Outcomes of Complicated Acute Appendicitis at a Central Academic Hospital in Johannesburg South Africa

Irini Bogiages

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

This research report is respectfully submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the academic requirements for the degree of Master of Medicine in the field of Surgery

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Declaration

I, Irini Bogiages, declare that this research report is my own. It is being submitted in partial fulfillment of the requirements for the degree of Master of Medicine in Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

The research was conducted under the supervision of Professor Deirdre Kruger and Professor Thifheli Luvhengo.

Student Number: 2219172

Signature: _____

Date: _____

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List of Abbreviations

CMJAH: Charlotte Maxeke Johannesburg Academic Hospital

CRP: C-reactive Protein

HB: Haemoglobin

HIV: Human Immunodeficiency Virus

IQR: Interquartile Ranges

LOS: Length Of Stay

MC+S: Microscopy, Culture and Sensitivity

ICU: Intensive Care Unit

UK: United Kingdom

US: United States

WCC: White Cell Count

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Irini Bogiages, Deirdre Kruger, Thifheli Luvhengo

1. Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, South Africa.
2. Department of Surgery, Charlotte Maxeke Johannesburg Academic Hospital Johannesburg, South Africa

DISCLAIMERS

The authors declare no conflict of interest. No funding source to be declared.

ETHICS DECLARATION

Ethical approval was obtained from the Human Research Ethics Committee of the University of Witwatersrand (Ethics No M220865 MED22-05-049) and permission to conduct the study was provided by the Chief Executive Officer of Charlotte Maxeke Johannesburg Academic Hospital. Due to the retrospective nature of this study, no patient informed consent was obtained.

Irini Bogiages: MBChB, Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, South Africa, +27827737398, ORCID: 0009-0002-2012-7760

Professor Deirdre Kruger: BSc, PGCertHE (UK), PhD (UK). Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, South Africa, +27 11 717 2276. Deirdre.Kruger@wits.ac.za, ORCID: 0000-0002-3604-7682.

Professor Emmanuel Thifhelimbilu Luvhengo, MBChB (Medunsa), FCS (SA), Head of General Surgery, Charlotte Maxeke Johannesburg Academic Hospital, Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, South +27 83995 2552, thfheliluvhengo@gmail.com, 0000-0002-2901-1809

Outcomes of Complicated Acute Appendicitis at a Central Academic Hospital in Johannesburg South Africa

Abstract

Background: Laparotomy remains the most practiced approach for complicated appendicitis in some countries, including South Africa. This study compared the outcomes of patients who had a laparotomy or laparoscopic surgery for complicated acute appendicitis.

Methods: A retrospective review of patient records that had either a laparotomy and appendectomy or a laparoscopic appendectomy was undertaken. Data collected included demographic information, duration of symptoms, length of hospital stay, time to surgery, type of surgery, need for ICU admission, number of relooks, microbiology and outcomes.

Records of 200 patients of whom 62 patients (31.0%) had a laparoscopic appendectomy and 138 patients (69.0%) had an open appendectomy were included. Eighty-two patients (59.4%) who had an open appendectomy had a midline laparotomy. Postoperative complications developed in 46.4% of laparotomy vs 17.7% of laparoscopy patients (P<0.001). The mortality rate was 9.5% overall, with significantly higher mortality in the laparotomy group at 13.0% vs 1.6% in the laparoscopic group (P=0.009). Patients who died had significantly higher rates of complications and need for relook surgery (P<0.001). Histology showed a normal appendix in 13/138 patients (9.4%), granulomatous lesions and parasitic infection each in 5 patients (3.6%).

Conclusion: The majority of patients with complicated acute appendicitis had a appendectomy via laparotomy and this group of patients developed significantly more postoperative complications. The mortality rate was also significantly higher in patients who underwent a laparotomy.

Key words: Appendicitis, Laparoscopy, Laparotomy, Mortality

Introduction

Acute appendicitis is a common surgical emergency worldwide (1,2). Whilst there is variation in geographic locations, the estimated lifetime risk of developing acute appendicitis in the western literature is nearly 10% (1,2). Globally appendicitis remains a burden on health care systems, not only due to morbidity and mortality rates for each country, but also due the associated economic costs (3).

Complicated appendicitis is an umbrella term for acute appendicitis that progressed to an inflammatory mass, appendix abscess or ruptured appendicitis with generalized peritonitis (1,3). In the US, UK and Norway, complicated appendicitis accounts for 13 to 20% of all presentations of appendicitis (1). Predictably those that present with a complicated appendicitis would have a longer duration of symptoms (1). However, the very young (<10 years old) and those presenting beyond the 5th decade of life (>50 years old) often present with complicated appendicitis within 48 hours of onset of symptoms (1).

The diagnosis of acute appendicitis uses a plethora of options and is often more a risk stratification than an absolute diagnosis as appendicitis can only be confirmed on histopathological examination (1). It is sometimes difficult to differentiate simple from complicated appendicitis on clinical examination alone (1), however it remains important to distinguish simple from complicated acute appendicitis as they are managed differently.

Individuals who are at risk of complicated acute appendicitis include women who are pregnant, patients above the age of 50 years and those with immune compromising condition, such as

diabetes mellitus or human immunodeficiency virus (HIV) infection (4). Patients with gangrenous complicated appendicitis are likely to have significantly elevated white cell count (WCC) and C-reactive protein (CRP) on admission (4).

The most feared complication of acute appendicitis is free rupture with generalized peritonitis as it is associated with higher rates of mortality (1,3,5). Patients with ruptured appendix often require admission to an intensive care unit (ICU) for organ support, in addition to surgical intervention (1,6). Some patients who have had laparotomy or laparoscopy for a ruptured appendix require a relook procedure, which may be planned or mandatory (1). Whilst there is no consensus on the absolute indication for a relook procedure, mandatory relook is recommended for extensive contamination or necrotizing fasciitis (1–3).

Although international guidelines recommend laparoscopy over laparotomy for complicated acute appendicitis with purulent peritonitis, the ultimate choice of the operative approach is influenced by the surgeon's experience, institutional policies, and availability of equipment (1). From the literature, complicated appendicitis managed laparoscopically has reportedly better outcomes than appendectomy via the open approach (6,7). Despite local studies demonstrating the safety and benefits of laparoscopy in complicated appendicitis, open laparotomy remains the most practiced approach for ruptured appendix in South Africa (3,6,7).

On admission, an empiric broad spectrum antibiotic is administered intravenously and antibiotics which are selected for the treatment of a patient with complicated acute appendicitis should cover both aerobic and anaerobic organisms (1,4). The most commonly cultured organisms from patients with acute appendicitis are *Escherichia coli, Streptococcus species*, *Enterococcus species*, and *Pseudomonas aeruginosa* (8,9,10,11).

