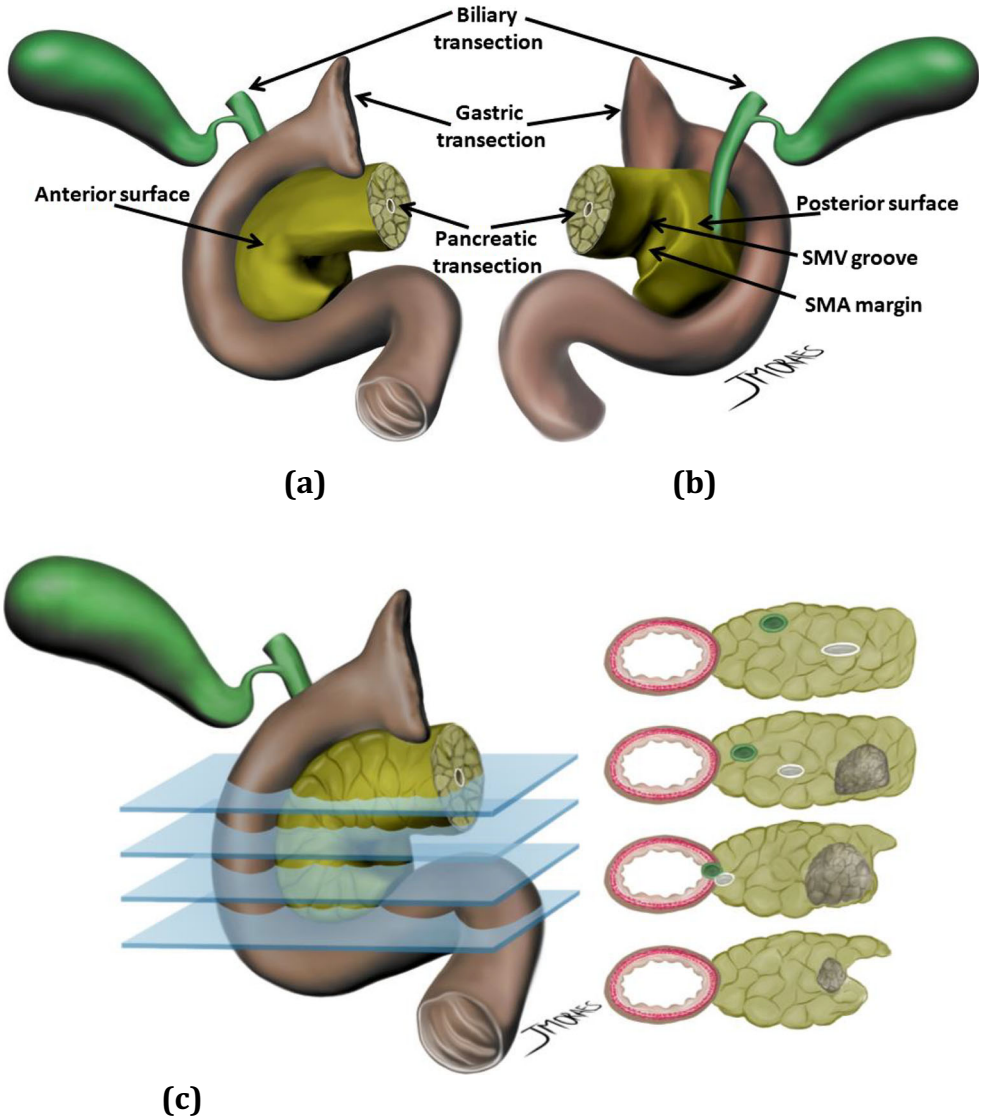

Fig. 5 Margins for pathological evaluation. **a** Anterior and **b** posterior view. The medial margin includes the SMV groove and superior mesenteric artery. **c** Slicing in the axial plane of the pancreatoduodenectomy specimen

