**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 63267

**Manuscript Type:** MINIREVIEWS

**Borderline resectable pancreatic cancer and vascular resections in the era of neoadjuvant therapy**

Mikulic D *et al*. Borderline resectable pancreatic cancer and vascular resections

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**Author contributions:** Mikulic D and Mrzljak A made contributions to the conception and design of the study, collecting of data and in drafting and revising the manuscript; both authors read and approved the final manuscript.

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**Received:** January 27, 2021

**Revised:** March 1, 2021

**Accepted:** May 27, 2021

**Published online:** July 16, 2021

**Abstract**

While pancreatic cancer is still characterized by early systemic spread and poor outcomes, the treatment of this disease has changed significantly in recent years due to major advancements in systemic therapy and advanced surgical techniques. Broader use of effective neoadjuvant approaches combined with aggressive surgical operations within a multidisciplinary setting has improved outcomes. Borderline resectable pancreatic cancer is characterized by tumor vascular invasion, and is a setting where the combination of potent neoadjuvant chemotherapy and aggressive surgical methods, including vascular resections and reconstructions, shows its full potential. Hopefully, this will lead to improved local control and curative treatment in a number of patients with this aggressive malignancy.

**Key Words:** Pancreatic adenocarcinoma; Borderline resectable; Neoadjuvant therapy; Venous resection; Arterial resection; Vascular reconstruction

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**Citation:** Mikulic D, Mrzljak A. Borderline resectable pancreatic cancer and vascular resections in the era of neoadjuvant therapy. *World J Clin Cases* 2021; 9(20): 5398-5407

URL: https://www.wjgnet.com/2307-8960/full/v9/i20/5398.htm

DOI: https://dx.doi.org/10.12998/wjcc.v9.i20.5398

**Core Tip:** Curative treatment of pancreatic ductal adenocarcinoma is only possible after margin negative surgical resection. Borderline resectable pancreatic cancer is characterized by vascular tumor involvement and the need to perform vascular resection to achieve radical resection. This report reviewed the characteristics of borderline resectable pancreatic cancer and the current treatment perspectives, including aggressive surgical approaches in the era of neoadjuvant therapy.

**INTRODUCTION**

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive disease with a dismal prognosis, currently the tenth most common cancer and the fourth leading cause of cancer-related mortality[1]. Its incidence is rising, and the current 5-year overall survival is only about 5%[2]. While major advancements have recently been made with systemic treatment, only a radical surgical resection gives the possibility of long-term survival and cure[3]. Long-term survival in non-resected patients has been reported only exceptionally[4]. Unfortunately, most pancreatic cancer patients are diagnosed with locally advanced or metastatic disease that precludes curative resection. Due to the aggressive nature of the disease and late onset of symptoms, only 10%-20% of patients present with resectable or borderline resectable disease[5].

Numerous studies have reported beneficial effects of neoadjuvant chemotherapy (NAT) in different cancers of the digestive system, namely rectal, gastric and esophageal carcinomas[6-8]. In recent years, promising results have appeared from clinical research of neoadjuvant chemotherapy and chemoradiotherapy for PDAC[9-12]. There are several possible benefits of NAT in PDAC. Firstly, the margin negative (R0) resection rates could be improved in borderline resectable pancreas cancer (BRPC). Only an R0 resection gives the chance of cure in PDAC, and it has been shown that an R0 resection with at least 1 mm margin correlates with improved survival[13,14]. Secondly, some patients with locally advanced (LA) PDAC, initially not amenable to surgical resection, could be downstaged with NAT, converting them from unresectable to resectable disease[9-12]. Finally, while adjuvant chemotherapy should be the standard of care after upfront resection for PDAC, almost half of the patients never receive adjuvant chemotherapy due to postoperative complications or poor performance status[15]. NAT, being independent of surgical morbidity, can increase the number of patients that receive chemotherapy leading to better systemic and local control of the disease translating into improved outcomes[16].

Due to the retroperitoneal location of the pancreas and its intimate contact with the neighboring vessels, vascular invasion by the tumor is a hallmark of PDAC. However, thanks to advancements in surgical techniques and perioperative management, tumor infiltration of the superior mesenteric vein/portal vein (SMV/PV), superior mesenteric artery (SMA), hepatic artery (HA), or celiac artery (CA) is no longer a contraindication to surgery. Over the last 20 years, resections and reconstructions of the diseased vessels have become the standard of care in experienced centers, and they play a major role when securing a curative resection. A number of innovative surgical modifications have appeared with the goal of safe and radical resection of all of the tumor-infiltrated tissue regardless of vascular involvement. Promising results of NAT appear to be central in the attempt to achieve optimal effects of these complex and challenging surgical procedures[3,17,18].

**BRPC**

The National Comprehensive Cancer Network first adopted the definition of borderline resectable pancreatic cancer (BRPC) in 2006, and it is based on the extent of arterial and venous involvement by the tumor. Specific anatomic factors include tumor contact with the superior mesenteric artery and/or celiac artery of less than 180 degrees without showing stenosis or deformity, tumor contact with the common hepatic artery without showing tumor contact with the proper hepatic artery and/or celiac artery, and tumor contact with the superior mesenteric vein and/or portal vein including bilateral narrowing or occlusion without extending beyond the inferior border of the duodenum[19]. Apart from anatomic factors, recent expert attempts were directed to broaden the definition of BRPC by including biologic and conditional dimensions (*e.g.*, positron emission tomography (PET) positivity, CA 19-9 Levels, Eastern Cooperative Oncology Group (ECOG) performance status), acknowledging the fact that resectability is not defined solely by anatomic factors, but that the biology of the tumor and performance status of the patient bear equal importance[20]. Different classifications of borderline resectable pancreatic cancer are presented in Table 1[18-20].

Despite surgical resectability in experienced centers, BRPC is burdened with an increased risk of positive resection margins and postoperative recurrence[21,22]. This is the rationale behind the idea of NAT for BRPC, and the current National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines recommend NAT for patients with BRPC[23].

