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REVIEW

Vascular invasion in pancreatic cancer: Imaging modalities, preoperative diagnosis and surgical management

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Abstract

Pancreatic cancer is associated with a poor prognosis, and surgical resection remains the only chance for curative therapy. In the absence of metastatic disease, which would preclude resection, assessment of vascular invasion is an important parameter for determining resectability of pancreatic cancer. A frequent error is to misdiagnose an involved major vessel. Obviously, surgical exploration with pathological examination remains the "gold standard" in terms of evaluation of resectability, especially from the point of view of vascular involvement. However, current imaging modalities have improved and allow detection of vascular invasion with more accuracy. A venous resection in pancreatic cancer is a feasible technique and relatively reliable. Nevertheless, a survival benefit is not achieved by curative resection in patients with pancreatic cancer and vascular invasion. Although the discovery of an arterial invasion during the operation might require an aggressive management, discovery before the operation should be considered as a contraindication. Detection of vascular invasion remains one of the most important challenges in pancreatic surgery. The aim of this article is to provide a complete review of the different imaging modalities in the detection of vascular invasion in pancreatic cancer.

Key words: Vascular invasion; Cancer; Pancreas; Management

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INTRODUCTION

The incidence of pancreatic cancer has gradually increased over the 20th century and in the early years of this century[1,2]. Cancer of the pancreas is the sixth most common cancer and fourth cause of death from cancer (22% of deaths among gastrointestinal cancers)[1-3].

Pancreatic cancer is associated with a poor prognosis, with less than 5% of patients surviving 5 years after the diagnosis[4]. Surgical resection remains the only chance for curative therapy in these patients[5-7]. Accurate preoperative staging of pancreatic cancer is essential to avoid unnecessary surgery in those with unresectable disease and, at the same time, in order not to deny the opportunity for cure in patients with resectable disease[5,6,8].

Only 16% of patients initially present a disease confined to the pancreas (stage I)[6,7]. Thus, of patients seen, 85%-90% have surgically unresectable tumors at the time of diagnosis[6,7,9-11].

There is no evidence-based consensus on the optimal preoperative imaging assessment of patients with suspected pancreatic cancer[6,8,12].

The criteria of unresectability are numerous[7,13-23]. However, in the absence of metastatic disease which precludes resection, assessment of vascular invasion is an important parameter for determining resectability for pancreatic cancer[5]. A frequent error is to misdiagnose an involved major vessel[11]. Vascular invasion is a relatively frequent discovery in pancreatic cancer; found in 21%-64% of patients, depending on the population studied[7,24].

From the point of view of arterial vessels, a tumoral infiltration of a large trunk (celiac axis, superior mesenteric artery, or hepatic artery) must be carefully analyzed because it constitutes a contraindication to surgery[25-27]. However, isolated involvement of smaller branches such as the gastro-duodenal artery will not preclude surgical resection[25]. The superior mesenteric vessels are the most frequently involved vessels in this cancer, due to their intimate relationship with the head, the uncinate process, and body of the pancreas[25,28].

Limited venous invasion does not represent an absolute contraindication for surgery[4,26,27,29-31]. Obviously, surgical exploration with pathological examination remains the "gold standard" in terms of evaluation of resectability, especially from the point of view of vascular involvement. However, current imaging modalities have improved and allow detection of vascular invasion with more accuracy. Detection is the key to the surgeon's preoperative planning, because the posterior and lateral surfaces of the portal and superior mesenteric vein can be evaluated only after the surgical procedure is well advanced[14]. Thus, the management of a suspicious tumoral adhesion to a vessel is one of the most important challenges in a Whipple type procedure.

In this review, the current imaging modalities for assessing vascular involvement of pancreatic cancer will be discussed. Subsequently, the management and outcome of vascular invasion in patients with pancreatic cancer will also be reviewed briefly.

COMPUTED TOMOGRAPHY

Computer tomography (CT) gives information about localization, size and extension of tumor[8,18], while being non-invasive[32]. A recent meta-analysis showed CT to be 91% sensitive and 85% specific for tumoral detection[33]. Phoa *et al*[34] showed that, with regard to tumor convexity towards a vessel, Grades D (concave contour of the tumor towards vessel) or E (circumferential involvement of vessel) have a risk of invasion of 88%; and a possibility of resection of 7% for the type D and of 0% for the type E[35]. Loyer *et al*[35] found that Grades A (fat plane separating the tumor from the vessel) and B (normal pancreatic tissue between tumor and vessel) had a resection rate of 95%, therefore these two grades are factors of better prognosis.

On the other hand, the length of tumor contact with the vessel (if it is greater than 5 mm) is a relatively good predictive factor for vascular invasion (78% for portal vein and 81% for superior mesenteric vein)[34].

