

# Surgical treatment of pancreatic cancer

## Authors' Contribution:

A – Study Design  
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## ABSTRACT:

The only way to cure the patient with adenocarcinoma of the pancreas (RT) is surgical excision of the tumor. The standard surgical treatment of resectable pancreatic carcinoma is considered the classic pancreatoduodenectomy (PD) with the Kausch-Whipple procedure, or the pylorus-preserving PD with the Traverso-Longmire method. The most difficult technically and at the same time the most important PD stage from an oncological point of view is the separation of the head of the pancreas from the superior mesenteric artery. Over the last decades several PD modifications have been developed, focusing on this maneuver in the early phase of the operation, i.e. before the pancreas is cut (an irreversible stage of the procedure). These procedures in the English literature are called “artery-first approach” or “SMA-first approach”. The term “mesopancreas” was created. Complete removal of the mesopancreas together with the proximal part of the jejunum is considered an R0 resection in the case of a tumor of the head of the pancreas with direct or indirect vascular invasion, or metastases to regional lymph nodes, and in English literature it is referred to as pancreatoduodenectomy with systematic mesopancreas dissection (SMDPD). Distal resection of the pancreas (DRT) due to cancer, is associated with a high percentage of positive margins, insufficient number of removed lymph nodes, low survival rates. A new technique was developed - a radical proximal-distal modular pancreatosplenectomy (RAMPS). In RAMPS, surgical operations proceed from the side of the pancreas head towards the tail, the pancreas is cut early, and the splenectomy is performed at the final stages of the procedure. Currently, following the PD model, attempts are made to further modify the original RAMPS technique, especially in the direction of SMA-first approach. In patients with borderline resectable pancreatic tumors or locally advanced tumors, after neoadjuvant treatment, a technique of radical resection with preservance of arterial vessels - “the TRIANGLE operation” has been elaborated. Despite the tremendous progress of surgical techniques, RT is still detected too late in the phase preventing effective resection.

In 2014, pancreatic cancer (PC) was the fourth most common cancer to which Europeans died [1]. This cancer is characterized by a very unfavorable prognosis, and the 5-year survival rate does not exceed 5% [2].

The only way to cure the patient with adenocarcinoma of the pancreas is surgical excision of the tumor [3]. Pancreatic resection is considered one of the most difficult operations in the gastrointestinal surgery, requiring not only excellent knowledge of the conditions and possible anomalies of the upper abdominal cavity, but also the ability to pre-operatively assess the severity of the disease. The difficulty of the operation is due to, i.a., the anatomic proximity of the pancreas and vital organs and structures such as: aorta, inferior caval vein, portal vein, hepatic, superior mesenteric and splenic arteries, bile ducts and duodenum.

## HISTORICAL OVERVIEW

The first successful operation due to pancreatic tumor was distal pancreatic resection (DPR) made in 1882 by Fryderyk Trendelenburg [4].

In 1903, Jan Mikulicz-Radecki described three barriers in pancreatic surgery [4,5], which today are still a challenge for operators. The first was to be the anatomical location of the pancreas. Another was the difficulty in early diagnosis of PC and its detection at the stage enabling effective resection. The last barrier according to Mikulicz was high perioperative mortality, which at the turn of the nineteenth and twentieth centuries resulted from the lack of intravenous fluid therapy, nutritional treatment and effective infection control [4,5].

Also in 1903, Theodor Kocher popularized the method of mobilizing the duodenum, allowing to overcome the first barrier of Mikulicz. He has undergone a surgical practice under the name of Kocher's maneuver [4].

The first successful pancreatoduodenectomy (PD) was performed in 1909 by Walther Kausch - son-in-law of Mikulicz and at the same time his successor at the Wrocław cathedral [4]. In order to minimize the risk of surgical complications associated with severe malnutrition and mechanical jaundice, Kausch decided to divide the treatment into two stages. In the first one he performed cholecysto-jejunostomy and Braun anastomosis [4]. Two months later, he performed an en-block resection of the distal part of the stomach, the proximal part of the duodenum and part of the head of the pancreas, followed by loop gastrojejunostomy and pancreatoduodenectomy. Nine months later, the patient died due to cholangitis [4].

In 1935, Allen O. Whipple described the method of anatomical PD as a two-step operation [6]. During the first treatment he performed gallbladder anastomosis and gastrojejunostomy. Three weeks after the first treatment he performed a second, based on the resection of the head of the pancreas and duodenum. In 1941, Whipple modified his operation so that both stages - resection and reconstruction - were a one-step, complete procedure [6]. The main factor responsible for Whipple's success was the use of silken sutures resistant to digestion by enzymes, unlike catgut sutures used previously [7].

