Clinical Profiles and Outcomes of Patients Receiving Acute Renal Replacement Therapy in the Cardiac Intensive Care Unit at a South African Tertiary Centre.

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Declaration

This thesis/dissertation has been submitted to the Turnitin module and I confirm that my supervisor has seen my report and any concerns revealed by such have been resolved with my supervisor.

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Date: 22 October 2021

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My Supervisors - Professor Mpiko Ntsekhe and Dr. Philasande Mkoko.
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Abstract

Background

At least a quarter of patients admitted to the Cardiac Intensive Care Unit (CICU) will develop Acute Kidney Injury (AKI) and some of these patients receive Renal Replacement Therapy (RRT). The clinical profiles and outcomes of CICU patients receiving RRT in resource constraint settings like South Africa is unknown.

Objectives

The objectives of this study were to determine the clinical profiles and outcomes of patients receiving RRT in the CICU in a South African Tertiary Centre.

Methods

In this retrospective study we included consecutive patients admitted and receiving RRT at the Groote Schuur Hospital CICU from 01/01/2012 to 31/12/2016.

Results

During the study period 3247 patients were admitted to the CICU and 46 received RRT. The RRT patients had a mean (SD) age of 52 (17) years, 56% were males, and 65% had a background history of systemic hypertension. Heart failure syndromes accounted for 60.9% of CICU admission in the RRT patient group, followed by acute coronary syndromes and arrhythmias, which accounted for 26.1% and 13.0% respectively. The RRT patient population had an in-hospital and 30-day mortality of 58.7% and 60.9% respectively. Baseline use of Angiotensin Converting Enzyme (ACE) inhibitor or Angiotensin Receptor Blocker (ARB) was associated with a reduced 30 day mortality, Hazards Ratio (HR) 0.43; 95% Confidence interval (95%CI) 0.20 – 0.93; p = 0.031. In addition, heart failure was associated with an increased 30 day mortality, HR 2.52; 95% CI 1.10 – 5.78; p = 0.029.

Conclusion

Heart failure syndrome accounts for a majority of RRT patients admitted to the our CICU. Patients receiving RRT in CICU have a high in-hospital and 30-day mortality.

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Background

The reported incidence of acute kidney injury (AKI) in patients managed in the cardiac intensive care (CICU) units is increasing.[1-3] This is partly because of the aging patient population and patients with complex comorbidities treated in the CICU. At least 25% of patients admitted with cardiovascular disease will develop AKI depending on the AKI definition used, including up to 56.1% in patients with acute decompensated heart failure and up to 30% in patients with Acute Coronary Syndromes (ACS)[4-6]. AKI complicating cardiovascular disease portends poor outcomes. For example, of the 118 465 patients admitted for acute decompensated heart failure evaluated in the ADHERE (Acute Decompensated Heart Failure National Registry) database, 56.1% developed moderate to severe acute renal impairment and had a 4-fold increase in in-hospital mortality when compared to those with mild or no renal impairment[7]. A recent systematic review suggested that approximately 3% of patients with ACS, acute decompensated heart failure and/or cardiogenic shock[8] admitted to the CICU received renal replacement therapy (RRT). Indeed, the need for RRT conferred a 10-fold increase in the risk of death and length of CICU stay[8].

In a study conducted by the international society of nephrology looking at the access to renal replacement therapy on a global scale, Qarni et al demonstrated that acute and chronic haemodialysis was available in most countries, although acute and chronic peritoneal dialysis access was severely limited in low income countries (24% and 35%, respectively)[9]. In centres where such advanced care is available there are frequently major resource related constraints which place a limit on the numbers of patients who can access care requiring careful selection of patients who are likely to benefit most. The ongoing epidemiological transition and increase in diseases such as coronary artery disease, diabetes and hypertension have led to a rapid rise in the demand for CICUs and advanced renal care. Given the persistently high burden of communicable diseases in South Africa requiring health resources,[10] important decisions about appropriate resource allocation require a thorough understanding of both the burden of non-communicable disease, and their related outcomes. Specifically, in a public sector, SA setting where patient demographics and cardiovascular risk factor profiles are different to that found in the global north,[11] the burden of AKI amongst patients admitted to hospital with acute cardiac syndromes and their related outcomes would be important to inform appropriate resource allocation and patient care.

