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Admission, management and outcomes of acute pancreatitis in intensive care

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Abstract

Background: A review of the management of acute pancreatitis (AP) at a tertiary intensive care unit (ICU) in Auckland, New Zealand, was published in 2004. This paper aims to update this series and identify changes in admission criteria, management and outcomes.
Methods: A retrospective review of patients admitted to the Department of Critical Care Medicine, Auckland City Hospital, with AP from 2003 to 2014 was undertaken and data compared with the previous study (1988–2001).
Results: Eighty-four patients (male 53, mean ± SD age = 56.9 ± 15 years) with 85 admissions to ICU from 2003 to 2014 were compared with 112 patients in the previous study. Maori were over-represented. Median duration of symptoms prior to admission to ICU decreased from 7 to 3 days. The proportion of total AP patients admitted to ICU halved and the mean Acute Physiology and Chronic Health Evaluation II score on admission decreased from mean 19.9 ± 8.2 SD to 15.4 ± 7.3 ($P < 0.001$). Two thirds of patients had persistent organ failure. The use of enteral feeding doubled from 46/112 (41%) to 71/85 (84%) ($P < 0.001$). The use of primary percutaneous drainage increased from 14/112 (13%) to 24/85 (28%) ($P = 0.007$). Rate of necrosectomy was similar (36/112 (32%) versus 20/85 (24%), $P = 0.205$), although minimally invasive necrosectomy was introduced. Overall hospital mortality decreased by 29% ($P = 0.198$).
Conclusion: There have been changes to the admission criteria and management in line with evolving guidelines and, overall, outcomes have improved.

Introduction

Despite a better understanding of the underlying pathophysiology of severe and critical acute pancreatitis (AP),[1] this subgroup of patients remains a major clinical and economic challenge.

In 2004, an audit from the same institution was published[2] on the management and outcomes of 112 patients with AP admitted to the intensive care unit (ICU) between 1988 and 2001. This included mostly patients with severe and critical AP, but not all. New approaches to management were adapted, including enteral feeding and abdominal decompression, but there was no reduction in the length of ICU stay or mortality, which was 31%.

More recent trends in the management of AP have included admitting all patients with predicted and actual severe AP to intensive care or high dependency units (henceforth 'ICU'), delaying the index computed tomography (CT) scan, recognizing the primacy of enteral (including gastric) nutrition, avoiding prophylactic antibiotics[3] and treating local complications by the 'step-up' approach.[4]

The aim of this study was to update the previous audit and document the evolution in management and outcomes.

Methods

A retrospective review of the medical records was undertaken for all patients with AP who were admitted to the ICU at Auckland City Hospital (ACH) between 2003 and 2014 (inclusive). Patients admitted to ICU primarily for another diagnosis were excluded. Patients transferred from other hospitals (tertiary admissions) were included but primary hospital records were not accessed. Multiple

admissions to ICU during the same hospital admission were combined and analysed as a single admission.

There were no standardized admission criteria to ICU and the decision to admit was by the on-call senior intensivist in discussion with the surgical team. Usually, the key criterion was the need for organ support. The patient was primarily managed by ICU staff, but decisions were made jointly with the surgical team.

The definitions used for data collection were consistent for both studies,[2] with the exception of 'cardiovascular failure' (defined as systolic blood pressure < 90 mmHg or the use of inotropes or vasopressors). Intra-abdominal abscess, while no longer an accepted term,[5] was defined, as per the original study, as an intra-abdominal infection of either necrosum or fluid. Oedematous interstitial pancreatitis was distinguished from necrotizing pancreatitis.[5] If the diagnosis of necrosis was not possible, because a CT scan or operation had not been performed, the patient was assumed to have interstitial pancreatitis despite being admitted to ICU. Extra-pancreatic infections were defined by the Centre for Disease Control Classification System.[6]

Predicted severity of AP was determined by the Modified Glasgow Criteria[7] within the first 48 h of admission to the primary hospital. The Acute Physiology and Chronic Health Evaluation (APACHE) II score[8] and Organ Failure Score[9] were calculated in the 24 h prior to ICU admission. Actual severity of AP was classified into four categories (mild, moderate, severe and critical) using the Determinants Based Classification.[1]

Statistical analysis was by Fisher's exact test for categorical data and Student's unpaired *t* test for continuous data. *P* values less than 0.05 were used to indicate statistical significance. Comparisons of medians between studies were not possible as the complete original data was unavailable. Graphpad Software (Graphpad Software Inc., San Diego, CA, USA) was used for all analyses.

