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Original Article

A Prospective Observational Study on Management of Infected Pancreatic Necrosis with Surgical Step-Up Approach and its Outcomes in a Tertiary Care Centre in Central India

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ABSTRACT

Introduction: Infected pancreatic necrosis is associated with high mortality and is virtually always an indication of invasive intervention. Currently, a step-up approach, either surgical or endoscopic, has superseded the conventional open necrosectomy for the management of infected pancreatic necrosis. However, the outcome of of the approach are not well defined in central Indian population. Thus, this study assessed the management of infected pancreatic necrosis with surgical step-up approach and evaluate the outcomes of this approach.
Methods: This prospective observational study was conducted in Department of General Surgery, Government Medical College and Hospital, Nagpur from August 2022 to August 2024. The study included 26 adult patients with IPN that were managed with surgical step-up approach and followed-up for six months.
Results: Out of 26 patients of infected pancreatic necrosis, 21(80.8%) were alcohol-induced and 5(19.2%) were gall stone induced. 18(69.2%) patients were confirmed radiologically on contrast enhanced computed tomography and 8(30.8%) were confirmed microbiologically on culture. 19(73.1%) patients were managed by drainage procedure only and 7(26.9%) patients required drainage procedure with operative intervention. Among operative intervention patients, 5(71.4%) patients underwent open necrosectomy and 2(28.6%) underwent video assisted retroperitoneal debridement. 21(80.8%) patients improved clinically, and 5(19.2%) succumbed. Among clinically improved patients, 13(61.9%) developed pancreatic fistula and 8(38%) developed exocrine insufficiency.
Conclusion: Surgical step-up approach leads to clinical improvement in patients with infected pancreatic necrosis. Mortality occurs in about one fifth of the patients. Pancreatic fistula and pancreatic exocrine insufficiency are frequent complications in clinically improved patients.

Keywords: Infected pancreatic necrosis, Surgical step up approach, Open necrosectomy, Video assisted retroperitoneal debridement.

INTRODUCTION

Acute pancreatitis, a common inflammatory condition of exocrine pancreas, has a global incidence of 30-40 cases per lakh population per year and mortality of 1-5%.[1] While 80% of the patients suffer from mild pancreatitis, 20% progress to necrotizing pancreatitis.[2] The acute necrotizing pancreatitis (ANP) leads to death in 8-39% cases.[3] The primary factor responsible for mortality is early organ failure accompanied by secondary infection of pancreatic and peri-pancreatic necrotic collection (PPN) resulting in sepsis and multiple organ dysfunction syndrome (MODS).[4]

ANP accompanies pancreatic necrosis as well as PPN. The collection can be sterile or infected. Though the management of sterile pancreatic/peri-pancreatic necrotic collection is usually non-operative, the infected pancreatic necrosis (IPN) is virtually always an indication for invasive intervention owing to increased risk of mortality.[5]

Over the last 20 years, the timing of surgical intervention in ANP has shifted from early necrosectomy irrespective of the state of infection to delayed intervention in those with documented or suspected infection of pancreatic necrosis. Postponing surgical intervention allows the immune system to encapsulate the necrotic tissue and facilitate necrosectomy and potentially reduces mortality.[6] Recent surgical guidelines by the International Association of Pancreatology state that surgical intervention should preferably be performed between 15 and 28 days (in third or fourth week) after admission.[7] The conventional management of ANP with superadded infection of necrotic tissue/collection is open necrosectomy (ON).[8,9] However, ON is associated with increased rates of complications (34 to 95%), mortality (11 to 39%), a risk of long-term pancreatic insufficiency, mainly owing to invasive nature.[5,10-15]

In PANTER trial, ON was formally challenged by the Dutch Acute Pancreatitis Study Group resulting in introduction of the step-up approach, which refers to less invasive alternatives that have the potential to be used with escalation in draining IPN. The step-up approach can be categorised into endoscopic step-up approach (consisting of endoscopic ultrasound-guided transluminal or transgastric drainage followed by endoscopic necrosectomy, if required) and surgical step-up approach (consisting of percutaneous catheter drainage followed by video assisted retroperitoneal debridement (VARD)/minimally invasive necrosectomy, if required, or ON).

Contrasting with ON, the step-up approach intends to minimise the infection rather than total extraction of IPN.[16-18] It decreases the rate of complications as well as death by reducing the trauma of operative intervention (i.e., tissue damage and a systemic pro-inflammatory response) in already severely ailing patients.[13,19]

In the last decade, the surgical step-up approach has superseded the conventional management of ON.[20,21] A randomised controlled clinical trial compared surgical step-up approach with primary ON and demonstrated that percutaneous catheter insertion as an initial intervention prevented the indispensability of necrosectomy in 35 to 50% cases.[20,22] Thus, this study aimed to assess the management of IPN with surgical step-up approach and evaluated the outcomes of this approach.

MATERIALS AND METHODS:
This prospective observational study was conducted in the Department of General Surgery, Government Medical College and Hospital, Nagpur over 24 months (August 2022 to August 2024). The study was approved by the Institutional Ethics Committee and written informed consent was obtained from the patients prior to enrolment.

Sample size calculation: Assuming that outcome variable measures should be binary (alive/dead) and possibility of success in each trial is p, possibility of failure is 1 - p and the sampling distribution of the sample proportion is approximated to normal. Applying the formula,
$n = Z^2_{1-a/2}P(1-P)/d^2$

where n = sample size, $Z^2_{1-a/2}$ = confidence interval, P = estimated precision, d = desired precision.
According to a study by van Santvoort HC et al.[20], percentage of patients who had major complications (death) after step-up approach (p) = 40%, absolute precision (d) = 20%, and desired confidence interval $Z_{1-\alpha/2}$ = 95%. Thus, minimum required sample size was calculated to be 23.

However, a total of 26 patients with IPN were enrolled and managed with surgical step-up approach.

Inclusion Criteria: The study included patients of either sex, aged 18 years or more, diagnosed with IPN, and underwent surgical intervention/step-up approach with possibility of placing a drain to remove the collection. IPN was elucidated as persisting sepsis or continued clinical worsening regardless of maximal aid in intensive care unit in a patient of pancreatic/peri-pancreatic necrosis, and confirmed microbiologically (positive microbial culture of pancreatic or PPN collection obtained by percutaneous needle aspiration or initial drainage intervention) or radiologically (visualisation of gas on contrast-enhanced computed tomography of abdomen and pelvis (CECT A+P).[23]

Exclusion Criteria: Patients aged less than 18 years, presenting with sterile pancreatic necrosis, or those with pancreatitis in whom emergency exploration was performed due to acute intra-abdominal events (including hollow viscus perforation, acute intra-abdominal haemorrhage, and abdominal compartment syndrome). Sterile pancreatic necrosis was defined as patient presenting as a case of pancreatic/peri-pancreatic necrosis managed conservatively and/or negative culture of pancreatic/peri-pancreatic necrosis.

Study Parameters: Following enrolment, demographic parameters, anthropometric details, comorbidities, presenting complaints, and duration of disease were collected. The patients underwent laboratory investigations, including white blood cell (WBC) count, C-reactive protein (CRP) level, and serum lipase. The causes of pancreatitis leading to IPN were

recorded (alcohol-based, gall stone-based, or others). Nutritional support given was recorded (oral/ enteral/ parenteral). Subsequently, Acute Physiology and Chronic Health Evaluation II (APACHE II) and quick Sequential Organ Failure Assessment (qSOFA) score were calculated. Moreover, the CECT A+P was performed and modified CT severity index (MCTSI) score was calculated.

Modalities for detection of IPN were noted (Radiologically confirmed - visualisation of gas on CECT A+P, or Microbiologically confirmed - positive microbial culture of pancreatic/PPN tissue). WBC count before the first intervention was recorded. Intervention I (drainage procedure), Intervention II, operative intervention (VARD/ON), and timing between them were noted. Blood loss and duration of surgical intervention were noted. Complications in the 6 months follow-up period were noted.

