A retrospective audit into the morbidity and mortality of open abdominal aortic aneurysm repair at Groote Schuur Hospital, Cape Town

By

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DECLARATION

I, *Gugulethu Tsakani Jenny Mhlanga*, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Gugulethu T.J. Mhlanga

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LIST OF ABBREVIATIONS

AAA	abdominal aortic aneurysm
AKI	acute kidney injury
AKIN	Acute Kidney Injury Network
ARF	acute renal failure
ASA	American Society of Anaesthesiologists
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CVVHD	continuous venovenous haemodialysis
EVAR	endovascular aneurysm repair
GFR	glomerular filtration rate
GSH	Groote Schuur Hospital
HIV	human immunodeficiency virus
ICU	intensive care unit
IHD	intermittent haemodialysis
IL-18	interleukin 18
KDIGO	Kidney Disease: Improving Global Outcomes
KIM-1	kidney injury molecule 1
NGAL	neutrophil gelatinase-associated lipocalin
OSR	open surgical repair
QALY	quality-adjusted life years
RIFLE	Risk Injury Failure Loss End-stage renal disease
RRT	renal replacement therapy
SLEDD	sustained low efficiency daily dialysis

Part A: Research Protocol

As approved by the Department Research and Human Research Ethics committees, University of Cape Town

RESEARCH PROTOCOL

A retrospective audit of morbidity and mortality associated with open abdominal aortic aneurysm (AAA) repair at Groote Schuur Hospital, Cape Town.

INTRODUCTION

Open AAA repair is a major, high risk surgery and is associated with significant morbidity and mortality. Current literature quotes an overall mortality of ruptured AAA at 85-90%, including those who do not reach the operating theatre. Mortality of elective AAA repairs is 4-8%[1].

Many patients presenting with abdominal aortic aneurysms are elderly and have pre-existing medical conditions, therefore putting them at high risk for numerous post-operative complications.

Causes of post-operative morbidity include: renal failure, pulmonary and cardiac complications, as well as paralysis. Such post-operative complications lead to potentially increased ICU and hospital stays.

JUSTIFICATION FOR RESEARCH

An audit into the morbidity and mortality at Groote Schuur has not yet been formally performed. Such a retrospective audit will be useful in establishing where this hospital stands in terms of mortality, as compared with published data from other centres.

In terms of morbidity, this research will chiefly focus on the development of renal dysfunction following AAA repair. It is known that renal dysfunction is one of the five preoperative risk factors that predict mortality following ruptured AAA repair. It is the most easily assessed risk factor for a retrospective audit.

Other risk factors include: age >76 years, haemoglobin less than 9 g/dL, loss of consciousness and ECG evidence of ischaemia[2]. If renal dysfunction results in failure (defined as a creatinine >335 µmol/L, according to the RIFLE criteria), and necessitates renal replacement therapy, mortality can then be as high as 50%, independent of other risk factors[3].

By conducting an audit of renal failure post AAA repair at Groote Schuur, we will gain valuable insight into the allocation of resources, such as renal replacement therapy.

OBJECTIVE

Primary outcome: perioperative mortality associated with open repair of abdominal aortic aneurysms.

Secondary outcomes: incidence of acute kidney injury, need for renal replacement therapy and duration of hospital and ICU stays.

STUDY DESIGN

A retrospective file audit of emergency and elective open abdominal aortic aneurysm repairs will be carried out.

The researcher will review folders of patients who have had repairs in the past five years, or a cohort of 100 patients. Each folder number will be assigned a study number in the database, to ensure anonymity of subjects.

SUBJECT SELECTION

Study subjects selected will be those having undergone open AAA repair in the five-year period between 01 July 2009 and 30 June 2014. *(The study period was amended to October 2006 until 31 December 2014, in order to reach the target of 100 patients; the amendment was approved by the Human Research Ethics Committee on 02 December 2016)*.

Folder numbers will be obtained from theatre operation notes, which are kept at the Groote Schuur Hospital main theatre complex. The folders will be obtained, with due permission, from the Medical Records Department. Pertinent information will be extracted, taking care not to reveal subject identities.

EXCLUSION CRITERIA

- Patients who have undergone endovascular aneurysm repair (EVAR)
- Patients with thoraco-abdominal aortic aneurysm repairs

- Patients who did not survive operation of AAA; that is, those who demised during the initial operation
- Patients for whom a complete set of data is not available

MEASUREMENT

Data will be collected using a specially designed case record folder (see Appendix). The data collected will be captured electronically on a Microsoft Excel™ spread sheet.

LIST OF VARIABLES

- Gender
- Date of birth
- Age at operation
- Comorbidities—any known comorbidities, which will be indicated in clinical notes
- Date of operation
- Elective/Emergency
- Type of aneurysm (Saccular/Fusiform)—description in operation notes
- Position of aneurysm—indicated in operation and/or clinical notes; commonly described as infrarenal, juxtarenal and suprarenal
- Position of aortic cross-clamp (supracoeliac/suprarenal/infrarenal)
- Duration of aortic cross-clamp
- Date of admission to ICU
- Date of ICU discharge
- Total length of ICU stay
- Days ventilated
- Date of death
- Cause of death
- Date of hospital discharge
- Renal replacement therapy (RRT) commenced (Yes/No)
- Creatinine on admission to hospital— information on blood results will be obtained either from the patient file, or our National Health Laboratory Services database, using folder numbers.
- Creatinine on commencement of RRT

- Creatinine on date of death, or on discharge from hospital
- Dialysis dependent at hospital discharge (Yes/No)

QUALITY CONTROL

The data will be collected solely by the primary investigator, to ensure that all necessary variables are collected.

PILOT STUDY

Data will initially be collected for the year from 01 July 2013 to 30 June 2014. It is estimated that this will hopefully yield at least 20 study subjects and their folders. Should this target not be met (i.e. 20 study subjects within the selected year), then data will be collected retrospectively for a prolonged period, in order to gain an overall study population of 100.

ANALYSIS

Data analysis will be performed using Stata 13, and will utilise the Mann-Whitney and Fisher's Exact tests.

ETHICS AND COMMUNICATION

1. ETHICS

As this is a retrospective file audit, there is no need for consent. Subjects will not be contacted in any way, and patients' identities will not be revealed. Ethical approval will be obtained from the University of Cape Town's Human Research Ethics Committee.

2. REPORTING AND IMPLEMENTATION

The outcome of this research will especially be communicated to the Department of Vascular Surgery, as well as the Department of Critical Care. The results of this audit could form a basis from which other studies can then be performed.

RESEARCH TIMETABLE

December 2014 to June 2015	Ethics approval; data collection; commencement of literature review
June 2015 to May 2016	FCA Part 2 examination preparation
May 2016 to November 2016	Data analysis, in conjunction with statistician; write-up of results
November 2016	Submission of dissertation

BUDGET AND OTHER LOGISTICS

There is no need for external funding. Costs will be borne by the primary investigator.

Folder numbers of subjects having undergone open repair of AAA, will be obtained from theatre operating notes. Files will be drawn from Medical Records Department, in order to collect pertinent information.

REFERENCES

1. van der Vliet J, Boll AP, Leger AS, et al. Abdominal aortic aneurysm. *Lancet*. 1997;349(9055):863-866. doi:10.1016/S0140-6736(96)07282-0.
2. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. *Lancet*. 2005;365:1577-1589.
3. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. *Lancet*. 2005;365(9457):417-430. doi:10.1016/s0140-6736(05)17831-3.

Part B: Literature Review

MORBIDITY AND MORTALITY ASSOCIATED WITH OPEN ABDOMINAL AORTIC ANEURYSM REPAIRS

1. OBJECTIVES OF LITERATURE REVIEW

The purpose of this literature review is to provide a brief overview on the topic of abdominal aortic aneurysms (AAAs) and the surgical repair thereof. The researcher will then examine the mortality and morbidity associated with open AAA repairs at different centres, paying special attention to acute kidney injury, and its outcomes following renal replacement therapy. Lastly, the researcher will review the costs associated with renal replacement therapy.

2. LITERATURE SEARCH STRATEGY

The researcher conducted PubMED and Google Scholar searches through the University of Cape Town's Faculty of Health Sciences' online library.

3. QUALITY CRITERIA

A PubMed MeSH search was conducted using the following keywords: Aortic aneurysm, abdominal AND acute kidney injury AND surgery. Using Google Scholar, a literature search to identify articles of relevance to this topic was conducted using the following keywords and phrases: abdominal aortic aneurysm repair mortality, emergency versus elective abdominal aortic aneurysm open repair mortality, renal failure AAA, renal replacement therapy costs, renal replacement therapy outcomes.

4. REVIEW AND CRITICAL APPRAISAL OF LITERATURE

4.1. OVERVIEW OF ABDOMINAL AORTIC ANEURYSM REPAIR

4.1.1. INTRODUCTION

Abdominal aortic aneurysm (AAA) is defined as a full-thickness widening or dilatation of the infradiaphragmatic aorta to a diameter of greater than 3.0 cm. The

normal diameter of the abdominal aorta in adults ranges from 2.0 to 3.0 cm. The underlying mechanism of the development of aneurysms is still unclear. However, it is pathologically marked by the degradation of the elastic media of the aorta. In most cases, non-specific degeneration and atheromatous changes of the aorta contribute to this degradation. Others aneurysms can be attributed to chronic infection such as tuberculosis, acute infection, trauma, inflammatory disorders and connective tissue disorders[1].

