



THE UNIVERSITY OF THE WITWATERSRAND

DEGREE OF MASTER OF MEDICINE IN

INTERNAL MEDICINE

**OUTCOME OF PATIENTS WITH ACUTE RENAL FAILURE IN AN
INTENSIVE CARE UNIT USING RIFLE CRITERIA IN SOUTH AFRICA**

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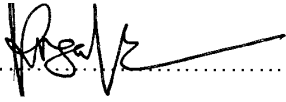
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A research report submitted for partial fulfilment of the requirements for the degree on Masters of medicine in Internal Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

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DECLARATION

I, **Dr.Leodegard Mujwahuzi**, hereby declare that this research report is my own work. It has not been submitted before for any publication, or degree at any other University. It is submitted for the degree of master of medicine in Internal medicine of the University of the Witwatersrand, Johannesburg, South Africa

Signature..........

Date27th.....Of January.....2012

DEDICATION

To my parents, Mr and Mrs S. Mujwahuzi (RIP) for their guidance and encouragement, my beloved wife Dr. Selina for her love and support, my children Byera and Bera for their understanding and patience, my teachers for their untiring mentorship and to my patients for allowing me to take care of them, treat them and learn from them.

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ABSTRACT

BACKGROUND: Acute renal failure (ARF) is a clinical syndrome characterised by a rapid deterioration of kidney function over hours to days which may recover/return to normal values following appropriate therapy. Various scoring systems currently exist to predict the severity and outcome in patients with ARF. Recently the Acute Dialysis Quality Initiative (ADQI) Group has established the RIFLE (Risk of injury, Injury to the kidney, Eailure of kidney function, Loss of kidney function, and End-stage kidney disease) classification which has become widely used globally. There is however, limited data on its use in Africa.

In order to provide data on the use of RIFLE criteria from an African facility, we conducted a retrospective chart review to assess the outcome of ARF in patients admitted in the Intensive Care Unit (ICU) at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). The data reviewed covered the period between January 1st to December 31st 2008.

METHODS: This was a retrospective chart review conducted in the adult multi-disciplinary intensive care unit at CMJAH between January 1st to December 31st 2008. Medical records of patients admitted during this period were reviewed and patients with acute renal failure were identified. Demographic data, relevant clinical information such as reason for ICU admission, number of organ(s) involved, presence of co-morbidity, RIFLE criteria on admission and on discharge, modality and duration of treatment of ARF, need for mechanical ventilation and or inotropic support were recorded. For the purpose of this study, serum creatinine based on RIFLE classification was used to define ARF. Statistical analysis was performed using the data collected and STATA version 11. The Primary outcome, which was

survival or death, was correlated with the maximum RIFLE classification during patients' ICU stay. The study was approved by the Human Research Ethics Committee medical (HRECM) of the University of Witwatersrand with Clearance certificate number M090906

RESULTS: One hundred and ninety three (193) patients with acute renal failure were included in the study. The mean APACHE II score was 19 ± 6.4 SD, with the maximum score documented being 38. Patient ages ranged from 21 – 92 years with a mean of $50.5 \text{ years} \pm 18.3\text{SD}$. Fifty two percent of the patients were male and 48% were female. Majority of patients were black (63%) with 36.8% being other race groups.

According to RIFLE criteria on admission, 40.9% had normal renal function, 23.3%, 14.0% and 21.8% were in RIFLE R, I and F classes respectively. The overall mortality in ICU was 59.9%. Of those patients discharged to the ward from ICU, 14.1% subsequently demised. Factors associated with mortality in ICU included race, chronic pulmonary disease, mechanical ventilation, inotropic support, need for ventilation and inotropic support, dialysis and maximum RIFLE criteria reached in ICU. After multivariate analysis using Cox proportion regression model, factors such as race, inotropic support, need for both ventilation and inotropic support and maximum RIFLE criteria were independently associated with mortality in ICU, whereas for patients discharged from ICU to the ward, only cancer was found to be independently associated with mortality. Based on RIFLE criteria, patients in R, I, and F class had 5.41, 3.17 and 5.69 greater risk of dying respectively as compared to patients with normal renal function (Adjusted HR 5.41 95%CI 2.66 - 11.0, p-Value 0.000 for **R** class, HR 3.17 95%CI 1.65 - 6.07, p-value 0.001for **I** class, and HR 5.69 95%CI 2.93 - 11.06, p-value 0.001 for **F** class)

CONCLUSION: RIFLE criteria is a useful tool for predicting the outcome of acute renal failure in the intensive care unit.

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LIST OF ABBREVIATIONS

ADQI	Acute Dialysis Quality Initiative Group
AKI	Acute Kidney Injury
AKIN	Acute Kidney Injury Network
ARF	Acute Renal Failure
ARI	Acute Renal Injury
ARFS	Acute Renal Failure Syndrome
APACHE	Acute Physiology and Chronic Health Evaluation
CI	Confidence interval
CKD	Chronic Kidney Disease
CRF	Chronic Renal Failure
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CRF's	Case record Forms
CRRT	Continuous renal replacement therapy
CVVHD	Continuous venovenous haemodialysis
DOS	Duration of Stay
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
HIV	Human Immunodeficiency Virus

HR	Hazard ratio
HRECM	Human research ethics committee medical
ICU	Intensive Care Unit
IHD	Intermittent haemodialysis
IRRT	Intermittent renal replacement therapy
K-M curve	Kaplan – Mayer curve
NOI	Number of Organ(s) Involved
RIFLE	<u>R</u> isk of acute renal failure, <u>I</u> njury to the kidney, <u>F</u> ailure of kidney function, <u>L</u> oss of kidney function, <u>E</u> nd-stage kidney disease
RRT	Renal Replacement Therapy
SARFS	Severe Acute Renal Failure Syndrome
S-creat	Serum Creatinine
SD	Standard deviation
SLED	Sustained Low Efficiency Dialysis
SOFA	Sequential Organ Failure Assessment
TB	Tuberculosis
TBSA	Total body surface area
UO	Urine Output
Yrs	Years

CHAPTER ONE

1. INTRODUCTION AND BACKGROUND

Acute renal failure (ARF) is a clinical syndrome characterised by a rapid deterioration of kidney function over hours to days which may recover/return to normal value following appropriate therapy.

It is serious common complication in critically ill patients and is associated with high morbidity and mortality (1). Depending on the exact definition used, the incidence and prevalence of ARF in the intensive care unit (ICU) has been reported to be between 11% and 67% (1,2,3,8). It is usually asymptomatic and nonspecific but depending on the severity may present with various complications such as a metabolic acidosis, uraemia with its associated complications, electrolyte and fluid balance disturbance, and multiple organ dysfunction.

The pathophysiological mechanism of acute renal failure in a critically ill patient differs depending on the causative/precipitating agents, but some generally accepted concepts include, metabolic derangement which is exacerbated in ARF and results in loss of renal homeostatic function. Once established this further stimulates several inflammatory cytokines (4) and ischaemic and toxic insults to the kidney result in a cascade of events (5), (figures 1 and 2).

Based on the mechanism and predisposing factors involved and or timing of appropriate management, the renal recovery may be complete (kidney function returns to baseline), partial (a persistent change but not persistent need for renal replacement therapy, (RRT)) (9) or RRT independent at ICU and hospital discharge

(16) or progression to chronic renal disease as demonstrated in figure1 (4) and figure 3 (11).

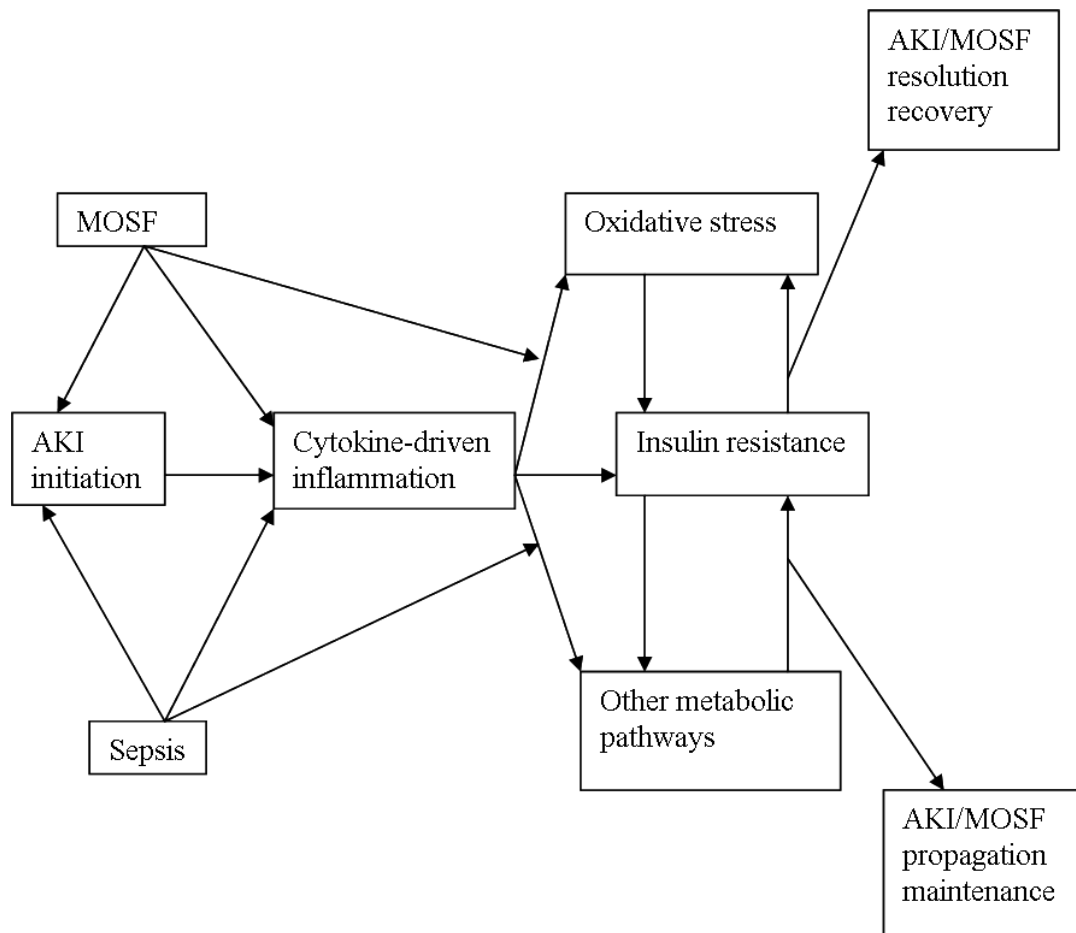


Figure 1: Proposed mechanism for dysmetabolism of AKI (AKI-acute kidney injury, MOSF-multiple organ systemic failure). **Adapted from** Himmelfarb J, Ikizler TA. Kidney International 2007; 71: 971–976.

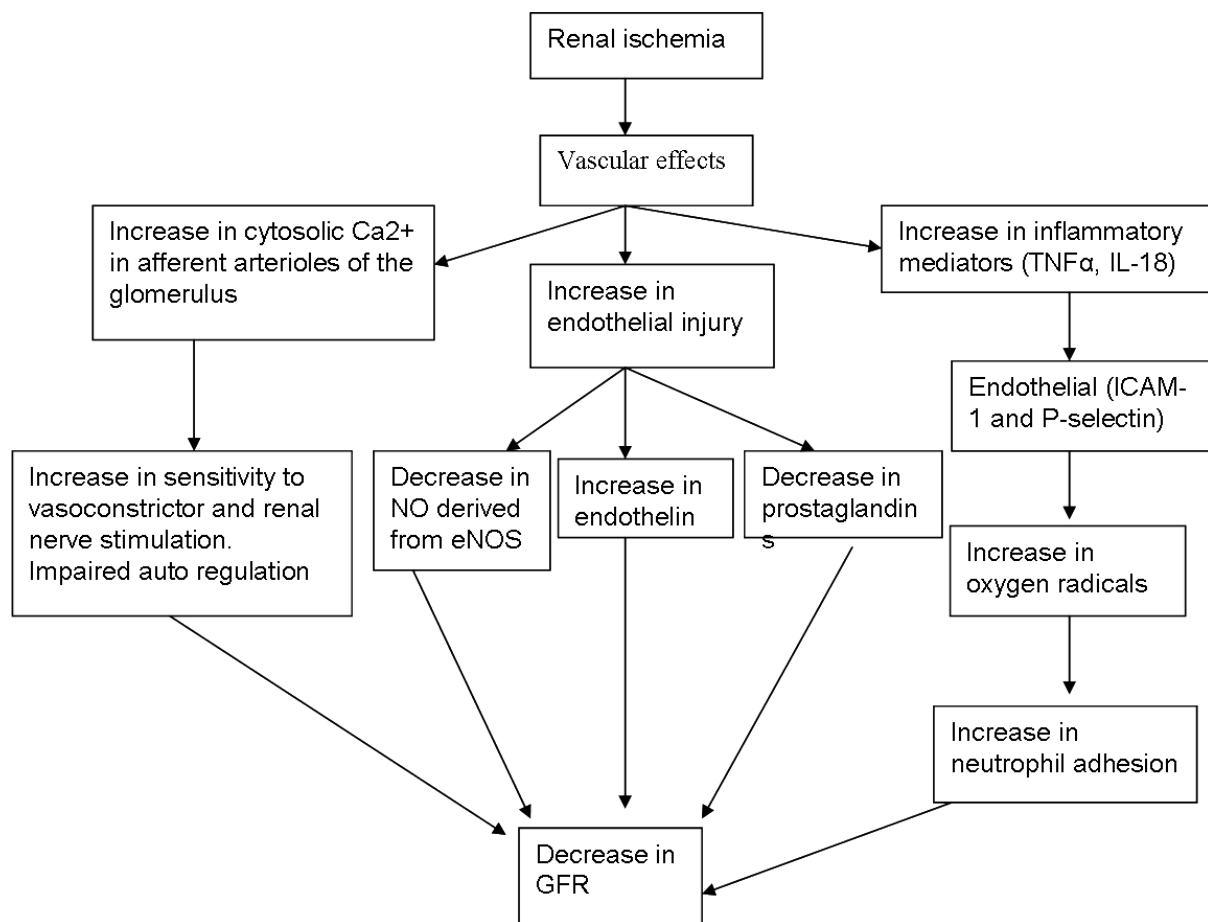


Figure 2.Pathogenesis of ischemic ARF. **Adapted from** Schrier RW et al, J Clin. Invest. 2004; 114:5-14

