RIGHT AND LEFT ATRIAL DIMENSIONS WITH 3 TESLA CARDIAC MAGNETIC RESONANCE IMAGING IN HEALTHY ADULT: HUSM EXPERIENCE

DR ZUBAIDAH MOHAMAD

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

AF	Atrial fibrillation Left Atrium
BMI	Body Mass Index
BSA	Body Surface Area
ch	Chamber
CMR	Cardiac Magnetic Resonance
CT	Computed Tomography
DM	Diabetes Mellitus
HPT	Hypertension
HUSM	Hospital Universiti Sains Malaysia
IVC	Inferior vena cava
LA	Left Atrium
LAV	Left Atrial Volume
LV	Left Ventricle
MRI	Magnetic Resonance Imaging
PACS	Picture Archiving and Communication System
RA	Right Atrium
RIS	Radiology Information System

RV	Right Ventricle
SD	Standard deviation
SNR	signal-to-noise ratio
SVC	Superior vena cava
SSFP	steady state free precession
1.5T	1.5 Tesla
2D	2 Dimensional
3D	3 Dimensional
3T	3 Tesla

ABSTRAK

Latar belakang: Resonans magnetik jantung (CMR) telah digunakan secara meluas kebelakangan ini. Pangkalan data mengenai dimensi jantung normal telah dibuat sebelum ini menggunakan pengimbas resonans magnetik 1.5 Tesla. Data mengenai gambaran klinikal, pengukuran dan isipadu jantung kanan adalah terhad. Nilai rujukan atrium normal yang tepat sangat penting dalam amalan dan penyelidikan klinikal. Tujuan kajian ini adalah untuk menilai dimensi atrium pada populasi yang sihat yang menjalani CMR 3 Tesla di HUSM.

Metod: Kajian kohort retrospektif dilakukan di Hospital Universiti Sains Malaysia (HUSM), Kota Bharu, Malaysia melibatkan 57 individu berusia 18 tahun hingga 60 tahun yang terdiri daripada bangsa Melayu, Cina dan India menggunakan resonans magnetik jantung (CMR) 3 Tesla antara Mei 2020 hingga November 2020. Sebanyak 29 orang peserta lelaki dan 28 orang peserta perempuan terlibat dalam kajian ini. Dua orang pemerhati terlibat secara langsung dalam proses analisa data. Dimensi atrium diukur dalam satah jantung yang berbeza pandangan (2 ruang (2ch), 3 ruang (3ch) dan 4 ruang (4ch)). Luas maksimum, diameter melintang dan membujur diukur. Korelasi dimensi atrium dan umur dianalisa menggunakan kaedah korelasi Pearson.

Keputusan: Untuk keluasan atrium kiri, had normal atas adalah 24.3 cm^2 (17.3 cm^2/m^2) pada pandangan 4ch, dan 24.7 cm^2 (15.4 cm^2/m^2) pada pandangan 2ch dan 21.8 cm^2 (11.5 cm^2/m^2) pada pandangan 3ch. Had atas atau normal bagi diameter dalam pandangan 4ch dan 2ch adalah membujur sebanyak 5.9 cm (4.0 cm/m^2) dan 5.5 cm

(3.7 cm/m^2), melintang sebanyak 5.1 cm (3.2 cm/m^2) dan 5.5 cm (3.5 cm/m^2), dan diameter melintang sebanyak 4.0 cm (2.3 cm/m^2) dalam pandangan 3ch.

Untuk keluasan atrium kanan, had atas normal adalah 25.5 cm^2 (15.5 cm^2/m^2) pada paparan 4ch. Had atas atau normal bagi diameter dalam 4ch masing-masing ialah sebanyak 5.8 cm membujur (3.5 cm/m^2) dan 5.7 cm melintang (4.4 cm/m^2).

Terdapat hubungan yang signifikan antara diameter membujur atrium kiri untuk 4ch, luas maksimum dan diameter membujur atrium kiri untuk 2ch, dan diameter melintang atrium kiri untuk 3ch dengan umur.

Kesimpulan: Kami telah menyumbang dalam menyediakan pangkalan data tempatan untuk dimensi atrium kanan dan atrium kiri menggunakan Pengimejan Resonans Magnetik (MRI) 3 Tesla.

Kata kunci: Dimensi atrial; Resonans magnetik jantung (CMR), Pengimejan Resonans Magnetik (MRI).