Worldwide studies indicate that median length of hospital stay (LOS) is about 3 days and approximately 2.4.3% of patients with acute appendicitis are admitted to ICU (1,4). In South Africa the mean LOS of patients with acute appendicitis is 5 days, whereas an estimated 9.6 % of patients require ICU admission (3). Additionally, South African data including both simple and complicated cases report a surgical site infection rate of around 19% (3). The Clavien-Dindo classification is currently one of the preferred methods to standardize reporting of post-operative complications (12).

In 1891 Mc Burney reported a 24.3% mortality in New York in patients with ruptured appendicitis(21). Currently, high income countries report an overall mortality rate of around 0.3% (1,3). However, mortality in low-income settings such as countries in Sub-Saharan Africa is reported to be as high as 5.4% (3,4,7).

This study's aims were to investigate the outcomes of all patients that had an appendectomy via laparoscopy or laparotomy during the period of January 2017 to March 2021 at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and audit the clinicopathological features associated with worse clinical outcomes.

Methods

This was a retrospective, cross sectional study investigating records of patients aged 18 years or older who had been admitted to CMJAH with a diagnosis of acute appendicitis from 1st January 2017 to 31st March 2021. All patients over the age of 18, that had a clinical assessment of acute complicated appendicitis were included in the study. Patients were diagnosed as having a complicated appendicitis by the admitting doctor that assessed the patient to have generalized peritonitis. Those patients who were initially managed non operatively and then

later complicated were also excluded from this study. Data collected included age, sex, race, comorbid conditions, HIV status, duration of symptoms, WCC, CRP, and haemoglobin (Hb) results on admission. Time to surgery, type of surgical intervention, admission to ICU, number of relooks, overall LOS, microbiology, histology and complications according to The Clavien-Dindo classification were also retrieved. Time to surgery was measured from the time of admission at the front desk of the hospital until the time the surgical consent was signed.

Data Analysis

An Excel spreadsheet of study data variables were imported into STATA v.16 (StataCorp, College Station, TX) for statistical analysis. Categorical variables are summarised as frequencies and percentages, whilst continuous variables are summarised as medians with interquartile ranges (IQRs). The chi-squared test or Fisher's exact test and the Mann-Whitney U test were applied to categorical and continuous data, respectively, to test for associations with the outcome variables of type of surgery (laparotomy vs laparoscopy) and mortality. Univariate logistic regression was used describe the relationship between predictor variables and mortality outcomes. All tests were performed at the level of significance set at $P<0.05$.

Results

In total 252 patients presented to the CMJAH Department of Surgery with a diagnosis of acute appendicitis during the study period. Fifty-two patients were excluded as their initial diagnosis of appendicitis was deemed incorrect upon further investigation. Therefore, 200 patient records were included in the study, of whom 62 patients (31.0%) had a laparoscopic appendectomy and 138 patients (69.0%) had an open appendectomy, or laparotomy procedure. In the open appendectomy group, 82 patients (59.4%) had a midline laparotomy, 43 patients (31.2%) underwent a Lanz incision and 13 patients (9.4%) had incision over McBurney's point. Of the 138 patients that had an open appendectomy, 49 (35.5%) had a relook procedure and 17 (12.3%) had more than one relook.

Demographic and clinical characteristics of the study participants

The demographic and clinical characteristics of the 200 study patients are shown in Table 1. The median age (IQR) at presentation of this adult population was 31 (24 to 40) years and most patients were male (70.0%).. The median (IQR) days of duration of symptoms leading up to presentation was 2 (1 to 3) days and ranged from 1 to 48 days, with those patients undergoing laparotomy having significantly longer duration of symptoms than those undergoing a laparoscopy (P=0.003). Patients were more likely to present during the summer or autumn months of the year. Length of hospital stay was a median (IQR) of 4 (2-8) days, with those receiving laparotomies staying significantly longer than laparoscopic patients (P=0.0003). Overall, 37.4.3% of patients reported complications, with the vast majority only reporting one complication (76.3%). Complications according to the Clavien-Dindo classification were significantly more likely in the laparotomy patients ($P<0.001$; Table 1 & Table 2). The mortality rate was 9.4.3% overall, with significantly higher mortality in the laparotomy group at 13.0% vs 1.6% in the laparoscopy group (P=0.009) (Table 1). Those who died were also significantly older at a median (IQR) of 51.0 (42.0-58.0) years vs 29.5 (22.5-38.0) years in those who were alive ($P<0.0001$).

Table 1. Demographic and clinical characteristics of the study population by surgical approach

Parameter	All (N=200)	Laparotomy (n=138)	Laparoscopy (n=62)	P-value
Age, median years (IQR)	31 (24-40)	31 (25-43)	29 (23-38)	0.06
Sex: Males, n (%)	140 (70.0)	106 (76.8)	34 (54.8)	0.002
Symptom duration, median days (IQR)	2 (1-3)	3 (1-4)	2 (1-3)	0.003
Day of presentation, n (%)				
Weekend (Friday-Sunday)	82 (41.0)	62 (44.9)	20 (32.3)	0.092
Weekday (Monday-Thursday)	118 (59.0)	76 (55.1)	42 (67.7)	
Season of presentation, n (%)				
Autumn	60 (30.0)			
Winter	49 (24.5)			
Spring	32 (16.0)			
Summer	59 (29.5)			
WCC ($x10^9$)	12.7 (9.6-16.9)	13.3 (9.9-17.4)	11.1 (8.7 -15.4)	0.02
CRP, mg/L	130 (44-292)	160 (63-304)	61 (19 - 87)	0.0004
LOS, median days (IQR)	4 (2-8)	5 (3-9)	3 (2-5)	0.0003
Complication(s) - *yes*, n (%)	75 (37.5)	64 (46.4)	11 (17.7)	<0.001
Mortality, n (%)	19 (9.5)	18 (13.0)	1 (1.6)	0.009

Abbreviations CRP, C reactive Protein; IQR, interquartile range; LOS, length of hospital stay; WCC, White Cell Count.

Table 2. Clavien–Dindo Classification of Surgical Complications

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications.
Grade IIIa	Requiring surgical, endoscopic or radiological intervention not under general anesthesia.
Grade IIIb	Requiring surgical, endoscopic or radiological intervention under general anesthesia.
Grade Iva	Life-threatening complication requiring ICU management with single organ dysfunction.
Grade IVb	Life-threatening complication requiring ICU management with multi-organ dysfunction.
Grade V	Death of a patient.

