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# Increasing Number of Comorbidities is Related to Delay to Surgical Management of a Perforated Peptic Ulcer in Patients who Died

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Authors APW, PMW and JBN developed the idea, authors TR-C and JA collected the data. All authors interpreted the data and contributed to the writing and revisions of the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

**Introduction:** The incidence of peptic ulcer disease has declined since the introduction of medical therapy, but the rate of perforated peptic ulcer and associated mortality has remained relatively constant. Delay to definitive treatment is known to adversely affect survival.
**Methods:** The Australian and New Zealand Audit of Surgical Mortality (ANZASM) retrospectively collects data on patients who died following surgery. To determine which patient characteristics are associated with delayed (not on the day of admission) surgical treatment of a perforated peptic ulcer, all patients who died in Queensland were identified from the ANZASM database.
**Results:** There were 39 deaths between 2007 and 2013 with a median age was 76 years. The median number of comorbidities was three and American Society of Anaesthesiologists (ASA) class

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was 4. Twenty nine patients had operative intervention on the day of admission and 10 underwent surgery later. Those with delayed surgery had a greater number of comorbidities (4 vs. 3; p = 0.016) but did not differ with respect to other demographics compared to those who underwent repair on the day of admission. The reviewing surgeon found no management issues in two thirds of patients.
**Conclusion:** Queensland patients with an increasing number of comorbidities were more likely to have delayed surgical intervention for a perforated peptic ulcer. Surgical delay is a known determinant of survival in patients with a perforated peptic ulcer and surgeons must be especially vigilant in multiply comorbid patients in making the diagnosis and expediting repair.

*Keywords: Mortality; audit; laparoscopy; duodenal ulcer; gastric ulcer; perforated ulcer.*

## 1. INTRODUCTION

Gastroduodenal ulceration usually occurs due to *Helicobacter pylori* infection or the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). While half the world's population is infected with *H. pylori*, less than 5% will develop gastroduodenal symptoms of this infection [1]. NSAIDs cause peptic ulceration by suppressing the production of protective gastric prostaglandins [2]. The mainstay of Gastroduodenal ulcer treatment is medical acid suppression and removing the causative agent. However, 1 in 10 peptic ulcers will perforate [3]. This complication is typically managed surgically. Selected patients may be managed medically (Taylor method) e.g. those aged < 60 years, less than 12 hours of symptoms, small volume pneumoperitoneum and normal haemodynamic status [2,3].

Open and laparoscopic repair of a perforated ulcer have the same mortality [4]. Delay to definitive treatment is known to adversely affect the chance of survival. A recent Dutch study has noted that reasons for delay are sparsely explored [5] but listed the following: out-of-hospital perforation, lack of peritoneal signs, late surgical review, attendance by junior surgical staff and lack of pulse oximetry. Given the above Dutch observation that hospital factors influence timing of surgery, we designed this study to identify the differences in demographics between patients who died following immediate versus delayed surgical management of a perforated peptic ulcer. As death from peptic ulcer perforation is an uncommon event, we used a national surgical mortality database to identify patients.

## 2. METHODS

All surgical deaths data were collected through the Australian and New Zealand Audit of Surgical Mortality (ANZASM) between August 2007 and October 2013. Deaths are reported to ANZASM by the hospital if the patient was an inpatient at the time of death and under the care of a surgeon, whether a surgical procedure was performed or not. ANZASM is a protected quality assurance activity in Australia under Part VC of the Health Insurance Act 1973 (gazetted August 2011).

The functioning, governance and objectives of ANZASM have been outlined elsewhere [6]. The treating surgeon provides the clinical data to ANZASM using a standard deidentified surgical case form (SCF). Every SCF is sent for first-line assessment to a surgeon from a different hospital (same specialty). Based on clinical judgment the assessor surgeon determines whether deficiencies in standard surgical care arose (e.g. communication issues, fluid balance issues, delay, inappropriate procedure). The case may then be closed or proceed to a non deidentified second-line assessment where a different assessor surgeon has access to the medical progress notes for that admission. The determinations of the assessor surgeons represent their own clinical opinions rather than that of ANZASM. Participation in ANZASM is mandatory as it forms a component of Continuing Professional Development requirement by the Royal Australasian College of Surgeons.

For this study, data were included if the patient died in a Queensland hospital following surgery for a perforated peptic ulcer. All data were extracted from the ANZASM database and analysed using IBM SPSS Statistics 19 (Armonk, NY: IBM Corporation, 2010). Chart review was not possible. Immediate surgery was defined as operation on the day of admission. Delayed surgery was defined as operation after the day of admission. The following demographic data were obtained: age, gender, day of admission, perforation site, length of stay, American Society of Anaesthesiologists class and number of comorbidities. A two tailed Student T test was

used to test the significance of a difference between groups using Microsoft Excel (Redmond, Washington: Microsoft, 2010). Differences in frequency counts between groups (binomial outcome) were tested using the Chi square test. Continuous variables are presented as medians. Categorical variables are presented as frequencies. P value < 0.05 was considered statistically significant.

## 3. RESULTS

There were 39 patients with an equal sex distribution who died following surgery for a perforated peptic ulcer. Twenty nine patients underwent surgery on the day of admission and 10 underwent surgery at a later date. The median age was 76 years. Age range was from 40 to 94 years but only six patients were younger than 60 years. The median number of comorbidities was three and median American Society of Anaesthesiologists (ASA) class was four.

The only statistically significant difference in demographics between patients who underwent delayed surgery and those who underwent surgery on the day of admission was a greater number of comorbidities (4 vs. 3 respectively p = 0.016) as is shown in Table 1. Twelve patients were admitted on a weekend (Friday, Saturday, Sunday) – 9 underwent surgery on the day of admission and 3 underwent surgery after the day of admission (31.0% vs. 30.0% respectively; p = 0.96).

However, there were differences clinically. Half of the patients who underwent surgery after the day of admission had an atypical presentation e.g. haemorrhage concurrent with perforation, elevated cardiac Troponin, no abdominal pain. Others had a complex medical background (e.g. immunosuppression, psychosis, rural residence) or lack of pneumoperitoneum on chest x-ray.

Two thirds of the ulcers were duodenal (27). Almost three quarters were repaired via laparotomy (31 including three conversions from laparoscopy). The median postoperative length of stay was seven days.

The treating surgeon identified a delay in diagnosis in nine patients. Just less than half the treating surgeons felt that in retrospect they would have managed their patient differently (17) without a statistically significant difference between the two groups (p = 0.980) as detailed in Table 2.

Death was due to single organ failure in 15 patients, abdominal sepsis in 12 patients, multi organ failure in seven and other causes in five.

There were no management issues identified in two thirds of patients according to the surgeon reviewers (24). In the remaining one third of patients between one and four management issues were identified. These were most commonly delays: delay in diagnosis / surgery / reoperation (14); but also technical or intraoperative issues (6); medical aspects of preoperative or postoperative care (4) and questionable decision to operate (3) were seen.

**Table 1. Demographic data**

| | Total (n= 39) | Surgery on day of admission (n = 29) | Surgery after the day of admission (n = 10) | P value |
|---|---|---|---|---|
| Female | 20 (51%) | 15 (52%) | 5 (50%) | 0.811 |
| Age (median) | 76 | 75 | 84 | 0.619 |
| Number of comorbidities (median) | 3 | 3 | 4 | 0.016 |
| ASA class (median) | 4 | 4 | 4 | 0.074 |
| DU : GU | 27 (69%): 12 (31%) | 20 (69%): 9 (31%) | 7 (70%): 3 (30%) | 0.586 |
| Open : commenced laparoscopically | 28 (72%): 11 (28%) | 19 (66%): 10 (34%) | 9 (90%): 1 (10%) | 0.431 |
| Postoperative length of stay | 7 | 7 | 9 | 0.447 |
| Delay in diagnosis | 9 (23%) | 5 (17%) | 4 (40%) | 0.217 |

*Note: DU= Duodenal Ulcer, GU= Gastric Ulcer, ASA= American Society of Anaesthesiologists*

**Table 2. Different actions as identified in retrospect by the treating surgeon**

| | Total | Surgery on day of admission (n = 29) | Surgery after the day of admission (n = 10) |
|---|---|---|---|
| Earlier treatment | 5 | 2 | 3 |
| Not operating | 5 | 4 | 1 |
| Intraoperative / technical issues | 4 | 4 | 0 |
| Postoperative management | 3 | 1 | 2 |
| TOTAL | 17 | 11 | 6 |

## 4. DISCUSSION

This study confirms that death following surgical management for a perforated peptic ulcer typically occurs in elderly patients with multiple comorbidities. Reassuringly, the day of admission was not related to delayed surgery. Perhaps surprisingly, only a quarter of patients did not undergo surgery on the day of admission. The finding that patients who had delayed surgery had more comorbidities and a complex medical background suggests that making a diagnosis in this group is more difficult and ultimately results in delayed surgery. Reviewer surgeons identified no management issues in two thirds of patients. In the remaining patients, deficiencies in management centred on the theme of delay: to diagnosis, surgery or reoperation.

The study's greatest strength is the fact that it includes all patients who died following surgical treatment for a perforated peptic ulcer in Queensland and were subject to at least a double blinded first-line assessment by a peer surgeon. ANZASM data is systematically collected by surgeons using a standard self-reporting tool and is thus clinically sound. Patients were identified from the operation description rather than based on administrative codes. The source population was large; it covered deaths in 20 public hospitals over a period of six and a half years; it conformed to recognized criteria for the assessment of surgical mortality. ANZASM data entry is checked for accuracy and loss to follow-up is low at 1% (unpublished data).

Half the world's population is infected with *H. pylori* but the vast majority will never develop symptoms of this infection [1]. *H. pylori* is identified in almost 95% of duodenal ulcers and two thirds of gastric ulcers [7]. Other recognised causes of peptic ulceration include non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, smoking, alcohol consumption and emotional stress [2]. The surgeon needs to address the causative agent as well as repair the life threatening perforation. Prognostic tools are seldom used because of complexity, subjective parameters or lack of specificity [8]: Boey score, Mannheim Peritonitis Index score, American society of Anaesthesiologists class and Acute Physiology and Chronic Health Evaluation (APACHE II) score [2]. A new simple score has recently been proposed: POMPP (Practical scoring system of mortality in patients with perforated peptic ulcer) which takes into account only age over 65 years, Blood Urea Nitrogen >45mg/dL and albumin <1.5g/L [8].

Patients with a perforated ulcer typically present with a sudden onset of severe epigastric pain [9]. Signs of generalized peritonitis are usually present [9]. Pneumoperitoneum on an upright chest x-ray or abdominal computed tomography (CT) scan is almost always present [9].

In a large population based study, 30-day postoperative mortality was increased by: increasing age (especially over 60 years), presence of malignancy, hypoalbuminaemia, hyperbilirubinaemia, delay to surgery over 24 hours from admission and acute renal failure [10]. Other clinical risk factors include: use of NSAIDs or steroids, preoperative shock, preoperative metabolic acidosis, tachycardia [11]. Parameters to improve survival following operative management of perforated peptic ulcer include: prompt clinical or radiological diagnosis, immediate administration of antibiotics and prompt surgery (laparoscopic or open) [11]. It is postulated delay predisposes the patient to developing severe sepsis [5]. Each hour that surgery is delayed increases 30 day mortality by 2.4%: less than 40% at 6 hours to more than 75% after 24 hours [5]. Which patients should be managed conservatively is currently poorly understood but this should not represent the initial treatment strategy [11].

Most duodenal ulcer perforations are smaller than 1cm and may be sutured directly [3] or repaired with a free (Graham) or pedicled

(Cellan-Jones) omental patch [2,12]. A gold standard technique is yet to be defined but the outcomes of open and laparoscopic repair are broadly similar [3]. A giant duodenal ulcer (>2cm diameter defect) may be managed with: subtotal gastrectomy, jejunal serosal patch, jejunal pedicle graft, free omental plug, gastric disconnection and controlled tube duodenostomy (tube gastrostomy, retrograde tube duodenostomy, feeding jejunostomy) [12]. Antibiotics, proton pump inhibition, thorough lavage with normal saline and avoidance of drains are routine [3]. There is no consensus on the use of nasogastric tube drainage but this is usually removed within 48 hours and oral feeding resumed [3].

Most perforated gastric ulcers can be closed (after wedge biopsy) either primarily or with a patch [3,13]. Simple procedures are associated with the lowest mortality rates[2]. Whereas almost no duodenal ulcers are malignant, between 4% and 16% of gastric ulcers will have a malignant etiology with less than one in three being diagnosed intraoperatively [13]. The majority of patients with a perforated malignant gastric ulcer will require two stage surgery (primary repair and secondary resection) [3].

Our retrospective hypothesis generating study has some limitations. The dataset is not able to determine the number of hours between hospital admission and surgery – we can only measure and report days. As surgeons self-submit data to ANZASM, there is a possibility of self-reporting bias by the treating surgeon. This study only includes in hospital deaths potentially missing patients who died after discharge from the primary surgical unit. Reviewer surgeons may demonstrate retrospective hindsight bias when assessing the care delivered to patients who are known to have died [14]. Our study covers only one Australian state (with a small sample size) and whether the findings are generalizable across the wider surgical population needs further study.

## 5. CONCLUSION

This study contributes to the literature by highlighting that patient factor i.e. the number of comorbidities may contribute to delay to surgical repair of a perforated peptic ulcer. Clinicians must be vigilant in not missing the diagnosis of a perforated peptic ulcer in multiple comorbid patients and expediting surgical repair.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

ANZASM / QASM is a protected quality assurance activity in Australia under Part Vc of the Health Insurance Act 1973 (gazetted August 2011) and as such ethical approval is not required.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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