

Mesopancreas in Pancreatic Cancer: Where do We Stand – Review of Literature

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Abstract Pancreatic cancer is associated with poor prognosis and surgery remains the main modality of treatment. Negative resection margin is an important prognostic factor for survival. Retropancreatic margin or the medial margin is the most common site of positive resection margin. Mesopancreas was proposed in analogy with mesorectum, which is considered as a fusion fascia formed embryologically during the development of pancreas. This mesopancreas lies posterior to the pancreas and contains pancreaticoduodenal vessels, lymphatics, nerve plexus and loose areolar tissue. Various technical modifications were proposed for better dissection of mesopancreas like posterior approach and artery first approach. There is an increased rate of R0 resection by these technical modifications but whether this will turn to increase in survival rates is yet to be established.

Keywords Mesopancreas · Total mesopancreatic excision · Retroportal lamina · Retropancreatic lamina

Introduction

Pancreatic cancer is one of the rare gastrointestinal cancer with worst prognosis and the age adjusted incidence rate is 1/1,00,000 population [1]. Complete surgical resection with R0 negative margins leads to 5 year survival rate of 5 to 20 %. Various studies showed the rate of noncurative resections of 15–35 % [2–5], but with modified pathological examination

(R1/R2) revealed the rate of R1 resection was higher ranging from 76–85 % [6–9]. Also autopsy studies in patients who died with pancreatic cancer showed 100 % local recurrence. Even patients with R0 resection had local recurrence which lead surgeons to attempt more radical approaches like regional pancreatectomies and extended lymphadenectomies. Fortner proposed regional pancreatectomies which initially showed promising results but follow up long term studies showed poor results [10]. Whether this discrepancy was caused by incomplete lymphnode dissection, perineural dissection and improper pathological examination was not yet known. Perineural invasion was detected in 77 % of specimens of resected pancreatic cancers [11].

Total mesorectal excision introduced by Heald's in treatment of rectal cancer lead to the path in applying the anatomical knowledge to help in better surgical resection. By dissecting in a plane between the fascia propria and presacral fascia, mesorectum was excised and had decreased the risk of local recurrence [12]. This concept of applied embryology and anatomy was introduced to various organs to increase rate of negative margins of resection. Mesopancreas, mesogastrum, mesoesophagus, mesohepatectomy and mesometria were described based on postulates in analogy with mesorectum [13–17]. Whether these descriptions and further refinement in surgical technique based on these postulates will give better results or not is not yet known.

Embryology

The pancreas develops from 2 buds one in the ventral mesogastrum which is the ventral bud and the other in the dorsal mesogastrum which is called as dorsal bud on the lateral aspect of duodenum. They receive blood supply from the gastroduodenal artery a branch of common hepatic artery, inferior pancreaticoduodenal artery a branch of Superior mesenteric artery (SMA) and splenic artery. The ventral bud

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rotates and fuses with dorsal bud to form the pancreas (Fig. 1). The duct of dorsal bud forms the accessory duct or duct of santorini. Duct of wirsung is formed proximally by the ventral pancreatic duct and the distally by the dorsal pancreatic duct (Fig. 2) [18].

Anatomy

Pancreas is related anatomically with the duodenum, kidneys and major vessels. Kidneys are covered by Gerotas fascia which constitutes anterior layer called as fascia of Toldt and a posterior lamina called as fascia of Zuckerkandl. The posterior lamina unites with anterior lamina close to the colon to form lateroconal fascia. Medially the extent of anterior lamina is doubtful with varying reports. The sheet of tissue behind the duodenum and pancreas formed by the fusion of embryological mesoduodenum with posterior abdominal wall after rotation lead to the formation of retroduodenopancreatic fascia of Treitz and was first described in 1853. The fusion fascia of the body and tail of pancreas due to fixation of dorsal wall of lesser sac was called as Toldt's fascia (Fig. 2). Pancreaticoduodenal arcades of arteries, veins and nerves are situated on the fusion fascia of treitz. This fascia also covers the extrapancreatic nerve plexus, superior mesenteric artery and portal vein [19]. Pancreatic cancer of head hence follows these arteries, veins, nerves and spread horizontally towards the SMA or celiac axis