Abdominal aortic aneurysms are categorised anatomically according to aetiology, morphology and position. The morphology of an aneurysm can be described either as fusiform or as saccular, and is linked to its aetiology. 'Fusiform' implies that the entire circumference of the aorta is involved. Fusiform aneurysms tend to be from non-specific, degenerative causes. 'Saccular' implies that only a part of the circumference is involved. Saccular aneurysms mostly have other, usually infective, aetiologies. The majority of AAAs are fusiform[27].

The position of the aneurysm is described in relation to the renal arteries. Suprarenal aneurysms involve that portion of the aorta that is above the renal ostia. Juxtarenal aneurysms are situated below the renal ostia, where there is no segment of non-aneurysmal aorta between the renal arteries and the aneurysm. Infrarenal aneurysms are situated below the level of the renal arteries, where there is a segment of nonaneurysmal aorta between the renal arteries and the beginning of the aneurysmal dilatation[27].

4.1.2 INCIDENCE OF AAA

AAAs affect more males than females, being more common in those older than 65 years of age. Studies place the prevalence of AAAs in males at 1.3-8.9%, and at 1.0-2.2% in females[1]. The greatest contributor to aneurysm formation and progression is tobacco smoking[2]. Other factors that have been identified include hypertension, hyperlipidaemia, chronic obstructive pulmonary disease (COPD) and a positive family history of AAA[1]. Patients presenting with AAAs are likely to have one or more comorbidities.

Aneurysmal dilatation of the aorta may be asymptomatic, being diagnosed on routine abdominal examination. Some patients do become symptomatic,

experiencing back, abdominal and/or flank pain, tenderness over the aneurysm, or the non-specific systemic symptoms of malaise and fever[27].

Elective surgical repair of AAAs is usually carried out in the asymptomatic patient with an aneurysm diameter exceeding 5.5cm, or in the symptomatic patient with an aneurysm of any diameter. Current guidelines state that operating in an asymptomatic patient with an AAA with a diameter of less than 5.5cm does not confer any benefit in terms of post-operative mortality or morbidity[3].

Ruptured AAAs require emergency repair. Rupture of the aorta occurs when arterial wall thickness deteriorates to such an extent as to result in extravasation of blood. Among the patients who present with ruptured AAAs, and who undergo emergency repair, the mortality rate is as high as 85-90%[1].

4.1.3 SURGICAL REPAIR OF AAA

The mainstay of surgical repair is via the open route, through either transperitoneal (midline or transverse) or retroperitoneal approaches[27].

Endovascular repair of abdominal aortic aneurysms (EVAR) has been gaining popularity since it was introduced in the early 1990s; currently it is reserved for those patients deemed unfit for open repair of the AAA[4].

EVAR is significantly less invasive, and better tolerated, than open AAA, as access to the aneurysm is obtained through groin dissection and cannulation. EVAR does not involve aortic cross-clamping, and so avoids the negative sequelae thereof. The aneurysm must, however, be anatomically suitable for EVAR; that is, there must be sufficient normal aorta above and below the aneurysm to adequately seat the graft.[5]

4.1.4 PHYSIOLOGY OF AORTIC CROSS-CLAMPING

Open surgical repair of AAAs, by whichever approach, involves exposure of the aorta, aortic cross-clamping, and placement of a graft. This is followed by aortic unclamping and reperfusion of the distal structures.[6]

The anatomical level of the aneurysm will determine the level of aortic cross-clamp placement. The physiological sequelae of cross-clamping depend on the level of cross-clamp placement, being more exaggerated with more proximal placement.

Cross-clamp placement results in increased systemic vascular resistance and arterial pressure, as well as an increased myocardial afterload. The increased afterload results in enhanced myocardial contractility and oxygen demand[7]. There is interruption of the blood supply to the lower body. Perfusion of structures distal to the clamp thus becomes dependent on collateral blood supply. During cross-clamping, organs with blood supply originating from the distal aorta are vulnerable to ischaemia and subsequent injury. Regardless of the level of the clamp, renal perfusion is affected; in fact, infrarenal clamps are said to decrease renal blood flow by up to 60%[6].

Unclamping of the aorta conversely results in sudden decrease in afterload, which may necessitate attenuation via the administration of fluids and/or vasopressors. Reperfusion of ischaemic tissue leads to the release of vasoactive substances, which suppress myocardial tissue and further exacerbate hypotension[7]. The decrease in afterload causes a decrease in coronary blood flow, which is likely to result in myocardial ischaemia if left untreated.

4.2 POST-OPERATIVE MORBIDITY AND MORTALITY

Hertzer et al[8] from the Cleveland Clinic published data collected from 1989 to 1998. In that period, there were 1 135 patients that underwent open repairs of infrarenal AAAs. The majority of those patients were male (985 versus 150 female); the median age was 70 years. They reported a 30-day mortality of 1.2%. Mortality was due to cardiac causes in three patients, pulmonary complications in three cases and multiorgan failure in four patients. Four (4) deaths were attributed to a category termed ‘other causes’.

Six patients (0.5%) required dialysis postoperatively, excluding patients who were on dialysis prior to surgery. Complication rates tended to be increased in those patients with COPD, prior congestive cardiac failure, pre-existing renal insufficiency, pre-operative dialysis, and increased age.

In the UK Small Aneurysm Trial[3], a total of 1 090 patients were randomised to two groups: early (aortic diameter 4.0-5.5cm) versus late (aortic diameter >5.5cm) open repair of AAAs. Five hundred and sixty-three (563) patients were assigned to the former, early group, and 527 were assigned to the latter, surveillance group. Five hundred and seventeen (517) of the early group ultimately underwent elective

repair, and a further two patients underwent emergency repair for aneurysm rupture. In the latter group, 321 patients eventually underwent elective repair. Patients in the two groups were comparable in terms of age and gender, and were followed up for a period of five years. In the early open surgery group, the 30-day mortality was 5.8%. Certain risk factors were associated with a higher risk of death. These included: increased age, larger aortic diameter, poorer lung function, and lower ankle/brachial index (a marker of severe peripheral vascular disease). In the surveillance group, 321 out of 527 underwent elective repair. One hundred and fifty (150) of these patients died during the trial. This group had 17 deaths from ruptured AAAs (compared with six deaths from the same aetiology in the early surgery group).

The 820 patients from the UK Small Trial who underwent elective open repair of their AAAs were further analysed, in order to ascertain identifiable risk factors for post-operative death. The 30-day mortality was 5.6%. The leading cause for death was cardiac, followed by pulmonary and renal causes of death.

Menard et al[9] followed a series of 572 patients undergoing surgical repair of unruptured infrarenal AAAs between 1990 and 2000. They separated these patients into low-risk and high-risk groups. Patients belonging to the high-risk groups were those with higher American Society of Anaesthesiologists (ASA) grading, age greater than 80 years, pre-operative serum creatinine greater than 3.0 mg/dL (265 µmol/L), pulmonary insufficiency (domiciliary oxygen use, FEV1 <20% of predicted or FEF25-75 <20% predicted), hepatic failure and cardiac dysfunction (LVEF <20%, congestive heart failure, unstable angina, coronary artery disease not amenable to grafting, and symptomatic aortic stenosis). One hundred and twenty-eight (128) of their patients met one or more criteria for high risk. The other 444 patients were classified as low risk. The 30-day mortality in the high risk group was 4.7%, and 0.0% in the low risk group. This brought the overall 30-day mortality of the cohort of 572 patients to 1.0%. The five year survival rate was 46% (high-risk) and 74% (low-risk). Morbidity was higher in those patients flagged as high-risk, than in their low-risk counterparts. The major complications were myocardial infarction, renal failure and pneumonia, as in the UK Small Trial. Renal failure occurred in 7% of patients in the high risk group, and <1% in the low risk group.

4.3 LONG-TERM OUTCOMES OF OPEN AAA REPAIR

Long-term outcomes are determined by evaluating beyond five-year mortality. Biancari et al[10] followed up on 208 subjects who underwent open AAA repair at their

centre, in order to evaluate the durability of repair, and reported on five-, 10-, and 15 year survival rates. The median follow-up period was 8.0 years. The 15-year survival rate was 18%. Late mortality was found to be due to myocardial ischaemia, cerebrovascular events, pulmonary diseases and cancer. Reoperation was necessary in 27 patients. Hertzer and Mascha in Cleveland documented a 15-year survival rate of 16%[11].

Long term survival is affected by graft durability. Graft related complications include: proximal and distal pseudoaneurysms and graft occlusions, graft-enteric erosion fistulae, graft sepsis, atheromatous plaque embolism, anastomotic leak, and colonic ischaemia[12].

4.4. POST-OPERATIVE RENAL COMPLICATIONS

Acute kidney injury (AKI), previously known as acute renal failure (ARF), refers to a sudden and sustained decrease in renal function[13] with subsequent accumulation of nitrogenous and non-nitrogenous waste products. It may also be associated with hyperkalaemia and metabolic acidosis.

The incidence of AKI in the general hospital population is reported at about 5%, and about 30-50% in intensive care unit patients[14].

AKI is an important negative prognosticator. Existing data of all-cause acute renal failure requiring renal replacement therapy in intensive care units, shows a mortality rate of between 40 and 80%[14,15]. The wide range in reported mortality may be attributed to the varying definitions of AKI that are used in different studies.

AKI rarely occurs in isolation, usually occurring in conjunction with failure of one or more other systems.

Korkeila et al[14] studied 3447 ICU patients admitted during the period 1992-1993. Sixty-nine of these patients (2%) required renal replacement therapy during their ICU stay. They showed an in-ICU mortality of 34%, and an in-hospital mortality of 45%. At six months, the mortality was 55%. This increased to 65% at 5 years.