ABSTRACT

Background: Cardiac magnetic resonance (CMR) has been widely used recently. The database on normal cardiac dimensions has long been established using 1.5 Tesla magnetic resonance scanner. Data on clinical and prognostic features of measurement and volume of atria are limited especially of the right atrium. Accurate normal atrial reference values are very important in clinical practice and research. The purpose of this study was to assess the dimensions of the atrium in healthy populations undergoing 3 Tesla CMR at HUSM.

Methodology: A retrospective cohort study was conducted in Hospital Universiti Sains Malaysia (HUSM), Kota Bharu, Malaysia on 57 healthy subjects aged 18 till 60 years old involving Malay, Chinese and Indian populations with 3 Tesla Cardiac magnetic resonance (CMR) between May 2020 and November 2020. Total of 29 males and 28 females were involved in this study. Two observers were responsible for the data analysis. Atrial dimensions were measured in different cardiac planes (2 chamber; 2ch, 3 chamber; 3ch, and 4 chamber; 4ch views) using a steady-state free precession sequence. Maximum area, transverse, and longitudinal diameters were evaluated. Correlation of atrial dimensions and age were analysed using Pearson's correlation method.

Results: For left atrial, the upper limits of area were 24.3 cm^2 (17.3 cm^2/m^2) in the 4ch view, and 24.7 cm^2 (15.4 cm^2/m^2) in the 2ch view and 21.8 cm^2 (11.5 cm^2/m^2) in the 3ch view. The upper limits for diameters in the 4ch and 2ch views were longitudinal 5.9 cm (4.0 cm/m^2) and 5.5 cm (3.7 cm/m^2), transverse 5.1 cm (3.2

cm/m^2) and 5.5 cm (3.5 cm/m^2) cm respectively, and an anteroposterior diameter of 4.0 cm (2.3 cm/m^2) in the 3ch view.

For right atrial, the upper limits of area were 25.5 cm^2 (15.5 cm2/m^2) in the 4ch view. The upper limits for diameters in 4ch was longitudinal 5.8 cm (3.5 cm/m^2) and transverse 5.7 cm (4.4 cm/m^2) respectively.

There was a significant linear correlation between LA longitudinal diameter for 4ch with age, maximum area for 2ch and LA longitudinal diameter for 2ch with age, and LA transverse diameter for 3ch with age.

Conclusion: We have helped to provide a local database for the right atrium and left atrium dimensions in accordance with age using 3T Magnetic Resonance Imaging (MRI).

Keywords: *Atrial dimensions, Magnetic Resonance Imaging (MRI), Cardiac magnetic resonance (CMR)*

CHAPTER 1: BACKGROUND

1.1 Introduction

The cardiovascular system consists of the heart, arteries, capillaries, and veins and may be further divided into two subsystems of circulation which are the pulmonary circulation that transports blood between the heart and lungs for exchange of blood gases, and the systemic circulation that transports blood between the heart and the rest of the body.

Heart acts as a pump to propel the blood throughout the body via the circulatory vessels. It is divided into two upper chambers, termed the right and left atria, and two lower chambers, called the right and left ventricles.

Normal left atrial (LA) contraction plays an important role in maintaining left ventricular (LV) end diastolic pressure, preserving LA pressure and normal blood flow through the cardiac chambers. Abnormalities in LV volume can cause changes in LA volume, function, and diameter. Knowledge of these changes relative to normal reference values is extremely important in the care of patients with atrial fibrillation (AF), and the changes may serve as biomarkers of cardiac and cerebrovascular events (Stojanovska *et al*., 2011). LA size is also related to cardiovascular morbidity and mortality.

Right atrial (RA) enlargement may occur in numerous conditions including congenital heart disease, acquired valvular heart disease, pulmonary disorder and heart failure. Recent data have shown that both RA and LA remodelling are equally associated with recurrence of AF after cardioversion. Other than that, RA size also act as an early marker of right ventricular (RV) dysfunction. It may provide significant prognostic information in patients with chronic systolic heart failure and pulmonary hypertension.

Many studies have produced database on the ventricular dimension, but fewer on atrial dimension. The LA and RA are not only reservoirs, but also have active emptying functions that contribute 15–30% of ventricular filling. LA impairment increases with age and in diseases such as hypertension, heart failure, atrial fibrillation, hypertrophic cardiomyopathy, and amyloidosis. In addition, LA enlargement and LA functional changes are associated with cardiovascular mortality or worse prognosis in patients with atrial fibrillation, non-ischemic dilated cardiomyopathy, hypertrophic cardiomyopathy, and in the general population with different cardiovascular risks.

