LN Ratio May Predict Survival in Pancreatic Ca

BY ALICIA AULT
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WASHINGTON — A retrospective look at the Surveillance, Epidemiology, and End Results database indicates that too few nodes are being evaluated in some patients with pancreatic cancer, which may result in understaging, Dr. Mark Slidell said at a symposium sponsored by the Society of Surgical Oncology.

In the analysis of more than 4,000 patients, those who did not have any nodes examined were 44% more likely to die during follow-up, Dr. Slidell said. Several investigators have suggested that extended lymphadenectomy should be performed routinely, but that has not been conclusively shown to improve outcomes in previous studies, he said.

In addition, the data showed that the lymph node ratio—total number of positive nodes divided by the total number of examined nodes—is an important predictor of survival, said Dr. Slidell, a resident at Georgetown University, Washington. He and his colleagues at Johns Hopkins University in Baltimore had hypothesized that the ratio of metastatic to examined nodes may be more important for staging and survival than the number of nodes harvested alone.

But data on this measure, the lymph node (LN) ratio, are limited, with most previous studies performed at single institutions and academic centers.

He and his colleagues identified 4,005 patients (2,042 men and 1,963 women) in the National Cancer Institute's SEER database who had resection for pancreatic adenocarcinoma between 1988 and 2003. The patients' median age was 66, and most had tumors that were larger than 2 cm.

The database included standard demographic information and tumor size, grade, LN involvement, total number of LNs examined, and the number of positive nodes. The authors calculated the LN ratio by dividing the total number of positive nodes by the total number of examined nodes.

The median tumor size was 3 cm. Most patients who had surgery had a pancreatectomy.

The median number of nodes examined was seven. Most patients had fewer than 12 nodes examined, and 390 patients (10.1%) had 0 nodes examined. Of the 3,478 patients who did have nodes examined, 1,507 (43.3%) had no metastases and were classified as N0, and 56% (1,971) had metastatic disease (classified as N1).

The mean number of nodes examined in the negative group was 8, while the mean in the node-positive group was 11.

Overall, median survival was 13 months and the 5-year survival rate was 17%.

With multivariate analysis, the prognostic factors related to survival included tumor stage, tumor grade, a tumor size of greater than 2 cm, the number of nodes examined, the LN ratio, and N1 disease.

Patients with zero nodes examined were at highest risk of disease-specific death, as they were 44% more likely to die during follow-up, Dr. Slidell said.

Dr. Slidell and his colleagues also evaluated whether a greater number of positive nodes was associated with decreased survival. N0 patients had significantly better survival than N1 patients, but within the group of patients with N1 disease, an increasing number of positive nodes was not significantly associated with poorer survival; however, it was associated with a nonsignificant trend toward decreased survival, said Dr. Slidell.

N1 disease also increased the risk of disease-specific death, as did a higher LN ratio. Five-year survival for N1 disease was 7%, compared with 18% for N0 disease.

LN ratio proved to be even more important. For a ratio of 0, the median survival was 17 months, for ratios of 0-0.2 it was 15 months, and for 0.2-0.4 it was 12 months. Median survival declined to 10 months for ratios greater than 0.4.

The LN ratio appears to be a better predictor of survival, and should be considered for use as a potential stratification method in future clinical studies, he said. ■

THE EFFECTIVE PHYSICIAN

Acute Pancreatitis

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Acute pancreatitis causes an estimated 210,000 hospitalizations in the United States annually, with overall mortality around 5%. The American College of Gastroenterology recently published updated guidelines for diagnosis and management of this condition.

Conclusions

The diagnosis of pancreatitis requires at least two of three criteria to be present: abdominal pain typical of acute pancreatitis, serum amylase and/or lipase three times the upper limit or higher, and characteristic findings on CT scan. Older patients, obese individuals, and those with organ failure at presentation are more likely to have severe disease.

Interstitial pancreatitis (the preferred term for "uncomplicated" acute pancreatitis) is defined as pancreatic enlargement with homogeneous increased contrast uptake on CT.