A number of studies, some of them within a controlled randomized setting, show promising data with NAT in BRPC. A Dutch multicenter controlled randomized study (PREOPANC) was recently published including patients with resectable PC and BRPC. The patients were randomized either to upfront surgery or NAT with gemcitabine combined with radiation, followed by surgery and adjuvant gemcitabine. The BRPC subgroup undergoing NAT had a significant advantage in survival (overall survival: 17.6 mo *vs* 13.2 mo), a higher R0 resection rate, and less chance of having positive lymph nodes[24]. A study by authors from Korea compared neoadjuvant chemoradiation with gemcitabine to upfront surgery in patients with BRPC and found better 2-year survival and median survival (40.7% and 21 mo *vs* 26.1% and 12 mo) for patients with NAT[25]. In a study from Japan, patients with resectable PC and BRPC were randomized to NAT with gemcitabine and S-1 or upfront surgery followed by adjuvant chemotherapy with gemcitabine. Patients from the NAT group had better overall survival (36.7 mo *vs* 26.6 mo) without differences in resectability rates or resection margins[26]. However promising, it should be noted that the results of these studies should be interpreted with caution. Some of the concerns include heterogeneity of NAT regimens, variable application of concurrent radiation, and lack of differentiation between cases with arterial abutment and the patients with venous involvement only. There are several more ongoing randomized trials that will supposedly shed more light on the effects of NAT on survival, resectability, and R0 rates in BRPC. The results from recent systematic reviews and meta-analyses are also encouraging, particularly those that are based on comparative studies with intention-to-treat analysis[27-29]. Resection rates and R0 rates in the analyzed reports are highly variable, again highlighting the heterogeneity of the patient populations. While resectability rates after NAT are not always superior to upfront surgery, R0 rates for BRPC after NAT reported in these systematic reviews are encouraging and often comparable to initially resectable PC.

**Venous resections**

Almost 50 years ago, Joseph Fortner first reported a series of patients treated with pancreatectomy combined with vascular resection and reconstruction[30]. Reported perioperative morbidity and mortality rates were high, but still comparable to the rates achieved with conventional pancreas resections performed at the time[31,32]. Despite such evidence, pancreatic surgeons were mostly reluctant to perform vascular resections and reconstructions concomitantly with pancreas resections well into the 1990s. Over the years, wider familiarity with vascular reconstruction techniques, centralization of PDAC patients in high volume centers, advancements in perioperative management and evolution of systemic therapies including NAT have led to pancreaticoduodenectomies (PD) being associated with venous resection in up to 25% in Europe and even more in Japan[33-36]. Distal splenopancreatectomies, on the other hand, require venous resections less often[37]. Radiologic classification of SMV/PV invasion includes: Type A: no invasion, Type B: unilateral narrowing, Type C: bilateral narrowing, Type D: stenosis or obstruction with development of collateral circulation[38]. The same group defined three grades of pathological vessel invasion: grade 0: no invasion, grade 1: tunica adventitia invasion, grade 2: tunica media invasion, grade 3: tunica intima invasion[39]. Notably, the extent of tumor venous invasion is often poorly evaluated in pathology reports, and its prognostic value is debatable[40,41]. Interestingly, the rate of true vascular infiltration is relatively low (between 47% and 60%), reflecting the difficulty to intraoperatively differentiate between venous tumoral invasion and fibrotic changes secondary to peritumoral inflammation, especially after NAT[42-44].

As for the surgical technique, reconstruction after resection of the SMV/PV can be performed as a lateral, tangential resection and primary suture, repair using a venous patch, end-to-end anastomosis, or reconstruction using an autologous or synthetic interposition graft, depending on the type and length of vessel involvement by the tumor[22]. Adequate mobilization of the mesenteric root usually provides for a safe, tension-free end-to-end anastomosis, even in vein resections ranging up to several centimeters[17]. The use of synthetic grafts may be associated with the risk of infection, particularly worrying in the setting of a pancreatic fistula and the associated risk of postoperative hemorrhage[45]. However, the type of reconstruction technique does not affect the outcomes in terms of perioperative morbidity or mortality[43,46]. Distal locations of SMV involvement are more challenging than proximal when it comes to reconstruction because of the smaller diameter and branching of the SMV. According to current guidelines, involvement of the SMV below the inferior margin of the duodenum is considered to be the marker of unresectability of BR PDAC[20]. The alternative classification proposed by the NCCN in 2016 defined resectability based on the contact of the tumor with the first and second jejunal venous branches; however, this is often difficult to assess intraoperatively[20].

Venous resection performed concomitantly with pancreas resection in patients with vascular involvement seems to result in similar surgical mortality and perioperative morbidity rates when compared to standard pancreas resections. A number of single and multi-center studies have reported no difference in overall complication rates and postoperative mortality after PD with or without venous resection in patients who underwent upfront surgery[47-49]. Notably, most of the patients in these studies had not undergone NAT before surgery. On the other hand, when considering factors that affect overall and disease-free survival, several studies have shown higher R1 rates in patients undergoing venous resection without NAT[50,51]. Other negative prognostic characteristics associated with tumors requiring venous resection include larger tumor size, higher lymph node invasion rates, and worse tumor differentiation[52]. Several meta-analyses compared the outcomes of VR with conventional resections. They have confirmed the higher incidence of negative prognostic characteristics in patients undergoing VR without NAT (R1 resections, larger tumors, higher perineural invasion rates), and they suggest that NAT should be recommended in the setting of a planned venous resection[53-55].

**Arterial resection**

Not long ago, PDAC resection requiring concomitant arterial resection and reconstruction was performed only exceptionally and considered a controversial procedure limited to a small number of centers[56,57]. Reasons are manifold. Firstly, there are the apparent surgical technical challenges and inherent risks that reportedly portend increased surgical mortality due to possible complications such as graft thrombosis and mesenteric/hepatic ischemia or fatal hemorrhage[58]. Secondly, the celiac trunk and the SMA are invested within dense neural and lymphovascular tissue, making a margin negative resection technically demanding. Finally, infiltration of the arteries and the perivascular tissue can be considered to be a marker of a biologically aggressive disease, so the oncologic rationale of arterial resection for local tumor clearance in such cases may be questioned.

The use of potent and effective NAT followed by more aggressive and complex operative resections has improved local and systemic control providing improved outcomes in patients with BRPC and LA PC[59-61]. Even in BRPC with arterial infiltration where upfront resection is possible from the technical standpoint, recent evidence leans towards NAT first[17]. This is based on the results of several studies that have reported 5-year survival rates of up to 20% for selected patients who undergo arterial resection after NAT[62,63]. Regardless of the NAT regimen applied, surgical exploration should be carried out after restaging, provided there are no signs of systemic spread. Notably, the historical criteria of resectability by cross-sectional imaging are no longer appropriate in patients after potent NAT therapies. Current imaging techniques are often unable to distinguish between post-NAT fibrosis and viable tumor and patients without the signs of systemic spread or tumor progression after NAT should be surgically explored[64].