Compared with the LA, the RA is less studied, although RA function is related to the severity and prognosis of pulmonary hypertension and congenital heart disease.

Complete evaluation of the heart often requires a multimodality approach that includes radiography, echocardiography, computed tomography (CT), magnetic resonance imaging (MRI), and invasive angiography (Malik *et al*., 2015).

Cardiac MRI (CMR) is a highly accurate, non-ionising method for the assessment of cardiac disease. It is especially suited for the assessment of cardiac function and morphology. It is the gold standard for morphological assessment of the heart, as well as the assessment of the right and left ventricular systolic and diastolic function and mass. Its high spatial and temporal resolutions allow accurate assessment of the morphology and function of both the atria and ventricles in healthy subjects as well as in patients with various structural heart diseases (Kuchynka *et al*., 2015).

Traditionally, two-dimensional (2D) echocardiography has been used to evaluate LA dimension and size, and the newer three-dimensional (3D) echocardiography has improved the accuracy of measurement of the atrial volume. CMR has advantages in the evaluation of atrial size and phasic function compared with echocardiography and cardiac CT. CMR can provide accurate measurements of dimension, volume, and structure of the atria, with high temporal and spatial resolution. The measurements are reproducible. CMR is the gold standard to evaluate ventricular volumes and should also be the standard for atrial volume and function assessment. Accurate normal atrial reference values are crucial in clinical practice and research. CMR provides high quality images of the atrium with high temporal resolution steady state free precession (SSFP) cine sequences (Maceira *et al*., 2010). Based on the previous study on cardiac dimensions, CMR is the best imaging modality for cardiovascular evaluation.

The normal reference values for atrial size and volume have been investigated at 1.5 Tesla (1.5T) in past years in a population of European descent. Recently, a study in China reported reference values for the left atrium volume, total left atrial ejection fraction, and right atrium area index measured by CMR at 3.0 Tesla (3T) (Li *et al.*, 2017). Buechel (2009) and Maceira (2010) have produced a database on the normal left atrial dimensions. A study by O'Neill (2018) demonstrates that South Asians have smaller LA volumes (LAV) compared with Caucasians. Maceira (2013) again published normal right atrial reference values derived from subjects of European descent. A study by Li (2017) produced reference value on both atrial size and phasic function among healthy Chinese adult.

Problem Statement

This study was conducted to evaluate the right and left atrial dimensions in healthy adult using the 3T CMR. CMR was chosen to measure the dimensions since this is the gold standard for this assessment. Many studies have produced databases on the ventricular dimension, but fewer on atrial dimension, particularly the RA is less studied compared with the LA. Most of the previous studies were based on the 1.5T MRI scanners, largely due to the availability of the machines compared with the 3T scanners. The earlier generation of 3T scanners also produced more susceptibility artefacts compared with 1.5T which made it less desirable for cardiac imaging. However, this issue has been addressed in the later scanner generation and was proven to produce equally good quality cardiac images, sometimes in a shorter period compared with the 1.5T. The 3T systems have demonstrated advantages over the 1.5T system on a broad range of clinical applications. The primary advantage of 3T over 1.5T is a higher signal-to-noise ratio (SNR), which can be used as such or traded off to improve spatial or temporal resolution and decrease acquisition time (Rajiah *et al.*, 2014). This system now is widely available and are being increasingly used in clinical practice. SSFP at 3T has further increased SNR for myocardium and blood, as well as myocardium-to-blood contrast-to-noise ratio. However, there are substantial challenges with 3-T cardiac MR imaging, including higher magnetic field and radiofrequency inhomogeneities and susceptibility effects, which diminish image quality. These artifacts can be managed by using higher-order shimming, frequency scouts, or low repetition times. B_1 inhomogeneities can be managed by using radiofrequency shimming, multitransmit coils, or adiabatic pulses.

Over the last couple of years, there has been a significant increase in the number of 3T MRI installations in the country.

This study is also conducted because the previous study showed there is a difference between the normal atrial reference values of different population. Previous study proved that South Asians have smaller LA volumes compared with Caucasians. Studies on cardiac dimensions are important since it provides reference values for clinicians which facilitate the management of their patients.

