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HOW-I-DO-IT ARTICLE

Pancreatic resection for cancer—the Heidelberg technique

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Abstract

Background Pancreatic cancer is associated with high recurrence rates, and any surgery should aim to prevent local recurrence. However, systematic resection of putatively tumor-infiltrated soft tissue adjacent to the celiac branches and superior mesenteric artery has not regularly been applied in pancreatic head resection.

Objective We describe a technique of vessel-oriented pancreatic head resection, allowing for extended removal of lymphatic and neural tissue that is situated in the TRIANGLE in between the celiac trunk, the superior mesenteric artery, and the portal vein.

Conclusions Vessel-oriented dissection or vascular resection facilitates complete removal of putatively tumor-infiltrated soft tissue, thus potentially reducing the risk of isolated local recurrence in pancreatic cancer.

Keywords Pancreatic cancer · PDAC · Pancreatoduodenectomy · Artery first · TRIANGLE · Local recurrence

Introduction

Standardized concepts of extended and radical surgical resection can reduce the occurrence of local recurrences and improve overall survival in patients suffering gastrointestinal malignancies. This holds particularly true for tumors hallmarked by early onset local and lymphatic expansion. In colorectal cancer treatment, for instance, the introduction of total mesorectal excision (TME) [1] and complete mesorectal excision (CME) [2] have represented major and lasting breakthroughs [3]. In pancreatic ductal adenocarcinoma (PDAC), however, standardized concepts of radical surgical clearance have not routinely been applied.

Unlike other tumors, PDAC has a distinctive propensity for perineural invasion [4]. This may cause extensive and early onset local tumor spread to autonomous nerves located alongside the superior mesenteric artery (sma) and the celiac trunk (ct), thus hampering complete tumor clearance at the medial and posterior resection margins following pancreatic head resection [5]. Microscopically incomplete resection represents a major risk factor concerning local and overall recurrence [6, 7]. Resection margin (R-) status and completeness of resection are, therefore, strong predictors of overall survival following resections for PDAC [8–10]. Currently, local recurrence occurs in about 25–45% of patients following surgical resection of PDAC [6, 11, 12]. Notably, improved chemotherapeutic and multimodal treatment strategies have made curative-intent surgical resection an option even in locally advanced pancreatic tumors [13, 14]. In this context, standardized and elaborated surgical treatment strategies that allow for improved local control may become ever more important [15].

The pancreatic head has traditionally been dissected in a medial-to-lateral direction, and conventional pancreatoduodenectomy has not encompassed systematic removal of putatively tumor-infiltrated neural and lymph tissue that is situated in between the celiac axis, the sma, and the portal vein. Here, we provide a step-by-step description of vessel-oriented pancreatic head resection, which represents our current HEIDELBERG standard for surgical treatment in PDAC.

Surgical technique

Exploration and mobilization of the pancreatic head

The initial steps of the operation are the same as in conventional partial pancreatoduodenectomy. The larger omentum is separated from the transverse mesocolon, and the right colic flexure mobilized to display the pancreas. When tumor infiltration into the portal or superior mesenteric vein is suspected

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mobilization of the right hemicolon and mesenteric root (Cattel-Braasch maneuver) should be performed, which will provide sufficient flexibility of the mesenteric root in case segmental resection and end-to-end venous reconstruction should become necessary [16]. An extended Kocher's maneuver completes the mobilization of the pancreatic head. The inferior vena cava is exposed at its junction with the left renal vein, the latter being secured with a vessel loop. The origin of the superior mesenteric artery, which is situated just above the left renal vein (Fig. 1b), can be palpated, displayed and secured with a vessel loop at this stage already. Dissection of the hepatoduodenal ligament completes the stage of surgical exploration. The left, right, and proper hepatic arteries are cleared in this process, and the gastroduodenal artery identified at its origin from the common hepatic artery (Fig. 1a). Lymphadenectomy is subsequently extended alongside the common hepatic artery towards the celiac trunk. In order not to jeopardize venous drainage of the stomach, it is prudent to secure and conserve the left gastric (coronary) vein (Fig. 1a), especially if tumor extension may necessitate total pancreatoduodenectomy and resection of the splenic vein. The common hepatic duct and the gastroduodenal artery are severed once technical resectability has been confirmed. Lymphatic tissue that is located to the lateral and posterior aspects of the portal vein is dissected to remain with the resection specimen. The right gastroepiploic vessels are subsequently severed at the ventral margin of the pancreatic head, and the distal stomach (or duodenal bulb in case of pylorus-preserving resection) is transected with the stomach being transposed to the left subphrenic space.