A circumferential contact of more than 180 degrees has been shown to have a good correlation with unresectability[34,36,37]. For this criterion, Lu *et al*[38] found a sensitivity of 84%, a specificity of 98%, a positive predictive value (PPV) of 95%, and a negative predictive value (NPV) of 93%, for unresectability. Furthermore, Phoa *et al*[34] reported a sensitivity of 60%, and a specificity of 90%, if tumor convexity Grades D or E were combined with circumferential involvement of > 90 degrees. In addition, a strongly narrowed vessel also has an important risk of being invaded[34,36], but prudence is essential, especially for a vein, due to the mass effect of the tumor without the presence of vascular invasion[10,39,40]. In addition, an artery may be completely invaded, with no apparent change in vessel caliber[36,39].

Concerning the irregularity of the vascular wall, Li *et al*[36] reported a sensitivity and a specificity of 45% and 99%, respectively, for tumor detection in arteries, and 63% and 100% in the case of veins.

Regarding the rare superior mesenteric vein teardrop sign, Hough *et al*[41] found a sensitivity of this CT sign of 91% and a specificity of 98%; similar findings were reported in other series[36].

Consequently, Li *et al*[36] reported that the CT criteria for arterial invasion might be: an arterial embedment in tumor, or the combination of tumor involvement of more than one-half of the circumference of the arteries with artery wall irregularity or with artery stenosis (sensitivity of 79%, specificity of 99%). The criteria for venous invasion might be venous occlusion, tumor involvement of more than one-half of the circumference of the veins, vein wall irregularity, vein caliber stenosis, and teardrop superior mesenteric vein sign (sensitivity of 92%, specificity of 100%).

From the point of view of the detection of vascular invasion, many studies have evaluated CT (Table 1). CT has improved much these last years. Technology has developed multi-slice with 4-64 detector rows, allowed thin-sections and dual-phase, with faster time of acquisition, and numerous possibilities of image post-processing (3D reconstructions, multiplanar reconstructions)[19,29,40,42-45].

Fourteen years ago, Yoshimi *et al*[46] reported one of the first cases of 3D vascular reconstruction, allowing the evaluation of portal invasion with a higher accuracy than angiography alone. Currently, pancreatic section thickness of 1 mm is obtained in approximately 20 s, allowing true volume acquisition, with vascular details better than angiography[28,47,48] useful when assessing vascular invasion[44]. Furthermore, CT angiography allows anatomical study of small pancreatic vessels with a remarkable degree of accuracy[49,50].

Moreover, dilation of the peri-pancreatic veins with no visualization of inferior branches on CT suggests tumor invasion of peri-pancreatic tissue[50].

Several studies have highlighted the importance of

Table 1 CT performance in the detection of vascular invasion in more than 50 patients with pancreatic cancer

Studies (yr)	*n*	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Megibow *et al*[24] (1995)	118	47	69	89	28
Raptopoulos *et al*[208] (1997)	82	NA	NA	NA	96
Sugiyama *et al*[91] (1997)	73	65[1]	77	NA	NA
McCarthy *et al*[16] (1998)	67	NA	NA	55/94[2]	95/94
Diehl *et al*[209] (1998)	89	86	NA	NA	NA
Böttger *et al*[10] (1998)	255	22.2[3]	96.4	72.7	74.1
Sugiyama *et al*[88] (1999)	91	64[4]	79	NA	NA
Nakao *et al*[105] (1999)	55	82.1[5]	74.1	76.7	80
Pietrabissa *et al*[130] (1999)	50	82	53	NA	NA
Gress *et al*[89] (1999)	151	15	100	100	60
Squillaci *et al*[69] (2003)	50	97	100	100	95
House *et al*[210] (2004)	115	85-87[6]	95-99	83-93	92-98
Soriano *et al*[8] (2004)	62	67	94	89	80
Li *et al*[36] (2005)	54	92/79[7]	100/99	NA	NA
Buchs *et al*[98] (2007)	153	54.5[8]	91.2	66.7	86.1

[1,3,4,5]Only evaluated for portal vein invasion; [2]PPV of 55% for venous invasion and 94% for arterial invasion; NPV of 95% for venous invasion and 94% for arterial invasion; [6]Sensitivity of 85% for the superior mesenteric and portal vein invasion, 86% for the superior mesenteric artery invasion, 87% for the celiac trunk invasion; specificity of 95% for the superior mesenteric vein and portal vein involvement, 97% for the superior mesenteric artery invasion, 99% for celiac trunk involvement; PPV of 90% for the superior mesenteric vein and portal vein invasion, 83% for the superior mesenteric artery involvement, 93% for celiac trunk invasion; NPV of 92% for the superior mesenteric vein and portal vein involvement, 98% for the superior mesenteric artery and celiac trunk invasion; [7]Sensitivity of 92% for venous invasion and 79% for arterial invasion; specificity of 100% for the veins and 99% for the arteries; [8]For multi-slice CT. CT: Computer tomography; PPV: Positive predictive value; NPV: Negative predictive value; NA: Not available.

