An evaluation of the accuracy of CT when determining resectability in pancreatic head adenocarcinoma locally advanced after neoadjuvant treatment

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Purpose

Complete surgical resection is currently the only potentially curative treatment for a pancreatic adenocarcinoma (1). However, only 10-15% of patients benefit from such treatment because their symptoms present late in the disease, and thus, the diagnosis is performed at a locally advanced or metastatic stage in more than 80% of cases (2).

The use of preoperative chemoradiotherapy may be responsible for a "downstaging" of the tumor in about 30% of patients, allowing us to extend surgical approaches to locally advanced lesions (3). In these cases, the rates of complete resection and survival are close to those that are found in patients who immediately undergo surgery (4).

The assessment of locoregional extensions in pancreatic cancer is currently largely based on computed tomography (CT) analysis because the negative predictive value of this modality is high (89-100%) (5). However, local changes that are secondary to chemotherapy and radiotherapy and due to inflammation, fibrosis, or necrosis may be difficult to evaluate or quantify by CT (6).

The aim of our study was to assess the ability of CT to predict the resectability of pancreatic head adenocarcinomas after neoadjuvant therapy.
Methods and Materials

Study

Between January 2005 and December 2010, 135 patients underwent surgery in our institution with the intent of curing a right pancreatic adenocarcinoma.

The pre-operative CT scans of 80 of these patients were in our possession.

38 of these 80 patients underwent neoadjuvant treatment: 36 patients because tumor was considered locally advanced on the initial CT scan, and 2 patients for presence of N2 lymphadenopathy during exploratory laparoscopy.

Image acquisition

The CT scans were all performed using multidetector CT scanners. The optimal protocol consisted of a routine injection of the iodinated contrast agent that was adapted to the patient's weight (2-3 ml/kg) and injected at a rate of 3-4 cc/s. The scans consisted of pancreatic image acquisition without an injection, an abdominal-slice acquisition in the arterial phase (40-45s), and a portal-phase acquisition in the thorax-abdomen-pelvis. Ten examinations did not have an arterial phase.

Image analysis

Two radiologists blinded to the clinical, operative and histological findings separately analyzed the preoperative CT scans of the 80 patients. In the case of a discrepancy, agreement was reached when the two readers followed a second reading.

The operability assessment was based on an evaluation of liver metastases, peritoneal carcinomatosis, N2-M1 lymphadenopathies. The histological resectability assessment was based on the tumor vascular contacts and their circumferential extent.

A tumor was classified as an R1 resection risk when one or more of the following signs were present:

• tumor abutment with the superior mesenteric artery (SMA),
• abutment or encasement of the hepatic artery (HA),
• contact with the celiac trunk and/or
• invasion of the spleno-mesenteric portal vein (SMPV) confluence superior than 180°, extended for more than 20 mm, or in association with a venous stenosis

Surgical technique and histological analysis

During surgery, resection of the retroportal pancreatic lamina was systematic and extended to the SMA. The orientation and marking of the resection was performed as part of the protocol that was followed by the surgeon in the operating room. A microscopic study was performed after standard HES staining. The posterior resection limit was routinely analyzed in our institution before the start of the inclusion period. In the final analysis, each tumor was classified according to its TNM classification. The type of resection (R1 or R0) and the distance from the smallest margin were recorded.
Results

1. Demographics and clinical data (table 1)

2. Operability

In the control group, only one patient could not undergo resection because of liver metastases that were invisible during the CT scan. One patient underwent a complete resection despite being classified as inoperable from the CT scan.

In the neoadjuvant group, 7 patients were determined to have unresectable tumors upon an exploratory laparotomy; 3 had peritoneal carcinomatosis, 1 had liver metastases, 1 had a positive N2 lymph node upon frozen sectioning, and 2 had unresectable tumor infiltration into the SMA. Of the 7 non-operable patients, 3 were suspected to have advanced regional tumor invasion based on their CT scans. Seven other patients benefited from resection, even though they were considered to be inoperable from their CT scans.

The ability of CT to predict operability was 95% in the control group versus 71% in the neoadjuvant group (p=0.005).

