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Management of Inflammatory Pancreatic Fluid Collections and Walled-off Pancreatic Necrosis: A Retrospective Study Over Five Years

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ABSTRACT

Background and objective: Acute pancreatitis (AP) is an inflammatory process of the pancreas, with variable involvement of peri-pancreatic tissues and remote organ systems. In this study we discuss surgical and conservative management of acute pancreatitis and its local complication.

Methods: This retrospective study was carried out on 128 patients, who were admitted to Gastrointestinal Surgery Unit, Main Alexandria University Hospital, Alexandria University, and who were complaining of acute pancreatitis with fluid collections and sequels (PP, ANC and walled-off pancreatic necrosis (WOPN). Medical information was retrieved retrospectively from patient's files recorded in Main Alexandria University Hospital and from computerized data system in Gastrointestinal Surgery Department, between October 2013 – October 2018.

Results: Forty-five patients with acute edematous pancreatitis with free collection were managed conservatively successfully. Thirty-two patients with PP underwent drainage, endoscopic (n=17), or open (n=15) approach. Twenty-three patients with WON underwent drainage and debridement whether by open (n=11), endoscopic (n=9), or PCD (n=3) approaches. Twenty-eight patients with necrotizing pancreatitis, 16 patients were managed conservatively, 12 patients needed intervention either, PCD (n=9) or open surgical necrosectomy (n=3).

Conclusions: The operative management of acute pancreatitis is focused on managing the acute complications, and the long-term sequelae. However, the evolution of videoscopic and endoscopic techniques have greatly expanded the tools available.

Keywords: Acute pancreatitis, Necrotizing pancreatitis, Pseudo pancreatic cyst, Walled off necrosis.

INTRODUCTION

Acute pancreatitis:

It is an inflammatory condition of the pancrease and clinically characterized by acute abdominal pain and elevated level of pancreatic enzymes in the blood, in some cases it can be fatal [(1)].

Worldwide, the incidence of acute pancreatitis ranges between 5 and 80 per 100,000 population, with the highest incidence recorded in the United States and Finland [(1)]. The incidence of acute pancreatitis in USA anges from 4.9 to 35 per 100,000 per year [(2)].

Etiology:

Common etiologies of AP are summarized as follows, provided that gallstones and alcoholism constitute 75% of causes [(3)]:

i. Obstructive (Gallstones, biliary sludge and microlithiasis, tumors, helminthes), and functional (Sphincter of Oddi dysfunction).
ii. Alcohol, toxins, drugs.
iii. Metabolic disorders (Hypertriglyceridemia, hypercalcemia).
iv. Iatrogenic e.g. post endoscopic retrograde cholangiopancreatography (ERCP).
v. Trauma [(4)].

- Acute pancreatitis has two distinct stages.

The first stage is related to the pathophysiology of the inflammatory cascade; usually lasts a week. During this phase, the severity of acute pancreatitis is related to organ failure secondary to the patient's systemic inflammatory response elicited by acinar cell injury. The second stage is characterized by local complications after one or two weeks (better assessed by CT Balthazar score), occurs only in patients with moderately severe or severe pancreatitis [(5)].

Diagnosis:

Acute pancreatitis is best defined clinically as the patient presenting with 2 of the following 3 criteria [(6)]:

(1) Symptoms, such as epigastric pain, consistent with the disease.
(2) A serum amylase and lipase greater than 3 times the upper limit of normal.
(3) Radiologic imaging consistent with the diagnosis via computed tomography (CT).

MANAGEMENT

- Conservative management:
  1. Intravenous fluid administration
2. Good analgesia
3. Antibiotics in sever pancreatitis

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4. Enteral nutrition if tolerated [7].

Pseudo pancreatic cyst:

Most cases of pseudo cysts can be managed conservatively and only need interventions in large symptomatic cysts [7].

Intervention:

A. Surgical drainage (open or laparoscopic)
B. Endoscopic drainage
C. Percutaneous drainage

Surgical drainage:

The surgical options include cystogastrostomy, cystoduodenostomy, and cystojejunostomy depending on the location of the pseudocyst for the best dependent drainage [7].

