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Review Article

Pancreatic head cancer – Current surgery techniques

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ABSTRACT

Pancreatic head cancer is a highly fatal disease. For now, surgery offers the only potential long-term cure albeit with a high risk of complications. However, the progress of surgical technique during the past decade has resulted in 5-year survival approaching 30% after resection and adjuvant chemotherapy. This paper presents current data on the recommended extent of lymphadenectomy, the resection margin, on the definition of resectable and borderline resectable tumors and mesopancreas. Surgical techniques proposed to improve PD are presented: the artery first approach, the uncinate process first, the mesopancreas first approach, the triangle operation, periarterial divestment, and multiorgan resection.

1. Introduction

Pancreatic cancer (PC) incidence is 11th in the world and 7th in western countries among all cancers.[1] In almost 75% of patients, it is found in the pancreatic head. The resectable (R–PHC) and borderline resectable (BR-PHC) pancreatic head cancers are treated surgically by pancreatoduodenectomy (PD). This procedure is challenging for surgeons, requires advanced technical skills, and poses a high risk of life-threatening complications. However, it is the only possibility of a long-term cure for the patient. It was not until the 1980s that the PD mortality rate diminished to less than 10%.[2] Nowadays, in high-volume reference centers for pancreatic surgery it was possible to reduce the mortality rate to 3% or below or to perform a series of more than 100 consecutive PDs without in-hospital or 30-day mortality.[2] The 5-year survival rate of patients with PHC after resection and adjuvant chemotherapy now reaches 30–40%.[3] The review presents current advances in surgical techniques in the treatment of PHC.

2. Lymphadenectomy

PC spreads through the lymphatic system and in most patients, if the lymph nodes are infiltrated by tumor cells, the metastases are found not only regionally but also in distant localizations.[4] It seems that regardless of how many lymph nodes are removed, the outcomes are the same.[5] Also, the ratio of lymph nodes with and without metastases was shown not to have any impact on treatment results.[5] This indicates that if lymph node metastases are present, the biological features of the primary tumor are very aggressive. The question is how to perform adequate lymphadenectomy and provide better outcomes without unnecessary risk. In 2013, a standard of lymphadenectomy was proposed.[6] It involves the removal of at least 15 lymph nodes during pancreatoduodenectomy.[6] The lymph node stations to be removed are presented in Fig. 1. However, this recommended number and location are still under debate.

Some publications report that more extensive regional lymphadenectomy improves the survival of patients with PC. In a US population-based study of 7685 patients with pancreatic cancer, removal of $\geq$20 lymph nodes vs $<$ 20 resulted in longer overall survival in patients both with and without nodal metastases.[7] In a meta-analysis of 5 randomized clinical trials (n = 546), however, survival time did not improve with extended lymphadenectomy (removal of 20–40 lymph nodes) compared with the standard procedure (removal of 13–17 lymph nodes). It is worth mentioning that extended lymphadenectomy had a higher postoperative morbidity rate.[8]

According to some authors, the extent of lymphadenectomy should depend on the anatomical location of the tumor.[9] This claim arose from the analysis of regional lymph node metastases and nodal recurrence, which showed differences between different locations of the tumor (the isthmus, the uncinate process, and the papilla of Vater).[9]

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List of abbreviations

pancreatic cancer PC
resectable pancreatic head cancer R—PHC
borderline resectable pancreatic head cancer BR-PHC
pancreatoduodenectomy PD
superior mesenteric artery SMA
International Study Group of Pancreatic Fistula ISGPS
locally advanced tumors LA-PHC
superior mesenteric vein SMV
hepatic artery HA
en bloc proximal peri-mesenteric clearance PPMC
TRIANGLE pancreatoduodenectomy TPD
laparoscopic pancreatoduodenectomy LPD
open pancreatoduodenectomy OPD
robotic-assisted pancreatoduodenectomy RPD
total pancreatectomy TP
portal vein PV
postoperative pancreatic fistula POPF

