

Step-up approach for the management of acute necrotizing Pancreatitis (ANP): Single institution experience

ABSTRACT

Introduction: Acute necrotizing pancreatitis causing infected pancreatic necrosis is a severe disease with high morbidity and mortality that needs critical care and judicious management decisions. With a step-up approach in the management of acute necrotizing pancreatitis, there is a significant reduction in complications. The aim of this study is to analyze the outcome of the step-up approach in a single tertiary care centre.

Methodology: Prospective observational study conducted between January 2021 and December 2022. Patients with pancreatic necrosis or peripancreatic necrosis detected on contrast-enhanced computed tomography scans were included in the study.

Results: A total of 53 patients were included in the study. Ethanol (75.5%) and biliary (11.3%) were the two most common etiology. 32 patients (60.4%) were managed conservatively initially and 19 (35.8%) with a step-up approach. Interventions were done in 24 patients (45.3%) –image-guided percutaneous drainage-14(26.4%) patients, Percutaneous drainage followed by necrosectomy- 5(9.4%) patients, Conservative management followed by direct necrosectomy -5 (9.4%) Patients. 14(73.7%) Patients were managed with Percutaneous drainage alone successfully. Overall mortality- 4 patients. Primary end points were- mortality 02(10.5%), Enteric fistula 03(15.9%), secondary end points- biliary stricture and Pseudocyst formation 01(5.3%), need of pancreatic enzymes 02(10.5%).

Conclusion: Step-up approach management reduces morbidity and mortality in patients with necrotizing pancreatitis and infected pancreatic necrosis, in two-thirds of patients percutaneous drainage obviated the need for necrosectomy.

Keywords: Infected pancreatic necrosis, walled-off necrosis, percutaneous drainage, direct necrosectomy, pancreatic pseudocyst.

Abbreviations and acronyms: ANP-acute necrotizing pancreatitis, INP-infected pancreatic necrosis, PCD- percutaneous drainage, TLC- total leukocyte count, WON- walled off necrosis, CECT- Contrast-enhanced computed tomography.

1. INTRODUCTION

Acute Pancreatitis is not an uncommon gastrointestinal emergency requiring hospitalization. Necrotizing pancreatitis develops in approximately 20% of patients with acute pancreatitis and is associated with a mortality of 8% to 39%¹. The conventional treatment of necrotizing pancreatitis with secondary infection is open necrosectomy so as to completely remove the infected necrotic material^{2,3}. This procedure is however associated with high mortality reaching up to even 40%⁴. Direct open necrosectomy has been replaced by a “step up” approach⁵ wherein necrotizing pancreatitis is treated sequentially with intravenous fluids and supportive/symptomatic, percutaneous /endoscopic drainage, and if required surgical necrosectomy⁶. The percutaneous drainage (PCD) approach alone circumvented the need for surgical intervention in infected necrotizing pancreatitis in 30-100% of cases^{7,8,9}. Endoscopic necrosectomy reduced the pro-inflammatory response as well as major complications and death compared with surgical necrosectomy.¹⁰ We prospectively studied the outcome of a step-up approach in managing patients with necrotizing pancreatitis (infected or non-infected) at our centre, a tertiary care surgical gastroenterology centre in southern India.

2. MATERIAL AND METHODS

Study design

This prospective observational study was conducted in the surgical gastroenterology unit at Tirunelveli Medical College and Hospital, Tirunelveli, Tamil Nadu state, between January 2021 and December 2022. A total of 53 consecutive patients with acute necrotizing pancreatitis were enrolled in the study. The Institutional Review Board approved the study in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients.

Inclusion criteria

All patients with pancreatic necrosis (with or without a wall) or peripancreatic necrosis with or without features of infection confirmed on contrast-enhanced computed tomography (CECT) and fulfilling Balthazar's criteria.

Exclusion criteria

Patients with non-necrotizing acute pancreatitis, peripancreatic fluid collection, pancreatic pseudocysts, and those discharged against medical advice. Patients undergoing endoscopic intervention for necrosectomy were excluded.

Methods

All patients admitted with acute pancreatitis requiring intensive care were followed up for the natural course of events. APACHE II score was done if the duration of symptoms was within 24 hours and BISAP (blood urea nitrogen, impaired mental status, systemic inflammatory response, age, and pleural effusion) if coming later. Patient data included demography, etiology, duration of abdominal pain, severity, and organ failure namely cardiovascular, respiratory and renal failure were recorded. Baseline and follow-up investigations included complete blood count, serum amylase, renal function tests and liver biochemistry. The need for organ support was also recorded at baseline and during follow-up.

