Appendicectomies performed >48 hours after admission to a dedicated acute general surgical unit

B March¹, D Gillies², J Gani^{1,2}

¹University of Newcastle, NSW, Australia

²John Hunter Hospital, Newcastle, NSW, Australia

ABSTRACT

INTRODUCTION Acute general surgical units (AGSUs) are changing the way in which acute appendicitis is managed. In the AGSU at John Hunter Hospital, some patients wait more than 48 hours from admission to undergo an appendicectomy, usually because they are not unwell enough to precipitate an operation before that time. We analysed this subgroup of appendicectomy patients to determine how effectively they are being managed and how this might be improved.

METHODS A retrospective review of prospectively collected data was conducted of all patients who received an appendicectomy while admitted under the AGSU at John Hunter Hospital in the five years between January 2009 and December 2013.

RESULTS A total of 1,039 appendicectomies were performed in the study period, with 81 patients (7.8%) waiting >48 hours for their operation (delayed appendicectomy group). Overall, the negative appendicectomy (NA) rate was 21.6%; the NA rate in delayed appendicectomies was 50.62% and a non-therapeutic operation occurred in 47% of this group ($n=38$). No significant difference was found in the incidence of perforation/gangrenous appendicitis between patients having surgery in <48 hours and the delayed appendicectomy groups (11.2% vs 9.9%, $p=0.85$). A combination of negative diagnostic imaging result, a normal white cell count and normal C-reactive protein (ie a negative 'triple test') was the best predictor of a negative appendicectomy ($p=0.0158$, negative predictive value: 0.91, 95% confidence interval: 0.59–0.99), in the delayed appendicectomy group.

CONCLUSIONS In the delayed appendicectomy group, the incidence of perforation/gangrenous appendicitis was not significantly different from that found in patients having appendicectomy performed sooner. However, the NA and non-therapeutic operation rates were unacceptably high. An appendix triple test can improve diagnostic accuracy significantly without an unacceptable rise in the rates of perforation/gangrenous appendicitis.

KEYWORDS

Appendicitis – Appendicectomy – Predictive value of tests

Accepted 11 September 2014

CORRESPONDENCE TO

Jon Gani, E: jongani@mac.com

In recent years, there has been a paradigm shift in major hospitals around Australia with the establishment of acute general surgical units (AGSUs). This has resulted in a change in the way acute appendicitis has been managed both surgically and non-operatively to a lesser extent. No longer is the appendicectomy performed in the middle of the night by an unsupervised registrar but, instead, it is more often undertaken the following day on a quarantined operating list under consultant supervision. Additionally, the rotation of on-call consultants results in an intrinsic second opinion for many patients.

John Hunter Hospital is a 750-bed tertiary referral hospital in Newcastle, New South Wales. Our AGSU has been in existence since 2007. The AGSU is run daily by an on-site consultant general surgeon, responsible for prioritising acute cases for the dedicated afternoon operating list. Despite this acute care surgery model, it is not infrequent

to find patients admitted for more than 48 hours with suspected appendicitis, still awaiting an operation. The surgical dilemma is whether, at this stage, these patients are best served by an operation given that their disease process has already withstood a significant period of conservative management and they are rarely acutely unwell. Conversely, conventional wisdom teaches that there is an increasing risk of perforation with time if appendicitis is the true underlying pathology. How the results of preoperative imaging and blood tests should be interpreted in these delayed cases is not well defined.

In our study, the outcomes in patients undergoing an appendicectomy more than 48 hours from the time of admission (delayed appendicectomy group) were analysed to determine the negative appendicectomy (NA) rate and the incidence of perforation/gangrene in the appendicectomy specimens. The results of preoperative imaging and

pathology tests in the delayed appendicectomy group were also analysed to determine the accuracy of these preoperative investigations.

Methods

A five-year retrospective study from 1 January 2009 to 31 December 2013 was undertaken. It was approved by the Hunter New England Human Research Ethics Committee. Patients were selected from a prospectively maintained database of AGSU cases at John Hunter Hospital. All appendicectomies performed in the AGSU in this period were included in the study.

