ABSTRACT

Background: Computed tomography (CT) is widely used to pre-operatively evaluate patients with pancreatic tumors.

Aim: The purpose of this study is to evaluate retrospectively, the ability of multi-detector computed tomography (MDCT) to predict resectability of pancreatic cancer on the basis of surgical outcome and pathologic correlation.

Patients and Methods: Sixty nine consecutive patients presenting between January 2007 and June 2010 with pancreatic head tumors were included in the study. The study group comprised patients with pancreatic head tumors from the local catchment area and others referred to our tertiary care center from surrounding hospitals. Sixty nine examinations were performed with the same 64 slice CT scan (Brilliant Philips). All patients were imaged using a standardized MDCT protocol. Patients with disease that was clearly inoperable were excluded from the study. The remaining patients (32) had their CT studies double-reported using a standard method. Images were scored for vascular involvement, tumor size and the presence of distant metastases. Surgical and pathologic reports were reviewed and compared to CT results. Frequencies, mean and range were used as descriptive statistics, positive predictive value (PPV) and negative predictive value (NPV) and sensitivity, specificity and accuracy were done using SPSS version 18 program.

Results: Of the 32 patients evaluated, 65.6% had successful resection of pancreatic head tumors; while 34.4% had a palliative procedure. When compared to surgical outcome, the positive predictive value of multi-detector computed tomography for resectability was 100%. On the basis of pathologic results (considering the surgical technique and the positive surgical margin as a microscopic picture), the negative predictive value of multi-detector computed tomography for resectable disease fell to 65.5%. Three patients deemed resectable following multi-detector computed tomography had positive margins at pathology.

Conclusion: There is improved prediction of resectability/unresectability with the introduction of MDCT. When compared to Helical computed tomography (HCT) studies, there is a rise in the rate of successful surgical resection with a concomitant decrease in the rate of palliative surgery. The positive predictive value of multi-detector computed tomography for resectable disease is lower when pathologic correlation, as opposed to surgical correlation, is used as the gold standard.

Key Words: Multidetector computed tomography (MDCT) – Resectability/unresectability prediction – Pancreatic head tumors.

INTRODUCTION

Pancreatic ductal adenocarcinoma is one of the most aggressive human malignancies. It represents the fourth most frequent cause of cancer-related death and the second most frequent cause, after colorectal cancer, when considering digestive tract cancers alone [1]. The incidence of pancreatic adenocarcinoma is still increasing. Because of its silent course, late clinical symptoms and rapid growth patterns, it has been named the “silent killer” [2,3]. About 15 to 20% of patients have resectable disease at the time of presentation [4]. Surgical resection offers the only chance for cure with reported 5-year survival rates of 8% to 21% [5]. Tumors are considered unresectable when metastatic or local vascular invasion is present. The most involved vessels are the celiac trunk, the hepatic artery, the superior mesenteric artery, as well as, the superior mesenteric vein and the portal vein [6,7].

Helical Computed Tomography (HCT) and more recently Multidetector Computed Tomography (MDCT) have been widely accepted as
the imaging technique of choice for the staging of pancreatic adenocarcinoma. Despite the advent of endoscopic ultrasound, computed tomography remains the mainstay of preoperative assessment [8-10]. The introduction of HCT, less than a decade ago, improved our ability to appropriately stage the disease. However, a significant number of patients are still incorrectly diagnosed as having resectable tumor on CT only while proved to be unresectable at surgery. The proportion of patients undergoing unnecessary laparotomy may vary between 21% and 44% [7,11,12].

The purpose of this study is to evaluate, retrospectively, the ability of MDCT to predict resectability of pancreatic cancer on the basis of surgical outcome and pathologic correlation at King Fahed Specialist Hospital-Dammam.

PATIENTS AND METHODS

Sixty nine patients presenting between January 2007 and June 2010 with pancreatic head tumors were included in the study. The study group comprised patients from the local catchment area and others referred to our tertiary care center from surrounding hospitals.

CT technique:

All examinations were performed with the same 64 slice CT scan (Brilliant Philips). Patients drank 1000ml of water to the distal ileum and delineate the pancreatic head region. Patients received an intravenous injection of 100ml of Xenetix 350 (Guerbet, France) at a rate of 4ml/s. The protocol of 64 MDCT is dual-phase performed with a detector width of 0.625mm, a section width of 1mm and an interval reconstruction of 0.5mm. The scan done by bolus tracking at (110 H.U.) threshold at the aorta at corresponding level of superior mesenteric artery. The delayed image at 20 second after threshold for pancreatic phase and the venous phase at 55 second after threshold.

All images were interpreted on a Picture Archiving and Communication System (PACS) workstation. Multi-planar reformations were obtained as a dedicated post processing workstation (Advantage® windows 4.0 General Electric Medical system, Milwaukee, WI, USA). Multiple Slices Computed Scans (MSCT) were analyzed to surgeons to determine resectability.