many centers. It is defined as early control of the SMA and dissection at the SMA margin, at the initial stage of resection, with the aims of identifying arterial tumor infiltration and assessing resectability, promoting adequate clearance of the right side of the SMA, performing radical lymphadenectomy, and minimizing bleeding by ligation of the IPDA [56–58]. In a review of published techniques, Pandanaboyana et al. [59] identified six different techniques for "artery-first" approaches to the SMA, including the superior approach (lesser sac), anterior approach, right posterior approach (through the retroperitoneum), left posterior approach, right/medial uncinate approach, and mesenteric approach (Fig. 6) [60, 61]. A meta-analysis by Ironside et al. [62] concluded that the artery-first approach may be associated with improved perioperative outcomes and survival compared with standard pancreatoduodenectomy. The posterior approach seems to offer an early selection of patients in terms of SMA infiltration and resectability and allows optimal exposure of arterial abnormalities, including replacement of the right hepatic artery from the SMA. The potential advantages of artery-first approaches are summarized in Table 3 [35]. However, to date, there are no prospective randomized trials evaluating the safety and efficacy of these different approaches for TME during pancreatoduodenectomy versus standard resection [35, 40, 41, 59, 61, 63]. However, there is an ongoing multicenter randomized trial comparing the mesenteric approach versus the conventional approach (MAPLE-PD trial) [64].

Operative technique

Levels of periarterial dissection

Inoue et al. [58, 65, 66] classified the extent of the dissection into four levels. Level 1 dissection does not include adequate lymph node dissection and is not indicated for pancreatic

Table 3 Advantages of the artery-first approach (SHARMA) [35]

1. Resection without breaching the tumor extension plane, thereby minimizing cell spillage
2. Increases curative (R0) resection, decreases local recurrence
3. Complete resection of peripancreatic retroperitoneal tissue around the plexuses
4. Increased lymph nodal clearance
5. Early assessment of non-resectability (SMA involvement), avoiding useless R2 resections
6. Better delineation of SMA and identification of RHA anomalies
7. Easier en bloc resection and reconstruction of SMV-PV by "no touch" technique
8. Reduced need for graft substitutions
9. Reduced operative time and blood loss (early ligation of IPDA/JA1)

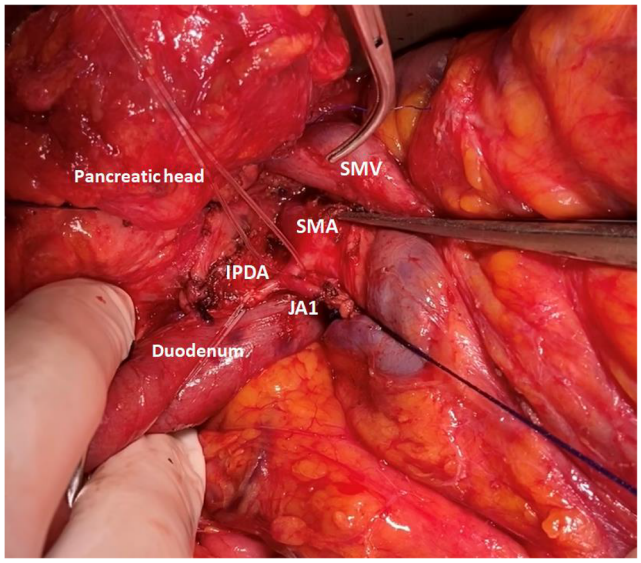

Fig. 7 Anatomic view of the SMA, IPDA, and JA1. Legend: SMV, superior mesenteric vein; SMA, superior mesenteric artery; IPDA, inferior pancreatoduodenal artery; JA1, first jejunal artery