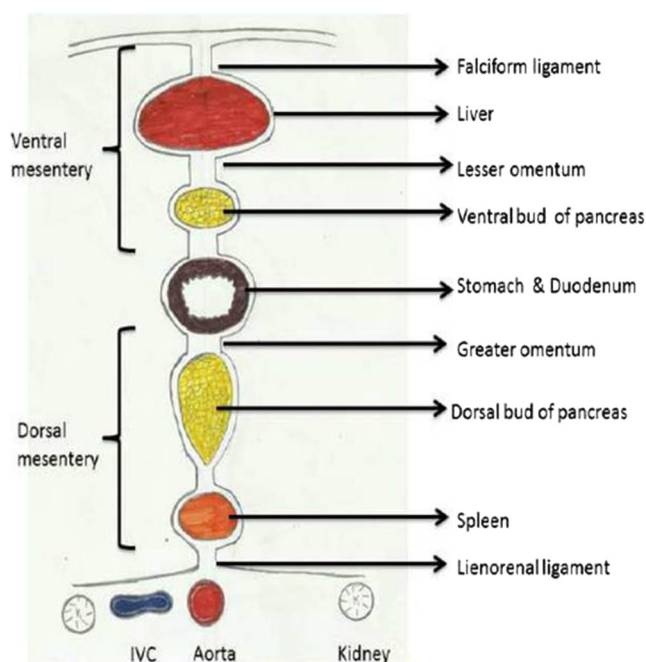


Fig. 1 Longitudinal section showing the dorsal and the ventral mesentery with development of liver and ventral bud of pancreas in ventral mesentery and dorsal bud of pancreas and spleen in dorsal mesentery

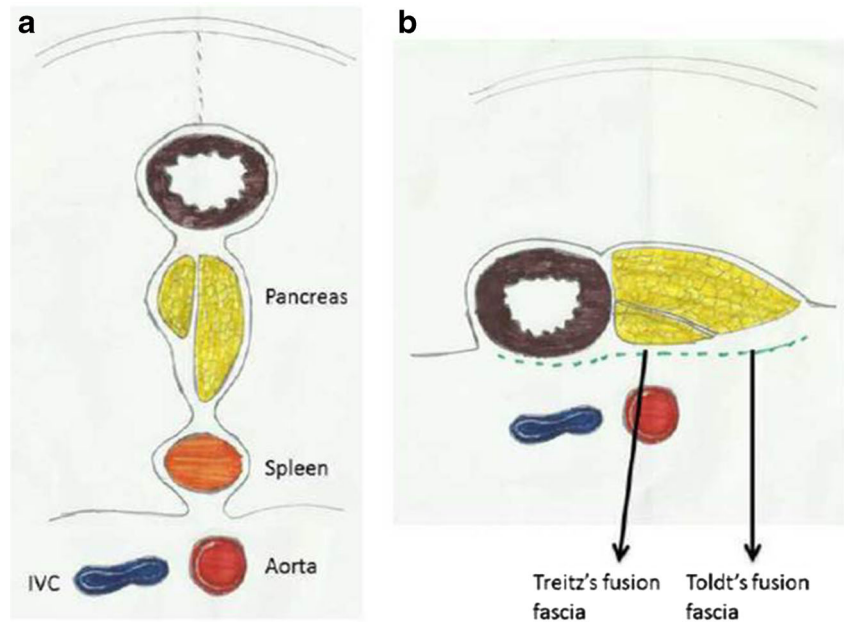
rather than posteriorly towards inferior vena cava (IVC). This soft tissue between the pancreatic head and SMA includes nerves, vessels, lymphatics and nodes which is called as the mesopancreas [13] (Fig. 3). But a cadaveric study failed to show a fascial covering over these structures [20]. The previous terminology used for mesopancreas include retroportal lamina or retroportal pancreas [21]. Some authors proposed that a total mesopancreatic excision for better achievement of curative (R0) resection [22].