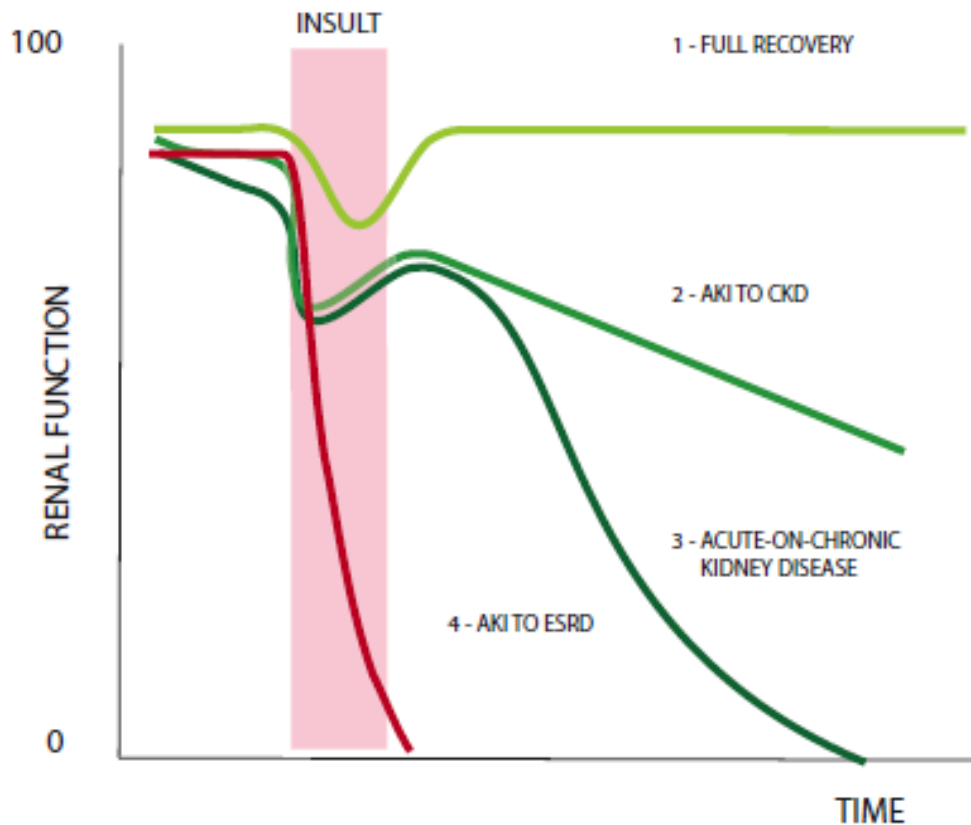


Figure 3. Natural history of ARF. **Reproduced from** Cerda J et al, Clin J Am Soc Nephrol 2008; 3: 881-886.

ARF is diagnosed on the basis of clinical presentation such as general patient's state, decreased urine production complimented with laboratory results and renal imaging. Urine output and characteristic laboratory findings have been used as the main parameters in defining and classifying ARF patients in ICU and hospital set up (9, 19,21).

1.1. SCORING SYSTEM.

Several scoring systems aimed at predicting risk of mortality and evaluating outcome in critically ill patients have been published and are in practice (10). Some of these scoring systems have no joint reference points and this has led to many definitions of Acute Renal Failure being used, which in turn has created confusion (9). Bellomo et

al. (2001) proposed a criteria derived from the acute lung injury/acute respiratory distress syndrome criteria to categorize different presentations of acute renal failure into three classified stages namely acute renal injury (ARI), acute renal failure syndrome (ARFS) and severe acute renal failure syndrome (SARF) based on absolute values of serum urea and serum creatinine, or urine output and the need for renal replacement therapy (Table 1) (21). Despite the fact that these criteria were not widely used, they became the foundation of the existing scoring systems. Recently the RIFLE classification (RIFLE stands for Risk of kidney injury, Injury to the kidney, Failure of kidney function, Loss of kidney functions, End-stage kidney disease) was established by Acute Dialysis Quality Initiative (ADQI) Group as represented in Figure 4 (9).

Table 1. Proposed criteria for ARI, ARFS, and SARFS.

ARI	ARFS	SARFS
Creat >120 μ mol/l and Urea >8mmol/l and/ or UO <800ml/24h or UO <200ml/6h	Creat >240 μ mol/l and Urea >16mmol/l and/or <400ml/24h or UO <100ml/6h	Need for RRT and either ARI or ARFS
If A/C ARI use increase in Creat of 60 μ mol/l or in urea of 4mmol/l and or UO same as above	If A/C ARI use increase in Creat of 1200 μ mol/l or in urea of 8mmol/l and or UO same as above	Need for RRT and A/C criteria for ARI or ARFS

ARI-Acute Renal Injury, ARFS-Acute Renal Failure Syndrome, SARFS-Severe Acute Renal Failure Syndrome, RRT-Renal Replacement Therapy, UO-Urine Output

Adapted from Bellomo R et al, Intensive Care Med 2001; 27:1685-8

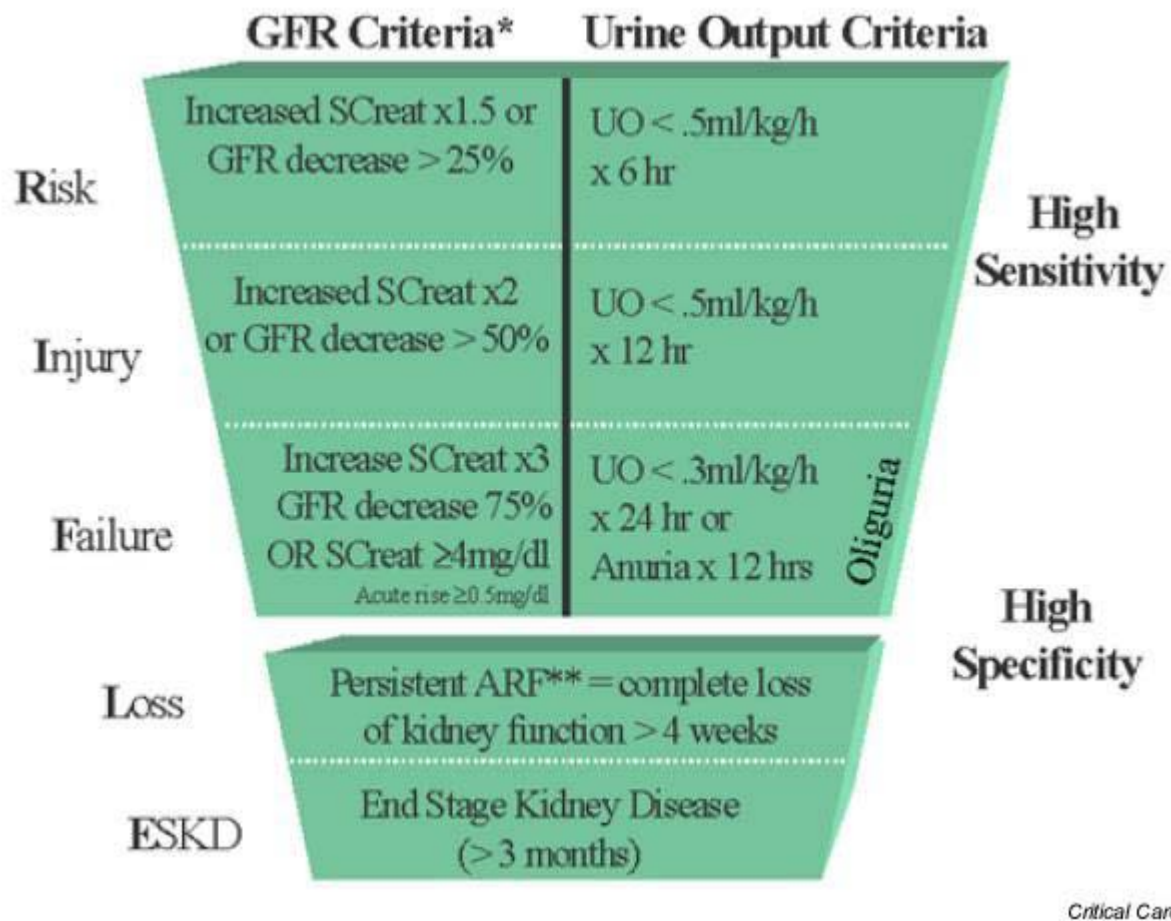


Figure 4: Classification for ARF using RIFLE criteria (acronyms for Risk of kidney injury, Injury to the kidney, Failure of kidney functions, Loss for kidney functions and End-stage kidney disease). **Reproduced from** Bellomo R et al, Critical care 2004;8:R204-12.

RIFLE classification evaluates various parameters as elucidated above and is now regarded as a useful tool for predicting mortality (5, 6, 7, 8, 26, 33) and outcome in ARF patients in ICU (6). Currently, AKIN (Acute Kidney Injury Network) has proposed a modification of RIFLE criteria into AKI staging system(19,20)as shown in Table 2. In both classifications each class increases with increase in severity but they differ in

their level of predicting outcome. Limited data exists with the use of these classifications in African ICU's.

Table 2: Classification/staging system for acute kidney injury (AKI).

AKI stage	Creatinine criteria	Urine output criteria
AKI stage I	Increase of serum creatinine by ≥ 0.3 mg/dl (≥ 26.4 μ mol/L) or increase to $\geq 150\%$ – 200% from baseline	Urine output < 0.5 ml/kg/hour for > 6 hours
AKI stage II	Increase of serum creatinine to $> 200\%$ – 300% from baseline	Urine output < 0.5 ml/kg/hour for > 6 hours
AKI stage III	Increase of serum creatinine to $> 300\%$ from baseline or serum creatinine ≥ 4.0 mg/dl (≥ 354 μ mol/L) after a rise of at least 44 μ mol/L or treatment with renal replacement therapy	Urine output < 0.3 ml/kg/hour for > 24 hours or anuria for 12 hours

Reproduced from Ostermann M et al, Crit Care 2008; 12(6): R144.

1.2. Statement of the problem and Justification

The mortality of patients with acute renal failure in intensive care unit irrespective of cause is considerable worldwide. Early detection of any renal function derangement and prompt initiation of appropriate management plays a significant role in altering the outcome of acute renal failure in critically ill patients. The delay in immediate management of patients with acute renal failure in the intensive care set up results in

potentially serious complications which further contribute to high morbidity and mortality (37, 38, 39). In order to address the above problem, various scoring systems such as RIFLE criteria and the AKIN staging system have been developed in an effort to improve the ability to predict the outcome of ARF patients in ICU. Despite the fact that both systems have been shown to predict hospital mortality and short-term prognosis, the RIFLE criteria has better discriminatory power and overall correctness than the AKIN criteria (21). The use of RIFLE criteria has not been documented in African ICUs' despite evidence that it represents a simple and useful tool for early ARF detection and prediction of its outcome in ICU and hospitals (18). This study therefore aims at assessing the outcome of ARF in patients admitted to an adult multidisciplinary ICU using the RIFLE classification. Given the above, it was deemed important to conduct this study using RIFLE criteria to determine the outcome of AKI in order to provide updated data from an academic African institution. A recent study at the same facility defined ARF as a rise in serum creatinine of more than twice the upper limit of normal (i.e. $240\mu\text{mol/l}$), and documented mortality rate in patients with ARF of 52.5% (24).