ductal adenocarcinoma. Level 2 dissection is selected for patients with a tumor located far from the SMA and insufficient performance status. The procedure includes the ligation of the IPDA at its root (Fig. 7) and the first jejunal artery (JA1) and the first jejunal vein (JV1), and the corresponding lymph nodes should be included in the mesopancreas specimen. Early ligation of the IPDA is related to minimal bleeding. Lymphadenectomy involves en bloc resection of anterior and posterior pancreatoduodenal nodes (nos. 17a, 17b, 13a, and 13b), hepatoduodenal ligament nodes (nos. 12a, 12b, 12p, and 12c), SMA nodes (nos. 14p and 14d), pyloric nodes (nos. 5 and 6), and nodes along the common hepatic artery (nos. 8a and 8p). Level 3 dissection is selected for suspected invasion into the mesopancreas without abutment of the SMA. The dissection includes the periarterial nerve plexus at the tumor oriented on the right side of the SMA. For tumors abutting the SMA up to 180° or more, extended level 3 up to complete circumferential removal of the periarterial plexus is indicated to secure horizontal margins. Circumferential dissection of the superior mesenteric-portal vein (SMV-PV) axis should be performed routinely. The SMV should be resected even in minimal abutment. Interaortocaval lymphadenectomy is not routinely performed [54–56]. Patients with complete circular (but not semicircular!) removal of the periarterial plexus around the SMA experienced profuse diarrhea. However, this

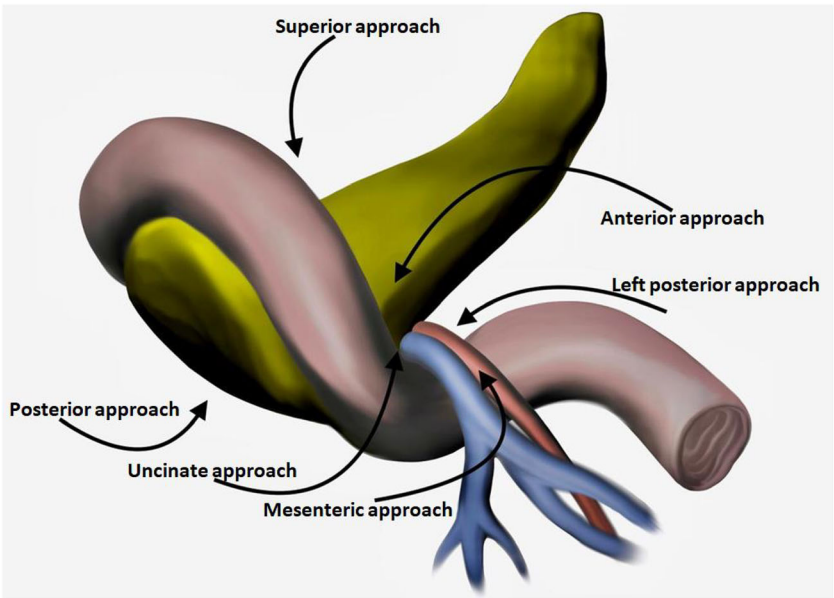

Fig. 6 Six different techniques of the artery-first approach

condition can be treated by medication (including pancreatin and loperamide) and ceases after some weeks [65–67].

Technique step by step

Identification of the posterior edge of the mesopancreas

To perform the right posterior approach, after extensive Kocher maneuver, expose the anterior surface of the inferior vena cava, left renal vein, and right genital vein, from the right side of the patient from the second portion of the duodenum to the left border of the aorta. Expose the space behind the head of the pancreas and PV. The SMA (the root of the mesopancreas) is identified at its origin from the aorta in the angle formed by the inferior vena cava and the left renal vein. Inspect and confirm if the SMA is involved. The SMA is controlled by a vessel loop at its origin. Anatomical variants such as a replaced right hepatic artery originating from the SMA close to its origin should be identified and preserved [37, 41, 50, 51, 59].

The SMA is isolated in the mesentery and skeletonized longitudinally from the origin of the middle colic artery up to its origin from the aorta. All the branches should be identified and ligated, including the first jejunal artery and IPDA (Fig. 7). The thick fiber nerves running down from the pancreatic head to the right celiac ganglion should be dissected along with the ganglion. The CT and common hepatic artery are exposed, and the proper hepatic artery and PV skeletonized. The proximal jejunum can be delivered to the upper quadrant by passing it behind the SMA and SMV [37, 41, 50, 51, 60].

