Introduction: Morphological and functional changes in the pancreas after surgical pancreatic necrosectomy have not been studied extensively. Aims: To study morphological changes in the pancreas, and exocrine and endocrine pancreatic function following pancreatic necrosectomy. Methods: Eighteen adult patients surviving at least one month after pancreatic necrosectomy for acute necrotizing pancreatitis were followed up. Contrast-enhanced computed tomography was done every six months. Stool fat was estimated at 3-month intervals, and need for and response to enzyme supplements were recorded. Blood sugar was measured every fortnight; in patients with hyperglycemia, need for oral hypoglycemic agents or insulin was recorded. Additional pancreatic imaging was done in some cases. Results: Six weeks after surgery, nine of 18 patients had exocrine insufficiency. Thirteen patients developed endocrine insufficiency, including 5 who also had exocrine insufficiency. At the end of the study, 13 patients had endocrine insufficiency and 2 had exocrine insufficiency. Pancreatic size was subnormal in all patients at the end of six months. Pancreatography in three cases did not reveal any ductal abnormality. Conclusions: Necrotizing pancreatitis affects pancreatic exocrine or endocrine function in more than half the patients. [Indian J Gastroenterol 2004;23:203-205] Key words: Pancreas: endocrine function, exocrine function, morphology, pancreatic necrosectomy

Necrotizing pancreatitis (NP) is a dreaded complication of acute pancreatitis. Despite advances in operative interventions and critical care, this condition often requires prolonged treatment, and causes substantial morbidity and mortality. Only limited data are available on long-term morphological and functional outcome after operative treatment of NP. There is lack of data from the Indian population. We therefore studied morphological and functional changes after pancreatic necrosectomy.

Methods
During a 30-month period (January 2001 to June 2003), 172 patients with acute pancreatitis were treated at our institution, a tertiary referral hospital. Of these, 43 had NP. Of the patients with NP, 17 with sterile necrosis and stable organ function were successfully managed conservatively. The remaining 26 patients underwent surgical necrosectomy for severe infected necrosis or sterile necrosis with multi-organ failure; of these, 18 (69%) survived more than one month following necrosectomy. These patients were followed up for 8 to 28 (median 19) months. Patients with documented or suspected chronic alcoholic pancreatitis, based on history of chronic alcohol intake and history of recurrent attacks of upper abdominal pain or other symptoms suggestive of pancreatitis, were excluded.

At initial admission, detailed history had been recorded regarding presence of etiological factors, duration of pain, and past history of occurrence of similar pain, administration of pancreatic enzyme supplements or diabetes prior to NP. The diagnosis of NP was made using contrast-enhanced computed tomography (CECT) and confirmed at surgery. Only patients with pancreatic or peripancreatic necrosis were included. The Atlanta classification for acute pancreatitis was used. Extent of pancreatic parenchymal necrosis was estimated as percent value based on a combination of CECT and intra-operative findings. All patients were admitted to the intensive care unit for hemodynamic instability, or single or multi-organ failure.

Following necrosectomy, patients were evaluated for clinically evident endocrine and exocrine pancreatic insufficiency, recurrent pancreatitis, abdominal pain, and return to work. The assessment was done during the postoperative hospital stay, at the time of discharge from the hospital, at 2-week intervals for the initial 2 months and every month thereafter.

Endocrine pancreatic insufficiency was defined as development of diabetes mellitus (fasting blood glucose higher than 200 mg/dL on repeated measurements in patients who were euglycemic before NP) or new development of insulin dependence in patients who had pre-existing diabetes mellitus. Need for insulin was assessed in conjunction with an endocrinologist, and was based on clinical data and blood sugar levels.

Patients who developed changes in stool frequency and/or consistency underwent measurement of fecal fat excretion; values exceeding 7 g/24 h was taken as evidence of exocrine pancreatic insufficiency. Need for
pancreatic enzyme supplementation (30,000 U lipase before each meal) was assessed in conjunction with a gastroenterologist, and was based on clinical data and stool fat.

Morphological changes in the pancreas were evaluated using CECT at six-month follow up and every six months thereafter. All CT scans were reviewed by the same radiologist, who was unaware of the patients’ clinical details. Necrosis of the head and neck of the pancreas was scored as 50 percent, that of the body as 30 percent, and that of the tail as 20 percent. Additional imaging was undertaken in patients with recurrent abdominal pain; this included endoscopic retrograde pancreatography (ERP) in three patients at 12, 10 and 9 months after surgery, and magnetic resonance pancreatography (MRP) in two of these patients 8 months after surgery.

Results

The 18 patients were aged 25 to 47 (median 36) years; all were men. The etiology of acute pancreatitis was: alcohol 10, gallstones 4, idiopathic 2, postoperative 1, and primary hyperparathyroidism due to parathyroid adenoma in one patient. The median duration of symptoms was 4 (range 2-32) days. The median duration of follow-up was 19 (range 8-28) months.