Posterior and anterior approach to the SMA

Vessel-oriented dissection of the pancreatic head now commences according to the "artery-first" approach [17, 18]. For this purpose, it is essential to display and secure the superior mesenteric artery (sma) at its aortic origin (*posterior approach to the sma*; Fig. 1b), and once again within the mesenteric root at the lower margin of the pancreatic corpus (*anterior approach to the sma*; Fig. 1c). While extended posterior mobilization of the pancreatic head provides standardized access to the sma at its aortic origin (Fig. 1b), the anterior approach to the sma needs to be adapted to the extent of peripancreatic tumor infiltration. In the absence of peripancreatic tumor infiltration, the superior mesenteric vein (smv) is dissected free at the lower margin of the pancreas, and the sma accessed to

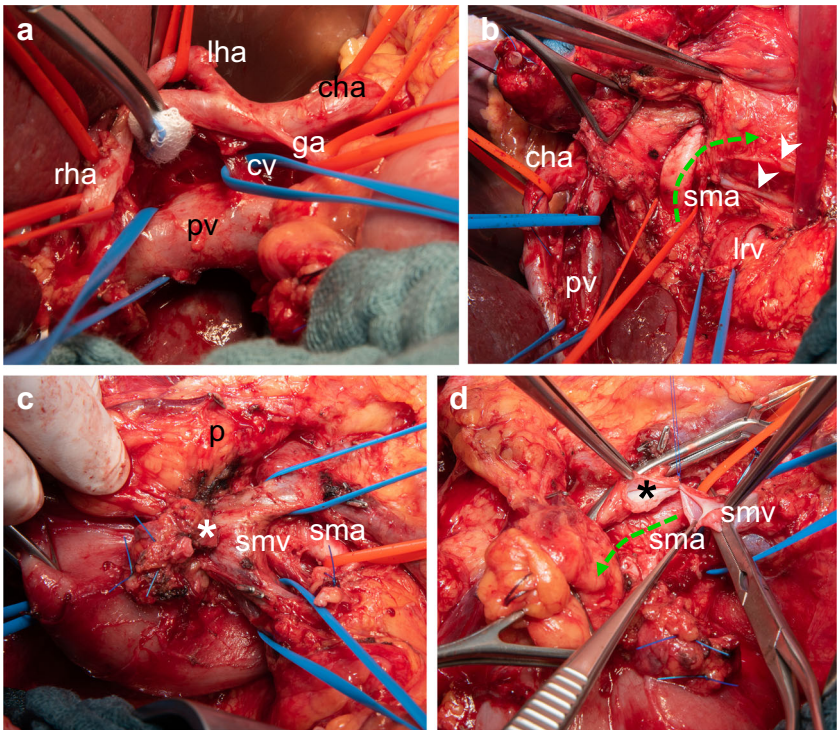

Fig. 1 Blood vessel-oriented approach to the pancreatic head. **a** Dissection of the hepatoduodenal ligament. *cha*, common hepatic artery; *cv*, coronary vein; *ga*, gastroduodenal artery; *lha*, left hepatic artery; *pv*, portal vein; *rha*, right hepatic artery. **b** Posterior approach to the superior mesenteric artery (sma) at its aortic origin. Green arrow indicates direction for pancreatic head dissection alongside the sma from posteriorly. *cha*, common hepatic artery; *lrv*, left renal vein, *pv*, portal vein. Note lymphatic vessels (arrowheads) adjacent to the sma. **c,d** Anterior approach to the superior mesenteric artery (sma), the superior mesenteric vein (smv), and its chief tributaries (blue vessel loops) within the mesenteric root at the lower margin of the pancreas (p). Asterisk in (*c*) indicates site of tumor infiltration into the smv. Asterisk in (*d*) indicates resection and end-to-end reconstruction of the smv. Green arrow in (*d*) indicates direction for further pancreatic head dissection alongside the sma from anteriorly

the left of the smv in the supramesocolic position. If the tumor infiltrates the transverse mesocolon, the sma needs to be approached from the inframesocolic position. For this purpose, the ligament of Treitz is opened and the small bowel transposed to the right. The sma is then displayed within the mesenteric root at the inframesocolic position and dissected in a cranial direction (Fig. 1c). The middle colic artery is severed at its origin from the sma in this process, and the tumor-infiltrated portion of the transverse mesocolon is resected to remain with the specimen. The first jejunal loop is subsequently divided, dissected from its mesentery, and transposed to the upper right side of the abdomen.

Systematic mesopancreatic dissection alongside the SMA

With vessel loops around the sma at the anterior and posterior positions serving as landmarks, systematic mesopancreatic dissection is now performed alongside the right lateral aspect of the sma, where no arterial branches are encountered (Fig. 1b, d). Sharp dissection alongside the sma can be carried out in a posterior-to-anterior direction (starting at the aortic origin of the sma; green dotted arrow in Fig. 1b), or in an anterior-to-posterior fashion (starting at the mesenteric root; green dotted arrow in Fig. 1d). It can be helpful to alternate between both directions of dissection, rendering the right lateral circumference of the sma free from all surrounding soft tissue once the anterior and posterior dissection planes have been joined. The common stem of the inferior pancreatoduodenal arteries is displayed, severed, and ligated at its origin from the sma in the process of this dissection. A replaced right hepatic artery originating from the sma, which is encountered in about 12% of cases [19], needs to be carefully dissected and preserved.

If dissection is hindered by venous tumor infiltration (asterisk in Fig. 1c), the smv and its chief tributaries are clamped, and the tumor-infiltrated area is excised followed by end-to-end portal venous reconstruction (Fig. 1d). If tumor infiltration involves a larger venous segment temporary bridging with a prosthetic graft can be applied, which may need to be shortened or replaced with end-to-end venous reconstruction once the pancreatic head has been removed, thus allowing for tension-free adaption of the smv and portal vein.

Larger lymphatic vessels which converge to the intestinal lymphatic trunk (arrowheads in Fig. 1b) are severed while dissecting alongside the sma, and all lymphatic and soft tissue is cleared from the space between the origin of the sma and the left renal vein (Fig. 1b). The pancreatic head is thus resected in a retrograde fashion from right to left and from posterior-to-anterior, with the pancreatic parenchyma being transected as the final step of resection (a technique referred to as “uncinate process first” [17]).

Dissection of the TRIANGLE

While the vascular-oriented dissection technique described above leaves the ventral and lateral aspects of the sma stripped from all surrounding soft tissue, a substantial portion of putatively tumor-infiltrated lymphatic and neural tissue remains within the triangular space that is bordered by the celiac trunk (ct) cranially, the sma caudally, and the portal vein anteriorly (Fig. 2a). We extend dissection to this specific area, which is a frequent site of isolated local recurrence [20]. For this purpose, the ct is dissected free at its origin from the aorta (Fig. 2a, b). The right lateral and anterior circumference of the ct is subsequently freed from residual soft tissue up to the origins of the splenic and common hepatic arteries (Fig. 2b). Sharp dissection alongside the ct has to be carried out cautiously, since its right lateral circumference is more susceptible to damage by sharp dissection than the sma. The right crus of the diaphragm is displayed in the process of clearing the triangle (Fig. 2a, b). Bleeding from the origin of the right phrenic artery may occur and should be controlled by suture ligation. Dissection of lymphatic and neural tissue that is situated in between the ct and the sma completes this final step of resection, rendering the triangle surrounded by the ct, the sma, and the portal vein devoid of putative tumor residues.

Discussion

Here, we describe a technique of strictly vessel-oriented pancreatic head resection, which has evolved from previous experience reported by ourselves [15, 17, 18] and others [21, 22]. In extension to our previous technical reports on this subject [17, 18], this technique does not only encompass systematic mesopancreatic dissection alongside the superior mesenteric artery (sma), but likewise integrates dissection of the celiac trunk (ct) into the procedure. It thus allows for standardized clearance of putatively tumor-infiltrated lymphatic and neural tissue that is situated in the triangle between the ct, the sma, and the portal vein. We believe that this approach may prove fundamental in reducing the risk of local recurrence of pancreatic adenocarcinoma.

Among the crucial technical requirements, this approach involves visualization and clearance of the sma early on in the dissection process. Another characteristic is that, rather than dividing the pancreas prior to or in the course of the dissection process, systematic mesopancreatic dissection is performed in a lateral-to-medial fashion, applying sharp dissection alongside the sma. The advantages of such an approach are twofold: first, it facilitates structured resection of the pancreatic head while at the same time reducing the risk of accidental injury to the major vessels surrounding the pancreatic head. Second, and probably more importantly, it enables the surgeon to remove all putatively tumor-infiltrated neural

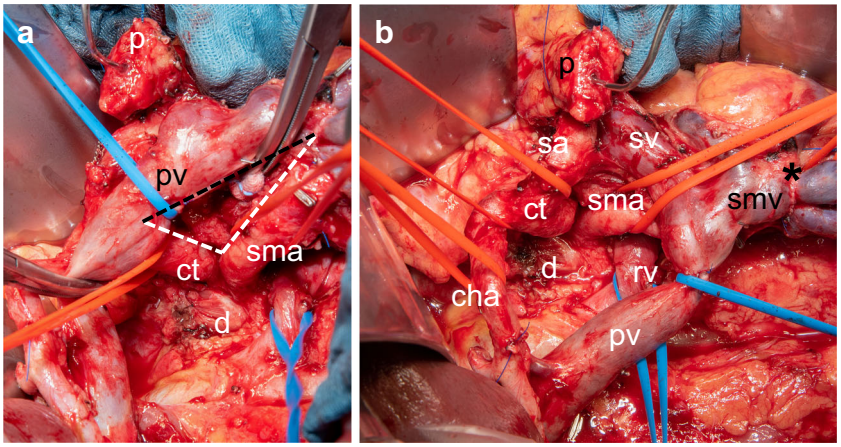

Fig. 2 Extended dissection of putatively tumor-infiltrated soft tissue (TRIANGLE). **a** Triangle bordered by the portal vein (pv), celiac trunk (ct), and superior mesenteric artery (sma). *d*, right crus of diaphragm; *p*, pancreas. **b** Surgical field after vessel-oriented pancreatic head resection. *cha*, common hepatic artery; *ct*, celiac trunk, *d*, right crus of diaphragm; *p*, pancreas; *pv*, portal vein; *sa*, splenic artery; *sma*, superior mesenteric artery; *smv*, superior mesenteric vein. Asterisk indicates site end-to-end reconstruction of the smv

and soft tissue that is situated alongside the origins of the ct and the sma, which is the site where most local recurrences occur following pancreatic head resection for PDAC.

Rather than to evaluate and compare our technique to alternative (more conservative) approaches, this article intends to provide reference and guidance for pancreatic surgeons in everyday clinical practice. In fact, albeit reasonable, it remains to be finally proven that our suggested mode of standardized vessel-oriented pancreatic head resection will indeed significantly reduce recurrence rates and improve survival in PDAC patients. It is, however, widely accepted that increasing the radicality of dissection beneath the ct, the sma, and the portal vein will increase the likelihood of obtaining a "true" R0 status (defined as a margin of > 1 mm between the tumor invasion front and the surgical resection margin [23]), which is paramount for improving oncologic survival. Of note, while the crucial impact of the R-status in predicting overall recurrence and survival is undisputed, its predictive value concerning the pattern of recurrence is a matter of debate [24]. In our collective of patients undergoing pancreatoduodenectomy for pancreatic adenocarcinoma, however, R0 resection (> 1-mm clearance) was associated with a median survival of 42 months, whereas R1 resection with < 1-mm clearance was associated with median survival of only 28 months [10].

