ORIGINAL ARTICLE

Minimally Invasive Necrosectomy versus Open Necrosectomy Approaches in a Tertiary Hepatopancreatobiliary Unit

Eugene Wong[1,2], Julia Jones[1], Justin S Gundara[1], Christopher Nahm[1], Sarah Cho[2,3], Ian Norton[2,3], Jaswinder S Samra[1,2], Anubhav Mittal[1,2]

[1]Upper Gastrointestinal Surgical Unit, Royal North Shore Hospital, St Leonards, NSW 2065, Australia
[2]University of Sydney, Camperdown, NSW 2006, Australia
[3]Department of Gastroenterology, Royal North Shore Hospital, St Leonards, NSW 2065, Australia

ABSTRACT

Introduction The minimally invasive "step-up" approach to acute pancreatitis with necrotic collection is now well established. This study aimed to retrospectively review the indications, specific techniques used and outcomes of pancreatic necrosectomy in an Australasian tertiary hepatopancreatobiliary unit. **Methods** Retrospective analysis of 21 patients with confirmed diagnosis of necrotising pancreatitis with necrotic collection admitted to a tertiary hepatopancreatobiliary unit between May 2010 and May 2016 was performed. Primary composite endpoint of morbidity or mortality as outlined by the PANTER were examined. **Results** Out of the 23 total patients included in the study, 7 patients were treated with traditional open necrosectomy and the remaining 16 patients underwent a minimally invasive step-up approach. There was no statistically significant difference between the minimally invasive and open necrosectomy groups in terms of the primary endpoint (p=0.29) or development of any Grade 3 complication (p=0.19). **Discussion** Based on the experience of a small cohort of patients managed at a tertiary hepatopancreatobiliary unit, we did not find an appreciable difference in measurable endpoint outcomes between patients who underwent minimally invasive step-up necrosectomy as compared to open necrosectomy. Further multi-centre trials are still required to investigate if the management of severe acute pancreatitis can be safely undertaken at adequately resourced hospitals but without access to MIN.

INTRODUCTION

Acute pancreatitis is a common acute surgical condition, with worldwide incidence variably reported to be between 4.9-73.4 cases per 100,000 people [1]. The incidence of acute pancreatitis continues to increase, and it is now reported to be the most common gastrointestinal indication for US hospital admission [2, 3]. With this, the burden of associated peri-pancreatic and multi-system related complications has increased and the health economic burden is large [3, 4]. Despite recent advances in technology and minimally invasive techniques, severe and critical pancreatitis continues to have high morbidity and mortality [5, 6].

BACKGROUND

Management of infected pancreatic necrotic collection in a patient with multi-organ dysfunction continues to pose an ongoing challenge. Historically, surgeons would embark on morbid open surgical debridement and accept the consequences of this treatment which were often ascribed to the disease process itself [7]. Over the last decade, surgical management of infected necrosis has evolved from a maximally invasive approach to a minimally invasive, "step-up" approach. More specifically, 2010 saw the publication of the "Open necrosectomy *vs.* step-up approach for necrotising pancreatitis" (PANTER) trial, the first randomised study of 88 patients to show that a minimally invasive "step-up" approach reduced organ failure rates but did not reduce mortality when compared with open techniques [5].

The PANTER trial and subsequent studies have resulted in a paradigm shift and minimally invasive approach has been rapidly incorporated into surgical practice [8, 9]. This is reflected in recent guidelines for management of acute pancreatitis recommending a minimally invasive approach, such as in the International Association of Pancreatology (IAP)/American Pancreatic Association (APA) guideline published in Pancreatology in 2013 [10].

Study Question

The primary aim of the study was to compare the composite endpoint of morbidity or mortality for minimally invasive step-up approach vs. open necrosectomy in a 'real world' high volume tertiary hepatopancreatobiliary (HPB)

Received August 04th, 2017-Accepted September 29th, 2017
Keywords Minimally Invasive Surgical Procedures; Pancreatitis
Correspondence Anubhav Mittal
GIT Surgery
University of Sydney
Royal North Shore Hospital
St Leonards, NSW 2065, Australia
Tel + 61 2 9463 2899
Fax + 61 2 9463 2080
E-mail anubhav.mittal@sydney.edu.au

unit. The secondary aims were to document differences between the two groups for the development of multiple-organ failure, multiple systemic complications, number of interventions during admission, hospital length of stay and the development of incisional hernia and diabetes.

METHODS

Study Design

All cases of acute necrotising pancreatitis with necrotic collection admitted between the 1st of May 2010 to the 1st of May 2016 to the Royal North Shore Hospital Campus of the University of Sydney were retrospectively identified by searching through the inpatient hospital database (PowerChart, Cerner, North Sydney, Australia) and a prospectively maintained surgical audit database. The following ICD-10 codes were used (K85.02, K85.12, K85.22, K85.32, K85.82, K85.92). Case notes and electronic records were then retrieved and retrospectively reviewed and data collected on a structured proforma. Only patients with imaging confirmed necrotising pancreatitis with collection were included in the study cohort **(Table 1)**.

Definitions

Endoscopic transgastric drainage – A side-viewing duodenoscope was used under conscious sedation and ultrasound guidance where possible. Extrinsic compression from a walled off pancreatic necrosis was determined from the endoscopic approach. After entry into the collection was achieved, two pigtail catheters were inserted. Traditionally, in medial retrogastric collections this approach is preferred.

Percutaneous drainage – A drain was introduced with Computed Tomography (CT) guidance into the pancreatic collection using a retro-peritoneal approach.

Minimally-invasive necrosectomy – Patients undergoing either percutaneous drainage, endoscopic transgastric drainage or a minimally-invasive necrosectomy as the first procedure were considered to have undergone a Minimally-invasive Approach (MIN) to management. The minimally invasive approach involved either a Minimally Invasive Pancreatic Necrosectomy (MIRP) or a Video-Assisted Retroperitoneal Debridement (VARD) [11, 12].

Open necrosectomy – Patients undergoing an open necrosectomy as the first procedure were considered to have undergone an open necrosectomy approach (ONec.) The abdominal cavity was accessed via a midline or subcostal incisions, and the pancreas exposed by dissecting the overlying omentum. Extensive debridement of pancreatic collections and nonviable tissue was then performed.

Outcome Evaluation

Primary outcome - The primary endpoint as defined in the PANTER trial protocol was a composite comprising of a number of major postoperative complications, which included new onset, multi-organ failure, severe pulmonary, circulatory or renal failure, systemic complication or development of visceral perforation, an enterocutaneous fistula or severe intra-abdominal bleeding requiring surgical, radiologic or endoscopic intervention [5].

Secondary outcomes: development of any Grade 3 or higher complication, hospital length of stay, number of procedures and development of new diabetes or incisional hernias.

Statistical Analysis

Unpaired student's t-test and multiple logistic regression analysis were performed as appropriate. Kaplan-Meier survival curves and the Cox Regression survival analysis were performed as necessary. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using Statistical Analysis Software v9.4 (SAS Institute Inc, Cary NC, USA.)

Ethics

This study was approved by the Northern Sydney Local Health District, Human Research Ethics Committee.

RESULTS

A total of 23 patients were identified as having acute necrotising pancreatitis admitted to the Royal North Shore

Table 1. The primary endpoint as per the PANTER protocol.

Complication	Definition
New-onset multiple-organ failure or systemic complications	New onset failure (not present at any time in the 24hr before the first intervention) of two or more organs or occurrence of two or more systemic complications at the same time
Organ Failure	
- Pulmonary failure	PaO_2 < 60 mmHg, despite FiO_2 of 0.30, or need for mechanical ventilation
- Circulatory failure	Circulatory systolic blood pressure <90 mmHg, despite adequate fluid resuscitation, or need for inotropic catecholamine support
- Renal failure	Creatinine level > 177 µmol/litre after rehydration or new need for haemofiltration or haemodialysis
Systemic complication	
- Disseminated intravascular Coagulation	Platelet count <100×10^9/litre
- Severe metabolic disturbance	Calcium level <1.87 mmol/litre
- Gastrointestinal bleeding	>500 mL of blood over 24 hr
Enterocutaneous fistula	Secretion of faecal material from a percutaneous drain or drainage canal after removal of drains or from a surgical wound, either from small or large bowel; confirmed via imaging or during surgery
Perforation of visceral organ	Perforation requiring surgical, radiologic or endoscopic intervention
Intra-abdominal bleeding	Requiring surgical, radiologic or endoscopic intervention

Hospital between the 1st of May 2010 and the 1st of June 2016. Of these, 7 patients were treated with the traditional open necrosectomy (ONec) approach as their first procedure while the remaining 16 patients underwent the minimally invasive step-up approach (MIN).

Demographics

The majority of patients in both groups were male: 75% (n=12) in MIN and 86% (n=6) in ONec. 12 patients were admitted directly from the Emergency department while the remaining 11 patients were admitted via an inter-hospital transfer from surrounding district hospitals. **Table 2** summarizes the demographic data for the cohort.

Aetiology

Of all 23 patients who were diagnosed with necrotising pancreatitis, 8 were secondary to alcohol use, 9 were biliary, 1 was due to hypertriglyceridemia, 1 post-ERCP procedure, 1 following Clostridium Difficile colitis, and 1 was following a distal pancreatectomy performed at a district hospital for excision of a neuroendocrine tumour. The remaining patient experienced idiopathic necrotising pancreatitis with no clear aetiology.

Number of Operations/Procedures

The median number of operations or procedures undertaken by patients in both the MIN group and ONec groups was 2 (MIN range 1-7, ONec range 1-6) in patients. This difference was not found to be statistically significant (p=0.77).

Of those who underwent MIN, eight patients (50%) underwent either percutaneous or endoscopic transgastric drain insertion as the initial intervention. The other eight patients (50%) began with a minimally invasive pancreatic necrosectomy via video-assisted retroperitoneal debridement (VARD) procedure. Only 1 patient who initially underwent MIN subsequently progressed to open necrosectomy, but was included in the MIN group for analysis **(Table 3)**.

Patients who underwent MIN had shorter time to first procedure when compared to ONec, but this difference was not found to be statistically significant (P=0.14.)

Hospital Length of Stay

The mean hospital length of stay in the MIN group was 2.21 months (months defined as 31 days; SD 1.10), compared to 3.31 months (SD 1.44) in the ONec group (p=0.46).

Primary Endpoint

Ten out of the 16 patients in the MIN group experienced the primary endpoint (63%), compared to 5 patients in the ONec group (71%). This difference was not statistically significant on univariate analysis (OR=2.4, p=0.29, 95% CI 0.22 – 26.8) or after adjusting for age, sex, number of operations and admission APACHE II score (OR=4.5, p=0.25, 95% CI 0.36-55.9) **(Table 4)**.

Grade 3 Complications

The complications were classified based on the Clavien-Dindo classification for surgical complications [13]. Nine of the 16 patients who underwent MIN experienced at least one Grade 3 complication (56%), compared to 5 patients who underwent ONec (71%). Again, this was not found to be statistically significant on univariate (OR=4.6, p=0.20, 95%CI 0.45-48) or multivariate analysis (OR=6.3, p=0.16, 95% CI 0.51–80)

Development of New Incisional Hernia or Diabetes

Two patients experienced new onset diabetes in the MIN group while 1 patient experienced this outcome in the ONec group (OR 1.17, p=0.91). One patient in the MIN

Table 2. Patient demographics.