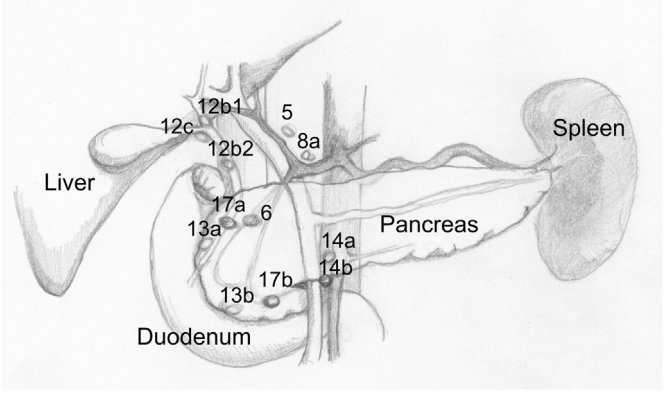

Fig. 1. Standard lymphadenectomy during pancreatoduodenectomy for adenocarcinoma: lymph node stations no. 5 (suprapyloric), 6 (infrapyloric), 8a (common hepatic artery), 12b1 and 12b2 (bile duct), 12c (cystic duct), 13a (posterior side of the upper pancreatic head part), 13b (posterior side of the lower pancreatic head part), 14a and b (right lateral side of the SMA), 17a (anterior surface of the upper pancreatic head part) and 17b (anterior surface of the lower pancreatic head part).

For now, routine removal of further lymph node stations (located on the left side of the superior mesenteric artery-SMA, the celiac trunk, splenic artery, or left gastric artery) is not recommended because in comparison with the lymphadenectomy recommended by ISGPS (International Study Group of Pancreatic Fistula) no improvement of the survival rates is observed, and the risk of complications is greater.[6] It might be considered though when in preoperative imaging tests extra-regional lymph node metastases are suspected. Also, in some patients with isolated lymph node recurrence after PD, surgical resection may be considered.[10]

3. The resection margin in PD

A group of tumors on the borderline between the completely resectable (R—PHC) and the locally advanced tumors which cannot be removed (LA-PHC) was at first called “marginally resectable",[11] and from 2006 the name “borderline resectable” (BR-PHC) is used.[12] Since then, numerous anatomical definitions of borderline resectable tumors have been established.[13,14] In BR-PHC, neoadjuvant chemotherapy seems crucial for a negative resection margin (R0).[15] Currently, there is still controversy regarding the impact of R1 resections (a microscopically positive margin) on the survival of PC patients. The lack of one definition of the resection margin likely caused differences in the results of studies. According to the Union for International Cancer Control, R0 resection meant no tumor cells in the line of excision i.e., a 0 mm distance from the tumor infiltration was sufficient. In Europe, at least 1 mm distance from the tumor was needed for an R0 margin. In 2014, the ISGPS established a final definition of R0 resection,[16] requiring a distance of at least 1 mm without tumor infiltration from the incision line. Also, a minimum of 7 margins is recommended to be reported: anterior, posterior, superior mesenteric vein (SMV) groove, SMA, bile duct, and bowel.[16] In a meta-analysis assessing the percentage of R0 resections in studies published before the new definition, the number of R0 resections diminished from 72% to 42% when the 1 mm tumor-free margin was considered R0 instead of 0 mm.[17]

What is important, if lymph node metastases are found, the resection margin does not have a significant impact on the patients' survival.[18] When no metastases are present, the R0 resection improves the survival time (R0- 45 months vs R1- 17 months).[18]

In a large study from John Hopkins Hospital, the R status had a significant effect on distant treatment outcomes. For R0 resections, median and 5-year survival was 20 months and 21% respectively, while for R1 resections, it was 14 months and 12%. The determinants of survival after resection were the resection margin, the tumor size, the occurrence of lymph node metastases, and tumor grading. In 56 patients out of 1175 who underwent PD for PC and had favorable pathological results in each of the four features, the median and 5-year survival were impressive 44 months and 43%, respectively.[19] Other studies also confirm that long-term survival after PC resection depends much on a negative resection margin.[20–22]

According to Strobel et al, the R status is independently associated with long-term survival.[20] The study showed that the median survival time for patients undergoing PD with R0 resection (tumor-free margin $\geq$1 mm) was 41.6 months vs 27.5 months after R1 resection, and the 5-year survival rates were 37.7% and 30.1%, respectively.

Also, a 3-center study of 305 patients with R—PHC and BR-PHC who were administered neoadjuvant therapy and PD confirmed that the margin status was an independent predictor of overall survival (31 months in R0 vs 16 months in R1).[21] According to the authors, an R0 margin may be used as a determinant of proper oncological resection.

In 2019 a randomized controlled trial was performed, aiming to analyze the association between the clinical features and margin status along with the impact of positive margin on the place of recurrence, and on overall and recurrence-free survival.[22] The data obtained confirmed that in R1 cases the overall and recurrence-free survival after surgery diminished substantially. Additionally, in these patients the risk of local tumor recurrence was greater.[22]

4. Vascular resections

4.1. Venous resections

Until the 1980s, locally advanced pancreatic head carcinomas infiltrating the portal vein and its branches through continuity were considered unresectable. Three events led the first surgeons to take up the new challenge of ‘en bloc’ resection of the pancreatic head with portal vasculature: improvement of postoperative morbidity and mortality rates, development of vascular prosthesis technology and extracorporeal circulation devices, and improvement of distant outcomes after extended removal of lymph nodes and soft tissues surrounding the tumor.

