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Acute necrotizing pancreatitis: Has conservative management replaced surgery? Perspective from a tertiary care centre in Pakistan: A cross-sectional study

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ARTICLE INFO

Keywords:

Acute necrotizing pancreatitis
Conservative
Mortality
Morbidity

ABSTRACT

Background: The main purpose of this study was to review the trends in management of patients presenting with acute necrotizing pancreatitis (ANP) over the last seven years and its effect on morbidity and mortality.

Methods: A cross-sectional study was conducted on all patients presenting with the diagnosis of acute necrotizing pancreatitis to the Aga Khan University Hospital in between the year 2008–2015. The study population was broadly categorized in to two groups based on the way these were managed. The first group consisted of patient who underwent surgery for acute necrotizing pancreatitis while the second group was composed of those patients with necrotizing pancreatitis who were conservatively managed. Patient outcomes were assessed in terms of hospital stay, complication rates and in-hospital mortality. Data was analyzed using SPSS version 20. Comparison of outcomes between two groups was done using chi-square test, Fischer exact test or *t*-test wherever applicable. A *p*-value of less than 0.05 was considered statistically significant.

Results: A total of *n* = 110 patients were included in the study with 68% (*n* = 75) males and 32% (*n* = 35) females. Nasojejunal route was found to be the most commonly utilized route of feeding in these patients consisting of around 49% (*n* = 54) patients with forty percent (*n* = 44) tolerating direct oral diet. The outcomes in both these groups in terms of hospital stay, complication rate, and in hospital mortality were not found to be statistically significant. The conservative group however was significant in terms of cost-effectiveness which was shown by a *p* value of (0.035). The management of this clinically important disease over the years showed an increased trend towards conservative approach in our institute.

Conclusion: Our study further substantiates the recent global trend of conservative approach towards managing patients with acute necrotizing pancreatitis as reflected in the recent available literature. Therefore surgeons of the developing world need to evolve and adapt to these new measures for better outcomes in patient management.

1. Introduction

Acute Pancreatitis (AP) is a fairly common and potentially fatal disease causing significant morbidity and mortality with more than 200,000 hospital admissions per year in the United States and incidence ranging from 4 to 45 per 100,000 patients per year in Europe [1,2]. Unfortunately about 20%–25% of these patients develop severe acute pancreatitis which is characterized by single or multiple organ failures persisting for greater than 48 h [1,3–5]. However about 10%–20% of severe acute pancreatitis cases develop necrosis of the pancreas which may be in the pancreatic parenchyma, its surrounding peri-pancreatic

tissues or both resulting in acute necrotizing pancreatitis (ANP) (See Fig. 1). [1,3,4,6]. If this necrotic tissue gets infected which happens in about 40–70% of patients of ANP, this may result in a substantially high mortality rate ranging as high as 35%–40% as shown in recent studies. However if this remains non infected it only carries a seven percent mortality [1,3,7,8].

Severe acute pancreatitis, if left untreated progresses in two phases with first phase lasting for 10–14 days and characterized by release of pro-inflammatory markers and severe systemic inflammatory response syndrome (SIRS), leading to one or more organ system failures in about 40% of patients as shown in Fig. 2 [1,3,7,9]. The second phase starts 2

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<https://doi.org/10.1016/j.amsu.2021.02.005>

Received 13 December 2020; Received in revised form 29 January 2021; Accepted 2 February 2021

Available online 18 February 2021

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weeks later resulting in immune-suppression and infection of the necrotic pancreatic tissue. This most commonly results from bacterial translocation from the gut and eventually leads to sepsis related complications [7,9]. Recent studies demonstrate that any surgical intervention should be delayed for up to 3–4 weeks as this allows clear demarcation between viable pancreatic parenchyma and necrosed tissue resulting in walled off necrosis (WON) [1,7,9,10]. This decreases the risk of hemorrhage and iatrogenic pancreatic endocrine or exocrine insufficiency resulting in a mortality benefit of around 41% by reducing mortality from about 56% to 15% if any intervention is delayed for a month [1,7,9,10].