AKI complicates the post-operative course of AAA repairs, partly due to pre-existing renal disease, and also because of reduced renal blood flow during periods of aortic cross clamping. Following the release of aortic cross clamping, reperfusion to the kidney may also contribute to AKI.

In the Cleveland Clinic's series of elective open infrarenal AAA repairs[8], 1.7% of their patients developed acute renal insufficiency post-operatively, defined in their study as an increase in serum creatinine of greater than 1 mg/dL (88.4 µmol/L). Six (6) patients who were not on dialysis prior to surgery required dialysis. In that series, 57 patients had a pre-operative serum creatinine of greater than 2 mg/dL (177 µmol/L). An additional nine patients were on renal dialysis prior to elective AAA repair[8].

Castagno et al[16] investigated the incidence of AKI in both open and endovascular repairs of infrarenal AAAs. In the open repair subgroup comprising 285 participants, 75 patients (26.3%) developed AKI. The study found that those who developed post-operative AKI had higher pre-operative serum creatinine concentration. Risk factors for the development of AKI included: current smoking, hypertension, chronic kidney disease, and arrhythmias.

In the study by Menard et al[9], renal failure complicated the post-operative course of 13 out of the total 572 patients, or 2.3% of their study population. The five-year survival rate (5YSR) was worse in those patients with a higher creatinine. Patients with a serum creatinine of greater than 3.0 mg/dL (265 µmol/L) had a 5YSR of 11%. Comparatively, in those with a serum creatinine of 2.0-3.0 mg/dL (177-265 µmol/L), the 5YSR was 45%[9].

Twenty to forty-six percent (20-46%) of patients with ruptured AAAs develop AKI. Barratt et al[17] looked specifically at the outcomes of patients developing renal failure following open repair of ruptured AAA. They retrospectively investigated cases admitted to the ICU from 1984 to 1996, excluding those who had had pre-existing, dialysis-dependent renal disease. The authors defined acute renal failure as an increase of serum creatinine to greater than 600 µmol/L, or the commencement of renal replacement therapy for hyperkalaemia, acidosis or fluid overload. Sixty-five cases were identified for analysis. It was observed that AKI occurred at a median of 4 days post-operatively. 75% of those who developed AKI died in hospital. Those who developed isolated AKI survived, whereas the development of multi-organ failure worsened outcomes. Of the survivors, 56% did not survive beyond five years after operation. This study did not report the percentage of patients with ruptured AAAs who developed AKI.

4.5. DETECTION OF ACUTE KIDNEY INJURY AND RIFLE/KDIGO CLASSIFICATION

Several groups have attempted to define classify acute kidney injury in recent years. In 2004, the Acute Dialysis Quality Initiative (ADQI) workgroup proposed the RIFLE (Risk Injury Failure Loss End-stage renal disease) criteria, which utilises glomerular filtration rate (GFR) and urine output in order to classify acute kidney injury[13], as in the table below.

	GFR criteria	**Urine output criteria**
Risk	Serum creatinine increased 1.5 times	<0.5 mL/kg/hour for 6 hours
Injury	Serum creatinine increased 2.0 times	<0.5 mL/kg/hour for 12 hours
Failure	Serum creatinine increased 3.0 times, or creatinine >355 µmol/L when there was an acute rise of >44 µmo/L	<0.3 mL/kg/hour for 24 hours or anuria for 12 hours
Loss	Persistent acute renal failure; complete loss of kidney function for longer than four weeks	
End-stage renal disease	End-stage renal disease for longer than three months	

Therefore, according to the RIFLE classification, acute renal failure was diagnosed when the serum creatinine had exceeded 355 µmol/L, had risen by more than 44 µmol/L, or had risen by more than three times the baseline creatinine.

In 2007, the Acute Kidney Injury Network (AKIN), which included members of the original ADQI group, proposed a change of terminology from ‘acute renal failure’ to ‘acute kidney injury’ in order to encapsulate the entire spectrum of renal dysfunction.

AKIN proposed that a diagnosis of acute kidney injury be made if there was an “abrupt (within 48 hours) reduction in kidney function, (then) currently defined as an absolute increase in serum creatinine of more than or equal to 26.4 µmol/L, a percentage increase in serum creatinine of more than 1.5 times the baseline value, or a reduction of urine output (<0.5 ml/kg/hour for 6 hours)”[18]. The diagnostic criteria for AKI closely mirror the criteria for ‘Risk’ under the RIFLE criteria.

More recently, there has been recognition of the need to unify global guidelines pertaining to the management of acute kidney injury. This is with the aim of improving patient outcomes. The Kidney Disease: Improving Global Outcomes (KDIGO) foundation in 2012 released clinical practice guidelines, which incorporated the RIFLE/AKIN criteria into a single definition, namely: an increase in serum creatinine by >0.3 mg/dL (>26.5 µmol/L) within 48 hours; an increase in serum creatinine to >1.5 times the baseline within seven days; or a urine volume <0.5 ml/kg/hour for six hours.

KDIGO goes on to grade the severity of acute kidney injury:

- Grade 1: the aforementioned definition of AKI, namely an increase in serum creatinine by >0.3 mg/dL (>26.5 µmol/L) within 48 hours; an increase in serum creatinine to >1.5 times the baseline within seven days; or a urine volume <0.5 ml/kg/hour for six hours
- Grade 2: serum creatinine increase of 2.0-2.9 times the baseline, or a urine output of <0.5 ml/kg/hour for a duration exceeding 12 hours
- Grade 3: a serum creatinine increase of more than 3.0 times the baseline, a serum creatinine of >353.6 µmol/L, initiation of renal replacement therapy, a decrease of estimated GFR to <35 ml/min per 1.73m^2, or anuria for >24 hours[19]

KDIGO grade 3 correlates with the RIFLE classification: Failure stage.

Serum creatinine as a marker for renal injury has its limitations, as the production of creatinine is dependent on muscle mass. Thus, creatinine may be falsely normal in the elderly, who develop sarcopenia. The search continues for the ideal marker of acute kidney injury. Several serum and urine biomarkers have been identified as being potentially useful in the early detection of renal injury, including serum- and urinary neutrophil gelatinase-associated lipocalin (NGAL), serum cystatin C, urinary kidney injury molecule 1 (KIM-1) and urinary interleukin 18 (IL-18)[20,21]. These assays are undergoing validation for use in humans, and have not been incorporated into any acute kidney injury classification system.

For the purposes of this dissertation, we chose to use serum creatinine changes in order to quantify the severity of acute kidney injury post AAA repair. Serum creatinine is an easier parameter to retrospectively audit than urine output in ICU. Furthermore, we used KDIGO stage 3 to denote those in need of renal replacement

therapy. Tests of serum or urinary biomarkers of renal dysfunction are not yet available at Groote Schuur Hospital.

4.6. INSTITUTION OF RENAL REPLACEMENT THERAPY

The institution of renal replacement therapy is at the discretion of attending clinicians. Historically, the indications for dialysis are:

- Refractory hyperkalaemia
- Severe or worsening metabolic acidosis
- Refractory pulmonary oedema
- Uraemic encephalopathy or pericarditis

There is no consensus regarding the optimal time to initiate dialysis. General consensus is that earlier RRT is associated with lower mortality. In a systematic review, Joannidis et al[22] concluded that initiating RRT before the onset of uraemic symptoms was associated with a better outcome. Bagshaw et al[23] demonstrated that late initiation of RRT (more than five days from ICU admission) was associated with prolonged RRT, hospital stay, and worsened renal recovery. There was, however, no definitive serum urea or creatinine concentration identified above which to commence RRT.

The KDIGO guidelines advise clinicians to monitor trends in urea and creatinine, rather than single values, when making the decision to institute RRT[19]. Apart from a comment on emergently initiating RRT in the case of life-threatening metabolic acidosis, hyperkalaemia or volume overload, KDIGO makes no recommendation on the optimal time to initiate RRT.

4.7. TYPES AND COST OF RENAL REPLACEMENT THERAPY

Renal replacement therapy is a broad term that can be used to describe haemodialysis, haemofiltration, haemodiafiltration, peritoneal dialysis and renal transplantation. In the post-operative and ICU settings, and for the purpose of this review and dissertation, RRT refers to haemodialysis.

Haemodialysis is broadly divided into two different modalities: namely, intermittent haemodialysis and continuous haemodialysis. Intermittent haemodialysis can further

be divided into intermittent haemodialysis (IHD), as well as prolonged intermittent haemodialysis, otherwise known as sustained low efficiency daily dialysis (SLEDD). Continuous venovenous haemodialysis (CVVHD) is the sole example of continuous haemodialysis.

Decisions pertaining to the type of renal replacement therapy instituted are determined by the clinical condition of the patient. The different modalities have implications on speed of solute and volume removal, and thus affect the patient's haemodynamic profile to varying degrees. CVVHD confers the greatest haemodynamic stability to its recipients. IHD is usually administered over a period of 4-6 hours, during which a large amount of fluid can be removed. It may have a negative effect on a patient's haemodynamics, which has negative implications on renal recovery[24]. SLEDD is occasionally described as a compromise between the aforementioned modalities. In a comparison between CVVHD and SLEDD, there was some evidence that SLEDD was associated with improved outcome in terms of higher post-dialysis mean arterial pressure and subsequently, a lower mortality[25]. The study was carried out on only 101 patients; therefore, that has yet to be tested on a larger population.

