Computer tomography in pre-operative staging of pancreatic cancer
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Chapter 2

The value of spiral CT in pre-operative staging of potentially resectable carcinoma of the pancreatic head

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Chapter 2

Abstract

Purpose
To assess the value of spiral CT in the pre-operative staging of potentially resectable pancreatic head carcinoma.

Methods
In 56 consecutive patients with pancreatic head carcinoma spiral CT findings were prospectively correlated with operative and histo-pathologic findings. Criteria for irresectability at CT were infiltration of the peripancreatic fat and vascular ingrowth grade D, on a scale A to F.

Results
At surgery 27 of 56 tumors were irresectable (48%). Small metastases were found in seven patients (12%). Ingrowth in portal or mesenteric vein was present in 19 patients (34%). Sensitivity and specificity of CT for irresectability were 78% and 76%. Resection rates with a vascular margin free of tumor were respectively for grade A: 100%, B: 63%, C: 44%, D: 15%, E: 0%, with a predictive value for ingrowth of 88% for grades D or higher. Resectability rate was 11% (1/9) when infiltration of the anterior peripancreatic fat was present and 61% when infiltration was absent ($\chi^2, p<0.01$).

Conclusion
Spiral CT with thin slices seems to improve detection of distant metastases and vascular ingrowth in patients with pancreatic head carcinoma.
Pre-operative staging

Introduction

Patients with a pancreatic head carcinoma have a poor prognosis and the only chance of cure is surgical resection. Pre-operative staging focusses on the detection of non-resectable disease in order to prevent an unnecessary laparotomy. Before the introduction of spiral CT, dynamic CT was regarded as the best technique for staging pancreatic head carcinoma, with a reported accuracy of 90-100% for predicting irresectability of the tumor. However, the predictive value for resectability of a tumor was reported as low as 28%. The predictive value for resectability was reported to be slightly better (56%) for spiral CT, in a series using CT with 8 mm thick sections. Undetected small metastases and vascular ingrowth (in the portal or the mesenteric veins) accounted for approximately 40% each, in causing a false negative spiral CT. Detection of liver lesions and visualization of anatomic details of pancreas and peripancreatic vessels can be improved using thinner sections in spiral CT.

The aim of this study was to evaluate the use of spiral CT with thin sections (5mm), for staging of patients with potentially resectable malignancy in the pancreatic head region. The CT findings were correlated with findings at surgery and histo-pathology in 56 patients with pancreatic head carcinoma, who underwent an as curative intended resection.

Patients and methods

Between June 1995 and December 1996, 113 consecutive patients, suspected to have a pancreatic head carcinoma underwent both a spiral CT and a duplex sonography (DUS) as pre-operative assessment.

In 14 patients benign disease was diagnosed: chronic focal pancreatitis in seven, obstructing bile duct stones in three, and no pancreatic abnormalities in four. In eight patients percutaneous biopsy proved metastases to the liver or to distant lymphnodes. In 16 patients the pancreatic mass was considered to be irresectable, due to the local extent of tumor, due to vascular occlusion or to perivascular mass, with narrowing of the vessel and with an abnormal Doppler shift. Ten patients presumed to have resectable tumors were unfit for surgery (n=1), refused operation (n=1), or were treated at other institutions (n=8).

The remaining 65 patients underwent a diagnostic laparoscopy with laparoscopic
sonography (DLUS) and subsequent surgery for attempted resection. In two patients no final diagnosis was obtained (in one patient extensive pancreatitis prohibited resection, the other patient died of cholangitis before surgery). In two patients surgery was delayed for more than two months after CT. Five patients underwent a resection but no carcinoma was found present (one carcinoid tumor was found and four cases of a chronic focal pancreatitis).

Our study consisted of the remaining 56 patients, with proven pancreatic head carcinoma, in whom CT could be correlated with surgical findings: 34 males and 22 females, with a mean age of 59.9 years (40-76 yr).

Spiral CT Technique
Spiral CT was performed on a Siemens Somatom Plus scanner. Unenhanced contiguous 10 mm slices of the liver and the pancreas were followed by contrast enhanced spiral CT of the pancreas (5 mm slice thickness, 24 rotations, pitch of 1). An iv contrast infusion rate of 2 ml/s was used for 130 ml megluminejoxithalamate 300 mg/ml (Guerbet), the scan delay was 55 seconds. A second spiral CT with 5 mm slice thickness was made through the liver.

