The effect of solid pancreatic mass lesions on pancreatic duct diameter at endoscopic ultrasound.

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ABSTRACT

Objectives: To evaluate the effect of solid pancreatic masses on the pancreatic duct (PD) at the endoscopic ultrasound (EUS) and the relationship of the location/size of a mass and PD dilation. Materials and Methods: Patients who underwent EUS for pancreatic indications from 2011 to 2013 at a single center were retrospectively identified. Those with biopsies that revealed adenocarcinoma or neuroendocrine tumors in the pancreas were identified and PD size was ascertained from EUS, computed tomography, or magnetic resonance imaging. Results: Of the 475 patients who had a pancreatic EUS, 239 had a dilated PD and 236 had a normal PD. Patients with a dilated PD had a significantly higher incidence of pancreatic malignancy than those with a normal PD diameter (106/239, 44.4% vs. 32/236, 13.6%, P < 0.001). Of the 138 patients with a pancreatic malignancy, 106 (76.8%) had a dilated PD at some location in the pancreas. Over 80% of patients with a mass within the head, neck, or body had a dilated PD. For a mass located at the uncinate process or the tail, PD dilation was 65% and 23%, respectively. Fifty-six (80.0%) of the masses in the head, 11 (78.6%) masses in the neck, and 16 (76.2%) masses in the body had a dilated PD upstream of the mass. In addition, a step-wise increase in the incidence of PD dilation was correlated with an increase in mass size. About 67.6% of patients with masses measuring in the 1st quartile had a dilated PD, while 77.8%, 91.0%, and 71.4% of those with masses measuring in the 2nd, 3rd, and 4th quartiles, respectively, had a dilated PD. Conclusion: PD dilation is a warning sign for pancreatic malignancies, however, small masses or masses at the uncinate process or the tail of the pancreas may not affect the size of the PD.

Key words: Endoscopic ultrasound, pancreatic cancer, pancreatic duct

INTRODUCTION

Pancreatic cancer is the eighth and ninth cancer leading cause of death in men and women, respectively, in the United States.[1] Pancreatic ductal adenocarcinoma is the most common type of pancreatic cancer, making up 85% of all cases.[2] In addition, the pancreatic neuroendocrine tumor is another growing type of...
pancreatic malignancy causing more attention than before. Approximately 60%–70% of pancreatic cancers are located in the head of the pancreas, while 20%–25% are located in the body and tail of the pancreas.\[2\] Unfortunately, all types of pancreatic cancers are often more difficult to be diagnosed than many other cancers of the abdominal viscera. The mean survival time of patients with pancreatic ductal carcinoma is 4 months without treatment.\[3\] As a result, more than 90% of patients diagnosed with pancreatic cancer die from the disease.\[2\]

Patients with pancreatic cancer typically present with asthenia, anorexia, abdominal pain, weight loss, and jaundice.\[4\] However, by the time symptoms present, cancer has metastasized beyond the point of surgical resection in approximately 80%–90% of patients.\[5\] Diagnostic methods of pancreatic cancer include imaging examinations such as computed tomography (CT) and magnetic resonance imaging (MRI). However, endoscopic ultrasound (EUS) has become a mainstay in making the diagnosis of pancreatobiliary disorders, particularly pancreatic cancer.\[6\] EUS has diagnostic rates higher than 90%, especially for masses <2–3 cm in size, for which the sensitivity rate is 99% versus 55% for CT.\[6\]

The pancreas is an organ made up of two major parts: the pancreatic parenchyma and pancreatic duct (PD) system. Pancreatic adenocarcinoma typically arises from and affects the PD system, which consists of the main PD, as well as side branches. On the other hand, pancreatic neuroendocrine tumor typically arises from the pancreatic parenchyma. While PD changes, especially dilation, can be seen in both types of cancer and are often reported on EUS, CT, and MRI, the clinical significance of this is not completely clear.

A previous study from our group conducted a retrospective analysis of 77 patients with dilated PD on CT and found that the most common causes of main PD dilation on CT were chronic pancreatitis and pancreatic cancer.\[7\] However, there are still many questions regarding the role of pancreatic cancer in dilation of the PD. In this study, we aimed to evaluate the significance of PD dilation on EUS, CT, or MRI in patients undergoing EUS for pancreatic indications. In addition, we evaluated the role of pancreatic mass lesions, including the size and the location of the mass, in the dilation of the PD.

