Does arterial encasement on CT always mean invasion at surgery in pancreatic cancer? If not, how can we assess resectability and what is the strategy?

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Purpose

The salient indication of pancreatic cancer (PC) unresectability is the superior mesenteric (SMA) and celiac artery (CA) encasement, signaling arterial invasion. Computed tomography (CT) is the gold standard for PC resectability evaluation.

How to extract patients with Stage II pancreatic cancer (who benefit from radical surgery) from Stage III group in which they have to be included according to present regulations if we use only CT (and this is general practice) for diagnostics of arterial involvement.
Methods and Materials

The data from the preoperative CT and EUS reports on 163 patients consecutively operated on for ductal adenocarcinoma were compared with the findings at 51 standard, 58 extended, 17 total pancreatoduodenectomies (PDs), 9 distal resections with the CA excision (DPCA) and 28 palliative bypasses for PDAC between June 2005 and July 2012. From all of these cases, 11 patients were found who had controversial data of CT and EUS in regard to peripancreatic arterial tumor invasion. They all had CT signs of arterial involvement, but curative R0/R1 procedures with or without an excision of the arteries were performed. Survival in above mentioned group was compared to the survival of 8 patients who underwent an R2 resection (Group B), and of 12 patients with locally advanced cancer in whom palliative bypass surgery were carried out (Group C). Sixteen patients who underwent bypass procedure were not included in the study due to the presence of distant metastases. In the remaining patients no distant metastases were detected at surgery.
Results

The diagnosis of ductal adenocarcinoma of the pancreas was histologically proven in all the cases. In all the cases of group A the arteries involved on CT were considered intact at surgery (Fig. 1-13). There were no difference between the groups for age and sex. The tumor size was significantly greater in the bypass group (Table 1), although real tumor size in these patients could not be measured because tumors were not removed and were assessed at surgery only approximately.

An attempt of pancreaticoduodenectomy or distal pancreatectomy in Group A was opted for as a result of the obvious discrepancies between the CT evidence and EUS findings: in each of the cases the CT imaging features displayed were consistent with the peripancreatic arteries (Table 1) being completely encased by the tumor while the EUS appearance was suggestive of the tumor merely abutting the arteries. In Group B palliative PDs were undertaken as motivated by the equivocal CT findings regarding the tumor resectability and the surgeon- disclosed SMA and/or CA tumoral involvement after the gland transection, that is, after having crossed "the point of no return".

Group A (Table 1). The tumor was located in the pancreatic head and body in 5 and 5 cases respectively and once the pancreas was totally involved. No CT-presumed encasement of the peripancreatic arteries by the tumor was noted in the surgical records to have been discovered at operation in group A (Fig. 1 -13). In all but one of the cases the level of an R1 resection was secured as conditioned by the artery-tumor contact, in 1 case an R0 resection was achieved. The status of a negative resection margin of the pancreas and clear soft tissues to the left of the SMA during pancreaticoduodenectomy (PD) and to the right of the SMA during distal pancreatectomy was therewith histologically confirmed at surgery in each of the cases. In 3 cases a classical PD was performed, in 2 - a pylorus-preserving PD, in 1 - pylorus-preserving total duodenopancreatectomy and in 5 - distal PD with the CA excision (the modified Appleby procedure). As this took place, three PDs necessitated the pancreatic body resection or removal and portal (PV) or superior mesenteric vein (SMV) resection. Basing on CT data in all the cases the tumor extension was clinically staged as T4 with regional spread suspected in 5 cases. In all the cases CT demonstrated the tumor to be unresectable because of the SMA involvement, in 6 cases, that of SMA and CA - in 1, of the CA and left hepatic artery (LHA) - 1, of the common hepatic artery (CHA) -1, replaced right hepatic artery (rRHA) - 1 and of the gastroduodenal artery (GDA) - 1 case.