CT staging
The CT examinations were prospectively scored by a radiologist, who was blinded for all clinical and other diagnostic information. Obstruction of the biliary or pancreatic duct and presence of a mass in the pancreatic head was noted. Tumors were scored as irresectable, if infiltration of peripancreatic fatplanes was present or when involvement of portal vein (PV) or superior mesenteric vein (SMV) was graded as D or higher. (Grade A: fatplane visible between tumor and vessel, grade B: normal pancreatic tissue between tumor and vessel, grade C: tumor adjacent to vessel with a convex contour towards vessel, grade D: tumor adjacent to vessel with a concave contour towards vessel, grade E: circumferential involvement of the vessel and grade F: vascular occlusion, after Loyer et al 8). Lesions were also scored as irresectable, when arterial encasement was present: complete circumferential involvement (cuff sign), narrowing or occlusion of the artery. All other lesions were scored as resectable, including liver lesions that could not be punctured percutaneously.

At DLUS and at surgical exploration tumor irresectability due to metastases or due to local tumor extent was always confirmed by biopsies. The CT findings were correlated with the findings at laparoscopy, at surgical exploration, and at histopathological examination. The Chi square test with one degree of freedom was used for statistical analysis.
Results

CT Diagnosis:
In 54 of the 56 malignant lesions CT demonstrated a mass in the pancreatic head. In two patients CT could only demonstrate dilatation of both the pancreatic duct and the common bile duct. Forty-nine of the 54 detected lesions (90%) were qualified by CT as being malignant (hypodense lesion, clearly demarcated from normal pancreas, with ductal obstruction). In five cases distinction from a pancreatitis was not possible by CT. The mean diameter of the tumors, visible at CT was 2.8 cm (range 1-4.5 cm). At pathology the average size of resectable lesions was 3 cm.

Surgical findings:
Twenty-seven of the 56 (48%) carcinomas were irresectable: liver metastases were found in six patients (11%) and peritoneal metastases were found in one patient. One patient also had distant malignant lymphnodes. In 21 patients without liver metastases, local irresectability of the tumor was proven with biopsies at trial dissection (19 patients had venous ingrowth).
Twenty-nine of the 56 (52%) carcinomas were resectable, and a resection was performed. Three patients underwent a sleeve resection of the vein, due to tumor ingrowth detected at a late phase of the resection (after transsection of the pancreas).

CT Staging
CT data were correlated with the overall resectability at surgical exploration, including patients who had metastases. In 28 patients CT scored the tumor as resectable, correctly in 22 (79%), six were proven irresectable due to vascular ingrowth. CT graded 28 tumors as irresectable, correctly in 21 patients. In seven of these a resection could be performed (three with tumor-positive vascular resection margins). All six patients with liver metastases were in the group scored as irresectable. Sensitivity, specificity and positive and negative predictive value of CT for irresectability at surgery were 78% (21/27), 76% (22/29), and 75% (21/28) and 79% (22/28), respectively. Excluding the patients with metastases, CT findings are correlated with local surgical resectability in Table 1. Sensitivity and positive predictive value for local irresectability were slightly lower than for overall resectability (71% and 68%, respectively).
A radical resection (tumor-negative resection margins at pathology) was obtained in 20 of 29 resected tumors, including in one case of a sleeve resection (Fig 1).
In Table 2 the resectability at CT is correlated with radicality of the resection, excluding
Table 1: Resectability at CT correlated with local surgical resectability

<table>
<thead>
<tr>
<th></th>
<th>Resectable</th>
<th>Irresectable</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resectable</td>
<td>22</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>Irresectable</td>
<td>7</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>29</td>
<td>21</td>
<td>50</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, positive and negative predictive value of CT for local irresectability at surgery were 71% (15 of 21), 76% (22 of 29), 68% (15 of 22), and 79% (22 of 28), respectively.

Fig 1: Small pancreatic head carcinoma (T). CT grade C contact with SMV with flattening of the vein (arrow). Radically resected lesion, sleeve resection necessary.

Table 2: Resectability at CT correlated with radicality at pathology.