Electronic records were reviewed for time/date of presentation to the emergency department, time/date of operation start and finish, operative findings, postoperative complications, length of stay and histopathology of the appendix. Patient records were reviewed for a further 30 days following surgery to identify complications. Clavien–Dindo complications classed as grade II–V were recorded.¹

Haematological and biochemical test results, together with histology reports, were collected through the hospital's pathology database and analysed using the laboratory's reference ranges: white cell count (WCC) 4.0–11.0/mm³ and C-reactive protein (CRP) >5.1mg/l. The hospital's radiology system and patient notes were used to assess the use and results of diagnostic imaging (ultrasonography or computed tomography) conducted prior to operation.

Definitions

Definitions of appendicitis, therapeutic and non-therapeutic operations were adapted from Douglas *et al.*² The diagnosis of appendicitis was given on histological evidence of transmural infiltration by neutrophil granulocytes. A NA was an operation when a non-inflamed appendix was removed. An operation was considered to be therapeutic if disease was found, when the disease was the likely cause for the patient's symptoms and when surgery was the appropriate management. All other operations were considered to be non-therapeutic, including if the only abnormality found was a faecolith or fibrous obliteration of the appendix lumen, in the presence of a non-inflamed appendix.

The appendix was considered to be perforated or gangrenous if the histopathologist identified gangrene or full-thickness necrosis, with or without perforation. Results of diagnostic imaging studies were designated positive, negative or equivocal using criteria adapted from Douglas *et al* for ultrasonography.² Time to operation was defined as the time in hours from admission to operation start.

Data analysis

Data were analysed using Prism® version 6.0 (GraphPad Software, La Jolla, CA, US). Continuous variables were analysed using the Student's unpaired t-test and categorical variables with Fisher's exact test.

Results

A total of 1,039 appendicectomies were performed while admitted under the AGSU team between 1 January 2009

Figure 1 Frequency distribution of time from admission to operation in all appendicectomies (n=1,038). The delayed appendicectomy group (time to operation >48 hours, n=81) is displayed in turquoise.

and 31 December 2013. Time from admission to operation is displayed in Figure 1, with the mean time to operation being 1.05 days. The majority (92.2%) of appendicectomies were performed within 48 hours of admission to hospital.

Over the five-year study period, histological evidence of appendicitis was found in 790 cases (76%). A histologically normal appendix was found in 224 cases (21.6%). Another pathology was found in 25 cases (2.4%), including carcinoid tumours, adenocarcinomas, appendiceal diverticula, endometriosis and enterobiasis.

The time to operation was >48 hours in 81 (7.8%) of these cases and it is this group on which we focused for further analysis. A diagnosis of appendicitis was found in 40 patients (49.4%) while a histologically normal appendix was found in 41 cases (50.6%). A therapeutic operation occurred in 45 patients (55.1%) and a non-therapeutic operation was performed on 38 patients (46.9%). Males accounted for 29 cases (35.8%).

Inflammatory markers

WCC, CRP and diagnostic imaging results in the delayed appendicectomy group are presented in Table 1. A normal CRP level had a significant negative predictive value (NPV) for appendicitis (NPV: 0.842, 95% confidence interval [CI]: 0.60–0.96) and a raised WCC had a moderate positive predictive value (PPV) (PPV: 0.824, 95% CI: 0.57–0.96).

Diagnostic imaging

Relevant inpatient preoperative imaging was performed in 64 patients (79%). Of this subgroup, ultrasonography was the primary imaging modality in 42 cases and computed tomography was the initial imaging choice in 22. Imaging was reported as positive for appendicitis in 28 cases, equivocal in 9, negative in 24 cases and yielded another diagnosis in 3 patients. The NA rate in the image positive group was 28.57% while the combined image negative and equivocal

Table 1 Laboratory values of white cell count (WCC) and C-reactive protein (CRP)

	Appendicitis	Negative appendicectomy	p-value
WCC (n=81)			
High	14	3	0.0026
Normal	26	38	
CRP (n=51)			
High	19	13	0.0033
Normal	3	16	
Imaging (n=64)			
Positive	20	8	0.0009
Negative / equivocal	10	26	

group had a NA rate of 69.44%. Image positive cases had a perforation/gangrene rate of 14.29% compared with a 8.33% NA rate in the image negative/equivocal group.