1.2 Objectives

1.2.1 General Objective

To evaluate the right and left atrial dimensions (area and diameters) in healthy adult with 3 Tesla cardiac magnetic resonance imaging.

1.2.2 Specific Objectives

1. To determine the atrial dimensions of right and left atria in healthy adult.
2. To determine the correlation between right atrial dimensions with age in healthy adult.
3. To determine the correlation between left atrial dimensions with age in healthy adult.

1.3 Research Question and Hypothesis

Specific objective 1: Are the right and left atrial dimensions of our local population similar to the previously reported dimensions among Asian population?

Alternative Hypothesis: The right and left atrial dimensions of our local population are similar to the previously reported dimensions among Asian population.

Specific objective 2: Is there any correlation between right atrial dimensions with age?

Alternative Hypothesis: There is correlation between right atrial dimensions with age.

Specific objective 3: Is there any correlation between left atrial dimensions with age?

Alternative Hypothesis: There is correlation between left atrial dimensions with age.

CHAPTER 2: LITERATURE REVIEW

2.1 Cardiovascular anatomy and function

Heart acts as a pump to propel the blood throughout the body via the circulatory vessels. It is divided into two upper chambers, termed the right and left atria, and two lower chambers, called the right and left ventricles.

In the normal heart, the RA receives deoxygenated blood from the body via the superior and inferior venae cava. The deoxygenated blood passes through the right atrioventricular or tricuspid valve into the RV. The RV contracts during systole and propels blood to the lungs through the pulmonary valve and pulmonary trunk, which bifurcates into the right and left main pulmonary arteries, respectively. Approximately 60% of deoxygenated blood enters the right lung, and approximately 40% enters the left lung.

The exchange of gases occurs at the capillary–alveolar level within the lungs, and the oxygenated blood is returned to the LA via the four pulmonary veins. Oxygenated blood flows from the LA to the LV via the left atrioventricular valve or mitral valve. The LV is responsible for pumping oxygenated blood throughout the systemic circulatory system. Oxygenated blood flows through the aortic valve into the aorta when the LV contracts.

A cardiac cycle consists of systolic (contraction) and diastolic (relaxation and filling) phases that are linked closely together for optimal function of the heart. Normal diastolic function allows adequate filling of the heart without an excessive increase in diastolic filling pressure both in the resting state and with stress or exertion. The diastolic phase is remarkably well designed to ensure that the ventricle is optimally filled for a given clinical condition. Basically, at the end of systole, LV relaxation begins as an initial diastolic process, and LV pressure falls rapidly as the LV expands. This relaxation phase is accompanied by active movement of the mitral annulus away from the apex. The velocity of LV dilatation and mitral annular movement during early diastole correlates well with how fast the LV fills and relaxes, respectively. Myocardial relaxation continues during early diastole to reach the minimal LV diastolic pressure.

Diastolic heart failure, a major cause of morbidity and mortality, is defined as symptoms of heart failure in a patient with reduced LV diastolic function. Diastolic dysfunction occurs when the left ventricular myocardium is non-compliant and not able to accept blood return in a normal fashion from the left atrium. This can be a normal physiologic change with aging of the heart. However, it can result in elevated left atrial pressures leading to the clinical manifestations of diastolic congestive heart failure.

2.2 Atrial pathology

RA pathologic findings can be broadly categorized into *(a)* congenital anomalies (cor triatriatum dexter, Ebstein anomaly, and aneurysm), *(b)* disorders of volume (tricuspid regurgitation, pathologic mimics such as a pseudoaneurysm, and atrial septal defect), *(c)* disorders of pressure (tricuspid stenosis, restrictive cardiomyopathy, and constrictive pericarditis), and *(d)* masses (pseudo masses, thrombus, lipomatous hypertrophy of the interatrial septum, lipoma, myxoma, sarcoma, and metastatic disease) (Malik *et al*., 2015).

RA enlargement may occur in numerous conditions including congenital heart disease, acquired valvular heart disease, pulmonary disorder, and heart failure. Recent data have shown that both RA and LA remodelling are equally associated with recurrence of AF after cardioversion. Other than that, RA size also act as an early marker of RV dysfunction. It may provide significant prognostic information in patients with chronic systolic heart failure and pulmonary hypertension.

LA size is related to cardiovascular morbidity and mortality. LA size increases for several reasons: (1) pressure overload caused by LV filling pressures or mitral stenosis; (2) volume overloads associated with mitral regurgitation or high cardiac output; or (3) AF. Dilatation of the LA has been repeatedly shown to be a strong marker of adverse cardiovascular outcomes (Kuchynka *et al*., 2015). LA size represents the integration of LV diastolic performance over time and is considered a reliable indicator of the duration and severity of diastolic dysfunction (Simek *et al*., 1995), regardless of whatever loading conditions are present at the time of the examination. It provides significant prognostic information both in the general population and in patients with heart disease including heart failure, acute myocardial infarction, cardiomyopathy, and mitral regurgitation. LA enlargement is commonly found in hypertensive heart disease and it is a risk factor for atrial fibrillation and stroke.

2.3 Imaging modality

Complete evaluation of the heart often requires a multimodality approach that includes radiography, echocardiography, CT, MRI, and invasive angiography.

Chest radiograph is the first line imaging for any patient presented with cardiac symptom. Although this imaging modality can offer only limited information about the anatomic structure and pathologic characteristics of the atria, it may provide the first clue to atria pathologic involvement. Nonspecific signs of pathologic involvement can be seen at radiography, such as atria enlargement, cardiomegaly, pulmonary vein engorgement or rarely, a calcified mass.

For assessment of atrial sizes, various echocardiographic techniques are available, including transthoracic, transoesophageal and intracardiac echocardiography. Transthoracic echocardiography is most used in daily clinical practice to assess atrial size. Some technical limitations in this study including limited echo window, spatial and temporal resolutions. For this reason, CMR is considered the most accurate technique for the non-invasive assessment because of the high spatial resolution and the excellent atrial border detection.

CT is an excellent tool for anatomic evaluation of the atria, especially when performed by using electrocardiographic gating. The advantages of CT include excellent spatial resolution, a fast single–breath-hold examination, and widespread availability. Disadvantages include exposure to ionising radiation, risk for contrast agent–induced nephropathy, and lower temporal resolution compared with MRI and echocardiography (Malik *et al*., 2015).

CMR is the gold standard for morphological assessment of the heart, as well as the assessment of the RV and LV systolic and diastolic function and mass. Its high spatial and temporal resolution allows accurate assessment of the morphology and function of both the atria and ventricles in healthy subjects as well as in patients with various structural heart diseases (Kuchynka *et al*., 2015). The advantages of CMR imaging include the absence of ionizing radiation, better temporal resolution than that provided with CT, the ability to obtain structural and functional information in a single study, and the absence of risk for contrast agent–induced nephropathy.

The excellent accuracy and reproducibility of CMR is well established, making it a gold standard technique for measurement of ventricular dimensions and function, for which reference ranges have been established from the SSFP technique (Maceira *et al*., 2006). SSFP yields excellent blood-endocardium and epicardium-fat contrast, higher acquisition speed, and the ability to greatly improve the temporal resolution of the cines without loss of image quality (Moon *et al*., 2002). However, atrial dimensions have not been extensively studied with CMR, and there is limited data on the influences of age, gender and body surface area (BSA) on atrial dimensions. Therefore, the aim of this study was to establish SSFP based reference values in normal subjects for atrial dimensions normalized, when necessary, for independent influences such as gender, body surface area and age.

The disadvantages of MRI include a generally lower spatial resolution than that provided with CT, the difficulty of imaging patients with claustrophobia, a longer study time than occurs with CT, and the risk for nephrogenic systemic fibrosis in patients with renal failure. Many international studies have been able to produce database on cardiac dimensions in relation to age, gender and risk factors using 1.5T. Most of the previous studies were based on the 1.5T scanners, largely due to the availability of the machines compared with the 3T scanners. 3T scanner using 2D cine SSFP technique have been able to provide high signal-to-noise and contrast-to-noise ratios, thus better image quality compared with the 1.5T machines (Gutberlet *et al.*, 2005).

2.4 Factors affecting atrial dimension

Many studies had produced databases on the ventricular dimension, but few on atrial dimension. Data on the clinical and prognostic characteristics of right atrial size and volume are limited. Compared with the LA, the RA is less studied, although RA function is related to the severity and prognosis of pulmonary hypertension and congenital heart disease. Measurement of RA volume is not routinely performed clinically although its prognostic value has been shown in several conditions as mentioned before.