Characteristic	Minimally Invasive	Open Necrosectomy	Univariate Analysis
Patients (n)	16	7	-
Male Sex (n, %)	12, 75%	5, 86%	P=0.96
Direct ED Admission (n, %)	7, 44%	5, 71%	P=0.18
Mean age (n, range)	57, 47-67	54, 28-80	P=0.72
Mean APACHE II Score (n, range)	14, 7-23	14, 11-20	P=0.99
Median SOFA (n, range)	2.6, 0-7	3.6, 1-6	P=0.33
Mean time from admission to first procedure (n, range)	0.6 months, 0.1-1.2	3.5 months, 1.8 months, 0.1-2.0	P=0.14
Number of Operations or Procedures (n, range)	2, 1-7	2, 1-6	P=0.77
Hospital Length of Stay (months, range)	2.21, 0.63-4.61	3.31, 0.59-4.57	P=0.46

Table 3. Causes of pancreatitis.

Cause	Minimally Invasive	Open Necrosectomy	Univariate P-value
Alcohol (number, %)	4, 25%	4, 57%	P=0.14
Clostridium Difficile colitis (number, %)	1, 6.3%	0, 0%	P=0.98
Gallstones (number, %)	7, 43.8%	2, 28.6%	P=0.50
Hypertriglyceridaemia (number, %)	1, 6.3%	0, 0%	P=0.98
Post ERCP (number, %)	1, 6.3%	0, 0%	P=0.98
Postoperative complication (number, %)	1, 6.3%	0, 0%	P=0.98
Other/Unknown cause (number,%)	1, 6.3%	1, 14%	P=0.91

group and 1 in the ONec group developed a new incisional hernia (OR 2.50, P=0.54). The patient who developed an incisional hernia in the MIN group underwent subsequent open necrosectomy [14, 15, 16].

In-hospital Mortality

During the index admission, 2 patients in the MIN group died as compared to no deaths in ONec. Given the small cohort size and that as no patients in ONec died, it was not meaningful to perform statistical survival analysis on this cohort of patients **(Table 5)**.

DISCUSSION

Here we present the experience of a high-volume HPB unit at a major metropolitan hospital (Royal North Shore Hospital, Sydney, Australia) in the management of severe acute pancreatitis with necrosis. There was no statistically significant difference in major surgical complications (Grade 3 or higher), ICU or hospital length of stay between MIN and ONec. In addition, MIN patients underwent more interventions compared to ONec patients.

The PANTER trial provided strong impetus for wide adoption of MIN in critically ill surgical patients needing pancreatic necrosectomy. However, there was no difference in the length of stay in ICU, hospital length of stay or mortality. The findings of the current study are consistent with the PANTER trial.

A meta-analysis performed by Cirocchi *et al*. comparing MIN and ONec published in 2013 pooled 4 clinical controlled trials (both non-randomised and randomised). This meta-analysis identified a statistically significant difference in incidence of multiple organ failure as well as development of incisional hernias and new-onset diabetes, but did not find any difference in the incidence of intra-abdominal bleeding, fistula formation or surgical re-intervention [17]. A retrospective case-control study from Liverpool (UK) over 16 years comparing 274 patients undergoing minimal

Table 4. Comparison of outcomes.

Complication	Minimally invasive	Open Necrosectomy	Multivariate analysis (OR, p-value, 95% CI)
In-hospital mortality	2, 13%	0, 0%	-
Primary Endpoint as per PANTER (n, %)	10, 62.5%	5, 71.4%	OR=4.5, p=0.25, 95% CI 0.36-55.9.)
Any Grade 3 Complication	9, 56.3%	3, 60%	OR=6.3, p = 0.16, 95% CI 0.51–80
New onset diabetes	2, 13%	0, 0%	OR 1.17, p=0.91
New incisional hernia	1, 6.3%	1, 20%	OR 2.50, P=0.54

Table 5. Detailed treatment information for each patient included in the study.