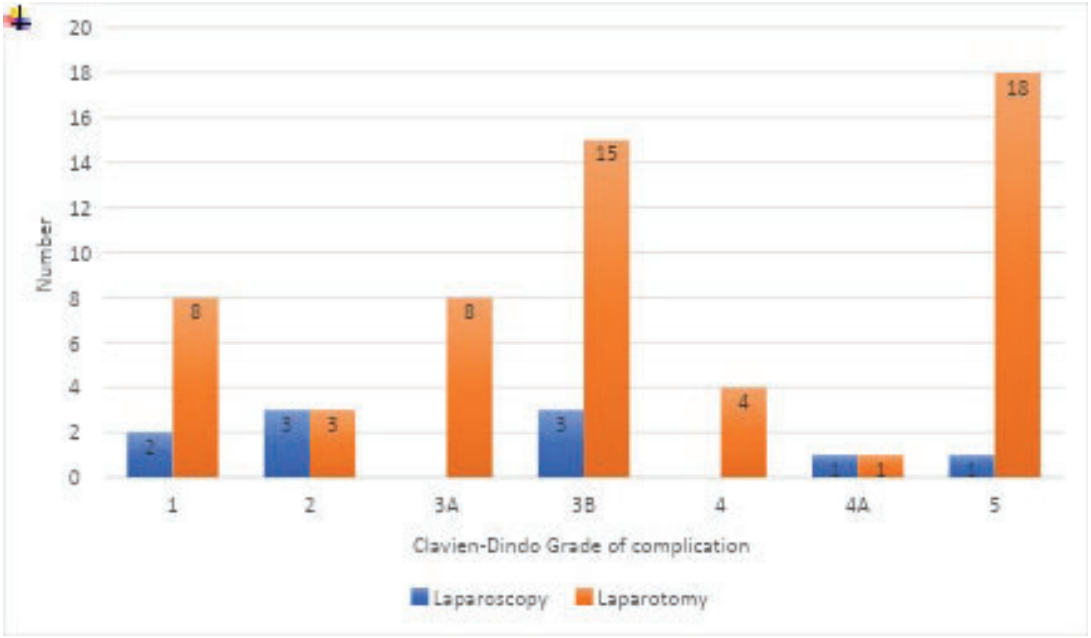

Figure 1. Number of Complications following of Laparoscopy vs Laparotomy using the Clavien-Dindo grading system

Clinicopathological features of patients following appendectomy via open laparotomy approach for clinically diagnosed complicated acute appendicitis

Table 3 shows the clinical parameters of the group of patients who received an open appendectomy via laparotomy according to mortality outcome. Patients who died following an open appendectomy were significantly older with a median (IQR) age of 51 (45-58) years compared to 30 (24-38) years in those who got discharged (P<0.0001). Patients who died had significantly higher rates of complications, need for relook surgery, raised CRP and raise Hb levels (Table 3). Amoxicillin/clavulanic acid was prescribed empirically in 132 patients (96%), while 5 (3%) had a combination of Amoxicillin/Clavulanic acid and Fluconazole.

Table 3. Demographic & clinical characteristics of patients who had laparotomy according to mortality

Parameter	Dead (n*=18)	Alive (n*=120)	P-value
Age, median years (IQR)	51 (45-58)	30 (24-38)	<0.0001
Sex: Males, n (%)	16 (88.9)	90 (75.0)	0.244
Symptom duration, median days (IQR)	3.5 (3-6)	2 (1-4)	0.04
LOS, median days (IQR)	6 (2-13)	5 (3-8)	0.373
ICU admission - *yes*, n (%)	16 (88.9)	9 (7.7)	<0.001
Complication(s) - *yes*, n (%)	17 (94.4)	47 (39.2)	<0.001
Relook(s) - *yes*, n (%)	14 (77.8)	35 (30.4)	<0.001
Antibiotic(s) - *yes*, n (%)	17 (94.4)	120 (100.0)	0.130
Biochemistry			

WCC (x10^9)	10.7 (8.6 -16.3)	13.5 (10.3-17.7)	0.131
CRP mg/L	312 (246-350)	134 (53- 291)	0.0001
Hb g/dl	12.8 (9.9-14.4)	14.8 (13.3-16)	0.004

*Not all parameters were available for each patient, percentages calculated per available denominator.
Abbreviations: CRP, C reactive protein; Hb, Haemoglobin; ICU, Intensive Care Unit; IQR, interquartile range; LOS, length of hospital stay; WCC, White Cell Count.

Laboratory and histopathological findings in patient undergoing appendectomy via open laparotomy approach

Overall, the median (IQR) WCC values upon admission for patients admitted with acute complicated appendicitis and undergoing a laparotomy was 13.3 x10^9 (9.9 to 17.4 x 10^9), and this did not differ according to mortality (Table 3). The median (IQR) CRP values was significantly higher at 312 (246-350) mg/L in those who died compared to 134.5 (53-291) mg/L in alive patients (P=0.0001). The median (IQR) Hb level on admission was significantly lower in those who died (P=0.004). Only six patients (4.3%) had CD4 counts and viral loads captured, therefore these results were excluded from the analysis.

The results of microscopy, culture and sensitivity (MC+S) of blood or fluid collected intra-operatively could be traced in 72 (52.2%) of the laparotomy patients. Results of MC+S showed no bacterial growth in 33 patients (45.8%), with cultures from 28 patients (38.9 %) growing only one species of bacteria and that of 20 patients (27.8%) showing polymicrobial growth. In 17 patients (35.4%) who had positive cultures, the organisms cultured were sensitive to Augmentin. Escherichia coli was cultured in 39 (76.2%), Bacteroides fragilis in 5(10.4%) and Pseudomonas aeruginosa in 4 (8.3%) of patients.

Overall, in 110 patients (54.3%) a diagnosis of acute appendicitis was confirmed on histological examination. Of the 28 patients that did not show acute appendicitis, 13 (9.4%) had a normal appendix, 5 (3.6%) had granulomatous lesions and 5 (3.6%) patients had a parasitic infection. One of the records had histological report of dysplasia in a patient who was lost to follow up and presented a few years later with metastatic colon cancer. Table 4 shows a list of all the incidental findings.

Table 4: Incidental findings in patients who had appendectomy for clinically complicated appendicitis diagnosed (n = 138)

Pathology	Number (%)
Normal appendix	13 (9.4%)
Tuberculosis or granulomatous disease	5 (3.6%)
Parasitic infection (Schistosoma species+ Ascaris species)	5 (3.6%)
Neuroma	2 (1.4%)
Lymphoid follicular hyperplasia	1 (0.7%)
Dysplasia	1 (0.7%)
No appendix in sample	1 (0.7%)

Time from admission to surgery

Overall, the median (IQR) time to surgery from admission was 21 (12-33) hours. The day of the week that the patient was admitted was reviewed to assess if there was a longer time to theatre on a weekend but showed no statistical difference (P=0.904). There was also no statistical difference in the likelihood of a patient undergoing a laparotomy or laparoscopy during the week or on the weekend (P=0.092).

A univariate analysis showed that each hour delay to theatre significantly increases the chance of mortality in the laparotomy group (Figure 2). After a delay of 16 hours, the chance of survival dropped from 99% to 89% post-laparotomy and this continued to drop per hour before tapering off after 58 hours. At hour 58 the survival rate was 71% in the laparotomy group compared to 98% in the laparoscopy group (P=0.011).

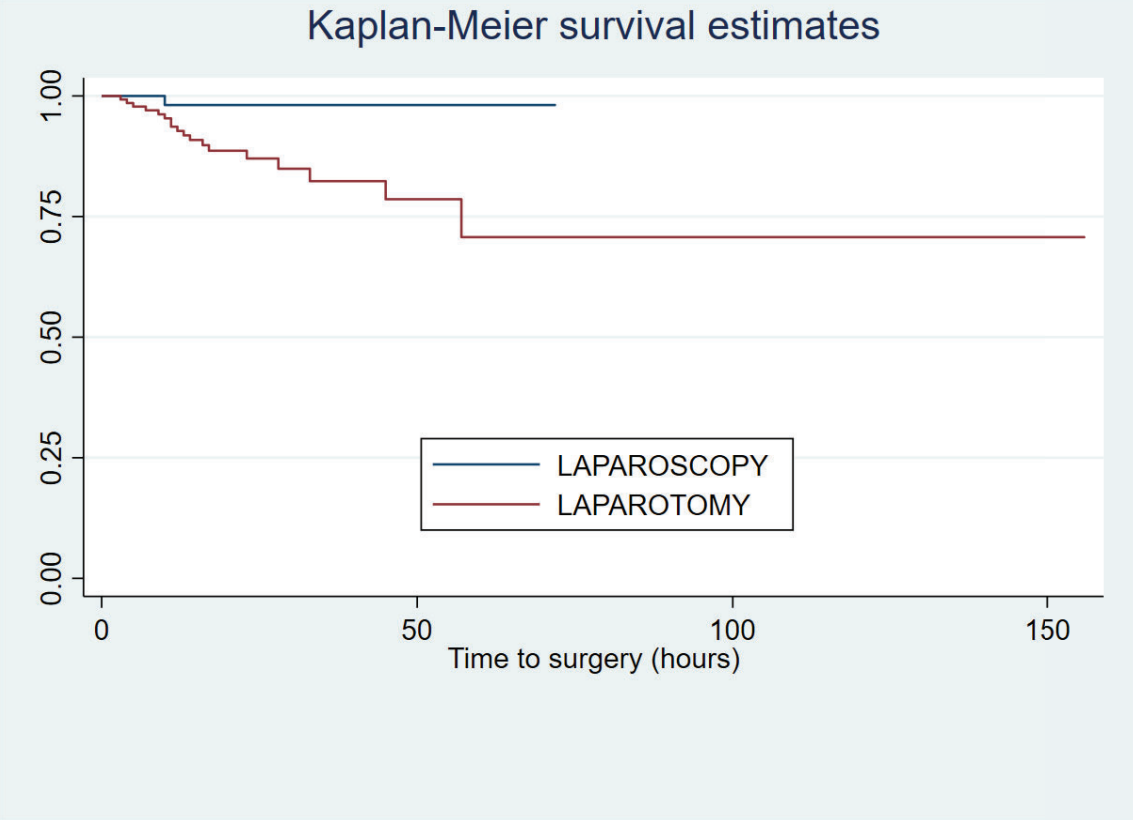

Figure 2. Kaplan-Meier survival estimate in laparotomy vs laparoscopy appendectomy patients.

Admission to ICU

Twenty-five (18 %) of patients that underwent an open appendectomy were admitted to ICU, which does not include patients that required ICU but there were no ICU beds available.

Table 5: Postoperative complications in patients who had laparotomy for complicated appendicitis (n = 75)

Complication	Number (%)
Paralytic ileus	15 (20.3)
Organ dysfunction	12 (16.2)
Bowel resection and stoma or primary anastomosis	10 (13.5)
Intra-abdominal collections	9 (12.1)
Surgical site infection	7 (9.5)
Iatrogenic small bowel injury	4 (5.4)
Cardiac complications	3 (4.1)
Pulmonary embolism	2 (2.7)
Iatrogenic urinary bladder injury	2 (2.7)
Re-admission	1 (1.4)
Bowel evisceration	1 (1.4)
Aspiration	1 (1.4)
Bleeding from anterior abdominal wall	1 (1.4)
Buttock abscess	1 (1.4)
Deep vein thrombosis	1 (1.4)
Tracheal Stenosis	1(1.4)
Urinary tract infection	1(1.4)
Retroperitoneal haematoma	1(1.4)
Upper gastrointestinal bleeding	1(1.4)
Unknown	1 (1.4)

Discussion

The study investigated 200 patients of whom the majority were male and 69% had an open appendectomy via laparotomy. The findings of this study report an overall mortality rate of 9.4.3% in patients with acute appendicitis, with a significantly higher rate of 13.0% in patients undergoing a laparotomy vs 1.6% in laparoscopy patients. This is higher than expected as mortality in low-income settings in the Sub-Saharan Africa is reported to be 5.4% (3,4).

The median age in this study population was 31 years, yet the median age was significantly older in those who died at 51 years. Age is a known risk for poorer outcomes, although a higher cut-off age of 65 years has been reportedly associated with mortality (10,13). In addition to age, a frailty index score should also be considered at admission. Males were significantly more likely to undergo a laparotomy at 75.7% vs 53.3% of females. In contrast to earlier published literature from South Africa, male sex was not associated with mortality in this study (6,7).