Many factors affect the atrial dimensions such age, gender, BSA and others. Study by Maceira (2010) stated that BSA was shown to have a significant independent influence on left atrial volume and most diameters. Subsequent study by Maceira (2013) demonstrated a significant independent influence of BSA on most RA parameters. The age-related changes in atrial size and function were inconsistent with previous reports. Study by Sievers (2005), showed that LAV did not correlate with age in healthy volunteers. Maceira (2010) also did not find an association between the LAV with age, and age was not an independent indicator for the LAV. However, the LA transverse and longitudinal dimensions were related with age. Meanwhile, another study in a large European population, including a younger age range, demonstrated a significant correlation between age and LAV (Le Ven *et al*., 2015). The differences among these studies might be caused by a bias in population selection, inconsistent analysis and limited sample size with different age groups. Sievers (2005), proved that age is not an independent predictor of left atrial maximal volume nor diameter in normal individuals. However, in study by Li (2017), age was mild to moderately correlated with the size of the RA and LA.

Men have a larger maximal left atrial volume compared to women (Hudsmith *et al*., 2005 and Maceira *et al*., 2010). All absolute right atrial volumes, diameters and areas were significantly large in male except transverse diameter in 2-chamber view (Maceira *et al*., 2013). Similarly, Sievers (2005) observed higher diameters in the 2 and 4-chamber views in males with no differences in the anteroposterior diameter. Anderson (2005) measured maximal RA area and depth in end-systole in the 4-chamber view and obtained an upper limit of normality of 23.5 cm^2 for area and 55.6 mm for depth, with no significant differences between men and women. There was no influence of age on atrial parameters and no influence of gender on atrial volumes (Sievers *et al*., 2007). This study proved that there was a significant decrease in absolute and normalized areas and transverse diameters, measured in the 2-chamber in males ($p < 0.001$), and in absolute and normalized areas in the 2-chamber view and normalized diameter in the 4-chamber view in females. All absolute right atrial volume, diameters and area were significantly larger in males, except transverse diameter in the 2-chamber view.

Maceira (2006) have produced a database on the right and left ventricular dimensions in relation to age and gender of normal healthy adults using SSFP technique. Hudsmith (2005) have added the normal left atrial dimensions to their study. A study by Buechel (2009) managed to obtain right and left ventricular parameters in normal children. Maceira (2013) again produced reference value for right atrial dimensions and volumes by SSFP CMR in 2013 of European descent.

A study by O’Neill (2018) demonstrates that South Asians have smaller LA volumes compared with Caucasians. South Asians also have reduced LV end diastolic volume and smaller LV mass indicating that the South Asian heart is proportionally smaller to the Caucasian heart and this is likely to be due to genetic factors. Reduced LA volume may confer a degree of protection against the development of re-entrant circuits and fibrosis within the atria and may explain why South Asians have a reduced prevalence of atrial fibrillation. Li (2017) produced reference value on both atrial size and phasic function among healthy Chinese adult.

We conducted this study to evaluate the atrial dimension in healthy population that undergo 3T CMR in HUSM.

2.5 Rationale of the Study

This study is conducted to evaluate the right and left atrial dimensions in healthy adult using the 3T cardiac magnetic resonance imaging (CMR). CMR is chosen to measure the dimensions since this is the gold standard for this assessment. Many studies had produced databases on the ventricular dimension, but fewer on atrial dimension, the RA is less studied compared with the LA. Most of the previous studies were based on the 1.5T MR scanners, largely due to the availability of the machines compared with the 3T scanners. Therefore, this study is conducted to ascertain the right and left atrial dimensions in healthy adult using the 3T scanner. 3T scanner can complete the examination in short period of time and provide excellent quality images compared to 1.5T. The 3T systems have demonstrated advantages over the 1.5T system in a broad range of clinical applications. This system now is widely available and are being increasingly used in clinical practice. Over the last couple of years, there has been significant increase in the number of 3T installations in the country.

This study is also conducted because the previous study showed there is difference between the normal atrial reference values of different population. Previous study proved that South Asians have smaller LA volumes compared with Caucasians. Studies on cardiac dimensions are important since it provide reference values for the clinicians which facilitate the management of their patients.

CHAPTER 3: METHODOLOGY

3.1 Study Design

This was a retrospective cohort study

3.2 Study Location and Duration

This study was conducted in Hospital University Sains Malaysia (USM), Kota Bharu for a period of 6 months from May 2020 to November 2020.