Results

The demographic, admission and severity data are compared in Table 1. The proportion of admissions with AP who were admitted to ICU decreased between studies. Maori were over-represented with the proportion twice as high as in the Auckland catchment population (22 versus 11%),[10] but this was not the case for other ethnic groups including Pacific and Asian. The distribution of the maximum severity of AP during the patient's hospital admission was 0 with mild AP, 21 moderate, 44 severe and 20 critical.

The use of CT scan during hospital admission (including referring hospital) increased (84/112 (75%) versus 73/85 (86%), $P = 0.074$). Mean time from symptom onset to first CT was 3.7 ± 5.2 days, with 21/54 patients having a CT within 24 h (tertiary referrals excluded).

The rates of complications and organ failure are shown in Table S1. Notably, there was no change in the rate of pancreatic/peri-pancreatic necrosis (60/112 (54%) versus 47/85 (55%), $P = 0.885$) or infected collections/necrosis (29/112 (26%) versus 29/85 (34%), $P = 0.269$). Extra-pancreatic infectious complications included respiratory infection in 54 patients, bacteraemia in 35, urinary tract infection in 21 and infected central line in 11 patients. These were not recorded in the first study. Cardiovascular failure was the most common type of organ failure (65/85) and the incidence of respiratory failure significantly decreased (99/112 (88%) versus 58/85 (68%), $P < 0.001$). Four patients had no organ failure, 25 had transient (<48 h) and 56 had persistent failure (>48 h).[11]

Rates of interventions are listed in Table S2. Antibiotic use increased between studies (94/112 (84%) versus 80/85 (94%), $P = 0.042$), and in this study, median time to commencement of antibiotics from symptom onset was 2 days (range: 0–66) (tertiary referrals excluded). There was no difference in the overall rates of endoscopic retrograde cholangiopancreatography between studies

Table 1 Admissions and demographics for patients admitted to ICU with AP for 1988–2001 and 2003–2014

	1988–2001	2003–2014	*P*-value
Demographics			
Age (mean ± SD)	57.3 ± 14.3	56.9 ± 15.4	0.851
Number of males (%)	69 (62)	53 (63)	0.882
Admissions			
Admissions to ICU with AP (*n*)	112	85	
Admissions as proportion of total admissions to ACH with AP (*n* (%))	112/1552 (7.2)	85/2243 (3.8)	<0.001
Admissions per year to ICU (mean ± SD)	8 ± 2.7	7.1 ± 3.4	0.459
Duration of symptoms prior to ICU admission (days, median and range)	7 (1–100)	3 (0–116)	Not available†
Transfers from other hospitals to ACH/ICU (*n* (%))	55 (49)	26 (31)	0.013
Aetiology			
Gallstones (*n* (%))	47 (42)	29 (34)	0.302
Alcohol (*n* (%))	32 (29)	27 (32)	0.641
Other (*n* (%))	33 (29)	29 (34)	0.537
Severity			
Predicted severe disease by MGS (≥3 criteria) (%)	68/109 (62)	45/72 (62.5)	1.000
APACHE II score (mean ± SD)	19.9 ± 8.2	15.4 ± 7.3	<0.001
OFS (mean ± SD)	7.3 ± 3.2	6.8 ± 3.8	0.318

†Complete data for analysis of difference of medians between studies was unavailable. ACH, Auckland City Hospital; AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; MGS, Modified Glasgow Score; OFS, organ failure score.

but a significantly higher rate of stent insertion was present (4/39 versus 14/31, $P = 0.002$). In this study, most patients had endoscopic sphincterotomy (22/31).

