PARTIAL PANCREATECTOMY WITH SPLENECTOMY IS THE BEST OPTION OF TREATMENT FOR INFECTED ACUTE NECROTISING PANCREATITIS: A PROSPECTIVE STUDY

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ABSTRACT

BACKGROUND

Pancreatectomy for severe acute necrotising pancreatitis has been associated with more mortality and hence replaced by piecemeal debridement and toileting either by the open or the laparoscopic technique. We had reported the results of deliberate subtotal pancreatectomy with splenectomy for infected pancreatic necrosis in acute pancreatitis.

METHOD

18 patients were studied for 6 years, out of which 9 patients were male. Average age was 61 years (36-69 years). The median time for operation after presentation was 27 days (Range 2-74). Microbiological culture confirmed infection in 14 (78%) patients. Most patients required ICU care. Prognosis is monitored not only by Ranson's, but also by APACHE, Glasgow and application of Balthazar score.

RESULTS

Three patients (17%) died within 30 days of operation. Twelve of the 15 survivors (80%) underwent a single operative procedure. Three patients required a further laparotomy, of whom 2 required colectomy for ischaemia. Median hospital and ICU stays were 43 (Range 30-57) and 5 (Range 4-6) days respectively. Six patients (40% of survivors) developed an infection of the left half of the chevron incision; however, all wounds were fully healed within 3 months. Long-term follow-up of survivors (n=14) revealed 8 (57%) to need at least occasional pancreatic enzyme supplementation and 5 (36%) to have diabetes mellitus. Two patients (14%) developed an incisional hernia.

CONCLUSIONS

About 20% of acute pancreatitis presented with severe necrotising pancreatitis, where more than 50% is the mortality. Timely laparotomy and distal pancreatectomy with removal of spleen and necrosectomy along with irrigation is the best option to reduce mortality and morbidity. Considering much fatality of the pathogenesis, the patients need to bring under Right to Health Act. Because this severe disease of pancreas needs community awareness for prevention and its high cost of treatment.

KEYWORDS

Acute Severe Pancreatitis; Necrotising; Radical; Splenectomy; Subtotal Pancreatectomy; Right to Health.

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BACKGROUND

The incidence of acute pancreatitis appears to have responsible for most deaths during the early phase.[1] The overall mortality rate for acute pancreatitis remains about 10%,[2,3] the majority of deaths (80%) occurring in patients with pancreatic necrosis.[4] Multiple Organ System Failure (MOSF) is responsible for most deaths during the early phase of the disease process[5] with secondary pancreatic sepsis accounting for later mortality.[6] Pancreatic resection, either partial or complete, was used in the management of severe acute pancreatitis for many years,[7,8] but the practice stopped owing to a high incidence of complications and associated mortality.[9,10] It is basically two types; mild oedematous and severe necrotising. Mild variety gets controlled by watch and observe with palliative measure, but severe necrotising variety needs surgical intervention at appropriate time to reduce mortality from its life-threatening complications and multiple organ failure syndrome.

Aldridge and Colleagues in 1985 demonstrated that timely excision of necrotic pancreatic tissue may help reduce the high mortality associated with this condition. Radical distal pancreatic resection aided by deliberate splenectomy to be an effective approach in infected pancreatic necrosis and is the treatment of choice[11] followed by continuous irrigation.

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MATERIALS AND METHODS

During the study period of 6 years, 18 patients (9 males) with severe acute pancreatitis underwent radical pancreatic resection. The median age was 61 years (Range 36-69). During the period from January 2007 to January 2013, prospective data were collected on all those patients who underwent operation for severe necrotising pancreatitis. This included details of age, sex, operative findings and procedure, Acute Physiology and Chronic Health Evaluation (APACHE II) score,[12] duration of Intensive Care Unit (ICU) stay, total duration of hospital stay, postoperative complications, microbiological data and histology. Follow-up data were available for every patient for at least 3 years.

The median time for operation after presentation was 27 days (range 2-74). Microbiological culture confirmed infection

in 14 (78%) patients. One patient (6%) died within 30 days of operation. Twelve of the 17 survivors (71%) underwent a single operative procedure. Three patients required a further laparotomy, of whom 2 required colectomy for ischaemia. Median hospital and ICU stays were 43 (Range 30-57) and 5 (Range 4-6) days respectively. Six patients (35% of survivors) developed an infection of the left half of the chevron incision; however, all wounds were fully healed within 3 months. Long-term follow-up of survivors revealed 8 (47%) to need at least occasional pancreatic enzyme supplementation and 5 (29%) to have diabetes mellitus. One patient (6%) developed an incisional hernia.[10] Patients who had cholelithiasis underwent cholecystectomy.