Over recent years several innovative surgical techniques have appeared when dealing with PDAC with arterial involvement. One of the widely used techniques is the “artery first” approach, where the SMA involvement is first assessed by dissection of the vessel from its origin. This can be accomplished *via* several anatomical routes, both inframesocolically and from the supracolic approach, from the left or right sides[65-67]. Once the infiltration of the SMA is confirmed or excluded, the type of reconstruction can be decided upon. The techniques used in arterial reconstruction include direct anastomosis, transposition of another artery (*e.g.*, splenic artery), and graft interposition with a venous graft, autologous or allogeneic artery. Microsurgical techniques used in liver transplantation have proven helpful and yielded excellent outcomes with minimal incidence of complications[68]. While splenic and left gastric artery can usually be resected and sacrificed without reconstruction, proper or common hepatic artery must be reconstructed to ensure hepatic perfusion. Distal pancreatectomy with celiac axis resection (DP-CAR) is an example of a long-known procedure that has shown excellent results in the era of NAT, sometimes combined with innovative techniques like aorto-hepatic bypass[69,70]. While there are some concerns regarding the safety of this procedure after reports of high postoperative mortality, most of the recent data show that this operation can be performed safely with acceptable median survival[71-73].

The struggle to achieve local control in patients with BR or LA PDAC has recently taken a new turn with the adoption of surgical strategies that take maximal advantage of the results of tumor downstaging in the era of NAT. The new techniques of periadventitial dissection or arterial divestment are applicable when the arterial adventitia is not affected by tumor invasion, and the periarterial neurolymphatic tissue can be dissected off the arterial wall by sharp dissection. This must include all of the soft tissue along the SMA and in the triangle between the CA, SMA, and the PV/SMV (mesopancreas excision or the triangle operation)[66,74,75]. This way, radical tumor clearance can be achieved without arterial resection and the associated morbidity[66,76,77]. In conclusion, survival rates after arterial resection for BRPC are encouraging, and postoperative morbidity and mortality rates, while once controversial, are acceptable today without a significant increase of the perioperative risk.

**CONCLUSION**

The combination of modern chemotherapy regimens, including those applied in the neoadjuvant setting and aggressive surgical methods, has shown promising results in the treatment of patients with pancreatic cancer. While most of patients with resectable PDAC still undergo upfront surgery, evidence shows that neoadjuvant therapy has benefits in patients with borderline resectable pancreatic cancer and locally advanced pancreatic cancer. Surgery for pancreatic cancer has taken advantage of several surgical innovations over the last 20 years. Venous resections are now part of a routine surgical approach to PDAC. Pancreatectomy combined with arterial resection is also feasible and should be considered in selected patients. Survival benefit exists in patients who undergo NAT before arterial resection. In conclusion, in the era of potent and effective systemic treatment, aggressive surgical operations for borderline resectable pancreatic cancer are justified and bring a clear survival benefit to a group of patients fraught with a history of poor outcomes.

**REFERENCES**

1 **Miller KD**, Goding Sauer A, Ortiz AP, Fedewa SA, Pinheiro PS, Tortolero-Luna G, Martinez-Tyson D, Jemal A, Siegel RL. Cancer Statistics for Hispanics/Latinos, 2018. *CA Cancer J Clin* 2018; **68**: 425-445 [PMID: 30285281 DOI: 10.3322/caac.21494]

2 **Global Cancer Observatory (Globocan)**. [cited 5 January 2021] Available from: https://gco.iarc.fr/

3 **Büchler MW**, Kleeff J, Friess H. Surgical treatment of pancreatic cancer. *J Am Coll Surg* 2007; **205**: S81-S86 [PMID: 17916525 DOI: 10.1016/j.jamcollsurg.2007.06.332]

4 **Oh SY**, Edwards A, Mandelson MT, Lin B, Dorer R, Helton WS, Kozarek RA, Picozzi VJ. Rare long-term survivors of pancreatic adenocarcinoma without curative resection. *World J Gastroenterol* 2015; **21**: 13574-13581 [PMID: 26730170 DOI: 10.3748/wjg.v21.i48.13574]

5 **Ryan DP**, Hong TS, Bardeesy N. Pancreatic adenocarcinoma. *N Engl J Med* 2014; **371**: 2140-2141 [PMID: 25427123 DOI: 10.1056/NEJMc1412266]

6 **Shivnani AT**, Small W Jr, Stryker SJ, Kiel KD, Lim S, Halverson AL, Talamonti MS. Preoperative chemoradiation for rectal cancer: results of multimodality management and analysis of prognostic factors. *Am J Surg* 2007; **193**: 389-93; discussion 393-4 [PMID: 17320541 DOI: 10.1016/j.amjsurg.2006.09.030]

7 **Cunningham D**, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, Scarffe JH, Lofts FJ, Falk SJ, Iveson TJ, Smith DB, Langley RE, Verma M, Weeden S, Chua YJ, MAGIC Trial Participants. Perioperative chemotherapy *vs* surgery alone for resectable gastroesophageal cancer. *N Engl J Med* 2006; **355**: 11-20 [PMID: 16822992 DOI: 10.1056/NEJMoa055531]

8 **Al-Batran SE**, Hofheinz RD, Pauligk C, Kopp HG, Haag GM, Luley KB, Meiler J, Homann N, Lorenzen S, Schmalenberg H, Probst S, Koenigsmann M, Egger M, Prasnikar N, Caca K, Trojan J, Martens UM, Block A, Fischbach W, Mahlberg R, Clemens M, Illerhaus G, Zirlik K, Behringer DM, Schmiegel W, Pohl M, Heike M, Ronellenfitsch U, Schuler M, Bechstein WO, Königsrainer A, Gaiser T, Schirmacher P, Hozaeel W, Reichart A, Goetze TO, Sievert M, Jäger E, Mönig S, Tannapfel A. Histopathological regression after neoadjuvant docetaxel, oxaliplatin, fluorouracil, and leucovorin *vs* epirubicin, cisplatin, and fluorouracil or capecitabine in patients with resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4-AIO): results from the phase 2 part of a multicentre, open-label, randomised phase 2/3 trial. *Lancet Oncol* 2016; **17**: 1697-1708 [PMID: 27776843 DOI: 10.1016/S1470-2045(16)30531-9]