### MATERIALS AND METHODS

This is a retrospective study performed at The Emory Clinic, a tertiary care facility in Atlanta, Georgia. The study was approved by our Institutional Review Board (IRB). The IRB number is IRB00075016. The software Endoworks (Olympus, Tokyo, Japan) was used to generate a list of all patients who received an EUS between January 1, 2011, and December 31, 2013. Abstraction of computer database records for each patient was completed using PowerChart (Cerner Corp, North Kansas City, MO). All patients who received an EUS for nonpancreatic indications were excluded from the study. The clinical course and final diagnosis of each patient who had an EUS for a pancreatic indication were reviewed and documented. Most patients received a CT or MRI in addition to an EUS at some point during their clinical course. In the few cases that the PD size was not charted in the EUS report, this information was gathered from the CT or MRI. PD dilation at a specific part of the pancreas, such as the head, the body, or the tail was also recorded. In addition, in cases with a pancreatic mass, the size of the mass in square centimeters and location of the mass were recorded from the electronic medical record.

The main PD diameter >3 mm in the head, 2 mm in the body, and 1 mm in the tail of the pancreas on the EUS was defined as PD dilation at this study. The diagnosis of pancreatic adenocarcinoma or pancreatic neuroendocrine tumor was based on pathology.

Our primary interest was to investigate the relationship between PD diameter and the size/location of pancreatic cancer, in other words, the geographic relationship of pancreatic cancer and PD dilation. We evaluated the role of PD diameter as a sign of pancreatic cancer by analyzing the number of patients with PD dilation that had cancer. In addition, we evaluated the location of mass and its effect on location of dilation as a more specific sign of pancreatic cancer. Furthermore, we evaluated the role of mass size on the likelihood of PD dilation. Finally, we explored the difference in adenocarcinoma and neuroendocrine tumor in relation to likelihood of PD dilation.

Fisher’s exact test was used to evaluate the difference in percentage of malignancy between patients with a dilated PD and those with a PD of normal
diameter. Mann–Whitney U-test was used to evaluate the differences in size of adenocarcinomas and neuroendocrine tumors. The student’s t-test was used to evaluate the differences in both likelihoods of PD dilation, as well as the location of adenocarcinomas and neuroendocrine tumors. A P < 0.05 was considered statistically significant.

RESULTS

From 2011 to 2013, 1165 patients underwent EUS at The Emory Clinic. Six hundred and ninety patients were excluded from the study due to the fact that the pancreas did not undergo ultrasound during the EUS. The majority of these excluded patients underwent EUS for esophageal or gastric indications. The remaining 488 patients had an EUS with indications including pancreatitis, pancreatic cyst, suspicion of mass, jaundice, elevated amylase or lipase, and dilation of common bile duct or PD as seen on CT or MRI. Of these, 239 patients had a dilated PD while 153 patients had a pancreatic malignancy (not all patients with malignancy have a dilated PD). However, 15 of the patients with a pancreatic malignancy were excluded: 12 did not have a PD diameter charted, 2 did not have a mass size charted, and 1 did not have either PD diameter or mass size charted. Finally, 236 patients had a normal PD diameter [Figure 1]. Patients with a dilated PD had a significantly higher incidence of pancreatic malignancy than those with a normal PD diameter (106/239, 44.4% vs. 32/236, 13.6%; P < 0.001) [Table 1].

Dilated pancreatic duct

The mean age of the 239 patients, 126 females and 113 males with dilated PD, was 64 years old. Ninety-four (39.3%) of these patients had pancreatic adenocarcinoma while 12 (5.0%) had a pancreatic neuroendocrine tumor. Of patients with a dilated PD in the head of the pancreas, 26 (23.6%) had adenocarcinoma and 4 (3.6%) had neuroendocrine tumor. Of those with a dilated PD in the body of the pancreas, 71 (46.7%) had adenocarcinoma and 8 (5.3%) had neuroendocrine tumor. Among patients with a dilated PD in the tail of the pancreas, 60 (52.6%) had adenocarcinoma and 5 (4.4%) had neuroendocrine tumor [Figure 2].

Pancreatic mass location

The mean age of the 138 patients, 70 females and 68 males, with a pancreatic malignancy was 65 years old. Seventy (50.7%) had a mass in the head of the pancreas, 14 (10.1%) in the neck, 21 (15.2%) in the body, 13 (9.4%) in the tail, and 20 (14.5%) in the uncinate process. Among patients with cancer in the pancreatic head, 61 (87.1%) were found to have

<table>
<thead>
<tr>
<th>Diagnosis, n (%)</th>
<th>Dilated PD</th>
<th>Normal PD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic malignancy</td>
<td>106 (44.4)</td>
<td>32 (13.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No pancreatic malignancy</td>
<td>133 (55.6)</td>
<td>204 (86.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 1. Comparison of patients with normal and dilated pancreatic duct

Figure 1. Patients selected for inclusion in analysis. PD: Pancreatic duct
a dilated PD. Of those with cancer in the pancreatic neck or body, 12 (85.7%) and 17 (81.0%) had a dilated PD, respectively. Only three (23.1%) patients who had a mass in the tail had a dilated PD. Finally, 13 (65.0%) of those with a mass in the uncinate process had a dilated PD. Patients with a mass at a particular location were found to have associated PD dilation upstream of the mass. For example, of the seventy patients with a mass in the head of the pancreas, 53 (76.8%) had PD dilation immediately upstream of the mass. These data are reflected in Table 2.