the moment of image acquisition. With regard to the pancreas, it seems that a portal venous phase (60 s after intravenous administration of iodinated contrast medium) or that a pancreatic phase (40-70 s) provides more information than an arterial phase (18 s) or that of a hepatic phase (70 to 100 s)[19,29,51-54]. McNulty *et al*[51] reported that an arterial phase can be reserved for patients in whom CT angiography is required.

Lastly, Imbriaco *et al*[55] showed that dual-phase helical CT (arterial: 20 s, and pancreatic late: 70 s) was interesting but was comparable with single-phase helical CT (pancreatic early: 50 s).

In conclusion, CT is the assessment of choice in first intention, permitting in one non-invasive examination a TNM staging evaluation.

From the vascular point of view, many criteria exist (especially circumferential involvement of vessel of more than 180 degrees, radiological absence of a fat plane between tumor and vessel, vascular occlusion with collaterals, teardrop sign) which allow accuracy in diagnosing vascular invasion. Development of new radiological techniques (3D reconstructions, multiplanar reconstructions) has improved accuracy of assessment of vascular invasion.

MAGNETIC RESONANCE IMAGING (MRI)

MRI with cholangiopancreatography gives much information for the evaluation of primary tumor and metastatic dissemination, improved by the use of gadolinium or mangafodipir trisodium[1,13,47,56-58]. Currently, the use of MRI in an "all-in-one" staging method (MRI, coupled with angiography and cholangiopancreatography) is a subject under deliberation[58-60].

MRI criteria for vascular invasion are: (1) occlusion of the vessel, with or without collaterals, (2) tumoral infiltration of peri-vascular fat tissue, (3) circumferential contact of more than 180 degrees between the tumor and the vessel, and (4) mass effect along one side of the vessel for more than 2 cm[7,56,60,61].

As regards the detection of vascular invasion, MRI has an accuracy of approximately 94% for enhanced T1-weighted imaging[62]. Romijn *et al*[58] found in their study an accuracy of 81% with mangafodipir trisodium (definitely higher than MRI without contrast medium).

Other studies have attempted to analyze the performance of MRI in the detection of vascular invasion. They found a sensitivity of 47%-83%[24,60], a specificity of more than 95%[7,59], a PPV of more than 70%[7,8], and a NPV of 23%-96%[24,60].

Modern MRI technology makes it possible to obtain 3D reconstructions, facilitating the study of the peri-pancreatic vessels[61,63,64]. Some series have also demonstrated the adequate time for vascular pancreatic image acquisition: biphasic imaging at 15 and 45 s after arrival of contrast material (gadolinium) in the abdominal aorta[65].

Accuracy of MRI for vascular visualization is quite similar to that of CT[56,66,67]. It consequently seems logical to reserve this expensive and time-consuming technology for those patients not able to benefit from CT (allergy to iodine, renal insufficiency, pregnancy) or if CT findings are inconclusive[68].

ANGIOGRAPHY

Currently, conventional angiography is no longer part of the diagnostic protocol in most centers[13], because this examination does not permit the detection of the tumor itself[1], and can easily be replaced by other less invasive methods which give more information on tumoral extension.

On the other hand, preoperative arteriography may visualize vascular abnormalities (anatomical variations, acquired stenosis), allowing a possible modification of surgical strategy (revascularisation, replacement hepatic artery, embolization of an aneurism)[17,69,70].

With regard to vascular invasion, angiographic criteria are: (1) vascular stenosis or occlusion, with or without collaterals, (2) thrombosis of a vessel, (3) acute angle appearing in the venous wall, and (4) envelopment of the vessel within tumor[69,71-74].

In at least 20% of cases, angiography misses the vascular invasion[10], because it gives only information about the lumen of the vessel[72]. Angiography depends upon displacement of vessels and distortion of vascular contours unless clear vessel occlusion is present. Furthermore, the tumor may completely encase and invade the small amount of fat surrounding the vessel, and yet not cause a distortion of the contour of the vascular lumen, which is required for detection on angiography. This feature can be visualized during endoscopic ultrasonography or CT. Thus, angiography requires more extensive vascular involvement in order for it to be detected[5,74,75].