Of 81 patients in the delayed appendicectomy group, 42 (52%) had complete 'triple test' results (WCC, CRP level and preoperative diagnostic imaging). A negative triple test (all three tests negative/equivocal) was a strong indicator of a NA ($p=0.0158$, NPV: 0.91, 95% CI: 0.59–0.99). However, 9% of patients with a negative triple test had appendicitis. Importantly, none of these had perforation or gangrene. Similarly, a positive triple test (combination of a positive imaging result, elevated CRP and a raised WCC) was a strong predictor of appendicitis ($p=0.0213$, PPV: 1.00, 95% CI: 0.40–1.00). Figure 2 demonstrates the NA rates with the various combinations of results of the triple test.

Complications

Among the delayed appendicectomy group, there were 11 representations or readmissions (13.6%) within 30 days following surgery. Three cases were not attributable to their earlier appendicectomy while eight presentations were a consequence of their operation and the readmission rate related to surgery was therefore 10%. The overall complication rate for the delayed appendicectomy group was 14.8%. Eight grade II complications were recorded (7 with appendicitis), one grade III complication was seen (in a NA) and three grade IVa complications were observed (1 NA). No reoperations were required and no 30-day mortality was recorded.

There was no significant difference in the perforation/gangrene rate in appendicectomies delayed more than 48 hours compared with those performed at less than 48 hours (9.9% vs 11.2%, $p=0.85$). One patient with perforated appendicitis required readmission and two grade II complications occurred in the context of perforation.

The reasons for delayed operation were extracted from the clinical notes (Table 2). Only the major reason that caused the operation to be delayed past 48 hours was recorded. One of the most common reasons for delay was postponement,

due to emergency caseload pressure on available operating time. Other reasons included diagnostic uncertainty and failed trial of non-operative management (persisting pain after observation and/or intravenous antibiotics).

Discussion

Acute appendicitis is a common cause of acute abdominal pain, and it is notorious for mimicking other abdominal and pelvic pathologies. 'Textbook' presentations are encountered in only about 60% of patients and accurate preoperative diagnosis has therefore been a longstanding challenge for even experienced surgeons.⁵ Current research continues to pursue improvements in diagnostic accuracy through imaging and investigations, thereby lowering the NA rate and its associated harms.⁴

The average NA rate for an Australian acute surgery unit is reported to be 26%.⁵ In our study, the overall NA rate was below this threshold but it was identified that those patients having an appendicectomy more than 48 hours after admission to hospital have almost double the NA rate.

The utility of preoperative investigations for the diagnosis of appendicitis, such as WCC, CRP and diagnostic imaging, has been the focus of extensive research. We observed that a negative or equivocal imaging result was associated with a very high NA rate while image positive cases had roughly the accepted average NA rate. The best predictor of a NA in this cohort was found to be a negative triple test: a negative diagnostic imaging result in addition to a

Table 2 Reasons for operative delay of >48 hours after admission

	Appendicitis	Negative appendicectomy	Perforation / gangrene	Total
Diagnostic uncertainty	11 (34%)	21 (66%)	2 (6.3%)	32
Initial operation cancelled / postponed	17 (63%)	10 (27%)	1 (3.7%)	27
Failed conservative management	11 (58%)	8 (42%)	5 (26.3%)	19
Other	1 (100%)	0 (0%)	0 (0%)	1
No identifiable reason	0 (0%)	2 (100%)	0 (0%)	2

normal WCC and normal CRP. Similarly, the best predictor of appendicitis was a positive triple test: positive imaging result combined with elevated CRP and raised WCC. A raised WCC is a highly significant finding where appendicitis is extremely likely and should therefore take precedence over other test results.

These findings add to the evidence from a previously published meta-analysis, which suggests that the interpretation of inflammatory markers in combination yields the greatest diagnostic accuracy.⁶ The added benefit of additional inflammatory markers such as procalcitonin is unknown.