Pancreatic mass size
The mean pancreatic mass size was 10.4 cm$^2$: 9.8 cm$^2$ in the head, 10.2 cm$^2$ in the neck, 11.1 cm$^2$ in the body, 8.0 cm$^2$ in the uncinated process, and 15.6 cm$^2$ in the tail. The patients with a mass were separated into quartiles based on mass size. Twenty-three (67.6%) patients with masses measuring in the 1st quartile had dilated a PD whereas 28 (77.8%), 30 (91.0%), and 25 (71.4%) of those with masses measuring in the 2nd, 3rd, and 4th quartiles, respectively, had a dilated PD. Among those with masses in the head measuring in the 1st, 2nd, 3rd, and 4th quartiles, 13 (72.2%), 15 (88.2%), 15 (93.8%), and 18 (94.7%), respectively, had a dilated PD. Among those with masses in the neck measuring in the 1st, 2nd, 3rd, and 4th quartiles, 3 (75.0%), 3 (100.0%), 3 (100.0%), and 3 (75.0%), respectively, had a dilated PD. Among those with masses in the body measuring in the 1st, 2nd, 3rd, and 4th quartiles, 3 (60.0%), 4 (80.0%), 6 (100.0%), and 4 (80.0%), respectively, had a dilated PD. Among those with masses in the tail measuring in the 1st, 2nd, 3rd, and 4th quartiles, 2 (66.7%), 2 (40.0%), 0 (0.0%), and 0 (0.0%), respectively, had a dilated PD. Finally, among those with masses in the uncinate process measuring in the 1st, 2nd, 3rd, and 4th quartiles, 3 (60.0%), 2 (40.0%), 0 (0.0%), and 3 (60.0%), respectively, had a dilated PD [Figure 3].

Pancreatic mass type
Of the 138 patients with a pancreatic mass, 116 (84.1%) had pancreatic adenocarcinoma and 22 (15.9%) had pancreatic neuroendocrine tumor. Patients with adenocarcinoma were significantly more likely to have a dilated PD than those with neuroendocrine tumor (94/116, 81.0% vs. 12/22, 54.5%; $P = 0.007$) [Figure 4]. There was no significant difference in the location of adenocarcinomas and neuroendocrine tumors [Figure 5]. However, the median size of pancreatic adenocarcinoma was significantly greater than that of the pancreatic neuroendocrine tumor (8.1 cm$^2$ vs. 2.7 cm$^2$; $P = 0.006$) [Figure 6].

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**Table 2. Pancreatic mass and associated pancreatic duct dilation at particular location**

<table>
<thead>
<tr>
<th>Location of mass</th>
<th>Head</th>
<th>Neck</th>
<th>Body</th>
<th>Tail</th>
<th>Uncinate process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>70</td>
<td>14</td>
<td>21</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>PD dilation (%)</td>
<td>61 (87.1)</td>
<td>12 (85.7)</td>
<td>18 (81.0)</td>
<td>3 (23.1)</td>
<td>13 (65.0)</td>
</tr>
<tr>
<td>Location of dilation (%)</td>
<td>20 (29.4)</td>
<td>1 (7.1)</td>
<td>2 (10.0)</td>
<td>1 (7.7)</td>
<td>6 (24.0)</td>
</tr>
<tr>
<td>Head</td>
<td>53 (76.8)</td>
<td>9 (64.3)</td>
<td>6 (30.0)</td>
<td>0</td>
<td>11 (55.0)</td>
</tr>
<tr>
<td>Body</td>
<td>33 (48.5)</td>
<td>8 (57.1)</td>
<td>16 (76.2)</td>
<td>2 (16.7)</td>
<td>6 (31.6)</td>
</tr>
</tbody>
</table>

PD: Pancreatic duct
DISCUSSION

To our knowledge, this is the first report of a comprehensive study on the relationship of the geography of pancreatic malignancy and the geography of PD dilation. One of our previous studies demonstrated that the most common causes for PD dilation on CT are chronic pancreatitis and pancreatic cancer.[7] However, we did not study the geography of pancreatic malignancy and the geography of PD dilation. In this study, we studied the size, location, and type of pancreatic malignancy and PD dilation. Furthermore, we analyzed the specific location of PD dilation.