<table>
<thead>
<tr>
<th></th>
<th>Radical resection</th>
<th>Non-radical resection</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resectable</td>
<td>16</td>
<td>12</td>
<td>28</td>
</tr>
<tr>
<td>Irresectable</td>
<td>4</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>20</td>
<td>30</td>
<td>50</td>
</tr>
</tbody>
</table>

The sensitivity, specificity, positive and negative predictive value of CT for a non-radical resection at pathology were: 60% (18 of 30), 80% (16 of 20), 82% (18 of 22), and 57% (16 of 28), respectively.
the patients with metastases. The positive predictive value of CT for a non-radical resection was 82%, with a sensitivity of 60%. If patients with metastases were included, the overall positive predictive value of CT for a non-radical resection would be 86%, with a sensitivity of 67%.

CT vascular grading.

In 19 patients local irresectability at surgery was due to venous ingrowth. Arterial ingrowth was found in 8 patients, but never without coexisting venous ingrowth. Excluding patients with metastases and using the highest CT grade for PV and SMV invasion as a single parameter, surgical resection rates for grades A-E were respectively: 100%, 75%, 67%, 31%, and 0% (Fig 2). The resection rate was 76% (25/33) at grades A-C and 24% (4/17) at grades D-E ($\chi^2$, p <0.001).

Fig 2 CT Grade of Venous Involvement correlated with Local Surgical Resectability

![Fig 2 CT Grade of Venous Involvement correlated with Local Surgical Resectability](image)

The sensitivity, specificity and positive and negative predictive values of CT for local irresectability at surgery (CT grade D and E) were: 61%, 86%, 76% and 75% respectively.

Fig 3 CT Grade of Venous Ingrowth correlated with Vascular Ingrowth at Pathology

![Fig 3 CT Grade of Venous Ingrowth correlated with Vascular Ingrowth at Pathology](image)

The sensitivity, specificity, positive and negative predictive value of CT (grades D and higher) for venous ingrowth at pathology were: 55%, 91%, 88% and 64% respectively.

(Grade A/B: fat/normal tissue between tumor and vein; grade C/D: convex/ concave contour of tumor; grade E: circumferential involvement.)

Venous ingrowth at histopathology could be assessed in 50 patients, after resection or if biopsies were taken of the vascular plane during trial dissection. A sleeve resection was considered as ingrowth, regardless of involvement of the resection margins. Venous ingrowth was thus found in 15 of 17 tumors with CT grades D or E, yielding a predictive value of 88% (Fig 3). Infiltration of peripancreatic fatplanes was one of the CT parameters...
for local irresectability. Correlation with local surgical resectability was examined for patients without metastases. Infiltration of the anterior peripancreatic fatplane was seen in nine patients and a resection could be performed in only one (11%) (Fig 4). If anterior fatplane infiltration was absent the resectability rate was 67% ($\chi^2$, $p < 0.01$). Posterior fat infiltration was present in 16 patients, and seven of these underwent resection (the resection margins were free of tumor in five). Furthermore, there were seven patients with indeterminate liver lesions at CT that could not be biopsied percutaneously. Sizes of these lesions were: < 15 mm in two, < 10 mm in two, and < 5 mm in three. Two lesions were proven malignant at LUS, and 4 were proven to be benign, 1 lesion had negative biopsies at LUS, but proved malignant on short follow up.

![Fig 4 Pancreatic head carcinoma (T). Subtle infiltration of anterior peri-pancreatic fat (arrows). No sign of venous invasion. At surgery irresectable tumor was found due to local extension of tumor.](image)

**Discussion**

CT has been regarded the most accurate diagnostic modality in pre-operative staging of pancreatic head carcinoma. The sensitivity and specificity for irresectability have been reported to be up to 100% (Table 3)\(^5\)\(^9\)\(^\text{12}\). The findings from the present study seem comparable with those of McCarthy\(^9\), but are less accurate compared to studies using a 3 mm helical CT technique\(^10\). Results should be interpreted cautiously, as variation in resectability rates could indicate differences in patient selection or in surgical strategy. In the present series with 5 mm slice thickness, small metastases were undetected or unproven after CT in 12% of the patients. As only patients with biopsy proven metastases were excluded from further work-up, this seems an improvement in pre-operative detection.
Pre-operative staging

of metastases compared to series using dynamic CT or helical CT with 8 mm slice thickness. Metastases were found at surgery in 40% of the patients, that were considered to have resectable tumors at CT in one series. This improved detection of metastases may partly be due to improved fine needle biopsy (FNB) techniques often performed under CT or US guidance, but it may also be partly due to patient selection.