Haemodialysis is a costly intervention. Factors which contribute to the high cost include human resource costs (staffing), as well as the cost of equipment and consumables. In terms of staffing, SLEDD is the cheapest modality. In terms of consumables, CVVHD (ZAR 2 727) is the most expensive when compare to IHD (ZAR 1 950) and SLEDD (ZAR 2 076). The prices quoted are the daily cost of each modality, but also include the initial cost of a vascular catheter, which is usually replaced at least every seven days to prevent line-related sepsis. These prices are correct as of August 2016.

Studies looking at the cost-effectiveness of renal replacement therapy must take into account patient survival at six months and five years, as well as quality of life. To adequately represent long-term cost-effectiveness, researchers utilise the concept of quality-adjusted life-years (QALYs). Overall, renal transplantation provides the best results in terms of QALYs[26].

In the study carried out by Korkeila et al[14], the quoted cost per 6-month survivor as USD 80 000, with good quality of life reported by the subjects. Moreover, the patients who did not survive ICU tended to have multi-organ failure, which prolonged ICU stay. Thus, the cost of care was ultimately greater.

4.8 IMPLICATIONS FOR RESEARCH

To our knowledge, the morbidity and mortality associated with open AAA repair at Groote Schuur has not been quantified. In view of the evidence in literature, this audit will focus on examining the mortality of both elective and emergency open AAA repair, comparing the mortality at GSH with current global trends. It will also examine the incidence and outcomes of RRT in the post-operative period. For the purposes of this dissertation, KDIGO stage 3 will be used to indicate those patients who meet the criteria for the institution of RRT.

REFERENCES

1. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. *Lancet*. 2005;365:1577-1589.

2. Wilmink TBM, Quick CRG, Day NE. The association between cigarette smoking and abdominal aortic aneurysms. *J Vasc Surg*. 1999;30:1099-1105.

3. UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet*. 1998;352(9141):1649-1655. doi:10.1016/S0140-6736(98)10137-X.

4. Prinssen M, Verhoeven E, Buth J, et al. A Randomized Trial Comparing Conventional and Endovascular Repair of Abdominal Aortic Aneurysms. *N Engl J Med*. 2010;351(16):2487-2498. doi:10.1056/NEJMoa1514204.

5. Greenhalgh RM, Brown LC, Kwong GPS, Powell JT, Thompson SG. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet*. 2004;364(9437):843-848. doi:10.1016/S0140-6736(04)16979-1.

6. Al-Hashimi M, Thompson J. Anaesthesia for elective open abdominal aortic aneurysm repair. *Contin Educ Anaesthesia, Crit Care Pain*. 2013;13(6):208-212. doi:10.1093/bjaceaccp/mkt015.

7. Gelman S. Pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82(4):1026-1060.

8. Hertzer NR, Mascha EJ, Karafa MT, O'Hara PJ, Krajewski LP, Beven EG. Open infrarenal abdominal aortic aneurysm repair: The Cleveland Clinic experience from 1989 to 1998. *J Vasc Surg*. 2002;35(6):1145-1154. doi:10.1067/mva.2002.123686.

9. Menard MT, Chew DKW, Chan RK, et al. Outcome in patients at high risk after open surgical repair of abdominal aortic aneurysm. *J Vasc Surg*. 2003;37(2):285-292. doi:10.1067/mva.2003.121.

10. Biancari F, Ylönen K, Anttila V, et al. Durability of open repair of infrarenal abdominal aortic aneurysm: A 15-year follow-up study. *J Vasc Surg*. 2002;35(1):87-93. doi:10.1067/mva.2002.119751.

11. Hertzer NR, Mascha EJ. A personal experience with factors influencing survival after elective open repair of infrarenal aortic aneurysms. *J Vasc Surg*. 2005;42(5):1-10. doi:10.1016/j.jvs.2005.08.003.

12. Hallett J, Marshall DM, Petterson TM, et al. Graft-related complications after abdominal aortic aneurysm repair: Reassurance from a 36-year population-based experience. *J Vasc Surg*. 1997;25(2):277-286. doi:10.1016/S0741-5214(97)70349-5.

13. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. *Lancet*. 2005;365(9457):417-430. doi:10.1016/s0140-6736(05)17831-3.

14. Korkeila M, Ruokonen E, Takala J. Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. *Intensive Care Med*. 2000;26(February):1824-1831. doi:10.1007/s001340000726.

15. Åhlström A, Tallgren M, Peltonen S, Räsänen P, Pettilä V. Survival and quality of life of patients requiring acute renal replacement therapy. *Intensive Care Med*. 2005;31(9):1222-1228. doi:10.1007/s00134-005-2681-6.

16. Castagno C, Varetto G, Quaglino S, et al. Acute kidney injury after open and endovascular elective repair for infrarenal abdominal aortic aneurysms. *J Vasc Surg*. 2016;64(4):928-933.e1. doi:10.1016/j.jvs.2016.02.048.

17. Barratt J, Parajasingam R, Sayers RD, Feehally J. Outcome of Acute Renal Failure Following Surgical Repair of Ruptured Abdominal Aortic Aneurysms. *Eur J Vasc Endovasc Surg*. 2000;168(August):163-168.

doi:10.1053/ejvs.2000.1078.

18. Mehta RL, Kellum JA, Shah S V, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2). doi:10.1186/cc5713.

19. Kellum J A, Lameire N, Aspelin P, et al. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl*. 2012;2(1):1-138. doi:10.1038/kisup.2012.7.

20. Nguyen MT, Devarajan P. Biomarkers for the early detection of acute kidney injury. *Pediatr Nephrol*. 2008. doi:10.1007/s00467-007-0470-x.

21. Devarajan P. Biomarkers for the early detection of acute kidney injury. *Curr Opin Pediatr*. 2011;23(2):194-200. doi:10.1097/MOP.0b013e328343f4dd.

22. Joannidis M, Forni LG. Clinical review: timing of renal replacement therapy. *Crit Care*. 2011;15(3):223. doi:10.1186/cc10109.

23. Bagshaw SM, Uchino S, Bellomo R, et al. Timing of renal replacement therapy and clinical outcomes in critically ill patients with severe acute kidney injury. *J Crit Care*. 2009;24(1):129-140. doi:10.1016/j.jcrc.2007.12.017.

24. Bell M, Granath F, Schön S, Ekbom A, Martling CR. Continuous renal replacement therapy is associated with less chronic renal failure than intermittent haemodialysis after acute renal failure. *Intensive Care Med*. 2007;33(5):773-780. doi:10.1007/s00134-007-0590-6.

25. Wu V-C, Wang CH, Wang WJ, et al. Sustained low-efficiency dialysis versus continuous veno-venous hemofiltration for postsurgical acute renal failure. *Am J Surg*. 2010;199(4):466-476. doi:10.1016/j.amjsurg.2009.01.007.

26. Haller M, Gutjahr G, Kramar R, Harnoncourt F, Oberbauer R. Cost-effectiveness analysis of renal replacement therapy in Austria. *Nephrol Dial Transplant*. 2011;26(February):2988-2995. doi:10.1093/ndt/gfq780.

27. Collins, KA. Overview of abdominal aortic aneurysm. In: *UpToDate*, Post TW (Ed), UpToDate, Waltham, MA (Accessed on 05 November 2016).

Part C: Publication-ready manuscript

TITLE PAGE

A retrospective audit of the mortality and morbidity associated with open abdominal aortic aneurysm (AAA) repair at Groote Schuur Hospital, Cape Town

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ABSTRACT

Background: Open AAA repair is a major, high risk surgery and is associated with significant morbidity and mortality. Current literature quotes an overall mortality of ruptured AAA at 85-90%, including those who do not reach the operating theatre. Mortality of elective AAA repairs is 4-8%. Many patients presenting with abdominal aortic aneurysms are elderly and have pre-existing medical conditions, therefore putting them at high risk for numerous post-operative complications, such as acute kidney injury, pulmonary and cardiac complications. These complications lead to potentially increased ICU and hospital stays.

Objectives: To the author's knowledge, an audit into the morbidity and mortality at Groote Schuur Hospital has not yet been formally performed. Such a retrospective audit will be useful in establishing where this hospital stands in terms of mortality, as compared with published data from international centres. In terms of morbidity, this research focused on the development of acute kidney injury following AAA repair.

Methods: The study design was an observational retrospective file audit, of both emergency and elective open abdominal aortic aneurysm repairs. 90 case reports of operations performed between October 2006 and December 2014 were analysed. The primary outcome measure was the incidence and causes of perioperative (30-day) mortality. The secondary outcome measure was the incidence of acute kidney injury and renal replacement therapy (RRT). We further analysed whether cross-clamp time and anatomical classification of the aneurysm had any effect on the subsequent need for RRT, utilising the Mann-Whitney test.

Results: Of the 90 patients, 76.7% were male (n=69). The study population had a mean age of 64.9 years. Overall perioperative (30-day) mortality of both emergency and elective cases was 15 out of 90 cases (16.6%); the mortality for emergency cases was 12 out of 31 (38.7%), as compared to 3/59 (5.1%) for elective cases. Seventeen patients (18.9%) developed KDIGO stage 3 AKI, and RRT was instituted in 12 cases (13.3% of all patients); seven patients survived, and no patients were dialysis-dependent on hospital discharge. AKI was not significantly associated with abdominal aortic cross-clamp time (46 minutes vs. 38 minutes, p=0.9021), but was significantly associated with anatomical classification of the aneurysm (supra-/juxtarenal vs. infrarenal, p=0.037).