The Kausch-Whipple procedure was standard in the treatment of resectable pancreatic cancer until 1972, when Traverso and Long-

**Tab. I.** Definition of borderline resectable pancreatic cancer according to various criteria; based on: Halperin DM, Varadhachary GR: Resectable, Borderline Resectable, and Locally Advanced Pancreatic Cancer: What Does It Matter? *Curr Oncol Rep* (2014) 16:366.

	MD ANDERSON	AHPBA	NCCN
SHX	adherence of tumor to vessel	adherence of tumor to vessel	adherence of tumor to vessel
CA	adherence of tumor to vessel	no contact between tumor and vessel	no contact between tumor and vessel
CHA	adherence or surrounding by tumor on a short section	adherence or surrounding by tumor on a short section	adherence or surrounding by tumor on a short section
SMV-PV	presence of venous thrombosis	adherence or surrounding of vessel by tumor or presence of thrombosis with preserved vessels on proximal and distal section of infiltration site	adherence or surrounding of vessel by tumor or presence of thrombosis with preserved vessels on proximal and distal section of infiltration site

SMA superior mesenteric artery, CA coeliac axis, CHA common hepatic artery, SMV superior mesenteric vein, PV portal vein

**Tab. II.** Criteria for pancreatic cancer resectability according to National Comprehensive Cancer Network version 2.2017.

PANCREATIC CANCER	RELATION TO ARTERIES	RELATION TO VENOUS VESSELS
resectable	The tumor does not adhere to large vessels (CA, SMA, CHA)	The tumor does not adhere to SMV and PV, or the adherence of the tumor to $\leq 180^\circ$ of the circumference of the vessel, without changing the shape of the venous vessel (SMV and / or PV)
potentially resectable	<p>Pancreatic head / hamulus tumor</p> <ul style="list-style-type: none"> <li>• Tumor adjacent to the common hepatic artery, not passing into the CA and CHA branch, conditions for safe and radical resection with reconstruction</li> <li>• tumor adhering to the SMA at <math>\leq 180^\circ</math> of its circumference</li> <li>• the presence of a vascular anatomical variant in the arterial system (e.g. an additional right hepatic artery) and its position relative to the tumor and / or infiltration by the tumor should be taken into account during the planning of the surgical technique</li> </ul> <p>Pancreas body / tail cancer</p> <ul style="list-style-type: none"> <li>• adherence of the tumor to CA at <math>\leq 180^\circ</math> of its circumference</li> <li>• adherence of the tumor to the CA at <math>&gt; 180^\circ</math> of its circumference without the features of pulling the wall of this vessel into the tumor, provided that the lesion is not in contact with the gastroduodenal artery (some experts believe that this criterion qualifies the case as inoperative)</li> </ul>	<ul style="list-style-type: none"> <li>• tumor adhering to SMV or PV at <math>\leq 180^\circ</math> of circumference, changing the shape of the vessel,</li> <li>• presence of venous thrombosis with preserved normal vessels on the proximal and distal part of the infiltration site, conditions for safe and radical venous resection with subsequent reconstruction</li> <li>• the tumor adheres to the inferior caval vein</li> </ul>
unresectable	<p>presence of distant metastases (including involvement of lymph nodes outside the regional lymph node group)</p> <p>Pancreatic head / hamulus tumor</p> <ul style="list-style-type: none"> <li>• adherence of the tumor to the SMA or CA at <math>&gt; 180^\circ</math> of the circumference</li> <li>• infiltration of the first ileal branch of SMA</li> </ul> <p>Pancreas body / tail cancer</p> <ul style="list-style-type: none"> <li>• adherence of the tumor to the SMA or CA at <math>&gt; 180^\circ</math> of the circumference</li> <li>• a tumor that adheres to CA and infiltrates the aorta</li> </ul>	<ul style="list-style-type: none"> <li>• no possibility of SMV / PV reconstruction due to infiltration or closure of vessel lumen</li> <li>• infiltration of the first ileal SMV branch</li> <li>• no possibility of SMV / PV reconstruction due to infiltration or closure of vessel lumen</li> </ul>

mire popularized the pylorus-preserving PD technique. This method was originally described in 1944 by Kenneth Watson [4]. In 1994 Gagner and Pomp performed the first laparoscopic PD, and in 2003 Giulianotti performed the first PD using a surgical robot [4].