The diagnosis of acute necrotizing pancreatitis was based on the documentation of necrotizing pancreatitis in CECT by modified CT severity index. Magnetic Resonance Cholangio Pancreatogram (MRCP) was also done in patients with acute biliary pancreatitis (cholangitis, common bile duct stones).

Based on the number of organ failures, laboratory investigations and imaging, patients were classified as mild, moderate, and severe pancreatitis based on Atlanta classification to prognosticate the outcome.

Treatment Protocol

All patients were managed conservatively in the initial 2 weeks, regardless of the severity of symptoms and organ failure. PCD was considered at the third week when the necrotic collection started getting become encapsulated. Surgical necrosectomy was done after 72 hours of PCD if indicated.

a. Conservative management

Included fluid resuscitation, nutritional supplementation, pain relief, antibiotics, and organ support as required. Patients who improved on conservative management were discharged and kept on follow-up.

b. Percutaneous Drainage

Indications included patients who had pancreatic/peripancreatic necrotic collection(s) with persistent infection and signs of clinical deterioration, in the form of multiorgan dysfunction, fever ($>100^{\circ}\text{F}$), leucocytosis ($>11000/\text{mm}^3$), persistent tachypnea (respiratory rate $>20/\text{min}$) and tachycardia (heart rate $>100/\text{min}$). The preferred route was through the left retroperitoneal approach for lateral compartment necrotic collection. A transperitoneal approach was done for necrotic collection in the central compartment. Image-guided PCD 12 /14 Fr was performed. Drains were flushed with 50 ml saline periodically (6 hourly).

For patients with multiple necrotic collections, multiple PCDs were done in the first sitting. PCD was considered successful if this was the only procedure done for recovery, with normalization of tachycardia, whole blood cell count, and could tolerate oral feeds. Patients were discharged with PCD in situ and was removed when the drain output was less than 20 mL on 3 consecutive days, with repeat CECT imaging confirming no and or minimal residual collection. Post PCD removal, patients were followed up for 6 months for any delayed complications like pancreatic pseudocyst, enteric fistula, and pancreatic insufficiency.

C. Surgical Necrosectomy:

This was indicated if after 72 hours of drainage, there was deterioration in general condition i.e. persistently elevated leucocyte count with or without fever, CECT abdomen showed persistent of necrotic material or the patient progressed to multi-organ failure of any of the 2 organs namely, circulatory, pulmonary, or renal function derangement. Based on the location of the collection retroperitoneal or transperitoneal route was considered for the procedure. For patients who had walled-off necrosis during follow-up and were symptomatic, a retro gastric location was considered i.e. transgastric necrosectomy with cystogastrostomy.

The step-by-step surgical necrosectomy consisted of the following steps Fig, 1 A and 1B).

C i. Retroperitoneal necrosectomy.

a. Position of the patient: Supine position with the left side elevated, 5-7 cm incision was made in the left flank under PCD guidance.

- b. With digital exploration drain was followed into the collection and necrosectomy was performed with ring forceps and a suction device (Fig 1A).
- c. Cavity was irrigated with normal saline and hydrogen peroxide multiple times.
- d. Two large bore 32Fr drains were placed in the cavity.
- e. Postoperatively saline irrigation was done via drain periodically.