In R2 group (B, Table 2) the neoplasm was sited in the pancreatic head in 7 and in the body of the pancreas - in 1 case. In 2 cases classical version of the standard PD, and in 6 - its pylorus-preserving variation were performed. In one case the modified Appleby operation was done. In all the cases the tumor extension was intraoperatively assigned T4 owing to the SMA invasion, and all the patients were found to have regional metastases (Table 2). Five patients in this group were examined by endoUS, which showed SMA
Involvement in one case, CA involvement in one case and in three cases the report was equivocal.

In bypass group (C, Table 3) the tumor was located in the pancreatic head and body in 9 and 2 cases correspondingly, and in 1 case the whole of the gland was affected. In all the cases CT identified the spread of the malignancy as T4 due to the SMA, and both the SMA and CA together being involved in 7 and 5 cases respectively. Regional spread was proven in 5 cases. In the other patient the pancreas biopsy was done, and that of the lymph nodes was not performed.

Eight patients in Group A, 6 in Group B and 8 in Group C received and/or are receiving gemcitabine chemotherapy. One patient with pancreatic body cancer from Group A was given gemcitabine and eloxatin neoadjuvant chemotherapy.

Perioperative characteristics were compared in groups A and B only, because there were no significant blood loss and ICU stay in bypass group (C). There were no difference between operating time ($P_{MW} = 0.368$), blood loss ($P_{MW} = 0.47$) and the length of ICU stay ($P_{MW} = 0.409$) between groups A and B. The overall hospital stay time was approximately the same ($P_{KW} = 0.165$) in all three groups.

There were significant differences in survival between the groups ($p = 0.0001$). The one-year survival was not attained in Groups B and C, notwithstanding the fact that the difference in survival between Groups B and C was considerable ($p = 0.003$). The median survival for Group B was 9.5 months (95%CI: 8.5 - 11 mo). The one-year survival rate in Group A was 88.9% (95%CI: 68% - 100%), two-year - 26.7% (95%CI: 0 - 68%) with a median follow-up period of 22 months (95%CI: 14 - 27 mo). The expected median survival has not been reached because more than half of patients in group A were alive at last follow-up. The difference in survival between groups A and B was significant ($p = 0.0029$) (Fig.14). The actuarial one-year survival in united resection group (Group A + Group B), i.e., in resections nonmettering factor R, was as high as 43.7% (95%CI: 19% - 68%), two-year - 13.1% (95%CI: 0 - 35%) with median survival of 12 months (95%CI: 9 - 19 mo). The median survival following palliative operations was 6 months (95%CI: 5 - 7 mo) and there were significant differences in survival between the groups ($# = 0.00024$) (Fig.15)

Table 1. Group A. Characteristics of the patients who underwent radical (R0-1) surgery for PDAC with circular arterial involvement on CT

<table>
<thead>
<tr>
<th>N</th>
<th>Stage R factor</th>
<th>Location</th>
<th>Artery involved on CT</th>
<th>ChT</th>
<th>DFS (mo)</th>
<th>Survival (mo)</th>
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<tbody>
<tr>
<td>1</td>
<td>#T4N#M0</td>
<td>Head</td>
<td>rRHA</td>
<td>+</td>
<td>17</td>
<td>19</td>
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<tr>
<td>2</td>
<td>#T4N#M0</td>
<td>Body</td>
<td>SMA</td>
<td>+</td>
<td>20</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>#T4N#M0</td>
<td>Body</td>
<td>SMA</td>
<td>+</td>
<td>19</td>
<td>22</td>
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Table 2. Group B Characteristics of the patients who underwent R2 resections for PDAC.