Exocrine insufficiency

At the time of discharge from the hospital, 13 patients had pancreatic exocrine insufficiency, and were receiving pancreatic enzyme supplements. At the end of six weeks, nine of these patients had exocrine insufficiency, including five who had endocrine insufficiency too. At 6-month follow-up, steatorrhea and enzyme supplementation were continued in all these 9 patients. On further follow-up, 7 of these 9 patients had resolution of symptoms, and discontinued enzyme supplementation (within 12 months in 2 patients and at 12-18 months in 5 patients); in two patients, steatorrhea persisted despite treatment.

Endocrine insufficiency

Thirteen patients had endocrine insufficiency (diet control 2, oral hypoglycemic agents [OHA] 8 and insulin therapy 3) till last follow up; of these, 5 also had exocrine insufficiency (Table 1). At the time of discharge, 12 patients were receiving insulin; one additional patient had blood sugar control with dietary measures alone but needed resumption of insulin treatment three months after surgery. In 5 of these 13 patients, blood sugar came under control after 3-14 (median 8.5) months, with dietary modifications, exercise and OHA. Eight patients required insulin supplementation beyond one year; four of these were controlled with diet and OHA within 18-20 months. Two of these patients no longer needed insulin from 22 and 26 months, respectively.

Two patients required increasing doses of insulin during follow up and are still on high-dose insulin. One patient developed diabetic nephropathy and chronic renal failure. Endocrine insufficiency was found in 7 of 10 patients with alcohol-induced NP as against 5 of 8 patients with other causes of NP (p=ns).

Pancreatic morphology

The extent of pancreatic necrosis at presentation ranged from 30% to 100% (median 45%). On follow-up CECT, 16 patients had small pancreatic size. ERP and MRP in selected patients did not show any ductal abnormality.

Two patients with normal postoperative pancreatic function had 30% pancreatic parenchymal necrosis (involving the pancreatic head in both the cases) during the acute phase. The extent of necrosis was 30% to 70% (median 55%) in four patients with persistent exocrine insufficiency alone, 30% to 70% (median 60%) in seven patients with endocrine insufficiency alone, and 60% to 100% (median 80%) among five patients with both endocrine and exocrine insufficiency. Seven patients with endocrine insufficiency alone had necrosis of the pancreatic body and tail.

Other follow-up features

Two patients had postoperative complications; one patient had colonic necrosis, and the other patient had upper gastrointestinal hemorrhage due to splenic artery pseudoaneurysm. Five patients complained of occasional abdominal pain, which was not accompanied by hyperamylasemia and did not need hospital care. Three patients were unable to return to work because of recurrent pancreatitis and abdominal pain (one case), or severe steatorrhea (2 cases).

Discussion

Although abnormalities in pancreatic endocrine and exocrine function are known to occur during acute pancreatitis, especially with NP, data on this aspect are limited.

Pancreatic insufficiency occurred in more than three-fourths of our patients, who were followed up for a median duration of 19 (range 8-28) months. Endocrine insufficiency occurred during the acute episode in more than two-thirds of the affected patients and either remained stable or worsened over time. Exocrine insufficiency occurred during the episode, but improved in about half of the affected patients. Development of endocrine and/or exocrine insufficiency was associated with more extensive pancreatic parenchymal necrosis.

Endocrine pancreatic insufficiency is the first sign of pancreatic dysfunction to develop in 22%-92% after treatment of NP;5 overt diabetes mellitus develops in 13%-54%.6,7 The temporal relation between the onset of NP and endocrine insufficiency is poorly understood. It
seems reasonable that endocrine insufficiency would manifest soon after parenchymal necrosis; indeed, one of the Ranson’s criteria is serum glucose greater than 200 mg/dL.8 Our study supports these data since 13 of our 18 patients needed insulin supplementation at the time of discharge. Of these, none was able to consume a full diet and needed some intervention for glycemic control till last follow up.

Limited and conflicting data exist on factors associated with the development of endocrine insufficiency. In our study, diabetes mellitus was associated with more extensive parenchymal necrosis. Endocrine insufficiency appears more frequently after alcohol-induced rather than gallstone-induced NP, possibly because of pre-existing pancreatic injury in chronic alcoholics.1 In our study, endocrine insufficiency was found in 7 of 10 patients with alcohol-induced NP as against 5 of 8 patients with other causes of NP. Endocrine insufficiency alone was associated with necrosis of the body and tail of the pancreas; this may be related to a higher islet cell concentration in the tail of the pancreas.9

Exocrine insufficiency in the postoperative period was observed in 72% of our cases undergoing NP. As has been reported previously,10-13 it developed before discharge, and improved over time. Thus, only two of our patients had persistence of exocrine insufficiency.

Necrotic debris, once removed, is replaced by scar tissue.6 In our study, similar findings were seen, except in two patients where up to 60% (50%-70%) uptake of contrast was seen in the residual pancreatic bed though there were no ductal abnormalities. This suggests that the necrosed tissue in the pancreatic bed is not fully replaced.

In conclusion, pancreatic exocrine or endocrine functions are affected in more than half the patients with NP; with the passage of time, these show partial improvement. A careful follow up is therefore necessary for the management of these patients.

References