Conclusions: In comparison with research from international centres, this study population was predominantly male, with a similar age profile to that quoted. The bulk of the perioperative mortality was from emergency AAA repairs, with the mortality associated with elective open AAA surgical repair being within the ranges quoted in international literature. Of the patients who received RRT, there was a mortality of 41.6%. There were many limitations in this study, as the population analysed was extremely heterogeneous, owing to the small sample size. There is great potential for further research, especially into the outcomes of open versus endovascular repairs of AAAs.

A RETROSPECTIVE AUDIT/STUDY INTO THE MORBIDITY AND MORTALITY ASSOCIATED WITH OPEN ABDOMINAL AORTIC ANEURYSM REPAIRS AT GROOTE SCHUUR HOSPITAL, CAPE TOWN

INTRODUCTION

Aortic aneurysm repairs, in various forms, have been performed since the 2nd century[1]. The first instance of abdominal aortic ligation was described in 1817, by Astley Cooper. Subsequently, significant advances have been made in the management of aortic aneurysms, with the modern techniques for open surgical repair (OSR) of abdominal aortic aneurysms (AAA) being developed in the 1940s and 1950s[1]. Endovascular repair of abdominal aortic aneurysms (EVAR) was introduced as an alternative to open repair in the early 1990s[2]. Despite the subsequent refinement of the endovascular technique, open abdominal aortic aneurysm (AAA) repair is still considered an important complementary treatment strategy, as it is still essential in patients who are not endo-suitable, or have a life expectancy exceeding five to ten years.

Open AAA repair is associated with significant morbidity and mortality, and remains classified as major, high-risk surgery. Published literature from centres in the UK reports a postoperative mortality of elective AAA repairs of 4-8%. The mortality rate of emergency open AAA repairs remains significantly higher, being 80-85%[3].

Data regarding the incidence of aortic aneurysms emanates predominantly from the developed world, currently reported as ~ 1.5% - 5%, where the life expectancy is greater (78.7 years in the US and 81.5 years in the UK) and health systems preferentially geared towards prevention, surveillance and treatment of AAA.

The magnitude of the problem in South Africa is difficult to ascertain, as there are limited published data. Abdominal aortic aneurysm is more prevalent in the adult Caucasian male population above 65 years. South Africa, as a developing country, has experienced an increase in life expectancy. As of 2015, national life expectancy stands at 61 years, having increased from 52 years in 2005[4]. It is reasonable to expect that there will be an increase in the incidence of AAAs as the population ages. At the moment, one can only speculate that the South African AAA case load is far lower than that of developed countries. A study by Tiemensma et al[5]

conducted in South Africa suggested that 1.3% of cases of sudden and unexpected death (8/601) were determined at autopsy to be due to ruptured aortic aneurysm.

South Africa is a severely resource-constrained developing country. Renal replacement therapy (RRT) is a resource-intensive intervention, and the development of acute renal failure in hospital is an independent predictor of mortality in all patients, and especially in patients undergoing open surgical AAA repair[6,7,8]. Questions are often raised as to whether instituting RRT is cost effective in terms of patient survival and quality of life post open surgical AAA repair. In observing the ethical principle of distributive justice, there is a need to ensure that resources benefit the majority of the population.

RATIONALE FOR RESEARCH

Groote Schuur Hospital (GSH) in Cape Town, South Africa, is the major academic hospital affiliated with the University of Cape Town. The vascular surgery unit at GSH receives referrals from the Cape Metropolitan area and as far afield as East London, approximately 1000 kilometres from Cape Town. Based on the number of entries in theatre ledgers, it is estimated that an average of 14 patients undergo open AAA repair annually.

All patients undergoing open AAA repair at GSH are admitted to the intensive care unit (ICU) for post-operative care. These patients are at risk of acute kidney injury and may require renal replacement therapy, potentially leading to prolonged hospital stays. Lengthy hospital stays, including total ICU stays, are costly for the health system, as well as for the patient, who is required to pay for hospital services while losing his or her income due to incapacity. According to the author's knowledge, there has not been a study conducted at GSH into the outcomes of these specific patients.

The primary objective of this research is to establish the perioperative (30-day) mortality associated with open AAA repair at GSH. The secondary objective is to determine whether a significant portion of patients who had an open AAA repair developed a need for renal replacement therapy, and what their clinical outcomes were.

METHODOLOGY

The design of the study was a retrospective observational study, which uses existing data that have been recorded for reasons other than research.

The study population included all patients who underwent open AAA repair at GSH between October 2006 and December 2014. Because the numbers of patients operated upon was relatively small, the author included both elective and emergency open AAA repairs. Patients who received an open or hybrid thoraco-abdominal aortic aneurysm repair, or an endovascular AAA repair (EVAR) were excluded from this study. Patients with incomplete clinical records were also excluded from this study.

Data from clinical hospital records, anaesthetic and vascular operative databases, were capture and recorded in clinical research folders created for each patient. Data capture included: patient age, gender, risk factors for AAA, and associated co-morbidities as documented in the hospital admission notes.

Abdominal aortic aneurysms were classified as infrarenal, juxtarenal (infrarenal neck less than 8 mm) or supra-renal based on preoperative Computed Tomographic Angiogram (CTA) imaging. The position of the abdominal aortic cross-clamp, as well as the duration of cross-clamp, was recorded from the operative and anaesthetic records. Post-operative data collection included: duration of ICU and hospital stay, change in creatinine, type and duration of RRT instituted and whether there was a need for outpatient RRT following hospital discharge. The 30-day mortality was recorded using hospital records as well as the national births and deaths registry.

Data on serum creatinine concentrations were obtained from the National Health Laboratory Service's Disa electronic database, and hospital records. Data pertaining to acute kidney injury, as defined by the Kidney Disease Improving Global Outcomes (KDIGO) working group, and the need for renal replacement therapy, were recorded. In this study, acute renal failure was defined as serum creatinine levels meeting the criteria for KDIGO Stage 3 renal injury, namely: an increase in serum creatinine of more than three times of the preoperative value, a serum creatinine of greater than, or equal to, 353.6 µmol/L, or the institution of renal replacement therapy[13]. Urine output criteria was not used, as there is great interpersonal variability in the accurate recording thereof.

Data were captured electronically on Microsoft Excel™ spread sheets. Data analysis was performed using Stata 13™. Secondary analyses were carried out using the Mann-Whitney and Fischer's Exact tests.

Ethical approval to perform the audit was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town (HREC reference number 914/2014). As no public electronic database of operations exists in the study setting, the researcher perused theatre ledgers of operations performed between October 2006 and December 2014, and identified all open abdominal aortic aneurysm repairs performed during that time.

RESULTS

One hundred and four open AAA repairs were performed during the study period October 2006 to December 2014. Of the 104 cases, 90 folders were retrieved from medical records. Fourteen patients were excluded because of inadequate clinical records. These 90 patients therefore constitute the study population.

The study population consisted of 76.7% (n=69) males and 23.3% (n=21) females. The mean age of the sample was 64.9 years (median 68 years, interquartile range 60-71 years). The minimum and maximum ages were 31 and 84 years respectively.

Seventy six percent (76.67%) of the patients had documented pre-operative hypertension and 30% had ischaemic heart disease, 28.9% had hyperlipidaemia, 6.67% were HIV (human immunodeficiency virus) positive, and 10% had established chronic kidney disease. Furthermore, 64.77% of patients were smokers, with 20.0% reported to have moderate to severe chronic obstructive pulmonary disease (COPD) based on clinical and radiological features and pulmonary function tests. **(Table 1)**

Of the 90 patients in the study, 65.6% (n=59) required elective open AAA repairs and 34.4% (n=31) required emergency open AAA repairs, 29 of these being for ruptured AAAs. With respect to the AAA classification, 61.1% (n=55) of the aneurysms repaired were infrarenal, with 37.8% (n=34) being juxtarenal, and only one case (1.1%) being suprarenal.

The perioperative (30-day) mortality rate (combined elective and emergency cases) was 16.6% (n=15). Most of the mortalities (n=12) followed emergency AAA repair. Most of the perioperative mortality was associated with emergency open AAA

repairs (12/31, 38.7%). The mortality in the elective repair group was much lower, at 5.1% of all elective repairs. **(Table 2)**

One elective patient survived in-hospital for 42 days, until succumbing to a suspected pulmonary embolism. The mean hospital length of stay in survivors was 11.71 days. In non-survivors, the mean survival was 10.31 days. The mean length of ICU stay was 4.09 days. **(Table 3)**

Aortic cross-clamp time was not recorded in 4 of the cases. Of the remaining 86 cases, the mean cross-clamp time was 39 minutes (median 32 minutes, IQR 24-55 minutes). An analysis of aortic cross-clamp times was performed according to the level of clamping. **(Table 4)**

The study identified 17 patients (18.9%) who developed KDIGO stage 3 renal dysfunction post-operatively. Three of those patients had pre-existing chronic kidney disease. Two patients had diabetes mellitus, and 15 patients had hypertension. One patient was HIV positive. Only 12 patients received RRT (13.3% of all patients). Of the 5 patients not commenced on RRT, two had a poor prognosis, and the other three patients had adequate urine output despite deranged serum creatinine concentration. Of the 12 patients who received RRT, five did not survive. Of the survivors, no patients were dialysis dependent at hospital discharge.