9 **Gillen S**, Schuster T, Meyer Zum Büschenfelde C, Friess H, Kleeff J. Preoperative/neoadjuvant therapy in pancreatic cancer: a systematic review and meta-analysis of response and resection percentages. *PLoS Med* 2010; **7**: e1000267 [PMID: 20422030 DOI: 10.1371/journal.pmed.1000267]

10 **Katz MH**, Shi Q, Ahmad SA, Herman JM, Marsh Rde W, Collisson E, Schwartz L, Frankel W, Martin R, Conway W, Truty M, Kindler H, Lowy AM, Bekaii-Saab T, Philip P, Talamonti M, Cardin D, LoConte N, Shen P, Hoffman JP, Venook AP. Preoperative Modified FOLFIRINOX Treatment Followed by Capecitabine-Based Chemoradiation for Borderline Resectable Pancreatic Cancer: Alliance for Clinical Trials in Oncology Trial A021101. *JAMA Surg* 2016; **151**: e161137 [PMID: 27275632 DOI: 10.1001/jamasurg.2016.1137]

11 **Mellon EA**, Hoffe SE, Springett GM, Frakes JM, Strom TJ, Hodul PJ, Malafa MP, Chuong MD, Shridhar R. Long-term outcomes of induction chemotherapy and neoadjuvant stereotactic body radiotherapy for borderline resectable and locally advanced pancreatic adenocarcinoma. *Acta Oncol* 2015; **54**: 979-985 [PMID: 25734581 DOI: 10.3109/0284186X.2015.1004367]

12 **Boone BA**, Steve J, Krasinskas AM, Zureikat AH, Lembersky BC, Gibson MK, Stoller RG, Zeh HJ, Bahary N. Outcomes with FOLFIRINOX for borderline resectable and locally unresectable pancreatic cancer. *J Surg Oncol* 2013; **108**: 236-241 [PMID: 23955427 DOI: 10.1002/jso.23392]

13 **Strobel O**, Hank T, Hinz U, Bergmann F, Schneider L, Springfeld C, Jäger D, Schirmacher P, Hackert T, Büchler MW. Pancreatic Cancer Surgery: The New R-status Counts. *Ann Surg* 2017; **265**: 565-573 [PMID: 27918310 DOI: 10.1097/SLA.0000000000001731]

14 **van Roessel S**, Kasumova GG, Tabatabaie O, Ng SC, van Rijssen LB, Verheij J, Najarian RM, van Gulik TM, Besselink MG, Busch OR, Tseng JF. Pathological Margin Clearance and Survival After Pancreaticoduodenectomy in a US and European Pancreatic Center. *Ann Surg Oncol* 2018; **25**: 1760-1767 [PMID: 29651577 DOI: 10.1245/s10434-018-6467-9]

15 **Russ AJ**, Weber SM, Rettammel RJ, Mahvi DM, Rikkers LF, Cho CS. Impact of selection bias on the utilization of adjuvant therapy for pancreas adenocarcinoma. *Ann Surg Oncol* 2010; **17**: 371-376 [PMID: 19851808 DOI: 10.1245/s10434-009-0759-z]

16 **Heinrich S**, Pestalozzi BC, Schäfer M, Weber A, Bauerfeind P, Knuth A, Clavien PA. Prospective phase II trial of neoadjuvant chemotherapy with gemcitabine and cisplatin for resectable adenocarcinoma of the pancreatic head. *J Clin Oncol* 2008; **26**: 2526-2531 [PMID: 18487569 DOI: 10.1200/JCO.2007.15.5556]

17 **Hackert T**, Schneider L, Büchler MW. Current State of Vascular Resections in Pancreatic Cancer Surgery. *Gastroenterol Res Pract* 2015; **2015**: 120207 [PMID: 26609306 DOI: 10.1155/2015/120207]

18 **Müller PC**, Frey MC, Ruzza CM, Nickel F, Jost C, Gwerder C, Hackert T, Z'graggen K, Kessler U. Neoadjuvant Chemotherapy in Pancreatic Cancer: An Appraisal of the Current High-Level Evidence. *Pharmacology* 2021; **106**: 143-153 [PMID: 32966993 DOI: 10.1159/000510343]

19 **Katz MH**, Pisters PW, Evans DB, Sun CC, Lee JE, Fleming JB, Vauthey JN, Abdalla EK, Crane CH, Wolff RA, Varadhachary GR, Hwang RF. Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. *J Am Coll Surg* 2008; **206**: 833-46; discussion 846-8 [PMID: 18471707 DOI: 10.1016/j.jamcollsurg.2007.12.020]

20 **Isaji S**, Mizuno S, Windsor JA, Bassi C, Fernández-Del Castillo C, Hackert T, Hayasaki A, Katz MHG, Kim SW, Kishiwada M, Kitagawa H, Michalski CW, Wolfgang CL. International consensus on definition and criteria of borderline resectable pancreatic ductal adenocarcinoma 2017. *Pancreatology* 2018; **18**: 2-11 [PMID: 29191513 DOI: 10.1016/j.pan.2017.11.011]

21 **Callery MP**, Chang KJ, Fishman EK, Talamonti MS, William Traverso L, Linehan DC. Pretreatment assessment of resectable and borderline resectable pancreatic cancer: expert consensus statement. *Ann Surg Oncol* 2009; **16**: 1727-1733 [PMID: 19396496 DOI: 10.1245/s10434-009-0408-6]

22 **Bockhorn M**, Uzunoglu FG, Adham M, Imrie C, Milicevic M, Sandberg AA, Asbun HJ, Bassi C, Büchler M, Charnley RM, Conlon K, Cruz LF, Dervenis C, Fingerhutt A, Friess H, Gouma DJ, Hartwig W, Lillemoe KD, Montorsi M, Neoptolemos JP, Shrikhande SV, Takaori K, Traverso W, Vashist YK, Vollmer C, Yeo CJ, Izbicki JR; International Study Group of Pancreatic Surgery. Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2014; **155**: 977-988 [PMID: 24856119 DOI: 10.1016/j.surg.2014.02.001]

23 **NCCN**. Clinical Practice Guidelines in Oncology (NCCN Guidelines): NCCN, Pancreatic Adenocarcinoma, Version 1. 2020. [Cited on 31 December 2020] Available from: https://www.nccn.org/professionals/physician\_gls/pdf/pancreatic.pdf