Indication for Pancreatic Resection - During the 6-year period of study, an early "baseline" contrast CT was performed in every case. Patients were supported with oxygen, intravenous fluids, enteral and/or parenteral nutrition and antibiotics and careful observation was made for any clinical/biochemical deterioration that might represent super infection. If the patient became septic as evidenced by pyrexia and a rise in inflammatory markers including CRP and rising APACHE II score 12, then in the absence of any other cause (e.g., chest, urine or line infection) it was assumed that pancreatic infection was present. CT was repeated and would normally confirm identical or progressive pancreatic necrosis (patchy or total). The primary reason for repeating CT was to identify a separate fluid collection/potential abscess that was amenable to percutaneous drainage using a radiologically-guided pigtail catheter. Operative intervention was considered in those patients who were not amenable to such percutaneous intervention.

Fine needle aspiration for microbiology of solid necrosis was not routinely performed and our practice was that of careful and sensitive observation, operating on patients is thought to have developed infection of pancreatic necrosis, but before they had decompensated, become profoundly septic or developed multi-organ failure. We found that a sudden rise in the inflammatory marker, C-Reactive Protein (CRP) was particularly useful in the regard.

In summary, this series represented a consecutive group of patients either admitted directly under the senior visiting surgeon or referred to him with complicated acute pancreatitis who having initially responded to conservative management of their pancreatic necrosis, subsequently developed signs of sepsis with CT evidence of a disorganised semi-solid mass within the pancreatic bed, sometimes containing gas and not amenable to percutaneous drainage.

Operative Technique

With the patient under general anaesthetic, the abdomen was opened using a chevron/rooftop (Bilateral subcostal with vertical extension) incision. The typical findings were as follows - the greater curvature of the stomach and the splenic flexure of the colon were matted down over the region of the pancreatic tail and spleen, often with a large pancreatic/peripancreatic swelling palpable in the lesser sac. Inspection of the root of the transverse colonic mesocolon often revealed an abscess "pointing" to the left of the middle colic vessels. Attempts to open the lesser sac by division of the gastrocolic omentum were usually inhibited by the posterior wall of the stomach, which was often fused with the pancreatic body as a result of inflammation. Peeling the stomach towards the midline was usually possible and gave a full view of the superior pancreatic border. The pancreatic tail was often masked by the inflammatory mass that involved the splenic flexure. The distal transverse colon, proximal descending colon and splenic flexure were fully mobilised to give views of the pancreas up to the junction of the body and neck. It was this region that often appeared to be the seat of the watershed between viable and necrotic tissue as judged by CT.

Entering the plane behind the mobilised spleen and the tail of the pancreas allowed complete resection/debridement of the infected/necrotic body and tail of the pancreas and peripancreatic fat. The pancreas at the neck often appeared to be viable, although it was sometimes impossible to over-sew the remnant pancreatic neck/head at this point. The splenic artery was usually palpable despite the inflammatory mass along the superior board of the pancreas in the region of the neck and this was pinched off and double tied at this point. The splenic vein was tackled after the spleen and body and tail of the pancreas had been reflected to the right, allowing clear visualisation of the splenic vein as it traversed the mid-part of the gland on the posterior aspect. The vein was suture ligated and divided whilst on the back of the pancreas and the remnant vein peeled back to lie within the retro-peritoneum leaving a 3- to 4-cm splenic vein stump proximal to its confluence with the superior mesenteric vein to form the portal vein. This was a surprisingly straightforward and controlled process, although difficult retroperitoneal bleeding was not unusual but controlled.

At the end of the procedure the left upper quadrant was clean with no macroscopic pancreatic necrosis or infection remaining. The duodenum was kocherized to allow placement behind the duodenum of a Romovac 16 size tube and one at hepatorenal pouch of Morrison. An irrigating tube inside the main channel was brought out through the side wall, making this a closed system. These drainage tubes are now manufactured with a cuff incorporated into the molding (Fehling Medizintechnik, Karlstein, Germany and can be obtained from Medical Bionics, Wokingham, UK). Thus two 16 drain tube was inserted to drain from removed inflamed pancreatic tail, allowing irrigation of the retro-peritoneum. An extra tube to place in tail area separately through left side. An irrigation, at a rate of 1 ltr/hour of 0.9% NaCI was maintained as long as peripancreatic fat and necrotic pancreas continued to drain, often for a period of 10-14 days. Cholecystectomy was performed of all 10 patients having gallstones. Postoperative nutrition was maintained by insertion of a feeding jejunostomy. Post-operative electrolytes derangement during peritoneal lavage by normal saline solution was though insignificant yet easily came under control by initiation of Ringer lactate saline with sometime Darrow's to compensate more potassium deficiency and as patients were supported with feeding jejunostomy nutrition could maintain with satisfaction.