Anterior portion of the mesopancreas

Expose and ligate the right gastroepiploic vein, dissect the anterior face of the transverse colon until the lower edge of the pancreas, and expose the SMV beneath the pancreatic neck. Skeletonize the hepatoduodenal ligament, and expose and ligate the right gastric artery. The gastroduodenal artery (GDA) is divided and ligated, and the root of the common hepatic artery and abdominal aorta is exposed. The antrum is divided 2 cm above the pylorus, and the pancreatic neck is divided to the left of the portomesenteric vein. Thus, the anterior portion of the mesopancreas is completely divided. The firm and well-vascularized mesopancreas is identified on the back surface of the pancreatic head. The pancreatic head and uncinate process are still connected to the posterior portion of the mesopancreas [37, 41, 58, 65, 66].

Posterior portion of the mesopancreas

The posterior portion of the mesopancreas becomes visible after exposure to the left edge of the inferior mesenteric vein (IMV). The lower margin of the posterior portion of the mesopancreas is at the level of the inferior mesenteric artery. The dissection of connective tissues around the SMA continues upwards until 2 cm above the root of CT, which is defined as the upper limit of resection of the posterior portion of the mesopancreas [24, 37, 41, 58, 65, 66]. The left posterior border for the resection of mesopancreas is the left genital vein, and the IMV is the left anterior border. The anterior and posterior portions of the mesopancreas are divided after transection of the jejunum from the ligament of Treitz. The SMA on the left side of the SMV is exposed, and dissection includes the first branch of the jejunum, lymphatics, and nerve tissues around the SMA until its root. Then, en bloc resection of the pancreas, duodenum, and anterior and posterior sections of the mesopancreas is completed. While arterial infiltration is ruled out by an artery-first approach, venous resection may frequently be necessary for up to a third of resections for cancer. The described technique results in complete mobilization of the tumor with the infiltrated portovenous axis, which allows safe venous resection as the last step of resection with direct reanastomosis [24, 37, 41, 50, 51, 60].

Conclusions

The mesopancreas is a vascularized structure composed of fatty tissue, the nerve plexus, and lymph nodes located in the pancreatic retroperitoneal region between the pancreatic head and superior mesenteric and celiac vessels. This structure is considered the most frequent site of a positive resection margin, although the name is not universally accepted. The TME was described to facilitate and to increase the surgical radicality (R0 rates) of resection thereby to reduce locoregional recurrence and to improve postresection survival in patients with pancreatic head adenocarcinoma. Artery-first approaches are important to achieve “en bloc” resection in the retroperitoneum and have become a standard practice in pancreatic cancer surgery worldwide. Standard operative techniques and adequate pathologic evaluation are defined as the best practice in this new era for the treatment of patients with pancreatic ductal adenocarcinoma in the head of the pancreas.

References

1. Neoptolemos JP, Stocken DD, Friess H, Bassi C, Dunn JA, Hickey H, Beger H, Fernandez-Cruz L, Dervenis C, Lacaine F, Falconi M, Pederzoli P, Pap A, Spooner D, Kerr DJ, Büchler MW (2004) A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. N Engl J Med 350:1200–1210