Review of Literature

A literature search on “mesopancreas” and “retroportal lamina” in Pubmed on July 2008 revealed 15 published articles of which 8 articles are reviewed which are related to the present subject (Table 1). Pancreaticoduodenectomy procedure was first published by Codvilla in 1898 [23]. Kausch and Whipple popularized the procedure of pancreaticoduodenectomy [24, 25]. Later more than 70 technical modifications have been described in literature most of them on the techniques of reconstruction [26]. Though the postoperative mortality had decreased from 20 % to 5 % in most of the centers, the 5 year survival varied from 5 to 20 % [22, 27]. R0 resection varied from 20 % to 90 % depending on the method of histopathological examination [28–32]. The most commonly involved margins were the medial margins (60–80 %) and the posterior margins [22]. Hence there is a need to achieve curative intent surgery i.e., R0 resection. Jamieson et al. studied the microscopic positive margin and the prognostic influence. Resection margins were classified as transection margin and mobilization margins [33]. Transection margins includes pancreatic transection and mesopancreas margin close to mesenteric vessels whereas the mobilization margins includes adjacent organs surfaces separated based on embryological development planned and includes anterior, posterior and lateral duodenal margins. These results showed significant poor prognosis for patients with R1 transection margin than for R1 mobilization margins. How much margin is required to decrease the incidence of local recurrence is not yet clear but 1 mm margin may be considered as a potentially curative resection [22].

The term mesopancreas was first proposed by Gockel et al. in the year 2007 in analogy to total mesorectal excision in rectal cancer [13]. They emphasized the need of new surgical classification involving mesopancreas. It can be considered as an anatomical space bounded anteriorly by the the posterior surface of the pancreatic neck, posteriorly by the pancreaticoduodenal coalescence fascia, medially by the mesenteric vessels with nerves, lymphatics and vessels as its contents. It is mandatory to excise the total mesopancreas

Fig. 2 **a** Ventral pancreas rotates in anticlockwise direction along with rotation of stomach and duodenum to get fused with dorsal pancreas. **b** Later pancreas and duodenum becomes retroperitoneal after fusion of dorsal mesentery and posterior peritoneal covering. This fusion fascia formed is called as Treitz's fascia for pancreatic head and as Toldt's fascia for body and tail of pancreas



during the surgery for pancreatic head adenocarcinoma which may increase R0 resections. A cadaveric study by Agarwal et al. found no fibrous sheath or fascia around the structures present in the area of mesopancreas [20].

Technical Modifications Proposed for Better Resection of Mesopancreas

There are various modifications proposed for better resection of the mesopancreas. Pessaux et al. proposed the “hanging maneuver” to achieve negative retroperitoneal margin [34]. Various other modifications like “posterior approach” and “artery first” were proposed because of the high propensity of positivity of the medial margin.

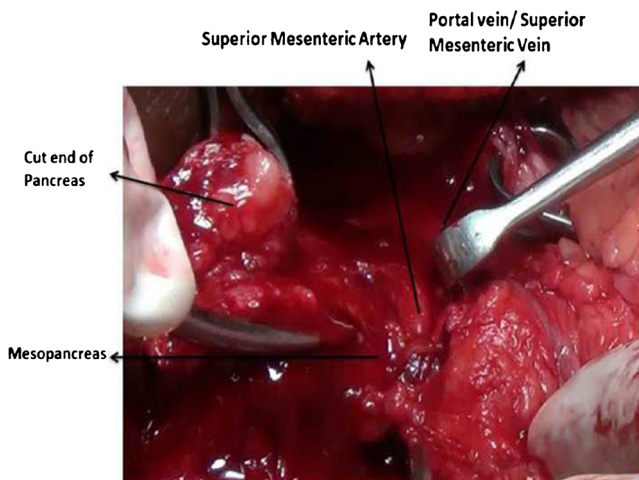


Fig. 3 Intraoperative image showing Superior mesenteric vein/portal vein, Superior mesenteric artery and mesopancreas