## CRITERIA FOR PANCREATIC RESECTION

There is no commonly accepted definition of resection of pancreatic tumor in the literature. Table 1 presents a comparison of the three most commonly cited definitions of pancreatic changes on the borderline of resection developed by the MD Anderson Cancer Center (MDACC), the American Hepato-Pancreato-Biliary Association (AHPBA) and the National Comprehensive Cancer Network (NCCN). The pancreatic resection criteria developed by

the NCCN are presented in Table 2.

By using the NCCN criteria when analyzing CT or MR images, tumor unresectability can be very well assessed (positive predictive value  $> 90\%$ ) [3]. Unfortunately, the value of these criteria for resection evaluation is much lower ( $> 50\%$ ). The European criteria are referred to by the European Society of Oncology ESMO in its guidelines of 2015 [3].

## PANCREATODUODENECTOMY

The standard surgical treatment of resectable pancreatic carcinoma is considered the classic PD with the Kausch-Whipple procedure, or the pylorus-preserving PD with the Traverso-Longmire

**Tab. III.** The anatomy of arterial supply to liver.

	TYPE	DESCRIPTION	%
Michels (n = 200)	1	Normal	55
	2	Replaced LHA from LGA	10
	3	Replaced RHA from SMA	11
	4	Replaced RHA + LHA	1
	5	Accessory LHA from LGA	8
	6	Accessory LHA from SMA	7
	7	Accessory RHA + LHA	1
	8	Type 3+5 or Type 2+6	4
	9	CHA from SMA	2.5
	10	CHA from LGA	0.5
Hiatt et al. (n = 1000)	1	Normal	75.7
	2	Replaced or Accessory LHA	9.7
	3	Replaced or Accessory RHA	10.6
	4	Type 2+3	2.3
	5	CHA from SMA	1.5
	6	CHA from aorta	0.2

LHA - left hepatic artery; LGA - left gastric artery; RHA - right hepatic artery; SMA – superior mesenteric artery; CHA - common hepatic artery

method [8]. During the classic PD Whipple method, the stomach is cut in half of its length, while in the Traverso-Longmire modification, the duodenum is cut about 2-3 cm after the pylorus. In 2016, a systematic review was published comparing both PDs in terms of survival, postoperative mortality, complications and quality of life after surgery [8]. The authors found no statistically significant differences between the two methods.

The most difficult technically and at the same time the most important from the point of view of the oncological PD stage is the separation of the head of the pancreas from the mesenteric artery [9]. In the classical technique, the neck of the pancreas is separated from the combination of the superior mesenteric vein and the portal vein. Then, the pancreas is cut along the venous plane. The uncinate process and the head of the pancreas can then easily be dissected from the surrounding tissues. Only at this stage of surgery can the surgeon attempt to separate the head of the pancreas from the mesenteric artery.

Over the last decades several PD modifications have been developed, focusing on this maneuver in the early phase of the operation, i.e. before the pancreas is cut, which is considered an irreversible stage of the procedure [9]. Procedures for obtaining a retroperitoneal margin around the upper mesenteric artery at the initial stage of PD in the English literature are named “artery-first approach” or “SMA-first approach”.

Various ways of artery-first approach have been developed. Del Chiaro et al. described a method based on a combination of the Koher maneuver and Cattell-Brascha maneuver [10]. The first step in this technique is to perform a wide Kocher maneuver, i.e.

mobilization of the descending duodenum by incision of the peritoneum along the lateral side of the duodenal. Next, the Cattell-Brascha maneuver is performed, which involves actuation of the caecum, the right half of the colon and the hepatic flexures from the right side in the medial direction, and mobilization of the posterior appendices of the small intestine in cranial direction [10]. In this way, large retroperitoneal space vessels - the aorta and the inferior vena cava - are very well displayed. The further part of the preparation is carried out in the cranial direction until the left renal vein and superior mesenteric artery are visible [10].

Another technique for SMA-first approach is Inferior Infracolic Superior Mesenteric Artery First Approach described for the first time by Weitz et al. [11]. Zhu et al. modified the Weitz method by abandoning the initial modified Kocher’s maneuver [12]. The first stage in their technique is transverse colon elevation. In this way, the superior mesenteric artery and vein are visible at the base of the mesentery of the transverse colon [12]. Then, both vessels are dissected and marked with ribbons. Further preparation takes place in the cranial direction, along the right surfaces of the superior mesenteric vessels up to the lower edge of the pancreas [12]. After cutting the gastrocolic ligament, the posterior surface of the pancreas is dissected and the ability to separate the head of the pancreas from the mesenteric artery is assessed [12]. Aosasa and Kawabata suggest upper access obtained by the release of duodeno-jejunal flexure (Superior mesenteric artery-first approach) [13,14].