In the past open necrosectomy was the gold standard for the treatment of ANP carrying a high morbidity and mortality which was obvious from the literature from that era [9]. As experience grew a subset of patients were identified who could undergo less morbid procedures which were being evolved at that time like percutaneous and endoscopic drainage of pancreatic necrotic collections including video assisted retroperitoneal debridement [4,11–15]. At the same time evidence emerged that some of these patients had a better prognosis if surgery was deferred for more than 4 weeks [7]. There even emerged publications which had reported quite a few cases that had been exclusively treated with radiological drainage and antibiotics [1,9,16]. These minimally invasive techniques had proven to decrease the risk of peri-operative complications like multi organ failure, enterocutaneous or pancreatic fistulae, perforation and bleeding [1,4,7,9]. They also reflected the improved outcomes in terms of lower morbidity and mortality and shorter hospital stay [1,4,7,9].

This evolution of change in patterns of treatment for this grave disease fascinated us to uptake this study and we aimed at understanding

the trends adapted by our surgeons from the developing world as to the management of acute necrotizing pancreatitis. As minimally invasive procedures including endoscopic and percutaneous video-assisted retroperitoneal debridement being unavailable in our region, we aimed to determine the differences in outcomes between those patients who were managed conservatively throughout their hospital course and in those patients who ultimately ended up having an open necrosectomy due to their progressively worsening disease.

2. Materials and methods

This was a cross-sectional study conducted at the Aga Khan University Hospital Karachi between the years 2008–2015. This included extensive review of charts for the patients who had been diagnosed as Acute Necrotizing Pancreatitis as evidenced by Computed Tomography Scan (CT). Those cases with incomplete records or the ones who had received prior treatment from outside hospitals were excluded from our study. The study was conducted after gaining approval from the Ethics Review Committee of our University.

ICD 9 coding was used to identify the number of the patients that had presented to our hospital with acute pancreatitis within the defined time period, which turned out to be 1562. Paediatric (less than 18 years of age) cases and those with incomplete medical records were excluded and the remaining files were reviewed for CT scans with evidence of necrosis (as shown in Figs. 3–6) resulting in a total sample size of 110 patients.

Patients were divided into two groups based on their management. The first group was the ‘operative’ group who ultimately underwent traditional open necrosectomy for acute necrotizing pancreatitis. They