2. Strobel O, Neoptolemos J, Jäger D, Büchler MW (2019) Optimizing the outcomes of pancreatic cancer surgery. Nat Rev Clin Oncol 16:11–26
3. Neoptolemos JP, Palmer DH, Ghaneh P, Psarelli EE, Valle JW, Halloran CM, Faluyi O, O'Reilly DA et al (2017) Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. Lancet 389: 1011–1024
4. Conroy T, Hammel P, Hebbar M, Ben Abdelghani M, Wei AC, Raoul J-L, Choné L, Francois E, Artru P, Biagi JJ, Lecomte T, Assenat E, Faroux R, Ychou M, Volet J, Sauvanet A, Breysacher G, di Fiore F, Cripps C, Kavan P, Texereau P, Bouhier-Leporrier K, Khemissa-Akouz F, Legoux JL, Juzyna B, Gourgou S, O'Callaghan CJ, Jouffroy-Zeller C, Rat P, Malka D, Castan F, Bachet JB (2018) FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. N Engl J Med 379:2395–2406
5. Jones RP, Psarelli EE, Jackson R, Ghaneh P, Halloran CM, Palmer DH et al (2019) Patterns of recurrence after resection of pancreatic ductal adenocarcinoma. A secondary analysis of the ESPAC-4 randomized adjuvant chemotherapy trial. JAMA Surg 154(11):1038–1048
6. Versteijne E, Suker M, Groothuis K, Akkermans-Vogelaar JM, Besselink MG, Bonsing BA, Buijsen J, Busch OR, Creemers GJM, van Dam RM, Eskens FALM, Festen S, de Groot JWB, Groot Koerkamp B, de Hingh IH, Homs MYV, van Hooft JE, Kerver ED, Luelmo SAC, Neelis KJ, Nuyttens J, Paardekooper GMRM, Patijn GA, van der Sangen MJC, de Vos-Geelen J, Wilmink JW, Zwinderman AH, Punt CJ, van Eijck CH, van Tienhoven G, for the Dutch Pancreatic Cancer Group (2020) Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer: results of the Dutch randomized phase III PREOPANC trial. J Clin Oncol 38: 1763–1773
7. Kalisvaart M, Broadhurst D, Marcon F, Pande R, Schlegel A, Sutcliffe R, Marudanayagam R, Mirza D, Chatzizacharias N, Abradelo M, Muiesan P, Isaac J, Ma YT, McConville C, Roberts K (2020) Recurrence patterns of pancreatic cancer after pancreatoduodenectomy: systematic review and a single-centre retrospective study. HPB 22:1240–1249
8. Delpero JR, Bachellier P, Regenet N, Le Treut YP, Paye F, Carrere N et al (2014) Pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: a French multicentre prospective evaluation of resection margins in 150 evaluable specimens. HPB (Oxford) 16(1): 20–33
9. Strobel O, Hinz U, Gluth A, Hank T, Hackert T, Bergmann F, Werner J, Büchler MW (2015) Pancreatic adenocarcinoma: number of positive nodes allows to distinguish several N categories. Ann Surg 26:961–969
10. Tarantino I, Warschkow R, Hackert T, Schmied BM, Büchler MW, Strobel O, Ulrich A (2017) Staging of pancreatic cancer based on the number of positive lymph nodes. Br J Surg 104:608–618
11. Niesen W, Hank T, Büchler M, Strobel O (2019) Local radicality and survival outcome of pancreatic cancer surgery. Ann Gastroenterol Surg 3:464–475
12. Strobel O, Büchler MW (2020) Chirurgie des Pankreaskarzinoms: Techniken zur vermeidung des lokalrezidivs. Chirurg 91(8):615–627
13. Strobel O, Hank T, Hinz U, Bergmann F, Schneider L, Springfeld C, Jäger D, Schirmacher P, Hackert T, Büchler MW (2016) Pancreatic cancer surgery: the new R-status counts. Ann Surg 265:565–573
14. Hank T, Hinz U, Tarantino I, Kaiser J, Niesen W, Bergmann F, Hackert T, Büchler MW, Strobel O (2018) Validation of at least 1 mm as cut-off for resection margins for pancreatic adenocarcinoma of the body and tail. Br J Surg 105:1171–1181
15. Verbeke CS, Leitch D, Menon KV, McMahon MJ, Guillou PJ, Anthoney A (2006) Redefining the R1 resection in pancreatic cancer. Br J Surg 93:1232–1237
16. Esposito I, Kleeff J, Berman F et al (2008) Most pancreatic cancer resections are R1 resections. Ann Surg Oncol 15:1651–1660
17. Campbell F, Cairns A, Duthie F, Feakins R (2019) Dataset for histopathological reporting of carcinomas of the pancreas, ampulla of Vater and common bile duct. The Royal College of Pathologists. www.rcpath.org
18. Westgaard A, Tafjord S, Farstad IN, Cvancarova M, , Eide TJ, Mathisen O, et al. Resectable adenocarcinomas in the pancreatic head: the retroperitoneal resection margin is an independent prognostic factor. BMC Cancer 2008; 8:1-10.
19. Tanaka M, Mihaljevic AL, Probst P, Heckler M, Klaiber U, Heger U, Büchler MW, Hackert T (2019) Meta-analysis of recurrence pattern after resection for pancreatic cancer. BJS 106:1590–1601
20. Ghaneh P, Kleeff J, Halloran CM, Raraty M, Jackson R, Melling J et al (2017) The impact of positive resection margins on survival and recurrence following resection and adjuvant chemotherapy for pancreatic ductal adenocarcinoma. Ann Surg 269:520–529
21. Chowdappa R, Challa VR (2015) Mesopancreas in pancreatic cancer: where do we stand - review of literature. Indian J Surg Oncol 6(1):69–74
22. Popescu I, Dumitrascu T (2011) Total meso-pancreas excision: key point of resection in pancreatic head adenocarcinoma. Hepatogastroenterology. 58:202–207
23. Gaedcke J, Gunawan B, Grade M, Szoke R, Liersch T, Becker H et al (2010) The mesopancreas is the primary site for R1 resection in pancreatic head cancer: relevance for clinical trials. Langenbeck's Arch Surg 395(4):451–458
24. Nagakawa Y, Yi SQ, Takishita C, Sahara Y, Osakabe H, Kiya Y, Yamaguchi H, Miwa Y, Sato I, Tsuchida A (2020) Precise anatomical resection based on structures of nerve and fibrous tissue around the superior mesenteric artery for mesopancreas dissection in pancreaticoduodenectomy for pancreatic cancer. J Hepatobiliary Pancreat Sci 27:342–351
25. Peparini N, Chirletti P (2013) Mesopancreas: a boundless structure, namely R1 risk in pancreaticoduodenectomy for pancreatic head carcinoma. Eur J Surg Oncol 39:1303–1308
26. Peparini N (2015) Mesopancreas: a boundless structure, namely the rationale for dissection of the paraaortic area in pancreaticoduodenectomy for pancreatic head carcinoma. World J Gastroenterol 21:2865–2870
27. Peparini N (2016) Para-aortic dissection in pancreaticoduodenectomy with mesopancreas excision for pancreatic head carcinoma: not only an n staging matter. J Gastrointest Surg 20:1080–1081
28. Yi SQ, Nagakawa Y, Ren K, Dai YD, Zhang M, Chen JF et al (2020) The mesopancreas and pancreatic head plexus: morphological, developmental, and clinical perspectives. Surg Radiol Anat 42: 1501–1508
29. Japan Pancreas Society (2017) Classification of pancreatic carcinoma, 4th edn. Kanehara & Co., Ltd., Tokyo
30. Muro S, Sirirat W, Ban D, Nagakawa Y, Akita K (2021) What comprises the plate-like structure between the pancreatic head and the celiac trunk and superior mesenteric artery? A proposal for the term "P–A ligament" based on anatomical findings. Anat Sci Int 96(3):370–377