Number	Age	Sex	Diagnosis	Approach	Initial Operation	APACHE	Last Follow-up
1	61	F	Gallstone	MIN	MIRP	23	Death
2	81	M	C.Difficile	MIN	MIRP	22	Alive, 4.6m
3	62	F	Pancreatic NET resection complication	MIN	Endoscopic transgastric drainage	16	Alive, 10.4m
4	32	M	Gallstones	MIN	MIRP	11	Alive, 2.8m
5	34	M	Alcohol	ONec	Laparotomy	12	Alive, 38.3m
6	47	M	Alcohol	MIN	Percutaneous drainage	7	Alive, 2.9m
7	83	M	Gallstone	MIN	MIRP	22	Death
8	60	M	Alcohol	MIN	1xPercutaneous drainage	9	Alive, 3.4m
9	63	M	Gallstone	ONec	Laparotomy	14	Alive, 18.1m
10	62	M	Alcohol	ONec	Laparotomy	11	Alive, 0.6m
11	66	F	Other/Unknown	MIN	MIRP	15	Alive, 19.2m
12	49	M	Alcohol	ONec	Laparotomy	20	Alive, 3.0m
13	62	M	Gallstone	MIN	MIRP	8	Alive, 2.2m
14	76	M	Gallstone	MIN	MIRP	14	Alive, 1.2m
15	31	M	Hypertriglyceridemia	MIN	Percutaneous drainage	13	Alive, 33.4m
16	66	M	Post-ERCP	MIN	MIRP	16	Alive, 33.1m
17	19	F	Gallstone	MIN	Endoscopic transgastric drainage	9	Alive, 63.7m
18	75	M	Gallstone	MIN	Endoscopic transgastric drainage	17	Alive, 36.1m
19	67	M	Alcohol	MIN	Endoscopic Transgastric	12	Alive, 56.9m
20	31	M	Alcohol	MIN	Endoscopic transgastric drainage	10	Alive, 37.8m
21	24	M	Alcohol	ONec	Laparotomy	12	Alive, 50.3m
22	80	M	Unknown	ONec	Laparotomy	17	Alive, 4.3m
23	67	F	Gallstone	ONec	Laparotomy	12	Alive 12.9m

Table of Patients

access retroperitoneal necrosectomy (MARPN) with 120 open necrosectomy also did not demonstrate significantly different mortality between the two groups [18].

These data are important because not all HPB units around the world will have access to the equipment or expertise required to perform MIN while they may have the necessary infra-structure to support a patient through ONec. Perhaps what is more important in determining outcome in these critically ill patients is an adequately resourced intensive care unit and interventional radiology departments [19]. Transfer of patients from a rural base hospital with adequte ICU to a high volume pancreatic centre will often displace them from their families and social support networks. Transfer of critically ill patients across long distances is complex, costly and difficult in many countries. For example, a retrospective review in 2005 found that 73% of patients with surgical emergencies transferred from rural Australian hospitals arrived out of normal working hours and may have thus had their care compromised [20].

The small cohort size and the retrospective analysis of prospectively collected data are limitations of the study. Despite the small numbers, the results are consistent with published literature. The small number of patients presenting to any single high volume HPB unit will continue to pose a problem for future researchers, but this study will undoubtedly contribute to the published literature on the topic.

CONCLUSION

The current study performed at a high volume and adequately resourced HPB unit at a major tertiary hospital failed to show any significant difference in composite endpoint of morbidity between MIN and ONec. While clinical equipoise may not exist in choosing between MIN and ONec at some centres, further multi-centre trials are still required to investigate if the management of severe acute pancreatitis can be safely undertaken at adequately resourced hospitals but without access to MIN or if these patients need to be transferred often adding to the complexity of managing these critically ill patients.

Conflict of Interest

The authors have declared that no competing interests exist.