The results reported for detection of vascular invasion by pancreatic cancer using angiography are: a sensitivity between 21%[5,8] and more than 80%[10,76], a specificity between 50%[72] and 100%[8,69], a PPV more than 60%[5,72], and a NPV between 50%[72] and 83%[10]. Late angiographic times allow visualization of the portal vein, and possible invasions. In addition, it is possible to inject contrast medium directly into the portal vein by a transhepatic access, for example at the time of intravascular ultrasonography (see below).

In conclusion, studies show that angiography is paradoxically relatively poor in the detection of vascular invasion. On the other hand, it permits the visualization of arterial and venous anomalies, allowing a change in surgical strategy.

ABDOMINAL ULTRASONOGRAPHY (US)

Abdominal US is often the first line examination for a patient presenting with jaundice and pain[13].

From the vascular point of view, US coupled with Doppler gives a reasonably reliable measure of vascular patency and can improve accuracy in assessing vascular invasion[13,77,78]. Its sensitivity ranges between 60%[79] and more than 90%[80]; its specificity has been reported to be higher than 90%[79,80], the PPV is higher than 90%[81], and the NPV is higher than 75%[82,83]. Very recently, authors reported US to be 93% accurate in detecting portal vein invasion, by using 3D vascular reconstruction technology[84].

Color Doppler sonographic criteria for vascular invasion are: (1) absence of hyperechoic tissue between the tumor and the vessel, (2) more than 2 cm continuity between tumor and vessel, (3) circumferential contact between the tumor and the vessel, (4) circumferential narrowing of vessel lumen, and (5) vascular occlusion or thrombosis[81-83,85-87].

In addition, perioperative US has been reported as 100% sensitive in identifying tumors, and 92% sensitive and specific in detecting portal invasion[88]. In 22% of patients with pancreatic neoplasms, US-Doppler makes it possible to modify therapeutic strategy[86].

In conclusion, US coupled with Doppler is a relatively accurate, cheap, and non-ionizing imaging modality for initial screening of patients with suspicion of tumors of the pancreas. However, US has demonstrated weakness in recognition of deeper localizations.

With regard to the detection of vascular invasion, studies have shown that US coupled with Doppler is a reliable method. However, these series evaluated almost exclusively the portal vein and its tributaries. Recent improvement in US imaging, allowing 3D reconstruction, offers new potential for this technology in the assessment of tumoral vascular involvement.

ENDOSCOPIC ULTRASONOGRAPHY (EUS)

EUS is a relatively new technique, providing direct ultrasonic imaging of the pancreas through the gastrointestinal lumen[2,13]. However, the probes are expensive and EUS requires a trained endoscopist[13,63].

EUS has been shown to be accurate in diagnosing and staging pancreatic cancer[89], with the help of fine needle aspiration (FNA), with 96.6% sensitivity, 99.0% specificity, 96.2% NPV, and 99.1% PPV[90].

EUS criteria for vascular invasion are: (1) loss of the hyperechoic vessel wall/tumor interface, (2) direct visualization of tumor within the vessel lumen, (3) vascular encasement or occlusion, (4) non-visualization of a major vessel, in the presence of collaterals, (5) proximity of the tumor (< 3 mm) to the vessel, and (6) irregularity of the vascular wall[5,8,11,89,91-96].

Sugiyama *et al*[91] reported that EUS is more accurate than CT, US, and angiography for the detection of portal invasion; similar findings were shown in other series[97,98]. In addition, Brugge *et al*[93] showed that EUS was highly sensitive in the detection of portal and splenic vein invasions.

Arterial invasion is assessed with more difficulty by EUS[92,98-100]. Globally, the sensitivity is 50%-100%[92,95,101,102], the specificity 58%-100%[92,102], the PPV 28%-100%[92,96], and the NPV 18%-93%[89,94].

Very recently, Fritscher-Ravens *et al*[103] reported the use of 3D linear EUS in the assessment of vascular involvement with very interesting results compared with classical EUS. Linear 3D EUS enhanced the evaluation

of vascular involvement of pancreatic lesions, especially in chronic pancreatitis.

In conclusion, it is appropriate to incorporate EUS in the preoperative assessment when there is suspicion of pancreatic cancer. From the point of view of the detection of vascular invasion, EUS has shown good accuracy, especially for venous invasion.

INTRAVASCULAR ULTRASONOGRAPHY (IVUS)

When a tumor appears to be contiguous with the portal vein or with the superior mesenteric vein, the diagnosis of vascular invasion can be difficult. Some limited reports have suggested that IVUS might allow the distinction between a simple compression by mass effect and invasion[71].

Moreover, IVUS makes it possible to detect intraportal thrombus, sometimes missed by CT[71]. IVUS is performed either by a transhepatic access, or by a transmesenteric catheterization (during operative time)[71,104-108]. Complications are rare[72,104-106].