Posterior and artery first approach proposed a direct dissection on SMA at its origin from aorta to decrease positive margin at the medial transection side. Weitz et al. proposed a modified artery first approach wherein the artery is identified below the pancreas on the left side of mesentery and dissection is carried upwards and helps in better dissection over the posterior part of artery [35]. Dissection on both sides of artery is not advocated because of increased risk of complications (eg: diarrhea). Horiguchi et al. proposed a mesenteric approach which is similar to the artery first approach [36]. Machado et al. proposed an alternative approach for patients who need portal vein resection which is similar to the Hiedelberg technique [37]. Hirota et al. proposed a “no-touch” technique wherein vessels are dissection first before mobilizing the tumor for pancreatic head tumors. This was proposed mainly for patients undergoing en-bloc superior mesenteric and portal vein resection [28]. Kawabata et al. described a total meso-pancreatoduodenum excision (tMPDe) in which a circumferential lymphadenectomy around the SMA together with mesopancreas was performed. Those patients who underwent tMPDE had no locoregional recurrence and there was increased number of lymph nodes dissected in this group compared with standard PD [38]. “The mesopancreas triangle” was proposed by Adham et al., with its anatomical boundaries formed by the posterior surface of the SMV and PV, a summit over the anterior surface of the aorta between Celiac trunk (CT) and SMA origin, and is limited on either side by the right semi-circumferences of the CT and SMA plexus (Fig. 4) [39]. An aberrant or replaced right hepatic artery is found in 15–20 % of people which can be better identified and dissected by the posterior

Table 1 Review of literature on mesopancreas and its importance

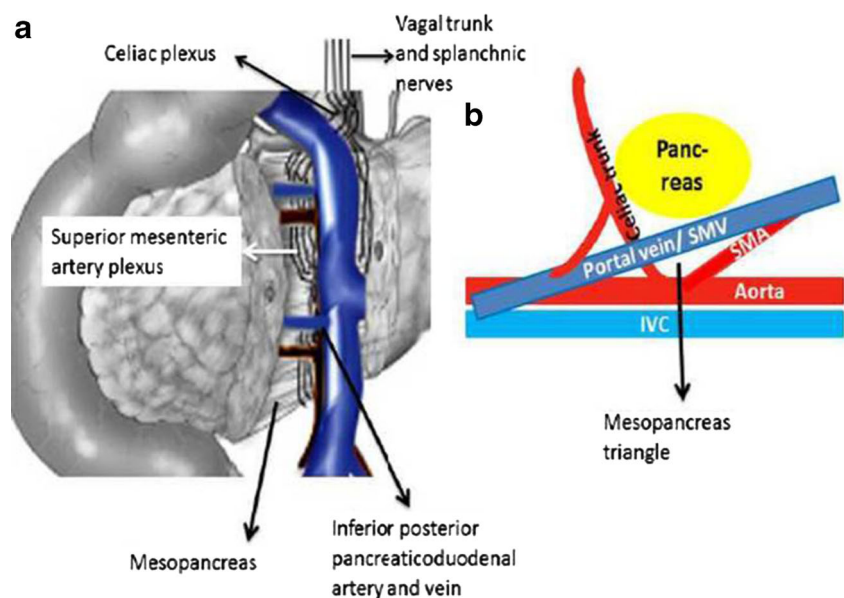
Author(year)	Number of patients/ corposes	R0 resection	Survival	Comments
Gockel et al. (2007) [13]	5 (corposes)	–	–	Defined mesopancreas as a perineural lymphatic layer
Pessaux et al. (2009) [34]	20 Patients	94 %	–	“Hanging maneuver” helps to achieve negative retroperitoneal margin
Agrawal et al. (2010) [20]	20 (corposes)	–	–	No fibrous sheath or fascia around the structures described as mesopancreas
Gaedcke et al. (2010)[41]	65	–	–	66.6 % had R1 resection was at mesopancreas margin, proposed standard histopathological examination of pancreatic head cancer specimens
Dumitrascu et al. (2010)[42]	21 – posterior approach vs 21- standard approach	No significant difference	No significant difference	Better delineation of vessel invasion, arterial abnormalities and less bleeding with no – touch technique and early ligation of vessels
Moldovan et al. (2012)[21]	16	11	–	Posterior approach facilitates superior mesenteric/portal vein resection
Kawabata et al. (2012)[38]	25- standard PD vs 14- tMPDe PD	60 % Vs 93 %	1 year survival - 47.8 % (sPD) Vs 76.2 % (tMPDe) Locoregional recurrence 3 Vs 0	Safe and more radical procedure with tMPDe
Adham et al. (2012)[39]	52	80.7 %	–	Posterior approach increases R0 resection

tMPDe total mesopancreaticoduodenum excision, sPD standard pancreaticoduodenectomy, PD Pancreaticoduodenectomy

approach [40]. A recent article by Sanjay.P et al., described 6 different approaches “artery-first”- posterior (through the retroperitoneum), medial uncinata, inferior infracolic (mesenteric), left posterior, superior(lesser sac) and the inferior supracolic(anterior). In the uncinata approach, the inferior pancreaticoduodenal vessels are ligated early and the aberrant right hepatic artery is identified lately, whereas in the posterior approach, the replaced right hepatic

artery is identified early [43]. These six approaches gives various options to determine early arterial involvement depending on the location of tumor and helps to decide on resectability before the ‘point of no return’. Though these approaches may help to know early resectability, whether these approaches would increase negative margins of resection, improve disease free survival and increase survival is not yet known.

Fig. 4 a Mesopancreas along with nerve plexus seen lateral to superior mesenteric artery after dissecting the superior mesenteric vein **b** Mesopancreas triangle which needs to be cleared for carcinoma head of pancreas lesions for better R0 resection



Surgical Implications of Mesopancreas and its Excision are

- i. An existence of definitive well define fascia enclosing the contents of mesopancreas is doubtful unlike as mesorectum
- ii. Most of the time it is a flimsy loose areolar tissue and at times it is difficult to define and dissect it preoperatively
- iii. But technical modifications like posterior and artery first approach help in better dissection of the mesopancreas
- iv. Total mesopancreaticoduodenum (tMPDe) excision helps in excision of tumor enmasse with increased curative (R0) resection
- v. Total mesopancreaticoduodenum excision decreases local recurrence
- vi. tMPDe helps in increased lymph nodal clearance
- vii. Other advantages of posterior and artery first approach are
 - a. Early selection of patients (to know about resectability)
 - b. Better delineation of SMA and its abnormalities (eg: aberrant right hepatic artery, Inferior pancreaticoduodenal artery and first jejunal branch)
 - c. Possibility of en-bloc resection of SMV-PV by no-touch technique
 - d. Complete clearance of the peripancreatic retroperitoneal tissue [21].

At present there is no definitive evidence supporting the superiority of posterior and artery first approach over the standard approach. But there is literature supporting the increased rates of R0 resection by performing a total mesopancreas excision which is better approached by artery first and posterior techniques. Whether total mesopancreas excision would lead to decreased local recurrences and thereby increase survival is not yet known. It needs future clinical trials to answer this question.

Summary

Positive resection margin in pancreatic cancer is associated with poor outcome and is an independent prognostic factor for survival. It is mandatory to perform a total mesopancreatic excision for better curative resection (R0) for pancreatic head cancers. It can be performed by either standard or posterior and artery first approaches. Newer modifications like posterior and artery first approach may help to decrease R1 resection and decrease the risk of local recurrence and improve survival. It needs further prospective trials to confirm the benefits of total mesopancreaticoduodenal excision.

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