Symptom duration was significantly longer in the patients who underwent laparotomies and in those who died. LOS stay was significantly shorter in the laparoscopy group by a median of 2 days and had no association with mortality. In the literature there is conflicting reports of whether delay to theatre or in hospital delay is a predictor of poor outcome, however it is generally accepted that duration of symptoms is associated with poor outcomes or longer LOS and increased surgical site infection (14-18). It is worth noting that the reports referenced here measure delays of over 13 hours from time of hospitalization to theatre, however we report a median length of time of 19 hours. The latter is most likely due to limited theatre space at our institution, but this needs further investigation. In a univariate analysis, our study that showed that each hour delay to theatre increased the likelihood of mortality. After a 16 hour delay from

admission to theatre, the chance of survival had dropped to 89% and continued to drop per hour until it tapered off at 58 hours with a survival rate of 71%. Hence, each hour is important and affects mortality. Our findings support a need to reduce the time to theatre from the time of hospitalization to improve mortality in our population undergoing appendectomy via laparotomy.

Although most of our study patients presented on a weekday, there was no was no statistically significant difference in time to theatre, which is not in keeping with the literature that shows a higher trauma burden on weekends which may affect time to surgery (19).

Although many scoring systems for appendicitis have been described, we mostly rely on clinical expertise and radiological findings when diagnosing acute appendicitis at our institution, as well as when determining which patients are complicated. Finding a suitable routinely measured biomarker that can aid in discriminating at risk patient populations in acute appendicitis would be valuable. WCC and CRP were significantly elevated in laparotomy vs laparoscopy patients, but only a raised CRP was significantly associated with mortality (P=0.0001). In addition, Hb was protective against mortality (P=0.004) but this may be an indicator of underlying chronic disease. Unfortunately, the mean cell volume and iron studies were not available from this data.

Overall we found a 37.5 % complication rate with significantly more patients in the laparotomy group developing complications at 46.4% compared to 17.7% in the laparoscopy group (P=0.0003). This may be due to the admission team being more likely to triage sicker patients to the laparotomy group, although this is in keeping with other studies that reported higher incidences of complications in laparotomy vs laparoscopy groups (6,7) Additionally, 94.4% of the patients who died developed complications vs 39.2% in the alive group. The most commonly reported complication was a paralytic ileus, followed by bowel resection. In other studies, the most commonly reported complications are related to intra-abdominal collections and surgical site infections (20,21). As to why our complications rates are higher than expected was not explored in this paper, one theory is that we may be better reporting our complications. Bowel resections and stoma are not reported in international studies as a documented complication.

Admission to ICU showed a remarkable association with mortality, in that 88.9% of those who died were admitted to ICU. This is not surprising in our setting as ICU beds are a rare commodity and only the most critically ill have access to ICU care (22). Significantly more patients in the mortality group also had a relook procedure at 77.8% compared to 30.4% in the alive group (P<0.001). In our study, empiric antibiotic use was not associated with mortality. The most common organisms included Escherichia coli that was cultured in 39 (76%) patients, followed by Bacteroides fragilis in 5 (10%) and Pseudomonas aeruginosa in 4 (8%) patients. These findings are similar to those reported in a Nigerian study (9).

In this study we report a negative appendectomy rate of 9 % in those who underwent a laparotomy and appendectomy.

The limitations of this study include that it was done retrospectively and from hospital records that may have had inaccuracies and missing data in recording. The sample size of the microbiology is not large enough to draw any conclusions.

Conclusion

Appendicitis is a common surgical emergency and we report higher mortality and morbidity rates from this study population than what is reported globally. The fast majority of our patients still have open appendectomies, even though access to laparoscopic equipment has improved. Factors that may predict the patient population most at risk of mortality in our setting include the duration of symptoms, delay to theatre, index CRP levels, number of relooks and type of surgery.

Despite numerous local studies demonstrating the safety and benefits of laparoscopy in complicated appendicitis, laparotomy remains the most practiced approach for ruptured appendix in South Africa (6,7). This may be driven by surgical expertise or bias, rather than lack of access to laparoscopic equipment.

Conflict of interest

No conflict of interest

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Ethical Approval

We received ethical approval from The University of the Witwatersrand Human Research Ethics Committee (MED22-05-049), as well as from the CEO of Charlotte Maxeke Hospital

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Appendix 1: Research Protocol

Candidate Name:	Irini Bogiages
Student Number:	2319172
Contact Number:	+27 82 773 7398
Candidate Email:	irinibogi@gmail.com
Supervisor Name:	Prof Emmanuel Thifhelimbilu Luvhengo (50%)
Qualifications:	MBChB (Medunsa), FCS (SA)
	Head of General Surgery
	Charlotte Maxeke Johannesburg Academic Hospital
Supervisor Name:	Prof Deirdré Kruger (50%)
Qualifications:	BSc, PGCHE, PhD (UK)
	Head of Research & Laboratories in Surgery
	Department of Surgery, University of Witwatersrand

Research proposal to be submitted as part of the research component in partial fulfilment of the Master of Medicine Degree in Surgery at the University of Witwatersrand, Johannesburg

Title:

Outcomes of Complicated Acute Appendicitis at a Central Academic Hospital in Johannesburg South Africa

Introduction

Acute appendicitis is a common surgical emergency worldwide[1-3]. Whilst there is variation in geographic locations, the estimated lifetime risk of developing acute appendicitis in the western literature is nearly 10%[1,3]. Since appendicitis was first described in 1886, incidence reports in developed nations have plateaued, contrasted to newly industrialized nations that report increasing incidence [1]. Globally appendicitis remains a burden on health care systems not only due to morbidity and mortality rates for each individual country, but also due the economic costs associated.

Acute appendicitis is a challenge for low- and middle- income countries due to limited resources and expertise[3]. In South Africa, the incidence of acute appendicitis is estimated to be less than 9 per 100,000[3].

Literature review

Traditionally the pathogenesis of acute appendicitis was described as a continuum[4,5] beginning with luminal obstruction secondary to a fecalith, lymphoid hyperplasia, a caecal tumour or intestinal parasites[4,5]. Luminal obstruction of the appendix is followed by bacterial overgrowth, ischaemia, necrosis of its wall and ultimately perforation[4,5]. Simple or non-complicated appendicitis is defined as appendicitis that presents before perforation, whilst complicated appendicitis is thought to be a consequence of appendicular perforation[4,5]. Newer hypotheses however suggest that the complicated appendicitis may be an entirely different biological process[4,6]. Moreover, simple and complicated appendicitis may not represent a natural progression of one disease process[4].

Whilst predominantly a disease of young males[1,3], acute appendicitis can occur in any age group and affect any gender. The classical symptom pointing toward appendicitis is a vague peri-umbilical pain which later migrate and become a localised right iliac fossa pain[3]. The pain of acute appendicitis is associated to a varying extent with fever, anorexia, nausea and vomiting[3]. Atypical or non-classical symptoms of acute appendicitis often do not include the migratory pain[1,3].