Nakao and his team were the pioneers of vascular resections. They developed a portal system resection technique with an antithrombogenic bypass catheter and recommended it for the cases when vascular resection could provide an R0 margin.[23] Initially, resections involving portal flow vessels did not gain widespread acceptance. Some have argued that they improve neither the rate of curative resections nor survival.[24]

However, in subsequent years when centers specializing in pancreatic surgery emerged, the perioperative mortality of patients who underwent PD with and without portal vein system resection became comparable. Similar survival times were reported in both groups, significantly better compared to the group of patients with only bypass anastomoses.[25]

In 2014, the ISGPS consensus was published,[16] recommending venous resection if the intraoperative assessment of the tumor indicates that it would enable complete tumor removal (R0). Nevertheless, the consensus notes that higher rates of intra- and postoperative complications must be taken into account if such resection is performed. Also, it has been proposed to classify the venous resections into four types: type 1 being partial venous resection with suturing of the wall defect; type 2, partial venous resection with patch reconstruction of the vessel; type 3, where after removal of a vessel segment, a primary end-to-end veno-venous anastomosis is performed; and type 4, resection of a vessel segment with a venous insert and two anastomoses or more (Fig. 2). Importantly, the ISGPS strongly suggests performing vascular resections in reference centers specializing in pancreatic surgery.

The latest French guidelines,[26] developed based on a literature review from 2008 to 2019 and published in 2020, emphasize that venous resection is recommended in patients with BR-PC when the tumor in a limited area infiltrates the lateral wall of the vessel or involves it circumferentially, but the lumen is patent and neither the celiac trunk nor the SMA is infiltrated. The importance of the good overall condition of the patients eligible for PD with vascular resection is emphasized, considering the greater risk of mortality and morbidity associated with this type of surgery.

While resection and reconstruction of the portal system vessels are now standard management for tumors infiltrating the portal vein or SMV over a limited segment, the cavernous transformation of the portal vein developing because of venous occlusion still poses a challenge for pancreatic surgeons. Some use specific vascular techniques for pancreatic resection, e.g., venous bypass between the SMV and inferior vena cava[27] or the SMV and portal vein in the hepatic hilum.[28] Such procedures are among the extremely difficult operations that are performed sporadically worldwide.

4.2. Arterial resections

The first arterial resections in advanced PHC were documented by Fortner in 1973.[29] Until now, treatment of PHC by extended PD with arterial resection is raising questions. According to the ISGPS guidelines, there is no strong scientific evidence to suggest that resection of arteries adjacent to the pancreatic head performed during PD benefits cancer patients and should certainly not be used routinely. They may even be detrimental, as high postoperative morbidity and mortality are observed.[16]

On the other hand, arterial resection may provide some patients with complete tumor removal (R0 resection) and thus be the only possibility to achieve long-term survival. Moreover, with the availability of new, increasingly effective adjuvant treatments, arterial resection may become important in the treatment of PC in the future. In terms of surgical technique, resection and reconstruction of the celiac trunk and hepatic artery (HA) should be distinguished from that of the SMA. Both procedures are feasible in hands of a skilled surgeon, but to achieve good therapeutic results extensive surgical experience of the operating team is required and an interdisciplinary approach to preoperative diagnosis and to the treatment of the postoperative complications is essential.[27]

According to the French guidelines from 2020 neoadjuvant therapy is recommended in cases of arterial infiltration, followed by surgery. The extent of the surgical procedure in these cases depends on the location and extent of the infiltration: for partial involvement of the common HA, resection with reconstruction is recommended. For SMA infiltration, a laparotomy with a biopsy of the periarterial tissues is recommended and PD should not be performed if cancer cells are found in the biopsy.[26]

5. Mesopancreas

The first anatomical definition of mesopancreas was given in 2007.[30] It consists of tissues (fat, nerves, blood vessels, and lymphatic structures) adjacent to the posterior wall of the pancreas and the SMV, throughout the space on both sides of the SMA and down to the inferior vena cava, and the aorta. The line of dissection of the uncinate process of the pancreas from the superior mesenteric vessels during PD lies within this space and this so-called “extravascular” resection margin often contains tumor cells responsible for R1 resection.[31] Lack of any kind of capsule around the mesopancreas causes identification problems during resection,[32] and to this day, discussion on its delineation continues.[31]