Contrast CT is the best way to assess severity and evaluate complications; it also might exclude other conditions from the differential diagnosis and provide insight into the etiology of pancreatitis. MRI's role is still being defined. Abdominal ultrasound is highly specific in detection of gallstones in acute pancreatitis, but has low sensitivity.

The degree of elevation of amylase and/or lipase does not correlate with the severity of pancreatitis; daily tracking of these enzyme levels has limited value. Increased serum lipase may be more sensitive and specific for pancreatitis than is serum amylase.

Serum hematocrit and APACHE (Acute Physiology and Chronic Health Evaluation) II score have the greatest clinical utility in predicting the severity of acute pancreatitis. Ranson's criteria have been shown in recent literature to be less predictive of severity than was previously reported.

Necrotizing pancreatitis has much higher morbidity and mortality than does interstitial pancreatitis (about 17% vs. about 3%). Similarly, organ failure at any time in the course of pancreatitis presages higher mortality.

Implementation

Hematocrit should be measured at admission and again at 12 and 24 hours to help guide fluid resuscitation. APACHE II score should be calculated daily for all patients during the first 3 days of hospitalization; increasing scores are suggestive of severe pancreatitis.

A CT scan is not required at admission for many patients who present with acute pancreatitis. Abdominal ultrasonography is useful if gallstone pancreatitis is suspected.

Liver chemistries and calcium and triglyceride levels measured within the first 24 hours might be useful in determining the etiology of acute pancreatitis.

Frequent measurement of vital signs (including oxygen saturation), aggressive fluid resuscitation, parenteral narcotics for pain control, and supplemental oxygen are recommended for at least 24 hours in all patients with acute pancreatitis. Intensive care is warranted for patients with sustained organ failure and other signs of severe pancreatitis. Blood gas analysis is suggested if oxygen saturation is 95% or less and/or there are other signs of hypoxemia. Central venous pressure monitoring is usually not needed.

C-reactive protein level higher than 150 mg/L (measured 48-72 hours after admission) strongly correlates with pancreatic necrosis.

Patients with acute gallstone pancreatitis who are strongly suspected to have common duct stones require rapid assessment for choledocholithiasis. Endoscopic retrograde cholangiopancreatography with biliary sphincterotomy and stone removal is indicated in patients with cholangitis and severe acute pancreatitis and in those who are strongly suspected or known to have bile duct stones.

Contrast CT might be indicated in patients with worsening pancreatitis after admission to assess for pancreatic necrosis. Follow-up CT scanning with contrast might be necessary in these patients to monitor for later development of other intra-abdominal complications.

Nutritional support should be initiated in patients unlikely to be able to tolerate oral intake for at least 5 days.

Enteral feeding is preferred over total parenteral nutrition (TPN) because of its lower cost and because of complications associated with TPN, but data are lacking on reduction in morbidity and mortality. Future research needs to further define the clinical benefits of different routes (nasojejunal vs. nasogastric) of enteric feeding and to further compare morbidity and outcomes with those of TPN-treated patients.

Pancreatic enzyme replacement is not beneficial in patients with interstitial pancreatitis.

Patients with necrotizing pancreatitis might benefit from pancreatic enzyme and proton pump inhibitors.

Prophylactic antibiotics are not recommended in patients with necrotizing pancreatitis. Appropriate antibiotic coverage is warranted while the patient is thoroughly assessed for infection as the source of the sepsis syndrome, which is common in pancreatic necrosis patients.

CT-guided percutaneous aspiration (for Gram stain and culture) is recommended when infected pancreatic necrosis is suspected. Surgical debridement is the standard treatment for patients with infected pancreatic necrosis if the patient is stable enough for the operation.

Sterile pancreatic necrosis should routinely be managed medically for at least 2-3 weeks; subsequently, debridement may be needed.

Reference

Banks, P.A., et al. Practice guidelines in acute pancreatitis. Am. J. Gastroenterol. 2006;101: 2379-400.

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