The proportion of patients who received enteral nutrition (EN) doubled between study periods (46/112 (41%) versus 71/85 (84%), $P < 0.01$). In this study, EN was via nasogastric tube (13/71), nasojejunal tube (45/71), feeding jejunostomy tube (3/71) or a combination at different times (10/71). Median time from symptom onset to commencement of EN was 4 days (range: 0–35) and median duration of EN was 7 days (range: 0–52) (tertiary referrals excluded). The proportion of patients receiving parenteral nutrition (PN) also increased between studies (32/112 (29%) versus 39/85 (46%), $P = 0.016$). All patients in this study on PN had already tried EN. There was a median time of 7 days (range: 1–53) to commencement from symptom onset and median duration was 11 days (range: 1–172) (tertiary referrals excluded).

The rate of primary percutaneous drainage of intra-abdominal collections (necrosis or fluid collection) doubled between studies (14/112 (13%) versus 24/85 (28%), $P = 0.007$). In this study, median time to drain insertion from symptom onset was 22 days (range: 7–110) and median number of drains per patient was 2 (range: 1–5). Percutaneous drainage was definitive treatment for collections in approximately half of these patients (Fig. 1). The number of open operations significantly decreased between the study periods ($P < 0.001$) (Fig. 2) and in this study, half of the necrosectomy procedures (10/20) were initially done using a minimally invasive technique.

The median stay in ICU was similar between study periods (4 versus 5 days) but median hospital stay decreased (29 versus 21 days). Mortality decreased by one third (35/112 (31%) versus 19/85 (22%), $P = 0.198$). The majority died in ICU in both studies (21/35 versus 15/19, $P = 0.229$) and median time to death from symptom onset was similar (11 versus 12 days). Mortality in each category of the Determinants Based Classification[1] was 0 for moderate, 14/44 for severe and 5/20 for critical. Cause of death was multi-organ failure for 13 patients, sepsis and multi-organ failure for three and other causes for three patients.

Discussion

This study describes the changes in intensive care and surgical management of patients with AP admitted to an ICU at a tertiary hospital. There have been few studies that have specifically investigated these patients. The data reveals how management has evolved between study periods.

Guidelines recommend ICU admission for patients classified as severe[3,12] and transfer to a specialist centre for these patients or those requiring intervention.[3] The lower proportion of patients with AP admitted to ICU is likely a result of less tertiary referrals, which is probably due to increased capacity/experience of other regional hospitals managing patients with severe and critical AP. This may highlight the need to reconsider the dispersed model of care, particularly for these relatively uncommon and high-risk patients. However, this data probably also reflects patients avoiding admission to ICU due to up-skilling of wards (unpubl. data). Increased bed pressure on ICU is also a possibility but is difficult to measure, especially in retrospect. The rate of ICU admission was low compared to other centres (12[13]–27%[14]).

It is also possible, although not proven from this data, that the threshold for admission to ICU decreased between the studies, with a shorter time from symptom onset to ICU admission and lower APACHE II score. However, other potential factors, such as an increased ICU capacity of ACH and provincial hospitals, would also affect this. The APACHE II score, however, remained considerably higher than the definition of 8 for severe disease.[15] The mean score for patients with severe AP admitted to ICUs across Australasia is 14.[16] There was likely a tendency to admit patients with a specific need for organ support rather than those at risk of developing it. This may also reflect the difficulties in accurate risk

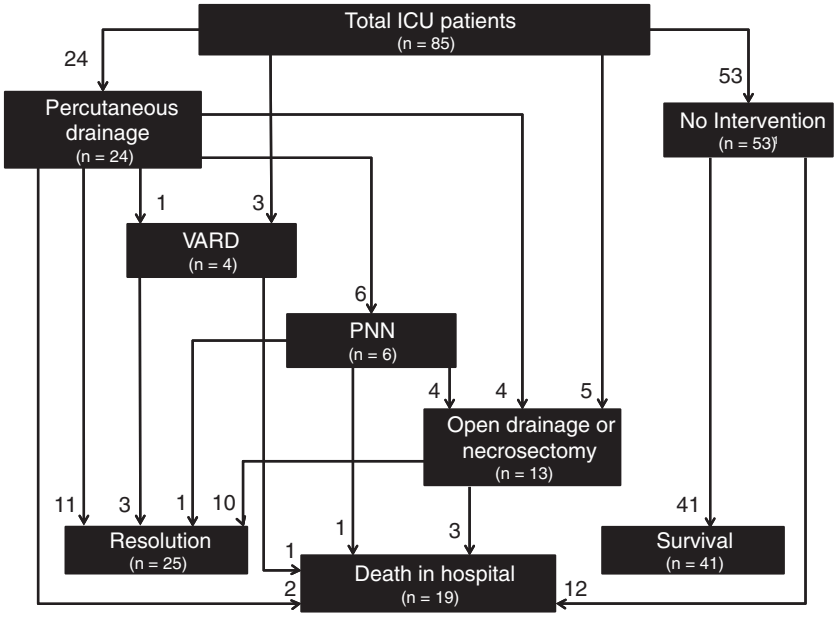

Fig. 1. Flowchart of interventions for necrosis and intra-abdominal abscess in patients admitted to ICU with AP during 2003–2014. [1]Patients who had a laparotomy for reasons other than abscess drainage or necrosectomy were included in this category. AP, acute pancreatitis; ICU intensive care unit; PNN, percutaneous nephroscopic necrosectomy; VARD, videoscopic-assisted retroperitoneal debridement.

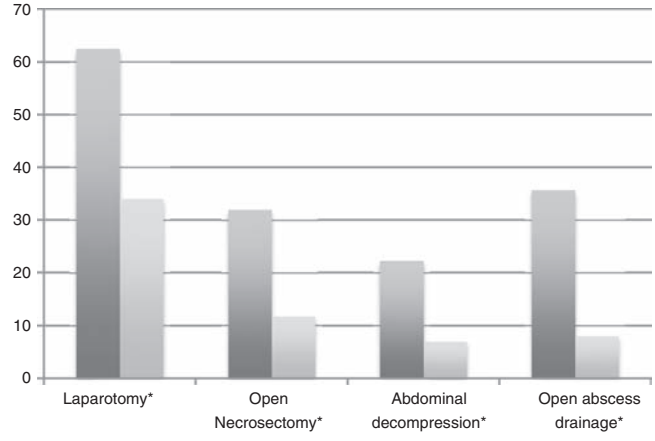

Fig. 2. Rate of open operations for patients admitted to intensive care unit with acute pancreatitis for (■), 1988–2001 and (■), 2003–2014. A statistically significant difference is denoted by *.

stratification, which is supported in this study where the Modified Glasgow Score only predicted 63% of those with actual severe AP.

Over-representation of Maori is in keeping with previously published results from South Auckland.[17] However, tertiary referrals may affect this data, as referring hospitals might include a higher proportion of Maori.

Current guidelines do not recommend the routine use of early CT for predicting severity,[3,12] as current clinical scoring systems are more accurate in predicting organ failure,[18] which is the best prognostic marker of mortality.[5,10] In spite of this evidence, the rate of early CT use in this study remained quite high. This has been shown elsewhere as well; one study reported that 90% of patients with severe AP had a CT scan within 3 days of admission.[19]

The rates of extra-abdominal infectious complications were high compared with other studies of ICU patients[20] as well as studies assessing all patients with AP.[14,21] These have been shown to increase the risk of infected pancreatic necrosis, as well as being a source of sepsis.[21] Prophylactic antibiotics have not been shown to be beneficial[22] and this is reflected in the current guidelines.[3,12,18] However, the high rate of antibiotics and short time to commencement suggest that prophylactic antibiotics were probably given for some patients, at least in the early period of this study. Antibiotic prophylaxis has been reported in other studies, where use solely as prophylaxis was seen in up to 53% of patients.[19]