Procedures for artery-first approach to retroperitoneal vessels are recommended because:

- They allow an early assessment of resection, without unnecessary prolongation of surgery, before the irreversible stage of surgery [9].
- They allow obtaining satisfactory parapancreatic margins of resection, especially medial and retroperitoneal [9].
- They facilitate the identification of common hepatic artery, especially in cases of anomaly of its course [7, Table 3].
- They protect against overfilling of venous vessels in the removed preparation before resection, which reduces intraoperative blood loss [9].

The complication of artery-first approach procedures is the possibility of severe diarrhea in the postoperative period [12]. Although it disappears after treatment with loperamide, it can significantly impair the post-operative comfort of patients [12]. The cause of diarrhea is skeletonizing of the superior mesenteric artery [12]. It can be prevented by maintaining the vascular arcade of the final section of the small intestine [12].

Simultaneously with the introduction of techniques of “artery-first approach” the terms „mesopancreas” and “systematic mesopancreas dissection” were created [9]. Mesopancreas is considered to be the nervous-vascular structure connecting the posterior surface of the pancreas, superior mesenteric artery with its surroundings and the right celiac ganglia [9]. Mesopancreas include: first and second nerve plexus around the head of the pancreas, inferior pancreaticoduodenal artery with its branches, arteries and veins of the jejunum and surrounding lymph nodes [9].

Complete removal of the mesopancreas together with the proximal part of the jejunum is considered an R0 resection in the case of a tumor of the head of the pancreas with direct or indirect vascular

invasion, or metastases to regional lymph nodes, and in English literature it is referred to as pancreatoduodenectomy with systematic mesopancreas dissection (SMDPD) [9]. Mesojejunum is considered to be a part of the small intestine vascularized by arterial branches from the superior mesenteric artery to the level of the inferior pancreaticoduodenal artery [9]. SMDPD is divided into three levels, depending on the extent of resection around and along the mesenteric artery. Qualification for a given level of resection depends on the type of tumor pathology [9]. For the first level of SMDPD, patients are qualified who do not need to undergo lymphadenectomy, i.e. with a low-grade lesion, pre-invasive cancer (carcinoma in situ) or intraductal papillary mucinous neoplasm; IPMN) [9]. On the first level of SMDPD, the nerve plexus around the superior mesenteric artery and arterial and venous jejunal branches is preserved, because removal of tissues to the left from the superior mesenteric vein is not necessary [9]. The indication for the implementation of SMDPD at the second level is carcinoma of the ampulla of Vater, duodenal carcinoma and carcinoma of the distal part of the common bile duct [9]. Resection at this level involves en bloc removal of the mesopancreas lymph nodes to the level of exit of the inferior pancreaticoduodenal artery, which is ligated at the base [9]. The third level of SMDPD is to remove all perivascular and lymphatic tissue to the right from the superior mesenteric artery. An indication to perform resection at this level is systemic PC or advanced cholestasis cancer [9].

The main branch of the celiac trunk is usually the common hepatic artery, which moves away from it cranially in relation to the pancreas. Before deciding on pancreatic resection, possible anomalies of this artery should be recognized. These atypical arteries may be both additional as well as the only vessels that supply the liver with arterial blood [7].

In 1966 Michels published a work written on the basis of 200 sectional examinations, in which he defined the basic variants of arterial liver vasculature [15, Table 3]. In 1994, Hiatt et al., based on the analysis of 1000 cases of patients undergoing orthotopic liver transplantation, modified the traditional Michels classification [16, Table 3]. In Michels' material, anomalies of liver arterial vascularization accounted for 45% of cases, whereas in Hiatta et al. 24.3% [15, 16, table 3].

## RANGE OF LYMPHADENECTOMY IN PD

The involvement of lymph nodes in patients with resective PC is an important prognostic factor. Lymphadenectomy is important for proper assessment of the stage of development (pN feature).