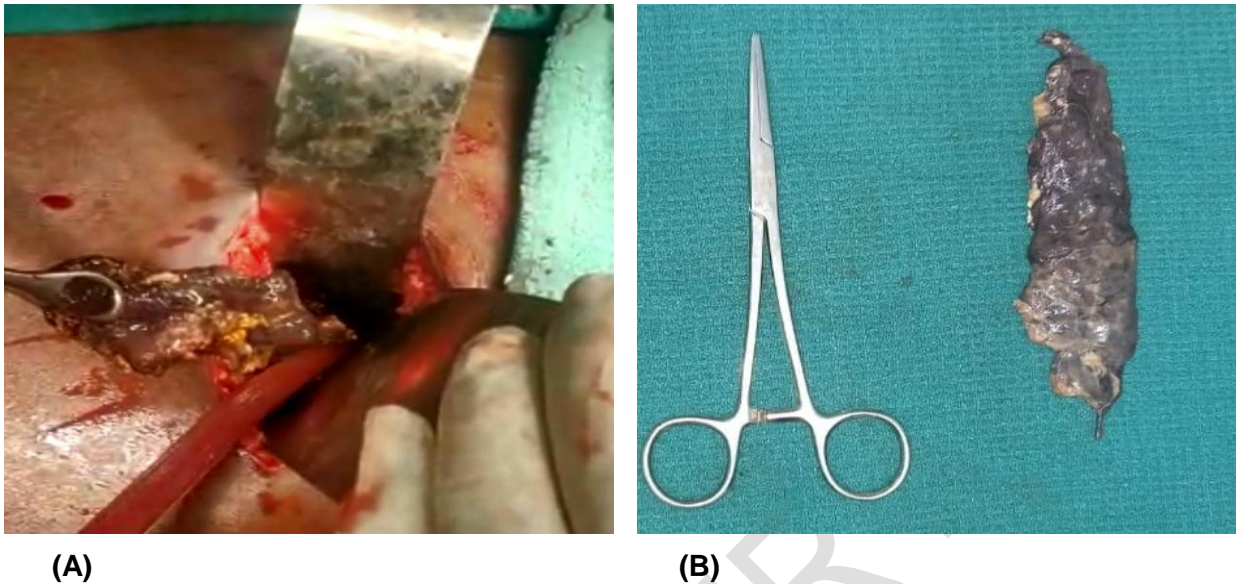


Figure 1A,1B. Retroperitoneal necrosectomy was performed with ring forceps and a suction device

C ii. Transperitoneal necrosectomy

Except for the left subcostal incision rest of the procedure was similar to the retroperitoneal route.

Postoperative management

CECT was repeated a week after surgical intervention. Catheters were removed if daily clear drain output was less than 20 ml/24 hours and there was a collapse of the cavity. Patients were discharged with catheters in situ and advised irrigation at home (normal saline irrigation 6 hourly via drains) if drain output persisted. The drain was removed on follow-up and the time of removal was recorded.

Follow-up

Post-procedure patients were followed up at weekly intervals in the first month and thereafter once a month for 6 months. The primary endpoint of the study was the occurrence of new-onset multi-organ failure or systemic complications, enteric fistula (either small or large bowel), bleeding requiring intervention, or death. The follow-up was completed at 3 months

The secondary endpoints of the study were at 6 months after discharge and included a physical examination and USG/CECT abdomen as and when indicated. The follow-up issues included the need for re-intervention for either the

presence of a persistent pancreatic fistula post-procedure at 3 months, new onset pancreatic pseudocyst, symptomatic biliary strictures, and incisional hernia or the need for pancreatic enzyme replacement therapy for pancreatic insufficiency.

Statistical Analysis

Data were described in terms of range; mean, standard deviation (\pm SD), median, frequencies (number of cases), and relative frequencies (percentages) as appropriate. For comparing categorical data, the McNemar test was performed. A probability value (p-value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

3. RESULTS AND DISCUSSION

Results

Fifty-three patients with acute necrotizing pancreatitis were admitted between 1 January, 2021 and 31 December, 2022. All patients were followed up for 6 months i.e. until 30 June, 2023.

Table 1 highlights the baseline characteristics of the patients. There were 48 males (90.6%), the median age being 35 years. The most common etiology being alcohol (40 patients; 75.5%) followed by gallstone disease (6 patients; 11.3%). Co-morbidities included coronary artery disease (6 patients, 11.3%) followed by diabetes mellitus (5 patients; 9.4%). The median duration of symptoms was 15 days (range 5-120 days) and the median duration of hospitalization was 14 days (Range 3-68days).

The APACHE II score was > 20 in 23 patients (43.4%). Thirty-two patients (60.4%) had leucocytosis. Based on the modified CTSI score, 30 patients had a score of 10 (56.6%) and 11 patients had extensive pancreatic necrosis (20.6%).