Endoscopic drainage :

Can be achieved through a transmural, transpapillary [8].

Transmural drainage can be performed either through the wall of the stomach or duodenum [8].

Transmural drainage was performed if there was a direct apposition of the PP against the gastric or duodenal wall

Endoscopic ultrasonography drainge:

Addition of endoscopic ultrasonography (EUS) for endoscopic drainage is a new and exciting development and may decrease the risks associated with endoscopic drainage [9].

Necrotizing pancreatitis:

Managed primarily by a conservative therapy [10]:

- Volume resuscitation.
- Pain management.
- Early enteral nutrition.
- Broad spectrum antibiotic

Indication for interventions [10]:

- Persisting sepsis after maximal conservative therapy.
- Persistent pain requiring narcotics > 8 weeks.
- The presence of gastric outlet obstruction.
- Abdominal compartment syndrome.
- Bleeding or bowel perforation.
- Worsening organ failure despite maximal support.
- Biliary obstruction and worsening jaundice.

Step-up Approach:

Step-up approach consisted of initial percutaneous (or in a few cases endoscopic) drainage, and if there was no clinical improvement within 72 h, a second drainage was performed followed by video-assisted retroperitoneal debridement (VARD); patients then underwent open necrosectomy if that strategy failed [11].

Walled off necrosis:

Symptomatic WOPN usually need some form of intervention to drain the organized necrotic material [3].

The drainage of WOPN can be done [3]: radiologically, endoscopically, surgically.

Surgical drainage:

Surgery has been the conventional treatment of pancreatic walled-off necrosis,

However, as WOPN contains a variable amount of solid necrotic material, The surgical procedures usually performed is trans-gastric necrosectomy (TGN) with internal drainage [12].

Endoscopic drainage

Patients with infected/symptomatic pancreatic necrosis/WOPN are being increasingly treated with endoscopic transluminal drainage (ETD) with or without necrosectomy [4].

ETD should be preferred for management of WOPN as it is associated with lower mortality, risk of major organ failure, adverse events, and length of hospital stay [12].

Percutaneous drainage

Percutaneous drainage involves placing single or multiple, 8–28 Fr drainage catheters in fluid collections. The catheters are placed into WOPN using combined ultrasound or CT guidance [13].

PATIENTS AND METHODS

- This retrospective study was carried out on patients, who were admitted to Gastrointestinal Surgery Unit, Main Alexandria University Hospital, Faculty of Medicine, and Medical Research Institute, General Surgery Department, Alexandria University, and who were complaining of acute pancreatitis with fluid collections and sequels (APFC, PP, ANC and WOPN) between October 2013 – October 2018.
- This retrospective study included 128 patients complaining of acute pancreatitis with fluid collections and sequels (45 patients with free collection, 32 patients with PP, 23 patients with WON, and 28 patients with NP).
- The following data extracted for every case whenever possible.
- Patient profile and **history**, medical and surgical history, date of admission and discharge.
- Findings on **examination**: (Jaundice, cachexia, fever, abdominal mass).
- Laboratory investigations: (Complete blood count, amylase and lipase, liver function tests, renal function test, C-reactive protein, alkaline phosphatase, serum bilirubin (total and direct), electrolytes (Na, K, Ca), cholesterol level, triglyceride level)

Radiological finding:

- Ultrasonography of the abdomen: Initial imaging study for all patients.

- Computed tomography: Gold standard noninvasive imaging.

Operative details:

- Date of operation.
- Type of intervention:
  - ✓ Surgical drainage
  - ✓ Percutaneous drainage
  - ✓ Endoscopic approach:
- Postoperative: Hospital stay, ICU admission, mortality, morbidity, need for re-intervention and follow up CT was obtained if available.

Ethical approval:

The study was approved by the Ethics Board of Alexandria University and an informed written consent was taken from each participant in the study.

Statistical analysis:

Data entry, coding, and analysis were conducted using SPSS, IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY: IBM Corp.USA. Description of quantitative variables was in the form of Mean and Standard Deviation (mean ± SD), description of qualitative variables was by frequency and percentage, chi square test was used to assess the relationship between two qualitative groups, t-test was to assess the relationship between two quantitative groups. P value ≤ 0.05 was set to be statistically significant.

RESULT

Forty-five patients with acute edematous pancreatitis with free collection were managed conservatively.

Thirty-two patients with PP underwent drainage; endoscopic drainage (n=17), or open drainage (n=15), There was no obvious indication in choosing endoscopic or open drainage approach, except if the PP was not related to the stomach. In this case, open drainage was indicated.

Twenty-three patients with WON underwent drainage and debridement whether by open (n=11), endoscopic (n=9), or PCD (n=3) approaches,

Twenty-three patients with WON underwent drainage and debridement whether by open (n=11), endoscopic (n=9), or PCD (n=3) approaches.

Table 1: Demographic data

	PP (n = 32)		WON (n = 23)		NP (n = 28)		Pancreatitis with free collection (n=45)	
	No.	%	No.	%	No.	%	No.	%
Sex								
Male	21	65.6	16	69.6	16	57.1	13	28.9
Female	11	34.4	7	30.4	12	42.9	32	71.1
Age (years)								
Min. – Max.	35.0 – 58.0		51.0 – 72.0		40.0 – 70.0		28.0—72.0	
Mean ± SD.	47.44 ± 5.02		61.0 ± 5.79		58.17 ± 9.25		49.44 ± 5.4	
Median	47.50		61.0		58.3		51.5	

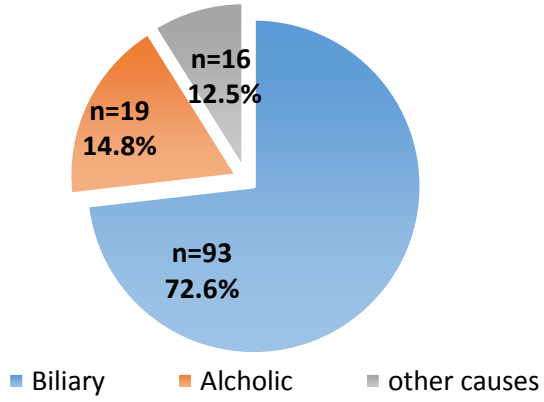

Figure 1: Etiology of acute pancreatitis

APACHE score was higher in NP patients, especially in those who underwent surgical necrosectomy (p=0.023*). Patients with NP, In the open surgery group, the score ranged from 14 to the maximum 17 with the median score 15, In the percutaneous drainage group, the score ranged from zero to 15 with the median score 5, and patients managed conservatively the score ranged from 2 to 13 with median score 5, While there was no significant difference between WON patients regardless the intervention performed.

Table 2: Distribution of WON and NP patients according to APACHE score

APACHE	Endoscopic (n = 9)	Surgery (n = 11)	PCD (n = 3)	T test	P value
WON					
Min. – Max.	0.0 – 11.0	1.00 – 12.0	0.0 – 4.0	0.166	0.920
Mean ± SD.	3.11 ± 3.48	3.45 ± 3.08	2.33 ± 2.08		
Median	3.0	3.0	3.0		
NP	**Conservative (n=16)**	**Surgery (n = 3)**	**PCD (n = 9)**	**T test**	**P value**
Min. – Max.	2.0—13.0	14.0 – 17.0	0.0 – 15.0	7.560*	0.023*
Mean ± SD.	6.25 ± 2.1	15.33 ± 1.53	5.33 ± 4.9		
Median	5.0	15.0	5.0		

In this study there were 3 mortality cases, one patient with WON who had endoscopic drainage. Two cases with ANP and one of them did surgical necrosectomy

According to preoperative CT scan, the size of PP ranged between 7 and 19 cm with a mean of 10.5 cm. Table 3 shows that there was no significance difference between endoscopic and open approaches as regards the size of the PP, revealing that the size of PP was not an indication for adopting the plan of management. The size of WON ranged between 5.5 and 30 cm with a mean of 13.2 cm. There was no significance difference between endoscopic, open, PCD approaches as regards the size of the WON, revealing that also the size of WON was not an indication for determining the plan of management.

Table 3: Comparison between different approaches of WON and PP according to size by CT

Size (cm)	Endoscopic (n = 9)	Surgery (n = 11)	PCD (n = 3)	T test	P value
WON					
Min. – Max.	5.5 – 18.0	6.0 – 30.0	7.0 – 23.0	0.955	0.402
Mean ± SD.	10.72 ± 3.82	14.0 ± 6.93	15.0 ± 8.0		
Median	10.0	13.0	15.0		
PP	**Endoscopic (n =17)**	**Surgery (n = 15)**	**-**	**T test**	**P value**
Min. – Max.	7.0 – 16.0	7.0 – 19.0	-	0.170	0.866
Mean ± SD.	10.59 ± 3.02	10.4 ± 3.25	-		
Median	10.0	9.0	-		

Intraoperative Blood Transfusion:

As regards management of PP, blood transfusion was not needed in either endoscopic or open approaches. In WON patients, only one patient -who managed surgically- needed blood transfusion. Patients with WON managed by endoscopic or PCD approaches did not need blood transfusion, see Table 4. All the three patients with NP who were managed surgically needed intraoperative blood transfusion.

Table 4: Comparison between different approaches of WON and PP management according to blood transfusion

Blood transfusion	Endoscopic (n = 9)		Surgery (n = 11)		PCD (n = 3)		□□	P value
	No.	%	No.	%	No.	%		
WON								
No	9	100.0	10	90.9	3	100.0	1.218	0.774
Yes	0	0.0	1	9.09	0	0.0		
NP	-		Surgery (n = 3)		PCD (n = 9)		□□	P value
No	-	-	0	0.0	9	100.0	1.333	0.509
	-	-	3	100.0	0	0.0		

Postoperative Assessment:

According to WON patients, PCD group patients did not need to be admitted to ICU. Only one patient in the endoscopic group needed ICU admission. While in the open group, three patients were admitted to ICU. There was no significant difference between the three groups, see Table 5. Fifteen patients with NP were admitted to ICU (33.3%). All the three patients treated surgically needed ICU admission. While six of the nine patients treated by PCD were indicated for ICU admission, and sex patients treated conservatively needed ICU admission.

Table 5: Comparison between different approaches of WON and PP management according to ICU admission

ICU admission	Surgery (n = 11)		PCD (n = 3)		Endoscopic (n = 9)		Total	□□	P value
	No.	%	No.	%	No.	%			
WON									
No	8	72.7	3	100.0	8	88.9	19	1.218	0.774
Yes	3	27.3	0	0.0	1	11.1	4		
NP	Surgery (n = 3)		PCD (n = 9)		Conservative (n=16)		Total	□□	P value
No	0	0.0	3	33.3	□□□□ □□□□	□□□□	13	1.333	0.509
Yes	3	100.0	6	66.7	6	37.5	15		

Postoperative Hospital Stay:

Table 15 shows that endoscopic drainage of PP had a significantly lower hospital stay than open surgery (p=0.001*). The median stay in PP patients treated by endoscopic approach was 3 days in comparison to that of open surgery which was 6 days. Also in patients with NP, it was noted that patients managed conservatively had a lower hospital stay (median=10.5) than patients managed by PCD (median=15.8), than patients managed by surgery (median = 22.6).