In 2012, Nimura et al. published the results of a multicenter randomized study conducted in Japan [17]. The study compared the value of PD with standard and PD with extended lymphadenectomy in patients without any complementary treatment (chemotherapy). The study included 112 patients operated between March 2000 and May 2003 in 14 leading Japanese centers [17]. The operations were performed by experienced surgeons, each of whom performed at least 50 PD with extended lymphadenectomy. Before the start of the study, technical details of the procedures were agreed, conditioning the study entry [17]. Surgeons considered standard lymphadenectomy to be the removal of lymph nodes stations no. 13a, 13b, 17a and 17b [17,18,19]. Additional removal of lymph node

stations no.8a, 8p, 9, 12a, 12b, 12p, 14p, 14d, 16a2, 16b1 [17,18,19] was treated as a radical operation. The average time of surgery, the number of lymph nodes collected and intraoperative blood loss were greater in the group undergoing extended lymphadenectomy [17]. The study showed that extended lymphadenectomy in radical PD does not bring benefits in the form of a longer post-operative survival [17]. Percentage of complications, postoperative mortality and quality of life were similar [17].

In 2014, the International Study Group on Pancreatic Surgery; ISGPS concluded that extended radical lymphadenectomy is not recommended [20]. The removal of the following nodes was considered a standard lymphadenectomy in PD: 5, 6, 8a, 12b1, 12b2, 12c, 13a, 13b, 14a, 14b, 17a and 17b [20].

The histopathologist should assess the following surgical margins: anterior, posterior, medial (superior mesenteric vein), superior mesenteric artery, pancreatic cutoff line, bile duct (common hepatic duct), small intestine [3]. Due to the high percentage of local recurrences, it is particularly important to assess the retroperitoneal area containing perineural connective tissue adjacent to the mesenteric artery [3].

A meta-analysis from 2015 highlights the wide variety of histopathological protocols and margin definitions for R0 and R1 resections [21]. Lack of standards for histopathologists causes a discrepancy in the reported frequencies of local recurrence after R0 resections in individual centers. This, in turn, translates into contradictory results from large retrospective studies, randomized trials and meta-analyses. Some confirm and others deny the prognostic significance of the R0 margin [22]. Without the adoption of uniform definitions and standards, it is not possible to conduct reliable studies comparing histopathological reports from surgical resections with adjuvant treatment, which hinders the progress in the treatment of resectable PC [22]. In recent years there have been several works from European centers proposing new standards for histopathological documentation, circular margins and new definitions of R0 and R1 margins [23]. The new definition of R0 resection includes cases where the cancer-free margin is 1mm, and R1 resection, when the margin is <1mm. The above definitions are included in the latest ESMO guidelines [3]. Authors from the center in Heidelberg compared groups of patients after resection R0 defined according to the new definition (average survival - 41.6 months, 5-year survival - 37.7%) and a group defined as R0 according to old findings, when the margin is 0 mm (average survival - 33.7 months, 5-year survival - 33.6%) [22]. A statistically significant increase in survival times in the first of these groups confirmed the clinical significance of the new standards [22].

## PREOPERATIVE DRAINAGE OF THE BILE DUCTS

One of the complications of malignant tumors around the Ampulla of Vater is the obstruction of distal bile duct sections. It causes cholestasis, mechanical jaundice and persistent pruritus. Cholestasis may, however, cause coagulation disorders, immune disorders and cholangitis, which in turn may cause an increase in PD complications, or even be contraindications to resection [24]. Preoperative drainage of the bile ducts performed in the endoscopic way, in cases of resectable PC is intended to relieve the symptoms and prevent acute cholangitis [24]. The procedure is associated with

1-30% of complications and mortality at 0.2-1% [24]. The most common complications are acute pancreatitis (1-15%), cholangitis, duodenal bleeding and duodenum perforation [24].

The lack of recommendations from scientific societies regarding bile duct drainage in cases of resection of tumors around the Ampulla of Vater and high efficiency (90-95%) of this procedure causes that it is performed routinely and, in some patients, unnecessarily. Indications which are the most frequently indicated in the literature for biliary drainage before the performance of PD are: high hyperbilirubinemia, cholangitis, persistent pruritus, decompression of cholestasis in patients with borderline resectable tumors for whom neoadjuvant treatment is planned [25]. The subject of the discussion is the cutoff point for the level of total bilirubin in blood serum, which would indicate the need for drainage. In most cases, it is between 200  $\mu\text{mol} / \text{l}$  (about 11.7 mg / dl) and 400  $\mu\text{mol} / \text{l}$  (about 23.4 mg / dl) [24]. Drainage should be considered in the case of elderly with additional diseases during an interview [24]. In young people, without additional burdens, resection should be planned in the foreground even with high hyperbilirubinemia [24].