The number of patients who underwent resection despite being deemed inoperable upon CT analysis (false positives) was 1/42 (2%) in the control group versus 7/38 (18%) in the neoadjuvant group (p=0.024).

3. Tumor size and T-staging (Table 2)

The tumor size measurements performed using CT showed a tendency to underestimate the lesion size in the control group and overestimate the lesion size in the neoadjuvant group.

The accuracy of the scanner to correctly grade the tumor stage T was significantly more robust in the control group compared to the neoadjuvant group (respectively 78% versus 39%, p=0.002).

4. Histologic resectability R0 (Table 3)

In the control group
7 of the 41 patients exhibited an R1 resection: 3 in the pancreatic section slice, 2 in the retroportal pancreatic lamina and pancreatic section slice, 1 in the superior mesenteric vein, and 1 in the bile duct.

Four of these R1 patients were classified as R1 upon CT analysis, while 4 other patients that were potentially classified as R1 on CT scan were R0 upon histology; 1 had >50% venous stenosis, 1 had <50% venous stenosis and <25% abutment of the SMA, and 2 had venous contacts <50% and SMA abutment <25%.

In the neoadjuvant group

6 of the 31 patients presented with an R1 resection: 3 in the retroportal pancreatic lamina, 2 in the SMA, and 1 in the pancreatic slice.

Five of these 6 patients were classified as R1 based on the CT analysis; while another 12 patients who were classified as R1 using the scanner had a complete R0 resection. Of these, 3 patients had an SMPV stenosis of >50%, 7 had venous contacts of >50%, 6 had contacts with the SMA, and 6 patients with HA abutments.

The CT ability to predict R0 resectability was reduced in the neoadjuvant group (p=0.039).

The number of patients who underwent complete resection (R0) while they were considered to have a high risk for R1 resection based on CT analysis (false positives) was overestimated in the neoadjuvant group.
<table>
<thead>
<tr>
<th>Table 1: Demographics and clinical data</th>
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<td><strong>Control Group</strong></td>
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<tr>
<td><strong>Number of patients</strong></td>
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<td>- female</td>
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<td>- male</td>
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<td><strong>Age (y) +/- SD</strong></td>
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<td><strong>Interval from CT scan to Surgery: median in days (IQR)</strong></td>
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<td><strong>Biopsy</strong></td>
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<td><strong>Biliary derivation</strong></td>
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<td><strong>Preoperative infectious complications</strong></td>
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<td><strong>Diffuse peri-pancreatic inflammation on CT scan</strong></td>
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<tr>
<td>Histologic median tumor size (mm)</td>
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<td>Variability in tumor size between histology and CT scan (mm)</td>
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<td>Histologic Tumor Staging</td>
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<td>- T0</td>
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<td>CT accuracy for T-staging</td>
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<td>Nature of T staging mistakes</td>
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**Table 2**: Tumor size and T-staging

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<table>
<thead>
<tr>
<th></th>
<th>Accuracy</th>
<th>Specificity</th>
<th>False positives</th>
<th>Negative Predictive Value</th>
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</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>34/41</td>
<td>88%</td>
<td>4/41 10%</td>
<td>91%</td>
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<tr>
<td>Neoadjuvant Group</td>
<td>18/31</td>
<td>52%</td>
<td>12/31 39%</td>
<td>93%</td>
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<tr>
<td>p-value</td>
<td>0.039</td>
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**Table 3**: Histologic resectability
Conclusion

The use of neoadjuvant therapy is commonly accepted as the initial step in the management of patients with "borderline" and locally advanced pancreatic head cancer to increase the likelihood of an R0 resection (7).

*In this study, we show that the ability of CT to evaluate operability, T-staging, and histological resectability is reduced after neoadjuvant therapy. The decrease in the diagnostic specificity of the scan is chiefly due to an overestimate of the tumor size and vascular contacts after preoperative treatment.*

Thus, our results validate the current attitude that seeks to focus on surgical exploration in any patient with a decrease in his or her tumor markers and the absence of tumor growth upon a CT revaluation performed at the end of neoadjuvant therapy. The persistence of vascular involvement upon post-radiochemotherapy scanning is not correlated with tumor invasion and therefore cannot contraindicate surgical exploration.
References