Intervention (Drainage Procedure) : Under the ultrasonography (USG) or computed tomography (CT) guidance percutaneous pigtail or drainage tube (minimum 12 Fr) was inserted in the pancreatic/PPN collection. Multiple drains were used in patients with massive or multiple necrotic collections. The left retroperitoneum was the most predisposed course. Alternative, transperitoneal course was used in cases with unfeasible retroperitoneal course. While the right retroperitoneal course was also permitted, depending on the feasibility of its application. The methods of continuous lavage were not instated. The inserted drains were irrigated with 50 cc normal saline (NS) thrice daily to maintain the patency. Additional NS was employed, determined by the appearance of the return liquid, the proportions of the collections on CECT, circulation among drains, and circulation among collections. Diurnal drain fluid balance was accounted. Failure was contemplated if there was clinical deterioration after drain placement and a follow-up CECT was performed to look at the position of the drain. On repeat CECT, if the drain position was adequate and no additional drainable collections are seen, the patient was considered for surgical intervention. In the presence of drainable collection on repeat CECT, a second pigtail or drain was inserted in the necrotic collection under USG/CT guidance.

Operative Intervention (Video assisted retroperitoneal debridement - VARD): The percutaneous retroperitoneal drain/pigtail inserted previously was utilised for VARD under supervision of an experienced surgeon. The preferred position for VARD was dorsal decubitus with elevation of left side. The entire abdomen and left flank was cleaned, painted, and draped. Pertaining to the location of the inserted pigtail/drain, a subcostal/intercostal incision of about five centimetres was made in the left loin. The retroperitoneal drain was trailed into the collection via finger dissection. Upon opening of collection, retroperitoneal debridement was carried out using ring forceps along with suction device. Through the retroperitoneal incision, a 10 mm trocar and a 10 mm zero degree laparoscope were placed. The cavity containing necrotic pancreas was examined using an laparoscope and persisting, loosely adhered necrotic pancreas was detached and taken out using laparoscopic graspers or ring forceps. Removal of entire necrotic pancreas was non-obligatory. Two 32 Fr abdominal drains were inserted in the collection through the incision. The skin amidst the drains was sutured. In cases where VARD was impractical technically, ON is carried out. Surgical competency was elucidated as experience of performing a minimum of 10 self-dependent VARD interventions.

Open necrosectomy (ON): ON was carried out using a bilateral subcostal/midline exploratory laparotomy incision. Lesser sac was entered after piercing the omentum and meticulously examined. Necrotic pancreatic tissue was bluntly debrided and sent for histopathological and microbiological analysis. Two wide bore drains of 32 FG were placed via distinct incisions and the tips of drains were placed in the lesser sac and necrotic cavities. The access to the lesser sac was meticulously secured to make an enclosed pocket for continuous peritoneal lavage. Obtained specimen of necrotic pancreatic tissue was sent for histopathological examination and culture.

Post-operative care: The post-operative care was comparable in both operative interventions. NS was used for instating continuous post-operative irrigation. Interventions (either drain insertion or operative procedure) were followed by CECT seven days after each intervention. The catheters were removed once the cavity collapsed (visualised on CECT along with contrast in the drains), and diurnal the drain output was reduced to less than 50 cc per day. The cases were discharged with drains in-situ and followed-up in OPD for removal of catheters/drains.

Outcomes (Definitions)

Clinical improvement referred to improvement of performance of minimum two body systems (cardiovascular, respiratory, renal) after intervention, or minimum 10% positive change in two among three parameters: WBC/pyrexia/CRP.

Mortality referred to cardiorespiratory arrest with unsuccessful revival at any point of time during the study, due to organ failure.

Organ failure referred to either pulmonary, renal, or multiorgan failure. Pulmonary failure was suggested by partial pressure of oxygen in arterial blood less than 60 mm Hg despite the fraction of inspired oxygen of 0.30 or need for mechanical ventilator. Circulatory failure was suggested by systolic blood pressure less than 90 mm Hg despite adequate fluid resuscitation or need for inotropic catecholamine support. Renal failure was suggested by creatinine level >177 micromol/litre after rehydration or new need for hemofiltration or hemodialysis. Multiorgan failure referred to failure of two or more organs on the same day.

Enterocutaneous fistula referred to persistent feculent discharge from percutaneous drain or from drain site following withdrawal of drains or from an operative site, either from small intestine or colon and diagnosed by radiological modality or during operative intervention.

Intraabdominal bleeding referred to bleeding requiring surgical, radiological or endoscopic intervention.
Pancreatic fistula referred to output, through a percutaneous drain or drainage canal after removal of drains or from a surgical wound, of any measurable volume of fluid with an amylase content more than three times the serum amylase level.
New-onset diabetes mellitus referred to insulin or oral anti-diabetic drugs requirement on 6-months follow-up and this need was absent prior to emergence of acute pancreatitis.

Exocrine insufficiency was defined as requirement of oral pancreatic enzyme supplementation to treat clinical symptoms of steatorrhea 6-months following discharge and this requirement was absent before onset of pancreatitis.

Incisional hernia referred to full thickness discontinuity in abdominal wall and bulging of abdominal contents, with or without obstruction, six months after discharge.

Wound infection referred to a superficial incisional surgical site infection (SSI), defined by following criteria: infection reported within a month following surgical intervention and involves only dermal and hypodermal layers. Additional criteria (one of four) to be fulfilled: First, pus discharge from the superficial incisional site. Second, microbes are grown out of an aseptically acquired culture of discharge from the superficial incisional site. Third, a minimum of one of the local signs of inflammation (that is rubor, calor, tumor, dolor) and superficial incisional site is intentionally incised by house-surgeon and has positive growth on culture or uncultured. Detection of no growth on culture does not fulfill this criterion. Fourth, superficial incisional SSI is diagnosed by the treating surgeon.

Statistical Analysis: SPSS (IBM, Armonk, NY, USA) version 23.0 for Windows was used to analyze the data. The categorical and continuous data were represented as frequency (percentage) and mean (standard deviation), respectively. The association between continuous data was assessed with independent sample t-test. A two-tailed $p<0.05$ was regarded as significantly significant.

RESULTS
In current prospective observational study, a total of 26 patients with IPN were enrolled and managed with surgical step-up approach.

Demographic and clinical characteristics (Table I):
The patients were predominantly males (84.62%) and the most frequently affected age groups were 21 - 30 and 31 - 40 years (each 30.8%). The mean body mass index was 25.3 ± 2.8 kg/m^2 with hypertension (11.6%) and diabetes mellitus (7.7%) being the most common comorbidities. The mean duration of illness was 4.8 ± 2.6 days with the patients mainly presenting with epigastric pain (100.0%) and vomiting (96.2%), and alcohol (80.8%) was the most common underlying cause of pancreatitis. The mean values of laboratory parameters, including WBC counts (12.9 ± 3.8 ×103/mm3), lipase (435.1 ± 200.4 IU/L), and CRP (251.2 ± 96.5 mg/dL), were raised.

Table I - Demographic and clinical characteristics

Characteristics	n (=26)	%
Age groups (years)		
18 - 20	1	3.9
21 - 30	8	30.8
31 - 40	8	30.8
41 - 50	6	23.1
51 - 60	2	7.7
61 - 70	1	3.9
Sex		
Male	22	84.6

Table I - Demographic and clinical characteristics		
Characteristics	n (=26)	%
Female	4	15.4
Anthropometry		
Height, m, mean ± SD	1.6 + 0.1	-
Weight, kg, mean ± SD	63.0 + 8.5	-
BMI (Body mass index), kg/m2, mean ±SD	25.3 ± 2.8	-
Comorbidities		
Hypertension	3	11.6
Diabetes mellitus	2	7.7
Thalassemia minor	1	3.9
Sickle cell disease	1	3.9
Presenting complaints		
Epigastric pain	26	100
Vomiting	25	96.2
Abdominal distension	15	57.7
Fever	10	38.5
Jaundice	1	3.9
Breathlessness	1	3.9
Duration of illness, days, mean ± SD	4.8 ± 2.6	-
Cause of pancreatitis		
Alcohol induced	21	80.8
Gall stone induced	5	19.2
Biochemical parameters at admission		
WBC counts, ×103/mm3, mean ±SD	12.9 ± 3.8	-
Lipase, IU/L, mean ± SD	435.1 ± 200.4	-
CRP, mg/dL, mean ± SD	251.2 ± 96.5	-
Biochemical parameters at intervention 1		
WBC counts, ×103/mm3, mean ±SD	24.82 + 8.21	

Disease severity (Table II):

Table II - Disease severity		
Characteristics	n (= 26)	%
APACHE II score, mean ± SD	6.92 ± 5.02	-

Table II - Disease severity		
Characteristics	n (= 26)	%
qSOFA score		
Score 0	9	34.6
Score 1	7	26.9
Score 2	5	19.2
Score 3	5	19.2
Pancreatic inflammation score		
0 - Normal pancreas	0	0.0
2 - Intrinsic pancreatic abnormalities with or without inflammatory changes in peri pancreatic fat	0	0.0
4 - Pancreatic or peri-pancreatic fluid collection or peri-pancreatic fat necrosis	26	100.0
Pancreatic necrosis score		
0 - None	0	0.0
2 - <30% necrosis	9	34.6
4 - >30% necrosis	17	65.4
Extra-pancreatic complications		
Pleural effusion	21	80.8
Ascites	17	65.4
Gastrointestinal complications	18	69.2
Vascular complications	8	30.8
Parenchymal complications	0	0.0
Modified CTSI score		
Score 8	12	46.2
Score 10	14	53.8

At presentation, the mean APACHE II score was 6.92 ± 5.02. Most of the patients had qSOFA score 0 (34.6%), pancreatic inflammation score 4 (100%), and pancreatic necrosis score 4 (65.4%). The most common extra-pancreatic complications were pleural effusion (80.8%), gastrointestinal complications (69.2%), and ascites (65.4%). Thus, most patients had MCTSI score 10 (53.8%).

Diagnosis and management of IPN (Table III):
In more than two-thirds of patients(69.2%), the diagnosis of infected ANP was reached radiologically (that is persistent sepsis/clinical deterioration with gas on CECT A+P) while in 30.8% patients IPN was diagnosed microbiologically (that is persistent sepsis/progressive clinical deterioration with positive culture report of necrotic tissue).

Half of the patients (50.5%) received oral nutritional support. Of 26 patients, 25 (96.2%) underwent USG-guided pigtail insertion (Intervention I). 8 patients required Intervention II, and half of them underwent USG-guided pigtail drainage (n=4, 50.0%). Finally, of the 7 patients that required operative intervention, 5(71.4%) underwent ON and 2(28.6%) underwent VARD.

Table III - Diagnosis and management of IPN		
Characteristics	n (= 26)	%
Diagnosis of infected ANP		
Radiologically	18	69.2
Microbiologically	8	30.8
Nutritional support		
Oral	13	50.0
Enteral via nasogastric or nasojejunal tubes	8	30.8
Parenteral	5	19.2
Intervention I		
USG guided pigtail insertion	25	96.2
Bilateral ICD insertion	1	3.8
Intervention II (n = 8)		
USG guided pigtail drainage	4	50.0
USG guided abdominal drain insertion	1	12.5
CT guided pigtail drainage	2	25.0
CT guided retroperitoneal drain insertion	1	12.5
Surgical intervention (n = 7)		
VARD	2	28.6
Open necrosectomy	5	71.4

Comparison between VARD and ON (Table IV):

Table IV - Comparison between VARD* and ON**				
Variables (Mean ± SD)	Surgical intervention		P value	Level of significance
	VARD (n = 2)	ON (n = 5)		
Blood loss, mL	90.0 ± 10.0	300.0 ± 100.0	0.038	Significant
Duration of intervention, min	125.0 ± 5.0	184.0 ± 25.8	0.029	Significant
ICU stay, days	4.5 ± 0.5	12.4 ± 3.0	0.017	Significant
Hospital stay, days	24 ± 2	21.6 ± 12.5	0.810	Not significant

*VARD: Video-assisted retroperitoneal debridement, **ON: Open necrosectomy

Compared to ON, VARD was associated with significantly lower blood loss (300.0 ± 100.0 mL vs 90.0 ± 10.0 mL, p = 0.038), shorter duration of intervention (184.0 ± 25.8 min vs 125.0 ± 5.0 min, p = 0.029), and shorter ICU stay (12.4 ± 3.0 days vs 4.5 ± 0.5 days, p = 0.017). While ON and VARD had comparable hospital stays (21.6 ± 12.5 days vs 24 ± 2 days, p = 0.810).

Timing between presentation and interventions of surgical step up approach (Table V):

Table V - Timing between presentation and interventions of surgical step up approach		
Timing (days)	Mean	Standard deviation
Presentation to Intervention I	11.2	6.2
Intervention I to Intervention II	10.0	4.1
Intervention II to operative Intervention	11.3	4.9

The duration between presentation and intervention I was 11.2 ±6.2 days, between intervention I and II was 10.0 ±4.1 days, and between intervention II to operative intervention was 11.3 ±4.9 days.

Organism grown on culture of IPN (Table VI):
On culture, the most commonly grown organisms were Klebsiella pneumoniae (30.8%), Pseudomonas aeruginosa (15.4%), Acinetobacter sp. (11.5%), and Escherichia coli (11.5%).

Table VI - Organism grown on culture of IPN		
Organism grown	n (= 26)	Percentage (%)
Klebsiella pneumoniae	8	30.8
Pseudomonas aeruginosa	4	15.4
Escherichia coli	3	11.5
Acinetobacter sp.	3	11.5
Staphylococcus aureus	2	7.7
Proteus sp.	1	3.9
Enterobacter sp.	1	3.9
Citrobacter sp.	1	3.9
Enterococcus sp.	1	3.9
Micrococcus	1	3.9
Mixed growth	1	3.9
Total	26	100

Outcomes of patients with IPN with surgical step up approach (Table VII):

Table VII - Outcomes of IPN with surgical step up approach			
Outcome	Clinical improvement	Mortality	Total
Drainage procedure only	16	3	19
Drainage and surgical intervention	5	2	7
Total	21 (80.8%)	5 (19.2%)	26 (100%)

Of 25 patients, 21(80.8%) showed clinical improvement with surgical step-up approach, while mortality occurred in 5(19.2%) patients. Of clinically improved patients, 16(76.2%) showed clinical improvement after drainage procedures only, while 5(23.8%) required drainage with operative intervention for clinical improvement. Out of 5 mortalities, 3 patients succumbed after a drainage procedure, while remaining 2 succumbed after operative intervention.

Complications in 6 months follow up period (Table VIII):
At 6-months follow-up, among 21 clinically improved patients, the most common complication was pancreatic fistula formation (n=13, 61.9 %) followed by exocrine insufficiency (n=8, 38%).

Table VIII - Complications in 6 months follow up

Complications on follow up	Frequency (N)	Percentage (%)
Pancreatic fistula	13	61.9
Exocrine insufficiency	8	38
Wound infection	2	9.5
New onset diabetes mellitus	1	4.8
Enterocutaneous fistula	0	0
Intra abdominal bleeding	0	0
Incisional hernia	0	0

DISCUSSION:
According to Atlanta classification[23], IPN is elucidated as persisting sepsis or continued clinical worsening regardless of maximal aid in intensive care unit in a patient of pancreatic/peri-pancreatic necrosis and confirmed microbiologically or radiologically. It can be managed by various methods, the decision to which is based on location of infected collections, extent of disease, availability of resources, and expertise to treating techniques.

The management of IPN requires precise strategies that are tailor-made for each patient. The primary goal is to decrease sepsis and systemic inflammatory response and prevent organ failure while inducing as little stress as possible. The first step in reaching the goal is the administration of fluids, analgesics, and antibiotics. This step delays (or sometimes) omits the need for early intervention. Several trials have compared various techniques of management/intervention. The PANTHER trial compared the benefits of surgical step-up approach to ON.[20] The PENGUIN trial similarly compared endoscopic transgastric drainage with surgical necrosectomy.[24] The TENSION trial compared benefits of endoscopic and surgical step-up approach.[25] Moreover, the MISER trial compared benefits of endoscopic step-up approach to minimally invasive surgery.[26]

The comparison between various study parameters used in current study group with step-up approach group in the PANTHER trial, surgical necrosectomy group in the PENGUIN trial, surgical step-up approach in the TENSION trial, and minimally invasive surgery group in the MISER trial (Table IX).

Table IX - Comparison of various parameters in the current study with published trials

Study parameters	PANTHER trial (Step-up approach group)	PENGUIN trial (Surgical necrosectomy group)	TENSION trial (Surgical step-up group)	MISER trial (Minimally invasive surgery group)	Current study
Mean Age (years)	57.6	64	60	52.9	36.8
Males	72%	80%	62%	66%	84.6%
Mean BMI	28	27	28	-	25.34
Alcohol as cause of pancreatitis	60%	20%	15%	34%	80.8%
Gall stone as cause of pancreatitis	3%	70%	64%	25%	19.2%
Median CTSI score	8	8	8	Mean 9	10 (mCTSI score)

Table IX - Comparison of various parameters in the current study with published trials					
Mean APACHE II score	14.6	11	10	21	6.92
Median SOFA score	3	-	1	-	1.5 (qSOFA score)
Time for first intervention (days)	30	59	41	35	11.23
Death	40%	40%	13%	6.3%	19.2%
Perforation with EC fistula	14%	20%	17%	28.1%	0%
Intraabdominal bleeding	16%	0%	21%	9.4%	0%
Pancreatic fistula	28%	70%	32%	28.1%	61.9%
Incisional hernia	7%	-	2%	6.3%	0%
New onset diabetes	16%	50%	22%	36%	4.8%
Exocrine insufficiency	7%	50%	32%	87.5%	38%
Wound infection	-	-	6%	6.3%	9.5%
Mean ICU stay (days)	Median 9	-	Median 2	6.6	8.25
Mean Hospital stay (days)	Median 50	Median 36	Median 65	23.3	22.73

In the current study, the mean age of patients was 36.8 years which is lower than that reported in the PANTHER trial (surgical step-up group: 57.6 years)[20], the PENGUIN trial (surgical necrosectomy group: 64 years)[24], the TENSION trial (surgical step-up group: 60 years)[25], and the MISER trial (minimally invasive surgery group: 52.9 years).[26] Thus, compared to the western world, younger Indian adults are affected by IPN.

In the current study, the majority of the patients were males (84.6%) which is comparable to that reported in PENGUIN trial (80%)[24], but higher than that reported by the PANTHER trial (72%)[20], the MISER trial (66%)[26], and the TENSION trial (62%).[25] Thus, males are predominantly affected by IPN that can be attributed to higher consumption of alcohol by the male sex.

In the current study, the mean BMI was 25.34 kg/m2, which is comparable to that reported in the PENGUIN trial (27 kg/m2)[24], the PANTHER trial (28 kg/m2)[20], and the TENSION trial (28 kg/m2).[25]

In the current study, the pancreatitis leading to IPN was mainly attributed to alcohol (80.8%) with 19.2% patients having gall-stone induced pancreatitis, which is significantly higher than that reported by the PANTHER trial (60% alcohol induced and 3% gall stone induced)[20], the MISER trial (34% alcohol induced and 25% gall stone induced).[26] While a reverse trend was observed in the PENGUIN trial[24], and the TENSION trial[25] with incidence of gall stone induced pancreatitis being higher than alcohol induced pancreatitis.