The latest literature - including 4 meta-analyses, one randomized multicenter study and one retrospective study - proves that unnecessary endoscopic biliary drainage in cases of resection of tumors around the Vater's papilla increases the incidence of serious perioperative complications (Clavien-Dindo > 2), including mortality perioperative and is not beneficial in improving the results of surgical resections [24,26,27,28,29,30]. Some studies prove an increased incidence of surgical site infections in patients after bile duct drainage [28,31,32]. A retrospective French study reports on isolated cases of local inflammatory fibrosis around the head of the pancreas initiated by bile duct drainage, which prevents the subsequent performance of safe PD [24]. The implementation of bile duct drainage extends the waiting time for surgery by about 33 days [24]. Sanjeevi et al. report an increase in the risk of progression of a resectable tumor to unresectable if the time between the diagnosis and the surgery is longer than 32 days, and Glant et al. if the period is longer than 35 days [33,34]. Extending the waiting time for resection associated with unnecessary drainage of the bile ducts can therefore make it unmanageable [24].

The issue of biliary drainage before planned PD shows how important it is to interdisciplinarily discuss each PC case before making any therapeutic intervention [24].

## CAN YOU PERFORM PANCREATODUODENECTOMY AND METASTASIS IN M1?

As shown by the survival curves, the only way to significantly extend and potential treatment of PC is radical R0 resection [35]. In reference to this, attempts were made to aggressive, extensive resections, extended to include lymphadenectomy of extra-regional lymph nodes and even metastasectomy of liver metastases [35]. The results of the published reports are different and depend on the center from which they come [36,37]. One of such reports is the publication of Shrikhande et al., in a retrospective analysis they compared a heterogeneous and small (n = 29) group of patients in whom R0 / R1 resection of pancreas combined with metastasectomy was performed, with a group of 287 patients without

metastatic changes (M0) also after R0 / R1 resection. The blood loss, mean length of hospitalization, post-operative complications and laparotomy in both groups was similar. The average survival time in the study group was 13.8 months. The authors state that pancreatic resection in M1 disease can be safe if performed in a specialized reference center in carefully selected patients [35]. However, such aggressive surgical treatment of generalized disease is not mentioned in the NCCN and ESMO guidelines, nor has it been subject to any meta-analysis.

## DISTAL PANCREATIC RESECTION (DRT)

About 25% of PC is localized in the head and tail of the pancreas, but rare types of cancer may also develop there, including: carcinoma of the acinar cells, intraspinal papillary mucinous neoplasm (IPMN), mucoid cystic tumor, pancreatoblastoma (Wilms tumor), neuroendocrine tumors, including those derived from cells of the endocrine part of the pancreas and hormone-producing (insulinoma, glucagonoma, VIPoma), serous cystadenocarcinoma; solid pseudopapillary neoplasm of pancreas (Hamoudi tumor).

Resectability of the pancreatic stem and tail tumors is smaller than resectability of tumors located in the head, because in these patients the tumor growth is not preceded by signaling symptoms, e.g. jaundice.

In the course of DRT, the pancreas is cut at the level of its isthmus, in the place of adherence of the portal vein / superior mesenteric vein [38].

Depending on the scope, we distinguish three types of DRT: DRT with splenectomy, DRT with preservation of the spleen and its main vessels as well as DRT with preservation of the spleen and resection of spleen vessels using the Warshaw technique. The choice of the type of resection depends on the type of pathology and intraoperative conditions. It should be remembered that ligation of the splenic artery does not require splenectomy, whereas in the case of ligation of the splenic vein it is necessary [7]. Preparing the vein and splenic artery is the most difficult stage of the second type of DRT mentioned above. During surgery with the Warshaw technique, the condition for preserving the spleen with simultaneous resection of splenic vessels is to save the short gastric arteries and vena gastroomentalis sinistra.

In recent years, many new solutions have been introduced in the treatment of resectable and borderline resectable pancreatic head cancer such as the „artery-first approach” technique, resection of the superior mesenteric vein / portal vein followed by vascular reconstruction, induction chemo-radiotherapy. All these activities are aimed at facilitating the achievement of R0 resection in PD traces. Due to the highly aggressive biology, the tendency to early involvement of regional lymph nodes and the less frequent occurrence, the cancer of the peripheral part of the pancreas was much less frequently the subject of clinical trials. Traditional DRT technique, due to cancer, is associated with a high percentage of positive margins, insufficient number of removed lymph nodes, low survival rates [39, 40]. The answer to the need to modify the traditional DRT technique was a study published in 2003 by Strasberg et al. describing a new technique, which they called the Radical Antegrade Modular Pancreato-Splenectomy (RAMPS) [41]. In the traditional surgical technique, the surgeon's direction