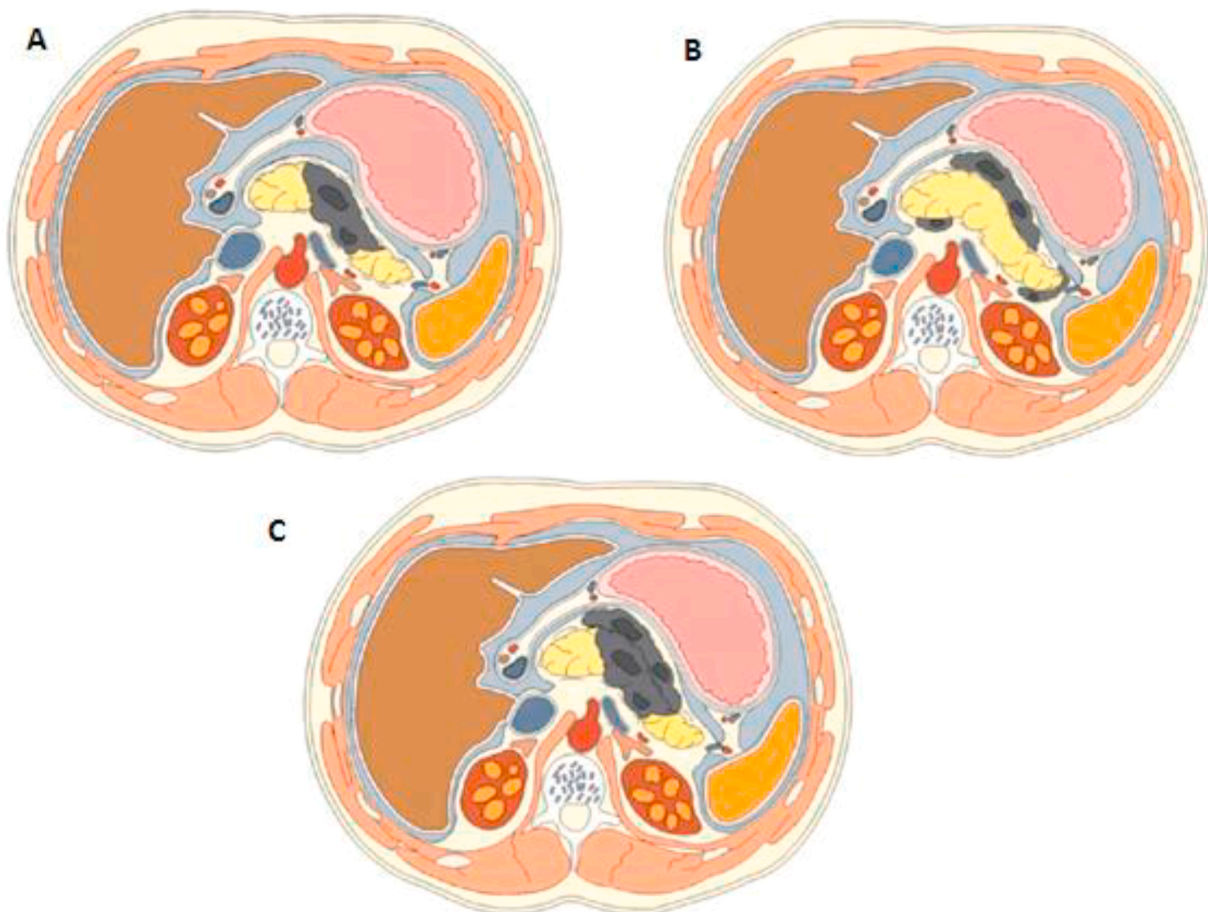


Fig. 1. Necrosis of the pancreas in the pancreatic parenchyma (A), surrounding peri-pancreatic tissues (B) or both (C). (Reproduced with permission from Shyu JY, Sainani NI, Sahni VA et al. Necrotizing pancreatitis: diagnosis, imaging, and intervention. *Radiographics*. 2014 Sep 10; 34(5):1218-39 [29]).

underwent surgery due to deterioration in their clinical condition with evidence of sepsis or septic shock, or multi-organ dysfunction. The surgeries were performed by experienced surgeons with at least greater than 5 years of experience. The second group was the non-operative or ‘conservative’ group of patients who were managed without any intervention or underwent only radiology guided percutaneous catheter drainage. (Other extensive minimally invasive procedures like endoscopic trans-luminal or laparoscopic necrosectomy is neither done in our institute nor in any other institute in our region).

Patient medical records were reviewed and data was gathered regarding their demographics, co-morbidities, clinical presentation, laboratory and radiological investigations, severity of the disease, route of feeding, any radiological and surgical procedures performed, and their outcome including hospital stay and mortality. They were followed only during their length of hospital stay.

Data was analyzed on SPSS version 20. All qualitative variables were presented as frequency and percentages and all quantitative variables as mean±standard deviation. Comparison of qualitative outcomes between two groups was done using chi-square test or Fischer exact test wherever applicable. Comparison of quantitative outcomes between two groups was done using *t*-test. Multivariate logistic regression analysis was done to adjust for the severity of illness based upon APACHE II score. A *p*-value less than 0.05 was considered statistically significant. The study has been reported in line with the STROCSS criteria [31]. This study has been registered with Research Registry (UIN: reaserchregisrity6340).

3. Results

A total of N = 110 patients were included in the study with 68% (n = 75) males and 32% (n = 35) females. They were divided into two groups based on their management. First group consisted of those who ultimately underwent surgical intervention (open necrosectomy) and these made up only 13.6% (n = 15) of the total sample size with only 10 males and 5 females. While the rest of the major chunk of around 86% (n = 95) of patients were included in the second group managed conservatively out of which only 16.8% (n = 16) underwent radiological guided

drainage.

The main etiology resulting in pancreatitis in our population turned out to be cholelithiasis with 54% (n = 59) of patients having gallstones at presentation. The other common causes were alcohol induced and post-ERCP cases as elaborated in Graph I.

Primary mode of nutrition in patients was also determined in the two study groups. Nasojejunal route was found to be the most commonly utilized feeding access used in 49% (n = 54) of all these patients. Forty percent (n = 44) of the patients in our study were fed orally while 7% (n = 7) required nasogastric feeding. The rest of the patients were administered total parenteral nutrition 4% (n = 5).

The severity of pancreatitis and patients’ condition on admission were determined and a comparison was made between the two groups. The mean age in the surgery group was 45 years while that in the non-surgery group turned out to be 47 years. The presence of systemic inflammatory response syndrome (SIRS), single or multi-organ failure and severity index scores including Ranson’s criteria, CT severity index score (CTSI) and the APACHE score (Acute physiology and chronic health evaluation score) was compared between the groups and results generated as displayed in Table 1.