As mentioned earlier, at presentation appendicitis is either simple or complicated. Complicated appendicitis is an umbrella term for acute appendicitis that progressed to an inflammatory mass, appendix abscess or ruptured appendicitis with generalized peritonitis[1,5]. In the US, UK and Norway, complicated appendicitis accounts for 13 to 20 % of all presentations[1]. Predictably those that present with a complicated appendicitis would have a longer duration of symptoms[1]. However, the very young (<10 years old) and old (>50 years old) often present with complicated appendicitis within 48 hours of onset of symptoms[1].

The diagnosis of acute appendicitis uses a plethora of options and is often more a risk stratification than an absolute diagnosis as appendicitis can only be confirmed on histopathological examination[1]. It is sometimes difficult to differentiate simple from complicated appendicitis on clinical examination alone[1]. There is also no single biomarker that is sensitive enough in diagnosing acute appendicitis[1]. The diagnosis of acute appendicitis is thus based on a combination of clinical findings, laboratory results, risk stratification scores and imaging[1,3]. It is also important to differentiate simple uncomplicated from complicated acute appendicitis as they are managed differently.

Individuals who are at risk of complicated appendicitis include women who are pregnant, patients above the age of 65 years and those with immune compromising condition such as diabetes mellitus or have tested positive for the human immunodeficiency virus[6]. There is an association with gangrenous complicated appendicitis and admission leucocytosis as well as an elevated CRP[6].

The mainstay of treatment of acute appendicitis is surgical[1,3,5] and appendectomy is among the most common emergency surgical procedures[1,3,5]. Appendicectomy may be performed either using the open or the laparoscopic approach[1]. The laparoscopic approach has longer operative times and higher operative costs but has lower postoperative pain, postoperative complications, shorter length of hospital stay and earlier return to normal function[1]. Current guidelines recommend the laparoscopic approach over the open approach for simple uncomplicated appendicitis[1].

The most feared complication of acute appendicitis is free rupture with generalized peritonitis as it is associated with a higher mortality rate[1,5,7]. Patients who have ruptured appendix often require organ support in addition to surgical intervention[1,11]. The management of a patient who has ruptured appendicitis follows the principles which are contained in the Surviving Sepsis Guidelines and include fluid resuscitation, administration of a broad spectrum antibiotics and early control of the source control of sepsis[13]. Source control is achieved in theatre via laparoscopy or laparotomy[1,5,11]. Irrespective of the approach, appendectomy and abdominal drainage is done for generalised peritonitis[1]. Thereafter the patient is taken to ICU for further resuscitation[13]. Some patients who have had laparotomy or laparoscopy for ruptured appendix require a relook procedure, which may be planned or mandatory[1]. Whilst there is no consensus

on the absolute indication for a relook procedure, mandatory relook is indicated for extensive contamination or necrotizing fasciitis[1,3,5].

Although current international guidelines recommend laparoscopy over laparotomy for acute complicated appendicitis with purulent peritonitis, the ultimate choice of the operative approach is influenced by the surgeon's experience, institutional policies, and availability of equipment[1]. However, complicated appendicitis managed laparoscopically has had better outcomes than appendectomy via the open approach[16-20]. Despite local studies by Thomson et al. (2015), Yang et al. (2015), Ndofor et al. (2016) and Fusi et al. (2017) demonstrating the safety and benefits of laparoscopy in complicated appendicitis, open laparotomy remains the most practiced approach for ruptured appendix in South Africa[21-24]. A 2014 prospective study from 2 public hospitals in Cape Town report that 24.7 percent of appendectomies were performed laparoscopically[22].

The treatment of non-generalised complicated appendicitis such as appendiceal abscess and appendiceal inflammatory mass is non-operative, as operative management increases the risk of ileo-caecal resection and postoperative intestinal fistulae[25,26]. An abscess or an inflammatory mass should be suspected in patients who present with features of acute appendicitis and have a palpable mass in the right lower quadrant of the abdomen. An appendix abscess is confirmed by ultrasound or CT scan of the abdomen. The preferred treatment of an appendix abscess is image guided percutaneous drainage[1].

On admission a patient with acute appendicitis will have laboratory tests done which include WCC, CRP and sometimes procalcitonin and lactate level. Thereafter, an empiric broad spectrum antibiotic is administered intravenously. Antibiotics which are selected for the treatment of a patient who has complicated acute appendicitis should cover both aerobic and anaerobic organisms oral antibiotic biogram[1,5]. The most common organisms cultured from

patients who have acute appendicitis are Escherichia coli, Streptococcus species, Enterococcus species, and Pseudomonas aeruginosa[29].

Worldwide studies indicate that median length of hospital stay is about three days and about 2.4.3% of all presentations of acute appendicitis are admitted to ICU1,5,11. In South Africa mean length of hospital stay is 5 days, whereas an estimated 9.6 % of patients require ICU22. Additionally South African data including both simple and complicated cases report a wound sepsis of 19 percent postoperatively22.

In 1891 Mc Burney reported a 24.3% mortality in New York in patients with ruptured appendicitis21. Currently, high income countries report a mortality rate of around 3 per 1000 patients1,3. However, mortality in low-income areas such as Sub-Saharan Africa is reported to be as high as 54 per 10003,5,11. The emergency Laparotomy Network in the UK published the outcomes of emergency laparotomies in the UK. The above team reported a remarkably high mortality rate of 14 percent of all patients undergoing emergency laparotomies for any surgical indication27,28. Their study did not however include cases of acute appendicitis28.Furthermore, the Clavien-Dindo classification is currently one of the preferred methods to standardize reporting of post-operative complications30.

Motivation for this study.

Acute appendicitis is a common surgical emergency with the potential for significant morbidity and mortality especially when complicated. Majority of patients who have acute appendicitis in low- and middle-income present late when it has already complicated. Acute appendicitis remains a significant cause of ICU admission and mortality in low- and middle-income countries including South Africa. There is a need to study the outcome of patients who had

laparotomy for acute complicated appendicitis to in order to develop treatment strategies which may improve the results.

Research question

What is the outcome of laparotomy for complicated acute appendicitis at a central academic hospital in Johannesburg South Africa?

Aim

To determine the outcome of patients who presented with complicated acute appendicitis and had midline laparotomy.

Objectives

a) To determine demographic, clinicopathological findings and other risk factors in patients who had complicated acute appendicitis and were managed with a midline laparotomy.
b) To determine the outcome as measured by admission to intensive care unit (ICU), length of ICU stay, over-all length of hospital stay, mortality, complications (Clavien-Dindo classification), following midline laparotomy for patients who had complicated acute appendicitis.
c) To determine the microbiology and antibiogram of specimen taken during midline laparotomy for complicated acute appendicitis.