Recent anatomical studies resulted in another term, “P-A ligament”, for the band of tissue located between the posterior surface of the pancreatic head (P) and the large vessels (the visceral trunk and the superior mesenteric artery with their branches) (A).[33] Some authors propose that because of morphologic, functional, and developmental features the duodenum should be included in the region's nomenclature and suggest the name “mesopancreatoduodenum” as more appropriate.[34] Other authors question the use of this term because of the vague borders of the mesopancreas.[35] They propose “en bloc proximal peri-mesenteric clearance (PPMC)", meaning lymphadenectomy together with removal of the tissues around the SMV and SMA.[35]

Improving the knowledge of the anatomy of the mesopancreas region and improving the technique of its excision is doubtlessly important in the pursuit of increasing the resectability of pancreatic head cancer.[36]

6. Surgical approaches

6.1. Artery first

“Artery first” is a surgical technique that exposes the SMA in the first stage of PD. Such early assessment of tumor infiltration which can disqualify the patient from the resection has undeniable advantages. Firstly, since the venous system may be safely resected, it is the infiltration of SMA which limits the resectability so it has to be assessed in the beginning of the surgery, before the irreversible maneuvres are performed. When access to the SMA is obtained in a traditional way, after cutting the isthmus of the pancreas, the PD must be completed. In the case of SMA infiltration, this results in R1or R2 resection, a high complication rate, and survival similar to that observed after bypass anastomosis. Apart from that, the resection of the medial-posterior edge of the pancreatic head is essential for the R0 resection and allows precise hemostasis.

Six routes have been described that can lead to the early exposure of the SMA.[37] In clinical practice, mainly 4 are used, most commonly the supracolic right posterior approach[38] (Fig. 3).

The first PHC resections with isolation of the SMA with a mesenteric approach were performed in the 1980s by Nakao and the procedure has been popularized over time in Japanese

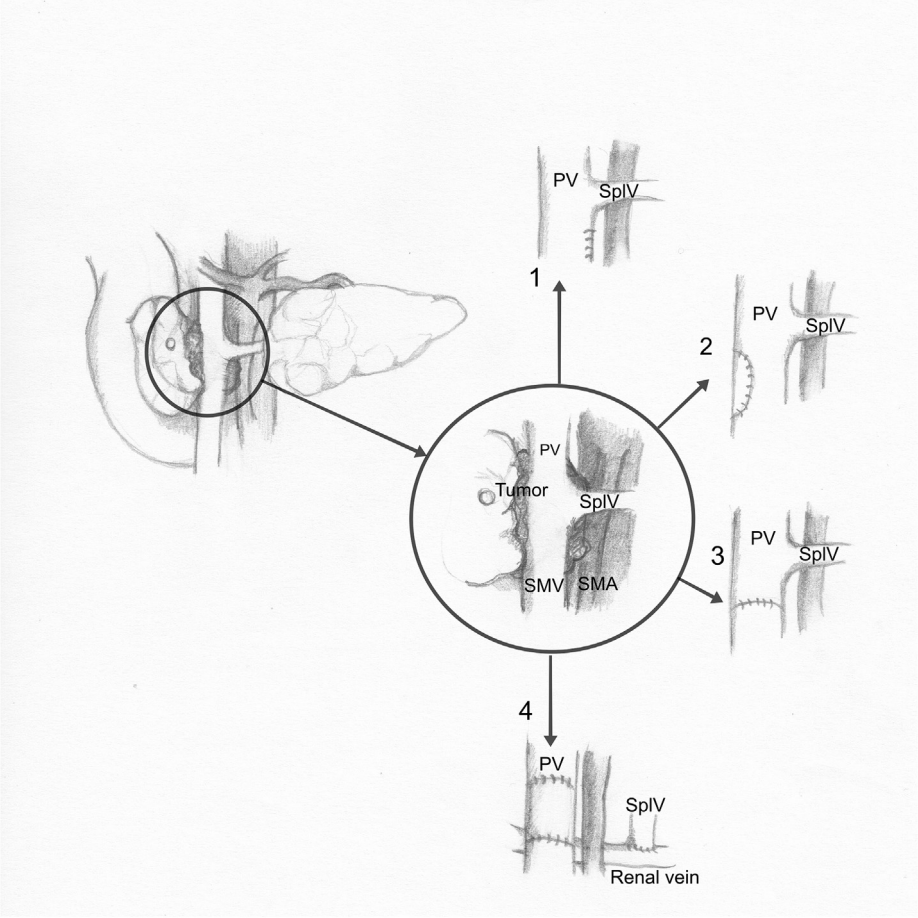

Fig. 2. Four types of venous resections. 1 - partial venous resection with suturing of the vessel wall; 2 - partial venous resection closed with the use of a patch; 3 - resection of a vessel segment with end-to-end veno-venous anastomosis; and 4 - resection of a vessel segment with a venous insert and at least two anastomoses.
The circled region contains the mesopancreas.