Laparoscopy and LUS have been advocated in pre-operative staging. In a recent report LUS with laparoscopy showed metastases, undetected pre-operatively in 35% of patients with pancreatic head carcinoma. DLUS with diagnostic puncture may be usefull in patients with indeterminate liver lesions at CT, that cannot be punctured percutaneously. In our study these patients were regarded potentially resectable and received further work-up by laparoscopy. CT was reported to detect a high number of small benign lesions, and our data agree with this finding (four of seven indeterminate lesions were proven to be benign).

Vascular encasement is the major cause of local irresectability and is found in approximately 50% of patients thought to have resectable tumors after CT. Data are hard to compare because different CT criteria have been used. When correlating findings with surgical resectability, results are also dependent on varying attitudes towards performing a venous resection. Complete encirclement of the vessels and total occlusion of a vessel are considered to be 100% specific for irresectability, but these criteria are not found in many of the patients. In a study that used thin-section helical CT, patients with more than 180 degrees of vessel encirclement were found to have vascular ingrowth in 88%. In our series the latter criterium represented 100% surgical irresectability, although it was only present in grade E tumors (that had complete

Table 3 Sensitivity and specificity of CT for irresectability, correlated with surgery

<table>
<thead>
<tr>
<th>Author</th>
<th>sens</th>
<th>spec</th>
<th>No of patients</th>
<th>Resection rate</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCarthy 98 *</td>
<td>72%</td>
<td>80%</td>
<td>67</td>
<td>48%</td>
<td>Pancreatic carcinoma</td>
</tr>
<tr>
<td>Diehl 98</td>
<td>91%</td>
<td>90%</td>
<td>76</td>
<td>28%</td>
<td>Pancreatic carcinoma</td>
</tr>
<tr>
<td>Bluemke 95</td>
<td>53%</td>
<td>100%</td>
<td>64</td>
<td>34%</td>
<td>Pancreatic carcinoma</td>
</tr>
<tr>
<td>Megibow 95</td>
<td>77%</td>
<td>50%</td>
<td>143</td>
<td>18%</td>
<td>Pancreatic neoplasms</td>
</tr>
<tr>
<td>Warshaw 90</td>
<td>56%</td>
<td>87%</td>
<td>55</td>
<td>29%</td>
<td>Pancreatic head ca.</td>
</tr>
<tr>
<td>Freeny 88</td>
<td>95%</td>
<td>100%</td>
<td>51</td>
<td>3%</td>
<td>Pancreatic carcinoma</td>
</tr>
<tr>
<td>Present series</td>
<td>78%</td>
<td>76%</td>
<td>56</td>
<td>52%</td>
<td>Pancreatic head ca.</td>
</tr>
</tbody>
</table>

* retrospective study
circumferential involvement of the vessel). In grade D tumors (concave contour of tumor towards vessel) the resectability rate was also low (25%), and all of these tumors had less than 180 degrees of venous involvement. If radicality is also taken into account, a resection with tumor free vascular margins could only be obtained in 13% of these grade D tumors. It is questionable, whether this criterium should be used to exclude patients from resection.

The sensitivity of 53% for vascular ingrowth seems low when correlating CT with pathology. This may partly be due to exclusion of patients, that had evident vascular encasement at pre-operative US and CT, and exclusion of patients, that had encasement at CT without histological confirmation, because of metastases that were found at surgery. In nearly one third of the patients that had undergone a resection, vascular ingrowth was found at pathology. Microscopic ingrowth seems therefore hard to predict at surgery as well. The predictive value of CT for vascular ingrowth at surgery was 76%. A recent study, using 3 mm spiral CT, found a predictive value for ingrowth of 70% for axial CT compared to surgical findings. In the same study CT with 3D rendering of the vessels showed a predictive value for ingrowth of 90% 20.

In conclusion spiral CT with thin slices seems to improve the detection of liver metastases and of vascular ingrowth in patients with carcinoma of the pancreatic head. Further studies should be performed to find definitive criteria that can exclude patients from laparotomy, because of a high predictive value for vascular ingrowth.
Pre-operative staging

References

7 Winter TC, Nghiem HV, Schmiedl UP, Freeny PC. CT angiography of the visceral vessels. Seminars in Ultrasound, CT & MR 1996;17:339-351.