It is hoped that the findings from this study will assist with future guidelines relating to the management of patients with ARF in ICU settings, particularly in developing countries.

1.3. Literature Review

A study from Belgium looking at predictive factors, incidence, comorbidity and outcome of ARF in patients with sepsis in a surgical ICU revealed that ARF developed in 16.2% of the patients admitted, among which 70.0% required dialysis. Advanced age, use of vasoactive therapy, mechanical ventilation and RRT were

associated with high mortality. Patients with ARF had higher mortality compared with patients without ARF (14).

Data from a multinational, multicenter prospective study involving 16 countries in Europe reported ARF to have occurred in 24.7% of 1411 patients. The identified risk factors for the development of ARF were older age (more than 65 years), acute circulatory or respiratory failure, presence of infection, past history of chronic heart failure, haematological malignancy, or cirrhosis. These factors at admission were also associated with increased ICU mortality. The mortality rate was higher in patients with ARF (42.8%) than in patients without ARF (14%) (31). Patients with ARF might have been underreported in this study since a cut-off creatinine of greater than 300 μ mol/l was used to define ARF.

A multicentre prospective study to assess prognostic factors in patients with acute renal failure due to sepsis in France revealed overall mortality of 74.5%. Factors associated with high mortality from this study included altered previous health status, previous hospital admission, need for mechanical ventilation, advanced age and sepsis. Mortality was much higher in elderly and septic patients with ARF (12).

Studies from Australian Intensive Care Units have demonstrated different incidences of ARF. A study conducted in more than 20 ICU's over 10 year period revealed that acute kidney injury occurred in a total number of 4,754 patients at the time of or within 24 hours of ICU admission. The incidence in this study population ranged from 4.6 to 6.9% with an estimated crude cumulative incidence of 5.2%(2). This is similar to that found from a multinational multicenter study which revealed that 5.7% of patients developed ARF during their ICU stay, with a period prevalence of 1.4% to 25% across all the study centers (1). A high incidence has been reported from the

same area (Australia) as demonstrated by data collected from Australia New Zealand Intensive Care Society Adult Patient Database (ANZICSAPD) between January 2000 to December 2005. One hundred and twenty thousand one hundred and twenty three patients were evaluated with an acute kidney injury occurring in 36.1% within 24 h of ICU admission. Maximum RIFLE category Risk occurred in 16.2% of the patients, Injury in 13.6% and Failure in 6.3%. The likelihood of developing AKI was higher in older patients (age $\geq$ 65 years), females and those with co-morbid disease (18).

Similar incidences have also been reported in Europe, Latin America, Asia, and the USA. A study in the UK and Germany involving 22,303 patients revealed that 35.4% to have AKI based on the AKI criteria. Of AKI patients, AKI stage I and II (same as RIFLE- R and I class) contributed 19.1% and 3.8% respectively and 12.5% AKI III. Twenty four percent of patients with AKI III had three or more organ failures as compared to 3.4% for AKI I and 6.4% for AKI II (19).

A study in Brazil, which included patients of all age groups, aimed at examining acute kidney injury after trauma. One hundred and twenty nine patients were included in the study. AKI was reported to have occurred in 40.3% of the studied patients (25). In another study from the same area with 381 ICU admissions, ARF occurred in 33.5% of patients. The main causes of ARF were shown to be hypotension (48.4%), sepsis (40.6%), nephrotoxic drugs (21.9%), rhabdomyolysis (9.1%), hepatorenal syndrome (3.9%), vasculitis (3.1%), and glomerulonephritis (1.6%). Co-morbidities reported included respiratory insufficiency (28.9%), cardiovascular disease (25.8%), hypertension (19.4%) and diabetes mellitus. Surgical complications contributed 9.4%, liver diseases 7.8% and malignancies

5.3%. Independent risk factors for death included need for mechanical ventilation, liver failure, use of vasopressors and sepsis. The mortality rate in this population was found to be 62.5% (26).

Data from a study conducted in Korea to evaluate the occurrence of AKI using RIFLE classification in the intensive care unit showed that AKI occurred in 41.3% of patients with maximum RIFLE-R, I and F class in 13.8%, 12.4%, and 15.1% respectively. The mean age (62.5 ± 15.9 years), occurrence of AKI, pulmonary disease and malignancy were independent risk factors for hospital mortality. The overall mortality rate of ICU patients was 25.7% (27).

A multicentre study from the USA which evaluated a total number of 5,383 patients has also reported that AKI developed in 67% of ICU admissions, with maximum RIFLE class R, I and F in 12%, 27%, and 28% respectively. The progression of severity from one class to the other was also noted and patients with maximum RIFLE class R, I and F had hospital mortality of 8.8%, 11.4% and 26.3% respectively (8)

A study in patients with major burns in Sweden (n=127) has shown that 24% of patients with major burns as defined by total body surface area (TBSA) $\geq 20\%$, developed AKI during their study period. In this study it was also reported that half of the patients who developed AKI (55%, 17 of 31) reached the level for Risk within the first 7 days, and 81% (25 of 31) within 14 days. All patients that developed AKI had systemic inflammatory response syndrome (SIRS) on day one and 87% of those were found to have sepsis within a week before reaching RIFLE- R class. Thirty nine percent of patients with AKI were on nephrotoxic antibiotics and in half of these

patients the derangement of renal function was noted after starting these agents (13).

Data from Canada in a large ICU study showed that 240 patients (4.2% of patient cohort) were diagnosed to have ARF and that the rate of ARF was higher in males and in those with age above 65 years. Risk factors for development of ARF were previous heart disease, stroke, pulmonary disease, diabetes mellitus, cancer, connective tissue disease and alcoholism (16). The recovery rate of renal function in ARF survivors at ICU and hospital discharge in this and other studies has been shown to range between 38% and 68 % (16, 17).

A study of 487 patients to determine factors predisposing and complicating ARF in a medical ICU in the Netherlands showed that 16% of patients had ARF and 63% of ARF patients required RRT. Factors such as advanced age, prior chronic disease, cardiovascular and pulmonary failure were independently associated with the development of ARF and all these factors together with RRT (except prior chronic disease) independently influenced the ARF mortality. The overall mortality in these patients was 63%. (15).

A study from the Western Cape, South Africa, which included a total of 198 medical patients admitted to a Medical ICU, reports that 23.2% of patients had or developed ARF. The leading causes noted in this study were acute tubular necrosis (82%) which resulted from sepsis, hypoperfusion and nephrotoxic medications. Other factors attributed to development of ARF included acute glomerulonephritis, malignant hypertension and vasculitis. Seventeen percent of patients with ARF needed acute renal replacement therapy. Mortality was higher in ARF patients (47.8%) compared with 17.5% of patients without ARF. Mechanical ventilation,

dialysis and multiorgan failure were noted to affect the outcome (23). Data from a study in Johannesburg, looking at the outcome of ICU patients requiring dialysis have also reported overall mortality of 52.5 % (24).

A prospective study from Germany which looked at 160 patients to assess the outcome of patients with ARF requiring daily as compared with alternate day haemodialysis, revealed an overall mortality of 37%. ARF patients who were on daily haemodialysis had a lower mortality rate of 28% as compared to the conventional (alternate day) haemodialysis group (37%) (22).

A National survey on the epidemiology and outcome of hospitalised ARF patients from the USA showed that ARF was commonly found in older patients, men, and black patients upon discharge. It was also common in patients with coexisting diseases such as congestive cardiac failure, cancer, chronic lung disease, and HIV infection. Among patients with ARF, 7.5% required dialysis. Patients with ARF had higher a mortality rate of 21.5% as compared to patients without ARF (2.3%) (28).

A study from Taiwan demonstrated that the mortality in patients with ARF progressively increased with each RIFLE class (RIFLE-R, I and F 63.2%, 69.2%, and 86.2% respectively). Factors associated with increased mortality in each RIFLE class included septic shock, liver cirrhosis and ARDS (29).

A study from Saudi Arabia showed that 9.0% of ARF patients required RRT, and was associated with a mortality of 64% .This study showed that high serum creatinine was an independent factor for better outcome while mechanical ventilation was an independent factor for worse outcome. It was generally found that the need for RRT in ICU was associated with high mortality (30). The association of high serum creatinine with better outcome is attributed to the absence or less co-morbid

conditions such as liver disease, decreased muscle mass and aging. These conditions are associated with decreased creatinine production and their absence may favour better outcome (30, 42).

Data from Pennsylvania in the USA in a multicentre study involving 1530 ICU patients with 254 ARF patients, showed an incidence of ARF of 17%. Eleven percent of these patients (ARF) needed dialysis. The mortality was higher in ARF patients (23%) as compared with 5% of non ARF patients. Patients with ARF on dialysis had a mortality rate of 57% (32).

Two studies looking at outcome of ARF in critically ill HIV patients from Portugal have shown that with and without using RIFLE criteria, 47.4% of the study population (97 patients) had some degree of renal dysfunction with an overall mortality of 43.3% (34,35). Factors independently associated with increased mortality in HIV patients with ARF included, age above 60 years, concomitant hepatitis C, and severity of illness (34). Based on RIFLE criteria, it was found out that in HIV patients with ARF, 26% of patients were in R class, 19.5% in I class and 54.3% in F Class. RIFLE I and F class independently predicted mortality (35).

Another study from France showed that the mortality in critically ill HIV infected patients admitted to ICU declined from 25% in 1996 to 8.6% in 2004 to 2005; this decline is attributed to the use of HAART and admission to ICU. Factors identified to be associated with increased mortality in these patients in ICU included delayed ICU admission, acute renal failure, hepatic cirrhosis, severe sepsis and ICU admission for coma (36).

A multicentre prospective study conducted in Belgium over a 3 year period between April 2001 and March 2004 to investigate the outcome of AKI and different treatment

options included 316 AKI patients on dialysis. In this study 144 patients were randomly assigned to receive intermittent renal replacement therapy (IRRT) and 172 patients to receive continuous renal replacement therapy (CRRT). There was no difference in duration of ICU or hospital stay and the mode of dialysis had no impact on outcome in ICU. Patients who were on IRRT had a mortality rate of 62.5% compared with 58.8% who received CRRT (43).

Another multicentre prospective study from Italy done between June 2005 and December 2007 to evaluate the dose of RRT and the outcome in patients with ARF, included 553 AKI patients on RRT. Three hundred and thirty three patients were on CRRT and 87 were on IRRT. This study showed no survival benefit among patients on higher dose of RRT (44).

An observational outcome analysis evaluating Intermittent Haemodialysis (IHD) versus CRRT for ARF in ICU from the USA which included 161 patients on RRT (84 on CCRT and 77 patients on IHD), showed that the RRT modality did not affect the likelihood of renal recovery, in-hospital survival, or survival during follow up (45).

Various studies have revealed that Sustained Low Efficiency Dialysis (SLED) is an efficient mode of RRT comparable to Continuous Venovenous Hemofiltration (CVVH) and has a cardiovascular tolerability profile in critically ill patients similar to CRRT (46).

1.4. Definition of terms

- **Acute renal failure** – As per RIFLE classification

- **Conservative treatment** – Patients who received other modes of ARF management, such as intravenous fluid and or furosemide infusion but not dialysis.
- **Chronic renal failure** – Complete loss of renal function for more than four weeks as per RIFLE Classification
- **Multidisciplinary ICU** – An Intensive Care Unit to which critically ill medical and surgical patients are admitted.
- **Recovery of ARF** – Either complete whereby kidney function returns to baseline classification within the RIFLE criteria, or partial i.e. a persistent change in RIFLE classification but not persistent need for RRT (9)
- **Outcome** – Patients Discharged dead or alive from ICU and hospital (for those discharged from ICU to the ward)

1.5. OBJECTIVES OF THE STUDY

1.5.1. Broad objective

The broad objective of the study was to assess the outcome of ARF in patients admitted to ICU using the RIFLE classification at CMJAH, January to December 2008.

1.5.2. Specific objectives

The specific objectives of this study were;

1. To determine the incidence of ARF in patients admitted to the multidisciplinary ICU at CMJAH, Johannesburg from January 1st to December 31st, 2008.

2. To determine factors associated with ARF recovery in patients admitted to the multidisciplinary ICU at CMJAH, Johannesburg from January 1st to December 31st, 2008.
3. To assess the mortality of patients with ARF admitted to the multidisciplinary ICU based on RIFLE criteria at CMJAH, Johannesburg from January 1st to December 31st, 2008.
4. To assess the factors that independently predict the mortality of patients with ARF admitted to the multidisciplinary ICU based on RIFLE criteria at CMJAH, Johannesburg from January 1st to December 31st, 2008.
5. To assess the factors that predict mortality in patients with ARF discharged from ICU to the ward based on RIFLE criteria at CMJAH, Johannesburg from January 1st to December 31st, 2008

1.6. Research question.

The primary research question of this study was to investigate whether the RIFLE criteria is a useful tool for predicting the outcome of acute renal failure in the intensive care unit.