IVUS criteria for vascular invasion are: (1) obliteration of the echoic band of the portal vein by the hypoechoic tumor, (2) tumor mass blended with the venous wall, and (3) tumor protrusion into the vascular lumen[71,72,76,104-106,109].

One of the limitations of IVUS is the lack of specificity in the case of pancreatitis[71,105]. Moreover, IVUS has a limited penetration, allowing only localised investigations. Another weakness remains the lack of spatial orientation, making the interpretation of the images difficult[72,106].

There are few studies concerning IVUS in detection of vascular invasion in pancreatic cancer. Moreover, they report only portal and superior mesenteric vein results, not evaluating arterial invasion. The results are: sensitivity more than 95%[71,76], specificity more than 90%[71,76], PPV more than 90%[105], and NPV more than 95%[105].

Kaneko *et al*[109], has pioneered the use of IVUS in staging of pancreatic cancer, recently using 3D reconstructions of IVUS with a high degree of accuracy. Tezel *et al*[110] also reported that a contact of more than 18 mm between the tumor and the portal or the superior mesenteric vein was a factor of poor prognosis. The use of IVUS allows stent placement[111], a possibility in the palliative treatment of portal stenosis.

In conclusion, studies show that IVUS is probably superior to CT and portography for the detection of vascular invasion. However, data is available only for the portal vein and for the superior mesenteric vein. To our knowledge, there are no data concerning the utility of IVUS in detecting tumoral arterial invasion.

Because IVUS is expensive and invasive, Nakao *et al*[105] recommend performing this examination only in cases in which the distinction between compression and invasion cannot be made by conventional imaging techniques.

LAPAROSCOPY AND LAPAROSCOPIC ULTRASONOGRAPHY (LUS)

For almost 30 years[112], laparoscopic examination of the abdominal cavity has offered an excellent, although invasive, visualization of peritoneum and the liver[13,47,63,113,114].

From the vascular point of view, incision of the gastrohepatic omentum allows a direct access to the underlying vessels[47,115]. However, it seems certain that laparoscopy alone cannot detect vascular invasion, in particular mesenteric, without help of perioperative ultrasonography[116].

Currently, routine laparoscopy is not recommended in cases of cancer of the head of the pancreas, because it influences further surgical strategy in only 14%-19% of cases[116,117]. On the other hand, a study showed that in the case of cancer of the body or the tail of the pancreas, laparoscopy could avoid up to 50% of the operations, because of metastases not identified during staging[116].

Obviously, laparoscopy can also be used with a palliative aim (double derivations), if the tumor is unresectable[21,117-120]. Laparoscopy has its limits: it only allows visualization of the liver surface; impossibility of analyzing the retroperitoneum and its vessels; technical problems due to adherences[21,47,63,120,121].

LUS was subsequently developed, and this allows detailed study of the liver, the lymphatic area, and the corresponding vessels[47,121-126]. Vascular structures can be accurately visualized by LUS in approximately 95% of patients with tumors in the head of the pancreas[126].

LUS criteria for vascular invasion are: (1) loss of the hyperechoic vessel - tumor interface, (2) obliteration or thrombosis of a vessel, (3) a fixed stenosis, (4) vessel encasement by tumor encirclement and rigidity, and (5) presence of invading tumor within the vessel lumen[122,127-129].

There are numerous studies evaluating resectability by LUS, but to our knowledge few have focused on vascular invasion. They have found a sensitivity of more than 50%[129], a specificity of more than 80%[130], a PPV of 93%[127], and a NPV of 73%[128].

Despite these encouraging results, several authors do not recommend systematic use of laparoscopy or LUS. They prefer to recommend this technique for doubtful cases[21,121,131-133].

POSITRON EMISSION TOMOGRAPHY (PET) AND POSITRON EMISSION TOMOGRAPHY COUPLED WITH COMPUTED TOMOGRAPHY

PET is a non-invasive imaging method, which gives information about cellular metabolic activity.

Currently, 18F-fluorodeoxyglucose (FDG) is injected and taken up preferentially by malignant tumors, and secondary localizations, rather than by healthy tissue[13,17,18,47,63,134-136]. The FDG is not metabolized and is trapped inside the cell[47], allowing it to be imaged in contrast to surrounding tissue[18].

PET is accurate in diagnosing small tumors (< 2 cm), as well as peritoneal implants and metastases[13,47,63,102,135,137-141]. In addition, PET is able to differentiate

inflammatory pathologies from tumoral ones[47,135,139,142,143]. PET differentiates malignant and benign pathologies with a sensitivity of 85%-100% and a specificity of 67%-99%; often higher than that of CT[135, 141,144-146].