Characteristics	Step-up Approach(N = 53)
Age-yrs	14-72yrs(median-35yrs)
Male sex(M:F)	48:5(Male-90.6%)
Etiology of pancreatitis	
Ethanol	40(75.5%)
Biliary	06(11.3%)
Metabolic	01(1.9%)
Trauma	01(1.9%)
Idiopathic	05(9.4%)
Comorbidities	17(32.1%)
Diabetic Mellitus	05(9.4%)
Renal insufficiency/Chronic kidney disease	01(1.9%)

Cardiovascular	06(11.3%)
Others	05(9.4%)
Total Leukocyte Counts > 11000mm ³	32(60.4%)
Serum Amylase(U/ml)	
Median	220
Range	15-118
APACHE II score>20	23(43.4%)
Modified CT Severity score	
Score 10	30(56.6%)
Range	4-10
No. of Patients with necrotic collections 2 or more	
Range of collections	15(28.3%) 1-3
Extensive necrosis extending to paracolic gutters	11(20.6%)
Duration of symptoms-	
Median	15days
Range	5-120days
Length of stay	
Median	14days
Range	3-68days

Management

I. Conservative

Of the 53 patients, 2 patients died during conservative treatment during the initial 2 weeks, remaining 32 patients (60.4%) were managed by a conservative approach initially. 27 patients (84.4%) did not require any further intervention. 5 patients (15.6%) presented with walled of pancreatic necrosis on follow-up and underwent transgastric necrosectomy with cystogastrostomy for mass effect (3 patients-open 9.4%, 2 patients laparoscopic 6.2%). These are 5 out of 32 patients which means only 27 were managed conservatively.(Figure 2)

ii. PCD

As a step-up protocol, 19 patients had PCD initially. Fourteen (73.7%) recovered with no further intervention during follow-up. The remaining five (26.3%) had necrosectomy. (3 left retroperitoneal approach, 2 transperitoneal approach) The median duration before PCD was 22 days (Range 13-49 days). The median duration for PCD was 22 days (range 5-62 days) after which either PCD was removed or the Patient underwent necrosectomy. A major PCD-related complication occurred in 1 Patient -fecal fistula and was managed conservatively.

In comparison with Pre-PCD and Post-PCD (72hrs after PCD insertion) Tachycardia, fever, and total count significantly reduced. Also, there was a significant reduction in creatinine levels and oxygen. The need for inotropic support was reduced from 26.3% to 10.5% but it was not statistically significant. The ventilator support requirement did not change

because both patients died within 72 hours of PCD. Most of the Patients who did not improve on PCD were those who underwent necrosectomy after 72 hours. (table 2)

Table 2: Comparison of Clinical, Lab Parameter, Renal, Respiratory, and cardiovascular functions in Pre-PCD and Post-PCD state

Parameters	Pre-PCD No of Patient (%)	Post-PCD No of Patient (%)	P value
1. Tachycardia PR>100/min	18(94.7%)	5(26.3%)	0.001
2. Fever (Temperature>100F)	16(84.2%)	6(31.6%)	0.002
3. Total Leukocyte count > 11000/ml	18(94.7%)	6(31.6%)	0.001
4. Serum Creatinine >1.5mg/dl	05(26.3%)	01(5.2%)	0.001
5. Respiratory Failure			
Oxygen requirement	09(47.3%)	03(15.8%)	0.031
Ventilator support	02(10.5%)	02(10.5%)	1
6. Cardiovascular failure			
Use of Inotropes	05(26.3%)	02(10.5%)	0.25

iii. Surgery

Overall ten of the 24 patients with intervention underwent surgical necrosectomy; 5 transgastric with internal drainage i.e. cystogastrostomy following conservative treatment, the remaining 3 had retroperitoneal necrosectomy and 2 had transperitoneal necrosectomy following PCD.

E coli was the most common organism isolated from fluid culture in 15 of the 24 patients (62.5%) and was sensitive to Amikacin /Gentamycin/Meropenam. Klebsiella was isolated in one patient (4.2%) who was sensitive to Piperacillin Tazobactam and clotrimoxazole antibiotic. Fluid was sterile in the remaining 8 patients (33.3%). (Table 3)

Table 3: Culture sensitivity		
Micro-organism	Antibiotic sensitivity	No of Patients, n=24
E. coli	Amikacin, gentamycin, ceftazidime+clavulanic acid, cefuroxime, Meropenam	15(62.5%)
Klebsiella	Piperacillin-Tazobactam, clotrimoxazole	01(4.2%)
No growth	NA	08(33.3%)