1.7. Variables

1.7.1. Outcome variables

- Mortality in ICU and Hospital (for patients discharged from ICU)

1.7.2. Explanatory variables

- Demographic factors such as age, sex, race,
- Clinical factors such as reason for ICU admission, inotropic support, ventilation support, combined ventilation with inotropic support and dialysis

- Comorbidities such as diabetes, chronic pulmonary disease, chronic cardiovascular disease, connective tissue disease, HIV status, HIV/TB coinfection, cancer

CHAPTER TWO

2. Materials and method

2.1. Study Design.

This was a retrospective chart review where medical records of patients with acute renal failure admitted to the multidisciplinary intensive care unit at CMJAH for a period of one year from January 2008 to December 2008 were reviewed.

2.2. Study site/ area

This study was conducted in the multidisciplinary ICU at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). CMJAH is an accredited central tertiary care academic hospital with 1088 beds serving patients from across the Gauteng province and neighbouring provinces. It is estimated to have more than 4000 professional and support staff offering a full range of specialized services to inpatients and outpatients.

It is located in Parktown and serves as a referral hospital for a number of hospitals in its referral chain.

The hospital is also a major teaching hospital for The University of the Witwatersrand, faculty of Health Sciences for undergraduate and post-graduate training in all area of health professions (47)

The multidisciplinary intensive care unit which is mainly run by the Respiratory Unit has an average of 1000 admissions a year with 12 ICU beds in ward 576 and 6 to 8 beds in high care, ward 579, all located in the medical block.

2.3. Study population.

The study reviewed medical records of patients admitted to the multidisciplinary ICU at Charlotte Maxeke Johannesburg Academic hospital from January 2008 to December 2008 and assessed for eligibility criteria.

2.4. Inclusion criteria

The study included medical records of patients with acute renal failure admitted to the multidisciplinary intensive care unit at CMJAH year 2008.

2.5. Exclusion criteria.

The following patients were excluded from the study

- All patients with chronic renal failure whether on dialysis or not.
- Patients admitted with acute on chronic renal failure.
- Readmitted patients who previously had ARF in ICU (only entered once in the data sheet)
- Patients who were less than 18years of age.
- Patients with ARF whose outcome data was missing in the record.

2.6. Sampling and sample size

A total number of 507 patients' files for the period of one year from January to December 2008 were available for review. Thirty seven patients with renal failure were excluded from the study (14 – Chronic renal failure, 6 – readmitted, so entered

once in the data set, 7 –less than 18 years of age, and 10 patients had no outcome indicated on discharge from ICU-missing data).Hence 193 study participants with acute renal failure were included in the study as summarised below

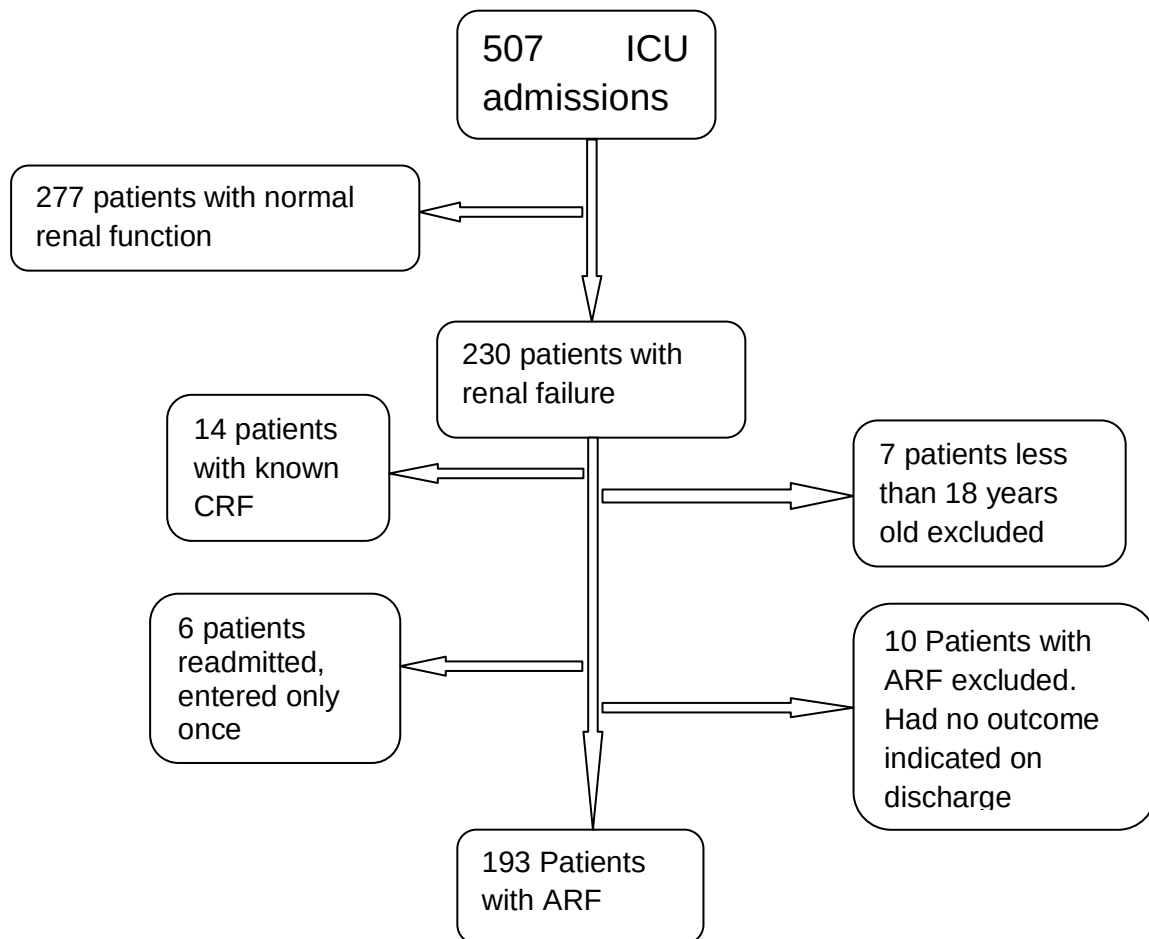


Figure 5.Flow diagram of the study population

2.7. Data management

2.7.1. Data collection

The following data were collected from the patients' records: demographic information, reason for ICU admission, presence of co-morbidity, RIFLE criteria for ARF on admission and on discharge, clinical details, modality and duration of treatment specifically for acute renal failure, use and duration of inotropic support and need for mechanical ventilation and its duration. Data on occupation, level of education, social habit such as alcohol intake and smoking were not documented in the majority of patients' files hence not recorded for analysis. For the purpose of this study, serum creatinine was used as per RIFLE classification to define ARF.

The above information was recorded and then entered in Microsoft Excel 2007 relational database software by the investigator. The data set was then transferred to STATA version 11 for; cleaning which involved removal of duplicates and checking for missing variables, grouping and coding, determining for internal consistency and statistical analysis.

2.7.2. Data analysis

The Primary outcome, which was survival or death, was then assessed in relation to the maximum RIFLE classification reached during patients' ICU stay.

Continuous variables such as age were described by determining their means, standard deviations, and ranges and categorical variables were presented in frequency distribution tables. The Chi-square test (bivariate analysis) was used to compare the proportions patients with acute renal failure or deaths between independent variables and chi-square of trend was used for ordered categorical

variables such as age and RIFLE criteria. A p value ≤ 0.1 was considered statistically significant where the chi-square test was used.

Variables that were found to be statistically significant in the bivariate analysis were then subjected to inferential statistics for univariate and/ or multivariate Cox hazards regression model to assess the outcomes and independent effects of the respective variables and control for confounding variables. A p-value ≤ 0.05 was used for inferential statistics. Survival analysis was also performed for each significant variable from the above regression model. This was presented by using Kaplan-Meier (K-M) curve and log-rank was used to test for significance.

2.8. ETHICAL CONSIDERATION

The study was unconditionally approved by the Human Research ethics committee (Medical), University of the Witwatersrand, Clearance certificate number M090906.

Only serial numbers were used to all patients' files reviewed in the study to maintain confidentiality.

CHAPTER THREE

3. Results

3.1. Descriptive analysis

3.1.2. Demographic characteristics of the study participants.

A retrospective chart review was conducted over a period of one year and a total number of 193 patients with ARF were enrolled in the study with a mean APACHE II score of 19 ± 6.4 SD, the maximum score documented being 38 (table 3).

The age of the study participants ranged between 21 and 92 years with a mean age of $50.5\text{years} \pm 18.3$ SD. 64.2% of all patients were above 41years of age.

The majority of patients were male (52.3%) and black (63%) (table 4).

Table 3.APACHE II score

Variable	Observation	Mean	SD	Min	Max
APACHE II	193	19.1	6.4	7	38

Table 4.Demographic characteristics of Patients with ARF

Variable	Number	Percentage (%)
Age		
18-40years	69	35.8
41-60years	62	32.1
> 60years	62	32.1
Sex		
Female	92	47.7
Male	101	52.3
Race		
Black	122	63.2
Other race groups	71	36.8

3.1.3. Comparison of patients by RIFLE criteria.

The majority of the patients on admission had normal renal function (40.9%) with RIFLE R, I and F class constituting 23.3%, 14.0% and 21.8 % respectively (Table 4).

Table 5.Distribution of patients based on RIFLE criteria

Variable	Number	Percentage (%)
RIFLE on admission		
Normal renal function	79	40.9
R class	45	23.3
I class	27	14.0
F class	42	21.8
Maximum RIFLE in ICU		
Normal renal function	63	34.4
R class	31	17.0
I class	46	25.1
F class	43	23.5

3.2. Bivariate analysis

3.2.1. Comparison of number of organ(s) involved with RIFLE classification

Patients with RIFLE I and F class had two or more organ involvement (Table 5).

Table 6.Comparison of NOI with maximum RIFLE

Variable	RIFLE Class				P-value
	NRF	R class	I class	F class	
NOI					
1	28(44.4%)	10(32.3%)	12(26.1%)	16(37.2%)	0.119
2	25(39.7%)	15 (48.4%)	30(65.2%)	17(39.5%)	
≥3	10(15.9%)	6(19.3%)	4(8.7%)	10(23.3%)	

NRF=Normal renal function, NOI= Number of organ(s) involved

3.2.2. Factors associated with acute renal failure recovery in the intensive care unit.

The Chi square test was performed to determine the difference between the distributions of factors associated with ARF recovery. A factor was considered for multivariate analysis if it had a P-value of ≤ 0.1 . Factors associated with ARF

recovery were: use of inotropic support, ventilatory support, need for both-ventilatory and inotropic support, and the need for dialysis.

Table 7. Comparison of factors on recovery of ARF in ICU

Variable	Recovered ARF Number (%)	ARF Number (%)	P-value
Age			
18- 40 years	26 (41.3%)	37 (30.8%)	0.259
41-60 years	16 (25.4%)	43 (35.8%)	
>60 years	21 (33.3%)	40 (33.3%)	
Sex			
Female	31 (49.2%)	56 (46.7%)	0.744
Male	32 (50.8%)	64 (53.3%)	
Race			
Black	38 (60.3%)	76 (63.3%)	0.689
Other race groups	25 (39.7%)	44 (36.7%)	
Reason for admission			
Cardiovascular disease	4 (6.4%)	10 (8.3%)	0.625
Gastrointestinal disease	2 (3.2%)	9 (7.5%)	
Metabolic disease	2 (3.2%)	6 (5.0%)	
Neurological disease	0 (0)	4 (3.3%)	
Poisoning	1 (1.6%)	3 (2.5%)	
Post-surgery	29 (46.0%)	51 (42.5%)	
Pulmonary disease	18 (28.6%)	25 (20.8%)	
Sepsis	7 (11.1%)	12 (10.0%)	
Diabetes			
No	56 (88.9%)	110 (91.7%)	0.539
Yes	7 (11.1%)	10 (8.3%)	
Chronic pulmonary disease			
No	51 (81.0%)	105 (87.5%)	0.235
Yes	12 (19.0%)	15 (12.5%)	
Chronic cardiovascular disease			
No	38 (60.3%)	80 (66.7%)	0.394
Yes	25 (39.7%)	40 (33.3%)	
HIV status			
No	37 (58.7%)	60 (50.0%)	0.407
Yes	12 (19.1%)	33 (27.5%)	
Unknown	14 (22.2%)	27 (22.5%)	
HIV/TB co infection			
No	39 (61.9%)	63 (52.5%)	0.434
Yes	4 (6.3%)	12 (10.0%)	
Unknown	20 (31.8%)	45 (37.5%)	
Cancer			
No	57 (90.5%)	112 (93.3%)	0.49
Yes	6 (9.5%)	8 (6.7%)	
Connective tissue disease			
No	62 (98.4%)	115 (95.8%)	0.352

Yes	1 (1.6%)	5 (4.2%)	
Re-operated			
No	52 (82.5%)	102 (85.7%)	0.572
Yes	11(17.5%)	17 (14.3%)	
Inotropic support			
No	25 (39.7%)	19 (24.0%)	
Yes	38 (60.3%)	101 (84.2%)	0.00*
Ventilatory support			
No	16 (25.4%)	13 (10.8%)	
Yes	47 (74.6%)	107 (89.2%)	0.10*
Ventilatory and inotropic support.			
No	29 (46.0%)	24 (20.0%)	
Yes	34 (54.0%)	96 (80.0%)	0.00*
Dialysis			
No	46 (73.0%)	39 (32.5%)	
Yes	17 (27.0%)	81 (67.5%)	0.00*
RIFLE on admission			
Normal	33 (52.4%)	42 (35.0%)	
R class	16 (25.4%)	28 (23.3%)	0.013*
I class	9 (14.3%)	17 (14.2%)	
F class	5 (7.9%)	33 (27.5%)	
RIFLE in ICU			
Normal	20 (32.3%)	9 (8.0%)	
R class	25 (40.3%)	23 (20.4%)	0.00*
I class	15 (24.2%)	39 (34.5%)	
F class	2 (3.2%)	42 (37.2%)	

*Statistically significant

3.3. Inferential statistics

3.3.1. Univariate Cox proportional Hazards regression

Factors with p-value ≤ 0.1 in the bivariate analysis were considered significant hence were evaluated further in the univariate Cox Proportional Regression model to assess their association with ARF recovery and the P-value 0.05 was considered significant. All factors were not statistically significant after univariate cox proportional regression analysis (Table 6)

Table 8. Factors associated with ARF recovery.