Aims and Objectives.

The overarching aim of this study was to review the local practice of acute renal replacement therapy in a typical South African tertiary centre Cardiac ICU; with regards to burden, patient profiles and patient outcomes.

The specific objectives were to:

- Determine the prevalence of AKI requiring RRT in the ICU over a 5 year period.
- Describe the profile of patients with specific reference to age, gender , pre-existing co-morbid conditions, current cardiac admission diagnosis.
- Describe the number of days in hospital and the case fatality rate.
- Determine which baseline variables predict mortality.

Methods

Study design and patient population

This was a retrospective folder review of all patients admitted to a 6 bed CICU at a large Tertiary Centre in Cape Town, South Africa, between 01 January 2012 to 31 December 2016.

After obtaining appropriate regulatory clearance from the hospital management and ethics permissions, ward admission records, renal replacement records and the electronic health information system for public sector hospitals and health care centres in the Western Cape Province of South Africa (CLINICOM) were searched for patient data and related information on all the patients admitted to the CICU during the study period. A standardized data collection form was used to extract and analyze relevant data on those participants receiving RRT from the above hospital records. The study was carried out with the approval UCT Human Subjects Research Ethics Committee (HREC 690/2020).

Approach to RRT in the CICU

The conventional indications for renal replacement therapy in acute renal failure are (a) volume overload (b) intractable hyperkalaemia (c) refractory metabolic acidosis (d) uremic signs or symptoms progressive azotaemia in the absence of uremia.[12] The selection of patients for renal replacement therapy depends on a number of factors , including but not limited to: age of the patient, with the younger candidates generally getting better preference; baseline functional class status, existence of co-morbid pre-existing conditions and disease control . Patients in the cardiac ICU needing renal replacement therapy will be referred by the consultant cardiologist to the consultant nephrologist, if they do not believe that there is reasonable prospect of renal recovery or the prognosis from the cardiac syndrome is dire, then the patients will not be accepted for renal replacement therapy.

Statistical Analysis

Normally distributed data are presented as means (standard deviation (SD)) or, where highly skewed, as medians (interquartile range (IQR)); discrete data are presented as numbers (percentages). Continuous data were compared using t-test or Mann-Whitney test, and categorical data using the Chi-square test or the Fisher exact test. Cox proportional hazard regression models were constructed to identify factors associated with 30-day mortality. All tests were two-sided, and a p-value < 0.05 was considered significant. Collected data were entered and analysed using IBM SPSS Statistical Software.

Results

During the 5 year study period 3247 patients were admitted to the CICU, of whom 46 (1.42%) patients received RRT for AKI. The patients receiving RRT in the CICU had a mean (SD) age of 52.6 (17.1) years and 56.5% were male. No record was available of the number of patients

who were actually referred for RRT over the study period, nor of the number of patients who were declined treatment. Furthermore, there is no record of the number of patients whose admission to the CICU was declined on the basis of being poor candidates for RRT. The baseline characteristics of the RRT cohort in CICU patients are presented in table 1.

Table 1: Baseline Characteristics of the patients who received Renal Replacement Therapy at the GSH Cardiac ICU

Variable	No: 46
Age, mean (SD)	52.6 (17.1)
Female, No (%)	20 (43.5)
Hypertension, No (%)	30 (65.2)
Diabetes Mellitus, No (%)	18 (39.1)
Dyslipidaemia, No (%)	16 (34.8)
Atrial fibrillation, No (%)	9 (19.5)
Peripheral Vascular Disease, No (%)	5 (10.9)
Current Smoking History, No (%)	15 (32.6)
History of Ischemic Heart Disease	12 (26.1)
Chronic Kidney Disease	11 (23.9)
ACE Inhibitor /ARB, No (%)	24 (52.2)
Beta Blocker, No (%)	14 (30.4)
Loop Diuretic, No (%)	16 (34.8)
Thiazide Diuretic, No (%)	10 (21.7)
Spironolactone, No (%)	4 (8.7)
Statin, No (%)	20 (43.5)
Sulfonylurea, No (%)	8 (17.4)
Metformin, No (%)	14 (30.4)
Insulin, No (%)	6 (13.0)
Warfarin, No (%)	6 (13.0)