31. Jamieson NB, Foulis AK, Oien KA, Going JJ, Glen P, Dickson EJ, Imrie CW, McKay CJ, Carter R (2010) Positive mobilization margins alone do not influence survival following pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. Ann Surg 251(6):1003–1010
32. Agrawal MK, Thakur DS, Somashekar U, Chandrakar SK, Sharma D (2010) Mesopancreas: myth or reality? JOP 11(3):230–233
33. Bouassida M, Mighri MM, Chtourou MF, Sassi S, Touinsi H, Hajji H, Sassi S (2013) Retroportal lamina or mesopancreas? Lessons learned by anatomical and histological study of thirty three cadaveric dissections. Int J Surg 11:834–836
34. Coffey JC, O'Leary DP (2016) The mesentery: structure, function, and role in disease. Lancet Gastroenterol Hepatol 1:238–247
35. Sharma D, Isaji S (2016) Mesopancreas is a misnomer: time to correct the nomenclature. J Hepatobiliary Pancreat Sci 23:745–749
36. Crippa S, Giannone F, Lena MS, Belfiori G, Partelli S, Tamburrino D et al (2020) R status is a relevant prognostic factor for recurrence and survival after pancreatic head resection for ductal adenocarcinoma. Ann Surg Oncol. https://doi.org/10.1245/s10434-020-09467-6
37. Xu J, Tian X, Chen Y, Ma Y, Liu C, Tian L, Wang J, Dong J, Cui D, Wang Y, Zhang W, Yang Y (2017) Total mesopancreas excision for the treatment of pancreatic head cancer. J Cancer 8:3575–3584
38. Quero G, Fiorillo C, Menghi R, Cina C, Galiandro F, Longo F, Sofo F, Rosa F, Tortorelli AP, Giustiniani MC, Inzani F, Alfieri S (2020) Total mesopancreas excision for periampullary malignancy: a single-center propensity score-matched comparison of long-term outcomes. Langenbeck's Arch Surg 405:303–312
39. Kawabata Y, Tanaka T, Nishi T, Monma H, Yano S, Tajima Y (2012) Appraisal of a total meso-pancreatoduodenum excision with pancreaticoduodenectomy for pancreatic head carcinoma. Eur J Surg Oncol 38:574–579
40. Dumitrascu T, David L, Popescu I (2010) Posterior versus standard approach in pancreatoduodenectomy: a case match study. Langenbeck's Arch Surg 395:677–684
41. Aimoto T, Mizutani S, Kawano Y, Matsushita A, Yamashita N, Suzuki H, Uchida E (2013) Left posterior approach pancreaticoduodenectomy with total mesopancreas excision and circumferential lymphadenectomy around the superior mesenteric artery for pancreatic head carcinoma. J Nippon Med Sch 80:438–445
42. Gockel I, Domeyer M, Wolloscheck T, Konerding MA, Junginger T (2007) Resection of the mesopancreas (RMP): a new surgical classification of a known anatomical space. World J Surg Oncol 5:44
43. Kim KS, Kwon J, Kim K, Chie EK (2017) Impact of resection margin distance on survival of pancreatic cancer: a systematic review and meta-analysis. Cancer Res Treat 49:824–833
44. Tummers WS, Groen JV, Sibinga Mulder BG, Farina-Sarasqueta A, Morreau J, Putter H, van de Velde CJ, Vahrmeijer AL, Bonsing BA, Mieog JS, Swijnenburg RJ (2019) Impact of resection margin status on recurrence and survival in pancreatic cancer surgery. Br J Surg 106:1055–1065
45. Demir IE, Jager C, Schlitter AM, Konukiewitz B, Stecher L, Schorn S et al (2018) R0 Versus R1 resection matters after pancreaticoduodenectomy, and less after distal or total pancreatectomy for pancreatic câncer. Ann Surg 268:1058–1068
46. Delpero JR, Jeune F, Bachellier P, Regenet N, Le Treut YP, Paye F et al (2017) Prognostic value of resection margin involvement after pancreaticoduodenectomy for ductal adenocarcinoma Updates from a French prospective multicenter study. Ann Surg 266:787–796