Table 6: Comparison between different approaches of WON and PP treatment according to hospital stay

Time hospital stay	Surgery (n = 15)	Endoscopic (n =17)	-	□□	P value
PP					
Min. – Max.	5.0 –10.0	2.0 – 18.0	-		
Mean ±SD.	6.67 ±1.54	4.71 ±4.48	-	40.500*	0.001*
Median	6.0	3.0	-		
NP	**Surgery (n = 3)**	**PCD (n = 9)**	**Conservative(n=16)**	□□	**P value**
Min. – Max.	3 –24.0	7.0 –37.0	7.0 –19.0		
Mean ±SD.	13.4 ± 6.45	18.1 ± 8.1	9.8 ± 4.2	6.224*	0.031
Median	22.6	15.8	10.5		

Postoperative Morbidity and Mortality

PP patients had low rate of morbidity after both endoscopic (11.8%) and open (26.7%) approaches. In the endoscopic drainage group, two patients experienced hematemesis attack after intervention, one was treated conservatively, while the other needed endoscopic management. In the open drainage group, two patients developed wound infection, one patient had chest infection, and one patient developed paralytic ileus, see Table 7. As regards WON patients, there was no significant differences in morbidity between the three approaches. The three patients managed by PCD had no morbidity, while 4 (36.6%) patients managed by open necrosectomy had post-operative complications; two patients had chest infection, one had pancreatic fistula and managed conservatively, and one had wound infection.

Table 7: Comparison between different approaches of WON and PP treatment according to morbidity

Morbidity	Endoscopic (n = 17)		Surgery (n = 15)		-		Total	□□	P value
	No.	%	No.	%	No.	%			
PP									
No	15	88.2	11	73.3	-	-		1.162	0.383
Yes	2	11.8	4	26.7	-	-	6		
WON	**Endoscopic (n = 9)**		**Surgery (n = 11)**		**PCD (n = 3)**		**Total**	□□	**P value**
No	7	77.8	7	63.6	3	100.0		1.338	0.543
Yes	2	22.2	4	36.4	0	0.0	6		

PP patients had no mortalities in both endoscopic and open groups. As regards WON patients, there was no significant differences in mortality between the three approaches. There were no mortality cases in open approach. In the endoscopic group, there was one mortality case. This patient was admitted to ICU due to respiratory failure, see Table 8.

Table 8: Comparison between different approaches of WON and PP management according to mortality

Mortality	Endoscopic (n = 9)		Surgery (n = 11)		PCD (n = 3)		Total	□□	P value
	No.	%	No.	%	No.	%			
PP									
No	17	100.0	15	100.0	17	100.0	0	-	-
Yes	0	0.0	0	0.0	0	0.0			
WON	**Endoscopic (n = 17)**		**Surgery (n = 15)**		-		**Total**	□□	**P value**
No	8	88.9	11	100.0	-	-	1	2.002	0.521
Yes	1	11.1	0	0.0	-	-			

Re-intervention or conversion to open surgery:

Regarding PP patients, 17 patients underwent endoscopic drainage procedure. The primary success rate was 82.4%. Of the three primary endoscopic failures (17.6%), two patients (11.8%) were managed successfully by a repeated endoscopic drainage procedure. Therefore, finally 16 patients (94.1%) were managed successfully with endoscopic drainage and one patient (5.9%) with primary endoscopic failures was salvaged by open surgical procedure.

Open cystogastrostomy (15 patients) were performed. No patients underwent a simultaneous procedure. The primary and overall success rate was 100%. There was a significant difference between the three approaches in WON treatment (p value =0.01). One of the three patients treated by PCD failed to be treated; and managed by open drainage and necrosectomy. Regarding re-intervention or conversion to open surgery in present study; in PP patients the primary success rate was 82.4%. Of the three primary endoscopic failures (17.6%), two patients (11.8%) were managed successfully by a repeated endoscopic drainage procedure. Therefore, finally 16 patients (94.1%) were managed successfully with endoscopic drainage and one patient (5.9%) with primary endoscopic failure was salvaged by open surgical procedure. Open cystogastrostomy (15 patients) were performed. No patients underwent a simultaneous procedure so the primary and overall success rate was 100%. Three of the nine patients treated endoscopically had successive upper GIT endoscopies; two patients needed two sessions of endoscopic necrosectomy and the last needed three sessions of endoscopic necrosectomy and no case converted to open necrosectomy. No patient in the open surgery group needed another operation or another intervention.