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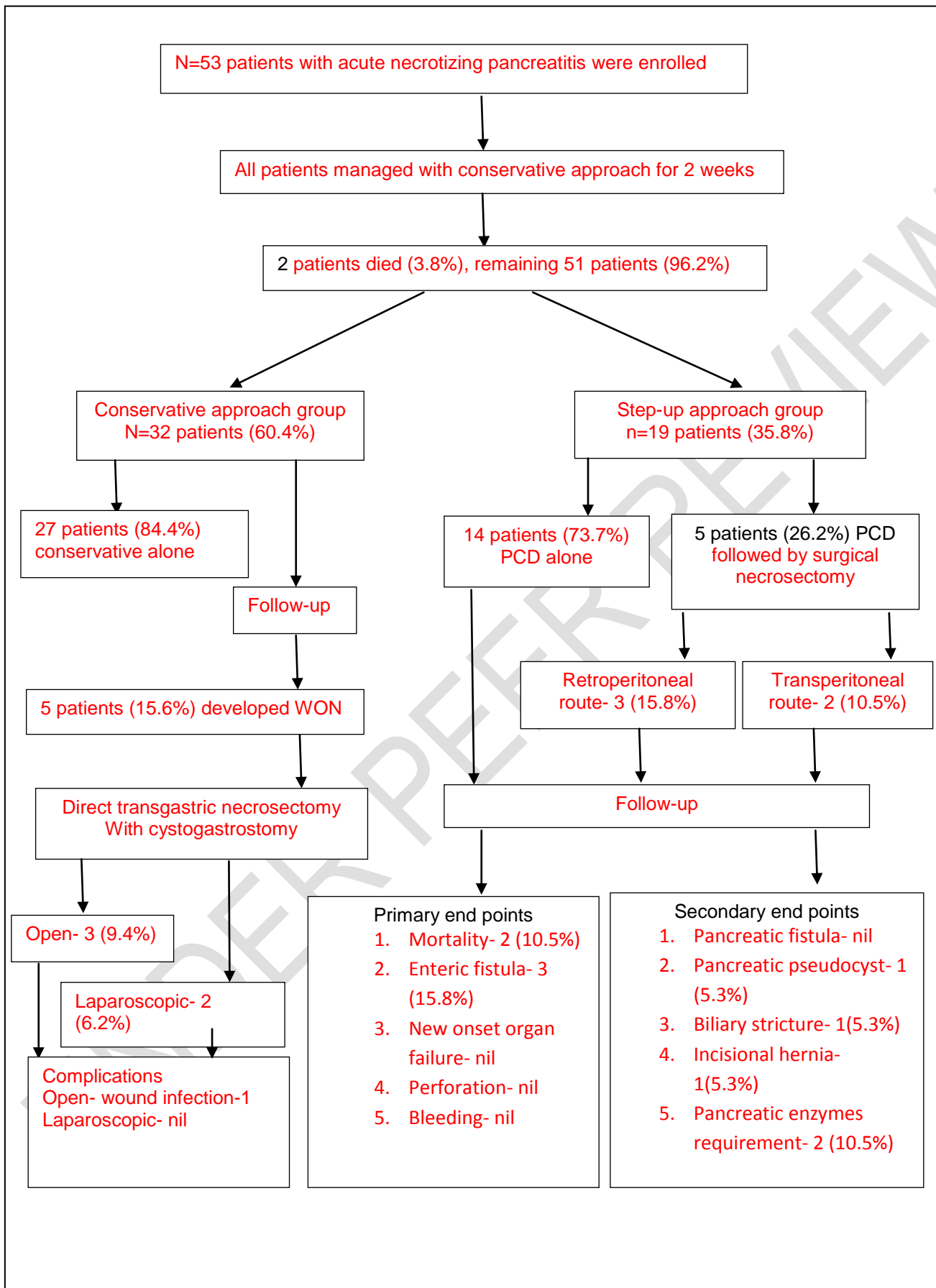


Fig 2 : Treatment algorithm

Follow up

Primary endpoint

Overall mortality was 4 patients; two patients (3.8%) in the conservative group, one with biliary pancreatitis with myocardial infarction and left hemiparesis, and the second a case of ethanol-induced pancreatitis and hemosuccus pancreaticus due to splenic artery pseudoaneurysm. There were 2 deaths in the step-up group. Among the step-up approach group, primary endpoints in the form of mortality occur in 2 patients (10.5%). Both mortality were seen in the PCD alone group- 1 patient was ethanol-induced Pancreatitis with old Pulmonary TB with multiple PCD died of severe sepsis, and another patient of biliary pancreatitis with Coronary artery disease died of Myocardial infarction. Three patients (out of 19) developed enteric fistula, one patient who had PCD and 2 following surgical necrosectomy. Diversion ileostomy was necessary in one of the 3 patients who had necrosectomy, the other two recovered with conservative management.