In the current study, the median modified CTSI score was 10, which was comparable to median CTSI score 8 in the PANTHER trial[20], the PENGUIN trial[24], as well as the TENSION trial[25], and 90% patients had score 8-10 in the MISER trial.[26]

In the current study, the mean APACHE II score was 6.92, which is lower than 14.6 in the PANTHER trial[20], median APACHE II score 11 in the PENGUIN trial[24], score 10 in the TENSION trial[25], and score 21 in the MISER trial.[26] In the current study, the median qSOFA score in current study was 1.5, which higher than median SOFA score of 1 in the TENSION trial[25] and lower than median SOFA score of 3 in the PANTHER trial.[20]

In the current study, the mean time for intervention from presentation was 11.23 days which is lower/earlier than 30 days in the PANTHER trial[20], 59 days in the PENGUIN trial[24], 41 days in the TENSION trial[25], and 28-42 days(50% patients) in the MISER trial.[26]

In the current study, the mortality rate was 19.2% which is lower than 40% in the PANTHER trial[20] and the PENGUIN trial[24], but higher than 13% in the TENSION trial[25] and 6.3% in the MISER trial.[26]

In the current study, pancreatic fistula was observed in 61.9% patients which is higher than that reported in the PANTHER trial (28%)[20], in the TENSION trial (32%)[25], and the MISER trial (28.1%)[26], but lower than 70% the PENGUIN trial.[24]
In the current study, 38% of patients had exocrine insufficiency, which is higher than 7% patients in the PANTHER trial[20], 32% in the TENSION trial[25], but lower than 87.5% in the MISER trial[26], 50% the PENGUIN trial.[24]

In the current study, 4.8% of patients had new onset diabetes mellitus, which is lower than 16% in the PANTHER trial[20], 22% in the TENSION trial[25], 36% in the MISER trial[26], and 50% in the PENGUIN trial.[24]

In the current study, none of the patients had enterocutaneous fistula, intra-abdominal bleeding, and incisional hernia, which is lower than respective complications in the PANTHER trial[20], the PENGUIN trial[24], the TENSION trial[25], and the MISER trial.[26]

In the current study, wound infection was observed in 9.5% patients, which is higher than 6% the TENSION trial[25] and 6.3% in the MISER trial.[26]

In the current study, the mean ICU stay was 8.25 days which is lower than median ICU stay of 9 days in the PANTHER trial[20], median ICU stay 2 days in the TENSION trial[25], and mean of 6.6 days in the MISER trial.[26]

In the current study, the mean hospital stay was 22.73 days which is lower than median hospital stay of 50 days in the PANTHER trial[20], 65 days in the TENSION trial[25], 36 days in the PENGUIN trial[24], and mean hospital stay of 23.3 days in the MISER trial.[26]

CONCLUSION:
To conclude, IPN are more prevalent in young and middle-age patients. Alcohol-induced pancreatitis are more likely to develop IPN than gall stone induced pancreatitis. Patients with IPN frequently complain of epigastric pain, vomiting, and abdominal distension and seek hospital care within a week. Patients with IPN stays in ICU for about half a month and in hospital for about a month.

With surgical step-up approach, patients with IPN improve clinically, with surgical procedure required in a quarter of patients. VARD leads to significantly lower blood loss, shorter duration of procedure, and shorter ICU stay than ON, but comparable hospital stays. IPN was associated with high mortality, and clinically improved patients may develop complications in follow-up, mostly pancreatic fistula and pancreatic exocrine insufficiency.

Declarations:
- All authors confirms that this study did not involve animal subjects or tissue.
- All authors declares that no financial support was received from any organisation for the submitted work.
- All authors declares that there are no competing interests.

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