The outcomes in both groups in terms of hospital stay, complication rate, and in hospital mortality was calculated which was not found to be significant. However when cost-effectiveness (total hospital cost was included only) was compared between the two groups which was 0.6 million in the surgery group and 0.4 million in the conservative group, it turned out to be statistically significant as shown in Table 2.

An overall increase in patients presenting with acute necrotizing pancreatitis was seen within the last seven years in our setup with recent trend in management shifting towards the conservative approach as illustrated by the Graph II (see Table 3). This may be due to increasing use of CT scan in acute pancreatitis for the diagnosis of acute necrotizing pancreatitis.

4. Discussion

Acute necrotizing pancreatitis (ANP), a subtype of severe acute

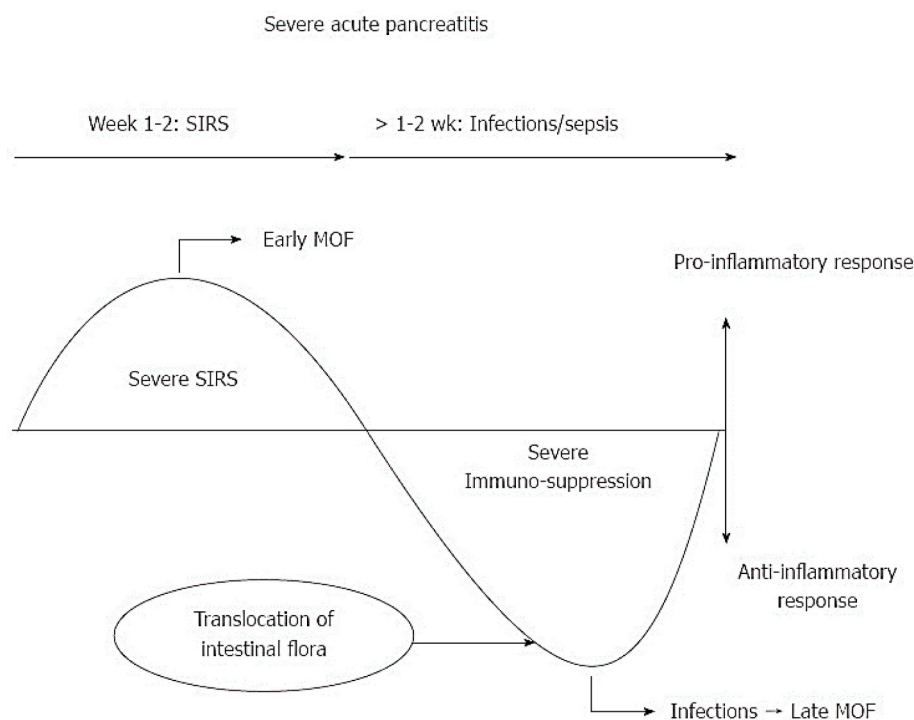


Fig. 2. Natural History of Acute Necrotizing Pancreatitis. (Adapted with permission from Zerem E. Treatment of severe acute pancreatitis and its complications. World Journal of Gastroenterology: WJG. 2014 Oct 14; 20(38):13879 [30].).



Fig. 3. CT scan cross-sectional image from a patient with acute pancreatitis. Diffuse emphysematous changes with necrosis of the pancreatic parenchyma seen. There is extensive peri-pancreatic fat stranding.



Fig. 4. CT scan cross-sectional view showing acute pancreatitis with swollen pancreas with peri-pancreatic fat stranding. There is extensive necrosis of the body and tail of the pancreas.

pancreatitis which is associated with significantly higher morbidity and mortality, and even more so if the necrosed pancreatic parenchyma becomes infected as happens in about 40–70% of cases [4,7]. A study conducted by Buchler MW et al. in Switzerland revealed that the mean age with which patients presented with ANP was 55.1 years with 61% men and 39% women [9]. These results were similar to our study in a way that male population dominated the spectrum of patients who present with ANP with 68% males and 32% females. However the mean age was less which was around 45 years.

The most common etiology resulting in acute necrotizing

pancreatitis in our study was biliary pancreatitis (54%) followed by alcohol induced pancreatitis (15%). These results were comparable to other several studies conducted throughout the world with similar results with the gall stone induced pancreatitis ranging from 40 to 50% in patients and alcohol induced pancreatitis from 10 to 40% of cases [9,17, 18].