In addition, false negatives exist in the case of strongly differentiated tumors, small periampullary tumors or in cases of hyperglycemia[63,135,146,147]. In the case of normoglycemic patients, PET has a sensitivity for tumoral detection of 93%-98%[135,137,146,148,149], although in the case of hyperglycemic patients, this falls to 63%, or even less[135,137,146,149], in parallel with the NPV which falls from 96% to 38%[146].

Concerning lymphatic invasion, PET detection has proved poor, probably due to the proximity of regional lymph nodes to the primary tumor[102,134,135,137,150], and the lack of anatomic detail[13,18,139]. PET alone is unable to visualize vessels and cannot assess vascular invasion[63,135,151]. Thus, the association of PET with CT (PET/CT) seems promising[139,152].

Heinrich *et al*[139] showed recently that PET/CT has a PPV for the differentiation between a benign and a malignant pathology of 91%, whereas its NPV is 64%. PET/CT detects a cancer of the pancreas with a sensitivity of 93%, and is more specific than CT alone (69% *vs* 21%, respectively, $P = 0.07$). However, data are lacking regarding the assessment of vascular involvement. The use of multislice CT coupled with PET, and angio-CT protocols, might allow better visualization of the vessels.

SURGICAL MANAGEMENT OF VASCULAR INVASION

Frequently, vascular invasion may be assessed only when the operation is already quite advanced (section of the pancreas, digestive transection)[22,27,153-156]. Palpation at the time of the Kocher maneuver (maneuver which permits exposure of structures behind duodenum and pancreatic head) is commonly performed to assess the relationship of a pancreatic head tumor to the superior mesenteric artery. However, if the tumor is large, if there is associated pancreatitis, or if the patient is undergoing reoperation, palpation is an inaccurate way to assess this critical tumor-vessel relationship prior to gastric and pancreatic transection[22].

The management of a suspicious tumoral adhesion to a vessel is one of the most important challenges in a Whipple procedure. In such a case, the surgeon is confronted with three options: (1) leave tumor attached to the vessel, resulting in a grossly positive margin of resection; (2) try to separate the tumor from the vessel, with a considerable hemorrhagic risk; and (3) or perform a partial or segmental resection of the portion of invaded vessel with reconstruction[22].

Arterial invasion

If the invasion of the superior mesenteric or portal vein is not in itself a criterion of unresectability[4,154,155,157], arterial invasion is a more controversial issue. Many authors regard this invasion as a contraindication to surgery[27,154,158], because of the high morbidity and mortality rates associated with arterial resection and reconstruction[159]. Furthermore, arterial invasion usually includes extensive involvement of the mesenteric neural plexus[160], rendering radical resection oncologically unsound because of the frequent finding of positive margins[154].

However, in many cases, the preoperative assessment cannot diagnose such an invasion. The surgeon must then adapt his surgical strategy. Fortner[161] recommended the resection of invaded arterial segment, if a reconstruction seemed possible.

From the arterial point of view, celiac or hepatic invasion, discovered during the operation, can be the object of a resection and a reconstruction, either by direct anastomosis, by interposition of a venous graft (for example reverse saphenous or internal jugular vein), or with a prosthesis[156,161-163]. An arterial graft (for example the splenic artery) can also be used[156,163]. These techniques seemed relatively reliable, with a mortality of 5%, in a recent study[164].

Regarding the modified Appleby's operation (*en-bloc* resection of the celiac trunk with distal pancreatectomy and total gastrectomy) for advanced cancers of body and tail of the pancreas, several Japanese groups propose an extended resection of the celiac trunk, splenic artery, common hepatic artery, and/or superior mesenteric artery, resulting in 5-6 mo of average survival. Hepatic vascularization must be maintained and evaluated during the whole operation, and if necessary, compensated, in order to avoid an acute hepatic insufficiency[163,165-168].

Recently, Gagandeep *et al*[169] reported their experience using celiac axis resection for pancreatic cancer with a prolonged survival, and proposed the consideration of this technique for central and distal pancreatic cancer invading the celiac trunk.

Hirano *et al*[170] reported a high R0 resectability rate (91%) with distal pancreatectomy with *en bloc* celiac axis resection.

When the superior mesenteric artery is invaded, an arterial jejunal branch is isolated. Heparin is injected there, in order to allow the clamping of the superior mesenteric artery with full safety. The artery is then reconstructed either by direct anastomosis, or by anastomosis to the aorta[161].

In the case of an invasion of the hepatic artery, techniques of reconstruction require a venous graft (jugular, reverse saphenous, gonadic veins) or prosthesis, or an arterial graft (splenic, gastro-epiploic, gastro-duodenal)[22,163,171-173].

In some cases of cancer of the body of the pancreas, with invasion of the common hepatic artery and celiac trunk, Kondo *et al*[174] tried to embolize the hepatic artery, obtaining a collateral pathway from the superior mesenteric artery. This allowed a distal pancreatectomy with *en bloc* resection of the celiac trunk, without hepatic ischemia.