Materials and methods

i. ***Design***: A single-centre retrospective study will be conducted using in-patient hospital records from the Department of General Surgery at Charlotte Maxeke Johannesburg Academic Hospital. The record review will span from 01 January 2016 to 31 March 2021.
ii. ***Site of study***: The study will be conducted at the Department of General Surgery at Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, Gauteng.

iii. ***Study period: 1st of January 2016 to the 31st March 2021.***

iv. ***Study population***: All patients treated surgically for complicated appendicitis.

v. ***Sample size estimation***: On average 2-5 patients are admitted with complicated acute appendicitis weekly meaning that around 8-20 are admitted monthly and therefore 56-240 per year.

vi. Inclusion Criteria

a) Records of patients 18 years and older who were admitted to the General Surgery Department
b) Records of all patients managed via laparotomy for purulent peritonitis secondary to acute appendicitis
c) Patient with confirmed acute appendicitis on histology

vii. Exclusion criteria

a) Negative appendectomies.
b) Records of patients that were referred after the initial surgery.
c) Records of patients with incomplete medical records for the outcome variables.

viii. ***Measuring tool***: An electronic tool will be used to manually extract data from the in-patient medical records and databases as well as from the National Health Laboratories Services (NHLS) database (Appendix A). The following data will be extracted: demographic data (age, gender and race), comorbid conditions (HIV and Diabetes), duration of symptoms, type of surgical intervention, number of relooks, admission to intensive care unit (ICU), length of ICU stay, over-all length of hospital stay, microbiology, histology, time to surgery, mortality, complications as measured by the Clavien-Dindo grading classification which is both reproducible and objective, smoking status, admission inflammatory markers (white

cell count, C-reactive protein or pro-calcitonin) and intra operative findings. The above data is available for collection in hospital records.

ix. ***Sources of bias***: As this is a retrospective study some records may be missing or incomplete. The data recorded will be reliant on clinicians' findings which is subjective and may have variations from one surgeon to the next. There may be missing or lost investigations. Further there may be option bias as we may be choosing open surgery on very ill patients

Data analysis

To establish the outcome as measured by mortality in patients presenting with complicated appendicitis. Categorical variables will be summarised as frequencies and percentages. Continuous variables will be summarised as mean and standard deviation or median with interquartile range. To determine whether the relationships between categorical variables are statistically significant, the chi-squared test or Fisher's exact test will be carried out. The T-test or ANOVA will be performed for normally distributed data depending on the number of groups in the outcome variable of interest i.e. mortality: alternatively for non-parametric data the Mann-Whitney U test or Kruskal-Wallis test will be applied. Multivariable logistic regression will be utilised to describe the relationship between multiple predictor variables and mortality outcomes. All tests will be performed at the level of significance α=0.04.3%, using STATA v.16 (StataCorp, College Station, TX).

Funding

The estimate cost is R500 for photocopying which will be covered by the researcher.

Ethics

Ethics clearance is essential for this study to proceed; no data will be collected before ethics has been obtained from the Human Research Ethics Committee (Medical) of University of the Witwatersrand. Approval will also be sought from the Head of Department of Surgery at CMJAH, CMJAH Research Committee and the CEO of CMJAH. The study will also be entered into the National Health Research Database (NHRD). Ethics is required for this study as it research is on humans; however, this is a retrospective study and will have no direct influence of the management of the involved patient. Patient information will remain confidential, and because of this informed consent is not required from the patient. Consent will be required from the gatekeeper of the data. This research will be submitted to a reputable journal with the intention of being published.

TIMING

	Jul-Aug 2021	Aug-Sep 2021	Sep-Dec 2021	Dec-Jun 2022
Preparing protocol	X			
Protocol assessment		X		
Submission to ethics committee		X		
Data collection			X	
Data analysis				X
Final write-up				X

Problems

Apart from bias additional challenges to the research study include availability of the medical in-patient data and the retrieval of these records. Problems are likely to include incomplete, or lost records. Furthermore, there may be potential difficulty in accessing patient records

databases due to inaccuracies/inconsistencies in patient details such as name or hospital number.

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UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PROTOCOL ASSESSORS MEETING

Candidate Full Name: **Irini Bogiages** Supervisors: **Luvhengo/Kruger**

Student Number: **2319172** Date: **4th November 2021**

School / Department / Division: **Department of Surgery, Division of General Surgery**

Degree: **MMED**

Title: **Outcomes of Complicated Acute Appendicitis at a Central Academic Hospital in Johannesburg South Africa**

1. **Type study** *(tick all that apply)*:

- Quantitative
- Qualitative
- Mixed Methods
- Laboratory
- Clinical ✓
- Other, please specify.....

2. **Is title of the study appropriate** (*preferably fewer than 20 words*)? Yes✓ No

Comments: The title of the study is appropriate

3. **Are the study objectives clear and linked to the research aim and title?** Yes No✓

Comments: Not entirely
- Clarify specific outcomes in objective 2
- Include in your objectives that you would evaluate risk factors associated with your outcomes

4. **Is the design of the study appropriate to meet the study objectives?** Yes✓ No

- Comments:

Appendix 2: Protocol Assessors Meeting And Faculty Approval Letter

5. **Are the proposed methods and tools appropriate to meet the research objectives?** Yes | No✓

- Not entirely
  - Clarify the Clavien-dindo classification in your methods
  - Please include in your protocol that the data being collected are available

6. **Is the study feasible within the resources of:**

a) The applicant? Yes✓ | No

b) The department? Yes✓ | No

c) The time frame? Yes✓ | No

7. **If this is a PhD protocol assessment:**

a) Is the content original? Yes | No

b) Does the content show the scope and depth of a PhD? Yes | No

Comments: _____

_____

_____

_____

Do you recommend:

i. Additional revision/amendment of the protocol? Please be specific on the recommendations being made:

- Check protocol for grammatical errors
- Time period in your sections "Study period" and "Study design" differ, please clarify
- Timeline should be adjusted
- In your literature review, ensure that you distinguish between acute appendicitis or just appendicitis. And that this is considered in the flow of your writing.

ii. The appointment of the proposed Supervisor? Yes✓ | No

Nominee/s: The assessors approve the appointed supervisors

_____

_____

iii. The appointment of the proposed Co-Supervisor/s and/or additional co-supervisors? | Yes | No✓