The early initiation of feeding through enteral route in ANP has been shown by numerous studies to be beneficial for prognosis due to better septic and metabolic profile with significant reduction in mortality, multi-organ failure and prevention of infections and at the same time is



Fig. 5. CT scan coronal section through the abdomen showing necrotic body and tail of the pancreas with small enhancing head of the pancreas.

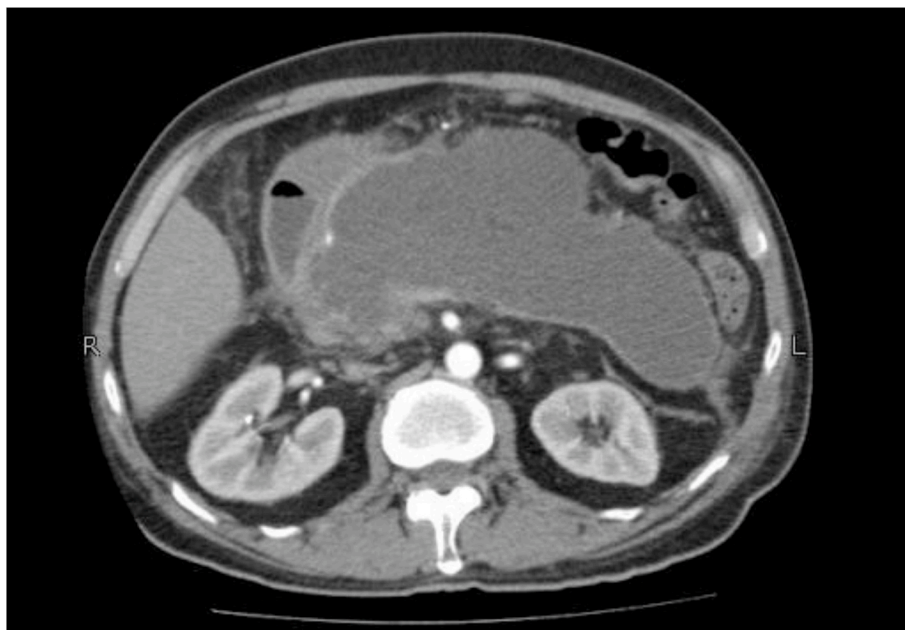
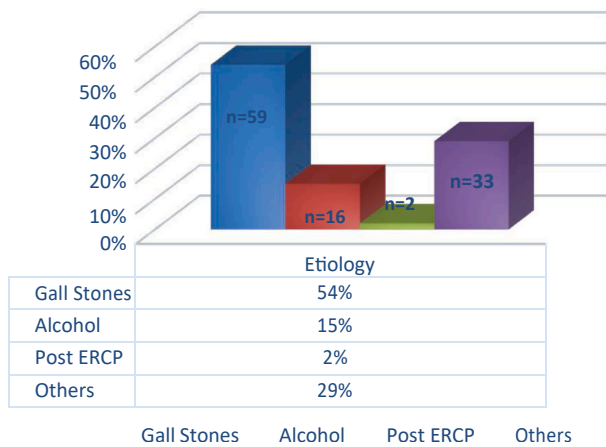


Fig. 6. CT scan image showing complete necrosis of the pancreas. Acute fluid collection developed in its place.

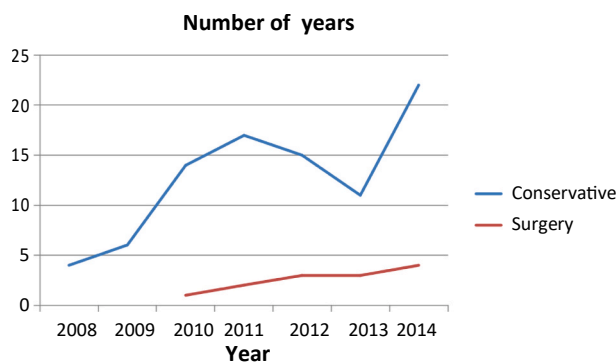
more cost-effective [1,19–22]. In our study, nasojejunal route was found to be the most common route used for feeding in 49% ($n = 54$) of patients while a large number of patients were also able to tolerate oral diet representing 40% ($n = 44$) of our patients and nasogastric feed was only used in 7% ($n = 7$) of cases. A study conducted by Alvi AR et al. also concluded that early enteral feeding in ANP patients resulted in better outcomes [7]. Multiple studies and randomized controlled trials comparing nasojejunal and nasogastric feeding concluded that these two routes did not have any significant differences in outcomes in regards to hospital stay, complications and mortality in necrotizing pancreatitis [4, 23,24]. Therefore patients can be started early on enteral nutrition with