Other authors have described more traditional techniques of resection-reconstruction, using the gastroduodenal artery[175]. Combined resection of the celiac trunk with a distal pancreatectomy has been found to improve the overall prognosis of patients with locally advanced cancer of the body and tail of the pancreas[176].

Venous invasion

Contrary to arterial involvement, the invasion of the superior mesenteric vein or portal vein is not in itself a criterion of unresectability[4,154,155,157,177].

In uncommon cases, the pancreatic tumor infiltrates the anterior surface of the inferior vena cava. It is possible to excise the invaded part, and to replace it with a synthetic prosthesis. Often, autologous tissues are preferred (jugular, saphenous veins)[22].

When the portal vein is involved, it is legitimate to attempt a resection, especially if the vein is invaded by more than 2 cm, in order to obtain negative margins (Table 2)[4,178-180]. Portal invasion is not a predictor of aggressive tumor biology, but rather a reflection of tumor size and location[153,157,177,179]. Up to 50% of tumors thought to have vascular invasion intraoperatively have been found subsequently to have only inflammatory adhesions to the portal vein after histologic examination[157,181,182]. This finding underlines the difficulty in determining tumoral venous invasion before and during surgery, since peritumoral inflammation may simulate true tumor infiltration[178]. Very recently, Fukuda *et al*[183] reported that the depth of portal vein invasion significantly alters survival after curative pancreatic resection combined with portal vein resection. The survival rate was similar for patients with no portal invasion and those with superficial invasion. However, a deeper portal invasion was associated with a poorer survival rate, similar to that of patients undergoing non-curative resection.

The excision is done either by a segmentary resection, or by a tangential resection[22,184,185]. The reconstruction requires an end-to-end anastomosis either by direct suture or by using an interposition venous or prosthetic graft[22,74,154,156,157,161,162,184-189]. The technical limit of portal vein resection without graft is 4 cm in the hepatic hilus and 7 cm after pancreatic resection[189]. For minimal tumor invasion into the portal vein, autologous saphenous vein patch has been described[27]. Wide resection of the portal vein may require transection of the splenic vein. To avoid segmental portal hypertension, end-to-side reanastomosis of the splenic vein to the interposition graft is recommended[184].

If the portal clampage lasts longer than 30 min, it is recommended to clamp also the superior mesenteric artery, in order to prevent intestinal congestion[22,189]. If the portal clampage lasts longer than 60 min, it is necessary to consider a bypass between the superior mesenteric vein and femoral vein[189,190].

Resection of the portal vein is associated with a higher morbidity rate (bleeding, infections, cardiopulmonary complications), than when this is not performed[4,185,191].

Table 2 Recent results of portal resections in pancreatic cancer

Studies (yr)	*n*	Mortality (%)	Survival at 1 year (%)	Median survival (mo)
Sindelar *et al*[159] (1989)	20	20[1]	50	12
Tashiro *et al*[189] (1991)	27	8.4	51.9	NA
Ishikawa *et al*[74] (1992)	35	5.7	NA	9+/-5
Launois *et al*[193] (1993)	9	0	NA	6.1
Takahashi *et al*[156] (1994)	79	16.5	17-61.5[2]	6-14
Allema *et al*[192] (1994)	20	15	30%	7
Nakao *et al*[211] (1995)	89	8	5.5-39.6[3]	NA
Nakao *et al*[190] (1995)	104	8	NA	NA
Roder *et al*[27] (1996)	31	0	39	8
Fuhrman *et al*[154] (1996)	23	4	NA	NA
Harrison *et al*[157] (1996)	58	5	59	13
Leach *et al*[196] (1998)	31	0	NA	22
Launois *et al*[188] (1999)	14	0	23	5
Bachellier *et al*[195] (2001)	21	3.2	NA	13
van Geenen *et al*[185] (2001)	34	0	55	14
Shibata *et al*[197] (2001)	23	4	31	6.8-20.6[4]
Hartel *et al*[212] (2002)	68	4	[5]	NA
Aramaki *et al*[194] (2003)	22	4.5	NA	NA
Nakagohri *et al*[213] (2003)	33	6	35-81	15
Li *et al*[164] (2004)	79	5[6]	NA	NA
Tseng *et al*[206] (2004)	110	1	85	23.4
Wagner *et al*[4] (2004)	51	7.7	NA	NA
Shimada *et al*[177] (2006)	86	1	[7]	14
Carrère *et al*[182] (2006)	45	4.4	[8]	15
Riediger *et al*[181] (2006)	53	3.8	[9]	NA
Fukuda *et al*[183] (2007)	37	2.4	47.7	NA

