A retrospective registry of patients presenting with cardiac tachyarrhythmia at a tertiary academic hospital in SA

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AUTHOR'S DECLARATION

This study represents original work by the author. It has not been submitted to any other tertiary institution. However, where the work by others is made use of, this has been duly acknowledged.

The research described in this dissertation was carried out in the Division of Cardiology at the Tygerberg Hospital located in the Western Cape under the supervision of Dr. J Moses (Consultant Electrophysiologist), Mr. J Steyn (Assistant Director of Clinical Technology), Prof AF Doubell (HOD: Cardiology) and under the supervision of Dr. Rosaley Prakaschandra in the Department of Biomedical and Clinical Technology, Faculty of Health Sciences, Durban University of Technology.

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DEDICATION

I dedicate this work to:

My fiancé, parents, and siblings for their love, support, and patience.

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CONTENTS PAGE

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF DEFINITIONS

DEFINITION	MEANING
Ablation	A medical procedure in which abnormal parts of the electrical conduction system of the heart are removed using either cold energy (cryoablation) or the heat generated from medium frequency alternating current (radiofrequency ablation).
Cardioversion	A medical procedure by which an abnormally fast heart rate or other cardiac arrhythmia is converted to a normal rhythm using direct current electricity or antiarrhythmic medications.
Pulmonary Vein Isolation	An ablation procedure to treat an abnormal heart rhythm called atrial fibrillation.

LIST OF ABBREVIATIONS

AF	Atrial Fibrillation
AFL	Atrial Flutter
AP	Accessory Pathway
ASE	American society of echocardiography
AT	Atrial Tachycardia
AV	Atrioventricular
AVN	Atrioventricular Node
AVNRT	Atrio Ventricular Nodal Re-entry Tachycardia
AVRT	Atrio Ventricular Re-entry Tachycardia
CAD	Coronary Artery Disease
CRF	Case Report Form
CRT	Cardiac Resynchronization Therapy
CTI	Cavotricuspid Isthmus
CVD	Cardiovascular Disease
CVRF	Cardiovascular Risk Factors
ECG	Electrocardiogram
EP	Electrophysiology
ICD	Implantable Cardiac Defibrillator
MI	Myocardial Infarction

NIMRR	Non-interventional Medical Records Review
NOAC	Novel Oral Anticoagulation
PASCAR	Pan African Society of Cardiology
PE	Pericardial Effusion
PND	Paroxysmal Nocturnal Dyspnoea
PTMC	Percutaneous Transvenous Mitral Commissurotomy
PVC	Premature Ventricular Contraction
PVI	Pulmonary Vein Isolation
RHD	Rheumatic Heart Disease
RVOT	Right Ventricular Outflow Tract
SA	South Africa
SNRT	Sinus Node Recovery Time
SSA	Sub-Saharan Africa
SVT	Supraventricular Tachycardia
VT	Ventricular Tachycardia
WHO	World Health Organization

ABSTRACT

Background:

Cardiac electrophysiology (EP) is a rapidly growing field in the health care sector globally. Evidence from European and American retrospective registries have shown that cardiac arrhythmias can be treated both medically and through intervention via catheter ablation. These registries have described disease burden, procedural success rates, and complication rates as well as patients' electrophysiological and clinical characteristics. Currently, there is minimal data describing these factors in South Africa (SA).

Aims and objectives:

The primary aim of this study was to describe the clinical characteristics, disease prevalence and the success and complication rates of EP procedures in the first year of a newly established service at a tertiary referral centre in SA.

Methodology:

Patients who were referred to the Tygerberg Hospital EP service in the year 2019 were retrospectively included. Clinical, electrophysiological, and echocardiographic data were anonymized, de-identified, and recorded into a password-protected Microsoft Excel case report form (CRF). For the continuous variables, means and standard deviations were used to analyse the data. For the categorical variables, the Pearsons chi-square tests and the Fisher exact tests were used. A p-value of <0.05 was regarded as statistically significant.

Results:

A total of 73 patients were retrospectively included in the study. Thirty-nine were males (53.0%) and 34 were females (47.0%). The mean age for this population was 49.5±14.3 years (males-mean 51.9±14.4 years; females-mean 46.8±13.7 years). Patients were symptomatic in the form of palpitations (n=55 [75.0%]), dyspnoea and pre-syncope (n=36 [49.3%] each).

Beta-blockers were the most commonly used medication to treat patients in this study, being prescribed to 64 (87.6%) patients. There were 13 (17.8%) patients treated with medical therapy alone, and 60 (82.2%) patients were advised to undergo an EP study (EPS) with catheter ablation if indicated. Three patients declined this treatment, and 57 EPS were performed.

Of the 57 patients undergoing an EPS, eight (14.0%) had diagnostic studies only, with four (7.0%) patients being non-inducible and four (7.0%) patients with arrhythmia substrate that were not ablated. The other 49 patients (86.0%) underwent catheter ablation. Twenty-one patients (39.6%) were diagnosed with atrial flutter (AFL), of which 19 (35.8%) underwent cavotricuspid isthmus (CTI) ablation. Twenty-nine (54.7%) patients were diagnosed with a paroxysmal supraventricular tachycardia (SVT). Of these 13 (24.5%) had atrioventricular nodal re-entry tachycardia (AVNRT), 15 (28.3%) had atrioventricular re-entry tachycardia (AVRT) and one patient had both AVNRT and AVRT. Atrial tachycardia (AT) was diagnosed in two patients (3.8%). In the 29 (54.7%) patients with SVT, 27 ablations were done in 26 patients, with 24 (92.3%) of the 26 patients having a successful procedure on the first attempt. Atrioventricular nodal ablations (AVNA) were performed on two patients with poorly controlled atrial fibrillation (AF). Only one (1.9%) patient underwent an EPS for ventricular tachycardia (VT) and this patient had a successful ablation for idiopathic right ventricular outflow tract (RVOT) VT. The success rate for ablation procedures in this cohort was 95.9%.

Echocardiograms were available for 57 (78.1%) of the study population. As was to be expected, structural heart disease was more common in the AFL group compared to the SVT group, with this group having larger atria, larger ventricles, poorer LV function and more diastolic dysfunction than the SVT group ($p<0.05$ for all of these variables).

At follow-up, patients reported a significant (78.6%) decrease in the prevalence of arrhythmia-related symptoms. Dyspnoea, palpitations, pre-syncope, and syncope were all significantly reduced, with a p-value <0.01. The need for cardioversion was also significantly reduced at follow-up with a p-value <0.01.

Conclusion:

This registry, the first of its nature in SA sought to identify disease prevalence, clinical characteristics of EP patients and the success and complication rates of ablation procedures. This provides novel setting-specific information. This study showed that referral for tertiary arrhythmia management was infrequent, with 73 patients referred in 2019. The most common arrhythmia was SVT, followed by AFL. Ablation procedures were safe and effective. Reasons for the low referral are likely to be multifactorial including lack of awareness on the part of patients and physicians, as well as logistical aspects

CHAPTER 1: INTRODUCTION

Globally, according to the World Health Organisation (WHO), the number one cause of mortality is cardiovascular disease (CVD), which was estimated in 2017 to be 17.8 million deaths, three-quarters of which occurred in low and middle-income countries (Kaptoge *et al.* 2019). Elevated blood pressures, hypercholesterolemia, diabetes, sedentary lifestyles with associated obesity, and a family history of CVD are strong predictors of the potential to develop CVD (Hajar 2017). Cardiovascular disease includes a vast number of conditions that can either be acquired or congenital. Coronary artery disease (CAD), strokes, arrhythmias, heart failure, and valve pathology are some of the most common conditions experienced by cardiac patients (Mayo Clinic 2021).

Cardiac arrhythmias can occur in structurally normal hearts or may have a congenital aetiology, which are electrical defects that are present at birth (Kulig and Koplan 2010; Zei and Soltys 2017). They can also be acquired as a result of structural changes in the heart usually secondary to other cardiac comorbidities (Gillespie, Lin and Prutkin 2014). These electrical abnormalities can be treated non-invasively with medical therapy or invasively, usually utilizing catheter ablation (Zei and Soltys 2017).

There are various types of cardiac arrhythmias, divided broadly into two categories, tachyarrhythmias and bradyarrhythmia's (Chin *et al.* 2016; Mustaqeem, Anwar and Majid 2018). Patients with symptomatic tachyarrhythmias form the bulk of the referrals to the arrhythmia outpatient service at Tygerberg Hospital and are the subject of this study. Tachyarrhythmias are further divided into sub-categories including broad complex tachycardias and narrow complex tachycardias, where broad and narrow are defined by the width of the QRS complex on a 12-lead electrocardiogram (ECG), and rhythms that are regular or irregular. See figure 1 displaying the classification of the different tachycardias (Chin *et al.* 2016).

The most important tachyarrhythmias have been well described. Atrial fibrillation is a supraventricular tachyarrhythmia and the most common narrow complex sustained tachycardiac rhythm. One of the leading triggers for this tachycardia is rapid electrical stimuli that occur in muscle sleeves located at the ostium of the pulmonary veins (Markides and Schilling 2003). Atrial flutter is an arrhythmia utilizing macro re-entry as its mechanism (Cosio *et al.* 1993). This tachycardia in its typical form is dependent on a portion of the right atrium known as the CTI (Chugh *et al.* 2006).

Atrioventricular nodal re-entry tachycardia (AVNRT), AVRT, and VT also usually utilize re-entry as a mechanism (Goyal *et al.* 2020). In patients with AVNRT, the slow pathway and fast pathway of the atrioventricular node (AVN) provide the substrate for re-entry due to their differences in conduction velocities and refractory periods (Kwaku and Josephson 2002). In AVRT, the tachycardia is bypass tract mediated and macro re-entrant in nature. It requires the presence of an accessory pathway (AP), and the difference in electrophysiologic characteristics between the AP and AVN allow for re-entry. Ventricular tachycardia is usually caused by a re-entry circuit in the ventricles due to the presence of scar, but can sometimes be caused by automaticity similar to AT (Goyal *et al.* 2020).

Cardiac arrhythmias are strongly associated with heart disease and significantly increase morbidity and mortality (Lüscher 2016). Treating cardiac arrhythmias is therefore important for the patients health and well being. Tachyarrhythmias can be treated medically or more recently by catheter ablation. Brugada et al suggest that recurrent symptomatic arrhythmia can and should be treated safely and effectively by catheter ablation (Brugada *et al.* 2020).

Cardiac electrophysiology (EP) is a rapidly growing field in the health care sector across the world (Valderrábano 2015; Zipes *et al.* 2015; Raymond-Paquin, Andrade and Macle 2019). A study comparing the impact of medical therapy and catheter ablation on health care costs and quality of life revealed that catheter ablation was better at improving quality of life and attaining complete permanent resolution of symptoms while having the same long term cost implications (Bathina *et al.* 1998).

Cardiac EP and catheter ablation can be highly effective and safe when performed on the right patient (Schilling 2002). The European Heart Rhythm Association position paper on the management of SVT provides recommendations regarding who would benefit the most from an EP procedure (Katritsis *et al.* 2017). When appropriately performed such as in patients with symptomatic AVNRT and AVRT, ablation therapy can be permanently curative. Availability of cardiac EP services differs greatly across the world. While EP services are widely available in European regions, in Sub-Saharan Africa (SSA) only SA offers complex ablation procedures (Bonny *et al.* 2020).

Evidence from European and American retrospective registries have provided important information on the management of arrhythmias. These registries have described disease burden, patients' electrophysiological and clinical characteristics, procedural success rates and complication rates (Scheinman and Huang 2000;

Cavaco, Morgado and Bonhorst 2016; Fontenla, García-Fernández and Ibáñez 2017). These registries have assisted their countries in identifying disease prevalence, tracking growth trends, treatment strategies and complication frequency, and in determining training capacities. Data from these registries have shown that catheter ablation is highly effective and safe. They have also shown that AF has become the most common arrhythmia treated via catheter ablation, surpassing AVNRT in the recent years.

Registries assist in creating data that is representative and relevant for the patient population involved. In addition, they assist in creating a body of knowledge that applies to, and is representative of, a real-world picture that assists a host of role players including but not limited to physicians, manufacturers, funders, and other stakeholders (Mkoko *et al.* 2020). Currently, most EP data published in the form of registries and consensus documents is published from European and North American cohorts (Scheinman and Huang 2000; Cavaco, Morgado and Bonhorst 2016; Fontenla, García-Fernández and Ibáñez 2017; Holmqvist *et al.* 2019). This results in a gap in the body of knowledge regarding EP in African countries (Bonny *et al.* 2018). Acquiring information in this specific population and economic climate will assist health care authorities to plan and distribute resources accordingly. There is very little information about the arrhythmia burden and patterns of referral in SSA. This sentiment is further substantiated by Bonny et al who state that no country in Africa records EP or ablation data in a national registry (Bonny *et al.* 2020).

This study intended to create and present the first EP registry from a tertiary academic hospital in a Sub-Saharan country. The aim of this study was to present the clinical and procedural data from all patient's referred to a specialist arrhythmia service at a tertiary centre in Cape Town, SA during the first year of that service being available.

This registry will allow a better understanding of disease burden, patient profiles, procedural success, and complication rates in the public sector in SA. This will also allow a comparison of the standard of care in this registry to American and European practices by comparing success and complication rates. In addition, the registry will allow medical professionals to better treat South African patients who, in some cases, have different causes for their arrhythmias such as rheumatic heart disease (RHD) (Diker *et al.* 1996). As cardiac EP is becoming increasingly available in African countries, this registry will contribute to a body of knowledge that is more relevant to physicians treating patients in SSA (Bonny *et al.* 2018).

The study was conducted in the Division of Cardiology, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, and Tygerberg Hospital in Cape Town, SA. Patients referred to the tertiary EP service at Tygerberg Hospital during the first year of service (2019) were included in the study. The study was quantitative, analytical, descriptive, and retrospective in nature. A registry was established whereby pre-procedural (clinical, echocardiographic, and ECG data), procedural (electrophysiological), and post-procedural (recurrence of symptoms and medical therapy) data was recorded and analysed from the patients first appointment at the EP service and their first follow up after treatment.

The data from 73 patients was studied. The results are displayed using graphs, tables, and pie charts. Continuous variables are described as means and standard deviations.

The categorical variables were analysed using the Pearson Chi-square test and the Fisher exact test and are displayed using categorized histograms.

CHAPTER 2: LITERATURE REVIEW

2.0 Introduction

Cardiac arrhythmia, in this study specifically tachyarrhythmia is described as an abnormal heart rhythm with a heart rate greater than 100 beats per minute (Sobotka *et al.* 1981; Mkoko *et al.* 2020). Arrhythmias such as AFL and AF have the ability to cause blood clots which can result in strokes. Persistent tachyarrhythmias can result in a tachycardia induced cardiomyopathy. A tachycardia induced cardiomyopathy occurs when there is impairment of systolic function and chamber dilation due to a persistent rapidly conducting arrythmia. These pathophysiological changes are normally reversible when normal sinus rhythm is re-established (Patel and Whittaker 2007). Cardiac EP is a sub-speciality in cardiology that primarily concerns itself with the establishment and maintenance of sinus rhythm. See figure 1 depicting the main types of tachyarrhythmias (Chin *et al.* 2016).

Patients who are referred to a cardiac EP service are usually symptomatic and have presented to the emergency room at some point. When evaluating a patient who experiences palpitations, dyspnoea and pre-syncope/syncope, an ECG at the time of the event and the mechanism of termination is extremely valuable in creating a differential diagnosis. Figure 1 provides a road map in creating a differential diagnosis when evaluating the tachycardiac ECG of a patient with a cardiac arrhythmia (Chin *et al.* 2016). The mechanism of termination of a narrow complex tachycardia can be useful in making a diagnosis. When the performance of a vagal manoeuvre terminates a narrow complex tachycardia it is likely a nodal dependant tachycardia such as

AVNRT or AVRT (Chin *et al.* 2016). While vagal manoeuvres will not terminate an AT, AF, or AFL it may illicit transient AV block which will expose the atrial activity of the arrhythmia and aid greatly in the making of a diagnosis. Finally, the baseline ECG may also provide insights into diagnosing the tachycardia such as the presence of a bundle branch block or pre-excitation (Chin *et al.* 2016). Once the tachyarrhythmia is diagnosed, patients can be treated medically or by catheter ablation therapy. According to the 2019 European Society of Cardiology (ESC) guidelines for the management of SVTs, catheter ablation is the recommended chronic therapy for patients with recurrent, symptomatic AT, AVNRT, AFL and AVRT (Brugada *et al.* 2020). See table 1 adapted from Brugrada et al for the success, complication and mortality rate for SVT procedures (Brugada *et al.* 2020).

