

Factors Influencing Mortality in Patients Undergoing Pancreatic Necrosectomy -Experience from a Tertiary Referral Centre in South India.

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Abstract

Background : Acute pancreatitis can present with a wide array of symptoms ranging from a self limiting illness to fatal illness. Acute necrotising pancreatitis is the most dreadful complication associated with mortality of approximately 15 %. The treatment of necrotising pancreatitis has changed from open procedures to minimally invasive procedures in experienced centres. This study focuses on the different factors which contribute towards mortality of patients undergoing pancreatic necrosectomy in a tertiary care setting

Materials and methods: In this prospective study, 428 patients were admitted to the hospital and diagnosed to have necrotising pancreatitis. 37 patients (8.64%) underwent open surgical necrosectomy and constitute the study population. Special proforma was designed to collect data about demographic profile, clinical profile of episode of acute pancreatitis, organ dysfunction during admission and following surgery, type of surgical procedure, use of radiologic intervention and follow up details and findings were noted.

Results: Significantly increased mortality was observed in those with presence of comorbidity, associated pleural effusion, renal failure, hypotensive and those requiring invasive ventilation prior to necrosectomy. ASA grade, requirement of post-operative ventilation and development of surgical complications or MODS in the post-operative period were noticed to have considerable increase in mortality rates.

Conclusion: Multidisciplinary management remains the key for effective management of necrotising pancreatitis and requires close communication between the interventional radiologists, critical care physicians and surgeons.

Key word: Acute necrotising pancreatitis, necrosectomy, multi organ failure, pancreatic necrosis

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I. Introduction:

Acute pancreatitis is complicated by the presence of necrosis in 20% of the patients¹. Infection of the pancreatic necrosis is associated with sepsis and multi-organ failure. It is responsible for the majority of the deaths occurring in 2 weeks after the onset of the disease². The recent decade has witnessed a paradigm shift in the surgical management of pancreatic necrosis, including the advent of minimally invasive approaches like retroperitoneal nephroscopic debridement or the laparoscopic and endoscopic approaches³. Many of these techniques are evolving and being increasingly employed in current clinical practice, as evidence for their use gathers momentum⁴. However tertiary centres which manage high volume of such cases, often resort to open pancreatic necrosectomy (PN) for those who have failed the minimally invasive approach. Therefore, it may be noted that the poorest outcomes will be observed in patients undergoing PN in comparison to the minimally invasive group.

The definite indication for PN is infected necrosis with associated organ failure². Pancreatic necrosectomy remains a formidable surgery despite improvements in intensive care, antibiotics and nutritional support with centres reporting mortality rates of up to 40%⁵. Post-operative course is often tumultuous,

characterized by the onset of or deterioration of organ function, development of loco-regional complications in the form of pancreatic abscesses, fistulas, bleeding and wound complications. Also there remains a high need for re-laparotomy, organ support therapy which substantially increases the cost of treatment.

The management protocols in our Institute adhere to the modern multidisciplinary care and incorporate the latest available evidence. As per the Mier's study⁶, surgical necrosectomy is delayed beyond the third week of onset of pancreatitis as far as possible. Aggressive drainage of collections under radiologic guidance is encouraged before and after PN. Step up approach⁴, forms the basis of our treatment philosophy. Operative necrosectomy is performed by blunt debridement of necrotic tissue along with aggressive lavage and adequate drainage. This report provides outcome data on a contemporary cohort of patients with acute necrotizing pancreatitis who underwent PN along with impact of perioperative factors on their mortality.

II. Materials and Methods:

Study Design: This is a single centre cohort study reporting outcome in a consecutive series of patients undergoing open pancreatic necrosectomy (PN).

Study Settings: Patients who were admitted and referred to Institute of Surgical Gastroenterology, Rajiv Gandhi Government General Hospital, Madras Medical College and were cared by a multidisciplinary team of surgical gastroenterologist, interventional endoscopist, interventional radiologist, intensivist and supporting personnel.

Study duration: April 1, 2011 to July 31, 2016,

Sample size: Out of the 428 patients, 37 patients (8.64%) underwent open surgical necrosectomy and constitute the study population

Materials: During the period April 1, 2011 to July 31, 2016, 428 patients were admitted to the hospital and diagnosed to have necrotising pancreatitis. 37 patients (8.64%) underwent open surgical necrosectomy and constitute the study population. Special proforma was designed to collect data about demographic profile, clinical profile of episode of acute pancreatitis, organ dysfunction during admission and following surgery, type of surgical procedure, use of radiologic intervention and follow up details.

Acute pancreatitis was classified based on the severity in accordance with the Revised Atlanta Classification. Organ failure defined according to the Marshall's organ failure criteria. Modified CT severity index was also used. SIRS criteria was used to assess the disease progress in the bed side. Preoperative assessment by anesthesiologist and assigning of ASA score from I through IV was done routinely.