3.3 Study Population and Sample

i. Reference population – Healthy adult in Kelantan.
ii. Source population – Healthy adult underwent cardiac MRI in HUSM, based on data recorded in RIS and PACS between July 2014 and July 2015.
iii. Target population – Healthy adult underwent cardiac MRI in HUSM.

3.4 Sampling Technique

Convenience sampling method was applied. All eligible patients that fulfilled the inclusion criteria were enrolled in the study.

3.5 Inclusion Criteria

1. Subjects above the age of 18 years and above.

2. Subjects with no clinical evidences of cardiovascular or cerebrovascular diseases (cardiac history, hypertension, hyperlipidaemia, diabetes mellitus, smoking, > obese class I; normal baseline ECG).

3. Blood profiles (fasting glucose and lipids) obtained within 1 month before CMR.

3.6 Exclusion Criteria

1. Images of non-diagnostic quality.

2. Images with incidental findings of congenital heart defect, cardiac mass, or significant lung disease.

3.7 Sample Size Calculation

Objective 1

For objective 1, which is to determine the right and left atrial dimensions (area and diameter) in healthy adult, sample size was calculated using single mean estimation (Arifin, 2020), which was shown in table 1 and table 2.

Table 1: Sample size calculation for objective 1 – LA

Variable	SD	precision	Sample size, n	Adjusted sample size, n + 10%	Reference
Max area – 4ch (cm^2)	3.7	1	53	59	Maceira et al. (2010)
Max area/BSA – 4ch (cm2/m^2)	1.8	0.5	50	56	
Longitudinal diameter – 4ch (cm)	0.7	0.2	28	54	
Longitudinal diameter/BSA – 4ch (cm/m^2)	0.4	0.15	28	32	
Transverse diameter– 4ch (cm)	0.5	0.2	25	28	
Transverse diameter/BSA – 4ch (cm/m^2)	0.3	0.1	35	39	
Max area – 2ch (cm^2)	4.7	2.0	22	25	Maceira et al. (2010)
Max area/BSA– 2ch (cm^2/m^2)	2.4	1	23	26	
Longitudinal diameter– 2ch (cm)	0.7	0.2	28	54	
Longitudinal diameter/BSA– 2ch (cm/m^2)	0.4	0.1	62	69	
Transverse diameter– 2ch (cm)	0.5	0.2	25	28	
Transverse diameter/BSA– 2ch (cm/m^2)	0.2	0.1	16	18	

Max area – 3ch (cm^2)	3.6	1	50	56	Maceira et al. (2010)
Max area/BSA– 3ch (cm^2/m^2)	1.8	0.5	50	56	
AP diameter– 3ch (cm)	0.5	0.2	25	28	
AP diameter/BSA– 3ch (cm/m2)	0.3	0.1	35	39	

A level: 0.05

Drop-out rate: 10%

Table 2: sample size calculation for objective 1 – RA

Variable	SD	precision	Sample size, n	Adjusted sample size, n + 10%	Reference
Max area – 4ch (cm^2)	3.8	1	56	63	Maceira et al. (2013)
Max area/BSA– 4ch (cm^2/m^2)	1.8	0.5	50	56	
Longitudinal diameter– 4ch (cm)	0.6	0.2	35	39	
Longitudinal diameter/BSA– 4ch (cm/m^2)	0.3	0.1	35	39	
Transverse diameter– 4ch (cm)	0.6	0.2	30	34	
Transverse diameter/BSA– 4ch (cm/m^2)	0.3	0.1	35	39	
Max area – 2ch (cm^2)	3.9	1	59	66	Maceira et al. (2013)
Max area/BSA– 2ch (cm^2/m^2)	2.3	1	21	24	
Longitudinal diameter– 2ch (cm)	0.5	0.2	25	28	
Longitudinal diameter/BSA– 2ch (cm/m^2)	0.3	0.1	35	39	
Transverse diameter– 2ch (cm)	0.7	0.2	48	54	
Transverse diameter/BSA– 2ch (cm/m^2)	0.4	0.1	62	69	

Objective 2 & 3

For objective 2 and 3, which is to determine the correlation of right and left atria dimension with age based on gender in healthy adult, sample size was calculated using Pearson's correlation estimation (Arifin, 2020), which was shown in table 3 and table 4.