Abbreviations: CICU, Cardiac Intensive Care Unit; RRT, Renal Replacement Therapy; PVD, Peripheral Vascular Disease; IHD, Ischemic Heart Disease; ACE, Angiotensin Converting Enzyme; ARB, Angiotensin Receptor Blocker; ACS, Acute Coronary Syndrome; SD, Standard Deviation; IQR, Interquartile Range; GSH, Groote Schuur Hospital.

Amongst the RRT cohort of patients, the majority were admitted to the CICU for decompensated heart failure, (60.9%), followed by acute coronary syndromes (26.1%) and unstable cardiac arrhythmias (13.0%) (Figure 1).

The median length of hospital stay for the cohort of patients who received RRT was 10 days. The in CICU case fatality rate was 58.7%, and 30-day mortality rate was 60.9%. Amongst the twenty seven patients who demised, the median time on RRT was 10 days (IQR: 5-17). Cox Regression analysis suggest that, the baseline use of Angiotensin Converting Enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARB) were associated with a reduced probability of a 30-day mortality, Hazards Ratio (HR) of 0.43; 95% Confidence interval [95%CI], (0.20 – 0.93); p = 0.03. In contrast, admission to the CICU for heart failure was associated with a 2.5 fold increase in probability of death in 30 days, HR = 2.52; 95%CI (1.10 – 5.78), P= 0.03 (Table 2).

Table 2: Hazards Ratios and 95% Confidence intervals for 30-day mortality in patients admitted to CICU and Receiving RRT

Variable	Hazard Ratio	95 % CI lower	95 % CI upper	P value
Age in years	1.01	0.98	1.03	0.685
Hypertension	0.65	0.30	1.385	0.262
Diabetes Mellitus	0.62	0.28	1.36	0.232
Atrial fibrillation	1.02	0.35	2.93	0.975
Atrial Flutter	0.64	0.09	4.70	0.659
Dyslipidaemia	1.11	0.51	2.40	0.796
PVD	0.85	0.26	2.81	0.784
Chronic Kidney injury	0.47	0.18	1.24	0.125
IHD	1.17	0.50	2.74	0.727
Metformin	0.56	0.23	1.37	0.204
Sulfonylurea	0.44	0.13	1.47	0.181
Insulin	0.74	0.22	2.46	0.624
ACE inhibitors/ ARB	0.43	0.20	0.93	0.031
Beta blockers	1.94	0.89	4.22	0.095
Atenolol	1.82	0.74	4.52	0.195
Carvedilol	1.15	0.40	3.32	0.795

Spironolactone	0.57	0.13	2.40	0.441
Statins	0.10	0.31	1.45	0.308
Furosemide	0.58	0.27	1.23	0.153
Warfarin	1.15	0.40	3.32	0.798
Hydrochlorothiazide	0.32	0.01	1.06	0.063
Aspirin	0.47	0.21	1.05	0.067
ACS	1.45	0.24	8.72	0.687
Cardiogenic shock	0.85	0.36	1.95	0.702
Heart failure	2.52	1.10	5.78	0.029

Abbreviations: CICU, Cardiac Intensive Care Unit; RRT, Renal Replacement Therapy; PVD, Peripheral Vascular Disease; IHD, Ischemic Heart Disease; ACE, Angiotensin Converting Enzyme; ARB, Angiotensin Receptor Blocker; ACS, Acute Coronary Syndrome.