24 **Versteijne E**, Suker M, Groothuis K, Akkermans-Vogelaar JM, Besselink MG, Bonsing BA, Buijsen J, Busch OR, Creemers GM, van Dam RM, Eskens FALM, Festen S, de Groot JWB, Groot Koerkamp B, de Hingh IH, Homs MYV, van Hooft JE, Kerver ED, Luelmo SAC, Neelis KJ, Nuyttens J, Paardekooper GMRM, Patijn GA, van der Sangen MJC, de Vos-Geelen J, Wilmink JW, Zwinderman AH, Punt CJ, van Eijck CH, van Tienhoven G; Dutch Pancreatic Cancer Group. Preoperative Chemoradiotherapy Versus Immediate Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Results of the Dutch Randomized Phase III PREOPANC Trial. *J Clin Oncol* 2020; **38**: 1763-1773 [PMID: 32105518 DOI: 10.1200/JCO.19.02274]

25 **Jang JY**, Han Y, Lee H, Kim SW, Kwon W, Lee KH, Oh DY, Chie EK, Lee JM, Heo JS, Park JO, Lim DH, Kim SH, Park SJ, Lee WJ, Koh YH, Park JS, Yoon DS, Lee IJ, Choi SH. Oncological Benefits of Neoadjuvant Chemoradiation With Gemcitabine Versus Upfront Surgery in Patients With Borderline Resectable Pancreatic Cancer: A Prospective, Randomized, Open-label, Multicenter Phase 2/3 Trial. *Ann Surg* 2018; **268**: 215-222 [PMID: 29462005 DOI: 10.1097/SLA.0000000000002705]

26 **Motoi F**, Kosuge T, Ueno H, Yamaue H, Satoi S, Sho M, Honda G, Matsumoto I, Wada K, Furuse J, Matsuyama Y, Unno M; Study Group of Preoperative Therapy for Pancreatic Cancer (Prep) and Japanese Study Group of Adjuvant Therapy for Pancreatic cancer (JSAP). Randomized phase II/III trial of neoadjuvant chemotherapy with gemcitabine and S-1 *vs* upfront surgery for resectable pancreatic cancer (Prep-02/JSAP05). *Jpn J Clin Oncol* 2019; **49**: 190-194 [PMID: 30608598 DOI: 10.1093/jjco/hyy190]

27 **Versteijne E**, Vogel JA, Besselink MG, Busch ORC, Wilmink JW, Daams JG, van Eijck CHJ, Groot Koerkamp B, Rasch CRN, van Tienhoven G; Dutch Pancreatic Cancer Group. Meta-analysis comparing upfront surgery with neoadjuvant treatment in patients with resectable or borderline resectable pancreatic cancer. *Br J Surg* 2018; **105**: 946-958 [PMID: 29708592 DOI: 10.1002/bjs.10870]

28 **Janssen QP**, Buettner S, Suker M, Beumer BR, Addeo P, Bachellier P, Bahary N, Bekaii-Saab T, Bali MA, Besselink MG, Boone BA, Chau I, Clarke S, Dillhoff M, El-Rayes BF, Frakes JM, Grose D, Hosein PJ, Jamieson NB, Javed AA, Khan K, Kim KP, Kim SC, Kim SS, Ko AH, Lacy J, Margonis GA, McCarter MD, McKay CJ, Mellon EA, Moorcraft SY, Okada KI, Paniccia A, Parikh PJ, Peters NA, Rabl H, Samra J, Tinchon C, van Tienhoven G, van Veldhuisen E, Wang-Gillam A, Weiss MJ, Wilmink JW, Yamaue H, Homs MYV, van Eijck CHJ, Katz MHG, Groot Koerkamp B. Neoadjuvant FOLFIRINOX in Patients With Borderline Resectable Pancreatic Cancer: A Systematic Review and Patient-Level Meta-Analysis. *J Natl Cancer Inst* 2019; **111**: 782-794 [PMID: 31086963 DOI: 10.1093/jnci/djz073]

29 **Unno M**, Hata T, Motoi F. Long-term outcome following neoadjuvant therapy for resectable and borderline resectable pancreatic cancer compared to upfront surgery: a meta-analysis of comparative studies by intention-to-treat analysis. *Surg Today* 2019; **49**: 295-299 [PMID: 30877550 DOI: 10.1007/s00595-019-01786-w]

30 **Fortner JG**. Regional resection of cancer of the pancreas: a new surgical approach. *Surgery* 1973; **73**: 307-320 [PMID: 4265314]

31 **Fortner JG**, Kim DK, Cubilla A, Turnbull A, Pahnke LD, Shils ME. Regional pancreatectomy: en bloc pancreatic, portal vein and lymph node resection. *Ann Surg* 1977; **186**: 42-50 [PMID: 195543 DOI: 10.1097/00000658-197707000-00007]

32 **Herter FP**, Cooperman AM, Ahlborn TN, Antinori C. Surgical experience with pancreatic and periampullary cancer. *Ann Surg* 1982; **195**: 274-281 [PMID: 6277259 DOI: 10.1097/00000658-198203000-00006]

33 **Hata T**, Motoi F, Ishida M, Naitoh T, Katayose Y, Egawa S, Unno M. Effect of Hospital Volume on Surgical Outcomes After Pancreaticoduodenectomy: A Systematic Review and Meta-analysis. *Ann Surg* 2016; **263**: 664-672 [PMID: 26636243 DOI: 10.1097/SLA.0000000000001437]

34 **Gooiker GA**, Lemmens VE, Besselink MG, Busch OR, Bonsing BA, Molenaar IQ, Tollenaar RA, de Hingh IH, Wouters MW. Impact of centralization of pancreatic cancer surgery on resection rates and survival. *Br J Surg* 2014; **101**: 1000-1005 [PMID: 24844590 DOI: 10.1002/bjs.9468]

35 **Okabayashi T**, Shima Y, Iwata J, Morita S, Sumiyoshi T, Kozuki A, Saisaka Y, Tokumaru T, Iiyama T, Noda Y, Hata Y, Matsumoto M. Reconsideration about the aggressive surgery for resectable pancreatic cancer: a focus on real pathological portosplenomesenteric venous invasion. *Langenbecks Arch Surg* 2015; **400**: 487-494 [PMID: 25940756 DOI: 10.1007/s00423-015-1305-z]

36 **Ramacciato G**, Nigri G, Petrucciani N, Pinna AD, Ravaioli M, Jovine E, Minni F, Grazi GL, Chirletti P, Tisone G, Napoli N, Boggi U. Pancreatectomy with Mesenteric and Portal Vein Resection for Borderline Resectable Pancreatic Cancer: Multicenter Study of 406 Patients. *Ann Surg Oncol* 2016; **23**: 2028-2037 [PMID: 26893222 DOI: 10.1245/s10434-016-5123-5]

37 **Rosso E**, Langella S, Addeo P, Nobili C, Oussoultzoglou E, Jaeck D, Bachellier P. A safe technique for radical antegrade modular pancreatosplenectomy with venous resection for pancreatic cancer. *J Am Coll Surg* 2013; **217**: e35-e39 [PMID: 24045139 DOI: 10.1016/j.jamcollsurg.2013.08.007]

38 **Nakao A**, Harada A, Nonami T, Kaneko T, Inoue S, Takagi H. Clinical significance of portal invasion by pancreatic head carcinoma. *Surgery* 1995; **117**: 50-55 [PMID: 7809836 DOI: 10.1016/S0039-6060(05)80229-6]

39 **Nakao A**, Kanzaki A, Fujii T, Kodera Y, Yamada S, Sugimoto H, Nomoto S, Nakamura S, Morita S, Takeda S. Correlation between radiographic classification and pathological grade of portal vein wall invasion in pancreatic head cancer. *Ann Surg* 2012; **255**: 103-108 [PMID: 22156923 DOI: 10.1097/SLA.0b013e318237872e]

40 **Malleo G**, Maggino L, Marchegiani G, Feriani G, Esposito A, Landoni L, Casetti L, Paiella S, Baggio E, Lipari G, Capelli P, Scarpa A, Bassi C, Salvia R. Pancreatectomy with venous resection for pT3 head adenocarcinoma: Perioperative outcomes, recurrence pattern and prognostic implications of histologically confirmed vascular infiltration. *Pancreatology* 2017; **17**: 847-857 [PMID: 28843714 DOI: 10.1016/j.pan.2017.08.005]

41 **Roch AM**, House MG, Cioffi J, Ceppa EP, Zyromski NJ, Nakeeb A, Schmidt CM. Significance of Portal Vein Invasion and Extent of Invasion in Patients Undergoing Pancreatoduodenectomy for Pancreatic Adenocarcinoma. *J Gastrointest Surg* 2016; **20**: 479-87; discussion 487 [PMID: 26768008 DOI: 10.1007/s11605-015-3005-y]

42 **Belfiori G**, Fiorentini G, Tamburrino D, Partelli S, Pagnanelli M, Gasparini G, Castoldi R, Balzano G, Rubini C, Zamboni G, Crippa S, Falconi M. Vascular resection during pancreatectomy for pancreatic head cancer: A technical issue or a prognostic sign? *Surgery* 2021; **169**: 403-410 [PMID: 32912782 DOI: 10.1016/j.surg.2020.08.002]

43 **Ravikumar R**, Sabin C, Abu Hilal M, Al-Hilli A, Aroori S, Bond-Smith G, Bramhall S, Coldham C, Hammond J, Hutchins R, Imber C, Preziosi G, Saleh A, Silva M, Simpson J, Spoletini G, Stell D, Terrace J, White S, Wigmore S, Fusai G. Impact of portal vein infiltration and type of venous reconstruction in surgery for borderline resectable pancreatic cancer. *Br J Surg* 2017; **104**: 1539-1548 [PMID: 28833055 DOI: 10.1002/bjs.10580]

44 **Kishi Y**, Nara S, Esaki M, Hiraoka N, Shimada K. Feasibility of resecting the portal vein only when necessary during pancreatoduodenectomy for pancreatic cancer. *BJS Open* 2019; **3**: 327-335 [PMID: 31183449 DOI: 10.1002/bjs5.50130]

45 **Müller SA**, Hartel M, Mehrabi A, Welsch T, Martin DJ, Hinz U, Schmied BM, Büchler MW. Vascular resection in pancreatic cancer surgery: survival determinants. *J Gastrointest Surg* 2009; **13**: 784-792 [PMID: 19137380 DOI: 10.1007/s11605-008-0791-5]

46 **Jain S**, Sharma GS, Kaushik M, Upadhyayula RS. Venous resection for adenocarcinoma of head of pancreas: Does extent of portal vein resection affect outcomes? *Surgeon* 2020; **18**: 129-136 [PMID: 31444075 DOI: 10.1016/j.surge.2019.07.004]

47 **Barreto SG**, Windsor JA. Justifying vein resection with pancreatoduodenectomy. *Lancet Oncol* 2016; **17**: e118-e124 [PMID: 26972858 DOI: 10.1016/S1470-2045(15)00463-5]

48 **Kelly KJ**, Winslow E, Kooby D, Lad NL, Parikh AA, Scoggins CR, Ahmad S, Martin RC, Maithel SK, Kim HJ, Merchant NB, Cho CS, Weber SM. Vein involvement during pancreaticoduodenectomy: is there a need for redefinition of "borderline resectable disease"? *J Gastrointest Surg* 2013; **17**: 1209-17; discussion 1217 [PMID: 23620151 DOI: 10.1007/s11605-013-2178-5]

49 **Beane JD**, House MG, Pitt SC, Zarzaur B, Kilbane EM, Hall BL, Riall TS, Pitt HA. Pancreatoduodenectomy with venous or arterial resection: a NSQIP propensity score analysis. *HPB (Oxford)* 2017; **19**: 254-263 [PMID: 28038967 DOI: 10.1016/j.hpb.2016.11.013]

50 **Yamada S**, Fujii T, Sugimoto H, Nomoto S, Takeda S, Kodera Y, Nakao A. Aggressive surgery for borderline resectable pancreatic cancer: evaluation of National Comprehensive Cancer Network guidelines. *Pancreas* 2013; **42**: 1004-1010 [PMID: 23532000 DOI: 10.1097/MPA.0b013e31827b2d7c]

51 **Ravikumar R**, Sabin C, Abu Hilal M, Bramhall S, White S, Wigmore S, Imber CJ, Fusai G; UK Vascular Resection in Pancreatic Cancer Study Group. Portal vein resection in borderline resectable pancreatic cancer: a United Kingdom multicenter study. *J Am Coll Surg* 2014; **218**: 401-411 [PMID: 24484730 DOI: 10.1016/j.jamcollsurg.2013.11.017]

52 **Delpero JR**, Boher JM, Sauvanet A, Le Treut YP, Sa-Cunha A, Mabrut JY, Chiche L, Turrini O, Bachellier P, Paye F. Pancreatic adenocarcinoma with venous involvement: is up-front synchronous portal-superior mesenteric vein resection still justified? A survey of the Association Française de Chirurgie. *Ann Surg Oncol* 2015; **22**: 1874-1883 [PMID: 25665947 DOI: 10.1245/s10434-014-4304-3]

53 **Giovinazzo F**, Turri G, Katz MH, Heaton N, Ahmed I. Meta-analysis of benefits of portal-superior mesenteric vein resection in pancreatic resection for ductal adenocarcinoma. *Br J Surg* 2016; **103**: 179-191 [PMID: 26663252 DOI: 10.1002/bjs.9969]

54 **Bell R**, Ao BT, Ironside N, Bartlett A, Windsor JA, Pandanaboyana S. Meta-analysis and cost effective analysis of portal-superior mesenteric vein resection during pancreatoduodenectomy: Impact on margin status and survival. *Surg Oncol* 2017; **26**: 53-62 [PMID: 28317585 DOI: 10.1016/j.suronc.2016.12.007]

55 **Zhou Y**, Zhang Z, Liu Y, Li B, Xu D. Pancreatectomy combined with superior mesenteric vein-portal vein resection for pancreatic cancer: a meta-analysis. *World J Surg* 2012; **36**: 884-891 [PMID: 22350478 DOI: 10.1007/s00268-012-1461-z]

56 **Settmacher U**, Langrehr JM, Husmann I, Eisele R, Bahra M, Heise M, Neuhaus P. [Reconstruction of visceral arteries with homografts in excision of the pancreas]. *Chirurg* 2004; **75**: 1199-1206 [PMID: 15248050 DOI: 10.1007/s00104-004-0899-4]

57 **Amano H**, Miura F, Toyota N, Wada K, Katoh K, Hayano K, Kadowaki S, Shibuya M, Maeno S, Eguchi T, Takada T, Asano T. Is pancreatectomy with arterial reconstruction a safe and useful procedure for locally advanced pancreatic cancer? *J Hepatobiliary Pancreat Surg* 2009; **16**: 850-857 [PMID: 19844653 DOI: 10.1007/s00534-009-0190-7]

58 **Mollberg N**, Rahbari NN, Koch M, Hartwig W, Hoeger Y, Büchler MW, Weitz J. Arterial resection during pancreatectomy for pancreatic cancer: a systematic review and meta-analysis. *Ann Surg* 2011; **254**: 882-893 [PMID: 22064622 DOI: 10.1097/SLA.0b013e31823ac299]

59 **Von Hoff DD**, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 2013; **369**: 1691-1703 [PMID: 24131140 DOI: 10.1056/NEJMoa1304369]

60 **Hackert T**, Sachsenmaier M, Hinz U, Schneider L, Michalski CW, Springfeld C, Strobel O, Jäger D, Ulrich A, Büchler MW. Locally Advanced Pancreatic Cancer: Neoadjuvant Therapy With Folfirinox Results in Resectability in 60% of the Patients. *Ann Surg* 2016; **264**: 457-463 [PMID: 27355262 DOI: 10.1097/SLA.0000000000001850]

61 **Truty MJ**, Kendrick ML, Nagorney DM, Smoot RL, Cleary SP, Graham RP, Goenka AH, Hallemeier CL, Haddock MG, Harmsen WS, Mahipal A, McWilliams RR, Halfdanarson TR, Grothey AF. Factors Predicting Response, Perioperative Outcomes, and Survival Following Total Neoadjuvant Therapy for Borderline/Locally Advanced Pancreatic Cancer. *Ann Surg* 2021; **273**: 341-349 [PMID: 30946090 DOI: 10.1097/SLA.0000000000003284]

62 **Miyazaki M**, Yoshitomi H, Takano S, Shimizu H, Kato A, Yoshidome H, Furukawa K, Takayashiki T, Kuboki S, Suzuki D, Sakai N, Ohtuka M. Combined hepatic arterial resection in pancreatic resections for locally advanced pancreatic cancer. *Langenbecks Arch Surg* 2017; **402**: 447-456 [PMID: 28361216 DOI: 10.1007/s00423-017-1578-5]

63 **Bachellier P**, Addeo P, Faitot F, Nappo G, Dufour P. Pancreatectomy With Arterial Resection for Pancreatic Adenocarcinoma: How Can It Be Done Safely and With Which Outcomes?: A Single Institution's Experience With 118 Patients. *Ann Surg* 2020; **271**: 932-940 [PMID: 30188399 DOI: 10.1097/SLA.0000000000003010]

64 **Ferrone CR**, Marchegiani G, Hong TS, Ryan DP, Deshpande V, McDonnell EI, Sabbatino F, Santos DD, Allen JN, Blaszkowsky LS, Clark JW, Faris JE, Goyal L, Kwak EL, Murphy JE, Ting DT, Wo JY, Zhu AX, Warshaw AL, Lillemoe KD, Fernández-del Castillo C. Radiological and surgical implications of neoadjuvant treatment with FOLFIRINOX for locally advanced and borderline resectable pancreatic cancer. *Ann Surg* 2015; **261**: 12-17 [PMID: 25599322 DOI: 10.1097/SLA.0000000000000867]

65 **Weitz J**, Rahbari N, Koch M, Büchler MW. The "artery first" approach for resection of pancreatic head cancer. *J Am Coll Surg* 2010; **210**: e1-e4 [PMID: 20113929 DOI: 10.1016/j.jamcollsurg.2009.10.019]

66 **Inoue Y**, Saiura A, Yoshioka R, Ono Y, Takahashi M, Arita J, Takahashi Y, Koga R. Pancreatoduodenectomy With Systematic Mesopancreas Dissection Using a Supracolic Anterior Artery-first Approach. *Ann Surg* 2015; **262**: 1092-1101 [PMID: 25587814 DOI: 10.1097/SLA.0000000000001065]

67 **Yamamoto J**, Kudo H, Kyoden Y, Ajiro Y, Hiyoshi M, Okuno T, Kawasaki H, Nemoto M, Yoshimi F. An anatomical review of various superior mesenteric artery-first approaches during pancreatoduodenectomy for pancreatic cancer. *Surg Today* 2020 [PMID: 32964249 DOI: 10.1007/s00595-020-02150-z]