Cardiac EP as a mainstream science can be described as relatively new in that the majority of the significant scientific breakthroughs have happened in the last few decades (Feld 1999; Zipes *et al.* 2015; Raymond-Paquin, Andrade and Macle 2019). Due to the high success rates and ability to reduce symptoms with minimal risk, these procedures have gained a considerable amount of traction in developed regions such as North America (Scheinman and Huang 2000; Shurrab *et al.* 2014). However, the EP platform is not well established in the developing world. High procedural costs, inadequate reimbursement, and the lack of structured fellowships have rendered it problematic to provide this service to public sector patients in developing countries (Bonny *et al.* 2018). In SA, most EP services are provided by private healthcare, i.e., to 16.9% of the population (Statistics South Africa 2019). Research is often undertaken in academic institutions, possibly explaining why, not only SA, but also Africa have failed to produce much research in cardiac EP. To the best of the researchers' knowledge, this will be the first EP registry of its kind published from SSA.

The information extracted from this registry will place SA and African EP in a global context and contribute to creating a reference for evidence-based medicine relevant to this patient population. Unfortunately, the major registries created to evaluate EP are few and are entirely based in developed countries (Scheinman and Huang 2000; Cavaco, Morgado and Bonhorst 2016; Holmqvist *et al.* 2019; Raymond-Paquin, Andrade and Macle 2019).

2.1 **Electrophysiology outside the continent of Africa**

2.1.1 The Portuguese National Registry on Cardiac Electrophysiology

2.1.1.1 The Portuguese National Registry on Cardiac Electrophysiology – 2016

The Portuguese National Registry on Cardiac Electrophysiology was first established in 1999 and has since been continuously maintained. This registry is conducted retrospectively. Their data evaluates all diagnostic EP studies, ablations, and Implantable cardiac defibrillator (ICD) implants. The data collection process involves sending questionnaires to all EP centres (private and public) in Portugal. The data collected is used to describe growth trends in Portuguese EP, disease prevalence, and procedural frequency and determine the training capacity of hospitals (Cavaco, Morgado and Bonhorst 2016).

In the year 2014, 3112 EP studies were done, of which 2325 lead to cardiac ablation. These procedures were done by 25 centres, of which only seven performed more than 100 procedures a year. The most common procedure done by these 25 centres was pulmonary vein isolation (PVI) for AF, which represented 29.6% of the total amount of procedures. It is important to note that although AF ablation was the most common procedure, it was primarily done by two high-volume centres. The registry also revealed that the number of AF ablation cases affected the complication rate of the centre. The complication rate decreased as high-volume centres became more experienced. This has provided information regarding what should be considered appropriate procedural exposure where the training of EP fellows is concerned (Cavaco, Morgado and Bonhorst 2016).

2.1.1.2 The Portuguese National Registry on Cardiac Electrophysiology - 2020

The Portuguese National Registry on Cardiac Electrophysiology presented their 2015-2016 data which became available online in June 2020. The number of centres that provided data to this registry decreased from 25 in 2015 to 21 in 2016. The centres that did not respond in 2016 were smaller volume centres assumed eventually to have terminated their services. For the year 2016, 21 centres had done 3486 EP procedures, 2974 (85.3%) resulted in ablations, the mean ablations per centre was 142, which increased from 103 in 2015; this is likely due to the exiting of smaller centres from the study. The median number of ablations also increased, from 44 in 2015 to 71 in 2016 (Gonçalves, Reis and Bonhorst 2020).

In the study period of 2016, AF ablation was the most common procedure and accounted for 29.7% of the total number of procedures, similar to the previous report in 2014, where AF ablations represented 29.6% of ablations. Next in line was AVNRT (23.6%), followed by CTI dependant AFL (17.5%), and lastly, ventricular arrhythmias (6.9%). The study describes an increase in the number of procedures from 2015 to 2016, which the authors welcomed. They comment that higher volume centres have decreased complication rates and increased procedural success (Gonçalves, Reis and Bonhorst 2020).

2.1.2 Spanish Catheter Ablation Registry

2.1.2.1 Spanish Catheter Ablation Registry - 2017

The Spanish catheter ablation registry, have reported similar methodology and findings to the Portuguese catheter ablation registry (Cavaco, Morgado and Bonhorst 2016). The data collection was done retrospectively by means of a questionnaire/detailed CRF. In the year 2016, 83 EP centres contributed to this registry by means of the CRF. There was a total of 13842 EP procedures done in that year (2016). The most common procedure was AVNRT ablation, with 3058 procedures, 22.7% of the total. The average success rate of the 83 centres was 97.0% for AVNRT, and there were 22 major complications noted for this procedure specifically (Fontenla, García-Fernández and Ibáñez 2017).

Interestingly, and in keeping with the Portuguese catheter ablation registry, for the first time in the 16 publications of this particular registry, AF ablation became the most common procedure. In addition, the data reveals an increase in the number of AF ablation cases and a decrease in the number of major complications as the registry progresses year by year (Fontenla, García-Fernández and Ibáñez 2017). Again, this is similar to the National Portuguese registry data (Cavaco, Morgado and Bonhorst 2016).

2.1.2.2 Spanish Catheter Ablation Registry -2018

The latest data from the Spanish catheter ablation registry is in keeping with the global trend of cardiac EP (Criado *et al.* 2019). Data from 100 centres were retrospectively collected via questionnaires. For the study period, 2018, 16566 procedures (the highest recorded number in this registry) were done by the 100 centres, with the median number of ablations per centre being 119. In keeping with the global trend in arrhythmia prevalence, AF was the most common ablation n=4234 (25.6%) (Cavaco, Morgado and Bonhorst 2016; Criado *et al.* 2019; Holmqvist *et al.* 2019; Gonçalves, Reis and Bonhorst 2020). This was followed by AVNRT n=3525 (21.3%), CTI dependant AFL 3425 (20.7), AP ablation n= 2148 (13%) and focal AT 464 (3.0%).

Point by point radiofrequency ablation, which is described as the placement of close proximity ablation lesions in the antrum of the pulmonary veins to cause atrio-pulmonary vein isolation was the more common approach to PVI, with 55.7% of cases being done this way and 43.6% were done by cryoablation (Hunter *et al.* 2015). The remainder of the procedures were done by multielectrode ablation catheters and lasers. The acute success rate for AF ablation was 94.1%, and the overall complication rate was 3.4% (n=145). This had slightly decreased from the previous year (2017), where the complication rate was 3.6%. There was only one complication that led to a fatality, and this was associated with ST-segment elevation. There were 49 vascular complications (1.2%), 33 PE (Pericardial effusion) (0.8%), 27 phrenic nerve palsies (0.6%), six embolisms (0.1%), five infarctions (0.1%), and three perforations (one requiring surgery), one aortic puncture. There were no atrioesophageal fistulae reported (Criado *et al.* 2019).

In the AVNRT cohort, the procedural success rate was reported at 96%. However, 11 (0.3%) severe complications were reported. There were three patients that had AV block requiring a pacemaker, six had vascular complications, one heart failure event, and one pulmonary thromboembolism.

Cavotricuspid Isthmus ablation procedures which were the third most common ablation, had a success rate of 94.0%. There were no fatal complications reported. The complications rate was 1.1% (n=38). This consisted of 18 vascular complications, nine AV block, two PE, two myocardial infarctions (MI), and one heart failure event.

Accessory pathway ablations occurred in 98.0% of the centres recruited, making it the most treated substrate among the centres in terms of substrate type. 2148 AP ablations were performed with a success rate of 91.0%. Manifest pathways were present 60.4% of the time, and concealed pathways 39.6%.In terms of location, as noted in previous editions of this registry, left-sided APs were the most common (51.2%), followed by inferoseptal (27.1%), right ventricular free wall (11.9%), and para-hisian (9.8%) (Cavaco, Morgado and Bonhorst 2016). The overall complication and mortality rate for this study was 2.2% and 0.04%, respectively.

2.1.3 Swedish Catheter Ablation Registry

The Swedish Catheter Ablation Registry was created when a gap in real-world data on procedural success and safety was noted. There were 11 ablation centres that provided data for this study in Sweden (Holmqvist *et al.* 2019). They prospectively / retrospectively recruited consecutive patients who were older or equal to the age of 18 and were undergoing catheter ablation in Sweden between 01 January 2006 and 31 December 2015. They recruited a total of 26642 patients aged (57+-15 years), 62.0% being male. The total number of ablation procedures was 34428 for the study period. They report 4034 AP ablations (12.0%), 7358 AVNRT ablations (21.0%), 1813 AT ablations (5.2%), 5481 typical AFL ablations (16%) 11916 AF ablations (35.0%), 2415 AVNA (7.0%), 581 premature ventricular complex (PVC) ablations (1.7%) and 964 VT ablations (2.8%). They report a change in the frequency of complex ablations over the years, with AF, VT, and PVC ablations becoming increasingly popular. They also report a doubling in the total number of procedures in the ten-year period, primarily driven by the increase in the number of AF procedures. Despite the increase in the frequency of AF procedures, they report a decrease in the need for repeat AF ablations. They report a low rate of adverse events (n=595, 1.7%). Death in the period following ablation was rare (n=116, 0.34%). They conclude that catheter ablation procedures generally appear safe, efficient and are associated with low risk for adverse events and mortality.

2.1.4 Greek Catheter Ablation Registry - 2020

The radiofrequency ablation procedures registry from the Hellenic Society of cardiology was created in 2008 to provide a report and interpretation of catheter ablation data submitted between 2008 and 2018 (Vassilikos *et al.* 2021). The registry received data from a total of 31 EP centres. In 2018 there were 2687 patients enrolled into the study. There were 2795 procedures performed for these patients. The mean age for this study cohort was 54.6 years old, with 34.2% of the population being female. With regards to the prevalence of tachyarrhythmias, as noted in previous European registries, the number of procedures done per year has increased year on year throughout the decade. AF again has been noted as the most frequent procedure (37.7%), with it surpassing AVNRT around the 2011-2012 period (Fontenla, García-Fernández and Ibáñez 2017; Gonçalves, Reis and Bonhorst 2020). Atrio-ventricular nodal re-entry tachycardia in this cohort of patients for 2018 accounted for 24,0% of the procedures, AFL was 7.9%, AT was 4.1%, AP ablation was 6.8%, VT 16.9%, and sinus node re-entry tachycardia (SNRT) being the lowest at 0.2%. The study describes that as the number of procedures increased each year, the success rates of the procedures became higher, and complication rates became lower. The authors attribute this trend to the increasing experience of physicians and the creation of high-volume centres.

2.1.5 Argentine Catheter Ablation Registry

The first Argentine catheter ablation registry was published in 2010 (López *et al.* 2010). They identified a deficiency in the body of knowledge regarding the use and outcomes of catheter ablation procedures in their environment. Their objective was to describe the number of EP procedures done, disease prevalence, and report on the success and complication rates of the procedures done. EP data was supplied by 30 centres. A total of 762 catheter ablation procedures were done, 98.7% were done utilizing radiofrequency ablation. The mean age was 42 years old, and 56.3 percent of the patient population were men, while 8% were regarded as paediatric (<14 years of age). 76.5% of this cohort had no underlying structural heart disease.

The registry reported procedural success rates of 93.4%.The disease prevalence encountered was described as follows AVNRT ablation 237 (30.0%), AF ablation 28 (3.6%), typical AFL ablation 160 (21.5%), EAT 34 (4.3%), Atypical AFL seven (0.8%), manifest APs 186 (24.0%), concealed APs 68 (8.6%), idiopathic VT 20 (2.5%), ischemic VT seven (0.9%), AVNA 15 (1.9%) and PVC seven (0.9%).

In the 253 patients treated for AVRT, 186 (73.5%) were manifest APs while the remainder were concealed. The patients with concealed APs were more symptomatic from tachyarrhythmias (100%) when compared to those who had manifest APs on baseline ECGs (15.6%). The success rate for manifest AP ablations was 92.0%, while concealed pathways had a success rate marginally lower at 90.8%. The most common AP location was left-sided 174 (68.0%). seven (2.7%) complications were registered for AVRT ablations (López *et al.* 2010).

The success rate for the 28 AF procedures performed was high. Access to the left atrium was acquired transeptally in all patients. Inability to fully isolate the pulmonary veins only occurred in one patient. They report no complications for these 28 procedures. In the AFL population, 160 (93.5%) patients had CTI dependant flutter, while 11 patients (6.5%) had non-isthmus dependant AFL. Bidirectional block was not achieved in eight patients. There were no major complications related to AFL ablations. Overall, this registry reported a low incidence of complications (3.0%). They concluded that cardiac EP procedures are considered safe as well as efficient.

2.1.6 Canadian Catheter Ablation Registry

The first Canadian cardiac EP registry was published in 2014 (Shurrab *et al.* 2014). The aim of this study was to create a period registry that reported information regarding EP laboratory infrastructure, human resources, and the spectrum and volume of EP procedures. A total of 25 centres were identified as EP centres; 19 of these centres responded to the invitation to participate in this study. On average, 8041 standard and complex ablations were performed per year by the 19 centres.

The Canadian cardiac EP registry had its most complete data set in the year 2012. Atrial fibrillation ablation, which was the most common procedure, was performed 1533 times (30.0%). The second most common procedure was AVNRT ablation which was performed 1178 times (23.0%), followed by CTI dependant AFL 987 (19.0%) and AVRT 568 (11.0%). Ventricular related ablations accounted for less than 10.0% of the workload.

A notable difference in first Canadian cardiac EP registry, compared to this study, is the decision not to report on success rates of the procedures and the nature and frequency of their complications. The authors have also not reported on the specifics of the arrhythmia’s substrate, e.g., AP location. They have, however, delved deeper into the details of logistics, technology, infrastructure, and human resources, which in this literature review was the only study to do so.

2.1.7 Latin American Catheter Ablation Registry

The first Latin American catheter ablation registry was established in 2012 (Keegan *et al.* 2015). The aim of creating this registry was to assess and analyse the results from catheter ablations in the larger part of Latin America. Cardiac EP procedural data for the study period 01 January 2012 to 31 December 2012 were retrospectively collected. The 13 countries that participated in this study recorded 15099 EP procedures from 120 EP centres. In this registry, AP ablation was the most common type of ablation done (31.0%), followed by AVNRT (29.0%), AFL (14.0%), and AF (11.0%) ablations.

The authors report an overall success rate of 92.0%. The complication rate for this cohort is reported at 4.0%. The authors attribute this higher complication rate to their more liberal reporting of complications, such as reporting all hematomas as complications (which accounted for more than 50% of the complications) compared to other registries that only reported hematomas that required treatment as blood transfusion and surgery.

The year this registry reports on (2012) likely explain why AF ablation is not the most common procedure, as it has become more prevalent in recent years. AF ablation is also a more complex procedure and usually requires advanced infrastructure such as an electro-anatomical mapping system. According to the authors, Latin America is primarily made up of developing countries, resulting in a poor socioeconomic climate.

This economic climate results in limitations, one of which could be the inability to offer advanced procedures like AF ablations. They stipulate that less than 50.0% of the centres had access to electro-anatomical mapping systems.

Critical dissection of these major registries has reinforced what is known about EP in the developed world. Most procedures are safe with high success rates. Complications rates are linked to centre volume and operator experience. The number of EP cases, and centres available to perform EP, are increasing yearly. AF ablation is a complex ablation procedure currently increasing in popularity (Scheinman and Huang 2000; Cavaco, Morgado and Bonhorst 2016; Fontenla, García-Fernández and Ibáñez 2017; Raymond-Paquin, Andrade and Macle 2019).