Management Policy: Patients with acute necrotising pancreatitis were managed in High Dependency Unit (HDU). Patients who tolerated oral feeds were encouraged to continue oral diet. Patients unable to tolerate oral feeds were kept NPO with IV fluid administration and total parenteral nutrition. Parenteral analgesics were given routinely. In patients with tachycardia >90/min, tachypnea >20/min, fever < 36°C (96.8°F) or >38°C (100.4°F) and elevated WBC counts (<4x10⁹/L, >12x10⁹ or 10% bands) antibiotics were initiated. Intravenous antibiotics were instituted in case of suspected infection of necrotizing pancreatitis and further intervention considered. Patients with respiratory failure were managed with ventilator support. Acute Kidney Injury was managed by the judicious use of intravenous fluids and if necessary, renal replacement therapy. Patients with persistent hypotension even after appropriate intravenous fluid resuscitation was started on inotropes and those who were not showing the improvement of clinical symptoms have undergone blood investigations and re-imaging. Patients with signs of sepsis, organ failure and not responding to initial supportive care and antibiotic therapy undergone image guided percutaneous catheter drainage and based on the culture sensitivity antibiotics fluid collected using percutaneous drainage method under USG/CT guidance by interventional radiologist.

Indications of Pancreatic Necrosectomy

(i) Early surgery indications :(<4 weeks of onset of symptom)

1. Patient with signs of peritonitis.
2. Bowel gangrene.
3. Vascular complication of pancreatitis splenic artery pseudo aneurysm with on-going bleeding in spite of resuscitation.
4. Failed angioembolization
5. Generalized peritonitis to the bowel perforation.
6. Failed endotherapy with signs of infected necrosis and sepsis.

(ii) Delayed Surgery Indications :(>4 weeks after the onset of symptom)

1. Patients with persistent of sepsis in spite of PCD and culture based antibiotics.
2. Patients without access for PCD with sepsis and multi organ failure.
3. Patients with multiple PCD having on-going sepsis.
4. Patients with bowel complications and signs of peritonitis
5. Patient with persistent unwell in spite of HDU conservative management

Technique of Pancreatic Necrosectomy

Patients with generalised peritonitis, multiple collections, post traumatic necrosis, suspected colon perforations, bowel gangrene mid line laparotomy done. Necrosis in the head and body were operated with bilateral subcostal incision. Left subcostal incision performed for necrosis of involving body and tail extending to perisplenic region, splenic artery pseudoaneurysm with failed angioembolisation. Left retroperitoneal approach performed for necrosis extending to paracolic gutter and perirenal space. We resorted to Video Assisted Retroperitoneal Debridement (VARD) for one patient with walled of pancreatic necrosis in the body and tail following PCD after 7 days. Necrosis located in the head and body undergone cystogastrostomy. Necrotic material removed with finger dissection technique with preservation of pancreatic parenchyma and adjacent structures. Necrotic fluid was sent for culture sensitivity and biochemical analysis. For necrosis adherent to stomach greater curvature stapled sleeve gastrectomy done. Necrosis extending to colon, transverse mesocolon, and colonic perforation segmental resection of colon with end ileostomy and mucus fistula performed. In patients with biliary pancreatitis and necrosis - cholecystectomy, CBD exploration with 14 Fr T insertion was done. Feeding jejunostomy performed for patients with necrosis extending in to gastric wall and prolonged nutritionally deprived patients. After the necrotic debridement 28 Fr drainage tube for lavage fluid and 32 Fr for out flow of the drainage fluid was placed in the necrotic cavity. Continuous irrigation of saline was administered till the drain fluid became clear without effluent.

Re-do Surgery indications

In the post-operative period, five patients with features of intra-abdominal collection had percutaneous drainage being performed and relaparotomy for lavage done for one patient. One patient underwent relaparotomy for post-operative intestinal obstruction. Two patients had post-operative bleeding through the drainage tube, while one patient had angioembolisation, packing was done for the other.

Statistical Analyses:

Continuous data were presented as medians with interquartile range (IQR). Discrete data were presented as percentages. To identify trends in management and outcome, the study group was divided into two subgroups according to death and survival. Factors were compared between the two groups using the Chi-Square test for discrete variables and the Mann-Whitney U-test for continuous variables. Minitab was used for the multivariate statistical analysis

III. Results:

Table 1 and 2 shows the patient clinical profile and demographics. Significantly increased mortality was observed in those with presence of comorbidity, associated pleural effusion, renal failure, hypotensive and those requiring invasive ventilation prior to necrosectomy. ASA grade, requirement of post-operative ventilation and development of surgical complications or MODS in the post-operative period were noticed to have considerable increase in mortality rates.