In a Mann-Whitney analysis of renal replacement therapy and aortic cross-clamp times, there was no significant difference in cross-clamp times between those patients who received RRT and those who did not (46 minutes versus 38 minutes, p=0.9021). Eight of the patients who received RRT had supra- and juxtarenal aneurysm; this was statistically significant (p=0.037). The type of RRT employed initially was continuous venovenous haemodialysis (CVVHD) in five patients, sustained low efficiency daily dialysis (SLEDD) in four patients, and intermittent haemodialysis (IHD) in three patients. The mean duration of RRT was 7.58 days (median 4 days, range 1- 20 days).

DISCUSSION

Patients presenting with AAA tend to be elderly and have numerous comorbidities. Potent risk factors for the development of AAA include: age of greater than 65 years, smoking and a positive family history of AAA[3]. The one consistent and modifiable factor associated with accelerated growth of aortic aneurysms is cigarette smoking,

with hypertension also contributing to aneurysm growth[9,10]. The normal adult aorta has a diameter of approximately 1.7-2.2 cm. Any abdominal aortic diameter beyond 3 cm or greater is classified as an abdominal aortic aneurysm. Elective open AAA repairs are indicated in all conventional risk patients with a symptomatic AAA irrespective of diameter, or an asymptomatic AAA that fulfils the one of the following criteria: diameter greater than 5.5 cm in males and 5.0 cm in females; saccular AAA diameter greater than 3 cm; or an associated iliac aneurysm with a diameter greater than 3 cm. For asymptomatic small AAA (4-5.5 cm in diameter), there is no survival advantage for OSR compared to surveillance and deferred repair[11].

Various risk factors for perioperative (30-day) mortality have been identified, including advanced age, smoking status, low forced expiratory volume in one second (FEV_1), pre-existing myocardial ischaemia, and a pre-operative serum creatinine greater than 160 µmol/L. Other, non-patient related risk factors included hospital case volumes, graft type, professional rank of surgeon, and surgeon case volumes and expertise (the number of AAA operations the surgeon had performed during the trial)[11].

Perioperative morbidity includes complications such as acute renal failure, acute pulmonary complications, colonic ischemia, myocardial ischemia and infarction, acute thrombo-embolic lower extremity complications, prolonged ileus, and paralysis due to spinal cord ischemia[12].

This study showed a similar mean age as is quoted in literature, with a similar risk profile, namely, hypertension, hyperlipidaemia, ischaemic heart disease and COPD. The study population had a 6.7% incidence of HIV; this is often not reported in the literature from developed countries. HIV infection tended to be in the younger patients (mean age 43.3 years) in this study. HIV infection is associated with the development of atypical aneurysm, postulated to be due either to opportunistic infections or accelerated atherosclerotic processes[13]. With an HIV infection prevalence of 10.2%[4], South African institutions will invariably encounter more of these atypical aneurysms.

In studies performed in countries in the developed world, elective AAA repairs carry a mortality of 4-8%, whereas emergency AAA repairs carry a much higher mortality of 85-90%[3]. In most of these studies, the researchers have focussed on outcomes following repair of infrarenal AAAs. In this study population, there were comparable mortality rates. The mortality among the elective AAA repair group (5.1%) is within the range quoted in literature.

Direct comparisons with international studies regarding renal failure are difficult to make, as wide variations exist in the definition of renal failure and in the timing of RRT. Most articles place the rate of renal failure in elective AAA repairs at 2%[14,15]. The incidence of renal failure following ruptured AAA repair is higher, at 20-46%[7]. The results showed that 17 of our patients (18.9%) developed acute kidney injury post open AAA repair, having fulfilled the criteria for KDIGO stage 3, which is analogous to the RIFLE criteria Failure stage[16]. Of the 12 patients who did receive RRT, five were emergency cases. At GSH, the decision to institute RRT was discretionary, and made by the attending nephrologist, as well as the intensivist who referred the patient to nephrology. The perioperative mortality rate in the RRT group was 41.67%. It is known that the development of acute renal failure is associated with an in-hospital mortality of 45%[17], and that the long-term prognosis is negatively impacted[17,15].

This study also found that duration of aortic cross-clamp time was not a significant factor in the subsequent development of renal failure. However, the anatomical classification of the AAA did seem to play a role in the subsequent development of renal failure. Juxta- and suprarenal aneurysms constituted the bulk of the patients receiving RRT (77.1%, p=0.037), presumably due to the level of cross-clamp placement and a greater burden of ischaemia. A similar observation was made by Crawford et al[18] in a study published in 1986. More recently, Chong et al[19] investigated the differences in outcomes in infrarenal and juxta-/suprarenal aneurysm (collectively termed suprarenal) repairs. They demonstrated a greater decline in renal function in the suprarenal group; mortality was not significantly different in these two groups.

Five patients were initiated on CVVHD, with another four initiated on SLEDD. Two of these patients were later placed onto the less labour intensive, and cheaper, IHD. Only three patients were placed on IHD as the first modality of RRT. At an estimated daily cost of ZAR 2 727 for CVVHD, ZAR 2 076 for SLEDD and ZAR 1 950 for IHD, the costs of RRT accrue[20]. The choice of RRT modality used is made by the attending renal physicians at Groote Schuur Hospital. This is informed not only by the patient's haemodynamic status, but also by the renal unit's staffing constraints.

Renal recovery, and subsequent quality of life, is an important consideration in patients who receive RRT. The on-going need for RRT would have an impact on the quality of life of these patients, in addition to placing additional financial burdens on

the patients and the healthcare system. Lin et al[8] found that 84.7% of survivors do recover their renal function following a period of dialysis. In this study population, none of our patients were dialysis dependent upon hospital discharge, and so did not face on-going financial constraints from the need to continue outpatient dialysis.

LIMITATIONS OF RESEARCH

The biggest challenge faced in carrying out this research was the inadequate clinical records in 14 patients. With the small number of cases retrieved, the author elected not to separate the different data sets between emergency and elective, or infrarenal and juxta-/suprarenal aneurysms in our sample; therefore, the patient population was heterogeneous. The small sample size also impacted on the ability to carry out univariate or multivariate analyses on the risk associations for the development of acute kidney injury. Conclusions regarding modifiable risk factors or preventative strategies can therefore not be made, but may signal future areas for research. A future study would also need to also look at long-term clinical outcomes.

CONCLUSIONS

This study confirmed in a local South African retrospective institutional audit that open AAA repairs are still associated with significant mortality and renal dysfunction. Perioperative mortality was similar to other international centres, at 5.1% and 38.7% for elective and emergency repairs respectively, with mortality in those requiring RRT being considerably high (41.67%), but definitely not futile. This has implications on the resource utilisation in providing these patients with renal support. The one factor found to have a bearing on the need for post-operative RRT, apart from pre-existing chronic kidney disease, is the anatomical classification of the abdominal aortic aneurysm ($p=0.037$). At this time, it is not prudent to draw any conclusions, as a larger number of patients would need to be studied.

The relatively small annual number of open AAA repairs at Groote Schuur is most likely indicative of a lower incidence of AAAs in the relatively young, predominantly black, South African population.

A number of questions arise from this study. Are there any modifiable risk factor associations contributing to the development of acute kidney injury? Do patients undergoing endovascular repair of AAAs in South Africa have better renal

outcomes? What role does HIV play in the development of renal complications? What are the perioperative renal outcomes in patients with inflammatory aneurysms?

Current clinical practice suggests AAA is also being diagnosed and treated in mixed ethnic populations. More atypical AAAs are being diagnosed and treated in the black population, whereas AAA is rare in Asian populations in South Africa. This study was not designed to examine the differences in racial groups in terms of type of aneurysm and age of operation. This is a potential future area of research.

The establishment of a computerised database of clinical records would definitely facilitate retrieval and analysis of outcome data. Multi-centre studies incorporating data from different centres in South Africa is also lacking. This further highlights the problem of a lack of research reflecting perioperative outcomes in the South African context, a problem which is gradually being addressed.

REFERENCES

1. Livesay J, Messner G, Vaughn W. Milestones in Treatment of Aortic Aneurysm Milestones in the Treatment of Aortic Aneurysm: Denton A. Cooley, MD, and the Texas Heart Institute. Texas Hear Inst J 2005;32(2):130-134.

2. Greenhalgh RM, Brown LC, Kwong GPS, Powell JT, Thompson SG. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. Lancet 2004;364(9437):843-848. [http://dx.doi.org/10.1016/S0140-6736(04)16979-1]

3. van der Vliet J, Boll AP, Leger AS, et al. Abdominal aortic aneurysm. Lancet 1997;349(9055):863-866. [http://dx.doi.org/10.1016/S0140-6736(96)07282-0]

4. Statistics South Africa. Mid-year Population estimates. *www.statssa.gov.za/publications//P03022014.pdf*. 2014;(July):1-18. [http://dx.doi.org/Statistical release P0302]. (Accessed 21 October 2016)

5. Tiemensma M, Burger EH. Sudden and unexpected deaths in an adult population, Cape Town, South Africa, 2001-2005. South African Med J 2012;102(2):90-94. [http://dx.doi.org/10.7196/samj.5363]

6. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. Lancet 2005;365(9457):417-430. [http://dx.doi.org/10.1016/s0140-6736(05)17831-3]

7. Barratt J, Parajasingam R, Sayers RD, Feehally J. Outcome of Acute Renal Failure Following Surgical Repair of Ruptured Abdominal Aortic Aneurysms. Eur J Vasc Endovasc Surg 2000;168(August):163-168. [http://dx.doi.org/10.1053/ejvs.2000.1078]