Figure 1A: Admission Diagnoses

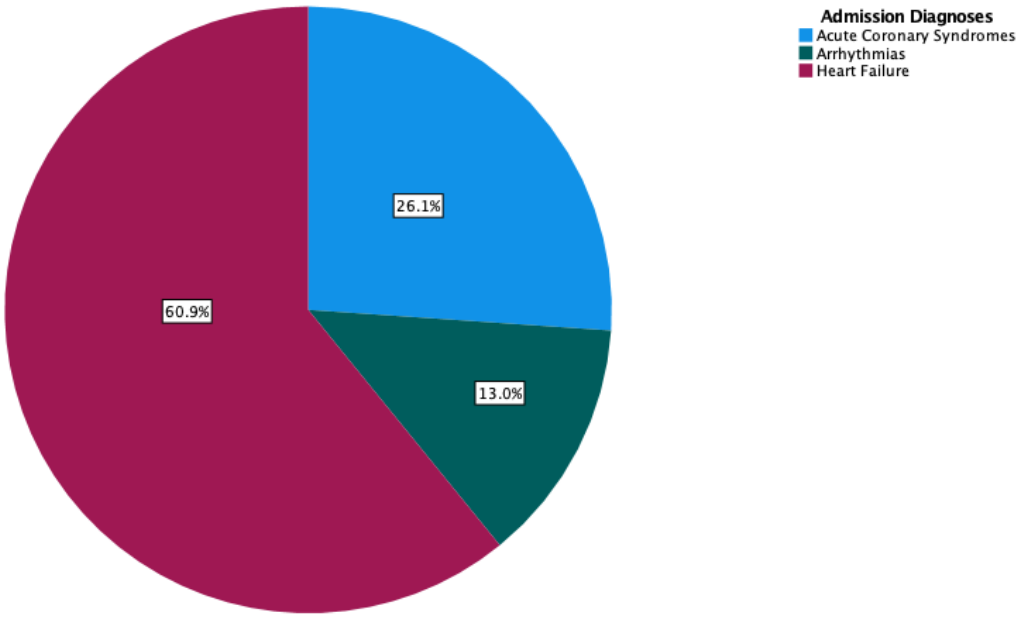


Figure 1 (b): Acute Coronary Syndromes

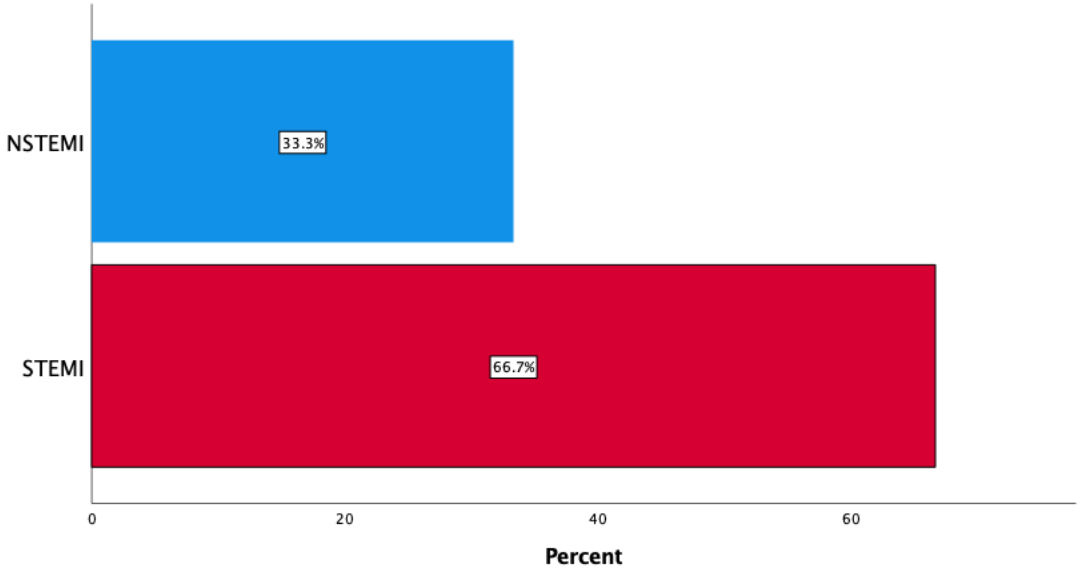
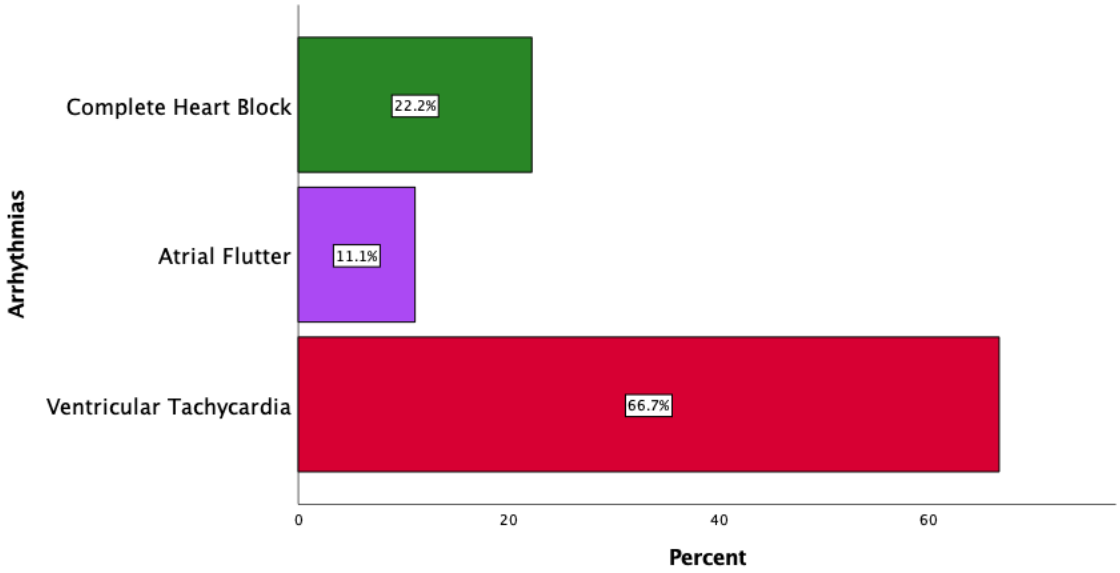


Figure 1C: Arrhythmias



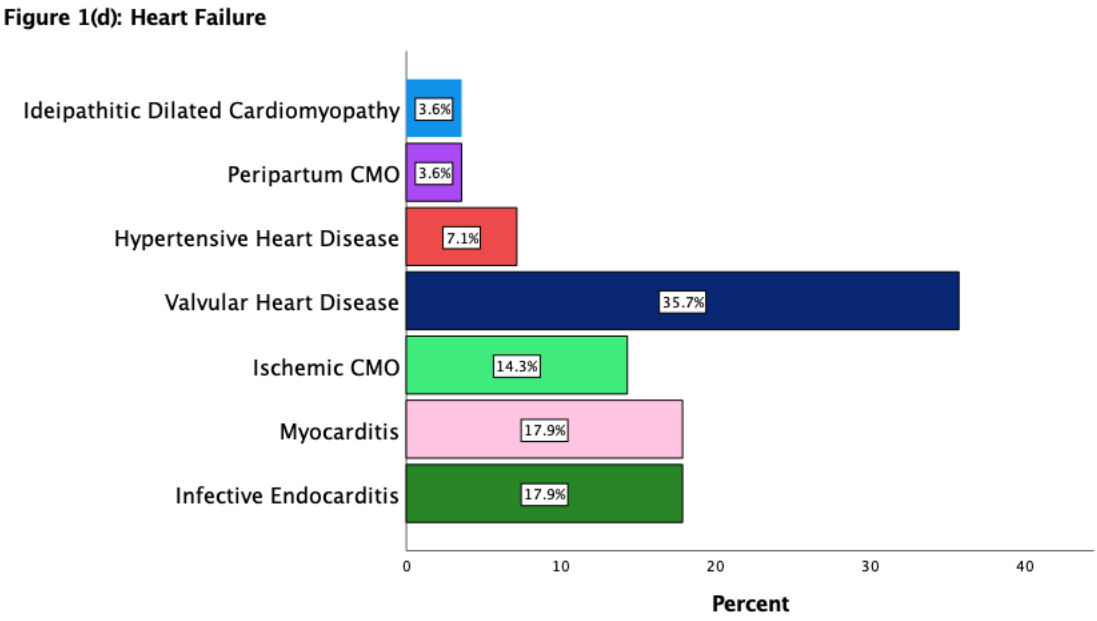


Figure 1: Pie chart depicting the indication for GSH CICU admission in patients treated with RRT. Abbreviations: NSTEMI, Non-ST Elevation Myocardial Infarction; STEMI, ST Elevation Myocardial Infarction.

Discussion

The main findings of this study are: 1) over the period of 5 years under review the proportion of CICU admissions receiving acute renal replacement therapy for acute kidney injury was low at 1.42 %; 2) patients who received the intervention were young [mean age (SD)] 52.6 (17.1) years, just over half (56.5%) were male, and the proportion with hypertension (65%) and diabetes (39%) was high. Approximately a quarter of the patients had a history of ischemic heart disease or chronic kidney disease ; 3) the main indication for RRT amongst patients was decompensated heart failure complicated by cardiorenal syndrome (60.9%) followed by patients with acute coronary syndrome. The main causes of acute kidney injury in those with ACS was shock and contrast nephropathy following angiography; 4) CICU patients treated with RRT have a high in-hospital and 30-day mortality at 58.7% and 60.95% respectively and the main predictor of mortality was cardiorenal syndrome associated with decompensated heart failure. The use of ACE-inhibitors or ARB at presentation appeared protective.

We searched for studies of a similar nature from low- and middle-income environments to compare our findings, however there was paucity of this type of data. We found similar studies from high income countries, where the age and risk factor profiles are known to be dissimilar to our setting. However, in a much larger study from the Mayo clinic reviewing data from 9311 CICU admissions over a 9 year period, the mean age of patients was 67.5[13], almost 15 years older than the mean age of the participants from our study. The Mayo Group cohort had more obese patients, more prior lung disease and prior cancer[13], which was a significantly different comorbidity profile from our cohort. In the same study, the proportion of patients admitted to the CICU who received acute RRT, was 3.5 % [13] compared to our setting where only 1.42% of patients received RRT. It is possible that this is in part due to the restricted access to RRT available in our setting[9]. The leading admission cardiac diagnosis amongst those requiring RRT in the Mayo Clinic study was heart failure (45 %), followed by acute coronary syndromes(44.1%) and shock (13%)[13]. Heart failure and acute coronary syndromes were also the two main cardiac conditions amongst those needing acute RRT in our study cohort but the proportions were very different.

We report an in-hospital and 30-day mortality of 58.7% and 60.9% respectively, findings consistent with those from larger studies from the developed world. [3,13-16] This highlights the complex adverse relationship of the sick heart and the kidneys and vice-versa, the cardio-renal syndrome[17]. In contrast to our findings where decompensated heart failure was the main predictor of mortality, Van Diepen and colleagues identified shock, cardiac arrest, significant liver disease, older age as predictors of in-hospital mortality in their CICU patients needing acute RRT [16].

The major limitations of this study are its small size, single centre and retrospective nature of its design. However in light of our study findings, a larger prospective study to confirm, the high mortality rate and better evaluate predictors of a poor outcome may be helpful to assist clinicians in similar setting with local evidence based decision making.

In conclusion, we set out to determine, how frequently acute renal replacement therapy was used in the CICU at this typical urban South African tertiary care center, and describe the clinical profile and outcomes of patients who were offered the intervention. We found that acute renal replacement therapy was used sparingly in a relatively young population ;the vast majority of who had decompensated heart failure with cardiorenal syndrome. In-hospital and

30-day mortality was high. The prevalence of baseline chronic renal impairment was high, although this may be related to the high prevalence of diabetes and hypertension. These findings highlight the need for more aggressive programs to screen for cardiovascular risk factors, and primary prevention interventions to reduce the burden of the need for both CICU admissions and acute kidney injury needing renal replacement therapy.

Figures and tables:

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Table 4: Hazards Ratios and 95% Confidence intervals for 30-day mortality in patients admitted to CICU and Receiving RRT

Figure 1A: Admission Diagnoses

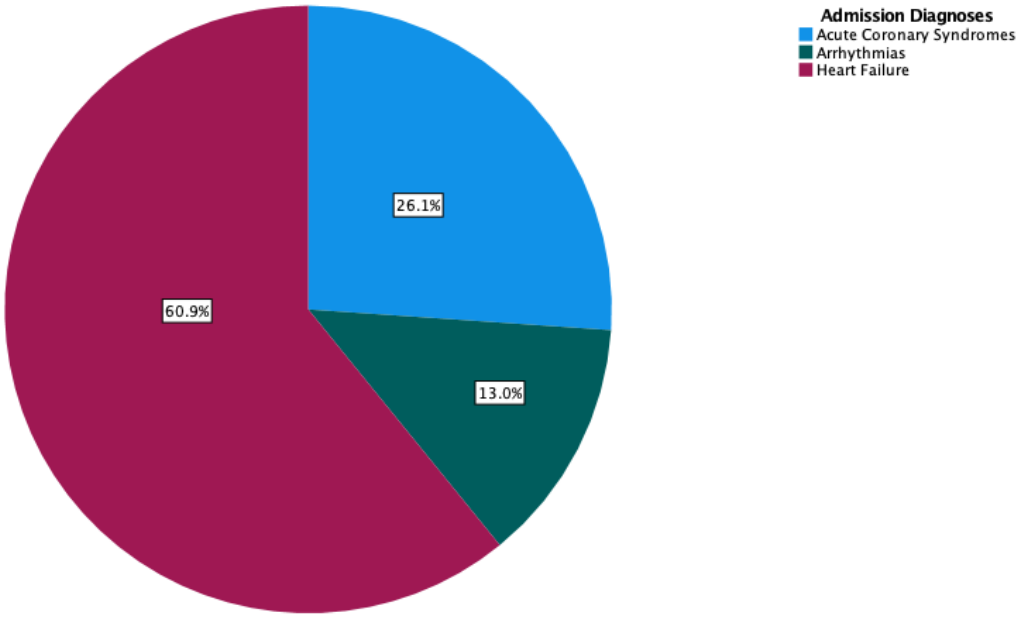


Figure 1 (b): Acute Coronary Syndromes

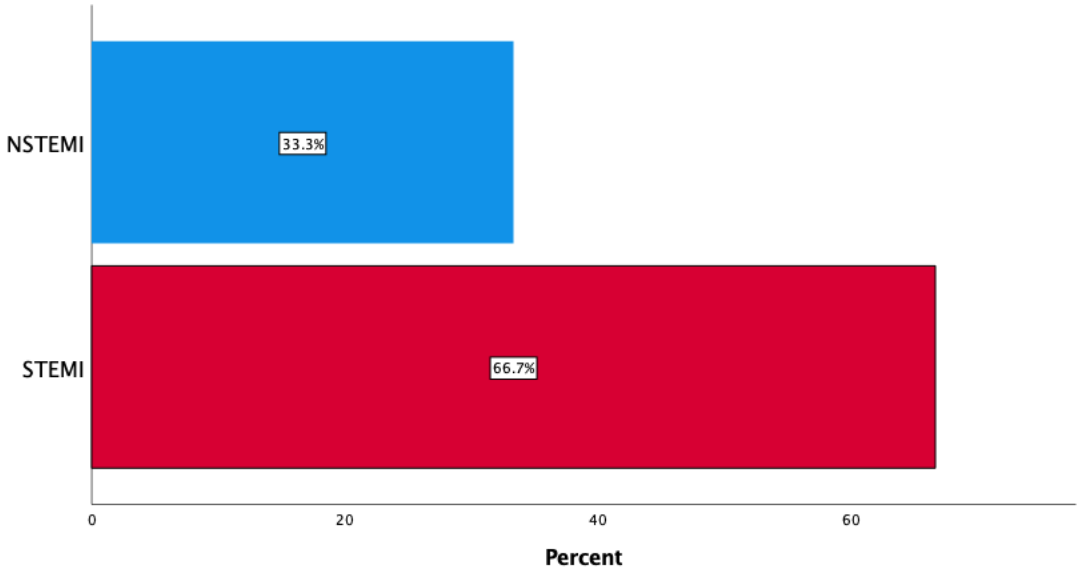


Figure 1 (c): Arrhythmias

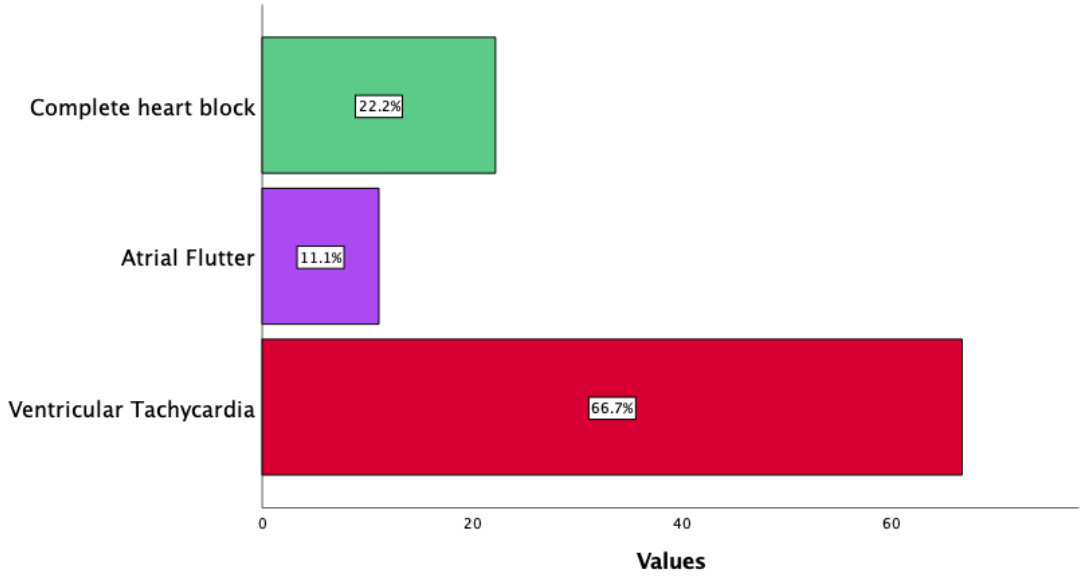
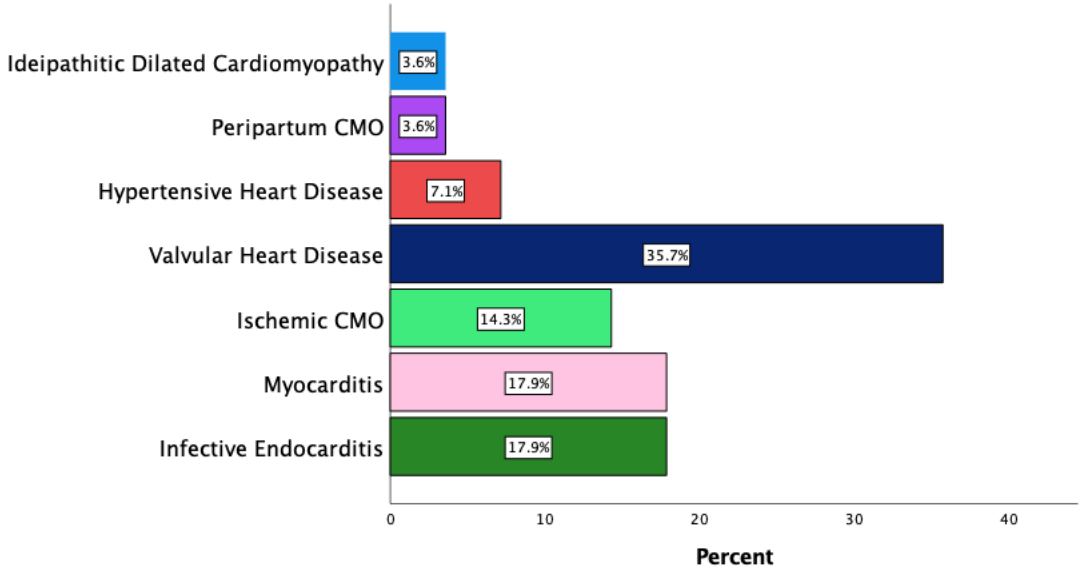


Figure 1(d): Heart Failure



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