Highlighting the main of the facts, at operation it was the intention to formally divide the pancreas at the neck after full mobilisation as described with the combination of linear stapler (Ethicon TLC-55, Ethicon, Bracknell, UK) and 2-O PDS (Ethicon). However, in 10 patients (56%) the neck proved too friable/necrotic to obtain any meaningful closure and was therefore transected and not over-sewn. This included the 1 patient who died postoperatively, all of whom had complete necrosis at operation. In no case was it possible to directly

suture the pancreatic duct remnant. The intention was to leave at least one irrigation drain for a minimum of 14 days, in order to allow development of a tract for egress of pus post-removal. In our experience, the right-sided abdominal drain was generally unproductive and was removed by day 10 in every patient. The irrigation fluid remained clear in this drain, despite reduction in the rate of inflow within the first 72 hours. The situation with the left-sided abdominal drain was different. Irrigation was maintained at a maximum rate (1 L/hour) for a minimum of 1 week. A reduction in the rate of inflow within that period was usually rewarded by an obvious thickening in effluent-containing tissue fragments. It was important to remain vigilant and milk the drain regularly in order to avoid blockage. This drain fell out on day 13 in 2 patients and was removed after a median of 20 days (Range 13-39) in the rest.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism Software (GraphPad Software, San Diego, CA, USA) and continuous variables expressed as medians (Interquartile range).

RESULTS

Eighteen patients underwent pancreatic necrosectomy of whom 9 were male. This accounted for 4.5% (18 out of 403) of the total number of patients admitted with acute pancreatitis during the study period. The median age of the group was 61 years (Range 36-69). The median time for operation after presentation was 27 days (Range 2-74). The median APACHE II score at the time of operation was 11 (Range 8-17). The aetiology was gallstones in 10 patients (54%), idiopathic in 5 (28%), alcohol in 1 (6%), trauma in 1 (6%), and post-parathyroidectomy in 1 (6%). Contrast-enhanced CT revealed diffuse or complete pancreatic necrosis in 9 patients (50%), necrosis of the neck and body in 6 (33%), of the head and tail in 1 (6%), of the body and tail in 1 (6%), and solely of the tail in 1 (6%). Microbiological culture confirmed infected necrosis in 14 patients (78%) and in 13 out of 17 patients (76%) who survived their operation.

One out of 18 (6%) patients died within 30 days of operation. That patient was in established multi-organ failure at the time of internal referral for operation; established renal failure and required preoperative ventilation. The patient had been admitted under the chest physicians with an empyema that was later proven to be related to a pancreatic abscess and had fulminant acute pancreatitis. The patients who died was 65 years old and had higher APACHE II scores (15) than the survivors. The procedure-related mortality was 1. The remainder survived their operation; however, of this group 1 an elderly man with chronic obstructive airways disease died of bronchopneumonia 63 days later. Since this occurred in a convalescent home technically associated with the hospital, this increased the overall hospital mortality to 11% (2 out of 18), even though this patient had previously been seen in outpatients for review and declared well. Of the 17 patients who survived the procedure, 12 (80%) required no further operations. Three underwent further laparotomies for sepsis, 2 of whom required a colectomy for ischaemia. Hemofiltration was required in 3 patients, 6 patients had episodes of septicaemia, 2 patients developed pneumonia and 2 suffered pulmonary emboli. Six patients (35%) developed a wound infection, which in all cases affected the left half of the chevron incision and resulted in a persistent discharge of pus in 4. However, all wounds were fully healed within 3 months. None of the patients developed a pancreatico-cutaneous fistula. Median hospital and ICU stays were 43 days (Range 30-57) and 5 days (Range 4-6) respectively.

Long-term follow-up (3 years post-inclusion of the last patient) has demonstrated 8 out of 14 (57%) of long-term survivors to require at least occasional pancreatic enzyme supplementation and 5 (36%) to have developed diabetes mellitus, of whom 2 have type 1 diabetes. One patient developed an incisional hernia.