8. Lin YF, Ko WJ, Chu TS, et al. The 90-day mortality and the subsequent renal recovery in critically ill surgical patients requiring acute renal replacement therapy. Am J Surg 2009;198(3):325-332. [http://dx.doi.org/10.1016/j.amjsurg.2008.10.021]

9. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. Lancet 2005;365:1577-1589. [http://dx.doi.org/10.1016/S0140-6736(05)66459-8]

10. Wilmink TBM, Quick CRG, Day NE. The association between cigarette smoking and abdominal aortic aneurysms. J Vasc Surg 1999;30:1099-1105. [http://dx.doi.org/10.1016/S0741-5214(99)70049-2]

11. Brady AR, Fowkes FGR, Greenhalgh RM, Powell JT, Ruckley C V, Thompson SG. Risk factors for postoperative death following elective surgical repair of abdominal aortic aneurysm : results from the UK Small Aneurysm Trial. Br J Surg 2000;87:742-749. [http://dx.doi.org/10.1046/j.1365-2168.2000.01410.x]

12. Al-Hashimi M, Thompson J. Anaesthesia for elective open abdominal aortic aneurysm repair. Contin Educ Anaesthesia, Crit Care Pain 2013;13(6):208-212. [http://dx.doi.org/10.1093/bjaceaccp/mkt015]

13. Robbs JV., Paruk N. Management of HIV Vasculopathy - A South African Experience. Eur J Vasc Endovasc Surg 2010;39(SUPPL. 1):S25-S31. [http://dx.doi.org/10.1016/j.ejvs.2009.12.028]

14. Hertzer NR, Mascha EJ, Karafa MT, O'Hara PJ, Krajewski LP, Beven EG. Open infrarenal abdominal aortic aneurysm repair: The Cleveland Clinic experience from 1989 to 1998. J Vasc Surg 2002;35(6):1145-1154. [http://dx.doi.org/10.1067/mva.2002.123686]

15. Menard MT, Chew DKW, Chan RK, et al. Outcome in patients at high risk after open surgical repair of abdominal aortic aneurysm. J Vasc Surg 2003;37(2):285-292. [http://dx.doi.org/10.1067/mva.2003.121]

16. Kellum JA, Lameire N, Aspelin P, et al. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2012;2(1):1-138. [http://dx.doi.org/10.1038/kisup.2012.7]

17. Korkeila M, Ruokonen E, Takala J. Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. Intensive Care Med 2000;26(February):1824-1831. [http://dx.doi.org/10.1007/s001340000726]

18. Crawford ES, Beckett WC, Greer MS. Juxtarenal infrarenal abdominal aortic aneurysm. Special diagnostic and therapeutic considerations. Ann Surg 1986;203:661-670.

19. Chong T, Nguyen L, Owens CD, Conte MS, Belkin M. Suprarenal aortic cross-clamp position: A reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair. J Vasc Surg 2009;49(4):873-880. [http://dx.doi.org/10.1016/j.jvs.2008.10.057]

20. Prices supplied by Dr Brian Rayner. Prices correct as of August 2016.

TABLES

Table 1 Baseline data

	N (%)
Total no. of patients	90 (100%)
Gender	
Male	69 (76.7%)
Female	21 (23.3%)
Age (years)	
Mean	64.96
Range	31.0-84.1
Positive smoking history	57 (64.8%)
Comorbidities	
Hypertension	69 (76.7%)
Ischaemic heart disease	27 (30.0%)
Hyperlipidaemia	26 (28.9%)
COPD	18 (20.0%)
HIV	6 (6.7%)
Chronic kidney disease	9 (10.0%)
Urgency of operation	
Emergency	31 (34.4%)
Elective	59 (65.6%)
Position of Aneurysm	
Infrarenal	55 (61.1%)
Juxtarenal	34 (37.8%)
Suprarenal	1 (1.1%)
Mortality (30-day)	**N=15**
Emergency	12 (38.7%)*
Elective	3 (5.1%)†

* *Percentage of all emergency cases*

† *Percentage of all elective cases*

Table 2 Cause of death

Cause of death	**N=15**
Cardiovascular	
Hypovolaemic shock/circulatory failure	6
Cardiac arrest	1
Myocardial infarction	1
Pulmonary embolism	1
Multi-organ failure, including renal	2
Gut ischaemia	1
Sepsis	2
Unknown	1

Table 3 Duration of ICU and hospital stay

	Mean	SD	p50	p25	p75	Min	Max
Duration of ICU stay (days)	4.09	3.25	3.5	2	5	1	22
Duration of postoperative ventilation (days)	1.16	2.20	0	0	1	0	14
Duration of post-operative hospital stay (days)							
Survivors (n=74)	11.72	7.79	9	7	13	4	47
Non-survivors (n=16)	10.31	13.49	3	2	14	1	42
Total (n=90)	11.47	8.98	9	6	13	1	47

Table 4 Duration of abdominal aortic cross-clamp

Clamp position	N	Mean	SD	p50	p25	p75	Min	Max
Infrarenal	29	49.69	21.74	49	32	61	15	100
Suprarenal	29	34.31	18.27	25	24	40	9	83
Supracoeliac	28	34.14	27.19	26	21.5	35.5	8	150
Total	**86**	**39.44**	**23.55**	**32**	**24**	**55**	**8**	**150**

Mean, SD, p50, p25, p75, min and max in minutes

Part D: Supporting Documents

Data Capture Form

Study number: _____

Folder number: _____

Date of operation: _____

Date of birth: _____ Age at operation: _____

Gender: _____

Type of aneurysm: Saccular / Fusiform (Circle applicable one)

Position of aneurysm: Suprarenal / Juxtarenal / Infrarenal (Circle applicable one)

Position of aortic cross-clamp: Supracoeliac / Suprarenal / Infrarenal (Circle applicable one)

Total aortic cross-clamp time (minutes): _____

Indicate: Emergency / Elective Ruptured? Yes / No

Patient comorbidities: _____

_____

_____

_____

Date of ICU admission: _____

Date of ICU discharge: _____

ICU length of stay (days): _____

Days ventilated: _____

Date of death: _____

Cause of death: _____

Renal replacement therapy (RRT): Yes / No

Number of days on RRT: _____

Type of RRT: _____

Creatinine on admission to hospital (prior to operation): _____

Creatinine on commencement of RRT: _____

Creatinine on hospital discharge/death: _____

Date of last recorded creatinine prior to discharge/death: _____

Dialysis dependent at hospital discharge: Yes / No

Date of hospital discharge: _____

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
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Email: Sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

11 December 2014

HREC/REF: 914/2014

Dr J Piercy
Anaesthesia & Critical Care
D-23
NGSH

Dear Dr Piercy

Project Title: A RETROSPECTIVE AUDIT INTO THE MORBIDITY AND MORTALITY ASSOCIATED WITH OPEN ABDOMINAL AORTIC ANEURYSM (AAA) REPAIR AT GROOTE SCHUUR HOSPITAL (Mmed-Dr G Mhlanga)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for approval.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year until the 30 December 2015.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

We acknowledge that the following student:-Dr Gugulethu Mhlanga is also involved in this project.

Please note that the on-going ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.

Hrec/ref:914/2014

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Hrec/ref:914/2014

South African Medical Journal Author Guidelines

The *SAMJ* has launched a new submission and tracking system. Authors will be required to register a profile on the Editorial Manager platform in order to submit a manuscript.

To submit a manuscript, please proceed to the *SAMJ* Editorial Manager website:

www.editorialmanager.com/samj

To access and submit an article already in production, please see the guidelines here.

Author Guidelines

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

SAMJ policies

- Types of articles considered by the SAMJ
- Authorship
- Conflict of interest
- Research ethics committee approval
- Clinical trials
- Protection of patient's rights to privacy
- Copyright notice
- Privacy statement
- Ethnic classification
- CPD

Manuscript preparation

- Preparing an article for anonymous review
- General article format/layout
- Preparation notes by article type
- Illustrations
- Tables

- References

From submission to acceptance

- Submission and peer-review
- Article Processing Charges
- Production process
- Changing contact details or authorship

Publication

- Online versus print
- Errata and retractions
- Indexing

SAMJ Policies

Type of articles considered by the SAMJ

The *SAMJ* will no longer limit the articles accepted to those that have 'general medical content', but is intending to capture the spectrum of medical and health sciences, grouped by relevance to the country's burdens of disease. This content will include research in the social sciences and economics that is relevant to the medical issues around our burden of disease. Please see 'A new vision for the *SAMJ* – and a call for papers' for a full discussion of the new directions for the *SAMJ*.

We accept the following types of articles:

- Research
- Reviews
- Clinical trials
- Editorials
- In Practice (Previously Forum incl. Case Reports)
- Correspondence
- Obituaries
- Book reviews
- Ad hoc supplements e.g. guidelines, conference/congress abstracts, Festschrifts*

The following articles are by invitation only:

- Guest editorial
- Continuing Medical Education (CME)

*Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Authorship

Named authors must consent to publication. Authorship should be based on: (*i*) substantial contribution to conceptualisation, design, analysis and interpretation of data; (*ii*) drafting or critical revision of important scientific content; or (*iii*) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structuresto ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchershave been adhered to.

Clinical trials

Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The *SAMJ* therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Protection of rights to privacy

Patient

Information that would enable identification of individual patients should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the *SAMJ*.

Copyright notice

Copyright remains in the Author's name. The work is licensed under a Creative Commons Attribution - Noncommercial Works License. Authors are required to complete and sign an Author Agreement form that outlines Author and Publisher rights and terms of publication. The **Author Agreement form** should be uploaded along with other submissions files and any submission will be considered incomplete without it.

Material submitted for publication in the *SAMJ* is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement. The *SAMJ* does not hold itself responsible for statements made by the authors.

Previously published images

If an image/figure has been previously published, permission to reproduce or alter it must be obtained by the authors from the original publisher and the figure legend must give full credit to the original source. This credit should be accompanied by a letter indicating that permission to reproduce the image has been granted to the author/s. This letter should be uploaded as a supplementary file during submission.

Privacy statement

The *SAMJ* is committed to protecting the privacy of its website and submission system users. The names, personal particulars and email addresses entered in the website or submission system will not be made available to third parties without the user's permission or due process. By registering to use the website or submission system, users consent to receive communication from the *SAMJ* or its publisher HMPG on matters relating to the journal or associated publications. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on

race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAMJ is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, *SAMJ* also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit MRP Consulting

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, which will delay publication.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

Preparation notes by article type

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text.

Structured abstract

- This should be 250-400 words, with the following recommended headings:
    - **Background:** why the study is being done and how it relates to other published work.
    - **Objectives:** what the study intends to find out
    - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
    - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.

    - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.

- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies

- trials
- systematic reviews.

CME

CME is intended to provide readers with practical, up-to-date information on medical and related matters. It is aimed at those who are not specialists in the field.

From January 2016, all CME articles will be printed in full in the *SAMJ*. Please try to adhere strictly to the guidelines on word count as we have a page limit for the print issue of the *SAMJ*. We reserve the right to place some tables and reference lists online if this is necessary for space.

In practice, this means that each CME topic usually covers two issues of the print issue of the *SAMJ*.

The guest editor, in consultation with the editor, is responsible for convening a team of authors, deciding on the subjects to be covered and for reviewing the manuscripts submitted. The suggestion is for 4 - 5 articles, although there is some room for flexibility contingent on discussions with the editor.

For queries about these guidelines please feel free to contact the CME editor, Dr Bridget Farham, by email (ugqirha@iafrica.com) or telephone (+27 (0)21 789 2331).

Review process

The guest editor reviews the articles and returns them to the CME editor for review and final approval.

Guest editorials

Guideline word limit: 1 000 words

- Include the guest editor's personal details (qualifications, positions, affiliation, e-mail address, and a short personal profile (50words)).
- If possible, include a photograph of the author(s) at high enough resolution for print. It is preferable to provide two guest editorials, one for each issue, so that the content of the articles in each issue is covered.

Articles

Guideline word limit: 2 000 - 3 000 words

- Each article requires an abstract of ±200 words.
- The editor reserves the right to shorten articles but will send a substantially shortened article back for author approval.

Personal details

Please supply: Your qualifications, position and affiliations and MP number (used for CPD points); Address, telephone number and fax number, and your e-mail address; and a short personal profile (50words)and a few words about your current fields of interest.

In Practice

Guideline word limit: 2 000 - 3 000words

This section includes articles that would previously have been accepted into the Forum section, and case reports.

In practice articles are those that draw attention to specific issues of clinical, economic or political interest regarding medicine and healthcare in southern Africa. They are assigned to a topic:

- Case report
- Clinical practice
- Clinical alert
- Issues in medicine
- Issues in public health
- Healthcare delivery
- Consensus/Position statement
- Medicine and the environment
- Medicine and the law
- Cochrane corner

An In Practice article should follow the following format – sub-headings are not necessary, but may be used for clarity:

- Author affiliations and qualifications: to be the same as for Research. Provide all authors' names and initials, qualifications and full affiliations, and corresponding author.
- Short abstract: does not need to be structured, but should capture the essential features of the article
- Introduction: the reason for the article and the issue being addressed
- Recent research, discussion, local policy around the issue – include your own research where appropriate
- All statements should be referenced and, if opinion only, this should be stated
- Discussion: how this article adds to the discussion around a particular topic
- If a clinical practice or policy point is at issue, this needs to be emphasised, using a box with highlights if appropriate.

Essentially In practice is an opportunity for a more discursive approach to topics of clinical, economic or political importance in southern African health systems. It is not an opportunity to put forward unsubstantiated opinions!

Case reports

The *SAMJ* has recently started to accept case reports. The cases must come from Africa, preferably southern Africa unless the condition is common to all African countries, and must be either a completely new description of a clinical condition or result (use Google!) or a case that highlights important practice or management issues.

Please use the following format for case reports:

- Title of case: do not include the words 'a case report' in the title
- Summary/abstract: up to 150 words summarising the case presentation and outcome
- Background: why is this case important and why did you write it up?
- Case presentation: presenting features, medical, social, family history as appropriate
- Case management: should be according to best practice, and if not, please explain why
- Investigations, if relevant: save space by simply saying 'normal' if, for example, renal function was completely normal, rather than listing normal results, highlight the abnormal – or indeed the normal if this is clinically significant
- Differential diagnosis, if relevant
- Treatment, if relevant
- Outcome and follow-up
- Discussion – a VERY BRIEF review of similar published cases
- Teaching points: 3 - 5 bullet points

- References: as per the *SAMJ* house style
- Tables and figures: keep to a minimum. Use clinical images where relevant – we need hi-res versions for print, and identifiable persons must have a consent form
- Patient consent: please include a statement about patient consent to a written case report. This should be uploaded as a supplementary file.

Clinical trials

Guideline word limit: 4000 words

As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The *SAMJ* therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Review articles

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners.

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 500 words

Letters to the editor should relate either to a paper or article published by the SAMJ or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Book reviews

Guideline word limit: 400 words

Should be about 400 words and must be accompanied by the publication details of the book. Provide a hi-res image of the cover if possible (with permission from the copyright holder).

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Guidelines

Guidelines should always be discussed with the Editor prior to submission.

Because of the intensive review process required to ensure Guidelines are independent, evidence-based and free from commercial bias, they are usually published as a supplement to the *SAMJ*, the costs of which must be covered by sponsorship, advertising or payment by the guideline authors/association. We will provide a quote based on the expected length of the guideline and whether it is to appear online only, or in print, which must be accepted by the body putting the guidelines together before submitting the work to the SAMJ.

The Editor reserves the right to determine the scheduling of supplements. Understandably, a delay in publication must be anticipated dependent upon editorial workflow.

All guidelines should be structured according to Agree II.

Please access this website before putting the guidelines together, download the Agree 11 instrument and use this to put the guidelines together.

All submitted guidelines will be sent to the local Agree II appraisal committee for review and must be endorsed by an appropriate body prior to consideration and all conflicts of interest expressed.

A structured abstract not exceeding 400 words (recommended sub-headings: *Background, Recommendations, Conclusion*) is required. Sections and sub-sections must be numbered consecutively (e.g. 1. Introduction; 1.1 Definitions; 2.etc.) and summarised in a Table of Contents.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.

- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

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- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
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    - Provide as follows, e.g.: http://dx.doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. DOI:10.1000/hgjr.182

- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references

• Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

• Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

• Acts:

South Africa. National Health Act No. 61 of 2003.

• Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

• Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

• Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

• Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

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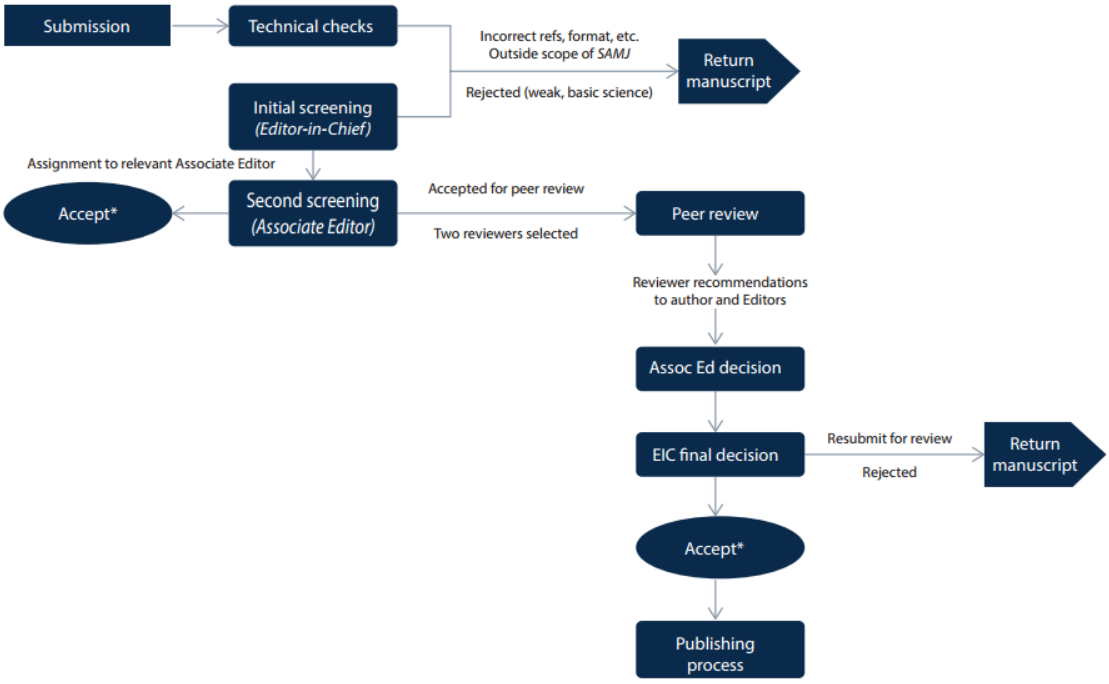

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