These registries have assisted the developed world by providing information regarding disease burden and procedural frequency, as well as describing the characteristics of the patient population. This information assists health care authorities in creating training criteria that will decrease complication rates and adequately prepare for the financial burden these procedures have. Data can also be extrapolated to make provisions for future years. This study will assist in providing this valuable information in an African setting.

2.2 **Cardiac arrhythmias in low and middle-income countries**

The gradual but ongoing improvement of the socioeconomic conditions in the low and middle-income countries globally is resulting in an epidemiological transition (Mkoko *et al.* 2020). While this is true, the level of effort in the prevention and treatment of CVD present in higher-income areas/developed countries is simply not seen in the developing world (Mkoko *et al.* 2020). The improvement in the socioeconomic situations of low and middle-income countries will impact life expectancy and the prevalence of non-communicable disease. Cardiac arrhythmias are expected to increase in prevalence as this transition happens (Jardine, Fine and Obel 2014).

The researchers postulate that while the prevalence of these arrhythmias will increase, treatment will not increase in the same fashion because it generally requires expert staff and expensive equipment, which is more readily accessible in the developed world. The disproportionality between disease prevalence and the ability to effectively diagnose and treat cardiac arrhythmias in developing and low-income areas is likely responsible for the disparity in the standard of care between the developing and developed world. While AF is the most common arrhythmia globally, its prevalence is much higher in the developed world. The difference may not be a true reflection of the actual disease prevalence but rather a result of the lack of published scientific data in these low-income areas (Jardine, Fine and Obel 2014).

The discrepancy in AF prevalence is evident in this literature review where in recent years, all registry data from developed countries show AF ablations as the most common ablation while the Argentinian and Latin American registries still report AVNRT ablations as the most common (López *et al.* 2010; Shurrab *et al.* 2014; Keegan *et al.* 2015; Criado *et al.* 2019; Gonçalves, Reis and Bonhorst 2020; Vassilikos *et al.* 2021). While, the prevalence of cardiac arrhythmias is expected to increase in the years to come, the scarcity of population prevalence studies, lack of adequately trained medical professionals, and rudimentary equipment and infrastructure will prove challenging to efficiently serve the needs of the populations of low and middle-income countries (Mkoko *et al.* 2020).

2.3 **Electrophysiology inside the continent of Africa**

The Pan African Society of Cardiology (PASCAR), to the researcher's knowledge, is the largest and most prominent working group for cardiac arrhythmias and pacing on the African continent. This working group was created to provide a comprehensive modern-day report on the access and use of cardiac services in Africa. Their second report was published in 2020 (Bonny *et al.* 2020). Their team received data from 21 counties in Africa. SA ranked third in the pacemaker implantation rate/million population behind Tunisia and Mauritius. Implantable cardiac defibrillators and cardiac resynchronization therapy (CRT) were used in 15 and 12 countries, respectively. Cardiac EP procedures were only performed in eight countries (35.0%), although complex cardiac EP procedures were only done in the Maghreb countries and SA. Patients with arrhythmias experience higher levels of morbidity and mortality due to the high cost of the necessary medical equipment required to perform these specialized procedures, the need for highly skilled experts required to treat complex arrhythmias, and inadequate public health policies. It is acknowledged in this article that no national EP or catheter ablation registry exists for any country in Africa (Bonny *et al.* 2020).

Atrioventricular node ablations were performed in six countries (26.0%), Typical AFL ablations in eight (35.0%), AVNRT ablations in seven (30.0%), AP ablations in seven (30.0%), AF ablation is only performed in four countries (17%) as is AT ablation is only available in four (17.0%) countries in Africa. This study reports that AF is becoming increasingly common in SSA, with 21.0% of the AF being associated with RHD (Bonny *et al.* 2020).

There is no data regarding the specific number of catheter ablations done in SA and Africa as a whole per annum, and as such, treating physicians are unaware if Africa follows the trend in global EP with an increase in the frequency of AF ablation procedures to match the rise in the number of AF patients. While, Africa as a continent needs to provide better access to cardiac arrhythmia treatments, services are notably lacking in SSA (Bonny *et al.* 2020). The data in this study aims to provide a snapshot of disease prevalence and treatment in a Sub-Saharan country. This will offer insight into the spectrum of cardiac arrhythmia services available in this setting as a tertiary institution in SA.

2.4 ***Cardiac electrophysiology in South Africa***

SA ranks highly in terms of ability to offer cardiac EP services (Bonny *et al.* 2020). While the researchers know that SA as a country offers a wide range of services, there is no data to determine how accessible these services are to the country's population. Anecdotally the researchers know that while only 16.9% of the SA population is insured by private medical aid the majority of the EP services are provided by private institutions (Statistics South Africa 2019). This means that 83.1% of SA's 58 million population is serviced primarily by public EP institutions. According to CASSA (Cardiac Arrhythmia Society of SA), there are only two dedicated public EP laboratories (Cardiac Arrhythmia Society of South Africa 2020). There is a significant gap in published data on EP in SA, in keeping with other low-income countries across the world. There is no national registry, and to the best of the researcher's knowledge, not a single centre in SA has published their disease prevalence, patient characteristics, success rates, and nature and frequency of complications. The researchers are optimistic that this attempt to report the first patient and procedural-specific data set in SSA will inspire other centres to do so, thereby setting up the foundation for a national registry.

2.5 ***Conclusion***

An extensive literature review was undertaken to establish the state of EP internationally, secondly at a Sub-Saharan level and then locally in SA. The researchers identified firstly that the number of ablation procedures are increasing yearly with most national registries indicating an increase in the number of centres participating. A consistent relationship was noted between high volume centres and low complication levels indicating a learning curve exists. In most international registries excluding the Latin American ablation registry and Argentine ablation registry (López *et al.* 2010; Keegan *et al.* 2015). Atrial fibrillation was noted as the most common arrhythmia. Keegan et al acknowledged that while ablation procedures are safe and effective, they are currently being under-utilized for complex procedures such as AF in Latin America. They postulate that this may increase with improvements in infrastructure and availability of technical resources which indicates the financial constraints currently being faced (Keegan *et al.* 2015).

At a Sub-Saharan level access to EP services drastically decreases as indicated by (Bonny *et al.* 2018) who state that in SSA only Senegal and SA offered an EP service and while SA has been offering complex ablation procedures for decades, Senegal only offers CTI ablation for AFL. The scarcity in availability of ablation services seems to have a direct impact on the amount of research done. Currently no country in Africa keeps a national registry and data regarding disease prevalence , clinical characteristics, and the success and complication rates of ablation procedures is largely unavailable. As acknowledged by Bonny et al SA offers the most comprehensive EP service in SSA and is therefore uniquely equipped to conduct this research (Bonny *et al.* 2018).

Therefore, the aim of the study was to describe the clinical characteristics, EP study findings, and short-term outcomes of patients referred to the EP service at Tygerberg Hospital.

The objectives were as follows:

1. To describe the clinical characteristics of patients referred to the cardiac EP service at Tygerberg Hospital.
2. To describe the echocardiographic findings of these patients.
3. To document the number of patients requiring invasive EP studies with ablation if necessary.
4. To describe the diagnoses made at EP study.
5. To ascertain the success rate of ablation procedures and to document all procedure-related complications.
6. To evaluate the patient's short-term follow-up for symptoms and arrhythmia recurrence.

CHAPTER 3: RESEARCH METHODOLOGY

Tygerberg Hospital is is a large tertiary referral hospital in the Western Cape, and is one of only two public institutions offering a regular EP service in SA. There is no published data to date describing the patient population referred to the EP service. In this retrospective study the researchers investigated the clinical characteristics, disease burden as well as the success and complication rates of invasive EP procedures. Assessment of real-world clinical data in a public sector tertiary referral centre will lead to a better understanding of current practices in SA and highlight the challenges faced, which will ultimately benefit patients' clinical care.

3.1 Aims:

The aim of the study was to describe the clinical characteristics, EP study findings, and short-term outcomes of patients referred for to the cardiac EP service at Tygerberg Hospital.

3.2 Objectives:

1. To describe the clinical characteristics of patients referred to the cardiac EP service at Tygerberg Hospital.
2. To describe the echocardiographic findings of these patients.
3. To document the number of patients requiring invasive EP studies with ablation if necessary.
4. To describe the diagnoses made at EP study.

5. To ascertain the success rate of ablation procedures and to document all procedure-related complications.
6. To evaluate the patient's short-term follow-up for symptoms and arrhythmia recurrence.

3.3 Study Location and setting

The study was conducted within the Division of Cardiology, Department of Medicine, Faculty of Health Sciences, Stellenbosch University, and Tygerberg Hospital, Cape Town, SA. Tygerberg Hospital is the teaching hospital for the Faculty of Health Sciences; University of Stellenbosch; University of the Western Cape and Cape Peninsula University of Technology. Tygerberg Hospital services a drainage area in the Western Cape with a population over 2.6 million people. The Northern Metro sub-districts, Khayelitsha north of Spine Road, Eastern Tygerberg, West Coast, Cape Winelands and the Overberg rural districts are all serviced by Tygerberg (Western Cape Government 2016)

3.4 Study design

The study design was quantitative, descriptive, and retrospective in nature. The quantitative study design was chosen because numerical statistical analysis was used to analyse data. The researchers described disease prevalence, trends, and other data such as success rate and complication frequencies, and patient data was collected and analysed retrospectively. The investigators examined the characteristics of patients referred to a tertiary EP service in SA. The researchers aimed to determine disease prevalence and report the clinical, as well as electrophysiological characteristics peri-procedurally and at follow-up.

3.5 Target and study population

All patients who met the inclusion criteria for this study and were referred to the cardiac EP service at Tygerberg Hospital from January to December 2019 were included in the study. The principal investigator (PI) performed a retrospective review of the patients' medical records from their first presentation to the EP service to their first follow up visit. All patients presented for their follow-up prior to ethical approval and were recruited retrospectively recruited.

3.6 Inclusion criteria

- All patients 18 years and older referred to the cardiac EP service at Tygerberg Hospital.

3.7 Exclusion criteria

- Patients for whom no clinical information was available.
- Patients below the age of 18 years old.

3.8 Sample Size

A statistician was consulted for statistical analysis. As this study included all patients referred to the EP service at Tygerberg Hospital over the first calendar year of the study (2019), no formal calculation of the sample size was done. All consecutive patients without exclusion criteria were retrospectively included in the study. Please find attached a letter from the statistician (see Appendix 1). The sampling technique used in this research process was purposive sampling which is a sampling technique where the researcher sets out to identify cases that meet a predefined criteria. In this study the researchers exclusively investigated patients that presented to the EP service, specfically those that presented with tachyarrythmias (Denieffe 2020).

3.9 Data collection and analysis

Data collection

Data collection was done exclusively by the PI. The clinical characteristics of patients at initial EP clinic visit and at follow-up were recorded from the electronic clinical record-keeping system at Tygerberg Hospital, ECM™. Echocardiographic data was obtained from the echocardiographic laboratory where images and reports were available on a storage system, Centricity™. Electrophysiology study/ablation reports were also available from the Centricity™ database. All EP measurements and assessments, including 3D mapping were available to the PI via two systems. The CLARIS™ recording system housed all analogue EP data such as standard EP studies and measurements. The Ensite PRECISON™ 3D mapping system stored information on all 3D mapping cases. All data was de-identified and recorded anonymously on a password secured CRF (Appendix 2).

3.10 Classification of abnormalities

3.10.1 Electrocardiography

All available ECGs were retrospectively reviewed by the PI. The ECGs were analysed according to the 2019 ESC guidelines for the management of patients with SVT (Brugada *et al.* 2020). Please see figure 2 below by depicting a pathway to diagnose narrow complex tachycardias (Brugada *et al.* 2020).

3.10.2 Echocardiography

All available echocardiograms were retrospectively reviewed by the PI. Two-dimensional, doppler, colour doppler and M-mode measurements were evaluated according to the American society of echocardiography guidelines, as is the standard practice at Tygerberg Hospital (Lang *et al.* 2015)

3.11 Classifications of complications

- Major adverse cardiac and cerebrovascular events
    - Death
    - Myocardial infarction
    - Stroke
- Severe non-fatal events
    - Major bleeding

- Pericardial Tamponade
- Need for emergency cardiac surgery

3.12 Data analysis

Data analysis was done in four stages:

Stage 1: Demographics of study cohort

The first stage of the analysis was done for the entire study population. All baseline clinical information including gender, age, co-morbid conditions, type of arrhythmia, medications and treatment strategy was recorded. This data was represented by way of means and standard deviations.

Stage 2: Data analysis per arrhythmia subtype

The second stage in the data analysis plan was to divide the study cohort into subgroups based on arrhythmia type-specific groups. Extracting and presenting information regarding clinical, echocardiographic and EP characteristics for each arrhythmia subgroup added value in characterising the study population. There were four arrhythmia groups: AFL, AF, SVT, VT. Firstly demographic data from the continuous variables per arrhythmia subgroup was presented. Categorical variables were also collected for each arrhythmia subgroup. Combined column charts were used, which were ideal for comparisons regarding the prevalence of cardiovascular risk factors (CVRFs), symptoms, medication used and the type of cardioversion, if this was performed. The echocardiographic data, which primarily comprises of continuous and categorical variables, is presented in a table. The table provides a value for each echocardiographic parameter correlated to a specific arrhythmia subgroup. The data being primarily continuous and categorical, is displayed as means and standard deviations and numbers and percentages.

Stage 3: Comparison data for the two large subgroups

When analysing the data, two dominant arrhythmia subgroups were identified. In consultation with the statistician, a decision to compare these two subgroups to identify any statistically significant differences in the data was taken. The two arrhythmia groups selected were the AFL and SVT groups.

For the continuous variables in these two subgroups, e.g. age, the data is displayed using histograms and tables. In the tabulated data numbers, percentages, means, and standard deviations are displayed for each group. The Mann-Whitney U test was applied to identify statistically relevant differences in the data. The Mann-Whitney U test tests for differences between two groups of non-normally distributed data (McKnight and Najab 2010).

The categorical variables were analysed using two-way summary tables (contingency tables) and displayed using categorized histograms. The chi-squared test was used to analyse this data to determine how independent of chance the results were, meaning how likely it was that the results obtained were not solely attributed to chance (McHugh 2013; Onchiri 2013). To determine whether the categorical data in each group varied in a manner that was statistically significant, the Fisher exact test was used.

Stage 4: Pre and post electrophysiology service comparisons

Analysis on specific parameters was done to establish whether there was a change from the first presentation and at follow-up. The Fisher exact test was utilized for this. The data is displayed using a histogram to provide a graphical description of the difference in the prevalence of symptoms at the first EP clinic visit and at follow-up.

3.13 Ethical Considerations

Data was collected retrospectively by the PI so this was very low risk to the patient. To further minimize the risk, data was collected on a password protected CRF created on the Microsoft Excel application (Appendix two). The data collected and entered into the password protected CRF was anonymized and de-identified of patient identifiers. A record of the data will be kept as long as the registry is active. After the registry is closed, data will be kept for a five-year period. Once that five-year period is over, all data will be deleted/electronically shredded.

The research proposal was sent to Durban University of Technology (DUT) for ethical approval (IREC 052/20.) (see Appendix 3) and to Stellenbosch University (SU) (S21/01/015) (see Appendix 4). A waiver of consent was granted. Once ethical approval was received, permission to conduct the research was obtained from the medical superintendent at Tygerberg Hospital (see Appendix 5). As this registry is observational only, recording real-world data, no procedure was specifically done for the sole purpose of this study.

When conducting research, there are various ethical issues to consider ensuring that both the participant and researcher are protected.

3.13.1 Principals Guiding Ethical Research

1) Autonomy and respect for the dignity of persons: It is important to ensure that participants are able to make their own decisions and for participants to fully understand their role in the study and what is required from them (Blanche *et al.* 2006). – This study was a retrospective non-interventional medical records review (NIMRR). Permission to access patient medical records was granted by the medical superintendent of Tygerberg Hospital who acts as a custodian.