centers.[39] The technique of accessing the SMA during PD by separation of the posterior surface of the pancreatic head from the retroperitoneal space vessels in the first stage of surgery was first presented by Pessaux et al in 2006.[40]

In a recently published meta-analysis of 18 clinical studies (n = 1483), two groups of patients were compared: one undergoing standard PD and the other artery-first PD.[41] The latter group had significantly lower postoperative morbidity, blood loss during surgery, and shorter hospital stay. A higher rate of R0 resection, a lower rate of local recurrence, and longer overall survival were also noted in this group.

Nevertheless, according to some authors, the artery-first method is not advisable for all patients[42] but should be employed mostly where resection and reconstruction of the portal vein are necessary. In this technique, once the resection is approaching completion, the parts prepared for removal are connected only by the portal vein and the anastomosis can be performed more easily and quickly, reducing the time of mesenteric ischemia. However, the possible prolongation of the surgery must be considered as well as the higher risk of lymph leakage and postoperative diarrhea. The routine use of the artery-first approach needs further evaluation, because it has been reported that when used non-selectively, it may not increase the R0 resection rate.[42]

6.2. Mesenteric approach

A modification of the artery-first approach was published and popularized by Nakao.[43] The so-called mesenteric approach omits the Kocher's maneuver and starts with incision of the mesentery, exposure of the SMV and SMA and determining the cancer-free margin. It enables early assessment of resectability, adequate lymphadenectomy and mesopancreas removal. According to some publications, this technique may result in a higher R0 rate than PD with Kocher's maneuver.[44]

6.3. Uncinate process first

When during the PD the first jejunal loop is transected and transposed to the right side to the upper abdomen, the pancreatic uncinate process is exposed and dissected from the retroperitoneal tissues, with good visualization of the superior mesenteric vessels. The SMA and SMV are approached from the right caudo-peripheral direction which allows for a lower risk of injury and bleeding. This maneuver, providing a high percentage of R0 resections, was described in 2007[45] and incorporated into a modification of the PD technique called “uncinate process first” described in 2010 by German surgeons from Heidelberg.[46] Such dissection of the uncinate process is also used in the laparoscopic PD to obtain a good view of the SMA, more often than the artery-first technique.[47]

6.4. Mesopancreas first

Recently, it has been proposed that a mesopancreas-first approach could complement the artery-first approach, reducing

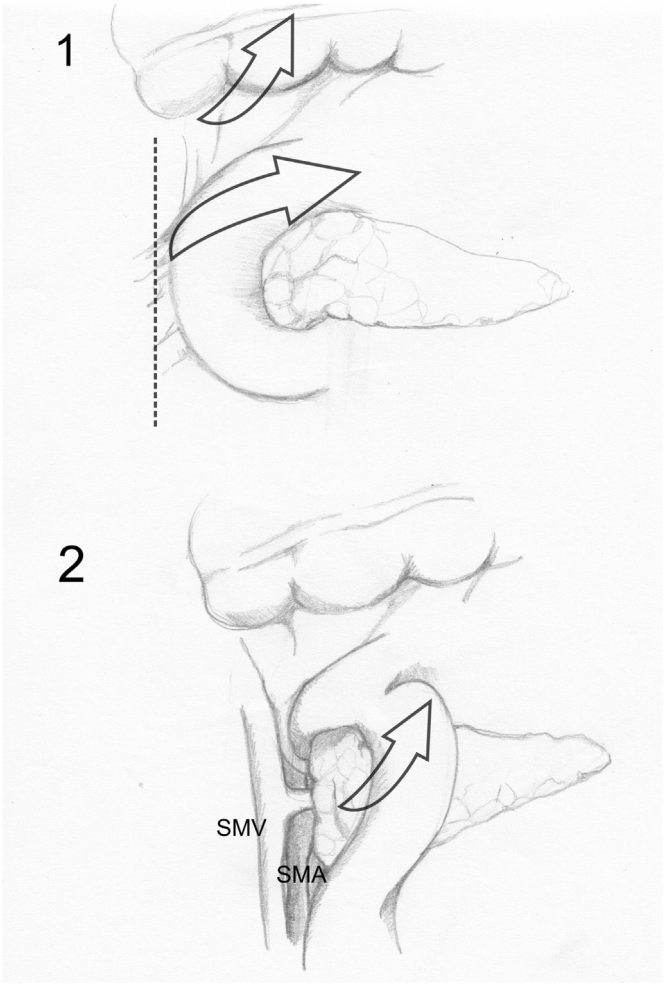

Fig. 3. Right posterior supracolic access to the superior mesenteric artery (SMA) and vein (SMV) in artery-first approach. The vessels are exposed by mobilizing of the ascending colon and moving it upwards (1) and by a Kocher maneuver (2).