[1]Included 3 arterial reconstructions. 17 patients benefited from adjunctive radiotherapy; [2]17% survival at 1 year if margins were positive (median survival: 6 mo) and 61.5% if margins were negative (median survival: 14 mo); [3]Survival at 1 year: 39.6% if the vessel was not invaded, 11.3% if the media was invaded, and 5.5% if the intima was invaded; [4]Median survival was 6.8 mo if the intima was invaded, 15.3 mo if the intima was spared, and 20.6 mo if there was no true vascular invasion; [5]5-year survival rate: 23%; [6]This mortality also includes arterial reconstructions (11 patients); [7]5-year survival rate: 12%; [8]3-year survival rate: 22%; [9]5-year survival rate: 17.9%.

In addition, Fuhrman *et al*[154] reported an operative time, an operative blood loss, and perioperative transfusion requirements of greater magnitude in patients who required venous resection. The mortality rate is also higher after portal vein resection but this value is not always significant[4,188,192,193]. These findings are not confirmed by other series[22,27,157,181,182,185,187,191,194-201]. Numerous authors have reported a mortality rate below 5%, similar to that of standard pancreatoduodenectomy[27,154,157,164,178,181,182,185,188,194-197].

In 62%-85% of cases, the vascular margins are found to be positive[27,31,185,192], explaining a very poor median survival. However, recently, Siriwardana *et al*[202] reported, in a systematic review of synchronous portal-superior mesenteric vein resection during pancreatectomy for cancer, a high rate (67.4%) of nodal involvement during the procedure. For the authors, this implied that by the time a pancreatic tumor involves the portal vein the risk of metastases is high, rendering the possibility of cure by surgery improbable[202].

If the tumor invades the superior mesenteric vein, it is not a criterion of unresectability. Various techniques exist to allow complete resection of the tumor,

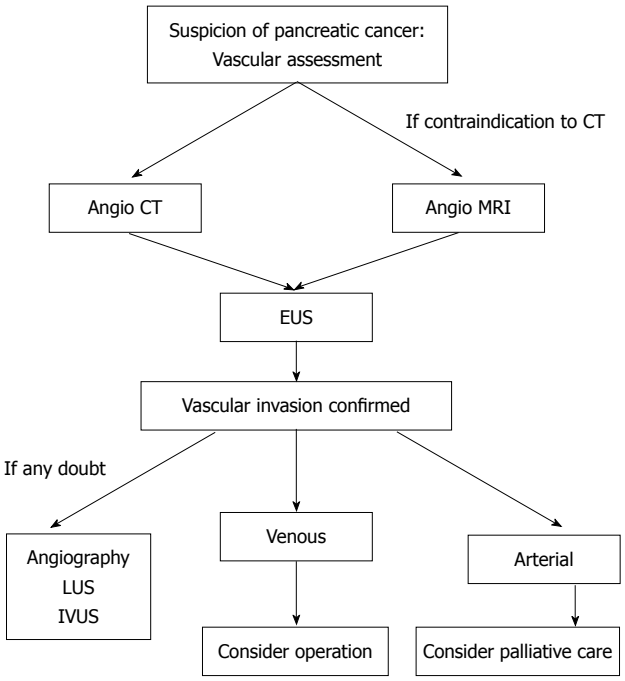

Figure 1 Proposed algorithm for the management of suspected vascular invasion in pancreatic cancer.

either by tangential excision, or by excision-reconstruction[153,155,161,162,185,197,203,204].

In conclusion, various studies show that venous resection in pancreatic cancer is a feasible technique and relatively reliable, at least with regard to mortality, but (importantly) at the price of a higher morbidity. However, a survival benefit is not achieved by curative resection in patients with pancreatic cancer and vascular invasion[205,206]. On the other hand, the discovery of an arterial invasion during the operation might require an aggressive management, using vascular reconstruction. Furthermore, neoadjuvant treatment (combination of 5-fluorouracil/cisplatin chemoradiation) showed only limited impact on survival but appeared to be associated with improved local control[207].

CONCLUSION

In the absence of metastatic disease, assessment of vascular invasion is a key aspect in the evaluation of resectability for pancreatic cancer. A frequent error is to misdiagnose an involved major vessel. Obviously, surgical exploration with pathological examination remains the "gold standard" in terms of evaluation of resectability, especially from the point of view of vascular involvement. However, current imaging modalities have improved and now allow detection of vascular invasion with more accuracy. Multi-slice CT has become the best imaging modality for this purpose, and the adjunction of PET might be a means to improve results further. EUS is useful, but it remains very operator-dependant. Data are still lacking for the exact role of MRI regarding this issue (Figure 1). Detection of vascular invasion remains one of the most important challenges in pancreatic surgery.

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