Table 9: Comparison between different approaches of WON and PP treatment according to re-intervention

Re-intervention	Endoscopic (n = 9)		Surgery (n = 11)		PCD (n = 3)		□□	P value
	No.	%	No.	%	No.	%		
WON								
No	6	66.7	11	100.0	2	66.4	11.241*	0.002*
Yes	3	33.3	0	0.0	1	33.3		
PP	**Endoscopic (n = 17)**		**Surgery (n = 15)**		-		□□	**P value**
No	14	82.4	15	100.0	-	-	2.921	0.229
Yes	3	17.6	0	0.0	-	-		

Recurrence rate at 6 months follow up:

Table 10 shows that there was no significance difference between recurrence rates of PP treated endoscopically or surgically, though there was no PP recurrence in the open drainage group, while there were two patients in the endoscopic group had PP recurrence (11.7%). These were redrained endoscopically through the previous cystogastrostomy with double pigtail stent, and had not recur on a further follow up of 6 months after stent removal. There was no recurrence in patients with WON that managed by open necrosectomy, and there was one recurrent case in endoscopic group that needed further endoscopic necrosectomy and one case managed by PCD that managed by surgery.

Table 10: Comparison between different approaches of WON and PP treatment according to recurrence rate

Recurrence	PCD (n=3)		Endoscopic (n = 9)		Surgery (n = 11)		□□	P value
	No.	%	No.	%	No.	%		
WON								
No	2	66.7	8	88.89	11	100.0	11.241*	
Yes	1	33.3	1	11.11	0	0.0		**0.624**
PP	**Endoscopic (n = 17)**		**Surgery (n = 15)**		-		□□	**P value**
No	15	88.2	15	100.0	-	-	1.882	0.486
Yes	**2**	**11.8**	**0**	**0.0**	-	-		

DISCUSSION

The size of PP ranged between 7 and 19 cm with a mean of 10.5 cm. In the study of Redwan et al. [(14)], mean size of PP was 10.5 cm, while in the study of Rasch et al. [(7)], mean size of PP was 8.5 cm.

The size of WON ranged between 5.5 and 30 cm with a mean of 13.2 cm. In the study of Nemoto et al. [(15)] and Driedger et al. [(16)], mean size of WON was 13 (5-30) and 14 cm respectively.

In patients with NP (28 patients), the extent of necrosis was assessed by preoperative CT scan. Nine patients (32%) had necrosis more than 50%. The other 19 patients with NP had necrosis less than 50%. In the study of van Santvoort et al.[(17)], (88 patients), 28 patients had necrosis more than 50%, the other 60 patients with NP had necrosis less than 50%.

In the study of Melman et al. [(18)], the primary success rate was 29 (82.9%) and (51.1%) respectively for endoscopic drainage, and (100%) and (81.2%) for open drainage respectively, while the overall success rate was 32 (91.4) and (81.2%) respectively for endoscopic drainage and (100%) and (90.9%) respectively for open drainage.

In our study, patients with WON that had open necrosectomy did not need another intervention so the primary and overall all success rate was 100%, while three patients managed endoscopically needed successive upper GIT endoscopies so, the primary success rate was 66.6% and overall success rate was 100%.

In the study of Nemoto et al.[(15)] three patients with WON (4%) of 83 cases failed the step up approach and required open necrosectomy.

CONCLUSION

1. EUSGD (Endoscopic ultrasound guided drainage of pancreatic fluid) of mature PFCs (Pancreatic fluid collections) can be achieved in the majority of symptomatic patients who require drainage.
2. ANP is managed primarily by a conservative therapy. In case of infected necrosis, interventional and minimally invasive approaches are the therapy of choice.
3. A step-up approach for interventions in necrotizing pancreatitis using primarily endoscopic techniques resulted in favorable outcomes with acceptably low morbidity and mortality.

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