the number of R1 resections.[48]

Inoue et al distinguished 3 levels of mesopancreas resection, each indicated in a different group of patients.[49] The first level allows for preservation of the mesojejunum, the nerves around the SMA and the small vasculature of the intestine. It is indicated in low-grade tumors when lymphadenectomy is not needed, e.g., in carcinoma in situ, pancreatic metastases, or an intraductal papillary mucinous neoplasm. The second level also preserves the periarterial nerves, but both the lymph nodes and the mesopancreas are excised. The inferior pancreaticoduodenal artery is ligated with the dissection running to the right of the SMA. This should be applied in duodenal and biliary tract tumors. In the third stage, ca. half of the SMA circumference is stripped of the nervous tissue, 'en bloc' with the entire mesopancreas. This most extensive dissection is indicated in PHC or locally advanced cholangiocarcinoma.[49]

Nagakawa et al proposed a new anatomical reference point for R0 resection that can be reached without the difficult dissection of the SMA from the surrounding nervous and fibrous tissues. The authors determined four areas of tissue around the SMA that should be removed, as well as three areas containing nerve plexuses that should not be excised. According to their study, this may become a new way of radical PD.[50]

Some authors suggest that the R0 resection rates can be improved by complete mesopancreas excision.[51] However, randomized controlled trials are needed to support this, as well as a universal definition of mesopancreas and a consensus on its excision technique.[52]

7. TRIANGLE operation

In 2017, a new type of surgical technique to improve radical PD was described, called TRIANGLE operation (TPD).[53] It is a variant of PD with radical removal of all soft tissues located in the triangular space limited by the SMA and the visceral trunk on one side, the SMV and the portal vein on the opposite side, and, from above, the common hepatic artery and the hepatic artery (Fig. 4). The TPD technique is recommended for patients with a stable disease with no apparent tumor regression, even if infiltration of the arterial vessels is suspected in radiological imaging. The authors justify the development of this procedure by the fact that patients receiving FOLFIRINOX as neoadjuvant treatment often have a desmoplastic reaction, changing the structure of the tissues surrounding the tumor, making it impossible to distinguish between fibrosis and tumor infiltration. The technique allows for tumor excision with a negative margin, without the dangers of arterial resection in this selected group of patients in whom there is a chance that finally the postoperative histopathology result will show no tumor cells in the perivascular fibrous connective tissue. TPD surgery for BR-PHC can also be safely performed laparoscopically in carefully selected patients.[54]

8. Periarterial divestment

Periarterial divestment is a procedure that involves the circular removal of soft tissue adjacent to the SMA wall and containing nerves, lymphatic structures, and tumor cells inactive after chemotherapy, which may have the potential for reactivation in the future and be responsible for distant local recurrence.[55]

The first report on this technique application for locally advanced PHC was published in 2016.[56] In 6 patients the authors removed the SMA infiltrate by separating the outer layer of the vessel (tunica adventitia) from the middle layer.

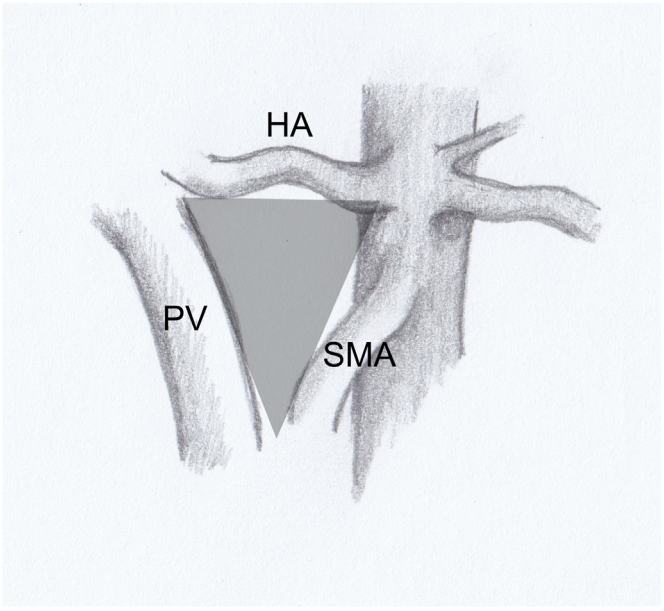

Fig. 4. TRIANGLE operation – removal of all soft tissues located in the space bordered on the sides by the superior mesenteric artery (SMA) and the visceral trunk (left), the superior mesenteric vein (SMV) and the portal vein (PV) (right), with the common hepatic artery and the hepatic artery (HA) from above.