of actions goes from the left to the right side of the patient, and the spleen and pancreas are triggered at the early stage of the procedure, before checking the large vessels and cutting the pancreas [40]. This method of surgical access is associated with limitations in visualization of the posterior resection plane, potential bleeding resulting from late vascular control and inadequate lymphadenectomy [40]. In RAMPS, surgical operations proceed from the side of the pancreas head towards the tail, the pancreas is cut early, and the splenectomy is performed at the final stages of the procedure [40]. According to the original Strasberg method, if the tumor in CT reoperative assessment does not infiltrate the posterior capsule of the pancreas, the course of the resection plane should reach up to the anterior renal capsule (anterior RAPMS) [41]. In the case of infiltration into the posterior pancreas, the posterior RAMPS procedure should be performed including left-sided adrenalectomy and Gerota's fascia [41]. The reason for such deep intervention in the retroperitoneal space is the tendency of PC to create microfoci penetrating deeper than suggested by CT images and palpation of the surgeon [41]. In the last decade, RAMPS has been increasingly performed, especially in Japan and Korea [39]. However, the number of patients using this method is still too small to carry out a randomized clinical trial comparing RAMPS results with those of traditional DRT [39]. Only one meta-analysis based on 6 retrospective works is available, comparing a group of 152 RAMPS patients with a group of 226 patients who have gone through traditional DRT [39]. Using the RAMPS technique, a higher percentage of R0 resections and a higher mean number of removed lymph nodes were obtained. The authors considered RAMPS a safe and beneficial oncological procedure [39]. However, they stressed the need for further studies assessing post-operative survival after this technique [39]. Currently, following the PD model, attempts are made to further modify the original RAMPS technique, especially in the direction of SMA-first approach.

Pancreas body and tail cancer is often recognized in the infiltration phase of the celiac trunk and its branch, i.e. at a stage that is traditionally considered to be inoperable. A chance for a radical resection for some of these patients is Appleby's surgery [42]. The procedure includes DRT with splenectomy and visceral resection. The success of this procedure depends on the presence of arterial collateral circulation through the superior pancreaticoduodenal artery and the gastroduodenal artery, which is to ensure the supply of arterial blood to the liver [42]. If the collateral circulation is inefficient, in order to ensure proper arterial vascularization for the liver and stomach, one must additionally perform a vascular reconstruction - a modified Appleby procedure. However, only single cases of this type of surgery in carefully selected patients are described in the literature. Before performing this type of resection, the surgeon must thoroughly analyze the anatomical variant of hepatic arterialization present in a given patient in order to perform appropriate vascular reconstruction if necessary [42].

In patients with borderline resectable pancreatic tumors or locally advanced tumors, after neoadjuvant treatment, Hackert et al. propose a technique of radical resection with preservation of arterial vessels, which they called „the TRIANGLE operation” [43]. CT scans often do not distinguish between neoplastic infiltration and arterial infiltration and chemotherapy-induced fibrosis (especially in the FOLFIRINOX scheme) [43]. Therefore, in some centers, patients after neoadjuvant treatment who have experienced regression of the tumor or in whom the disease has stabilized, de-

spite radiological suspicion of arterial infiltration, are subjected to resection [43]. After exclusion of peritoneal and hepatic metastases, Hackert et al. suggest using one of the methods of early access to retroperitoneal vessels [43]. From the place suspected of neoplastic infiltration onto the superior mesenteric artery or the celiac trunk, a section is taken for intraoperative histopathological examination [43]. If the neoplastic character of the infiltration is confirmed, resection is usually withdrawn [43]. Otherwise, you go to the next stage of surgery, which is a careful dissection of the superior mesenteric artery and the celiac trunk, to the adventitia [43]. If the tumor infiltrates neural or lymphatic plexuses, the arteries should be dissected to the place of their departure from the aorta [43]. The next stage is complete lymphadenectomy of the area [43]. One should carefully remove all soft tissues within the triangle delimited by the superior mesenteric artery, the celiac trunk and the portal vein [43]. In the case of DRT, the superior mesenteric artery and the celiac trunk should be thoroughly stripped from the left side, during the PD from the right side and during the total pancreatoduodenectomy in a circular manner [43]. Using this technique during total pancreatoduodenectomy, the left vena cava is usually subject to damage, which requires distal or even subtotal gastrectomy [43]. Heckert et al. emphasize that the technique they describe should be reserved only for centers of high referentiality, because preparation in the layer of adventitia of large arteries can result in their damage and the necessity of performing arterial resection followed by reconstruction [43].