Univariate Cox Proportional Hazards regression analysis

Factor	Univariate
	HR, 95%CI, P-value
Inotropic Support	
No	1
Yes	1.26 (0.77 2.06) 0.36
Ventilatory support	
No	1
Yes	0.79 (0.44 1.42) 0.42
Ventilatory and inotropic support	
No	1
Yes	1.21 (0.77 1.89) 0.41
Dialysis	
No	1
Yes	1.44 (0.98 2.13) 0.06

NOTE HR =Hazard ratio, CI = Confidence interval

3.4. Mortality in patients with ARF in the intensive care unit

The Chi square test was performed to determine the distributions of factors associated with mortality. A factor was considered statistically significant if it had a P-value of ≤ 0.1 . The overall mortality in patients with ARF was 59.95%. Factors significantly associated with mortality were: age, race, Cancer, inotropic support, ventilatory support, need for ventilation and inotropic support, dialysis, chronic pulmonary disease and maximum RIFLE class in ICU.

Table 9. Factors associated with mortality in patients with ARF in ICU.

Variable	Alive	Dead	P-value
Age			
18-40years	35 (44.9%)	34 (29.6%)	0.024*
41-60years	26 (33.3%)	36 (31.3%)	
>60years	17 (21.8%)	45 (39.1%)	
Race			
Black	57 (73.1%)	65 (56.5%)	0.019*
Other race groups	21 (26.9%)	50 (43.5%)	
Sex			
Female	36 (46.2%)	56 (48.7%)	0.729
Male	42 (53.8%)	59 (51.3%)	

Maximum RIFLE			
Normal	48 (61.5%)	15 (14.3%)	0.00*
R class	9 (11.5%)	22 (21.0%)	
I class	12 (15.4%)	34 (32.4%)	
F class	9 (11.5%)	34 (32.4%)	
Diabetes			
No	71 (91.0%)	104 (90.4%)	0.890
Yes	7 (9.0%)	11 (9.6%)	
Chronic cardiovascular disease			
No	53 (68.0%)	75 (65.2%)	0.694
Yes	25 (32.0%)	40 (34.8%)	
HIV status			
No	39 (50.0%)	60 (52.2%)	0.948
Yes	20 (25.6%)	29 (25.2%)	
Unknown	19 (24.4%)	26 (22.6%)	
HIV/TB co infection			
No	42 (53.9%)	62 (53.9%)	0.471
Yes	5 (6.4%)	13 (34.8%)	
Unknown	31 (39.7%)	40 (11.3%)	
Cancer			
No	69 (88.5%)	109 (94.8%)	0.107*
Yes	9 (11.5%)	6 (2.2%)	
Connective tissue disease			
No	76 (97.4%)	111 (96.5%)	0.720
Yes	2 (2.6%)	4 (3.5%)	
Chronic pulmonary disease			
No	71 (91.0%)	94 (81.7%)	0.072
Yes	7 (9.0%)	21 (18.3%)	
Inotropic support			
No	35 (44.9%)	9 (7.8%)	0.00*
Yes	43 (55.1%)	106 (92.2%)	
Ventilatory support			
No	20 (25.6%)	9 (7.8%)	0.001*
Yes	58 (74.4%)	106 (92.2%)	
Ventilatory and inotropic support			
No	39 (50.0%)	14 (12.2%)	0.00*
Yes	39 (50.0%)	101 (87.8%)	
Dialysis			
No	46 (59.0%)	44 (38.3%)	0.005*
Yes	32 (41.0%)	71 (61.7%)	

*Statistically significant

3.5. Inferential statistics

3.5.1. Univariate and Multivariate Cox Proportional Hazards regression

Factors with p-value ≤ 0.1 in the bivariate analysis were considered significant hence were evaluated further in the univariate Cox Proportional Regression model to

assess independent association with mortality.

All variables with $p\text{-value} \leq 0.05$ in the Univariate Cox Proportional Regression model were considered significant. Race, inotropic support, a need for both-ventilation with inotropic support and maximum RIFLE criteria were retained in the final multivariate Cox Proportional Regression model. After Univariate analysis Race, inotropic support, ventilation with inotropic support and maximum RIFLE criteria variables were statistically significant. After multivariate analysis race, inotropic support, maximum RIFLE class and need for both-ventilation and inotropic support remained statistically significant. Non-blacks had 1.56 fold greater risk of dying as compared to blacks (adjusted HR 1.56, 95%CI 1.07 - 2.28; $p\text{-value}$ 0.02). Those on inotropic support had 2.36 fold greater risk of dying as compared to those who were not (adjusted HR 2.36, 95%CI 1.02 – 6.18; $p\text{-value}$ 0.04). Those who needed both-ventilation and inotropic support had 1.14 greater risk of dying as compared to those who were not (adjusted HR 1.14, 95%CI 1.09 – 2.53, $p\text{-value}$ 0.01). With RIFLE criteria, patients in R, I, and F class had 5.41, 3.17, 5.69 greater risk of dying respectively as compared to patients with normal renal function (adjusted HR 5.41 95%CI 2.66 - 11.0, $p\text{-Value}$ 0.000 for R class, HR 3.17 95%CI 1.65 - 6.07; $p\text{-value}$ 0.001for I class, and HR 5.69 95%CI 2.93 - 11.06, $p\text{-value}$ 0.001 for F class). The results are shown in the table below.

Table 10 . Factors associated with mortality.

Univariate and Multivariate Cox Proportional Hazards Regression results

Factor	Univariate	Multivariate
	HR, 95%CI, P-value	HR, 95%CI, P-value
Age Categories		
18 to 40 years	1	
41 to 60 years	1.07 (0.67 1.72) 0.77	

> 60 years	1.39 (0.89 2.19) 0.14	
Race Blacks Other race groups	1 1.63 (1.13 2.39) 0.01	1 1.56 (1.07 2.28) 0.02*
Inotropic support No Yes	1 2.76 (1.39 5.46) 0.004	1 2.36 (1.02 6.18) 0.04*
Ventilatory support No Yes	1 1.18 (0.59 2.35) 0.64	
VS and IS No Yes	1 2.17 (1.23 3.79) 0.007	1 1.14 (1.09 2.53) 0.01*
Dialysis No Yes	1 1.11 (0.76 1.63) 0.59	
Chronic pulmonary disease No Yes	1 1.09 (0.67 1.77) 0.73	
Maximum RIFLE class Normal R class I class F class	1 5.21 (2.59 10.45) 0.000 3.63 (1.91 6.89) 0.000 4.95 (2.59 9.43) 0.000	1 5.41 (2.66 11.0) 0.000* 3.17 (1.65 6.07) 0.001* 5.69 (2.93 11.06) 0.001*

Assessing proportional hazard assumptions.

The global test for the proportional hazard assumption of all variables in the Univariate and Multivariate model analysis didn't show evidence that the model specified violates proportional hazard assumptions (P-value > 0.05).

Therefore factors independently associated with mortality after multivariate analysis were Race (other race groups), Inotropic support, RIFLE class on discharge and a need for ventilatory and inotropic support (VS and IS)

3.6. Survival analysis

3.6.1. Incidence

Patients were at risk for a total of 1268 person days of follow up. The acute renal failure incidence rate was 95 /1000 person days.

By 3rd, 7th and 13th day, ARF had occurred in 25%, 50% and 75% of the study participants respectively as shown in figure 6.

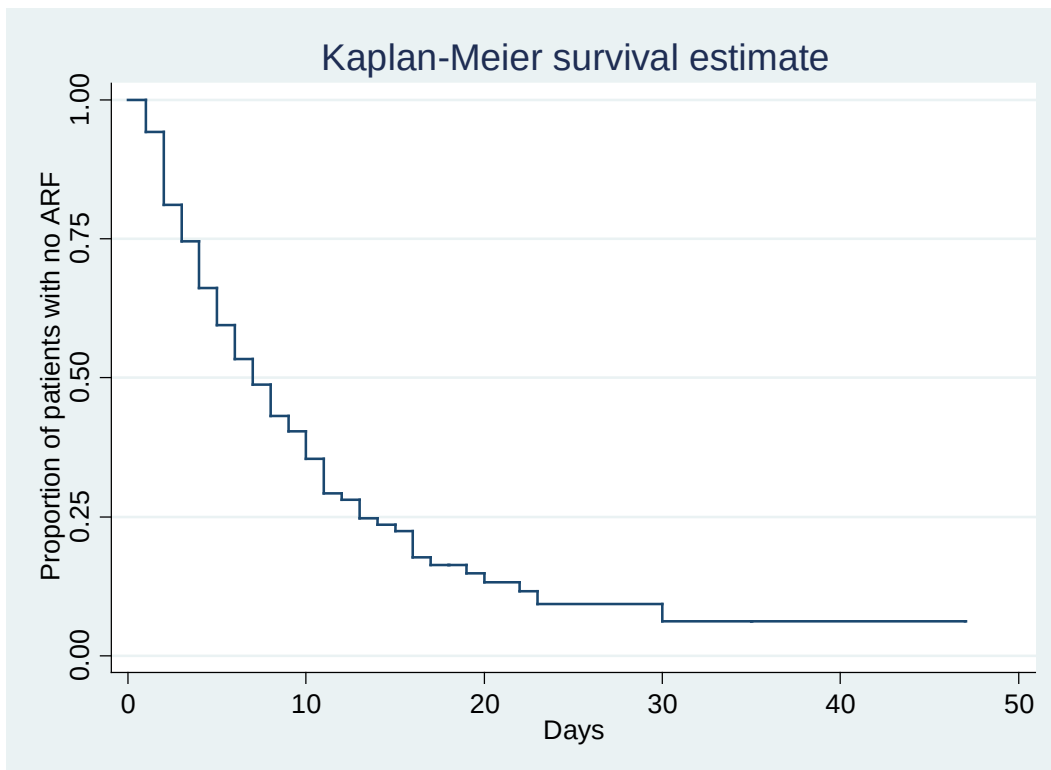


Figure 6. Kaplan – Meier curve for occurrence of ARF in ICU patients

3.6.2. Mortality in ICU

Patients were at risk for a total of 1268 person days of follow up. The death incidence rate was 9/100 person days. Twenty five percent of the patients who died survived more than 16 days of follow up.

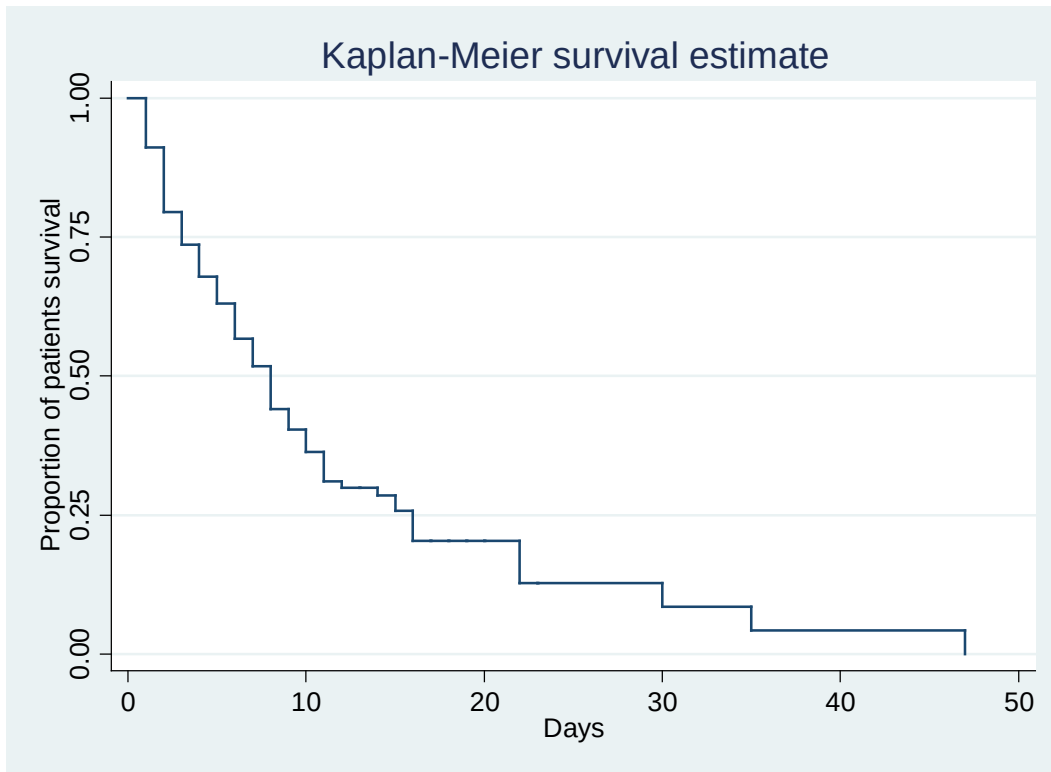


Figure 7. Kaplan – Meier survival curve for ICU patients

3.7. Survival curves for each significant factor after bivariate analysis.

Survival curve by Race

There is a difference in survival among patients in race categories. Blacks had improved survival as compared to other race groups. The log-rank test P-value was 0.006

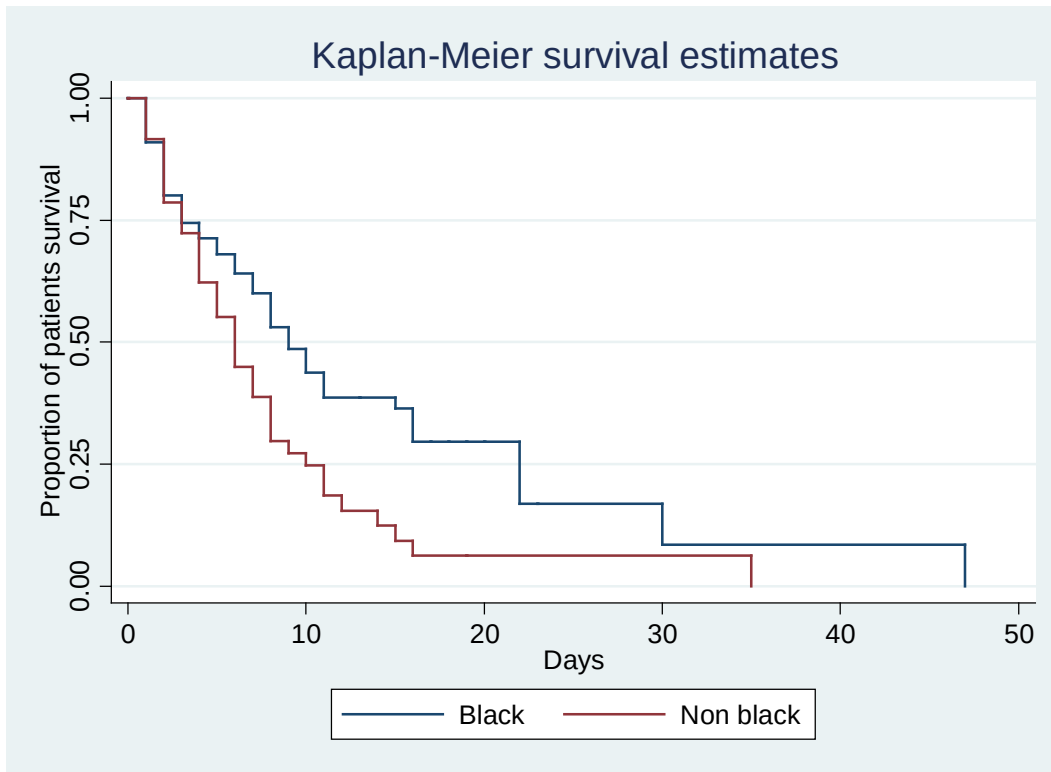


Figure 8. Kaplan – Meier survival curve for ICU patients by race

Survival curve by inotropic support

Those not on inotropic support had better survival than those who required inotropic support. The log-rank test P-value is 0.001 which is statistically significant.

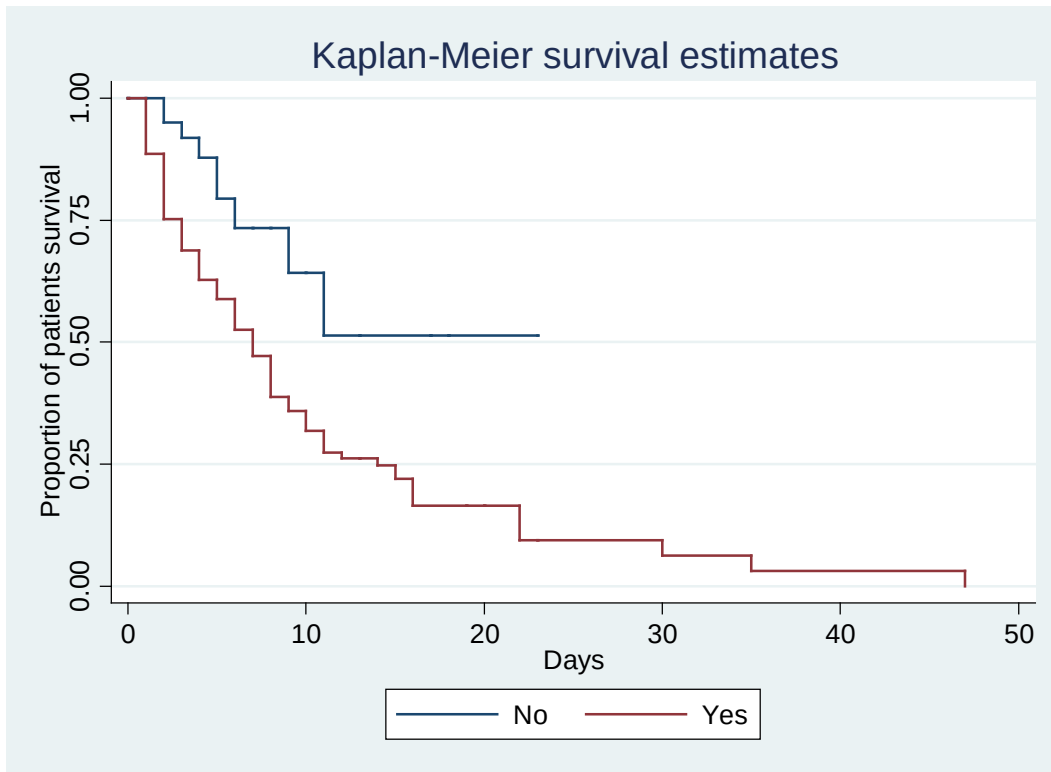


Figure 9. Kaplan – Meier survival curve for ICU patients by inotropic support.

Survival curve by ventilation and inotropic support

Patients who did not require ventilation and inotropic support had better survival than those who needed both supportive measures. The log – rank test P-value is 0.004 which is statistically significant.

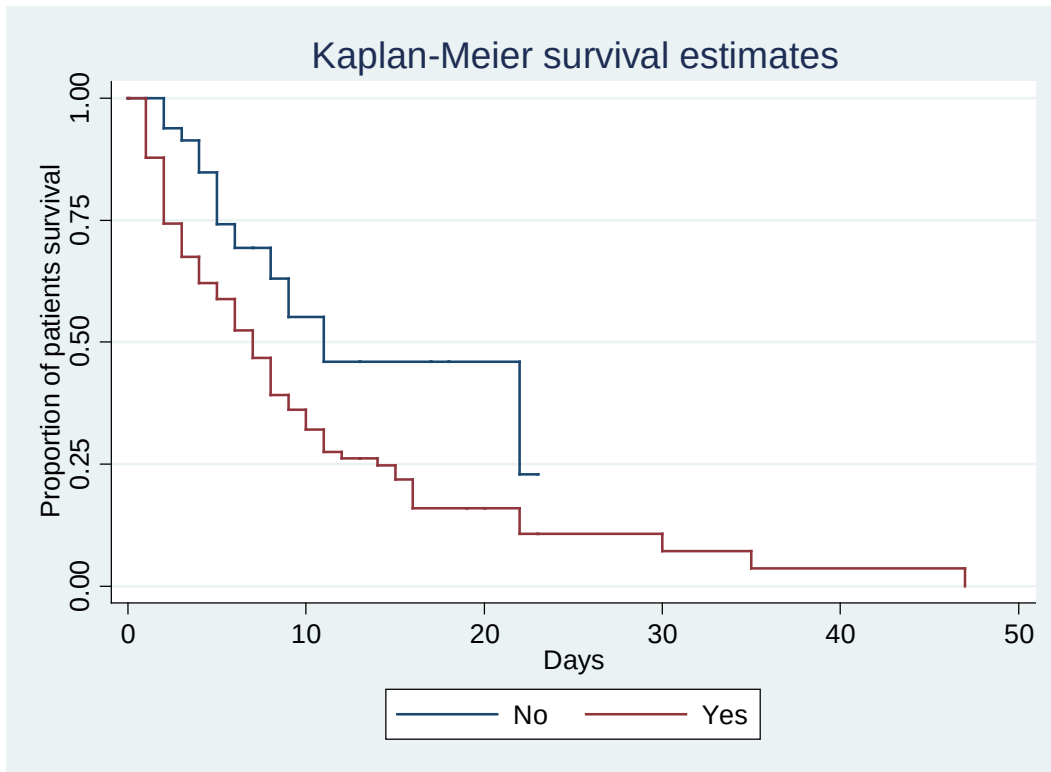


Figure 10. Kaplan – Meier survival curve for ICU patients by ventilation and inotropic support.

Survival curve by maximum RIFLE class

From the graph, patients with normal renal function have better survival than those with ARF based on RIFLE criteria. The log-rank test p-value is 0.000

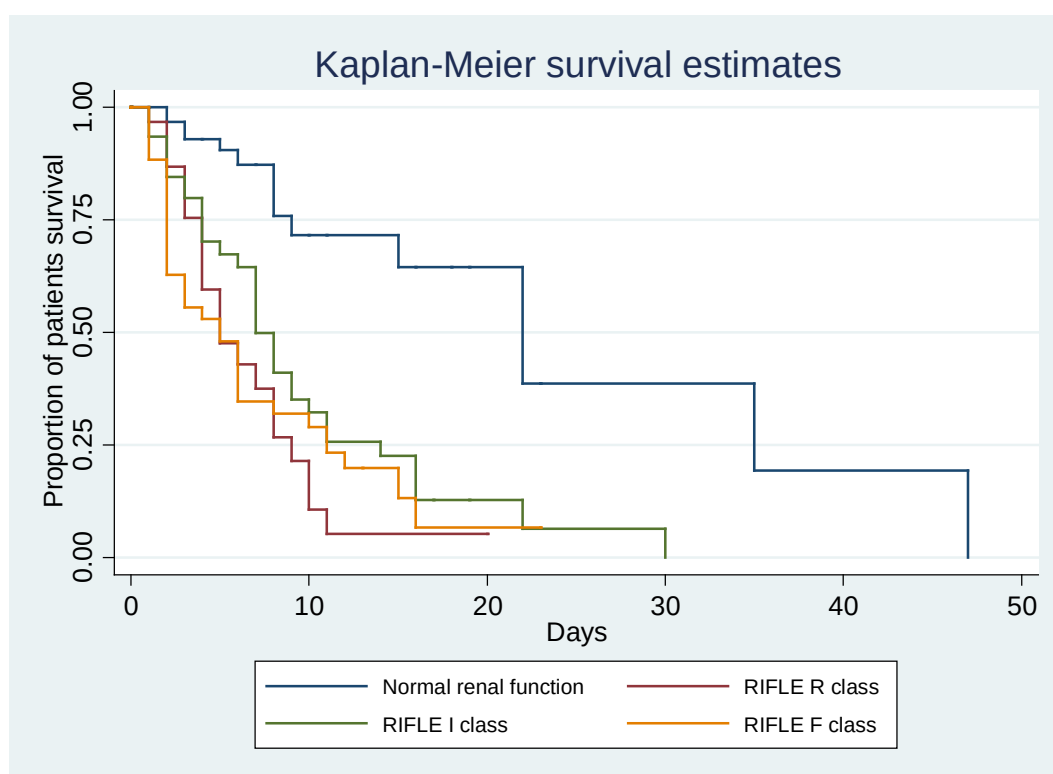


Figure 11. Kaplan – Meier survival curve for ICU patients by maximum RIFLE criteria

3.8. Race

Overall the majority of the study participants were young and black with less co-morbidities as compared to other race groups. HIV and or coinfection with TB was predominantly found in those of black race

Table 11.Comparison of factors with Race

Variable	Black	Other race groups	P-Value
Age			
18-40	60 (49.2%)	9 (12.7%)	0.000*
41-60	39(32.0%)	23 (32.4%)	
≥61	23 (18.9%)	39(54.9%)	
Chronic cardiovascular disease			
No	96(78.7%)	31(43.7%)	

Yes	26(21.3%)	40(56.3%)	0.000*
Chronic pulmonary disease			
No	113(92.6%)	53(74.6%)	
Yes	9(7.0%)	18(25.4%)	0.000*
HIV status			
Negative	47(38.5%)	52(73.2%)	
Positive	46(37.7%)	3(4.2%)	0.000*
Unknown	29(23.8%)	16(22.6%)	
HIV/TB coinfection			
No	52(42.6%)	52(73.2%)	
Yes	17(13.9%)	1(1.4%)	0.000*
Unknown	53(43.5%)	18(25.4%)	
Cancer			
No	116(95.1%)	62(87.3%)	0.031*
Yes	6(4.9%)	9(12.7%)	
Connective tissue disease			
No	120(98.4%)	68(95.8%)	0.133
Yes	2(1.6%)	4(4.2%)	
Number of organ involved			
1	42(34.4%)	28(39.4%)	
2	59(48.4%)	34(47.9%)	0.588
≥3	21(17.2%)	9(12.7%)	

*Statistically significant

In summary the results from this study in ICU have shown that in the bivariate analysis, multiple factors are associated with mortality in ICU. Factors such as race (other race groups), need for inotropic support, need for both –ventilation and

inotropic support, and maximum RIFLE criteria reached are independently associated with high mortality.

3.9.0 MORTALITY IN HOSPITAL

3.9.1. Bivariate analysis

3.9.2. Overall mortality

Total number of patients discharged to the ward from ICU was 78 patients, with the overall hospital mortality of 14.1% (11 patients died 14.1%, and 67 patients alive 85.9%).

The Chi square test was performed to determine the distributions of factors associated with mortality. Factors which were statistically significant after bivariate analysis (P-value ≤ 0.1) were sex, maximum RIFLE class, cancer, connective tissue disease, need for both-ventilation and inotropic support and conservative treatment as shown in the table below.

Table 12. Factors associated with mortality in patients with ARF in Hospital.

Variable	Alive	Dead	P-value
Age			
18-40years	31 (46.3%)	4(36.4%)	0.450
41-60years	23 (34.3%)	3(27.3%)	
>60years	13 (19.4%)	4 (36.4%)	
Race			
Black	49 (73.1%)	8 (72.7%)	0.977
Other race groups	18 (26.9%)	3 (27.3%)	
Sex			
Female	28 (41.8%)	8 (72.7%)	0.056*
Male	39 (58.2%)	3 (27.3%)	
Reason for admission			
Cardiovascular disease	3 (4.5%)	1 (9.1%)	0.751
Gastrointestinal disease	3 (4.5%)	0 (0.0%)	
Metabolic disease	5 (7.5%)	0 (0.0%)	
Poisoning	1 (1.5%)	0 (0.0%)	

Post-surgery	32 (47.5%)	6 (54.6%)	
Pulmonary disease	18 (26.9%)	2 (18.2%)	
Sepsis	5 (7.5%)	2 (18.2%)	
Maximum RIFLE criteria			
Normal	43 (%)	5 (45.5%)	
R class	9 (13.0%)	0 (0.00%)	
I class	10 (14.9%)	2 (18.1%)	0.031*
F class	5 (7.5%)	4 (36.4%)	
Diabetes			
No	62 (92.5%)	9 (81.8%)	0.249
Yes	5 (7.5%)	2 (18.2%)	
Chronic cardiovascular disease			
No	47 (70.2%)	6 (54.5%)	0.030*
Yes	20 (29.8%)	5 (45.5%)	
HIV status			
No	34 (50.8%)	5 (45.5%)	
Yes	18 (26.9%)	2 (18.2%)	0.580
Unknown	15 (22.4%)	4 (36.4%)	
HIV/TB co infection			
No	37 (55.2%)	5 (45.5%)	
Yes	4 (6.0%)	1 (9.0%)	0.812
Unknown	26 (38.8%)	5 (45.5%)	
Cancer			
No	61(91.0%)	8 (72.7%)	0.078*
Yes	6 (9.0%)	3 (27.3%)	
Connective tissue disease			
No	67 (100%)	9 (81.8%)	0.00*
Yes	0 (0.0%)	2 (18.2%)	
Chronic pulmonary disease			
No	61 (91.0%)	10 (90.9%)	0.988
Yes	6 (9.0%)	1 (9.1)	
Inotropic support			
No	32 (47.8%)	3 (27.3%)	0.205
Yes	35 (52.2%)	8 (72.7%)	
Ventilatory support			
No	19 (28.4%)	1 (9.1%)	0.175
Yes	48 (71.6%)	10 (90.9%)	
Ventilatory and inotropic support			
No	37 (55.2%)	2 (18.2%)	0.023*
Yes	30 (44.8%)	9 (81.8%)	
Conservative treatment			
IVF	50 (74.6%)	5 (45.5%)	
IVF and Lasix infusion	15 (22.4%)	6 (54.5%)	0.078*
No	2 (3.0%)	0 (0.0)	
Dialysis			
No	41 (61.2%)	5 (45.5%)	0.325
Yes	26 (38.8%)	6 (54.5%)	

3.9.3. Inferential statistic

3.9.4. Univariate Cox Proportional Hazards Regression

Statistically significant factors qualified for inferential statistics by Cox proportional hazard regression. The significant criteria here is taken as a p-value ≤ 0.05 . Those who had cancer were 7.48 fold more at risk of hospital death as compared to those who had no cancer, summarised in the table below.

Table 13. Factors associated with hospital mortality.

Factor	Univariate
	HR, 95%CI, P-value
Sex Female Male	1 0.29 (0.07 1.16) 0.08
Cancer No Yes	1 7.48 (1.48 37.77) 0.015
Connective tissue disease No Yes	1 2.28 (0.42 12.32) 0.338
Conservative treatment No Yes	1 0.68 (0.59 2.35) 0.64
VS and IS No Yes	1 1.78 (0.34 9.22) 0.49
RIFLE on hospital discharge Normal R I F	1 5.89 (0.79 2.69) 1.00 2.13 (0.37 12.13) 0.39 1.25 (0.29 5.28) 0.76

NOTE: Cancer is the only significant factor after Univariate analysis (Adjusted HR 7.48, 95%CI 1.48 – 37.77, p-value 0.015).No need for multivariate model

3.9.5. Survival analysis

Patients were at risk for a total of 1398 person days. Death incidence rate was 0.0078. By the 55th day of follow up, 75% of patients had already died.

Survival curves.

Twenty five percent of patients who died in hospital survived for more than 55 days of follow up.

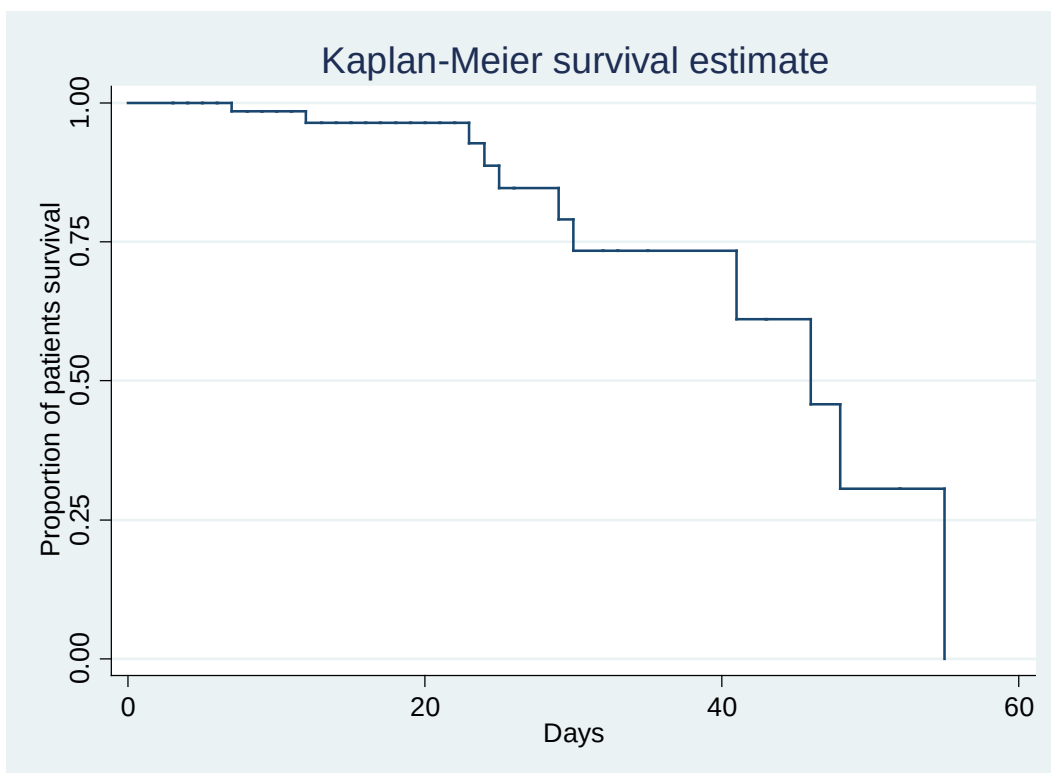


Figure 12. Kaplan – Meier curve for hospital patients mortality

Survival curve by Sex

From the graph males seem to have improved survival as compared to the females.

The log-rank test P-value is 0.06 which is not statistically significant. However, a trend is noted.

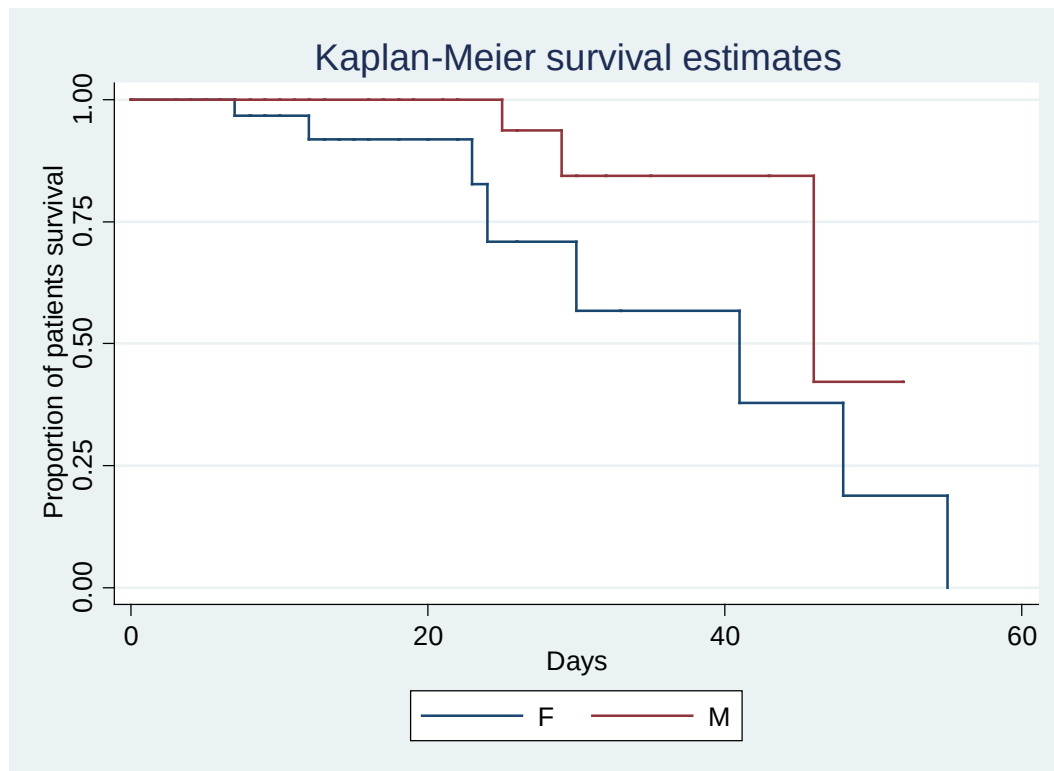


Figure 13. Kaplan – Meier survival curve for hospital patients by sex.

Survival curve by Cancer

Those with no cancer have improved survival as compared to those with Cancer.