Secondary endpoints

One patient developed a significant pancreatic pseudocyst and biliary stricture. This patient had a cystogastrostomy and choledocho-duodenostomy. One other patient developed an incisional hernia (5.3%) and 2 patients (10.5%) had steatorrhea requiring pancreatic enzyme replacement therapy.(Figure 2)

Discussion

This study shows that the step-up approach reduced the mortality rate and long-term complications, and more than two-thirds of patients were successfully treated with percutaneous drainage alone.

Acute Necrotizing Pancreatitis patients are often in critically ill conditions with organ failures or its complications and have poor tolerance for direct surgical stress. If direct surgery in the form of laparotomy is performed bleeding, intestinal fistula, diffuse abdominal infection, or multiple organ dysfunction may worsen, with an average mortality rate of 30.8%.^{11,12} In this single-center study, we analyzed the outcome of PCD in 19 out of 53 patients of acute necrotizing pancreatitis who were managed using a “step-up” approach. 27(50.9%) out of 53 patients were managed with a conservative approach. Percutaneous drainage alone was sufficient to deal with organ failure in 14 out of 19 patients (73.7%). In a study by Kochhar et al successful outcome of PCD was seen in 56.6 patients¹³.

The timing of PCD is controversial. We performed PCD after a median duration of 22 days (Range-13-49days) Though the current recommendations are to delay the drainage as much as possible for at least 4 weeks from onset, a number of studies have shown that patients with persistent organ failure or infected necrosis do benefit from PCD done as early 9–14 days.^{14,15,16} We believe that in the initial 2 weeks, patients should be managed with IV fluids and supportive treatment in the ICU. From 3rd week onwards when collection starts to become localized or walled off, PCD is to be done if indicated.

The improvement in patients with necrotizing pancreatitis after PCD has been explained by various mechanisms. In infected necrosis, source control via drainage of infected fluid is believed to act as the principal mode of action, and

catheter drainage of pancreatic enzyme-rich necrotic fluid helps by reducing inflammation, and endotoxins are also reduced^{17,18}. A Study by Liu et al.¹⁹ has shown that PCD results in a decrease in inflammatory markers and a reduction of inflammatory cytokine cascade.

In our study, *E. coli* was the most common microorganism, identified in 15 patients (62.5%) from culture, and was sensitive to Amikacin and Meropenam antibiotics. Mowbray et al. performed a retrospective analysis and found that *E. coli* is one of the most frequently cultured microorganisms in infected pancreatic necrosis and it is an opportunistic pathogen derived from the gut by bacterial translocation.²⁰ Adequate penetration by carbapenems, piperacillin, fluoroquinolones and cephalosporins in necrotic pancreatic tissue has been demonstrated in a study by Buchler et al.²¹

The favourable outcome of the step-up approach may be seen due to infected necrosis being similar to an abscess because both contain infected fluid (pus) under pressure and after the infected fluid is drained, the pancreatic necrosis can be left in situ⁹. Although we used an open approach for necrosectomy similar to VARD with a slightly bigger incision. PANTER study trial also did not prove that VARD is superior to open necrosectomy in patients in whom percutaneous drainage has failed.

Some patients did not qualify for step-up approach criteria and were managed conservatively in the initial period. Later they were presented with walled-off necrosis with mass effect in the follow-up period. We performed direct trans-gastric necrosectomy with cystogastrostomy for sterile pancreatic necrosis in 5 patients with minimum morbidity and nil mortality.

4. CONCLUSION

Our results suggested that the preferred treatment for patients with infected pancreatic necrosis should be a step-up approach consisting of percutaneous drainage followed, if necessary, by necrosectomy, although direct necrosectomy can be performed with minimal complications in sterile walled of necrosis patients, those who in clinically stable condition.

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

Ethical Approval:

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

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