Image analysis:

Standard axial images, multi-planar reconstructions, maximum-intensity projections, and volume-rendered images were used as appropriate. A standardized reporting proforma was used. Tumor size and the presence of distant metastases were recorded. Vascular involvement (for the superior mesenteric vessels, celiac artery, and portal vein) was estimated using the scheme devised and validated by Lu et al. [6] (grade 0, no contiguity of tumor to vessel; grade 1, tumor contiguous less than one quarter of circumference; grade 2, between one quarter and one half; grade 3, between one half and three quarters; grade 4, greater than three quarters) [6]. A Lu grade of 0 to 2 was considered operable, whereas grades 3 and above were considered radiologically inoperable depending upon other radiological findings. Patients were therefore assessed for operability.

Patients with inoperable disease or for whom curative surgery would not be possible due to co-morbid disease were excluded. This left a group of patients who were fit for surgery with favorable imaging (Thirty-two patients). Images for these patients were double-reported by a second radiologist who was blinded to the initial results. In case of reporting discrepancy, a consensus was reached (Table 1).

Patients in the potentially operable group, CT was followed by laparoscopy. If no contraindication to surgery was found, patients proceeded to formal laparotomy and trial of dissection. Double or single surgical bypass was performed in patients found to be inoperable. Pathologic reports were reviewed to determine if the surgical margins were free of tumor. Criteria for surgical inoperability are listed in Table (2).

Finally, the MDCT findings were correlated with surgical outcomes to assess accuracy in predicting resectability.

Data analysis:

Accuracy, positive and negative predictive values for resectability of MDCT were calculated by using surgical outcome as a reference standard. The same parameters were also calculated by using pathologic findings, particularly the presence or absence of tumor infiltration at the surgical margins. Frequencies, mean and range were used as descriptive statistics. Positive predictive value (PPV), negative predictive value (NPV), technical success rate, and inter-rater reliability were calculated. Inter-rater reliability was assessed using the Kappa test.
value (NPV), sensitivity, specificity and accuracy were done using SPSS version 18 program.

RESULTS

Sixty nine patients presented to our institution with pancreatic head tumor in a 3-year and 7 months period. After radiological and clinical assessment, 37 (53.6%) were not suitable for curative surgery, while 32 (46.4%) patients had favorable radiological findings with good performance status and were eligible for surgical resection. This group constituted our study. There were 19 (59.4%) males and 13 (40.6%) females, with mean age of 53 years (range 31-69 years). Twenty-one patients (65.6%) underwent a Whipple procedure, whereas 11 patients (34.4%) underwent a palliative procedure. The mean interval between MDCT and surgery was 17.5 days (range 3-97 days). The mean diameter of the lesions was 4.4cm (range from 2-9cm). Surgical and pathologic reports were reviewed and compared to CT results. Perioperative staging by MDCT is presented in Table (3).

In our study, CT showed no vascular encasement in 23 (71.9%) patients (grade 0) and 9 (28.1%) patients had vascular encasement (grade 1-3). CT diagnosed liver metastases in 2 (6.2%) patients. According to Lu classification for vascular involvement, 29 (90.6%) patients were resectable (grade 0-2) and 3 (9.4 %) patients were considered unresectable (grade 3) (Table 4). Of the 11 unresectable patients during surgery, 3 cases were proved to be inoperable by CT (Lu grade 3, for portal vein encasement), 3 cases had infiltration of both portal vein and superior mesenteric vein (SMV), 2 cases with uncinate process mass infiltrating the superior mesenteric artery (SMA), SMV and root of mesentery. One case had locally advanced disease with encasement of the hepatic artery and portal vein, and another patient had liver metastasis not diagnosed by CT preoperatively, while the last case had severe pancreatitis with teasing of the portal and SMV vein hindering the resection. This could be due to CT underestimation of the disease.

On the basis of pathologic results (considering the surgical technique and the positive surgical margin as a microscopic picture), three of the 21 (14.3%) patients, who underwent a Whipple procedure and were believed to be resectable on the basis of MDCT, were found to have positive surgical margins (Table 5). So the negative predictive value of MDCT for overall respectability fell to 65.5% (19/21) (Table 3).

Follow-up scans obtained within 6 months of surgery in one of these patients showed local recurrence of the tumor.

Table (6) shows the pathological characteristics of the patients.
DISCUSSION

The accurate determination of resectability in patients with pancreatic cancer is the most important contribution of pre-operative staging; the goal being to reduce needless surgery to a minimum [13]. Laparotomy in patients with pancreatic cancer carries significant perioperative morbidity (20-30%), even in expert hands, [14]. Moreover, prognosis is not improved for patients whose tumors are resected with positive margins or vascular invasion [15,16]. On the other hand, for patients with unresectable lesions, laparotomy for palliative procedures has become unnecessary because of recent advances in endoscopic and percutaneous methods of biliary and duodenal decompression [13].

This study examined the preoperative staging ability of MDCT in a group of patients with pancreatic head tumors. For patients who had surgery, direct comparison with the radiological findings was done. We undertook this study because, although CT is the most widely used staging modality, there is relatively little published work quantifying the accuracy of modern MDCT. Lu et al. has demonstrated that involvement of vessel wall, as judged by degree of physical contact, is highly specific for inoperability [6]. In a series of 25 patients, those with grades 2 and 3, corresponding to one half to three quarters of the vessel circumference, yielded the lowest number of false negatives for unresectability [6].

The improvement in CT technology has been paralleled by an improvement in the ability of CT to predict resectability. In a meta-analysis, Bipat et al. found a sensitivity and specificity of HCT for determining resectability of 81% and 82%, respectively [17]. This represented a significant improvement over conventional CT. Predictive values of HCT for resectability ranging from 56% to 79% have been reported [7,11,12,16,18]. Most of these studies reported better results when predicting unresectability, with predictive values ranging from 96% to 100%.

Several articles have hinted at the potential of MDCT in this area, but evidence of a definite increase in preoperative staging sensitivity is lacking [19-25]. A small series of 27 patients was examined by Laghi et al., using isometric data sets, positive predictive value was 80% for resectability and 93.3% for irresectability [24]. In another study by Catalano et al., sensitivity and specificity for predicting resection were 96 and 86%, respectively [26]. However, Ellsmere et al., found sensitivity and specificity of 96% and only 33%, respectively, and a PPV of 61% [27]. Also Smith et al., found that MDCT had an accuracy, sensitivity, specificity, PPV, and NPV of 72.7%, 81.8%, 68.2%, 56%, and 88.2%, respectively [28]. In a series of 69 patients, Maire et al., found a PPV of 86% and concluded that laparoscopy is needed in all cases when there is preoperative uncertainty [29]. Computed tomography has been compared with other staging modalities; Soriano et al., examined the efficacy of CT, endoscopic ultrasound, magnetic resonance imaging, and angiography. They concluded that CT had the highest accuracy for assessing the extent of the

Table (4): Lu classification for vascular involvement.

<table>
<thead>
<tr>
<th>Grade</th>
<th>No./Percentage</th>
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<tbody>
<tr>
<td>No contiguity</td>
<td>grade 0 23 (71.9)</td>
</tr>
<tr>
<td>Contiguous less than one quarter</td>
<td>grade 1 2 (6.2)</td>
</tr>
<tr>
<td>Between one quarter and one half</td>
<td>grade 2 4 (12.5)</td>
</tr>
<tr>
<td>Between one half and three quarters</td>
<td>grade 3 3 (9.4)</td>
</tr>
<tr>
<td>Greater than three quarters</td>
<td>grade 4 0</td>
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</tbody>
</table>

Table (5): Local resectability at MDCT correlated with pathological results.

<table>
<thead>
<tr>
<th></th>
<th>Free margins (n=18)</th>
<th>Positive margins (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT resectable</td>
<td>18 (100%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>CT unresectable</td>
<td>0</td>
<td>0</td>
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Table (6): Pathological criteria.

| Malignant (n=25)                      | 88% |
| Adenocarcinoma of pancreas           | 24 (85%) |
| Invasive serous cystadenocarcinoma    | 1 (3%) |
| Benign (n=7)                         | 22% |
| Lymphoplasmacytic sclerosing pancreatitis | 1 (3%) |
| TB pancreas                          | 1 (3%) |
| Muscinous cystic neoplasm            | 1 (3%) |
| Micromucinous cystadenoma of pancreas| 2 (6%) |
| Intraductal papillary mucinous neoplasm| 2 (6%) |

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local tumor (73%), local extension (73%), vascular invasion (83%), metastases (88%), and resectability (83%). Endoscopic ultrasound had the highest accuracy in determining tumor size and lymph node involvement, but with a sensitivity of 65% only [30].

In our study, the comparison between the MDCT and surgical result (as standard practice), showed that the accuracy, sensitivity, specificity, PPV and NPV for vascular invasion were 91%, 76.6%, 100%, 100%, 86.6%, respectively. For liver metastases, it was 97%, 66.7%, 100%, 100%, 96.7%, respectively, and for resectability, it was 75%, 27.3%, 100%, 100%, 72.4%, respectively. From these results, we can notice that the sensitivity of MDCT is low for the resectability, and this may be due to inability to diagnose small liver metastases, and/or underestimate local vascular invasion. Perhaps, it is important to make the distinction between resectable (curable) and operable disease. Tumors that can be removed, but with a positive pathological margin using the standard surgical definition, are not truly resectable. It is possible that our preoperative staging accuracy is higher than presented because, we are assuming that a technically successful Whipple procedure is curative, which is not always correct. So comparing CT results to pathologic findings modifies the results somewhat. When the absence of positive margins is considered the requirement for successful resection, the accuracy, sensitivity and NPV of MDCT for overall resectability fall to 69%, 23.1%, 76.9%, respectively.

In conclusion, there is improved prediction of resectability/unresectability with the introduction of MDCT. When compared to HCT studies, there is a rise in the rate of successful surgical resection with a concomitant decrease in the rate of palliative surgery. Despite technology advances, a group of patients remains with early but locally invasive pancreatic tumors, where anatomical imaging is unable to predict inoperability. Pancreatic surgeons should be aware of this intrinsic limitation of preoperative CT.

REFERENCES

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