The log-rank test p-value is 0.004 which is statistically significant.

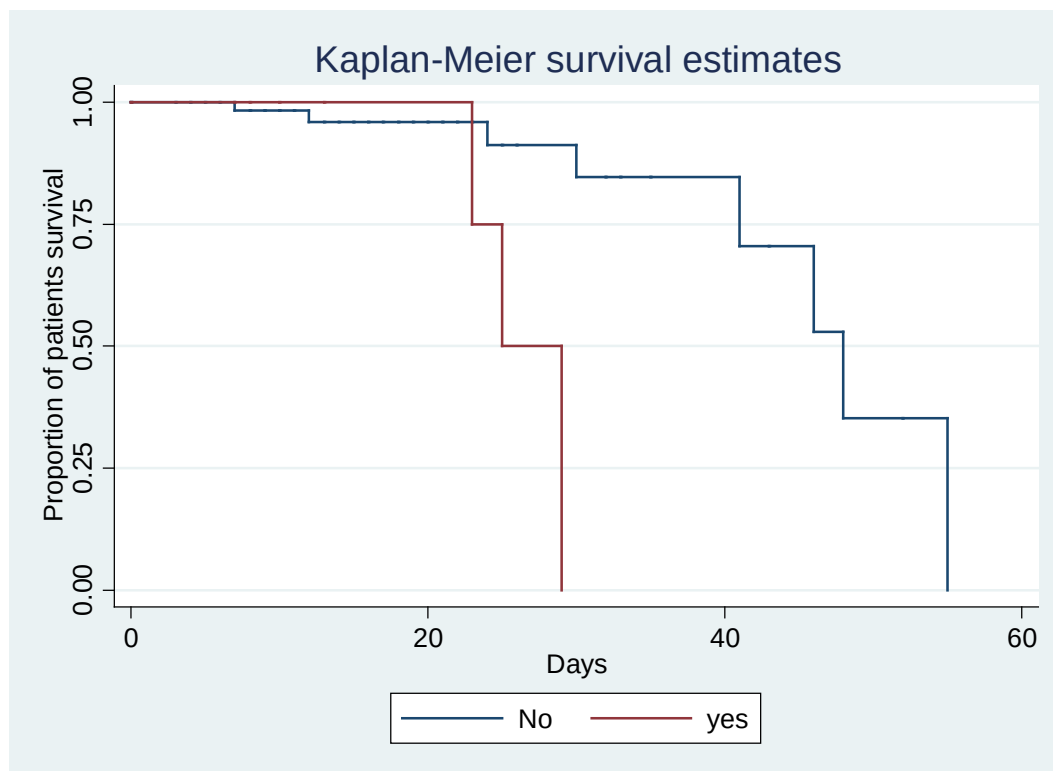


Figure 14. Kaplan – Meier survival curve for hospital patients by cancer

The results from hospital patients in this study show that despite the fact that multiple factors are associated with mortality in patients with ARF in hospital in the bivariate analysis, univariate Cox hazards regression analysis reveals cancer to be the only factor that is independently associated with mortality.

CHAPTER 4: DISCUSSION

4.0. Discussion

This was a retrospective chart review that aimed at assessing the outcome of patients with Acute Renal Failure (ARF) in the Intensive Care Unit (ICU). We screened a total number of 507 patients admitted in ICU, and according to RIFLE criteria, 193 patients with ARF were included in the study. This accounted for 38.1% (193/507) of all patients who were admitted to ICU during the study period. This incidence is similar to that reported in other studies (11, 18, 25, 26). Of those patients with ARF on admission 40.9% (79 patients), had normal renal function, 23.3% (45 patients), 14% (27 patients), and 21% (42 patients) were in R class, I class, and F class respectively with maximum RIFLE class during ICU stay was 17%, 27%, and 23% for R, I, and F class respectively. The range of maximum RIFLE class observed in this study is consistent with that published in other studies (8, 26). In this study dialysis was initiated in 53.4% (103/193) of all patients with ARF.

The mean age of the study population was 50.5 ± 18 years, with the majority of patients being in the age group of 18 years to 40 years. The majority of the patients were black (63.2%). This may be explained by the demographics in South Africa (48). The mean age in the present study was similar to that previously reported (24, 41) and was younger than that found in other study (56). This may be explained by the predominance of young age group found in this study.

With regard to predisposing factors for ARF in ICU, neither demographic characteristics such as age, race and sex, reason for admission, nor comorbidity present in this study were associated with ARF. This is in contrast to the data reported from other studies (15, 18, 28). The possible reasons for this include the

fact that majority of patients were relatively young, had two or less organ involvement on admission and throughout the ICU stay, and that the number of patients with co-morbidity and normal renal function on admission, were insignificant to show statistical association with the development of ARF. The recovery rate in the present study was 34.5% which was consistent to other reported data (16).

In this study, the overall mortality rate in patients with ARF was found to be 59.9%. This finding is similar to that found in other studies performed in Brazil, Saudi Arabia and the United Kingdom (25, 30, 49). It is however, slightly higher than that previously reported in South Africa (23, 24). In the bivariate analysis, we found that factors such as age, race, inotropic support, ventilatory support, need for both - ventilatory and inotropic support, dialysis, chronic pulmonary disease and maximum RIFLE class in ICU were significantly associated with mortality. With the exception of the need for both – ventilatory and inotropic support, the influences of other factors on the mortality in this study have also been reported in other studies (12, 14, 15, 26, 30). Factors such as race, inotropic support, maximum RIFLE class and need for both (ventilation and inotropic support) were subjected to multivariate regression analysis after remaining statistically significant in the univariate analysis which revealed that when present, they are independently associated with mortality. This is in accordance with data from other studies (25).

With RIFLE criteria, patients in R, I, and F class had more than 3 fold risk of dying as compared to patients with normal renal function (adjusted HR 5.41 95%CI 2.66 - 11.0; p-value 0.000 for R class, HR 3.17 95%CI 1.65 - 6.07; p-value 0.001 for I class, and HR 5.69 95%CI 2.93 - 11.06; p-value 0.001 for F class). This correlation and predictive ability of maximum RIFLE criteria in critically ill ARF patients with respect

to mortality is consistent with results found in other studies (29, 35, 49). This finding adds to the paucity of information from African facilities.

It was found in this study that other race groups had 1.56 fold greater risk of dying compared to blacks (adjusted HR 1.56, 95%CI 1.07 - 2.28, p-value 0.02). This observation has previously been published and although the reason for this finding is not clear, it may partly be explained by more comorbid conditions in non-black patients (other race groups), young age in black patients as compared with their counterparts, and possible biological differences between the two groups (40).

The currently available evidence supports the fact that the use of inotropic support in critically ill patients with ARF is independently associated with mortality (14, 25). In this study we found that patients with ARF on inotropic support had 2.36 fold greater risk of dying as compared to those who were not (adjusted HR 2.36, 95%CI 1.02 – 6.18; p-value 0.04).

This study further demonstrated that those who needed both ventilatory and inotropic support had a 1.14 greater risk of dying as compared to those who were not (adjusted HR 1.14, 95%CI 1.09 – 2.53; p-value 0.01). This finding has mainly been reported in paediatric oncology patients where the mortality rate among patients on ventilation and those on combined ventilation with inotropic support was 39% and 65% respectively (50). The above finding may be explained by the fact that patients who need inotropic support, ventilation or both are usually extremely ill, often with multiple organ failure and hence poorer outcome. The result that mechanical ventilation is associated with high mortality is consistent with other published data (12, 23, 25, 30, 41).

We found that the majority of patients discharged from ICU to the ward survived - 85.9% discharged alive versus 14.1% who died. Amongst those who died, 25% demised after 55 days of follow up in the hospital. In the bivariate analysis, we found that factors associated with mortality in the ward were sex, maximum RIFLE class, cancer, connective tissue disease, need for both-ventilatory and inotropic support and conservative treatments of ARF (Intravenous fluid and or furosemide infusion). However, after univariate analysis only cancer showed independent association with mortality. This is consistent with previous published data in which patients with malignancy were shown to have higher in-hospital mortality and lower survival (51, 52). We found in the survival analysis that males had improved survival as compared with females (Figure 12) although the log-rank test (p-value 0.06) was not statistically significant. This finding is in contrast to other studies that have reported male gender as a predictive factor of in-hospital mortality (53, 54). Furthermore Mitter N et.al; showed no mortality difference between the gender of patients with post-operative renal injury (55). The reason for this observation is not clear, but one of the possible explanations is the difference in testosterone levels. Of interest, a study by Kyriazis J et.al; demonstrated that testosterone deficiency in male haemodialysis patients was associated with all-cause mortality (57).

4.1. Limitations

This study had several limitations which include

- It is a single centre study so the results may not be representative of all university affiliated ICU's.
- Relatively low number of study participants

- It is a retrospective study

4.2. Strength of the study.

Despite the above limitations, the study;

- Has contributed data and information on the use of RIFLE criteria and its predictive ability for the mortality in an African ICU.
- Findings on the association of risk factors with mortality were consistent with previous studies.

4.3. Conclusion

This study found that according to RIFLE criteria, the overall occurrence rate of ARF was 38.1% (193/507) in ICU and that each maximum RIFLE class reached demonstrated its predictive ability of the outcome in terms of mortality and lower survival among patients with ARF in ICU. We have further added information on the usefulness of RIFLE criteria from an African institution where there is paucity of data regarding its use in predicting outcomes in patients with ARF.

4.4. Recommendations

Given the findings from this study, we recommend;

- The routine use of RIFLE criteria, which is a useful tool for early detection and improvement of outcome in critically ill patients with ARF.
- Further studies regarding various factors that influence the favourable outcome among black patients compared to other race groups.

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Appendices



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01 February 2010
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PAG

Dear Dr Mujwahuzi

Master of Medicine (In the specialty of Internal Medicine): Approval of Title

We have pleasure in advising that your proposal entitled "*Outcome of acute renal failure in ICU using rifle criteria in South Africa*" has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

A handwritten signature in black ink, appearing to read 'S Bonn'.

Mrs Sandra Bonn
Faculty Registrar
Faculty of Health Sciences

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

R14/49 Dr Leodegard Mujwahuzi

CLEARANCE CERTIFICATE

M090906

PROJECT

Outcome of Acute Renal Failure Using Rifle
Criteria in the Adult Multidisciplinary Intensive
Care Unit, South Africa

INVESTIGATORS

Dr Leodegard Mujwahuzi.

DEPARTMENT

Department of Internal Medicine

DATE CONSIDERED

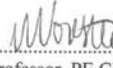
2009/10/02

DECISION OF THE COMMITTEE*

Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 2009/10/02

CHAIRPERSON 
PP (Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof M Mer

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Case report form for capturing data from the files

1. Serial number-----

2. Demographic information

i. Age -----

ii. Sex Female/ Male

M/F

3. Race i. Other race groups

Yes/No

ii. Black

Yes/No

4. Reason for ICU admission

i. Sepsis

Yes/No

ii. Pulmonary disease

Yes/No

iii. Post-surgery

Yes/No

iv. Cardiovascular disease

Yes/No

iv. Gastrointestinal disease

Yes/No

v. Neurological disease

Yes/No

vi. Poisoning/overdose

Yes/No

vii. Metabolic disease Yes/No

5. Number of organ(s) involved

i. One system

Yes/No

ii. Two systems

Yes/No

iii. Three or more systems

Yes/No

6. Patients' habit

I. Alcohol

Yes/No

ii. Smoking

Yes/No

iii. Substance abuse

Yes/No

7. Comorbidity

- | | |
|------------------------------------|----------------|
| i. Diabetes mellitus | Yes/No |
| ii. Chronic cardiovascular disease | Yes/No |
| iii. Chronic pulmonary disease | Yes/No |
| iv. HIV status | Yes/No/unknown |
| V. HIV/TB co infection | Yes/No/Unknown |
| V. Cancer | Yes/No |
| vi. Connective tissue disease | Yes/No |
| v. Reoperation | |

8. RIFLE class (based on the increase in serum Creatinine)

- i. RIFLE on admission
- ii. RIFLE in ICU
- iii. RIFLE on discharge

9: Treatment modality

A: Conservative treatment i. Intravenous fluid

ii. Intravenous fluid and diuretics

iii. Duration of conservative treatment--

B: Dialysis

A. Type of dialysis

i. Haemodialysis (HD)

ii. Sustained Low Efficiency Dialysis (SLED)

iii. Continuous Veno-Venous Haemodialysis(CVVHD)

B. Duration of dialysis -----

10: Duration of Inotropic support—

11: Duration of ventilatory support--.

12. Ventilatory and inotropic support

Yes/No

13. Duration of combined ventilation with inotropic support

14. Duration of stay 1. ICU ----

2. Hospital (discharged patients from ICU to the ward) ---

12: Outcome -discharged from

i. ICU 0: Dead

1: Alive

ii. Hospital 0: Dead

1: Alive