<table>
<thead>
<tr>
<th>N</th>
<th>Stage</th>
<th>PDAC location</th>
<th>Artery involved</th>
<th>ChT</th>
<th>Distant mets (mo)</th>
<th>Survival (mo)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>cT3NxM0</td>
<td>pT4N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>cT3NxM0</td>
<td>pT4N1M0</td>
<td>Body</td>
<td>SMA</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>cT3N1M0</td>
<td>pT4N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>cT3NxM0</td>
<td>pT4N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>cT3N1M0</td>
<td>pT4N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>cT3NxM0</td>
<td>pT3N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>cT3NxM0</td>
<td>pT4N0M0</td>
<td>Head</td>
<td>SMA</td>
<td>-</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>cT3NxM0</td>
<td>pT4N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>6</td>
</tr>
</tbody>
</table>

* alive. # In case 6 there were two SMA segments involved on CT.

Table 3. Group C. Characteristics of the patients who underwent bypass procedures for locally advanced PDAC

<table>
<thead>
<tr>
<th>N</th>
<th>Stage</th>
<th>PDAC location</th>
<th>Artery involved</th>
<th>ChT</th>
<th>DFS (mo)</th>
<th>Survival (mo)</th>
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<tbody>
<tr>
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<td>SMA and CA</td>
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<td>4</td>
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<table>
<thead>
<tr>
<th></th>
<th>Description</th>
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<th>Vessel</th>
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<tr>
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<td>#T4N#M0</td>
<td>Head</td>
<td>SMA</td>
<td>-</td>
<td>NA</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>#T4N#M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>#T4N#M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>4</td>
<td>6,5</td>
</tr>
<tr>
<td>5</td>
<td>#T4N#M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>NA</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>#T4N1M0</td>
<td>Body</td>
<td>SMA and CA</td>
<td>+</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>#T4N#M0</td>
<td>Total</td>
<td>SMA and CA</td>
<td>-</td>
<td>NA</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>#T4N#M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>9</td>
<td>#T4N#M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>#T4N1M0</td>
<td>Head</td>
<td>SMA and CA</td>
<td>+</td>
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<td>6</td>
</tr>
<tr>
<td>11</td>
<td>pT4N1M0</td>
<td>Body</td>
<td>SMA and CA</td>
<td>-</td>
<td>NA</td>
<td>6</td>
</tr>
<tr>
<td>12</td>
<td>pT4N1M0</td>
<td>Head</td>
<td>SMA</td>
<td>+</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

SMA - superior mesenteric artery, #A - celiac trunk, GDA - gastroduodenal artery, LHA - left hepatic artery, CHA - common hepatic artery, rRHA - replaced right hepatic artery.
Fig. 1: In this 65-year old man (case #10) pancreatic body DAC with 360° celiac (CA), splenic (SA) and superior mesenteric artery (SMA) encasement was established on CT (A,B), but endoUS data didn't confirm that, finding a plane between the tumor and the SMA (C,D, arrows)

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Fig. 2: Distal pancreatectomy with excision of the celiac artery (CA) and left adrenalectomy was performed and no SMA involvement was identified at surgery (E). The level of resection was R1 because of the contact of the SMA with the tumor.

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**Fig. 3:** In this 64-year old woman (case #7) circular encasement of celiac, common hepatic, left gastric, left hepatic and splenic arteries by PDA on the background of aberrant arterial anatomy - replaced right hepatic artery (rRHA, Michels, type VIIIb) was identified on CT (A-D)

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Fig. 4: Case #7. Photograph of operating field after distal pancreatotomy R0 with excision of the celiac (CA), common (CHA), left gastric (LGA), and left hepatic artery (LHA) and resection of gastroduodenal artery (GDA) was performed and there were no major arteries involvement was identified at surgery and histopathology; Blood supply to stomach is routed from SMA via PDAs and then through GDA with the latter’s proximal segment being resected and ligated (E)

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Fig. 5: Removed specimen under microscope (case #7). The tumor (DA) was less than 2 cm and was surrounded with thick layer of fibrotic tissue (A-D). No signs of involvement of major peripancreatic (CHA, GDA, LHA) arteries. A. CHA section obtained from close to the point of its transection (white arrow) amid fibrotic zone (black arrow) along pancreas margin. No evidence of tumor growth x5; B. Celiac plexus and trunk area of diffuse fibrosis (f) x5; A - artery; N - nerve plexus with large ganglion. C. Pancreatic tissue with apparent diffuse fibrosis (f), groups of islets left (I) and that of glandular formations of ductal adenocarcinoma of pancreas (DA) x50. D. Structures of DA throughout fibrotic tissue (F) containing remnants of pancreatic tissue (atrophic islets and ductules) x 50. H+E.