68 **Zhang Q**, Wu J, Tian Y, Duan J, Shao Y, Yan S, Wang W. Arterial resection and reconstruction in pancreatectomy: surgical technique and outcomes. *BMC Surg* 2019; **19**: 141 [PMID: 31601220 DOI: 10.1186/s12893-019-0560-2]

69 **APPLEBY LH**. The coeliac axis in the expansion of the operation for gastric carcinoma. *Cancer* 1953; **6**: 704-707 [PMID: 13059764 DOI: 10.1002/1097-0142(195307)6:4<704::aid-cncr2820060410>3.0.co;2-p]

70 **Klompmaker S**, Boggi U, Hackert T, Salvia R, Weiss M, Yamaue H, Zeh HJ, Besselink MG. Distal Pancreatectomy with Celiac Axis Resection (DP-CAR) for Pancreatic Cancer. How I do It. *J Gastrointest Surg* 2018; **22**: 1804-1810 [PMID: 30105677 DOI: 10.1007/s11605-018-3894-7]

71 **Cesaretti M**, Abdel-Rehim M, Barbier L, Dokmak S, Hammel P, Sauvanet A. Modified Appleby procedure for borderline resectable/Locally advanced distal pancreatic adenocarcinoma: A major procedure for selected patients. *J Visc Surg* 2016; **153**: 173-181 [PMID: 26775202 DOI: 10.1016/j.jviscsurg.2015.11.014]

72 **Klompmaker S**, de Rooij T, Korteweg JJ, van Dieren S, van Lienden KP, van Gulik TM, Busch OR, Besselink MG. Systematic review of outcomes after distal pancreatectomy with coeliac axis resection for locally advanced pancreatic cancer. *Br J Surg* 2016; **103**: 941-949 [PMID: 27304847 DOI: 10.1002/bjs.10148]

73 **Klompmaker S**, Peters NA, van Hilst J, Bassi C, Boggi U, Busch OR, Niesen W, Van Gulik TM, Javed AA, Kleeff J, Kawai M, Lesurtel M, Lombardo C, Moser AJ, Okada KI, Popescu I, Prasad R, Salvia R, Sauvanet A, Sturesson C, Weiss MJ, Zeh HJ, Zureikat AH, Yamaue H, Wolfgang CL, Hogg ME, Besselink MG; E-AHPBA DP-CAR study group. Outcomes and Risk Score for Distal Pancreatectomy with Celiac Axis Resection (DP-CAR): An International Multicenter Analysis. *Ann Surg Oncol* 2019; **26**: 772-781 [PMID: 30610560 DOI: 10.1245/s10434-018-07101-0]

74 **Hackert T**, Strobel O, Michalski CW, Mihaljevic AL, Mehrabi A, Müller-Stich B, Berchtold C, Ulrich A, Büchler MW. The TRIANGLE operation - radical surgery after neoadjuvant treatment for advanced pancreatic cancer: a single arm observational study. *HPB (Oxford)* 2017; **19**: 1001-1007 [PMID: 28838632 DOI: 10.1016/j.hpb.2017.07.007]

75 **Kawabata Y**, Tanaka T, Ishikawa N, Hayashi H, Tajima Y. Modified total meso-pancreatoduodenum excision with pancreaticoduodenectomy as a mesopancreatic plane surgery in borderline resectable pancreatic cancer. *Eur J Surg Oncol* 2016; **42**: 698-705 [PMID: 26995116 DOI: 10.1016/j.ejso.2016.02.241]

76 **Diener MK**, Mihaljevic AL, Strobel O, Loos M, Schmidt T, Schneider M, Berchtold C, Mehrabi A, Müller-Stich BP, Jiang K, Neoptolemos JP, Hackert T, Miao Y, Büchler MW. Periarterial divestment in pancreatic cancer surgery. *Surgery* 2020 [PMID: 33032819 DOI: 10.1016/j.surg.2020.08.030]

77 **Habib JR**, Kinny-Köster B, van Oosten F, Javed AA, Cameron JL, Lafaro KJ, Burkhart RA, Burns WR, He J, Thompson ED, Fishman EK, Wolfgang CL. Periadventitial dissection of the superior mesenteric artery for locally advanced pancreatic cancer: Surgical planning with the "halo sign" and "string sign". *Surgery* 2020 [PMID: 33036782 DOI: 10.1016/j.surg.2020.08.031]

**Footnotes**

**Conflict-of-interest statement:** The authors have any conflict of interest to declare.

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**Manuscript source:** Invited manuscript

**Peer-review started:** January 27, 2021

**First decision:** February 25, 2021

**Article in press:** May 27, 2021

**Specialty type:** Surgery

**Country/Territory of origin:** Croatia

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Tan CL, Wang YF, Wang XB **S-Editor:** Ma YJ **L-Editor:** Filipodia **P-Editor:** Yuan YY

**Table 1 Definition of borderline resectable pancreatic cancer in different classifications**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **AHPBA classification[20]** | **NCCN classification[20]** | **JPS classification[18]** |
| Venous  PV/SMV |  |  |  |
| Contact or encasement | Contact > 180 or ≤ 180 with contour irregularity or thrombosis of the vein | SMV/PV: Tumor contact/invasion of 180° or more/occlusion not exceeding the inferior border of the duodenum. |
| Short venous segment occlusion |
| Reconstructible | Reconstructible | SMA, CA, CHA: no tumor contact/invasion. |
| Arterial |  |  |  |
| SMA | Contact ≤ 180° | Contact ≤ 180° | SMA, CA: Tumor contact/invasion of less than 180° without stenosis/deformity. |
| CHA | Direct contact | Contact without extension to CA or HA bifurcation | CHA: tumor contact/invasion without showing tumor. |
| Short segment encasement |  |  |
| CA | No contact | Contact ≤ 180° | contact/invasion of the PHA and/or CA.  (In case of contact/invasion to both portal vein and peripancreatic arteries, it was graded as BR-A.) |
|  |  | Contact > 180°without contact of aorta/uninvolved GDA |

AHPBA: American Hepato-Pancreato-Biliary Association; CA: celiac artery; CHA: common hepatic artery; GDA: gastroduodenal artery; HA: hepatic artery; JPS: Japan Pancreas Society; NCCN: National Comprehensive Cancer Network; PHA: proper hepatic artery; PV: portal vein; SMA: superior mesenteric vein; SMV: superior mesenteric vein.



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