2) Non-maleficence (Do no harm): No harm should befall any participant of the study, directly or indirectly. It is important for the researcher to be cautious ensuring that the participant is put in no danger (physical or emotional) (Blanche *et al.* 2006). – No patient was placed at any risk of direct or indirect physical harm as a result of this study as the study was retrospective and observational.

3) Beneficence (Benefits): Research should be beneficial not only to the researcher but to the participants and population being studied. This can be provided by possible solutions to the problem being studied (Blanche *et al.* 2006). – The retrospective nature of this study does not allow direct benefit to the research participants but has the possibility to benefit the patient population as a whole by identifying challenges faced and possible differences in standard of care and for the South African patients suffering from arrhythmias. This will allow targeted interventions to improve patient care.

4) Justice: It is important to ensure that participants are treated fairly and with respect. This includes the responsibility to provide care and solutions that patients may need

(Blanche *et al.* 2006). – This study was a retrospective observational study and as such, did not interfere in anyway with the treatment offered to the study participants. At all times the patient was treated as deemed appropriate by the treating physician.

CHAPTER 4: RESULTS

Cardiac EP services in the public health care sector in SA are sparsely available. Research in the field of EP regarding disease prevalence, clinical characteristics of the patient population and success and complication rates is lacking in SA and Africa as a whole, as no country has a national EP registry.

This study aimed to describe the demographics, clinical characteristics, EP study findings, procedural success rates, procedural complications as well as the short-term outcomes of patients referred to the new EP service established at Tygerberg Hospital in 2019.

4.1 Electrophysiology clinic referrals and population demographics

In the year 2019, there were 86 referrals to the Tygerberg Hospital cardiac EP service. Of these 86 referrals, 75 were referrals requiring management for cardiac tachyarrhythmias. Two patients were excluded for being under 18 years of age (see figure 3) such that 73 patients were included in this study. The spectrum of patients regarded as non-EP referrals included patients referred for high-end device implants, and patients where there was inadequate information. The study population comprised of 53% (n=39) males, and the mean age was 49.5±14.1 years. The youngest patient was 20 years of age, and the oldest was 76 (see figure 4). The median age was 52 years.

4.2 Patient symptoms

Symptoms were common and reported across the spectrum of arrhythmia subgroups (see figure 5). The most common cardiac symptoms were palpitations (n=55 [75.0%]), dyspnoea and pre-syncope (n=36 [49.3%] each). Pre-syncope and syncope in combination, were reported by 33 (45.0%) patients. Symptoms of heart failure such as peripheral oedema, orthopnoea and paroxysmal nocturnal dyspnoea (PND) were less frequently experienced by EP patients, being reported in five (6.9%), five (6.9%) and six (8.2%) patients respectively.

4.3 Associated cardiovascular disease and co-morbidities

Cardiovascular risk factors were present across all arrhythmia subtypes. Hypertension was the most common CVRF present, seen in 37 patients (50.6%). This was followed by smoking (n=22, 30.1%), dyslipidaemia (n=19, 26,0%) and coronary artery disease (CAD) (n=16, 21.9%) (see figure 6). Males had more CVRFs than females (see figure 7).

Hypertension was more common in the AFL group 70.8% vs 37.5% in the SVT group (p=0.02). The only other CVRF to show statistical significance between these two arrhythmia subtypes was smoking. Smoking was significantly higher (45.8%) in the AFL group and 20.0% of the SVT group smoking (p=0.05). Diabetes, being recorded in 33.3% of the AFL group and 15.0% of the SVT group (p=0.12), alcohol use (AFL=25.0%, SVT=7.5%, p=0.07), obesity (AFL=16.7%, SVT=10.0%, p=0.46), known CAD (AFL=37.5%, SVT=17.5%, p=0.13), dyslipidaemia (AFL=37.5%, SVT=20.0%, p=0.15), and obstructive sleep apnoea (AFL=12.5%, SVT=5.0%, p=0.35) all showed no statistical difference between the two groups, although the numbers are small (see figure 8).

4.4 Type of arrhythmias

In 2019 the most common referral to the cardiac EP service at Tygerberg Hospital was that of SVT at 54.8% (n=40). This group includes AVNRT, AVRT and AT, in whom a definitive diagnosis was made of 15 AVNRTs, 16 AVRTs and 2 ATs (see figure 3). In the remaining patients, a definitive SVT diagnosis was not possible because they were either managed medically or non-inducible at EP study, leaving the 12 lead ECG as the only diagnostic tool. SVT was followed by AFL 32.9% (n=24) with fewer patients being referred with AF 5.5% (n=4) and VT 6.9% (n=5, see figure 9). The demographic data for each cohort is summarised in table 3. SVT, the largest group comprised of 42.5% males. The mean age for this group was young at 45.8±15.0 years. The AFL population consisted of 79.2% males and was older, with a mean age of 56.7± 8.2 years. The AF group was small consisted of 50% males. This group was young for an AF population with a mean age of 58.5±8.2 years. Only 20.0% of those referred with VT were male. This was also a young group of patients with the mean age of the group being 38.2± 15.9 years.

4.5 Echocardiographic data

Echocardiograms were available for 57 (79.5%) of the 73 patients included in this study. Echocardiographic data was not available for nine patients (12.3%) in the SVT group, six patients (8.2%) in the AFL group and one (1.4%) in the AF group. Table 4 summarises the echocardiographic data for the study population as a whole. Just under half the patients had atrial dilatation, and most patients (73.7%) had normal left ventricular (LV) size and function (64.9%) according to the American Society of Echocardiography (ASE) guidelines (Lang *et al.* 2015).

The echocardiographic findings for each arrhythmia subtype are summarised in table 5. The data was compared for the two larger arrhythmia subtypes (SVT and AFL), to identify any significant differences related to the type of arrhythmia. Echocardiographic abnormalities were more common in patients with AFL, with this group having larger atria, larger ventricles, poorer LV function and more diastolic dysfunction than the SVT group. The LVEF was lower in the AFL group (48.6±9.4 vs 50.5±6.5% in the SVT group, $p<0.01$).

4.6 Medical therapy

There were 13 (17.8%) patients treated with medical therapy alone. In addition to these three (4.1%) patients were offered an EP study but declined, bringing the total number of patients treated medically to 16 (21.9%).

Beta-blockers were the most commonly used medication to treat patients in this study, being prescribed to 64 (87.6%) patients. The second most commonly used medication was an ACE-inhibitor in 35 (48.0%) patients. The most frequently prescribed antiarrhythmic drug was amiodarone, prescribed in 8 (11.0%) patients. Sotalol was prescribed to one patient (1.4%) and flecainide was not prescribed for any patients in this cohort. Warfarin was the most frequently used anticoagulant, being prescribed for 33 (45.2%) patients. Novel oral anticoagulant (NOAC) use was minimal with only two

(2.7%) patients being on a NOAC. Digoxin was infrequently prescribed with only one patient (1.4%) being on this drug (see figure 10).

4.7 Cardioversion

Half of the 73 patients studied, (n=37 [50.7%]) had a cardioversion of some type. The most common was direct current cardioversion (DCCV), and it was most frequently performed in the AFL group. Chemical cardioversion was used in 11 (15.1%) patients, all of whom presented with SVTs which were cardioverted with intravenous adenosine (90.9%) and amiodarone (9.1%). In the group of 36 (49.3%) patients that did not receive either DCCV or chemical cardioversion, 27 (37.0%) were noted to have spontaneously cardioverted. The most common arrhythmia subtype to spontaneously cardiovert was the SVT group with 18 patients having spontaneously cardioverted in this group (45.0%). See figure 11.

4.8 Electrophysiology studies

Fifty-seven (78.1%) of the 73 patients studied underwent an invasive EP study. Of these eight patients (14.0%) had diagnostic studies only with four (7.0%) patients being non-inducible and four (7.0%) patients with arrhythmia substrate that were not ablated (see figure 3), with a definitive diagnosis being made in 53 patients. 49 of these 53 patients (67.1%) underwent catheter ablation. There were 21 (39.6%) patients were diagnosed with AFL. There were 19 (35.8%) patients that had a CTI ablation for the typical form, one had an ablation for peri-mitral AFL and one patient with atypical AFL had their ablation deferred to a later stage. Twenty-nine (54.7%) patients were diagnosed with an SVT, 12 (41.3%) of which were AVNRT, 14 (48.3%)

were AVRT, two were AT (6.9%) and one patient had a combination of AVNRT and AVRT. In the 29 (54.7) patients with SVT, 27 ablations were done in 26 patients, with 24 of the 26 patients (92.3%) having a successful ablation procedure on the first attempt. One of the two patients with SVTs that were not ablated was a 21-year-old gentleman referred for the evaluation of presumed pseudosyncope with a documented SVT on an exercise stress test. He was found to have a slow-slow AVNRT for which he was asymptomatic, without palpitations or syncope and the decision was taken to not ablate and follow up at EP clinic. The other patient was a 74-year-old female who was found to have multiple ATs from different foci and frequent episodes of AF during the study. It was decided to treat her medically in the first instance and re-book the procedure with 3D mapping should she remain symptomatic despite additional medical therapy. Of all the patients who underwent EP studies, only one had VT and underwent a successful ablation procedure for idiopathic RVOT VT. Two patients had atrioventricular node ablations (AVNA) for permanent AF which was poorly rate controlled.

Table 6 displays the various types of AP location and their prevalence. Manifest APs were present in 12 (75.0%) of the 16 APs, and four (25.0%) were concealed. Right posteroseptal APs were the most common with four (26.67%) right postero-septal APs being ablated. This was followed by left posterior (n=3 [20.0%]). A parahissian location was noted in three (20.0%) patients, two being mid-septal and one antero-septal If, left postero-lateral, left lateral and left anterolateral were combined into a broad group of left lateral pathways it would also be the most common type of AP four (26.7%).

The only complication was a left atrial thrombus at the site of transeptal puncture in a patient with severe mitral stenosis who underwent a balloon PTMC and ablation of a left posterior AP. The success and complication rate for ablation procedures in this cohort was 95.9% and 1.8%, respectively.

4.9 Follow up

Only 44 (60.3%) of the 73 patients presented to the EP clinic for follow-up while 29 (41.1%) did not. Of the 29 patients who did not follow up at the EP clinic, 16 (55.2%) were scheduled to follow up at a general cardiology clinic, a pacemaker device clinic, or at their local community clinic. The remaining 13 (44.8%) of the 29 patients were scheduled for an EP clinic follow up but did not attend their appointment. In other words, 17.8% of the 73 patients defaulted their follow-up.

Figure 12 shows the percentage prevalence of patients with various cardiac symptoms at first EP clinic visit (pre) and at EP clinic follow-up (post) as well as the prevalence of symptoms of the entire population at first EP clinic visit and at follow up. Most patients had their symptoms reduced at EP clinic follow-up. Dyspnoea, palpitations, pre-syncope, and syncope were all significantly reduced at follow-up with p-values of <0.01 for each of these. Overall, referral to the EP clinic and the treatment received had a significant impact in reducing patient symptoms (94.5% vs 15.9%, p<0.01). At follow up the percentage of patients requiring DCCV was reduced from 35.6% (n=26/73) to 2.3% (n=1/44, p-value <0.01), see table 7.

CHAPTER 5: DISCUSSION

In the year 2019, Tygerberg Hospital in Cape Town, Western Cape began offering an EP service and by doing so, became one of two public institutions in SA offering regular adult cardiac EP procedures. The EP service consisted of a specialist arrhythmia outpatient clinic every second week alternating with a high-end device clinic and one theatre list for invasive EP procedures per week. Little is known about disease prevalence and clinical characteristics of patients suffering from arrhythmias in the South African public health care setting. Likewise, the success and complication rates of invasive EP procedures have not previously been documented by a SSA center. Documenting this will assist in guiding clinical practice and inform areas where South African public sector EP does not meet international standards. This will assist health authorities and funders to allocate resources appropriately (Mkoko *et al.* 2020).

A retrospective registry was established to characterise arrhythmia patients in a tertiary academic hospital in SA. Registry data for an EP service in SSA has not been reported before. The first year's results are presented in this study.

In the year 2019, 84 patients were referred to the Tygerberg Hospital EP service. This is a small number of referrals, given that Tygerberg Hospital services a population of 2.6 million. Of these referrals, 75 (89.2%) were for tachyarrhythmias. This high percentage of tachyarrhythmia referrals was expected as the EP service at Tygerberg is a tertiary level service, and patients are referred after having been evaluated by general practitioners, primary and secondary level physicians, and general cardiologists before warranting tertiary level EP assessment.

5.1 Demographics

There were 73 patients who met criteria and were included in the study. The mean age was 49.5 $\pm$ 14.12 years. About half of the patients were male (n=39, 53.0%). This is in line with other data published, such as the first Argentine catheter ablation registry, where the mean age was 42 years, and 56.3% were men (López *et al.* 2010).

The cohort's relatively young age is not surprising if one considers the type of arrhythmia referred to this EP service. Supraventricular tachycardia, the dominant arrhythmia subtype, generally affects younger patients compared to arrhythmias such as AF which more often affects older patients due to myocardial fibrosis and atrial dilation associated with aging (Karamichalakis *et al.* 2015). This finding was also observed in the first Latin American registry where catheter ablation data in Latin America, an area with a similar socio-economic status was assessed (Keegan *et al.* 2015).

5.2 Disease prevalence

As mentioned, the most common arrhythmia referral to the EP service was SVT at 54.8% (n=40), followed by AFL 32.9% (n=24) with AF 5.5% (n=4) and VT 6.9% (n=5) being much less common. The low number of referrals for AF was notable as in most of the registries reviewed for this study AF was the most common arrhythmia treated (Scheinman and Huang 2000; Shurrab *et al.* 2014; Cavaco, Morgado and Bonhorst 2016; Criado *et al.* 2019; Holmqvist *et al.* 2019; Gonçalves, Reis and Bonhorst 2020;

Vassilikos *et al.* 2021). Atrial fibrillation has shown an upward trend in its prevalence and has doubled in the last decade in the general population (Zoni-Berisso *et al.* 2014). This upward trend is possibly attributed to advancements in the ability to treat cardiac and non-cardiac diseases which increases life expectancy with the result of an aging population that is at higher risk for developing AF. In addition, there have been advancements in the ability to detect AF.

A possible explanation for the low numbers of AF referrals is that the year 2019 marked the initiation of the EP service at Tygerberg Hospital. The way in which invasive EP procedures were introduced was to start with less complicated procedures and to gradually progress to more complicated procures such as AF and VT ablations. This may have influenced the referrals to the EP service, with patients with AF not being referred for assessment before catheter ablation was readily available, and explains why for the year 2019, no AF ablations were done at Tygerberg Hospital.

Another explanation is suggested by the only two registries that showed a similar disease referral pattern to this study, where AF was not the most common arrhythmia subtype seen, the Latin American catheter ablation registry and the Argentine Catheter Ablation Registry (López *et al.* 2010; Keegan *et al.* 2015). The similarity between these registries and this study is that they are all in developing countries/regions. This may be due to the fact that SVTs are more common in developing countries than in Europe and North America, where AF is the most common arrhythmia, but it is likely to be a reflection of an inability to adequately detect, refer and treat AF(Shurrab *et al.* 2014; Criado *et al.* 2019; Gonçalves, Reis and

Bonhorst 2020; Vassilikos *et al.* 2021). The prevalence of AF increases with the ability to effectively treat cardiac and non-cardiac diseases as well as advances in the ability to detect AF, could serve as a possible explanation for the low numbers of AF patients found in this study (similar to other developing world cohorts) due to lack of awareness, education and funding in the public healthcare sector in SA (Zoni-Berisso *et al.* 2014).

The socioeconomic situation that developing countries usually find themselves in, including the lack of infrastructure and funding for resource-heavy procedures like AF ablations which are very expensive invasive procedures, dramatically reduces their ability to provide such a service (Khaykin and Shamiss 2012).