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Fig. 14: The differences in survival between the groups were significant ($p = 0.0002$). Explanation is in the text.

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Fig. 13: Intraoperative photograph. Extended Whipple procedure was performed. There were no signs of rRHA and SMA involvement at surgery. The level of resection was R1 because of the contact of the rRHA with the tumor. SMA - superior mesenteric, rRHA - replaced right hepatic, LHA - left hepatic, RGEA - right gastro-epiploic arteries, CT - celiac trunk, SMV - superior mesenteric, PV - portal, LRV - left renal vein. T - tumor, PS - pancreatic stump.

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Fig. 12: In this 75-year old woman (case #1) 360° PDAC encasement of the replaced right hepatic artery (rRHA) was diagnosed on CT, while endoUS data described only tumor abutment to the artery. Arterial phase. Frontal image. CT evidences circumferential infiltration of the rRHA.

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Fig. 11: CT-angiography 3 months postsurgery. No relapse and no narrowing of the SMA.

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Fig. 10: Intraoperative photograph. Extended Whipple procedure was performed. There were no signs of SMA involvement at surgery. The level of resection was R1 because of the contact of the SMA with the tumor. SMA - superior mesenteric artery, SMV - superior mesenteric, PV-portal, IVC - inferior caval, LRV - left renal veins.

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Fig. 9: In this 59-year-old man (case #4) 360° PDAC encasement of SMA were diagnosed on CT (A-D), while endoUS data described only tumor abutment to the SMA. A-C. CT. Arterial phase. Axial images. CT evidences circumferential infiltration of SMV. The celiac artery (CA) is intact; D. CTA. Local narrowing of the SMA at the site where it was circumscribed by tumor.

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Fig. 8: (case #6)...there were no signs of SMA and hepatic arteries involvement at surgery and extended Whipple procedure with pancreatic body, portal, splenic and superior mesenteric vein resection was performed with the use of superficial femoral vein autograft (next picture) The level of resection was R1 because of the contact of the SMA with the tumor. A- aorta, SMA - superior mesenteric, RHA- right hepatic, LHA - left hepatic, SA - splenic, RGEA- right gastro-epiploic arteries, SMV - superior mesenteric, PV-portal, LRV- left renal veins, T- tumor, Pancr - pancreatic tail stump.

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Fig. 7: Case #6. "Organoleptic" signs of unresectability (both hepatic arteries were embedded in the tumor) at surgery, but...

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Fig. 6: In this 61-year old woman (case #6) 260° and 360° PDAC encasement of SMA segments were diagnosed on CT (A-E), while endoUS data described only tumor abutment to the SMA. A. B. Venous phase. Frontal view. CT evidences circumferential involvement of the SMV and PV. C., E. Arterial phase. Frontal view. The distal SMA segment (6-7 cm from the origin) presents circumferential adjacency to pancreatic head ductal adenocarcinoma. The celiac artery (CA) is unaffected; D. Arterial phase. Axial image. At least 260° of the proximal SMA segment (2.5-3 cm from the origin) is circumscribed by tumor

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Fig. 15: The median survival following palliative operations was 6 months (95%CI: 5 - 7 mo) and there was significant difference in survival between the palliative group (C) and united resection group (Group A + Group B).

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Conclusion

Arterial encasement on CT does not necessarily signify arterial invasion. Whenever PC is considered unresectable endoUS should be used. In selected cases, radical resection may be possible and provide survival benefit.