DISCUSSION

Pancreatic necrosis may occur in severe acute pancreatitis[13] and is defined as diffuse or focal area(s) of non-viable pancreatic parenchyma, typically associated with peripancreatic fat necrosis. A complex and fulminant process, it is associated with substantial use of hospital resources and expense.[14] There are substantive differences in the reported incidence of pancreatic necrosis in various study cohorts presenting with acute pancreatitis varying between 4% and 20%.[15,16] The introduction of the Atlanta classification,[13] the APACHE II scoring system and CT classification[17] has facilitated a more meaningful comparison of the incidence of necrosis and the results of therapeutic intervention.

The degree of pancreatic necrosis and peripancreatic inflammation can be assessed using bolus contrast-enhanced CT[18]; however, unless gas is seen within the pancreas or peripancreatic tissues, CT is of no value in identifying those patients with super infection. Some advocate the use of CT-guided fine-needle aspiration;[4] however, this is not without problems including false-negative results (20%),[19] and has the theoretical risk of introducing infection into sterile necrosis. In the present series, fine-needle aspiration was not routinely used and the decision to proceed to operation was based on a combination of clinical, radiological and biochemical factors.

Infected pancreatic necrosis is associated with substantial mortality. Beger et al[20] found hospital mortality to be significantly higher for those patients with infected necrosis compared with those patients with sterile necrosis. Whilst it is universally accepted that infected pancreatic necrosis requires surgical intervention,[21] the management of patients with sterile pancreatic necrosis is more controversial.[4,22] Those who advocate operation in patients with sterile pancreatic necrosis claim that these patients are as acutely ill as their infected counterparts, and that operation can be a favourable turning point for those patients with organ failure if carried out with acceptable mortality and complication rates.[19,22] Fernandez-del Castillo et al[22] studied 64 patients who underwent pancreatic necrosectomy and found no difference between infected and non-infected pancreatic necrosis in terms of outcome and overall mortality rate. Others maintain that most patients with sterile pancreatic necrosis should be managed conservatively. Rau et al[23] reported a series of 172 consecutive patients with sterile necrosis, in which 107 patients required debridement and 65 were treated conservatively and found no significant difference in mortality rates. The authors concluded that most patients with limited sterile necrosis do not require debridement, persisting or increasing organ complications being the only indication for operation. Bradley and Alien[4] reached a similar conclusion,

comparing 11 patients with sterile necrosis, treated conservatively with 27 patients with infected necrosis treated by open drainage. Early surgical intervention may also be associated with the theoretical risk of introducing infection and increased mortality. Uomo et al[24] reported a study of 169 patients with sterile pancreatic necrosis of whom 23 (14%) underwent surgical debridement. They found that the mortality rate was significantly lower (10% vs. 22%) in the non-operated group than in the surgical group. Despite a lack of prospective controlled data on the subject, it would appear that most patients with sterile necrosis can be managed with aggressive supportive therapy with only those patients with progressive deterioration requiring necrosectomy.[25] This was the policy adopted in the current study.

Most surgeons would agree that a maturation period between the initial pancreatic insult and subsequent necrosectomy is desirable,[26] making differentiation between viable and non-viable pancreatic tissue easier and allowing the endarteritis obliterans process to become complete.[27] This is supported by one of the few prospective randomised studies performed in necrotising pancreatitis patients by Mier et al.[28] They randomise patients to either early or late necrosectomy and found a difference in mortality rates of 56% vs. 27% with an odds ratio for mortality of 3.4 times higher in early necrosectomy patients, although this did not reach statistical significance. The exact length of time that is desirable before performing necrosectomy is undetermined, but most authors recommend a period of 1 month from the onset of the illness if possible.[22,28] In the present study, the median number of days from initial insult to intervention was 27 days. The timing was not deliberate, although it was recognised that allowing a period for the necrosis to mature made surgical resection easier. Instead, the decision to operate was made after careful support of the patient, usually with a combination of enteral and parenteral nutrition and careful observation. The typical scenario was one of initial attack followed by a period of stability and then subtle deterioration, most often evidenced by pyrexia and a rise in inflammatory markers and with no cause other than the pancreatitis likely. Under those circumstances, CT was arranged to exclude the possibility of a drainable collection and if not possible surgical laparotomy was performed. This paper demonstrates the results in all patients managed in this way under the senior author's care, but does not include data relating to every patient admitted to our Institution with acute pancreatitis, as only those with complicated disease requiring operation were referred to.

Whilst it is agreed that infective necrosis demands operative intervention, there is no consensus or clear guidelines on the correct surgical approach.[29] Excellent results have been obtained with debridement and closed packing[22] debridement and local lavage[20,30] and debridement with open drainage.[31] A review of the literature performed by D'Egidio and Schein[32] found mortality rates of 36%, 23% and 25% respectively for the above three techniques. The authors concluded that the surgical approach should be tailored to the individual operative findings, surgical experience and clinical course. A minimally invasive approach offers some obvious potential benefits.[33] However, this must be compared with a logical gold standard of controlled removal of all retroperitoneal sepsis.