EN has been shown to be safe and is the preferred approach to nutritional support.[3] It is associated with a decrease in infectious complications,[23] organ failure, surgical intervention and mortality[24] compared to PN. The shift from PN to EN occurred during the first study period, but interestingly the use of both increased during the second study period. However, all patients were started on EN first and supplemental PN was added in keeping with current guidelines[3] where it is required to reach the caloric requirements. The proportion of patients receiving combined nutritional support is at the high end of published results,[25] but the use of supplemental PN is higher than the published 14–17%.[19,25] It is unknown if the time to commence EN should be improved. Early EN (within 48 h of hospital admission) has been associated with reduced infectious complications, length of stay and mortality in a recent meta-analysis.[26] However, it is not known whether delayed EN increases the chance of feeding intolerance and the need for PN. A recent randomized-controlled trial comparing early EN (within 24 h) to delayed oral diet (after 72 h) found no difference in infectious complications or mortality.[27]

A major change in the approach to surgical intervention has occurred over the study periods. Firstly, there was a delay in definitive treatment, which was often facilitated by the use of prior percutaneous drainage. Secondly, in keeping with the PANTER (PAncreatitis, Necrosectomy versus sTEp up appRoach) randomized-controlled trial,[4] there was a change to a step-up approach (endoscopic or percutaneous drainage followed by minimally invasive necrosectomy (MIN) if required) rather than an open necrosectomy for infected fluid collections and walled off necrosis. The premise for this is to control infection by drainage, rather than achieve complete debridement, allowing delay of a (less likely) major surgical procedure in an already unwell patient. It is associated with less new-onset organ failure and a reduced composite outcome of major complications and death.[4] The significant decrease in rates of open surgical necrosectomy in this study paralleled the increased use of percutaneous drainage and the introduction of MIN. Patients with less invasive initial procedures who later required an open procedure are more than that required in the 'step-up' arm of the PANTER trial[4] (2/43, 5%), but less than another recent series (52%).[28] Most recently, a number of patients have not required admission to ICU because of timely and more effective use of percutaneous drainage, and this will require more study (unpubl. data).

Median ICU stay was probably shorter than other published studies that have reported means of 18–23 days.[25,28] There is a wide range of reported mortality rates for similar patients, ranging from 8 to 60%,[16,25] which is mainly accounted for by differences in the groups studied. The mortality rate of this study must be interpreted in light of how severe this subgroup of patients is. The mortality rate following MIN in this study was comparable to other reviews.[29] However, the mortality rate following open necrosectomy is lower than expected for this severe and biased subgroup of patients where the denominator includes only those admitted to ICU and who have failed the step-up approach. Other series report mortality rates of 25–30% following open necrosectomy.[30]

This study was susceptible to the limitations of retrospective analysis, including the inability to assign causality or to establish the basis for changes in practice. There was a potential difference between the two groups due to the subjective criteria for ICU admission. The data collected for the first study used the original Atlanta Classification[31] and this was retained to allow comparison between the first and second studies, despite the recent revision.[5] There is also an inherent weakness in aggregating data over a long period during which significant changes to guidelines and clinical practice have occurred.

The observed changes are largely in keeping with recent evidence-based guidelines and are associated with a modest decrease in mortality. In the search for further outcome improvements, there are aspects of care that may warrant further evaluation, including optimal timing of ICU admission for higher risk cases,

improving prediction of AP severity, the appropriate use of antibiotics and the efficacy of percutaneous drainage and MIN. Also, adoption and adherence to guideline recommendations can be improved based on this data. One of the important implications from this study is that the development of improved management strategies, including advanced interventions, requires a critical volume of cases and expert multidisciplinary care. The experience reported here showed a decrease in tertiary referrals, which is not supported by guidelines, but likely reflects improvements in intensive care and surgical management in regional hospitals.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Number of patients with organ failure and local complications admitted to intensive care unit with acute pancreatitis for 1988–2001 and 2003–2014

Table S2. Interventions for patients admitted to intensive care unit with acute pancreatitis for 1988–2001 and 2003–2014