Recognition of the fact that R0 resection is most difficult to obtain at the (posteromedial) sma margin [25] has led to the development of the artery-first concept in surgical management of PDAC, which involves radical mesopancreatic and periadventitial dissection alongside the sma. While different approaches to the sma exist [22], all variations of the artery-first approach have in common that dissection is performed within the tunica adventitia of this artery. In a recent meta-analysis of mostly retrospective (and, therefore, putatively biased) data, comprising close to 1500 patients overall, artery-first approaches were associated with enhanced rates of R0 resections and improved overall survival as compared with standard resection techniques [26]. Interestingly, this study likewise revealed reduced blood loss and surgical morbidity in patients undergoing artery-first approaches. A currently ongoing randomized controlled trial (PancER; DRKS-ID: 00013552) compares the oncological benefits of an uncinate first, vessel-oriented extended pancreatoduodenectomy approach versus conventional partial pancreatoduodenectomy for the resection of PDAC, with the rate of curative resections (defined as microscopically complete (> 1 mm) margin clearance, R0) as the primary endpoint, and overall survival and local recurrence rates among the secondary endpoints. Another ongoing randomized controlled trial (MAPLE-PD, NCT03317886) evaluates the advantages of an artery-first mesenteric versus a conventional approach during pancreatoduodenectomy, with survival from surgery to death as the primary outcome measure [27]. We are confident that these trials will provide more solid evidence concerning the oncological advantages of the blood vessel-oriented approach in surgical treatment of PDAC patients.

Obviously, the suggested oncological benefit of radical and vessel-oriented surgery in pancreatic adenocarcinoma needs to be balanced against an enhanced surgical risk profile. Indeed, extended resection of neural and lymphatic tissue bears a risk of increased surgical morbidity, encompassing adverse effects such as postoperative bleeding, therapy-refractory ascites, and diarrhea. However, in an initial series of patients undergoing the TRIANGLE operation as described above at our center, functional outcome was favorable in a majority of patients despite the extended approach of dissection [28]. These observations are consistent with those made by other authors, reporting that, when performed in high volume centers, surgical morbidity is acceptable even in patients undergoing extended pancreatectomy procedures compared to those treated with standard pancreatectomies [29].

Surgical approaches enabling radical local tumor clearance are of particular value in patients suffering locally advanced but non-metastasized tumors, who underwent neoadjuvant treatment [14]. Indeed, surgical resection becomes feasible in up to 60% of PDAC patients following neoadjuvant treatment protocols [13, 15]. In this collective of patients, a vessel-oriented approach comprising sharp dissection within the adventitia of the sma and the ct may allow for complete tumor clearance without the necessity of arterial resection [28].

Oncologic benefits of radical local tumor treatment are ultimately restricted by systemic disease recurrence, which represents a frequent event following surgical resection of PDAC [6]. In order to enhance the rationale for radical surgical concepts, it is thus desirable to identify subgroups of patients who are more prone to develop local than systemic treatment failure and will, thus, benefit most from extensive surgery. While clinicopathological factors may provide some limited insight into predicted recurrence patterns [6], it will in this context become essential to decipher biologic characteristics that are either intrinsic to the tumor [30] or the tumor environment [31], and which determine individual patients' risk of local versus systemic recurrence. Combination with such tools, allowing for prediction of local or systemic disease patterns, may, in future, provide a strong rationale for enhanced surgical radicality in local treatment of PDAC.

Conclusions

We suggest a vessel-oriented technical approach of pancreatic head resection, including eradication of all putatively tumor-infiltrated soft tissue beneath the celiac and superior mesenteric trunks. We believe that standardized application of this approach is suited to improve the rate of R0 resections in patients undergoing pancreatoduodenectomy for treatment of PDAC, and especially in patients undergoing resection of locally advanced tumors following neoadjuvant treatment. Solid evidence from randomized controlled trials is ultimately required prior to advocating this approach of extended and vessel-oriented approach as the standard for surgical resection in PDAC.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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