Some authors claim that periarterial divestment surgery violates all principles of oncologic surgery because cutting through the infiltrate results in R1 resection and increases the risk of the tumor spreading and local recurrence.[57] Additionally, this technique may significantly increase the number of both intra- and postoperative vascular complications. It causes weakening of the vessel wall, which can lead to life-threatening bleeding or thrombosis. Therefore, instead of vessel-sparing procedures, arterial resections 'en bloc' with the tumor is suggested as a better solution, when performed in experienced surgical centers.[57] However, the value of periarterial divestment needs to be assessed in clinical trials and as an alternative to arterial resection it is currently not recommended as a solution for locally advanced PC.

8.1. Multi-organ resection

In oncological surgery, a multiorgan resection is the excision of two or more organs in contact with each other to obtain a tumor-free resection margin. PD involves the pancreas, duodenal or gastric bulb, small intestine, gall bladder, and the bile duct, and sometimes portal vein.

Currently, only about 3% of patients require multi-organ resection during PD, most frequently involving the colon, stomach, and liver.[58] Unfortunately, multi-organ resection is accompanied by an increase in the in-hospital morbidity and mortality rates and no improvement in distant outcomes (5-year survival 7%). However, some authors show that extended resections can have good outcomes with no negative impact on in-hospital morbidity rates.[59]

A meta-analysis[60] published in 2014 evaluated 273 of 9927 patients (3%), who underwent PD with multiorgan resection (defined as additional removal of the colon, small intestine, stomach, kidney, or adrenal gland). 3-fold higher mortality and significantly higher morbidity were noted in this group when compared with standard surgery. An independent factor for increased morbidity was colectomy.

Therefore, it appears that multiorgan resection during PD is a method fit for reference centers and particular groups of patients because although it can increase the number of patients cured of cancer, the morbidity and mortality rates exceed these noted after standard procedure.[61]

9. MIPR-minimally invasive pancreas resection

Since 1992, when the first laparoscopic PD (LPD) was performed,[62] there has been a steadily growing interest in this technique. The first experiences with laparoscopic pancreatic resection were not encouraging and even the pioneers of this method doubted they benefited the patients.[63] The procedure was time-consuming, with high conversion rates and many complications. With the growing popularity of less invasive surgery, however, the method also becomes more appealing for pancreatic surgeons skilled in laparoscopy. The concerns that laparoscopy can worsen oncologic outcomes are refuted by current publications. A meta-analysis of 2 randomized and 26 retrospective studies confirmed the feasibility and the possible benefits of LPD over open PD (OPD).[64] Both techniques showed similar in-hospital morbidity and mortality. Compared to OPD, during LPD more numerous lymph nodes were removed and a higher occurrence of R0 was observed. Another meta-analysis comparing LPD and OPD and published in 2020 did not find any difference in 5-year survival between the examined groups.[65] The LPD surpassed the OPD in terms of the R0 resections rate and the number of lymph nodes removed. It also resulted in less postoperative bleeding, and shorter hospital stay. These results indicate the possibility of enhanced early outcomes with no deterioration of distant results after LPD for PHC.

On the other hand, a comparison of perioperative outcomes from 3 randomized controlled trials[66] published in 2020 showed that LPD did not exhibit advantages over OPD. In the opinion of experts, despite the continuous development of the LPD technique and increasingly better results, OPD remains the standard treatment for PC. LPD should be reserved for surgeons in reference centres specialized in this method.[67]

The first robotic-assisted PD (RPD) was performed in 2001.[68] The long-term outcomes and associated oncological aspects of RPD in patients with pancreatic adenocarcinoma were evaluated in a US cohort study[69] published in 2020. The study groups included 626 (RPD) and 17,205 patients (OPD), respectively. The mean number of lymph nodes removed, and the proportion of adequate lymphadenectomy ($\geq$12 lymph nodes) was higher in the RPD group vs the OPD group. The resection margins status was similar in both groups. The median overall survival did not differ between RPD (22.0 months) and OPD (21.8 months), neither did the 5-year overall survival rates (19% in both methods). The overall survival was not affected by robotic surgery employment. A meta-analysis published in 2021, including 24 studies (12,759 patients- 2175 RPD, 10,404 OPD), showed that RPD provided a better surgical efficacy compared to OPD (R1 resection 15.6% vs 19.9%). On average, 3 more lymph nodes were removed during RPD, but with longer operation time (+75.17 min) and higher costs.[70]