Table 3: Sample size calculation for objective 2 – LA

Variable	Expected correlation, r	Precision	Sample size, n	Adjusted sample size, n + 10%	Reference
LA longitudinal – 2ch (cm)	0.34	0.25	50	56	Li et al. (2017)
LA transverse – 2ch (cm)	-0.15	0.25	60	67	
LA longitudinal – 3ch (cm)	0.56	0.25	32	36	
LA AP – 3ch (cm)	0.21	0.25	58	65	
LA longitudinal – 4ch (cm)	0.30	0.25	53	59	
LA transverse – 4ch (cm)	0.07	0.25	62	69	

Table 4: Sample size calculation for objective 3 – RA

Variable	Expected correlation, r	Precision	Sample size, n	Adjusted sample size, n + 10%	Reference
RA longitudinal – 2ch (cm)	0.28	0.25	54	60	Li et al. (2017)
RA transverse – 2ch (cm)	-0.5	0.25	37	42	
RA longitudinal – 4ch (cm)	0.12	0.25	61	68	
RA transverse – 4ch (cm)	0.07	0.25	62	69	

Based on calculated sample size, the estimated required sample size to achieve all the objective was 62 samples.

3.8 Research Tools

1. MRI scanner Philips 3 Tesla Achieva 2011 (Best, The Netherland); SENSE Torso/Cardiac coil 32 element piased-array coil Achieva 3.0T TX compatible; Wireless Physiology for respiration Vector Cardiography (VCG) plethysmography (peripheral pulse unit) with Invivo Process patient monitoring system – for cardiac MRI image acquisition.

2. Clinical workstation - Philips IntelliSpace Portal 10 MR Cardiac Analysis (Best, The Netherland).

3. SPSS version 24 was used for data analysis.

3.9 Variable Definition

Healthy Adult

- Subjects above the age of 18 years and above.

- Subjects with no clinical evidence of cardiovascular or cerebrovascular diseases (cardiac history, hypertension, hyperlipidaemia, diabetes mellitus, smoking, > obese class I; normal baseline ECG).

BMI

BMI formula: Weight in kilograms / (Height in meters)^2. BMI is categorized according to World Health Organization.

Category BMI (range kg/m^2)

Severely underweight: < 16.0

Underweight: 16.0 – 18.4

Normal: 18.5 – 24.9

Overweight: 25.0 – 29.9

Obese Class I: 30.0 – 34.9

Obese Class II: 35.0 – 39.9

Obese Class III: > 40.0

BSA

The Mosteller formula takes the square root of the height (cm) multiplied by the weight (kg) divided by 3600.

The average adult BSA was 1.7 m^2 (1.9 m^2 for adult males and 1.6 m^2 for adult females)

Anatomical boundary for RA and LA:

Atrial area boundaries:

Right atrium:

- superior end: Superior vena cava (SVC) orifice
- inferior end: Inferior vena cava (IVC) orifice
- posterior wall: interatrial septum, faces anterior and to the right, marked by depression (fossa ovalis) in lower part of the septum with crescenteric upper margin called the limbus)
- anterior and right lateral wall: cardiac wall
- left lateral extent: right atrioventricular valve

Left atrium:

- anterior: transverse pericardial sinus
- posterior: ostia of pulmonary veins
- separated from right atrium by interatrial septum
- separated from left ventricle by atrioventricular valve

3.10 Data Collection

Patient Cohort

1. Data of previous MRI study from July 2014 till July 2015 were collected from Radiology Information System (RIS) and Picture Archive Communication System (PACS) in HUSM. Initial subjects were collected under the previous short-term grant project involving healthy volunteers aged 18 till 60 years old. Total of 29 males and 28 females were involved in this study (43 Malay, 11 Chinese and 3 Indians). Short term grant account (304/PPSP/61313132) in 15/4/2015 until 14/4/2018. The access for the data has been granted by previous principal investigator and head of department of radiology.

2. The data were to be only accessible to the researchers and involved personnel only.

3. The data were calculated using clinical workstation with Cardiac Explorer software application.

4. Data obtained were validated by Consultant Radiologist. Relevant information was obtained from medical record.

Cardiac MRI protocol

This was performed using MRI scanner Philips 3 Tesla Achieva 2011 (Best, The Netherland); SENSE Torso/Cardiac coil 32 element phased-array coil Achieva 3.0T TX compatible using the surface coils and retrospective ECG triggering. All scans were performed by the same operator. End-expiratory breath-hold cine were obtained in the vertical and horizontal long axis planes followed by contiguous short axis cine