## SCOPE OF LYMPHADENECTOMY IN DRT

SGPS concluded that in cases of pancreatic body and tail carcinomas, standard lymphadenectomy should include lymph node stations 10, 11 and 18 [18]. In the presence of metastases onto lymph nodes outside the standard scope of resection, ISGPS accepted both pancreatic resection (in carefully selected patients) and unresectable palliative treatment [18] as an acceptable form of treatment.

## DRAINAGE AFTER RESECTION OF THE PANCREAS

The purposefulness of draining the postoperative field in gastrointestinal surgery has recently undergone numerous discussions. In 2017, a meta-analysis evaluating the usefulness of drainage after resection of the pancreas appeared [44]. The study did not show any significant differences in 30-day post-operative mortality, general morbidity, and the frequency of surgical re-interventions between the group of patients in whom the postoperative field was drained compared to the group without drainage [44].

## THE ROLE OF HIGH-REFERENTIALITY CENTERS IN PANCREATIC SURGERY

The key role of high reference centers in pancreatic surgery has been repeatedly proven in numerous publications [45,46]. Centers in which a large number of such operations are performed have significantly fewer complications, lower post-operative mortality, and longer post-operative survival. In 2010-2012, a population study was conducted in Italy, which included all patients undergoing PC operative treatment in this country [47]. The probability of performing palliative surgery in Italian hospitals was much higher

in centers with very low referentiality than in centers with the highest referentiality values [47]. The authors believe that in low-referentiality centers there was an abuse of operational unresectable procedures, which, according to the standards in pancreatic surgery, should be performed rarely [47]. The study also showed that patients without metastatic changes had a better chance of resection in higher-grade facilities [47]. Different factors can influence these differences between centers. One of them may be the low quality of CT scans performed in smaller hospitals and less experience of radiologists assessing them. Another factor is the surgeon's lower experience, which can overestimate vascular involvement or not be able to perform vascular resection [47]. During the restaging performed in a high referentiality facility, it turned out that the majority of patients without metastatic lesions after an earlier attempt of resection in the center with less experience had an anatomically resectable tumor [47]. The third factor may be too frequent resolution of bile obstructive problems in the surgical path, instead of endoscopic, which often results from the lack of ERCP access in field hospitals [47]. Too frequent surgical palliative procedures were considered by the authors as abuse of healthcare. According to the definition, it is a benefit in which the damage exceeds the benefits, and the low quality of the services provided generates costs [47].

## LAPAROSCOPIC SURGERY

Due to the numerous advantages of laparoscopy, in the 90s of the last century, it was introduced to pancreatic surgery. At the beginning, mainly enucleations and distal pancreatic resections were performed from the laparoscopic approach, with time also pancreaticoduodenectomy.

According to the meta-analysis from 2011, DRT in the open procedure takes less time and is associated with a greater number of removed lymph nodes [48]. The benefits resulting from the minimally invasive procedure were shorter hospitalization time and shorter convalescence time.

In 2017, a meta-analysis comparing minimally invasive PD with

an open procedure was published [49]. The study showed that the laparoscopic procedure lasts longer, is associated with less intraoperative blood loss, shorter hospitalization time and a comparable number of postoperative complications. The authors emphasized, however, that laparoscopic PD should be performed only in centers specialized in pancreatic surgery, having at the same time extensive experience in laparoscopic surgery. The main obstacles in the dissemination of PD by laparoscopic method are: difficulties in obtaining an appropriate retroperitoneal margin, a complicated reconstructive phase, a longer period of surgery, and lack of evidently proven scientific advantages in comparison with the classical technique [50].

## SURGERY USING SURGICAL ROBOTS

The main advantages of robotic surgery are a three-dimensional image with the possibility of scaling, seven degrees of freedom in the manipulation of robot tools imitating human wrist work and allowing for greater motion precision, intuitiveness of the system and thus a shorter learning curve than in laparoscopy. Operation with a robot is more like an open technique than traditional laparoscopy, which is why it is considered a safe procedure [50]. However, there are no studies comparing open, laparoscopic and surgical methods in pancreatic surgery, as well as reports from long-term follow-up after resection of the pancreas using a robot, including the assessment of long-term survival after this type of surgery. Robotic surgery generates high costs, and its availability is limited to large centers.

## SUMMARY

The enormous advances in surgical techniques and postoperative care have overcome two of the three barriers to pancreatic surgery described by Mikulicz. Still, PC is detected too late in the phase preventing effective resection. In addition, its high aggressiveness and resistance to modern chemo-radiotherapy are associated with low rates of long-term survival.

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