References

1. Yadav D, Lowenfels AB. Trends in the epidemiology of the first attack of acute pancreatitis: a systematic review. Pancreas 2006; 33:323-330. [PMID: 17079934]

2. Nesvaderani M, Eslick GD, Cox MR. Acute pancreatitis: update on management. Med J Aust 2015; 202:420-423. [PMID: 25929504]

3. Peery AF, Dellon ES, Lund J, Crockett SD, McGowan CE, Bulsiewicz WJ, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology 2012; 1179:e1-3. [PMID: 22885331]

4. Fagenholz PJ, Fernandez-Del Castillo C, Harris NS, Pelletier AJ, Camargo CA. Direct medical costs of acute pancreatitis hospitalisations in the United States. Pancreas 2007; 35:302-307. [PMID: 18090234]

5. Van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A step-up approach or open necrosectomy for necrotising pancreatitis. NEJM 2010; 362:1491-1502. [PMID: 20410514]

6. Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, et al. A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis. Am J Gastroenterol 2012; 107:612. [PMID: 22186977]

7. Beger HG, Buchler M, Bittner R, Oettinger W, Block S, Nevalainen T. Necrosectomy and postoperative local lavage in patients with necrotising pancreatitis: results of a prospective clinical trial. World J Surg 1988; 12:255-262. [PMID: 3394351]

8. Bang JY, Holt BA, Hawes RH, Hasan MK, Arnoletti JP, Christein JD, et al. Outcomes after implementing a tailored endoscopic step-up approach to walled-off necrosis in acute pancreatitis. Br J Surg 2014; 101:1729-1738. [PMID: 25333872]

9. Da Costa DW, Boerma D, Van Santvoort HC, Horvath KD, Werner J, Carter CR, et al. Staged multidisciplinary team step-up management for necrotising pancreatitis. Br J Surg 2014; 101:e65-e79. [PMID: 24272964]

10. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology 2013; 13:e1-15. [PMID: 24054878]

11. Van Santvoort HC, Besselink MG, Horvath KD, Sinanan MN, Bollen TL, van Ramshorst B, et al. Videoscopic assisted retroperitoneal debridement in infected necrotizing pancreatitis. HPB 2007; 9:156-159. [PMID: 18333133]

12. Connor S, Ghaneh P, Raraty M, Sutton R, Rosso E, Garvey CJ, et al. Minimally invasive retroperitoneal pancreatic necrosectomy. Dig Surg 2003; 20:270-277. [PMID: 12748429]

13. Dindo D, Dermartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240:205-213. [PMID: 15273542]

14. Begg S, Vos T, Barker B, Stevenson C, Stanley L, Lopez AD. Burden of disease and injury in Australia in the new millennium: measuring health loss from diseases, injuries and risk factors. Med J Aust 2008; 188:36-40. [PMID: 18205562]

15. Tan V, Charachon A, Lescot T, Chafai N, Le Baleur Y, Delchier J, et al. Endoscopic transgastric versus surgical necrosectomy in infected pancreatic necrosis. Clin Res Hepatology Gastroenterology 2014; 38:770-776. [PMID: 25153999]

16. Howard TJ, Patel JB, Zyromski N, Sandrasegaran K, Yu J, Nakeeb A, et al. Declining morbidity and mortality rates in the surgical management of pancreatic necrosis. J Gastro Surg 2007; 11:43-49. [PMID: 17390185]

17. Cirrochi R, Trastulli S, Desiderio J, Boselli C, Parisi A, Noya G, et al. Minimally invasive necrosectomy versus conventional surgery in the treatment of infected pancreatic necrosis: a systematic review and meta-analysis of comparative studies. Surg Laparosc Endosc Percutan Tech 2013; 23:8-20. [PMID: 23386143]

18. Gomatos AP, Halloran CM, Ghaneh P, Raraty MG, Polydoros F, Evans JC, et al. Outcomes from minimal access retroperitoneal and open pancreatic necrosectomy in 394 patients with necrotizing pancreatitis. Ann Surg 2016; 263:992-1001. [PMID: 26501713]

19. Wilmer A. ICU management of severe acute pancreatitis. Eur J Intern Med 2004; 15:274-280. [PMID: 15450983]

20. Wong K, Levy RD. Interhospital transfers of patients with surgical emergencies: areas for improvement. Aust J Rural Health 2005; 13:290-294. [PMID: 16171503]