Whether the small number of AF patients referred to the EP service at TBH reflects a truly low AF prevalence, or a factor of 2019 being the first year of this service with AF ablation not yet being offered, will become apparent as further data from the registry is available.

5.3 Echocardiographic data

The registries reviewed for this study such as the Canadian web based registry, the first Latin American registry and the first Argentine catheter ablation registry did not specifically evaluate the echocardiographic parameters of their patient population but did comment on the availability of intra-cardiac echocardiography (López *et al.* 2010; Shurrab *et al.* 2014; Keegan *et al.* 2015). Tygerberg Hospital does not utilise intra-cardiac echocardiography.

Echocardiographic data was available for 79.5% of the patients in this study. Most patients were found to have normal sized LVs (73.7%) with normal LV function (64.9%). Patients with AFL, in general, had more echocardiographic abnormalities than those with SVT. Compared to the SVT population, AFL patients had more structural abnormalities, including a higher prevalence of dilated atria, and dilated left ventricles. Myocardial dysfunction was also more common in the AFL population, with the AFL population having lower LVEF and higher rates of diastolic dysfunction. Only 27.8% of patients in the AFL had normal LV systolic function compared to 80.7% of patients in the SVT group.

In the AFL group just under half (44.4%) of patients had a dilated ventricle with impaired systolic function compared to only 12.9% in the SVT group. This finding is compatible with the current understanding of the aetiology of SVT and AF. Heart failure, chronic pulmonary disease, and age are prominent predisposing factors for the development of AFL, which is an arrhythmia more often associated with structural heart disease and other CVRF including age. Atrial flutter can also precipitate cardiac dysfunction such as a tachycardia induced cardiomyopathy (CMO) (Rahman *et al.* 2016).

The primary mechanism for the development of AFL is the presence of an anatomical barrier in the atrium which acts as an area of slow conduction thereby facilitating re-entry. In typical AFL, which is macro-re-entrant in the right atrium, the area of slow conduction is the CTI (Daoud and Morady 1998; Cosío 2017). Conversely, paroxysmal

SVTs occur more often in younger patients with structurally normal hearts due to the presence of dual AV nodal physiology or the presence of an AP which are not dependent on the presence of structural abnormalities and are usually congenital (Knight, Link and Downey 2017).

If SVT occurs in people with structurally abnormal hearts these patients tend to be older. Chamber enlargement and valve lesions create the substrate for the development of arrhythmia (Orejarena *et al.* 1998). According to Orejarena et al patients with SVT and associated CVD had a mean age of 69 years, where patients with lone SVT had a mean age of 37 (Orejarena *et al.* 1998). This cohort of SVT patients had a mean age of which was 45,8±15.0 years and the AFL cohort was 56.7±8.2 years old. The four (12.9%) patients with SVTs that had dilated LVs with impaired systolic function were older, with a mean age of 53.5±12.3 years.

5.4 Cardioversion

All patients, but one patient who was rate controlled for an atypical flutter and two who had AVNA for AF, were managed with a rhythm control strategy, and half of the patients underwent a cardioversion as part of this strategy. The most common type of cardioversion performed was DCCV, mostly performed in the AFL population. This is not unexpected because DCCV is known to have a high success rate in converting AFL to sinus rhythm (Ambrosi *et al.* 2011).

Supraventricular tachycardias are known to be paroxysmal and can self-terminate (Medi, Kalman and Freedman 2009). This explains why 18 patients in the SVT group were noted to have spontaneously cardioverted. Arrhythmias can sometimes self-terminate due to the circuit requiring very specific conditions in order for the tachycardia to maintain itself. Physiological changes such as changes in vagal tone can disrupt these conditions and terminate the tachycardia. Despite this, patients with SVTs frequently present to the emergency room (Kotadia, Williams and O'Neill 2020). For patients that present to the emergency room in SVT, the current guidelines for the first-line treatment of acute narrow complex tachycardia are a vagal manoeuvre followed by intravenous adenosine (Katritsis *et al.* 2017; Brugada *et al.* 2020). In this study all the chemically cardioverted patients (37.0%) had SVTs which were terminated with adenosine.

This study noted a statistically significant drop in the need for DCCV at follow-up ($p<0.01$). Since DCCV was done primarily for the AFL population and no patient had a recurrence of CTI dependant AFL, a dramatic drop in the need for DCCV is therefore expected and welcomed. While this finding is welcomed the researchers are aware that the poor rate of patient follow-up may have had an effect on this finding. The high success rate for AFL ablation is in keeping with current literature, such as a meta-analysis of ablation of AFL and SVT, which reported an AFL ablation success rate of 91% (Spector *et al.* 2009). The high success rate associated with AFL ablation is likely due to the advanced understanding of the mechanism of AFL (Tai and Chen 2009). The CTI has been proven to be a critical part of the AFL circuit and the electroanatomical approach to AFL ablation resulting in a targeted ablation strategy greatly increases the procedural success rate (Cosio *et al.* 1993).

5.5 Supraventricular Tachycardia

Supraventricular tachycardia was the most common arrhythmia subtype in this study. There were 40 patients diagnosed with SVT at the EP clinic. Four (10.0%) of the 40 patients were treated with medical therapy only. Of these four patients, three had minimal symptoms and one patient referred with palpitations had primary hyperthyroidism. The other 90.0% of patients presenting with an SVT were offered an EP study and catheter ablation. While both medical therapy and catheter ablation have the ability to reduce symptoms and have similar long-term cost implications, ablation therapy results in complete reduction of symptoms and arrhythmia non-recurrence more consistently. General improvement in quality of life is also more common in the population undergoing ablation (Bathina *et al.* 1998). As demonstrated by this study and the registries reviewed for this study, ablations are safe and effective and as such the guidelines for the management of SVTs now promote a more liberal use of catheter ablation. It is encouraging to note that this is possible in the public healthcare sector in Cape Town (Brugada *et al.* 2020).

5.5 Subtypes of Supraventricular Tachycardia:

5.5.1 Atrioventricular Nodal Re-Entry Tachycardia

A total of 15 (20.5%) people were diagnosed with AVNRT. This finding is similar to registries in Sweden, Latin America and Canada who quoted AVNRT prevalence's of 21.0%, 29.0% and 23.0% respectively (Shurrab *et al.* 2014; Keegan *et al.* 2015; Holmqvist *et al.* 2019). There were nine (60.0%) females, and the mean age for this group was 44.6±11.3 years. This female predominance is expected as females are more likely to develop AVNRT (Ghani *et al.* 2011).

Two patients were treated with medical therapy as they became asymptomatic, and slow pathway ablations were performed in 12 (80.0%) of the patients diagnosed with AVNRT at EP study. A 21-year-old male, who had one episode of documented SVT and a history of presumed pseudosyncope was referred by neurology for evaluation. At EP study an atypical AVNRT was induced, of which the patient was asymptomatic. Since this tachycardia was not associated with syncope and he had never complained of palpitations in the past, a decision to not ablate was taken. Incidentally his syncopal episodes also resolved after the EP study.

There were no complications for the AVNRT ablations, and the immediate success rate of the procedure was 100% which correlates well with the Greek ablation registry who quote a 99.6% success rate for their 2017 registry data (Vassilikos *et al.* 2021). This success rate is also in keeping with guidelines that quote success rates for AVNRT ablation to be >95% (Page *et al.* 2016).

5.5.2 Wolff-Parkinson-White Syndrome and Atrioventricular Re-entry Tachycardia

The prevalence of APs varies greatly between registries. In the Swedish catheter ablation registry, the prevalence of AVRT was 12.0%, while in the Latin American, Canadian, and Greek catheter ablation registries the prevalence of AVRT was 31.0%, 11.0%, 17.9% respectively (Shurrab *et al.* 2014; Keegan *et al.* 2015; Holmqvist *et al.* 2019; Vassilikos *et al.* 2021). In this cohort, a total of 16 (21.9%) patients were diagnosed with AVRT, and 13 (81.3%) of these patients had an AP ablated. Manifest APs were present in 12 (75.0%) of the 16 APs, and four (25.0%) were concealed. This finding is consistent with a study by Adão et al who quote a 28.0% prevalence of concealed APs (Adão *et al.* 2011).

The three patients who were not ablated included a 43-year-old male originally from east Africa with Wolff-Parkinson-White (WPW) and pre-excited AF which was subsequently cardioverted. He was healthy with no CVRFs. He was offered an EP study/ablation but declined despite counselling. He opted to travel back to his home country on medical therapy only as he did not have the required documentation to be in SA. A 31-year-old female who presented for the first time to her local clinic with AF requiring DCCV, was referred for evaluation because her sinus rhythm ECG had a short PR interval without pre-excitation. She was thought to have Lown-Ganong-Levine syndrome at EP study, where no tachycardia was inducible and a third patient who present to Tygerberg hospital with atypical chest pain, palpitations, presyncope and a diagnosis of WPW on ECG. At EP clinic the patient was noted to be in normal sinus rhythm without pre-excitation, at this time a decision to retrieve his physical file to view his pre-excited ECGs and to follow him up at EP clinic was taken.

Accessory pathway ablation was successful in 11 patients (84.7%). In two patients the procedure was unsuccessful. In one patient with a left anterior AP, only the retrograde limb was successfully ablated. The antegrade limb was ablated successfully with a repeat procedure. The other patient had severe mitral stenosis and a left posteroseptal AP. She underwent a hybrid procedure with percutaneous transvenous mitral commissurotomy (PTMC) and AP ablation in the same setting. The procedure was complicated by the development of left atrial thrombus. The AP was subsequently successfully treated in a second procedure once the thrombus had resolved.

Left lateral APs are the most common APs (Fox *et al.* 2008). These were common in this study as well, with 26.7% of the AVRT patients having left lateral pathways. Equally common were right posteroseptal APs. Although left lateral pathways were common in this study, the Spanish catheter ablation registry quoted a percentage as high as 51.2% (Criado *et al.* 2019). A possible explanation for this difference is the small sample size in this study. Posteroseptal and anteroseptal pathways are present 24.0% and 5.0% respectively (Cain, Luke and Lindsay 1992). Our findings were similar with posteroseptal pathways making up 26.7% and anteroseptal pathways being present in 6.7%. There were three parahissian pathways in our cohort and all three were successfully ablated without any complications. Ablation of parahisian pathways carries an increased risk for unintentional damage to the AVN (Schlüter and Kuck 1992). In an attempt to minimize this risk, non irrigated catheters and low wattages were used.

5.5.3 Atrial Tachycardia

There were two patients (2.7%) who presented to the EP laboratory with AT. This finding was similar to the first Latin American registry where the AT prevalence was 4.0%. A low right atrial septal tachycardia was successfully mapped with 3D mapping and ablated without any complication in one of the patients, the second patient who was noted to have multiple ATs as well as AF at EP study was not ablated and was treated medically with amiodarone.

5.5.4 Atrial Flutter

Atrial flutter was present in 24 (32.9%) patients. This is higher than the prevalence of AFL quoted in other registries. The prevalence of AFL in these registries were as follows: the Swedish catheter ablation registry 16.0%, the Latin American registry 14.0%, the Canadian catheter ablation registry 19.0%, the Greek catheter ablation registry 11.0% and the Portuguese national registry 17.5%. One possible explanation for this is the small sample size of this study. Another is that AFL is a common arrhythmia in our patient population. Further study is required to ascertain whether AFL is more common in the South African patient population.

Medical therapy or DCCV only was used in three patients (12.5%), Of these three patients one patient had a well rate controlled atypical flutter and two patients were asymptomatic with no recurrence of their flutter after DCCV at EP clinic visit. There were 21 (87.5%) patients were referred to the EP lab for ablation. Typical counter clockwise AFL was diagnosed in 18 (75.0% of those with AFL, 24.7% of the entire cohort) of these patients and one had reverse typical (clockwise) AFL, bringing the total of CTI dependent AFL to 19 patients (79.2% of AFL patients, 26.0% of the cohort). There were two patients that had atypical AFL and one of the two had mitral isthmus dependant AFL which was successfully ablated, and the second patient, with a left sided AFL and a prosthetic mitral valve, had their ablation deferred to be rebooked with 3D mapping support. There were no complications noted for any of the AFL ablations. At follow up there was no recurrence of CTI dependent AFL. There was one patient who had a previous CTI dependent AFL which was ablated was found to have an atypical AFL. The CTI was confirmed to be blocked at the follow-up EP study where mitral isthmus dependent AFL was diagnosed and treated.

5.5.5 Ventricular Tachycardia

There were five patients (6.9%) that were referred to the EP service with suspected ventricular arrhythmia. Of these patients three had idiopathic VT, one of which was referred to EP study and underwent a successful RVOT VT ablation, the other two were successfully treated with medical therapy. There were two patients that presented with frequent PVC and both of these patients were also treated medically. There were no referrals for ischaemic or scar VT. PVCs and idiopathic VT have different recommendations for treatment depending on the site of origin (Priori *et al.* 2015). RVOT VT / PVC has a class I recommendation for catheter ablation as well as for medical therapy, whereas the recommendation for VT / PVCs from the LVOT is to manage them medically in the first instance. Given this, the patients in this cohort were managed within guideline recommendations.

5.6 Complications

In the 57 (78.1%) patients undergoing EP study in this cohort, one complication was reported. The complication occurred in a patient who underwent a PTMC and ablation for WPW sequentially in the same sitting. The attempt to ablate the left posteroseptal AP following PTMC was unsuccessful. At post-procedure echocardiography, the patient was found to have a large LA thrombus at the site of the transseptal puncture, which subsequently resolved on warfarin anticoagulation without any thromboembolic sequelae. This gives an overall complication rate for patients undergoing EP study and ablation at Tygerberg Hospital to be 1.8%. This is similar to complication rates noted in international registries such as the Spanish national registry at 2.2%, the first Argentine catheter ablation registry at 3.0% and the first Latin American catheter ablation registry at 4.0% (López *et al.* 2010; Keegan *et al.* 2015; Criado *et al.* 2019).

5.7 Follow up at electrophysiology service

Fourty-four (60.3%) patients presented to the EP clinic for follow-up. There were 16 (21.9%) patients of the initial cohort who were discharged from the EP clinic to follow up at either their local primary or secondary facility, or at a general cardiology clinic. There were 13 (22.8%) patients who were expected to follow up but did not attend their EP clinic appointment. One possible explanation for this high percentage of patients defaulting follow-up, is that patients are referred to Tygerberg Hospital from a large drainage area and often rely heavily on public transport, which is not always safe or reliable in SA (Vilakazi and Govender 2014). The cost of transport to a follow-up visit may also be a contributing factor for some patients from very low socioeconomic areas. Other registries have commented with inconsistency on follow-up visits. The Hellenic cardiology society ablation registry from Europe, where socio-economic circumstances are better did not report a significant number of patients defaulting a 6 month follow up (Vassilikos *et al.* 2020). Noticeably some registries such as the Portuguese national registry, the first Latin American registry and the Swedish catheter ablation registry did not follow up patients formally and relied on the presence of a redo procedure to determine success or failure of the initial ablation procedure (Keegan *et al.* 2015; Cavaco, Morgado and Bonhorst 2016; Holmqvist *et al.* 2019).

A further possible explanation for patients not following up is simply that they were less symptomatic after catheter ablation and therefore found a follow-up visit unnecessary. Patients can experience significant improvements in quality of life and number and duration of episodes after catheter ablation (Wood *et al.* 2010). This was true for our patients as well, with dyspnoea, palpitations, pre-syncope, and syncope, which were all common symptoms in patients at the time of referral, were all significantly reduced at follow-up. The high procedural success rate of 95.9% in our study is in keeping with published data (Ghzally, Ahmed and Gerasimon 2020).

CHAPTER 6: CONCLUSION

This study aimed to describe the demographics, clinical characteristics and EP study findings as well as the short-term outcomes of patients referred to the new EP service established at Tygerberg Hospital in 2019. There were 73 patients that were retrospectively included, and data was recorded for their initial EP clinic visit, EP study and at their first follow-up.

The study provides much needed information about the spectrum and scope of a local EP service. The data has revealed novel information about an EP service in this unique setting. The study reinforces the knowledge that catheter ablation procedures can be safe and highly successful.

The disease prevalence in this cohort was found to be different to developed world cohorts. Unlike the developed world, AF was not noted as the most common arrhythmia, and it is postulated that this is likely due to under-referral and not true disparities in disease prevalence. This highlights the need to generate more local data and to create awareness regarding the detection and treatment of AF.

6.1 Strength, limitations, and recommendations

This study takes advantage of a unique research opportunity in SA since Tygerberg Hospital is one of only two dedicated public sector EP centres in the country. The public sector serves the majority of the SA population and arrhythmias and cardiac EP procedures are not well documented for this population. This study provided information regarding disease prevalence and invasive EP procedural success and complication rates that is contextually novel and relevant to the SA setting. Limitations of this study include it’s retrospective nature and the low numbers referred to the service in its first year. Around 22% of the study cohort that were booked to follow-up at the EP clinic did not attend. This could have an effect on the follow up data presented. A significant limitation of this study when compared to other registries is that it was done by a single centre and only one-year data is presented. Other South African centres, including private centres, should be encouraged to join the registry to transform this initiative into a representative national registry. This will allow for a more accurate representation of EP services in SA.

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TABLES

Table 1 : Success, complication, and mortality rates for Supraventricular tachycardia procedures

	Acute Success(%)	Complications (%)	Mortality (%)
Focal AT	85	1.4[a]	0.1
CTI dependant AFL	95	2[b]	0.2
AVNRT	97	0.3[c]	0.01
AVRT	92	1.5[d]	0.1

[a]Vascular complications, AV block and pericardial effusion
[b]Vascular complications, stroke, myocardial infarction, and pericardial effusion.
[c]Vascular complications, AV block and pericardial effusion
[d]Vascular complications, AV block, myocardial infarction, pulmonary thromboembolism, and pericardial effusion.
AT=atrial tachycardia; AVNRT=atrioventricular nodal re-entrant tachycardia; AVRT=atrioventricular re-entrant tachycardia; CTI = Cavotricuspid isthmus

Table 2 : Parameter tested, and statistical test used

Objective no.	Parameters to be analysed	Statistical test used
1	Population Demographics	Mean±SD
1	Disease Prevalence	Sum/Count
1	Subgroup Demographics	Mean±SD
4	Accessory pathway locations	Sum/Count
1	CVRF Prevalence	Sum/Count
1	Symptoms	Sum/Count
1	Cardioversions	Sum/Count
1	Medication prevalence per arrythmia subgroup	Sum/Count

2	Echocardiographic data	Mean±SD
2	AFL/SVT Echocardiographic comparison	Chi-square/Fisher exact test
1	AFL/SVT CVRF Prevalence comparison	Chi-square/Fisher exact test
6	Change in prevalence of cardioversion at EP clinic follow-up	Chi-square/Fisher exact test
6	Change in prevalence of cardiac symptoms at EP clinic follow-up	Chi-square/Fisher exact test

AFL= Atrial flutter; CVRF= Cardiovascular risk factor; EP= Electrophysiology; SVT=Supraventricular tachycardia

Table 3: Patient demographic summary according to arrhythmia subtype.

Patient Subset	**Male gender n (%)**	**Mean Age (mean±SD)**
Entire cohort	39 (53.4%)	49.5±14.4
Atrial flutter	19 (79.2%)	56.71± 8.2
Atrial fibrillation	2 (50.0%)	58.5±8.2
Supraventricular tachycardia	17 (42.5%)	45.75±15.0
Ventricular tachycardia	1 (20.0%)	38.2± 15.9

Table 4: Mean echocardiographic values for cardiac chambers

Echocardiographic	
LA diameter - Mean±SD	39±8.9
LA area -Mean±SD	22.7±9.0
RA area -Mean±SD	18.44 ±7.5
LVEDD -Mean±SD	52.40± 10.6
Dilated LA size (n)(%)	26 (45.6%)
Dilated RA size (n)(%)	24 (42.1%)
Normal LV size	42 (73.7%)
LVH (n)(%)	6 (10.5%)
Normal LV systolic function (n)(%)	37 (64.9%)
Normal Diastolic function (n)(%)	22 (38.6%)
Normal RV size	41 (71.9%)
Normal RV function	43 (75.4%)

LA= Left atrium; LV = Left ventricle; LVH=Left ventricle hypertrophy; LVEDD= Left ventricle end diastolic diameter; RA=Right atrium; RV =Right ventricle;

Table 5: Echocardiographic data per arrhythmia subtype

ECHO PARAMETER	ATRIAL FLUTTER	ATRIAL FIBRILLATION	SUPRAVENTRICULAR TACHYCARDIA	VENTRICULAR TACHYCARDIA	P-value
Dilated LA size (n)(%)	n=15 83.3%	n=4 100%	n= 10 32.3%	n=1 20.0%	<0.01*
LA Diameter (mm) mean±SD	46.0 ±8.2	41.8±10.8	35.4±7.4	34.8± 2.6	<0.01*
LA Area (mm) mean±SD	28.8 ±8.7	29.9 ±12.7	20.6 ±6	18.1 ±4.8	<0.01*
Dilated RA size (n)(%)	n= 14 77.8%	n=1 25.0%	n=9 29.0%	n=1 20.0%	<0.01*
RA Area (mm)	21.6 ±6.8	22.9 ±17.7	13.9 ±1.4	15.1 ±3.6	<0.01*
Normal LV size Mean ±SD	n=9 50.0%	Mean=2 50.0%	n=26 83.9%	n=5 100%	0.02
LVEDD (mm)	56.4 ±7.8	62.3 ±15.7	51.8 ±9.2	46.6 ±3	<0.01*
LVH (n)(%)	N=2 11.1%	N=1 25.0%	N=3 9.7%	N=0 0.0%	
Normal LV systolic function (n)(%)	n= 5 27.8%	n=2 50.0%	n=25 80.7%	n=5 100%	<0.01*
LVEF (%) Mean ±SD	48.6 ±9.4		50.5 ±6.5		<0.01*
Normal Diastolic function (n)(%)	n=2 11.1%	n=0 0.0%	n=14 45.2%	n=4 80.0%	<0.01*
Normal RV size(n)(%)	n=10 55.6%	n=3 75.0%	n=25 80.7%	n=4 80.0%	0.05*
Normal RV function(n)(%)	n=10 55.7	n=4 100%	n=25 83.3%	n=4 80.0%	<0.01*
ECHO NOT DONE	n=6	n=1	n=9	n=0	

*p-value AFL vs SVT comparison
LA= Left atrium; LV = Left ventricle; LVH=Left ventricle hypertrophy; LVEDD= Left ventricle end diastolic;LVEF=Left ventricle ejection fraction; diameter; RA=Right atrium; RV =Right ventricle;

Table 6: Accessory Pathway location

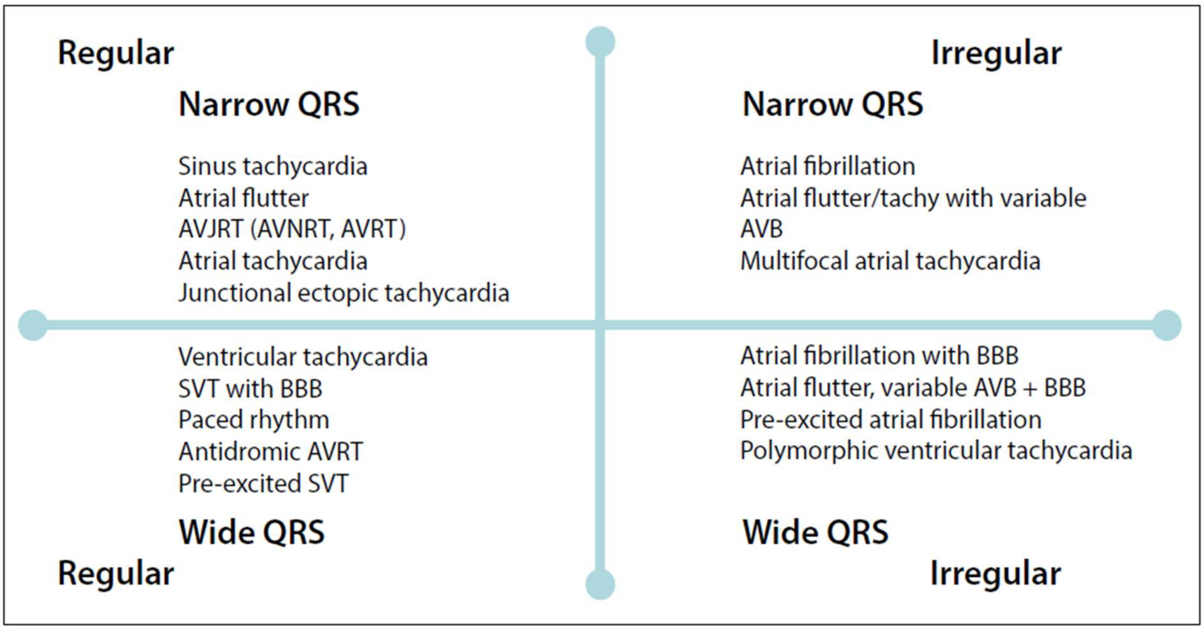
Accessory pathway location	**Total n=**
Right antero-septal	1
Right anterior	0
Right lateral	0
Right postero-lateral	0
Right posterior	0
Right postero-septal	4
Mid-septal	2
Coronary sinus	0
Left postero-septal	1
Left posterior	3
Left postero-lateral	1
Left lateral	2
Left antero-lateral	1

Table 7: Two way summary table showing difference in direct current cardioversion at follow up

Direct current cardioversion		
Initial presentation (n=73)	**Follow up (n=44)**	**P-value**
N=26	N=1	<0.01
%=35.6	%=2.3	<0.01

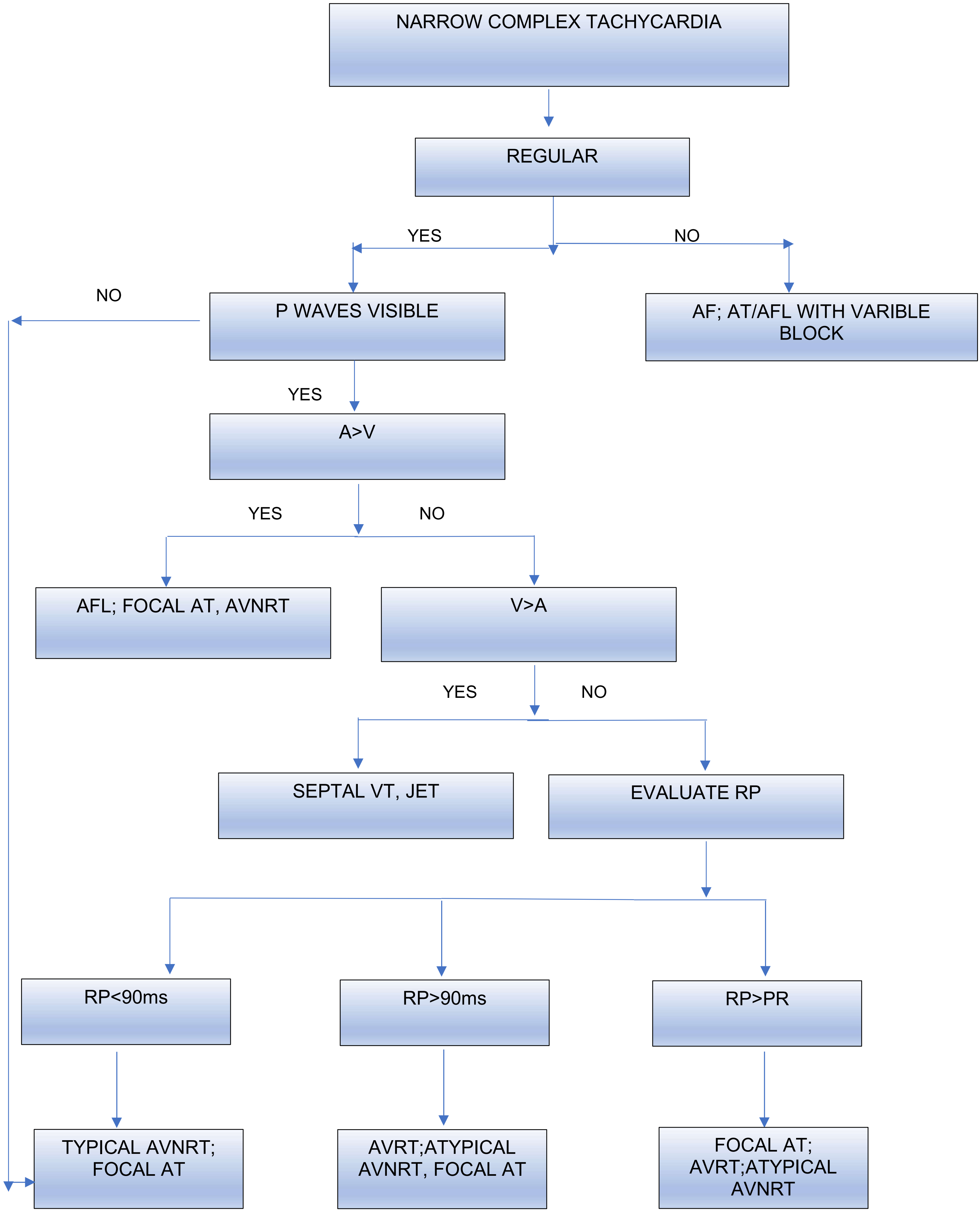
FIGURES

Figure 1 : Classification of tachyarrhythmias.



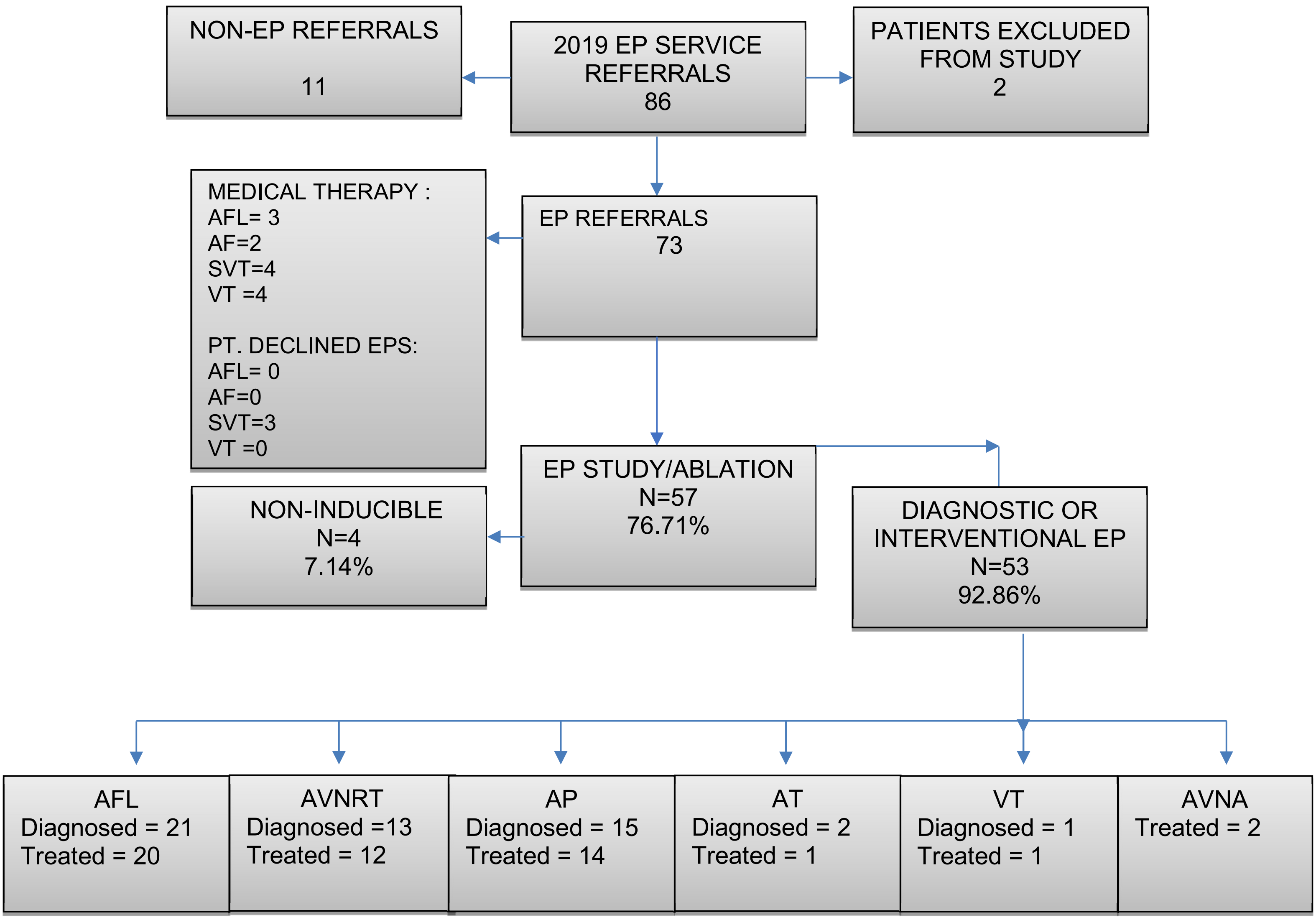
AVJRT = atrioventricular junctional re-entrant tachycardia; AVNRT = atrioventricular nodal re-entrant tachycardia; AVRT = atrioventricular re-entrant tachycardia; SVT = supraventricular tachycardia; BBB = bundle branch block; AVB = atrioventricular block

Figure 2: Pathway to diagnose Narrow complex tachycardias



AF = atrial fibrillation; AT = atrial tachycardia; AV = atrioventricular; AVNRT = atrioventricular nodal re-entrant tachycardia; AVRT = atrioventricular reentrant tachycardia; JET = junctional ectopic tachycardia; RP = RP interval; VT = ventricular tachycardia. Reproduced from Eur Heart J, Volume 41, Issue 5, 1 February 2020, Pages 655–720, https://doi.org/10.1093/eurheartj/ehz467

Figure 3: Flow chart of patients referred to the EP service.



AF = atrial fibrillation; AFL= atrial flutter; AT = atrial tachycardia; AV = atrioventricular; AVNRT = atrioventricular nodal re-entrant tachycardia; AP = accessory pathway; AVNA= Atrioventricular nodal ablation; VT= ventricular tachycardia; EP= Electrophysiology

Figure 4: Age distribution for the electrophysiology referrals.

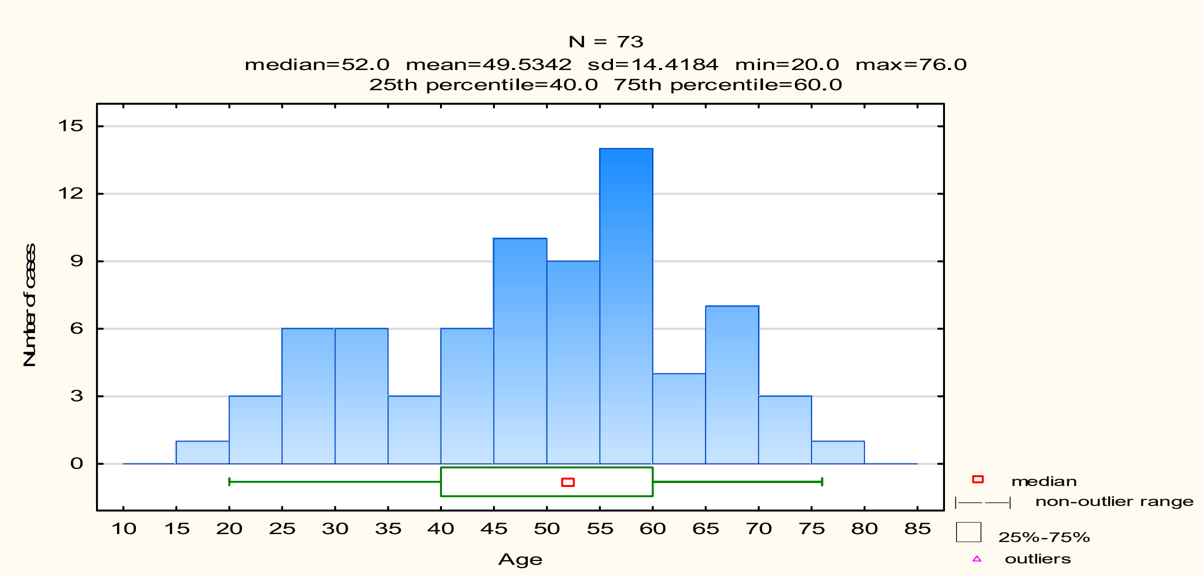
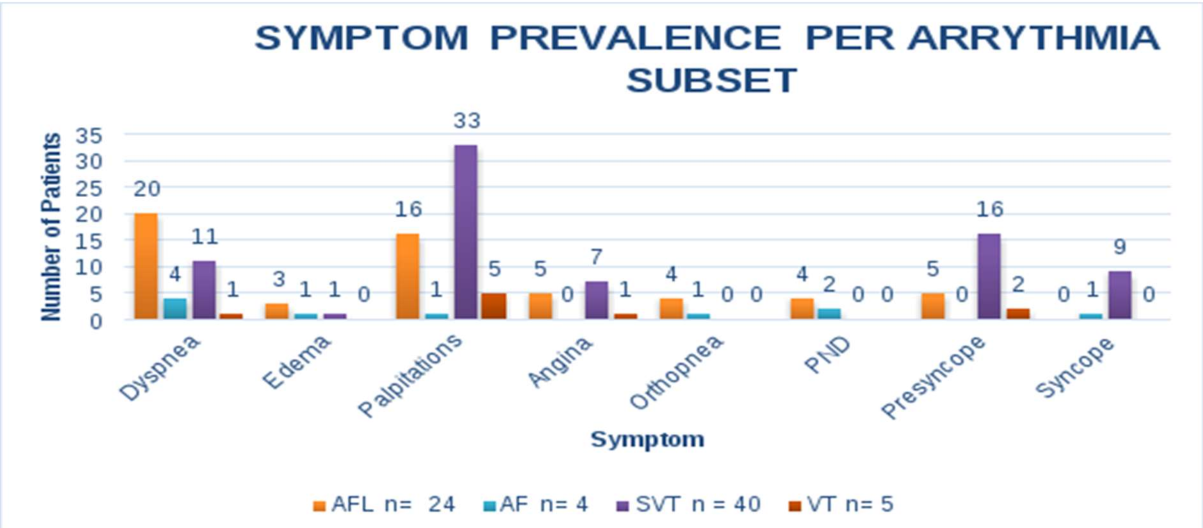
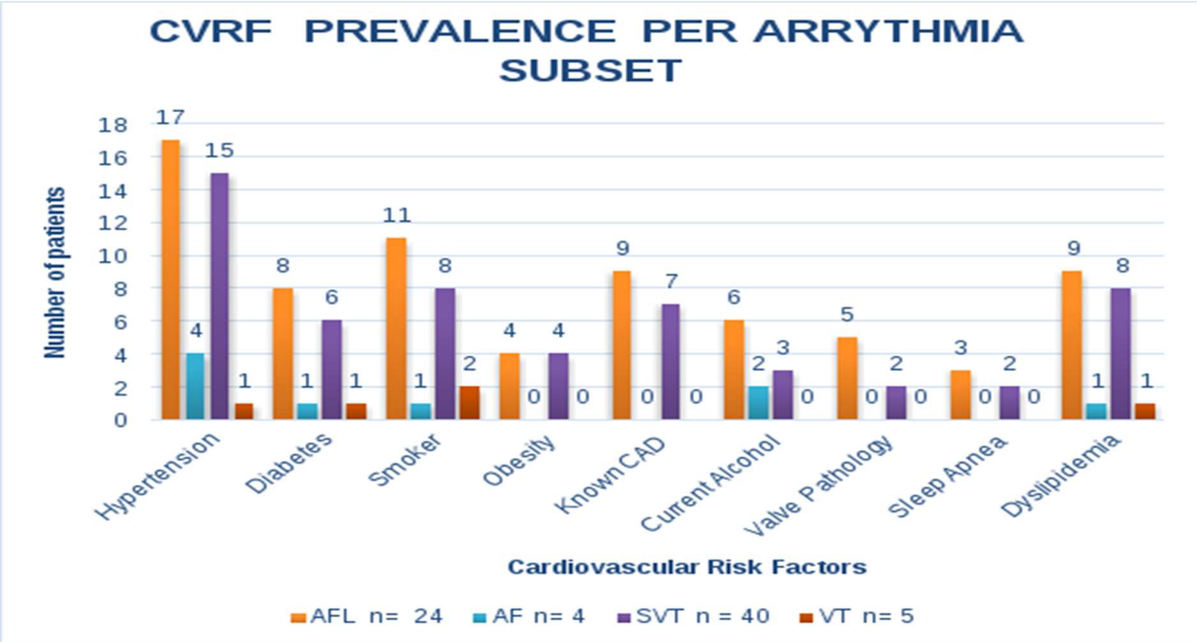


Figure 5: Symptom prevalence per arrhythmia subset



AFL= Atrial flutter; AF=Atrial fibrillation; SVT= Supraventricular tachycardia;VT=Ventricular tachycardia; PND= Paroxysmal nocturnal dyspnea

Figure 6: Cardiovascular risk factors prevalence per arrhythmia subset



AFL= Atrial flutter; AF=Atrial fibrillation; CAD=Coronary artery disease ;SVT= Supraventricular tachycardia;VT=Ventricular tachycardia;

Figure 7: Prevalence of cardiovascular risk factor according to gender

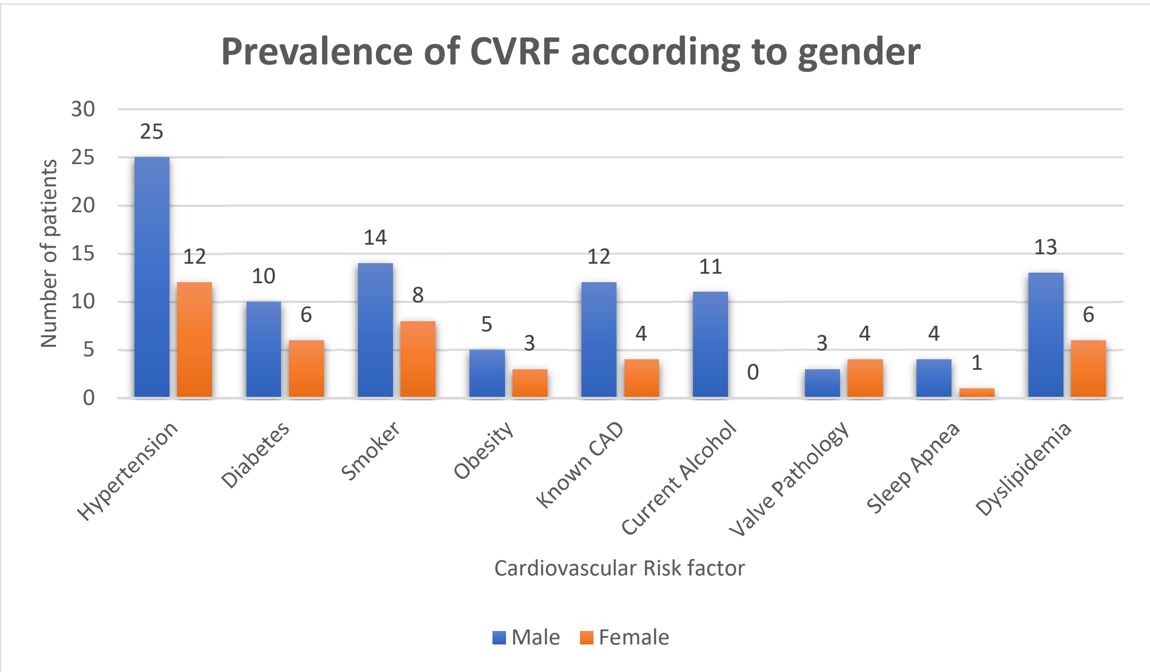
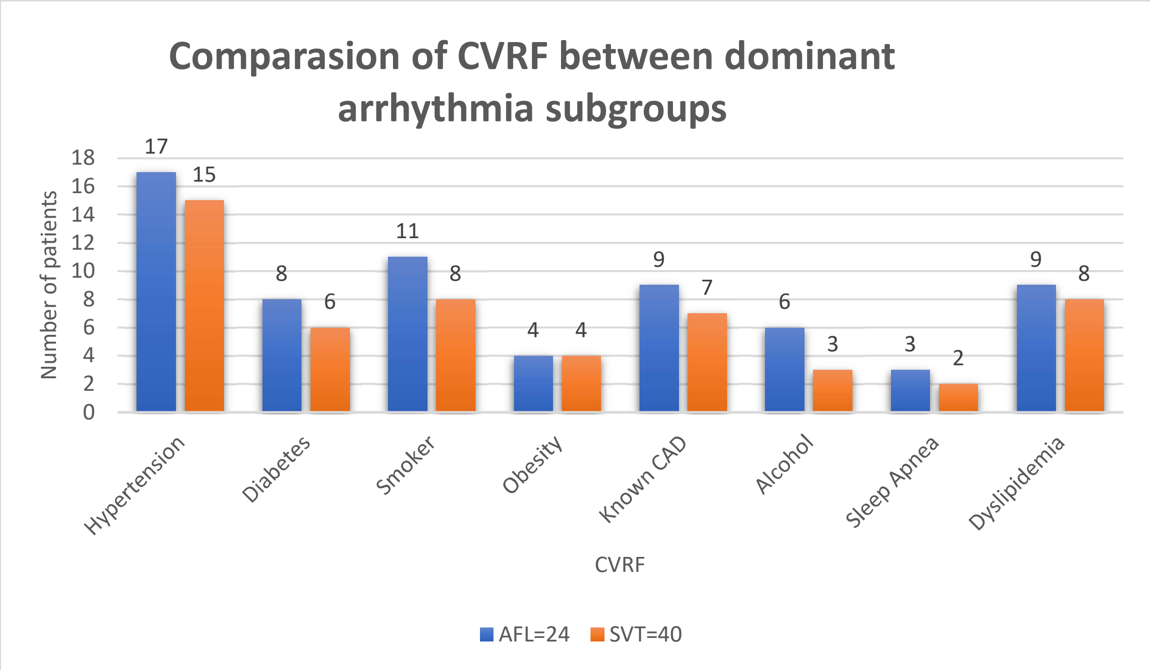


Figure 8: Comparison of cardiovascular risk factor between the dominant arrhythmia subgroups



AFL= Atrial flutter; CAD=Coronary artery disease; SVT= Supraventricular tachycardia

Figure 9: Disease prevalence per arrhythmia subtype

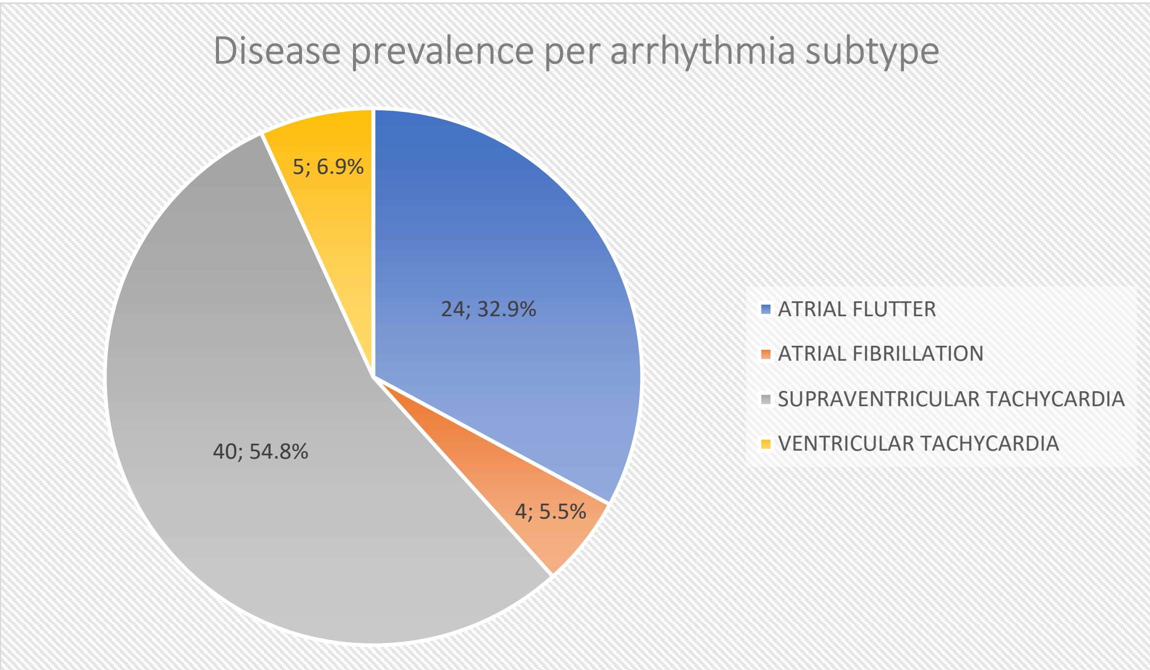
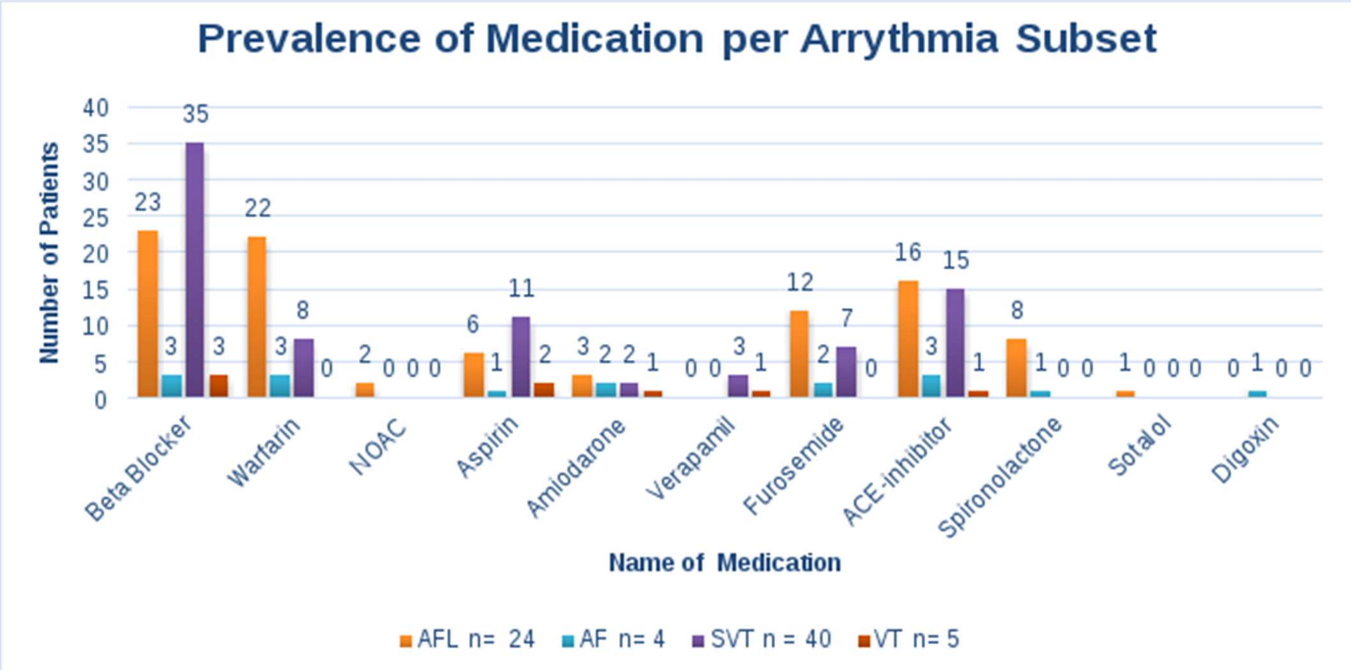
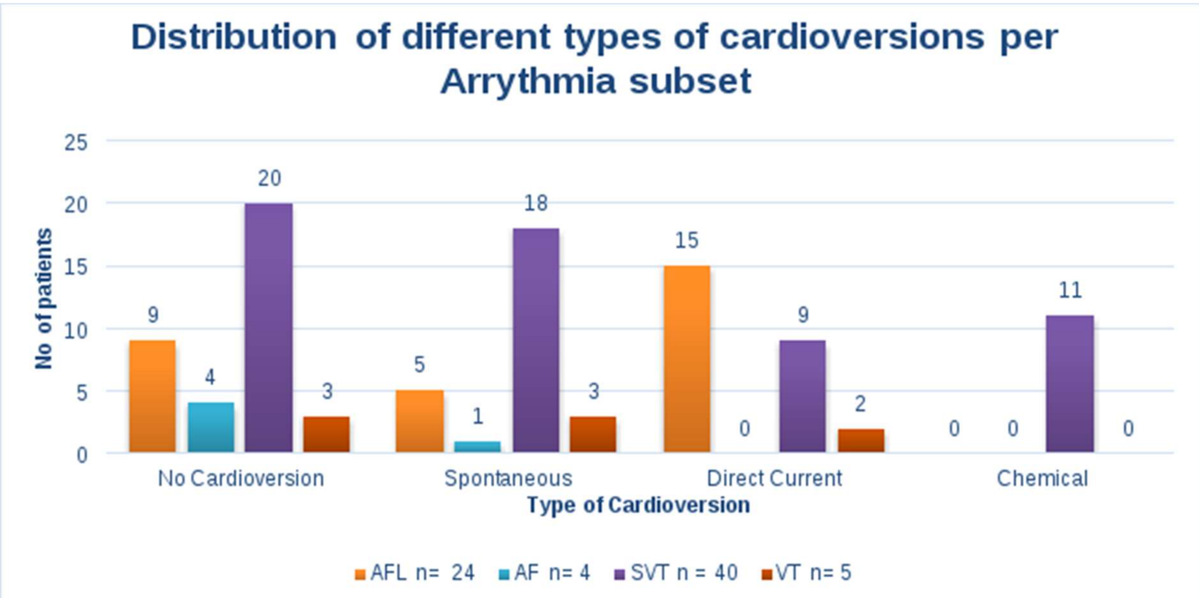


Figure 10: Prevalence of medication per arrhythmia subset



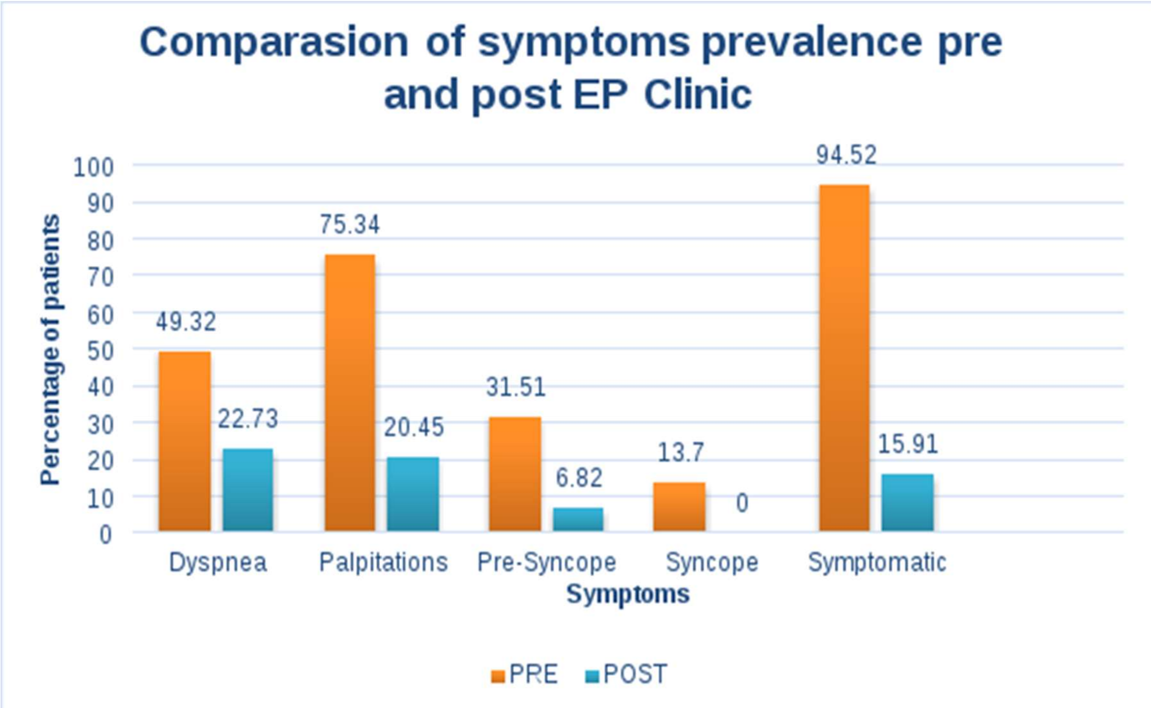
AFL= Atrial flutter; AF=Atrial fibrillation; NOAC= Novel oral anticoagulants; SVT= Supraventricular tachycardia;VT=Ventricular tachycardia

Figure 11: Distribution of different types of cardioversions per arrhythmia subset



AFL= Atrial flutter; AF=Atrial fibrillation; SVT= Supraventricular tachycardia;VT=Ventricular tachycardia

Figure 12: Comparison of symptom prevalence pre and post electrophysiology service



APPENDICIES

Appendix 1: Sample size collection letter from Statistician

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

2019-09-25

To whom it may concern.

SAMPLE SIZE DETERMINATION FOR STUDENT KUMESHIN MOODLEY

I hereby confirm that student Kumeshin Moodley, did consult with me regarding his research project, and that the sample size issue was discussed.

I am of the opinion that due to the dependence of recruiting patients from their registry, which is a fixed number, and due to the descriptive nature of the study, that no formal sample size calculation is necessary for this project.

MARTIN KIDD
Director: Centre for Statistical Consultation

Appendix 2: Case Report Form

CASE REPORT FORM

Age	Sex = Male	CVRFS	Hypertension	Diabetes	Smoker	Obesity	Known CAD	Current Alcohol	Valve Pathology
Sleep apnoea	Dyslipidemia	Heart Failure	Dyspnea	Edema	Palpitations	Angina	Orthopnea	PND	Pre-Syncope
Syncope	Fatigue	No Cardioversion	Spontaneous Cardioversion	Direct current cardioversion	Chemical cardioversion	AVR	MVR	Severe AS	Severe AR
Severe MS	Severe MR	Severe PS	Severe PR	Severe TR	Severe TS	No symptoms	B-blocker	Warfarin	NOAC
Aspirin	Amiodarone	Verapamil	Furosemide	ACE-inhibitor/ARB	Spironolactone	Sotalol	Digoxin	Previous stroke/TIA	CHA2DS2-VASc
Echocardiogram	Dilated LA size	LA diameter	LA area	Dilated RA size	RA area	Normal LV size	LVEDD	LVH	Normal LV systolic function
LVEF	Normal LV diastolic function	Normal RV size	Normal RV function	TAPSE	Refer for EP study	Medical therapy and F/U TBH	Medical therapy and F/U CHC	EP STUDY	

Kumeshin Moodley

Data collection case report form

Appendix 3: Durban University of Technology ethical clearance letter

Institutional Research Ethics Committee
Research and Postgraduate Support Directorate
2nd Floor, Berwyn Court
Gate 1, Steve Biko Campus
Durban University of Technology

P O Box 1334, Durban, South Africa, 4001

Tel: 031 373 2375
Email: lavishad@dut.ac.za
http://www.dut.ac.za/research/institutional_research_ethics

www.dut.ac.za

10 September 2020

Mr K Moodley
9 Gordon Road
Fairfield Estate
Parow
Cape Town

Dear Mr Moodley

The establishment of a bi-directional registry of patients presenting with cardiac arrhythmia at a tertiary academic hospital in South Africa

I am pleased to inform you that Approval has been granted to your proposal.

The Proposal has been allocated the following Ethical Clearance number **IREC 052/20**. Please use this number in all communication with this office.

Approval has been granted for a period of **ONE YEAR**, before the expiry of which you are required to apply for safety monitoring and annual recertification. Please use the Safety Monitoring and Annual Recertification Report form which can be found in the Standard Operating Procedures [SOP's] of the IREC. This form must be submitted to the IREC at least 3 months before the ethics approval for the study expires.

Any adverse events [serious or minor] which occur in connection with this study and/or which may alter its ethical consideration must be reported to the IREC according to the IREC SOP's.

Please note that any deviations from the approved proposal require the approval of the IREC as outlined in the IREC SOP's.

Please be advised that all relevant gatekeeper permission letters must be submitted to the IREC.

Yours Sincerely

Professor J K Adam
Chairperson: IREC

Appendix 4: Stellenbosch ethical clearance letter

UNIVERSITEIT
STELLENBOSCH
UNIVERSITY

Approval Notice

New Application

09/03/2021

Project ID :18602

HREC Reference No: S21/01/015

Project Title: Retrospective Electrophysiology Registry

Dear Mr. Kumeshin Moodley

The **New Application** received on 29/01/2021 was reviewed and **approved** by members of **Health Research Ethics Committee** via **expedited** review procedures on 09/03/2021.

Please note the following information about your approved research protocol:

Protocol Approval Date: 09 March 2021

Protocol Expiry Date: 08 March 2022

Please remember to use your Project ID 18602 and Ethics Reference Number S21/01/015 on any documents or correspondence with the HREC concerning your research protocol.

Please note that the HREC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

After Ethical Review

Translation of the informed consent document(s) to the language(s) applicable to your study participants should now be submitted to the HREC.

Please note you can submit your progress report through the online ethics application process, available at: Links Application Form Direct Link and the application should be submitted to the HREC before the year has expired. Please see *Forms and Instructions* on our HREC website (www.sun.ac.za/healthresearchethics) for guidance on how to submit a progress report.

The HREC will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit.

Please note that for studies involving the use of questionnaires, the final copy should be uploaded on Infonetica.

Provincial and City of Cape Town Approval

Please note that for research at a primary or secondary healthcare facility, permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Please consult the Western Cape Government website for access to the online Health Research Approval Process, see: https://www.westerncape.gov.za/general-publication/health-research-approval-process. Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.

For standard HREC forms and instructions, please visit: Forms and Instructions on our HREC website https://applyethics.sun.ac.za/ProjectView/Index/18602

If you have any questions or need further assistance, please contact the HREC office at 021 938 9677.

Yours sincerely,

Mrs. Melody Shana

Coordinator

Appendix 5: Gatekeeper permission from Tygerberg Hospital manager

Western Cape Government
Health

TYGERBERG HOSPITAL
REFERENCE:
Research Projects
ENQUIRIES: **Dr GG Marinus**
TELEPHONE:**021 938 5752**

Ethics Reference: IREC 052/20

TITLE: **The establishment of a bi-directional registry of patients presenting with cardiac arrhythmia at a tertiary academic hospital in South Africa.**

Dear Mr Moodley

PERMISSION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL.

1. In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009, permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg Hospital.

2. Researchers, in accessing Provincial health facilities, are expressing consent to provide the Department with an electronic copy of the final feedback within six months of completion of research. This can be submitted to the Provincial Research Co-Ordinator (Health.Research@westerncape.gov.za).

DR GG MARINUS
MANAGER: MEDICAL SERVICES

Date: 2/9/2020

Administration Building, Francie van Zijl Avenue, Parow, 7500 Private Bag X3, Tygerberg, 7505
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