nasogastric (NG), nasojejunal feeds (NJ) or direct oral feed if tolerated to gain favorable outcomes in these patients, with NG feed being relatively safe and requiring less expertise as compared to NJ feed.

The incidence of single organ failure in our study was found to be 54% in the conservative group as compared to surgery group which was 40%. However multi-organ failure was found to be 8% in the surgery group with only 5% in the conservative group. The mean hospital stay and in-hospital mortality was decreased in the conservative group with complication rate being higher in the conservative group. However these were found to be non-significant when compared with the surgery group. Despite of this the recent trend in the management of ANP



Graph I. Common causes of pancreatitis.



Graph II. Recent trend in management of ANP. X-axis: years. Y-axis: No of patients with ANP in that particular year.

Table 1 Severity markers of ANP in two groups.

	SURGERY	CONSERVATIVE
Age	47yrs	45yrs
SIRS	19(40%)	59(54%)
Single organ failure	7(14%)	26(24%)
Multi-organ failure	4(8%)	5(5%)
Ranson's	2	2
CTSI	8	8
APACHE	7	7

Table 2 Differences between outcomes in two groups. Overall complication rate of acute necrotizing pancreatitis was seen which included both minor and major complications such as multi-organ failure was seen.

	Conservative	Surgery	
Mean Hospital stay	12 days	20 days	p = 0.072
Complication rate	38.95%	33%	p = 0.677
In hospital mortality	8.4%	20%	p = 0.165
Mean Cost in Pakistani rupees	402,154	654,730	p = 0.035

patients has been shifting towards the conservative approach with increased usage of minimally invasive techniques like radiological drainage in our setup. We also noticed that we technically lacked in terms of offering minimally invasive procedures like VARD and endoscopic hybrid procedures which could be included in the conservative arm. These conservative techniques could have generated results

Table 3 Demographics table.

Total N = 110	Conservative Management	Surgical Management
Male	n = 65	n = 10
Female	n = 30	n = 5
	n = 95 (86%)	n = 15 (13.6%)

reflecting improved outcomes as shown by literature with reduced morbidity and mortality in these patients [1,9,16].

A study conducted by Buchler MW et al. determined that the mortality rate was 21% with the surgery group compared to only 7% in the group of patients with ANP managed conservatively. The rate of single and multiple organ failures were 32.7% and 34.8% respectively with an overall complication rate of 44% [9]. This high rate of multi-organ failures may have resulted due to open necrosectomy leading to new-onset multi-organ failure. Another study conducted by Alvi AR et al. had similar results to our study with mortality rate of 6.9% in conservatively managed patients versus 19.7% in surgically managed patients [7]. However the rate of complications were decreased significantly in conservatively managed patients and so were the hospital stay and in-hospital mortality making conservative management to be more favorable for prognosis of ANP [7]. This previous study from our centre by Alvi and colleagues also highlights the fact that though our mortality is within acceptable international standards however in advancing years no further reduction in death rates has been observed even when our results showed increased utilization of the conservative options. Similar results were also shown by another study conducted by van Santvoort HC et al. in which 62% of patients with necrotizing pancreatitis were managed conservatively resulting in a mortality rate of only 7% [25]. Few other studies have also concluded that open necrosectomy for management of ANP has resulted in severe complications including entero-cutaneous and pancreatico-cutaneous fistula formation with a much higher morbidity of 95% and mortality rates of about 25% [26, 27]. In contrast the conservative management and the minimally conservative approach results in a significantly decreased risk of complications and therefore death rate [28].

The strengths of this study were that this is the second study from our region specifically comparing the differences in the outcomes of ANP between patients managed with open surgery versus the conservative management on acute necrotizing pancreatitis. It also highlighted the deficiencies in our region which could be resolved by educating and training our surgeons, endoscopists and radiologist for using minimally invasive techniques to add to the armamentarium of options for treating this condition. Though our study did not show any difference in outcomes between the two treatment arms however it did reflect the cost effectiveness in patients treated with conservative options. The limitations of the study were its small sample size and the fact that it was a single-centre study. Also the patients were not followed after being discharged from the hospital to determine the effects of treatment on their quality of life. The authors recommend large multi-centre studies to determine outcomes between different minimally invasive procedures and open surgery.

5. Conclusion

A rise in trend towards conservative management was seen in more recent years in our set up. Outcomes in terms of hospital stay, complication rate and mortality were similar in both groups. The new advancement in minimally invasive endoscopic and percutaneous approaches means that our surgeons in developing world need to evolve and adapt to these techniques for better outcomes in patient management.

Ethical approval

Ethical approval was taken from Ethical Review committee of Aga Khan University Hospital.

Consent

Consent of all participants were taken before including in the study.

Author contribution

Fatima Mannan: Literature review, Study concept, design, data collection and analysis, writing and critical review of paper and its finalization. Roger Christopher Gill: Study concept, design, data collection and analysis, writing and critical review of paper and its finalization.

Abdul Ahad Sohail: Literature review, Study concept, design, data collection and analysis, writing and critical review of paper and its finalization.

Rehman Alvi: Study concept, design, data collection and analysis, critical review of paper and its finalization.

Khabir Ahmad: Study concept, design, data collection and analysis, critical review of paper and its finalization.

Registration of research studies

UIIN: researchregistry6340 <http://www.researchregistry.com>.

Guarantor

Fatima Mannan.
Roger Christopher Gill.
Abdul Ahad Sohail.

Funding disclosure

None.

Provenance and peer review

Not commissioned, externally peer-reviewed

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.02.005>.

References

- [1] S. van Brunschot, O.J. Bakker, M.G. Besselink, et al., Treatment of necrotizing pancreatitis, *Clin. Gastroenterol. Hepatol.* 10 (11) (2012 Nov 1) 1190–1201.
- [2] D. Yadav, A.B. Lowenfels, Trends in the epidemiology of the first attack of acute pancreatitis: a systematic review, *Pancreas* 33 (4) (2006 Nov 1) 323–330.
- [3] I. El Boukili, G. Boschetti, H. Belkhdja, et al., Update: role of surgery in acute necrotizing pancreatitis, *J. Visceral Surg.* 154 (6) (2017 Nov 4) 413–420.
- [4] C. Boumitri, E. Brown, M. Kahaleh, Necrotizing pancreatitis: current management and therapies, *Clin. Endosc.* 50 (4) (2017 Jul) 357.
- [5] M. Portelli, C.D. Jones, Severe acute pancreatitis: pathogenesis, diagnosis and surgical management, *Hepatobiliary Pancreat. Dis. Int.* 16 (2) (2017 Apr 15) 155–159.
- [6] C.L. Moura, P.P. Barros, C.M. Oliveira, et al., Minimally invasive endoscopic treatment of necrotizing pancreatitis: a case report with images and review of the literature, *Rev. Assoc. Méd. Bras.* 63 (3) (2017 Mar) 207–209.
- [7] A.R. Alvi, G.M. Sheikh, S.F. Kazim, Delayed surgical therapy reduces mortality in patients with acute necrotizing pancreatitis, *J. Pakistan Med. Assoc.* 61 (10) (2011) 973.
- [8] L. Sorrentino, O. Chiara, M. Mutignani, et al., Combined totally mini-invasive approach in necrotizing pancreatitis: a case report and systematic literature review, *World J. Emerg. Surg.* 12 (1) (2017 Dec) 16.
- [9] M.W. Büchler, B. Gloor, C.A. Müller, et al., Acute necrotizing pancreatitis: treatment strategy according to the status of infection, *Ann. Surg.* 232 (5) (2000 Nov) 619.
- [10] M. Arvanitakis, J.M. Dumonceau, J. Albert, et al., Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines, *Endoscopy* 50 (2018 May) 524–546.
- [11] T.L. Ang, A.Y. Teoh, Endoscopic ultrasonography-guided drainage of pancreatic fluid collections, *Dig. Endosc.* 29 (4) (2017 May 1) 463–471.
- [12] P.C. Freeny, E. Hauptmann, S.J. Althaus, et al., Percutaneous CT-guided catheter drainage of infected acute necrotizing pancreatitis: techniques and results, *AJR. Am J. Roentgenol.* 170 (4) (1998 Apr) 969–975.
- [13] M. Wroński, W. Cebulski, B. Witkowski, et al., Comparison between minimally invasive and open surgical treatment in necrotizing pancreatitis, *J. Surg. Res.* 210 (2017 Apr 1) 22–31.
- [14] P.L. Fagniez, N. Rotman, M. Kracht, Direct retroperitoneal approach to necrosis in severe acute pancreatitis, *BJS* 76 (3) (1989 Mar 1) 264–267.
- [15] M.C. van Baal, H.C. van Santvoort, T.L. Bollen, et al., Systematic review of percutaneous catheter drainage as primary treatment for necrotizing pancreatitis, *Br. J. Surg.* 98 (1) (2011 Jan 1) 18–27.
- [16] V.P. Mouli, V. Sreenivas, P.K. Garg, Efficacy of conservative treatment, without necrosectomy, for infected pancreatic necrosis: a systematic review and meta-analysis, *Gastroenterology* 144 (2) (2013 Feb 1) 333–340.
- [17] J.P. Neoptolemos, E.A. Kemppainen, J.M. Mayer, et al., Early prediction of severity in acute pancreatitis by urinary trypsinogen activation peptide: a multicentre study, *Lancet* 355 (9219) (2000 Jun 3) 1955–1960.
- [18] H. Isayama, Y. Nakai, R. Rerknimitr, et al., Asian consensus statements on endoscopic management of walled-off necrosis Part 1: epidemiology, diagnosis, and treatment, *J. Gastroenterol. Hepatol.* 31 (9) (2016 Sep 1) 1546–1554.
- [19] F. Kalfarentzos, J. Kehagias, N. Mead, et al., Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial, *BJS* 84 (12) (1997 Dec 1) 1665–1669.
- [20] A.C. Windsor, S. Kanwar, A.G. Li, et al., Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis, *Gut* 42 (3) (1998 Mar 1) 431–435.
- [21] M.S. Petrov, K. Whelan, Comparison of complications attributable to enteral and parenteral nutrition in predicted severe acute pancreatitis: a systematic review and meta-analysis, *Br. J. Nutr.* 103 (9) (2010 May) 1287–1295.
- [22] P.E. Marik, G.P. Zaloga, Early enteral nutrition in acutely ill patients: a systematic review, *Crit. Care Med.* 29 (12) (2001 Dec 1) 2264–2270.
- [23] F.C. Eatock, P. Chong, N. Menezes, et al., A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis, *Am. J. Gastroenterol.* 100 (2) (2005 Feb) 432.
- [24] A. Kumar, N. Singh, S. Prakash, et al., Early enteral nutrition in severe acute pancreatitis: a prospective randomized controlled trial comparing nasojejunal and nasogastric routes, *J. Clin. Gastroenterol.* 40 (5) (2006 May 1) 431–434.
- [25] H.C. Van Santvoort, O.J. Bakker, T.L. Bollen, et al., A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome, *Gastroenterology* 141 (4) (2011 Oct 1) 1254–1263.
- [26] B. Rau, A. Bothe, H.G. Beger, Surgical treatment of necrotizing pancreatitis by necrosectomy and closed lavage: changing patient characteristics and outcome in a 19-year, single-center series, *Surgery* 138 (1) (2005 Jul 1) 28–39.
- [27] S. Connor, N. Alexakis, M.G. Raraty, et al., Early and late complications after pancreatic necrosectomy, *Surgery* 137 (5) (2005 May 1) 499–505.
- [28] H.C. van Santvoort, M.G. Besselink, O.J. Bakker, et al., A step-up approach or open necrosectomy for necrotizing pancreatitis, *N. Engl. J. Med.* 362 (16) (2010 Apr 22) 1491–1502.
- [29] J.Y. Shyu, N.I. Sainani, V.A. Sahni, et al., Necrotizing pancreatitis: diagnosis, imaging, and intervention, *Radiographics* 34 (5) (2014 Sep 10) 1218–1239.
- [30] E. Zerem, Treatment of severe acute pancreatitis and its complications, *World J. Gastroenterol.* WJG 20 (38) (2014 Oct 14) 13879.
- [31] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, for the STROCSS Group, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery, *Int. J. Surg.* 72 (2019) 156–165.