Nearly half of the patients with a dilated PD on EUS had pancreatic cancer in this study. This finding was consistent with that of our prior study.[7] On the other hand, a little over one-eighth of patients whose PD was not dilated had pancreatic cancer. Those patients usually have cancer at the tail or in the uncinate process of the pancreas. The results indicated that PD dilation is a warning sign for pancreatic malignancy, but about 10% of pancreatic malignancy can present without PD dilation. During EUS examination, it is important to examine the tail and the uncinate process of the pancreas carefully when PD dilation is not seen. Of those with nonmalignant dilated PD, the spectrum of diseases included chronic pancreatitis, pancreatic pseudocyst, pancreatolithiasis, and idiopathic duct dilation. Furthermore, a progressive step-up in the percentage of patients with pancreatic adenocarcinoma was seen from dilatation in the head to dilatation in the body to dilatation in the tail of the pancreas. We propose a theory for this that is central to many of our results. In the case of pancreatic adenocarcinoma, the mass typically arises from the duct. As the mass grows in size, it likely obstructs the duct, preventing fluid from flowing downstream through the duct toward the major duodenal papilla. As a result, the duct becomes dilated upstream of the mass.

Over half of patients enrolled in our study who had pancreatic cancer had a mass in the head of the pancreas. The majority of these patients had a dilated PD, most commonly upstream of the mass. While fewer patients had masses in the neck and body, a similar majority was found to have upstream PD dilation. About 10% of patients had a mass in the tail. A minority of patients with a mass in the tail had dilation of the PD as there is little duct upstream of the pancreatic tail. Finally, out of the approximately 15% of patients with a pancreatic mass in the uncinate process, more than one-third of those patients had a normal size PD.

There was a gradual increase in average mass size moving from head to tail of the pancreas. There was a general correlation between mass size and likelihood of PD dilation. This was most evident
in patients with masses in the pancreatic head. In pancreatic adenocarcinoma, as the mass grows from the duct, a larger mass will more likely obstruct the duct and cause upstream dilation. To a lesser extent, in pancreatic neuroendocrine tumors, as the mass grows from the pancreatic parenchyma, it will obstruct the duct through compression and cause upstream dilation. While this phenomenon was seen in quartiles 1 through 3 for all masses, the 4th quartile had a smaller percentage of patients with PD dilation. We attribute this to the fact that the mean size of tail masses was quite a bit larger than that of all other masses. This is not unusual as tail masses often times become quite large before causing symptoms due to the anatomical location of the pancreatic tail.\(^\text{[8,9]}\)

As a result of the fact that tail masses rarely have upstream PD dilation, and many of the 4th quartile masses were tail masses, there were fewer 4th quartile masses that had associated PD dilation than was expected. This also was the case for neck and body masses but likely can be attributed to the fact that there were not enough patients in these groups to see the correlation.

Our study had over five times as many patients with adenocarcinoma as with neuroendocrine tumor. There was a noticeable difference in the effect of pancreatic adenocarcinoma and pancreatic neuroendocrine tumor on the PD. Pancreatic adenocarcinoma was significantly more likely to dilate the PD than pancreatic neuroendocrine tumor was. There is likely an inherent cause of this difference due to the fact that adenocarcinomas arise from the duct and thus are likely to cause obstruction at a smaller size while neuroendocrine tumors must become quite large before compressing the PD and causing upstream dilation. In addition to this cause, we explored other possibilities. We first evaluated a potential difference in mass location. If adenocarcinomas were more likely to be found in the head and neuroendocrine tumors were more likely to be found in the tail, this would explain the difference. However, we found that there was no significant difference in location of mass between adenocarcinoma and neuroendocrine tumor at any location. We then also evaluated a potential difference in size of the mass. A larger mass is more likely to obstruct the duct and cause upstream PD dilation. We found that adenocarcinomas were significantly larger than neuroendocrine tumors, and this accounted for the difference in the likelihood of PD dilation.

In summary, our study demonstrated a number of interesting findings about pancreatic cancer and the effect on the PD: The majority of patients with pancreatic cancer have PD dilation; the site of PD dilation is upstream from the mass and is more likely to be seen as the mass grows in size; nearly half of patients who have a dilated PD on EUS have pancreatic cancer. Therefore, patients with a dilated PD are significantly more likely to have pancreatic cancer than those without a dilated PD on EUS. Finally and most importantly, about 10% of patients with pancreatic malignancy had normal size of PD. Most of those patients had malignancy in the tail or in the uncinate process of the pancreas.

Our study was limited by the fact that it was a retrospective chart review and a prospective study evaluating this would be helpful to confirming our findings. However, based on our findings, it is important that patients with a dilated PD on EUS receive a full evaluation for pancreatic cancer, and in patients without a dilated PD on EUS, special attention should be paid to the tail and uncinate process of the pancreas during EUS examination as they still may have cancer.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES