

Prospective study of biliary strictures to determine the predictors of malignancy.

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Abstract:

Background: There have been few prospective studies regarding the investigation of biliary strictures, principally because of rapid technological change. The present study was designed to determine the sensitivity of various imaging studies for the detection of biliary strictures. Serum biochemistry and imaging studies were evaluated for their role in distinguishing benign from malignant strictures.

Methods: Thirty-one patients with suspected noncalculous biliary obstruction were enrolled consecutively in the study. A complete biochemical profile, ultrasound, Disida scan and cholangiogram (endoscopic retrograde cholangiopancreatography [ERCP] or percutaneous cholangiogram) were obtained at study entry. Stricture etiology was determined based on cytology, biopsy and/or clinical follow-up at one year.

Results: Twenty-nine of 31 patients had biliary strictures, of which 15 were malignant. The mean age of the malignant cohort was 73.9 years versus 53.9 years in the benign cohort ($P < 0.001$). Statistically significant differences between the malignant and benign groups, respectively, were as follows: alanine transaminase 235.2 versus 66.9 U/L ($P = 0.004$), aspartate transaminase 189.8 versus 84.5 U/L ($P = 0.011$), alkaline phosphatase 840.2 versus 361.1 U/L ($P = 0.002$), bilirubin 317.8 versus 22.1 $\mu\text{mol/L}$ ($P < 0.001$) and bile acids 242.5 versus 73.2 $\mu\text{mol/L}$ ($P = 0.001$). Threshold analysis using receiver operative characteristic (ROC) curves demonstrated that a bilirubin level of 75 $\mu\text{mol/L}$ was most predictive of malignant strictures. Intrahepatic duct dilation was present in 93% of malignant strictures versus 36% of benign strictures ($P = 0.002$). Common hepatic duct dilation was less discriminatory (malignant 13.5 versus benign 9.6 mm; $P = 0.11$). Ultrasound was highly sensitive (93%) in the detection of the primary tumor in the bile duct or pancreas, or in the visualization of nodal or liver metastases. In benign disease, ultrasound failed to detect evidence of intrahepatic or extrahepatic biliary dilation in most cases. Disida scans were not able to distinguish between malignant or benign strictures and could not accurately localize the level of obstruction. The sensitivity of Disida scan for the diagnosis of obstruction was 50%. Cholangiographic characterization of strictures revealed an equal distribution of smooth (eight of thirteen) and irregular (five of thirteen) strictures in the malignant group. Ten of thirteen benign strictures were characterized as smooth. Malignant strictures were significantly longer than benign ones - 30.3 versus 9.2 mm ($P = 0.001$). Threshold analysis using ROC curves showed that strictures greater than or equal to 14 mm were predictive of malignancy (sensitivity 78%, specificity 75%, log odds ratio 11.23).

Conclusions: A serum bilirubin level of 75 $\mu\text{mol/L}$ or higher, or a stricture length of greater than 14 mm was highly predictive of malignancy in patients with a biliary stricture. Ultrasound was useful in predicting malignant strictures by detecting either intrahepatic duct dilation or by

visualizing the tumor (primary or metastases). Strictures with a 'benign' cholangiographic appearance are frequently malignant. Disida scan did not add additional information. ERCP is necessary to diagnose benign strictures, which tend to be less extensive at presentation.

Comments:

Strengths/uniqueness: This report includes a comprehensive evaluation of biliary strictures, evaluating all of the commonly used laboratory and imaging approaches. It uses a prospective approach, and radiologists doing the imaging studies were blinded to the results of the patient's previous diagnostic studies.

Weaknesses: Over the one year period of enrollment, only 31 patients were included, which without reference to other studies would seem a relatively small cohort. Although there is comment that studies in this area are lacking, as well as some literature reference to specific imaging procedures, it is unclear whether this study is truly unique.

Relevance to Palliative Care: This report is extremely useful for palliative care practitioners in highlighting the poor value of making a diagnosis based on the visual appearance on ERCP. It is not uncommon for those of us working in palliative care to see patients who have been declared palliative based on the visual appearance of the stricture. In the absence of the other highly predictive features for malignant etiology demonstrated in this report, such as a serum bilirubin level of greater than 75 $\mu\text{mol/L}$, or a stricture length of greater than 14 mm, this report could be used to press for further investigation where the patient's other clinical circumstances might make this appropriate.