47. Ramia JM, De-la-Plaza R, Manuel-Vazquez A, Lopez-Marcano A, Morales R (2018) Systematic review of the mesopancreas: concept and clinical implications. Clin Transl Oncol 20:1385–1391
48. Kawabata Y, Tanaka T, Ishikawa N, Hayashi H, Tajima Y (2016) Modified total meso-pancreatoduodenum excision with pancreaticoduodenectomy as a mesopancreatic plane surgery in borderline resectable pancreatic cancer. Eur J Surg Oncol 42:698–705
49. Kawabata Y, Hayashi H, Ishikawa N, Tajima Y (2016) Total mesopancreatoduodenum excision with pancreaticoduodenectomy in lower biliary tract cancer. Langenbeck's Arch Surg 401:463–469
50. Adham M, Singhirunnusorn J (2012) Surgical technique and results of total mesopancreas excision (TMpE) in pancreatic tumors. Eur J Surg Oncol 38(4):340–345
51. Wu W, Wang X, Wu X, Li M, Weng H, Cao Y et al (2016) Total mesopancreas excision for pancreatic head cancer: analysis of 120 cases. Chin J Cancer Res 28(4):423–428
52. Azagra JS, Rosso E, Pascotto B, de Blasi V, Henrard A, González LG (2021) Real robotic total mesopancreas excision (TMpE) assisted by hanging manoeuver (HM): standardised technique. Int J Med Robot. https://doi.org/10.1002/rcs.2259
53. Hackert T, Strobel O, Michalski CW, Mihaljevic AL, Mehrabi A, Müller-Stich B, Berchtold C, Ulrich A, Büchler MW (2017) The TRIANGLE operation – radical surgery after neoadjuvant treatment for advanced pancreatic cancer: a single arm observational study. HPB 19:1001–1007
54. Weitz J, Rahbari N, Koch M, Büchler MW (2010) The "artery first" approach for resection of pancreatic head cancer. J Am Coll Surg 210:e1–e4
55. Moldovan SC, Moldovan AM, Dumitraæcu T, Andrei S, Popescu I (2012) The advantages of retropancreatic vascular dissection for pancreatic head cancer with portal/superior mesenteric vein invasion: posterior approach pancreatico-duodenectomy technique and the mesopancreas theory. Chirurgia (Bucur) 107(5):571–578
56. Chandrasegaram MD, Goldstein D, Simes J, Gebski V, Kench JG, Gill AJ, Samra JS, Merrett ND, Richardson AJ, Barbour AP (2015) Meta-analysis of radical resection rates and margin assessment in pancreatic cancer. BJS 102:1459–1472
57. Sabater L, Esteban Cugat E, Serrablo A, Suarez-Artacho G, Diez-Valladares L, Santoyo-Santoyo J et al (2019) Does the artery-first approach improve the rate of R0 resection in pancreatoduodenectomy? A Multicenter, Randomized, Controlled Trial. Ann Surg 270:738–746
58. Inoue Y, Saiura A, Yoshioka R, Ono Y, Takahashi M, Arita J, Takahashi Y, Koga R (2015) Pancreatoduodenectomy with systematic mesopancreas dissection using a supracolic anterior artery-first approach. Ann Surg 262(6):1092–1101
59. Pandanaboyana S, Takaori K, Govil S, Shrikhande SV, Windsor JA (2012) Artery-first' approaches to pancreatoduodenectomy. Br J Surg 99:1027–1035
60. Georgescu S, Ursulescu C, Grigorean VT et al (2014) Hind right approach pancreaticoduodenectomy: from skill to indications. Gastroenterol Res Pract 2014:210835
61. Nakao A (2016) The mesenteric approach in pancreatoduodenectomy. Dig Surg 33:308–313
62. Ironside N, Barreto SG, Loveday B, Shrikhande SV, Windsor JA, Pandanaboyana S (2018) Meta-analysis of an artery-first approach versus standard pancreatoduodenectomy on perioperative outcomes and survival. Br J Surg 105:628–636
63. Hirono S, Kawai M, Okada KI, Miyazawa M, Shimizu A, Kitahata Y, Ueno M, Shimokawa T, Nakao A, Yamaue H (2017) Mesenteric approach during pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. Ann Gastroenterol Surg 1:208–218

64. Hirono S, Kawai M, Okada KI, Fujii T, Sho M, Satoi S et al (2018) MAPLE-PD trial (Mesenteric Approach vs. Conventional Approach for Pancreatic Cancer during Pancreaticoduodenectomy): study protocol for a multicenter randomized controlled trial of 354 patients with pancreatic ductal adenocarcinoma. Trials 19(1):613. https://doi.org/10.1186/s13063-018-3002-z
65. Inoue Y, Saiura A, Tanaka M, Matsumura M, Takeda Y, Mise Y, Ishizawa T, Takahashi Y (2016) Technical details of an anterior approach to the superior mesenteric artery during pancreaticoduodenectomy. J Gastrointest Surg 20:1769–1777
66. Inoue Y, Saiura A, Oba A, Kawakatsu S, Ono Y, Sato T, Mise Y, Ishizawa T, Takahashi Y, Ito H (2019) Optimal extent of superior mesenteric artery dissection during pancreaticoduodenectomy for pancreatic cancer: balancing surgical and oncological safety. J Gastrointest Surg 23:1373–1383
67. Diener MK, Mihaljevic AL, Strobel O, Loos M, Schmidt T, Schneider M, Berchtold C, Mehrabi A, Müller-Stich BP, Jiang K, Neoptolemos JP, Hackert T, Miao Y, Büchler MW (2021) Periarterial divestment in pancreatic cancer surgery. Surgery 169: 1019–1025