Table 1 : Patient demographics and clinical profile

Characteristics	Death (n=11)	Survival (n=26)	P-Value
Age	40 (33 - 43)	35 (31.5 - 42.5)	0.38
Male	7(64%)	22(85%)	0.16
Female Gender	4 (36%)	4 (15%)	0.16
Infected Necrosis	9 (82%)	16 (62%)	0.23
Duration of Symptom	30 (10 - 60)	19.5 (9 - 45)	0.39
No of days between symptom and surgery	60 (22 - 100)	35 (18 - 92)	0.28
No of pre transfer dates >= 1 day	1 (0 - 4)	1.5 (0 - 3)	0.49
No of days hospital stay >= 21 days	16 (5 - 40)	21.5 (13.75 - 31.25)	0.51
CT SI Score	8.5(8-10)	7(6-10)	0.62
No of PCDs – 0	5 (45%)	12 (46%)	0.49
No of PCDs – 1	3 (27%)	10 (38%)	0.98
No of PCDs – 2	2 (18%)	4 (15%)	0.83
No of PCDs – 3	1 (9%)	0 (0%)	0.12

Presence of comorbidity	7 (64%)	5(19.2%)	0.01
Preoperative ventilator support provided	5 (45%)	4 (15%)	0.05
B/L Pleural effusion	7 (64%)	4 (15%)	<0.01
Left sided Pleural effusion	2 (18%)	13 (50%)	0.07
No Pleural effusion	2 (18%)	9 (35%)	0.32
Renal failure	4 (36%)	2 (8%)	0.03
Hypotension	7 (64%)	3 (12%)	<0.01
USG – Ascites	10 (91%)	24 (92%)	0.89
Body and tail necrosis location	5 (45%)	16 (62%)	0.37
Head and body necrosis location	2 (18%)	4 (15%)	0.83
Head body and tail necrosis location	4 (36%)	6 (23%)	0.41
Presence of air pockets	7 (64%)	8 (30.7%)	0.45
E.coli Organism	4 (36%)	10 (38%)	0.90
Klebiseiella grown Organism	4 (36%)	3 (12%)	0.08
Other organism grown	1 (9%)	3 (12%)	0.83
No organism	2(18%)	10(38%)	0.23
ASA/PS SCORE I	0 (0%)	4 (15%)	0.17
ASA/PS SCORE II	1 (9%)	14 (54%)	0.01
ASA/PS SCORE III	5 (45%)	7 (27%)	0.27
ASA/PS SCORE IV	5 (45%)	1 (4%)	<0.01
Presence of Post op complications	11 (100%)	13 (50%)	<0.01
Post op ventilator support provided	10 (91%)	6 (23%)	<0.01

Table 2

Characteristics	Death n= 11 (29.7%)	Survived n=26 (70.3%)	P value
Age	40 (33 - 43)	35 (31.5 - 42.5)	0.38
Duration of symptom to referral	30(10-60)	19.5(9-45)	0.39
Symptoms to surgery(in days)	60(22-100)	35(18-92)	0.28
Duration of stay in hospital	16(5-40)	21.5(13.75-31.25)	0.51
PCD Performed	6(54%)	14(53.8%)	0.97
Co-morbidity	7(63%)	5(19.2%)	0.01
Respiratory failure	5(45%)	4(15%)	0.05
Bilateral pleural effusion	7(64%)	4(15%)	<0.01
Renal failure	4(36%)	2(8%)	0.03
Hypotension	7(63%)	3(12%)	0.03
Head,body and tail necrosis n=10/37=27%	4(36%)	6(23%)	0.41
Head and body necrosis n=6/37=16.2%	2(18%)	4(15%)	0.83
Body and tail necrosis n=21/37=56.7%	5(45%)	16(62%)	0.37
E.coli	4(36%)	10(38%)	0.90
Klebsiella grown	4(36%)	3(12%)	0.08
ASA/PS score IV	5(45%)	1(4%)	<0.01
Presence of Post op complications	11 (100%)	13 (50%)	<0.01
Post op respiratory failure	10(91%)	6(23%)	0.01
Post of MODS	11(100%)	2(8%)	<0.01

Table 3 compares the various types of surgical procedures carried in our patient population in relation to patients who survived and those who succumbed. We noticed that patients who developed bleeding had increased mortality. Table 4 shows the patients with infected necrosis had a significantly higher rate of mortality. Table 5 shows the cause of pancreatitis and we noticed that the aetiology did not play a contributing factor to mortality in our series.