Another meta-analysis[71] published in 2020 comparing the results of 2 minimally invasive methods (LPD and RPD) with OPD showed that all 3 appear to be equally safe in terms of early complications. R0 margins and the total number of lymph nodes retrieved were similar in all 3 treatments. The authors recommend surgeons choose the preferred surgical method according to their experience.

The current international guidelines for minimally invasive surgery of the pancreas from 2020 state that the available data does not suffice to recommend minimally invasive techniques over OPD for the treatment of PC.[72] However, both minimally invasive methods and OPD are appropriate management options for selected patients with pancreatic head adenocarcinoma.

10. Total pancreatectomy (TP)

Postoperative complications after pancreatic resection are mainly related to problems with the pancreatic anastomosis. To avoid pancreatic anastomosis complications, Ross introduced total pancreatectomy (TP) in 1954.[73] Until recently, the procedure was considered very risky due to high rates of short- and long-term complications and did not show evidence of oncologic advantages. TP is followed by several potentially mortal metabolic consequences such as unstable diabetes and severe hypoglycemia. Chronic complications of unstable diabetes (cardiac and vascular diseases, neuropathy, nephropathy, and retinopathy) also cause increased morbidity, mortality and worsening of quality of life. However, recent studies have shown that although TP-induced diabetes negatively impacts select activities and functions, overall quality of life is comparable with that of patients who undergo a partial pancreatic resection.[74]

On the other hand, although total pancreatectomy compared with partial resection was associated with a higher rate of R0 resection, median survival was not significantly different[75] and the number of TP performed has decreased over time.[76]

Currently, advances in surgical techniques, improvement in perioperative care, new insulin formulations and modern pancreatic enzyme substitution have allowed good short- and long-term results and better quality of life, especially in high-volume centers. TP may be considered a viable option not only for patients affected by extensive pancreatic cancer (with the benefit of

achieving complete tumor resection and negative margins), but also in multifocal parenchymal diseases or involving the entire pancreas (intraductal papillary mucinous neoplasms, pancreatic neuroendocrine tumors, multiple endocrine neoplasia, and renal cell metastases). In addition, TP can be indicated for selected patients with soft pancreatic parenchyma which does not hold sutures, with the aim of avoiding anastomosis-related complications. Finally, TP can be performed in the emergency setting to control bleeding in the event of intraoperative iatrogenic vessel injury or when removal of the whole pancreatic remnant is performed for sepsis control in a postoperative pancreatic fistula (POPF) after a partial pancreatectomy.[77]

Additionally, prophylactic TP is suggested for rare cases of high risk of development of ductal pancreatic adenocarcinoma (hereditary pancreatitis, ductal or mixed intraductal papillary mucinous neoplasm).[78]

11. Pancreatic anastomoses

In the reconstructive stage of PD, the anastomosis between the pancreatic remnant and digestive tract poses the greatest challenge. If POPF occurs it may be fatal, reaching 26% mortality in the most severe cases.[79] The pancreas can be anastomosed either with stomach or with jejunum, with the stump invaginated into the small intestine or anastomosed in duct-to mucosa manner.[80] Numerous modifications of these standard techniques emerge in pursuit of lowering the risk of POPF, e.g., adding mattress sutures to cover the previous layer of sutures.[81] So far, none of the techniques have been proven significantly superior to others, therefore, the anastomosis must be tailored according to the surgeon's skills and experience.[82] Other factors that must be considered are the consistency of the pancreatic parenchyma and the size of the main pancreatic duct.[83]

12. Conclusions

Surgery of PHC has significantly advanced in the last years. The survival rates are growing thanks to better and courageous surgical techniques and neoadjuvant treatment. Some formerly unresectable cancers are now considered borderline resectable, which means that in expert centers with well−trained pancreatic surgeons this new group of patients has a chance for tumor removal and longer life. We still need an evaluation of some of the new techniques to assess if the risk is acceptable but for now, with the lack of effective chemotherapy, the only way to provide a better cure for PHC patients is the progress of surgery.

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Declaration of competing interest

The Authors declare that there is no conflict of interest.

Appendix A. Supplementary data

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