The safety of delaying appendicectomy has been debated in the medical literature. Dittillo *et al* found the prevalence of advanced pathology is correlated positively with a prolonged interval from surgery.⁷ Likewise, Papandria *et al* reported that greater inpatient delay before appendicectomy was associated with increased perforation rates for adults.⁸ Conversely, a meta-analysis from 2014 concluded that there was no increase in the rate of perforation between appendicectomies performed before or after 48 hours.⁹ Our findings would support this as we observed no significant difference in the rate of perforation/gangrene between appendicectomies performed <48 hours and >48 hours after admission.

Giraud *et al* reported a significantly increased complication rate between delayed (≥ 24 hours) and early (<24 hours) appendicectomy groups¹⁰ while two retrospective studies found no significant differences in the complication rate between early (<12 hours) or late (12–24 hours) groups.^{11,12} Meta-analysis has shown that delays beyond 48 hours are associated with an increased rate of wound infection.⁹ Our study found the complication rate in the delayed appendicectomy group to be 14.8%, which was comparable with published complication rates for laparoscopic appendicectomy.¹³

The subgroup of patients in whom 'failed conservative management' was deemed the reason for delay was further analysed, to ensure this group did not have an increased rate of negative outcomes due to a deliberate management strategy. The NA rate was 42% ($n=8$); there were five cases of perforation/gangrene (26.3%), three grade II complications, one grade IVa complication and one readmission for persistent abdominal pain. These outcomes do not differ significantly from those of the rest of the delayed appendicectomy group. However, the trend towards a higher incidence of perforation/gangrene in this subgroup requires further study.

Conclusions

Half of all patients who wait more than 48 hours from the time of admission to an appendicectomy will have a normal appendix removed at a non-therapeutic operation. This is a significantly higher NA rate than for patients operated on within 48 hours of admission. However, the perforation/gangrenous appendices rates are not significantly different. Better defined indications for surgery are needed in this group. An appendix triple test (diagnostic imaging, recent WCC and CRP) can improve diagnostic accuracy significantly without an unacceptable rise in the rate of perforation/gangrenous appendicitis.

Acknowledgements

The authors wish to thank Dr Julie M Burrows and Dr Karin Fisher for their contribution to statistical analysis.

References

- Dindo D, Demartines N, Clavien PA. Classification of surgical complications. *Ann Surg* 2004; **240**: 205–213.
- Douglas CD, Macpherson NE, Davidson PM, Gani JS. Randomised controlled trial of ultrasonography in diagnosis of acute appendicitis, incorporating the Alvarado score. *BMJ* 2000; **321**: 919–922.
- Ma KW, Chia NH, Yeung HW, Cheung MT. If not appendicitis, then what else can it be? A retrospective review of 1492 appendectomies. *Hong Kong Med J* 2010; **16**: 12–17.
- Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. *Arch Surg* 2002; **137**: 799–804.
- Brockman SF, Scott S, Guest GD *et al*. Does an Acute Surgical Model increase the rate of negative appendicectomy or perforated appendicitis? *ANZ J Surg* 2013; **83**: 744–747.
- Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. *Br J Surg* 2004; **91**: 28–37.
- Dittillo MF, Dziura JD, Rabinovici R. Is it safe to delay appendectomy in adults with acute appendicitis? *Ann Surg* 2006; **244**: 656–660.
- Papandria D, Goldstein SD, Rhee D *et al*. Risk of perforation increases with delay in recognition and surgery for acute appendicitis. *J Surg Res* 2013; **184**: 723–729.
- Safety of short, in-hospital delays before surgery for acute appendicitis: multicentre cohort study, systematic review, and meta-analysis. *Ann Surg* 2014; **259**: 894–903.
- Giraud G, Baracchi F, Pellegrino L *et al*. Prompt or delayed appendectomy? Influence of timing of surgery for acute appendicitis. *Surg Today* 2013; **43**: 392–396.
- Abou-Nukta F, Bakhos C, Arroyo K *et al*. Effects of delaying appendectomy for acute appendicitis for 12 to 24 hours. *Arch Surg* 2006; **141**: 504–506.
- Surana R, Quinn F, Puri P. Is it necessary to perform appendicectomy in the middle of the night in children? *BMJ* 1993; **306**: 1,168.
- Katkhouda N, Mason RJ, Towfigh S *et al*. Laparoscopic versus open appendectomy. *Ann Surg* 2005; **242**: 439–448.