In Leeder's study[34] of acute pancreatitis in a specialist referral centre, over half of the 144 patients were transferred from other hospitals and the mortality associated with pancreatic debridement was 70%. If the expectation is that a single procedure along with postoperative irrigation can eradicate sepsis safely, but with the theoretical morbidity associated with splenectomy and removal of viable pancreas, then this must be balanced against high mortality rates and also the morbidity of repeated surgical intervention. Beger[35] describes controversy surrounding the different approaches to necrosectomy and prefers closed management with postoperative lavage of the lesser sac after extensive surgical debridement. However, he does emphasise the dominant role in the survival of these patients being served by the extent and completeness of necrosectomy. Beger feels that semi-open techniques involving multiple re-operations are associated with prolonged ICU stay, the risk of local bleeding, intestinal failure, mechanical ileus and incisional hernia. We share this prejudice and although our approach has been associated with an incidence of diabetes of 5 out of 14 (35%) on long-term follow-up, we have had no GI fistulae and emphasised that 12 out of 15 patients required a single procedure. The technique of careful piecemeal necrosis removal can be associated with significant haemorrhage (26% in the study by Sarr et al[36]) and is less likely with controlled anatomical resection. The technique developed over the early course of this study evolved and changed to a more formal resection with deliberate splenectomy and distal pancreatectomy and compares with the philosophy adopted by Aldridge et al.[11] This allowed a more complete clearance of the pancreatic bed and allowed attempted control of the main pancreatic duct remnant, which has been reported to be ruptured in up to 70% of patients requiring surgical intervention compared with 23% of patients treated conservatively.[24] Whilst we are aware this may mean resection of some normal pancreatic tissue, we feel this is outweighed by the advantages of a more thorough debridement.

It is accepted the limitations associated with this prospective, but clearly non-randomised and selective group of patients. However, they do represent a consecutive series of patients managed in a specific and consistent way. Continuous postoperative lavage as opposed to open packing has been demonstrated to allow safe evacuation of devitalised tissues without the need for routine reoperation[30] with minimal risk of gastrointestinal fistula formation or postoperative haemorrhage.[32,37] The authors are aware of the recognised risks following splenectomy,[38,39] but feels this to be small compared with the advantages to be gained from a more complete one-off debridement set against the background of a condition with at least 20% mortality. There was no significant electrolytes abnormality during pre- or post-operative period. However, the nutrition and biochemical stability could easily be controlled by feeding jejunostomy and parenteral fluid therapy of specific type.

CONCLUSIONS

There is a belief that operative intervention in infected necrotising pancreatitis should be aggressive with a view to removing all macroscopic infected necrotic tissue, whilst allowing effective subsequent drainage of residual disease. We are uncomfortable with piecemeal removal of floating sequestra, leaving portions of infected necrotic pancreas. We accept the planned removal of the spleen at pancreatic debridement to be controversial, but have little doubt that at

the end of the procedure described we have radically removed all macroscopic pancreatic and peripancreatic sepsis. Whilst we accept that we are unable to remove all macroscopic dead tissue when necrosis is associated predominantly with the head of the gland, we feel that by removing the body and tail we are in a position to wash out remnant necrosis associated with the head by continuous postoperative irrigation. We would not recommend acute resection of the pancreatic head in view of the likely risk of significantly higher morbidity and mortality; however, necrosis located solely within the head is unusual.

The timing of surgical debridement (Approximately 28 days into the illness) was in keeping with that suggested by others. The fact that infection of pancreatic necrosis was confirmed in 78% of our cases confirms to us that surgical debridement was necessary. The majorities of surviving patients had a single operation, were housed for a relatively short period on the ICU and underwent retroperitoneal irrigation for a few weeks. Mortality and morbidity were favourable when compared with published data. We recognise that our numbers are relatively small and that centralisation of the management of this condition within a tertiary centre is advantageous as long as patients are referred early enough and before the onset of multi-organ failure. However, we do feel there is a place for radical anatomical resection in the management of complicated acute severe type of pancreatitis. We also agreed that this type of pancreatitis with highest morbidity and mortality with requirement of much financial support should bring under Right to Health Act, so that counselling, awareness and community based analytical approach to prevent the disease by abolishing the most deadliest effect of alcohol intake apart from other common causes of acute pancreatitis and its consequences. The consensus cannot be denied that Every Life Matters. And protection of life is of Nation's responsibilities.

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