Nominee/s: No co-supervisors required

_____

_____

iv. Has the Chair of the Assessor Group signed the RECOMMENDATION FOR APPOINTMENT OF SUPERVISOR(S) OF RESEARCH REPORT, DISSERTATION OR THESIS form? Please attach. | Yes | No✓

v. Has the Chair informed the student and supervisor about the Wits ethics requirements, and that if required, they must have either a Wits Human Research Ethics clearance certificate or a Wits Animal Research Ethics clearance certificate? | Yes✓ | No

vi. Based on the protocol provided (including any proposed changes by the protocol assessor group), does the student require:

1. Human Research Ethics clearance certificate	Yes✓	No
2. Animal Research Ethics clearance certificate	Yes	No
3. No human or animal ethics certificate is required	Yes	No
4. Unclear, will seek appropriate guidance from the HREC/AREC committees	Yes	No

vii. Has the Postgraduate student and supervisor/s signed the ethics declaration form | Yes | No✓

Overall recommendation regarding the protocol:

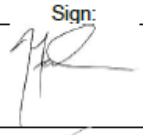
i. Revision of the protocol to the satisfaction of the Supervisor (**NB: if HoD approval is also required, please specify**): | Yes✓ | No
*(**Candidate**: one copy, list of corrections with page numbers and Supervisor approval letter – submit to PG Office).*

ii. Revision of the protocol to the satisfaction of the Assessor Group/Chair: | Yes | No
*(**Candidate**: one copy, list of corrections with page numbers, Supervisor approval letter – submit to PG Office and PG Office to forward to the Assessor Group Chair).*

iii. Revision of the protocol and resubmission of the revised protocol to the next Assessor Group Meeting: | Yes | No
*(**Candidate**: six copies, list of corrections with page numbers, Supervisor approval letter – submit one copy to PG Office / 5 to school assessor group administrator / for PhD, all six copies to be submitted to the PG Office).*

iv. Candidate goes ahead (*no revision required*): | Yes | No

Details of Assessors:

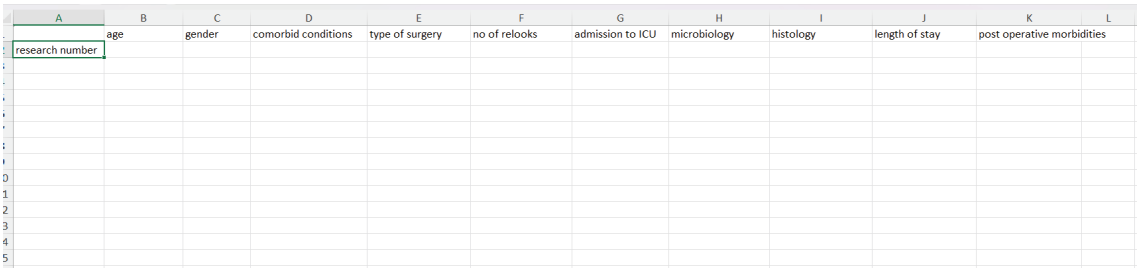
Name:	Email:	Sign:
Dr June Fabian	june.fabian@mweb.co.za	
Dr Daniel Surridge	surridge.daniel@gmail.com	

Details of Assessor Group Chair:

Name:	Email:	Sign:
Dr Ekene Nweke	Ekene.nweke@wits.ac.za	

Date: **10th November 2021**

Appendix 3: Data Collection Sheet



	A	B	C	D	E	F	G	H	I	J	K	L
1		age	gender	comorbid conditions	type of surgery	no of relooks	admission to ICU	microbiology	histology	length of stay	post operative morbidities	
2	research number											
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Appendix 4: Ethics Clearance Certification

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr I Bogiages

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220865

NAME: (Principal Investigator)	Dr I Bogiages
DEPARTMENT:	School of Clinical Medicine Department of Surgery Medical School University
PROJECT TITLE:	*Outcomes of complicated acute appendicitis at a central academic hospital in Johannesburg, South Africa*
DATE CONSIDERED:	2022/08/26
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Professors T Luvhengo and D Kruger
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2023/03/30

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **August** and therefore reports and re-certification will be due in the month of **August** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator _____ Date _____

Appendix 5: Plagiarism Declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I ____Irini Bogiages_____ (Student number: _____2319172_____) am a student registered for the degree of _____Master Of Medicine in Surgery _____ in the academic year ___2025____.

I hereby declare that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.

- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: irini bogiages Date: 25/05/2025

Appendix 6: Turnitin Report

Dr Bogiages MMed V7 01.05.2025_DKedits 020525_for Turnitin.docx

ORIGINALITY REPORT

6%	6%	4%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	academic.oup.com Internet Source	1%
2	www.wjgnet.com Internet Source	1%
3	www.ijlbpr.com Internet Source	1%
4	Zenon Pogorelić, Ivana Janković Marendić, Tin Čohadžić, Miro Jukić. "Clinical Outcomes of Daytime Versus Nighttime Laparoscopic Appendectomy in Children", Children, 2023 Publication	<1%
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Appendix 7: Letter Of Approval to conduct Research By Medical Advisory Committee

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG
ACADEMIC HOSPITAL

Enquiries: Ms N. Mzila
Email: Nolwazi.Mzila@gauteng.gov.za
Tel: 011 488 3365
Ref: 1/7/2
Date: 27 May 2023

GP_202205_029

Dear Irini Bogiages

RE: FINAL APPROVAL OF STUDY
TITLE: OUTCOMES OF COMPLICATED ACUTE APPENDICITIS AT A CENTRAL ACADEMIC HOSPITAL IN JOHANNESBURG SOUTH AFRICA.

Permission is granted for you to conduct the above-mentioned study as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic Hospital will not in any way incur or inherit costs as a result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall always be observed.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the HOD and Unit Manager or Sister in charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Supported / ~~Not Supported~~
Signed by:Jayshina Punwasi
Signed at:2023-06-01 08:54:18 +02:00
Reason:Witnessing Jayshina Punwasi

Dr J. Punwasi
Clinical Director

Approved / ~~Not Approved~~
Signed by:Gladys Magugudi Bogoshi
Signed at:2023-06-02 07:22:15 +02:00
Reason:Witnessing Gladys Magugudi Bo

Ms G. Bogoshi
Chief Executive Officer: CMJAH

Appendix 8: Approval Of Title

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

14 March 2022
Person No: 2319172
PAG

Dr I Bogiages
413 Queens Crescent
Lynnwood
0081
South Africa

Dear Dr Irini Bogiages

Master of Medicine in Surgery: Approval of Title

We have pleasure in advising that your proposal entitled *Outcomes of complicated acute appendicitis at a Central Academic Hospital in Johannesburg South Africa* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences