Evaluation of endoscopic ultrasonography and intraoperative ultrasound for vascular invasion in pancreatic tumors

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ABSTRACT

Background: Pancreatic cancer is a growing source of cancer related death and it has poor survival rates which have not improved in the last few decades so it requires early detection and surgical intervention. This intervention necessitates proper preoperative assessment especially the relation to adjacent blood vessels to determine its resectability.

Objective: To evaluate the role of endoscopic ultrasound (EUS) and intraoperative ultrasound (IOUS) in the assessment of pancreatic tumors and their relation to adjacent blood vessels.

Patients and methods: A Prospective study that was conducted among 30 patients with resectable and borderline pancreatic tumors and fit for surgery attending to Theodor Bilharz Research institute [TBRI] and Al-Azhar University Hospitals during the period from September 2019 to May 2021.

Results: Both EUS and IOUS examination showed high diagnostic accuracy in assessment of pancreatic tumors especially the relation to adjacent major blood vessels and were superior to the conventional imaging modalities like multidetector computed tomography (MDCT).

Conclusion: The correct diagnostic identification, reached by combination of different imaging modalities and techniques, has allowed to select patients with cancer really resectable, and endoscopic ultrasound examination and intraoperative ultrasound assessment increased the diagnostic accuracy of vascular invasion evaluation in pancreatic tumors that was higher than other conventional imaging modalities.

Keywords: Cancer; Pancreas; Endoscopic; Intraoperative; Ultrasound.

INTRODUCTION

Pancreatic tumor is one of the major causes of cancer related death. It has a poor 5-year survival rate of around 8–9%. This is mainly due to the majority of patients with pancreatic adenocarcinoma progress to either metastatic or locally advanced disease while in the asymptomatic phase.¹

Traditionally, the clinical indications for conventional imaging for pancreatic tumors include determination of resectability, detection distant metastasis, and measurement of treatment response.²

Endoscopic ultrasound (EUS) is considered the most sensitive method to detect early malignancy in the pancreas. Indeed, a direct comparison of radiological modalities in the recent era showed that EUS identified pancreatic abnormalities in individuals liable to have
high risk for developing pancreatic cancer 43% of the time, compared to 33% and 11% for MRI and CT, respectively.³

Vascular invasion is an important point for resectionability and deciding the therapeutic management for pancreatic tumors.⁴

The high-resolution depiction of the relation of a tumor to vascular structures by intraoperative US is often of value, particularly when preoperative imaging features are suggestive of borderline resectability or when a difficult resection is faced.⁵

**PATIENTS AND METHODS**

This was a prospective study that was conducted in Theodor Bilharz Research Institute and Al-Azhar University Hospitals during the period from September 2019 to May 2021. This study included 30 patients with resectable and borderline pancreatic tumors and fit for surgery.

**Inclusion criteria:**

Patients with resectable and borderline pancreatic tumors and fit for surgery.

**Exclusion criteria:**

Patients with unresectable pancreatic lesions (e.g: extensive vascular invasion, distal metastasis, ascites…etc)

Patients with diagnosed pancreatic tumors but unfit for surgery (e.g: respiratory distress, coagulopathy, cardiomyopathy…etc).

Criteria of resectability of pancreatic cancer are mentioned below and describe the differences between resectable and borderline resectable pancreatic cancer according to the current NCCN (the National Comprehensive Cancer Network) guidelines.⁶

Resectable:

Arterial: Clear fat planes around the coeliac axis (CA), SMA and HA.

Venous: The SMV or PV abutment but no distortion of the vessels.

Borderline Resectable:

- Arterial (Head of Pancreas): Gastroduodenal artery encasement up to the HA with either short segment encasement or direct abutment of the HA but without extension to the CA. Tumour abutment of the SMA <180° of the circumference of the vessel wall.

- Venous: Venous involvement of the SMV or PV with distortion or narrowing of the vein or occlusion of the vein with suitable vessel proximal and distal, allowing for safe resection and replacement.

All included patients were subjected to laboratory investigations (CBC, liver function tests, renal function tests, coagulation profile and tumor markers CEA, CA 19-9 and AFP), CT abdomen and pelvis with intravenous and oral contrast, Preoperative anesthetic assessment for any contraindication, endoscopic ultrasound and intraoperative ultrasound.
Statistical analysis
The data were analysed using Microsoft Excel 2016 and statistical package for social science ‘IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA)’. Continuous normally distributed variables were represented as mean±SD. with 95% confidence interval, while non normal variables were summarized as median with 25 and 75 percentile, and using the frequencies and percentage for categorical variables; a p value < 0.05 will be considered statistically significant. To compare the means of normally distributed variables between groups, the Student’s t test was performed, and Mann-whitney U test was used in non-normal variables. $\chi^2$ test or Fisher’s exact test w used to determine the distribution of categorical variables between groups. The diagnostic performance of the studied modality was assessed by receiver operating characteristic (ROC) curves. The area under the ROC (AUC) was calculated as an accuracy index for prognostic performance of selected tests.

RESULTS
Patients were in their third to seventh decades of life with mean age of all patients (56±8) years and male predominance (56.7%) (Table 1). Whipple's procedure was done for 28 patients while triple bypass anastmosis was done for 2 patients.

MDCT imaging detected pancreatic lesions in 22 patients while EUS and IOUS examination detected pancreatic lesions in all the patients (Table 2).

Regarding assessment of pancreatic tumors and its relation to adjacent blood vessels, Sensitivity and accuracy of EUS and IOUS in the diagnosis of malignant vascular invasion (83.3% and 66.67% [CI, 72.4% to 94.3%]; P = 0.001) and (80% and 60% [CI, 68.2% to 91.8%]; P = 0.001) with sensitivity 83.3% and 80% respectively and were more than MDCT with specificity and accuracy (70% and 40% [CI, 56.5% to 83.5%]; P = 0.01) (Table 3).

We had two cases of pancreatic adenocarcinoma in which MDCT showed invasion of adjacent blood vessels while endosonography examination and IOUS assessment supported their resectability. However, The surgical decision was changed according to the surgical findings and triple bypass anastmosis was performed (Table 4).

Comparison between the sensitivity, specificity and accuracy of EUS, IOUS and MDCT was elicited and showed statistical significance between results of MDCT and results of both EUS and IOUS (Table 5).
Table 1. Demographic data of the studied patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Min - Max</th>
<th>Mean±SD Or F(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>29.0 - 65.0</td>
<td>56.3±8.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13(43.3%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17(56.7%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Specificity and accuracy of the studied modality regarding mass detection

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>AUC</th>
<th>95% C.I</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDCT</td>
<td>73.33%</td>
<td>73.33%</td>
<td>46.67%</td>
<td>0.733</td>
<td>0.603 - 0.864</td>
<td>0.002**</td>
</tr>
<tr>
<td>EUS</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
<td>1.000 - 1.000</td>
<td>0.001**</td>
</tr>
<tr>
<td>IOUS</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>1.000</td>
<td>1.000 - 1.000</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

Table 3. Specificity and accuracy of the studied modality regarding tumor respectability

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>AUC</th>
<th>95% C.I</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDCT</td>
<td>70.0%</td>
<td>70.0%</td>
<td>40.0%</td>
<td>0.700</td>
<td>0.565 - 0.835</td>
<td>0.01*</td>
</tr>
<tr>
<td>EUS</td>
<td>83.33%</td>
<td>83.33%</td>
<td>66.67%</td>
<td>0.833</td>
<td>0.724 - 0.943</td>
<td>0.001**</td>
</tr>
<tr>
<td>IOUS</td>
<td>80.00%</td>
<td>80.00%</td>
<td>60.00%</td>
<td>0.800</td>
<td>0.682 - 0.918</td>
<td>0.001**</td>
</tr>
</tbody>
</table>
Fig. 1: ROC Curve to discriminate the Specificity and accuracy of the studied modality regarding tumor resectability

<table>
<thead>
<tr>
<th>SURGICAL PROCEDURE</th>
<th>MDCT</th>
<th>EUS</th>
<th>IOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not detected</td>
<td>Whipple</td>
<td>Whipple</td>
</tr>
<tr>
<td></td>
<td>N=28</td>
<td>N=28</td>
<td>N=28</td>
</tr>
<tr>
<td></td>
<td>8(26.7%)</td>
<td>21(70.0%)</td>
<td>25(89.3%)</td>
</tr>
<tr>
<td></td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
</tr>
<tr>
<td>Whipple</td>
<td>N=28</td>
<td>N=28</td>
<td>N=28</td>
</tr>
<tr>
<td></td>
<td>1(3.3%)</td>
<td>2(100.0%)</td>
<td>3(10.7%)</td>
</tr>
<tr>
<td>Triple anastomosis</td>
<td>N=28</td>
<td>N=28</td>
<td>N=28</td>
</tr>
<tr>
<td></td>
<td>0(0.0%)</td>
<td>2(100.0%)</td>
<td>0(0.0%)</td>
</tr>
</tbody>
</table>

Table 4. The associations between the studied modality evaluation and the surgical procedure as a gold standard
**DISCUSSION**

Pancreatic carcinoma is a leading source of cancer related death that has poor survival rates in the last years. Clinical presentation of this disease may include weight loss, obstructive jaundice, malabsorption, pain, vomiting, dyspepsia and nausea; however, many patients are asymptomatic with no early worrisome signs have been established for early detection of pancreatic cancer.\(^7\)

Vascular involvement was found in 21%-64% of patients with pancreatic carcinoma.\(^8\)

The accuracy of CT in assessment of vascular invasion is not strong, with the most recent studies showing a sensitivity of only 60% and specificity 94% when determining involvement of surrounding vessels.\(^9\)

EUS is also used as a reliable tool for local staging, as studies have shown a

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**Table 5. Comparison between the sensitivity, specificity and accuracy of the studied modalities.**

<table>
<thead>
<tr>
<th></th>
<th>MDCT</th>
<th>EUS</th>
<th>IOUS</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EUS Vs MDCT</td>
<td>IOUS Vs MDCT</td>
<td>IOUS Vs EUS</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>70.0%</td>
<td>83.33%</td>
<td>80.0%</td>
<td>0.001**</td>
</tr>
<tr>
<td>Specificity</td>
<td>70.0%</td>
<td>83.33%</td>
<td>80.0%</td>
<td>0.001**</td>
</tr>
<tr>
<td>Accuracy</td>
<td>40.0%</td>
<td>66.67%</td>
<td>60.0%</td>
<td>0.001**</td>
</tr>
</tbody>
</table>
sensitivity and specificity of 72% and 90% respectively for T1-2 staging, 90% and 72% respectively for T3-T4 staging, and 87% and 92% respectively for vascular invasion.\textsuperscript{10}

Intraoperative ultrasound (IOUS) allows confirming and verifying the preoperative assessment. In many cases it allows clear determination of the severity of the disease, safe surgical strategy and shortening its duration, proper evaluation of anatomic structures during the surgery and evaluation of the operating field after the treatment termination that permits more reliable assessment of radical treatment.\textsuperscript{11}

This study showed sensitivity and specificity of MDCT and EUS examination in detecting pancreatic tumors were 73.3\% (n = 22/30; [CI, 60\% to 86\%]; P = 0.002) and 100\% (n = 30/30; [CI 100-100\%]; P=0.001) respectively which was in agreement with Agarwal and his colleagues\textsuperscript{12} who evaluate the role of endoscopic ultrasound-guided fine needle aspiration and multidetector spiral CT in the diagnosis of pancreatic cancer and reported that the accuracy of spiral CT, EUS, and EUS-FNA was 74\% (n = 60/81, CI 63-83\%), 94\% (n = 76/81, CI 87-98\%), and 88\% (n = 73/81, CI 81-96\%), respectively, for diagnosing pancreatic cancer.

The current study showed that the sensitivity and accuracy of EUS and IOUS in the diagnosis of malignant vascular invasion were (83.3\% and 66.67\% [CI, 72.4\% to 94.3\%]; P = 0.001) and (80\% and 60\% [CI, 68.2\% to 91.8\%]; P = 0.001) with sensitivity 83.3\% and 80\% respectively and were superior to MDCT with specificity and accuracy (70\% and 40\% [CI, 56.5\% to 83.5\%]; P = 0.01).

This result was in agreement with Sugiyama and colleagues\textsuperscript{13} who assessed portal venous invasion in pancreaticobiliary cancers and found sensitivity and specificity of MDCT 65\% and 74\% respectively and less than reported in Bipat meta analysis study\textsuperscript{14} in which Sixty-eight articles fulfilled all inclusion criteria, Sensitivity and specificity of MDCT were 81\% and 82\% respectively.

In this work, Diagnostic value of EUS in assessment of vascular invasion in pancreatic tumors showed close results as Sun's study\textsuperscript{15} who reported that the sensitivity, specificity, and accuracy of EUS for malignant vascular invasion ranged from 42 to 91\%, 89 to 100\%, and 40 to 100\% respectively.

Rösch and colleagues\textsuperscript{16} reported that the sensitivity and specificity of EUS in the diagnosis of venous invasion were 43\% and 91\%, respectively, when using predetermined parameters such as visualization of tumor in the lumen, complete obstruction, or collateral vessels.

Also this results in agreement with Ćwik's study\textsuperscript{17} who reported significant advantage of sensitivity, specificity and accuracy of IOUS in diagnosing malignant invasion to the portal vein flow, as compared to CT, IOUS accuracy was determined at 89.7\%, as compared to the average of 64.1\% for CT.

This results in agreement with Werra and colleagues\textsuperscript{18} who reported that IOUS had reached to high level of sensitivity and specificity in the determination of resectionability of lesions, reported a sensitivity of 92-93\% and specificity of 95\% while CT results reach lowest values of sensitivity (71.4-90\%).

Contrary to our results, Aslanian and colleagues\textsuperscript{19} compared EUS with surgical findings
of vascular adherence reported that sensitivity and specificity of EUS were 63% and 64 for vascular adherence (tumor adherence requiring vascular resection) and 50%, 58% for vascular invasion (histologic invasion), respectively.

Also our results in disagreement with DeWitt and his colleagues who compared EUS with surgical findings of vascular adherence and reported that EUS was superior to CT for tumor staging accuracy but with lower statistically rates (67% vs. 41%; p < 0.001). In the current study, IOUS assessment during surgical procedures has not changed the surgical strategy in any case in comparison with Kolesnik and his colleagues who applied IOUS during 76 surgical interventions for pancreatic tumors and observed additional tumor invasion into portal or superior mesenteric vein in 8 patients (10.5%) that not detected in preoperative imaging and reported that the IOUS assessment changed the surgical strategy in 30% of patients included in their study.

CONCLUSION

It can be concluded that endoscopic ultrasound examination and intraoperative ultrasound assessment increased the diagnostic accuracy of vascular invasion in pancreatic tumors and were superior to other conventional imaging modalities but intraoperative ultrasound has a little role in changing the surgical strategy.

REFERENCES

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