Table 3 Comparison of death and survival for various surgical techniques:

Surgical techniques	Death n= 11 (29.7%)	Survived n=26 (71.2%)	P value
Feeding jejunostomy / NJ jejunostomy	3	5	0.59
Distal pancreatectomy splenectomy with sleeve gastrectomy	2	2	0.34
Distal pancreatectomy splenectomy	0	1	0.50
Cholecystectomy, CBDE, T tube insertion	1	0	0.11
Cholecystectomy	0	1	0.50
Resection of small bowel	1	0	0.11
Fecal diversion Ileostomy/Transverse colostomy	2	2	0.34
Bleeding post-operative	2	0	0.02
Splenic artery pseudo aneurysm	1	2	0.88
Re do surgery	2	2	0.34

Table 4: Comparison of infected and sterile between death and survived groups

Death	Infected	Sterile	P-Value
Necrosis Type	9	2	<0.01

Survival	Infected	Sterile	P-Value
Necrosis Type	16	10	0.10

Table 5 Comparison of etiology of pancreatic necrosis in the survival and mortality groups.

Etiology Causes	Death n= 11 (29.7%)	Survived n=26 (71.2%)	P value
Ethanol	3	10	0.51
Biliary	3	5	0.58
Ethanol + Biliary	2	5	0.94
Traumatic	1	1	0.51
Not known	2	5	0.94

IV. Discussion:

Severe acute pancreatitis remains a significant medical problem and is responsible for considerable morbidity and mortality. Management aims to blunt the systemic response to inflammation and is non-specific. Prophylactic antibiotics for pancreatic necrosis ⁷ and early ERCP⁸ for acute biliary pancreatitis are the only specific therapies for acute pancreatitis. Although it comes as a respite that only minority of pancreatitis belongs to the severe form, what remains a concern is the high mortality rates of up to 40% ⁹. Refractory multiple organ failure leads the cause of early mortality, while late death is often due to intra-abdominal sepsis.

Pancreatic necrosectomy is an infrequent critical intervention and we had to resort to it in only 37 patients in our cohort of 428 diagnosed to have necrotising pancreatitis. However, patients undergoing necrosectomy often belong to the critically ill group and our likely to have high complication rates. Minimally invasive approaches have become popular over the last two decades, as they avoid surgical insult associated with open necrosectomy ³ The arena of management of pancreatic necrosis is undergoing major changes, as our

understanding of the disease improves along with the evolving techniques in minimal access surgery. This creates a necessity to have outcome data from traditional necrosectomy series, which can be compared to newer approaches.

Our policy of open necrosectomy has evolved along with the minimal invasive attitude. In our cohort, 54% (20) patients underwent radiologically guided percutaneous drainage of collections preceding surgical interventions. In relation to the surgical conduct of open necrosectomy, the median delay from admission to surgery was 42.4 (18–100) days and the aim of surgery was blunt debridement of necrosis together with drainage of fluid collections. Patients with biliary pancreatitis had cholecystectomy concomitantly during necrosectomy, whenever feasible.

Detailed analysis of our cohorts revealed that the mortality was significantly increased in patients with comorbidities ($p=0.01$), requirement of invasive ventilation prior to necrosectomy ($p=0.05$) and those with bilateral pleural effusion. We also noted that renal failure and hypotensive episodes prior to necrosectomy were also significant factors influencing mortality ($p=0.03$). Interestingly, location of the necrosis, etiology of necrosis or timing of necrosectomy did not influence the outcome. ASA score was a significant risk factor, with higher grades correlating with increased mortality rates as expected. Requirement of post-operative invasive ventilation and MODS was significantly associated with increased mortality rates. Infected necrosis was significantly associated with mortality, as infection often leads to sepsis, hypotension and multiple organ failure. Development of haemorrhagic complications in the post necrosectomy status was independently associated with significantly increased mortality ($p=0.02$).

Direct comparison of our cohort with others in the literature is difficult due to differences in demographics and changes in the management of pancreatic necrosectomy have evolved over various time periods. Data presented by us are reflective of the patients we encounter in a typical tertiary referral centre in India. Despite the improvements in critical care and recent changes in management strategies for pancreatic necrosis, we encountered a mortality rate of 29.7% in patients undergoing necrosectomy and 2.57% for patients diagnosed to have pancreatic necrosis respectively.

V. Conclusion:

In summary, improving outcomes in patients with acute necrotizing pancreatitis remains a formidable challenge even in the current scenario. Despite being a benign condition, pancreatic necrosis carries high rates of mortality and often responsible for prolonged hospitalisation. Multidisciplinary management remains the key, and requires close communication between the interventional radiologists, critical care physicians and surgeons. Advent of radiologically guided interventions and minimal invasive approach are now established protocols in managing pancreatic necrosis, which should be compared with traditional open necrosectomy. Indications for conventional open necrosectomy are on the decline, but will still remain in the armamentarium of pancreatic surgeons for some more time.

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