

## Editorial

# ERCP and Pancreatic Cancer

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The early diagnosis of pancreatic cancer remains one of the most difficult challenges faced by clinicians. Advances in pancreatic imaging, especially multidetector high-resolution computerized tomography (CT),<sup>1</sup> magnetic resonance imaging, and endoscopic ultrasound (US),<sup>2</sup> have improved our ability to detect very small lesions. Unlike these newer technologies, endoscopic retrograde cholangiopancreatography (ERCP) has been used for more than 30 years in pancreaticobiliary disease and, for much of this time, it has played a central role in the evaluation of suspected pancreatic neoplasms.<sup>3</sup> Because of its invasiveness and morbidity, diagnostic ERCP has been supplanted by less invasive and more sensitive techniques.<sup>4</sup> Yet, ERCP is still performed in certain clinical situations (e.g., the evaluation and treatment of pancreatitis and biliary obstruction) where it crosses paths with patients with small, potentially resectable pancreatic cancers.

In this issue of the *Annals of Surgical Oncology*, Kalady et al.<sup>5</sup> from Duke University Medical Center use their institution's large and prestigious experience with ERCP to further our understanding of the likelihood of an underlying pancreatic malignancy when a pancreatic duct stricture is found. From a database of more than 7000 ERCP, they found 355 patients with pancreatic strictures from which to ascertain clinical features that were predictive of an underlying pancreatic malignancy. Some of their results were useful, albeit predictable, confirmations of our knowledge of the clinical presentation of pancreatic cancer. For example, univariate analysis of their data showed that age, jaundice, concomitant

biliary strictures, strictures of the pancreatic head or neck, and a lack of clinical or pancreatographic evidence of acute or chronic pancreatitis were all associated with a higher risk of a malignant stricture. Using multivariate analysis, they produced a formula that included the top three factors that affected the likelihood of a malignant stricture: stricture location, side branch abnormalities consistent with chronic pancreatitis, and a prior history of pancreatitis. Using this formula they could group their patients into high, intermediate, or low risk strictures. They propose that this formula could be used in other centers to guide management of patients found to have a pancreatic duct stricture on an ERCP.

Their study suffers from the usual issues involved in retrospective analyses: lack of both complete data and of prospective confirmation. Whether a stricture is associated with a mass by some other imaging modality would almost certainly affect the likelihood of malignancy. Prior pancreatic imaging data in the form of abdominal CT or US were apparently available for 80% of their patients and, of these, reportedly no mass was seen in 68%. No detail is given to the percentage of these patients having CT versus US nor was information provided on the quality of the CT or whether the US examinations were able to image the pancreas. The reality of the clinical evaluation of a pancreatic stricture today is that it would almost certainly be interpreted in association with at least concomitant CT information to whether a mass existed. False-negative pancreatograms with pancreatic cancer do occur in 5% to 10% of patients.<sup>6</sup> The frequency of this occurrence in an expert center and the patient characteristics where this occurs would also have been helpful information. Prospective confirmation of the predictive power of their equation is also necessary before their conclusions are fully incorporated into clinical practice. Remember, other institutions with different patterns of patient referral for ERCP may not have the same results.

Nevertheless, this study provides us with some useful information on dealing with the patient found to have a

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pancreatic duct stricture at ERCP. Importantly, they found that patients with pancreatic strictures of the body or tail who have either side branch changes of chronic pancreatitis, a history of pancreatitis, or both; or who have pancreatic head or neck strictures with both of these features have a less than a 2% likelihood of an underlying malignancy. Based on these data, such patients can be managed with careful clinical follow-up rather than invasive intervention, as long as they do not have any discernible mass by other imaging modalities. On the other hand, patients with a pancreatic head stricture with either a pancreatitis history or side branch changes (but not both) or an isolated body or tail stricture with neither feature have malignancy risks of 12%, 41%, or 26%, respectively. This degree of risk would certainly warrant much more aggressive work-up. Patients with isolated pancreatic head or neck strictures and no history of pancreatitis or side branch changes of chronic pancreatitis have a strikingly high 94% chance of their stricture being malignant. This last group is especially interesting, because this risk of malignancy is as high as the highest reported rates of definitive cytologic diagnosis by endoscopic US-guided fine-needle aspiration (EUS-FNA) of pancreatic masses.<sup>7</sup> Using their data, little point would seem to exist in attempting any kind of preoperative cytologic diagnosis in this group of patients, either by ERCP<sup>8,9</sup> or EUS-FNA<sup>10</sup> because the pretest likelihood of cancer is so high, unless, of course nonoperative management is planned (e.g., neoadjuvant chemoradiation).

About 5% of pancreatic cancers present with acute pancreatitis.<sup>11</sup> The current study confirms this frequency in that the data show that eight (6.7%) patients with a history of pancreatitis among the 118 were ultimately found to have pancreatic cancer. A new feature added by their data, however, indicates that only malignant strictures of the pancreatic head or neck were associated with pancreatitis. Speculatively, this is related to more pancreatic parenchyma being obstructed by head lesions or that closer proximity to the biliary tree or gut lumen enhances the risk of reflux of their contents into the obstructed pancreatic system setting off the enzyme activation cascade.

What then is the appropriate role of ERCP in pancreatic cancer? This has been reviewed extensively elsewhere.<sup>4,12</sup> Other than in the evaluation and therapy of obstructive jaundice and chronic pancreatitis and unusual lesions (e.g., intraductal papillary mucinous tumors),<sup>13</sup> ERCP would seem to now be relegated to a secondary or tertiary diagnostic procedure in the patient with suspected pancreatic neoplasia. Even using ERCP in suspected malignant obstructive jaundice may now be problematic. Because no conclusive evidence indicates that

preoperative decompression of malignant obstructive jaundice affects surgical outcomes,<sup>4</sup> less morbid techniques (e.g., CT, MRCP<sup>14</sup> or EUS/EUS-FNA<sup>15</sup>) may provide enough diagnostic and staging information as well as cytologic confirmation to move directly on to resection. This places ERCP in the role of a purely therapeutic procedure for decompression of patients with nonresectable disease or patients who are going on to neoadjuvant therapy. The special problem of diagnosing pancreatic cancer in the setting of underlying chronic pancreatitis remains one of the most difficult clinical dilemmas in medicine and ERCP certainly can play an important role. ERCP, however, has no better specificity than other diagnostic modalities.<sup>4,12</sup> Future advances in the molecular diagnosis of pancreatic neoplasia from pancreatic juice aspirates<sup>16</sup> could reinvigorate the role of ERCP in the early diagnosis of this deadly disease, especially in patients at high risk (e.g., those with hereditary pancreatitis or familial pancreatic cancer syndromes).<sup>17</sup> The authors are to be congratulated for adding to our understanding of the role of ERCP in pancreatic cancer.

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