ASSESSMENT OF LEFT ATRIAL FUNCTION IN FELINE HYPERTROPHIC CARDIOMYOPATHY BY USING TWO DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY

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การประเมินการทำงานของหัวใจห้องบนซ้ายในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติโดยการตรวจคลื่นเสียงสะท้อนความถี่สูงด้วยวิธีสเป็กเกิล แทรกกิงแบบสองมิติ

น.ส.อริศรา เกียรติศิลปนันต์

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โรคกล้ามเนื้อหัวใจหนาตัวผิดปกติเป็นหนึ่งในโรคที่พบมากที่สุดของโรคกล้ามเนื้อหัวใจในแมว โดยปกติแล้วการทำงานของหัวใจห้องบนซ้ายมีความสำคัญที่ช่วยชดเชยการทำงานของหัวใจห้องล่างซ้ายที่มีการคลายตัวผิดปกติ เพื่อคงระดับของเลือดที่ออกจากหัวใจในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติ ปัจจุบันมีหลากหลายวิธีที่ใช้ในการประเมินการทำงานของหัวใจห้องบนซ้าย แต่มักจะมีข้อจำกัดในแต่ละวิธี เพื่อข้ามข้อจำกัดเหล่านั้น วิธีการตรวจคลื่นเสียงสะท้อนความถี่สูงด้วยวิธีสเป็กเกิล แทรกกิง แบบสองมิติ นั้นเป็นวิธีใหม่ที่ช่วยในการประเมินการทำงานของหัวใจห้องบนซ้าย ในปัจจุบันยังไม่พบว่ามีการศึกษาเกี่ยวกับการทำงานของหัวใจห้องบนซ้ายในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติโดยใช้การตรวจคลื่นเสียงสะท้อนความถี่สูงด้วยวิธีสเป็กเกิล แทรกกิง แบบสองมิติ การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อประเมินการทำงานของหัวใจห้องบนซ้ายในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติเปรียบเทียบกับแมวปกติโดยการตรวจคลื่นเสียงสะท้อนความถี่สูงด้วยวิธีสเป็กเกิล แทรกกิง แบบสองมิติ ซึ่งประกอบด้วยแมวปกติจำนวน 20 ตัว และแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติจำนวน 17 ตัว โดยพบว่าการทดสอบความแปรปรวนของการใช้วิธีสเป็กเกิล แทรกกิง แบบสองมิติของค่า peak atrial longitudinal strain (PALS) ในผู้วัดคนเดียวกันอยู่ที่ร้อยละ 4.17 และต่างผู้วัดอยู่ที่ร้อยละ 14 ค่าเฉลี่ยและค่าเบี่ยงเบนมาตรฐานของ PALS ในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติอยู่ที่ร้อยละ 13.16 ± 8.64 มีค่าน้อยกว่าแมวปกติซึ่งอยู่ที่ร้อยละ 28.54 ±10.31 อย่างมีนัยสำคัญทางสถิติ ($p < 0.001$) ในส่วนของผนังหัวใจห้องบนซ้ายแต่ละส่วน พบว่า ด้านผนังกั้น (septal) และผนังด้านนอก (lateral) นั้นมีการลดลงอย่างมีนัยสำคัญทางสถิติในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติ เมื่อเทียบกับแมวปกติ และส่วนบนสุด (roof) ของหัวใจห้องบนซ้ายนั้นมีค่าเฉลี่ยต่ำที่สุด ค่า PALS มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับค่าพารามิเตอร์ที่เกี่ยวข้องกับการทำงานของหัวใจห้องบนซ้าย กล่าวคือ fractional shortening (LA-FS%) ($r=0.538$, $p=0.001$) ejection fraction (LA-EF%) ($r =0.797$, $p<0.001$) และ fractional area change (FAC%) ($r =0.746$, $p<0.001$) กล่าวโดยสรุปคือ PALS สามารถใช้ในการประเมินการทำงานของหัวใจห้องบนซ้ายในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติได้ และเป็นวิธีที่สามารถทำซ้ำได้ในการประเมินหน้าที่ของหัวใจห้องบนซ้ายในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาตัวผิดปกติ

สาขาวิชา	อายุรศาสตร์สัตวแพทย์	ลายมือชื่อนิสิต .....
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Arisara Kiatsilapanan : ASSESSMENT OF LEFT ATRIAL FUNCTION IN FELINE HYPERTROPHIC CARDIOMYOPATHY BY USING TWO DIMENSIONAL SPECKLE TRACKING ECHOCARDIOGRAPHY. Advisor: Assoc. Prof. Sirilak Surachetpong, D.V.M., M.Sc., Ph.D.

Hypertrophic cardiomyopathy (HCM) is one of the most common myocardial diseases in cats. The left atrial (LA) function plays an essential role in compensatory mechanism of left ventricle with diastolic dysfunction to maintain cardiac output in cats affected with HCM. Nowadays, there are several echocardiographic techniques used to evaluate the left atrial function; however, each technique has limitations. To overcome the limitations, two-dimensional speckle tracking echocardiography (2D-STE) is a novel technique for assessment the LA function. To date, no study focusing on assessment of the left atrial function by 2D-STE in feline HCM has been reported. The objective of this study was to evaluate changes in LA function in HCM cats compared to normal cats by using 2D-STE. Twenty healthy control cats and seventeen client-owned cats affected with HCM were included in this study. The intra-observer and inter-observer measurement variability of peak atrial longitudinal strain (PALS) were 4.17% and 14%, respectively. The mean value and standard deviation of PALS in the HCM group (13.16 ± 8.64%) was lower than those of the control group (28.54 ±10.31%) ($p < 0.001$). The atrial longitudinal strain of septal and lateral regions was significantly reduced in the HCM group compared to the normal group. The atrial longitudinal strain was lowest at the LA roof region. The PALS correlated with the percentage of fractional shortening of the LA (LA-FS) (r=0.538, p=0.001), the percentage of the LA ejection fraction (LA-EF) (r =0.797, p<0.001), and the LA fractional area change (FAC) (r =0.746, p<0.001). In conclusion, the PALS can be used to evaluate changes in LA function in HCM cats. It is a reproducibility method for assessing the LA function in cats affected with HCM.

Field of Study:	Veterinary Medicine	Student's Signature .....
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Arisara Kiatsilapanan

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CHAPTER I

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is one of the most common myocardial diseases in humans and cats, but rare in dogs. The cause of idiopathic HCM in cats is either inheritance or unknown. Feline HCM mostly appears in male middle-age cats with certain breeds such as Maine Coon, Persian, Ragdoll, and American Shorthair (Nelson and Couto, 2009). The prevalence of feline HCM is approximately 10-15% of cats. HCM becomes more common with increasing age (Paige et al., 2009; Payne et al., 2013). Clinical signs of feline HCM include tachypnea, dyspnea, syncope, or sudden death, depending on the disease severity. HCM relates to heart failure and arterial thromboembolism (ATE) (Silva et al., 2013). HCM is characterized by an increased left ventricular thickness (equal or more than 6 mm), a smaller left ventricular chamber size and the progressive diastolic dysfunction. All of above structural and functional changes lead to decreasing of ventricular volume, reducing cardiac output, increasing left ventricular pressure, decreasing left atrial contractile function, and dilating left atrium, respectively (Nelson and Couto, 2009). Finally, left-sided congestive heart failure (CHF) or arterial thromboembolism may develop.

The left atrial function is an integral part of the cardiac function that is often overlooked. Typically, left atrium contributes 20-30% of total left ventricular stroke volume. Left atrium has three main functions, namely reservoir, conduit, and booster pump function. The major role of the left atrial function is to compensate for left ventricular function or maintain optimal cardiac output (Cianciulli et al., 2010). In addition, left atrial volume and function may also indicate chronicity, severity and progression of diastolic dysfunction (Linney et al., 2014). The left atrial volume and function are related to survival time (Payne et al., 2013). Therefore, the assessment of the left atrial function is useful for disease management and helps to predict adverse cardiac events, especially congestive heart failure, arterial thromboembolism, and atrial fibrillation. A recent study has suggested that atrial function may be more important than left atrial size for predicting cardiac event outcomes of congestive heart failure in cats (Johns et al., 2012; Linney et al., 2014).

Echocardiography is a non-invasive method to diagnose feline HCM and to assess the left atrial function. Nowadays, there are several echocardiographic techniques used to evaluate the left atrial function in humans, dogs, and cats including conventional echocardiography, i.e., two- dimensional and spectral Doppler echocardiography. Two-dimensional echocardiography is used to measure the left atrial phasic volume. This technique has the limitation due to the measurement depending on cardiac volume changes. Another method, tissue Doppler imaging (TDI) measures tissue motion velocities. The limitation of this method is time-consuming. In addition, tissue velocities are influenced by angle and translation from neighboring myocardium. Therefore, it is sometimes difficult to measure accurate atrial myocardial tissue velocities.

To overcome these limitations, two-dimensional speckle tracking echocardiography (2D-STE), a novel echocardiographic technique, can be used for assessing the left atrial by tracking acoustic speckle patterns of the left atrial wall and analyzing the myocardial motion directly. The advantages of this technique are angle-independence, feasibility, and reproducibility. The reliability of 2D-STE is influenced by image quality (Roşca et al., 2011). In humans, this technique has been used for assessing left atrial mechanics in common cardiac diseases such as atrial fibrillation, hypertension and hypertrophic cardiomyopathy, and for detecting early left atrial dysfunction before structural changes (Todaro et al., 2012). The newer parameters derived from 2D-STE are less depending on cardiac volume changes and have higher sensitivity in assessing left atrial function than conventional echocardiographic parameters (Cianciulli et al., 2010; Roşca et al., 2011). 2D-STE has been used to study the left atrial deformation and function in dogs with myxomatous mitral valve disease (Baron et al., 2017). There is a study using 2D-STE in HCM cats to assess the left ventricular longitudinal function (Sugimoto et al., 2015).

To our knowledge, no study focusing on assessment of left atrial function by 2D-STE in feline HCM has been reported. This study aims to evaluate changes of left atrial function in HCM cats compared to normal cats by using two-dimensional speckle tracking echocardiography (2D-STE).

Objectives of this study

To evaluate changes in left atrial function in hypertrophic cardiomyopathy (HCM) cats compared to normal cats by using two-dimensional speckle tracking echocardiography (2D-STE).

Hypothesis

Left atrial function changes can be detected in hypertrophic cardiomyopathy cats compared to normal cats by using two-dimensional speckle tracking echocardiography (2D-STE).

Keywords (Thai): แมว โรคกล้ามเนื้อหัวใจหนาตัวผิดปกติ หัวใจห้องบนซ้าย สเป็กเกิล แทรกกิง

Keywords (English): feline, hypertrophic cardiomyopathy, left atrium, speckle tracking

Advantages of the study

The peak atrial longitudinal strain of LA assessed by 2D-STE can be utilized to evaluate changes in LA function in HCM cats. This method is repeatability and reproducibility and may be valuable for diagnosis and management cats affected with HCM.

CHAPTER II

LITERATURE REVIEWS

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is one of the most common myocardial diseases in humans and cats, but rare in dogs. The cause of idiopathic HCM in cats is unknown. HCM has been proved to be an inherited disorder in some breeds of cats (Meurs et al., 2007). Similar to human HCM, gene mutation in myosin binding protein C (MYBPC3) has been reported in Maine Coon and Ragdoll cats (Maron and Fox, 2015). HCM mostly appears in male middle-age cats with certain breeds such as Maine Coon, Persian, Ragdoll, and American Shorthair. (Meurs et al., 2005; Nelson and Couto, 2009). HCM is commonly found in apparently healthy cats. The prevalence of feline HCM is approximately 10-15% (Paige et al., 2009; Payne et al., 2015). The disease becomes more common with increasing age (Paige et al., 2009; Payne et al., 2015). The characteristic of feline HCM is defined as left ventricular wall thickness at end-diastole of 6 mm or more with a smaller chamber size than normal. An increased wall thickness can occur in the left ventricular posterior wall, interventricular septum, or both. All of the above structural changes lead to decreasing of ventricular volume and cardiac output, increasing left ventricular pressure, decreasing left atrial function, and dilating left atrium, respectively (Nelson and Couto, 2009). HCM is a major cause of morbidity and mortality in cats and related to heart failure, sudden death, and arterial thromboembolism (ATE) (Silva et al., 2013).

HCM can be classified into two types including idiopathic HCM or primary HCM which contributes to 57% of the cause of feline HCM and secondary HCM resulted from other causes such as hyperthyroid, systemic hypertension, aortic stenosis, and acromegaly (Häggström et al., 2015). Some cats with HCM can be asymptomatic at the early stage of the disease. The clinical signs of HCM include tachypnea, dyspnea, syncope, or sudden death. The appearance of clinical signs depends on the disease severity (Silva et al., 2013).

Humans with HCM may have left atrial enlargement and a decrease of left atrial contractile function (Blume et al., 2011). According to Frank staring law applied to the left atrium, when the left atrial diameter increases, left atrial contraction increases to maintain stroke volume. Whenever severe left atrial dilation occurs, the optimal sarcomere length of the left atrium exceeds, and the left atrial dysfunction will develop (Roşca et al., 2011). Left atrial size has been studied in recent years for assessing the disease severity and progression (Linney et al., 2014); however, a few studies have been performed for assessment left atrial function in feline HCM (Payne et al., 2013; Linney et al., 2014).

Left atrial function

Left atrial function is an integral part of cardiac function that is often overlooked. The major role of the left atrium is compensating the left ventricular function or maintaining an optimal cardiac output (Cianciulli et al., 2010). Normally, left atrium contributes 20-30% of total left ventricle stroke volume. Three main functions of the left atrium are reservoir, conduit, and booster pump function. First, the reservoir phase is the phase that the left atrium receives blood from the pulmonary veins during left ventricular systole. Second, the conduit phase is the phase that the left atrium passively transfers blood to the left ventricle during early diastole. The third phase is the booster pump is the phase that the left atrial contraction during the late diastole (Roşca et al., 2011). The reservoir, conduit, and booster phases contribute 40%, 35%, and 25% of total stroke volume, respectively. A previous retrospective study indicates that the left atrial dysfunction is one of the important prognostic indicators in cats with HCM(Payne et al., 2013). The left atrial dysfunction can increase the risk of cardiac death secondary to arterial thromboembolism, congestive heart failure, and sudden death (Payne et al., 2015). The assessment of the left atrial function also helps to indicate chronicity, severity, and progression of the disease (Linney et al., 2014). Left atrial function is also related to survival time in cats with HCM (Payne et al., 2013). In humans, the clinical applications of assessing left atrial function use for prognostic implications, prediction cardiac event outcomes (e.g., atrial fibrillation and congestive heart failure), and application for disease prevention (Blume et al., 2011; Roşca et al.,

2011). A poorer left atrial function is associated with left-sided congestive heart failure in cats (Johns et al., 2012). It has been suggested that left atrial function may be more important than the left atrial size for predicting cardiac event outcomes in congestive heart failure cats.

Echocardiography

Echocardiography is a non-invasive tool to diagnose feline HCM and to evaluate the left atrial function. Several methods have been used to assess the left atrial function in humans including 2D, 3D echocardiography, computed tomography, and magnetic resonance imaging (Vizzardi et al., 2012). Two-dimensional echocardiography can be used to assess the left atrial function by measuring the left atrial phasic volume changes. The limitation of this technique is the volume dependence. Tissue Doppler imaging (TDI) is another method that can be used for assessing left atrial function by measuring the left atrial ejection fraction at the peak velocity of mitral annulus in the late diastole. Atrial myocardial velocities assessed by TDI are influenced by angle and translation velocities from neighboring myocardium which is not able to distinguish between the velocity from mitral annulus and atrial myocardium. One of TDI limitations is time-consuming (Roşca et al., 2011). This technique measures the regional tissue motion velocity. The global tissue motion cannot be assessed. The myocardial motion of the atrial roof may not include for measuring (Cianciulli et al., 2010).

Two-dimensional Speckle Tracking Echocardiography (2D-STE)

To overcome limitations from methods mentioned earlier, two-dimensional Speckle Tracking Echocardiography (2D-STE), a novel technique, can be used for assessing the left atrial function by tracking the acoustic speckle patterns of the atrial wall, the interatrial septum, and the atrial roof in an apical four-chamber view, then analyzing myocardial motion directly by an offline software. 2D-STE allows the study of the regional atrial myocardial deformation parameters, including strain and strain rate (SR). Strain definites myocardial deformation, and strain rate definites speed at which myocardial deformation occurs (Todaro et al., 2012). 2D-STE is an accurate assessment of segmental strain deformation. The measurement can be tracked along

the direction of the wall, by frame to frame with angle-independence in greyscale image analysis. 2D-STE is a feasible and reproducible method that provides better quantification of regional and global myocardial deformation. Furthermore, the sensitivity of this technique is higher than the conventional echocardiography (Cianciulli et al., 2010; Roşca et al., 2011).

2D-STE technique has been used for the assessment of left atrial function in human patients with HCM. This technique is also used for assessing the left atrial mechanics in common cardiovascular problems such as atrial fibrillation and systemic hypertension. In addition, 2D-STE can detect the early left atrial dysfunction before structural changes(Todaro et al., 2012; Huang et al., 2018). 2D-STE has been used to assess the left atrial deformation and function in dogs with myxomatous mitral valve disease (MMVD)(Baron et al., 2017; Caivano et al., 2018). Several studies showed that 2D-STE could be used to differentiate healthy dogs and dogs with MMVD at different stages (Baron et al., 2017; Caivano et al., 2018). Previous studies indicated that speckle tracking echocardiography provides quantitative measurements of LA longitudinal deformation and can be used to assess LA phasic function in healthy dogs (Baron et al., 2017; Caivano et al., 2018). 2D-STE has also been used to assess the left ventricular longitudinal function in feline HCM (Sugimoto et al., 2015). 2D-STE is feasible to detect myocardial dysfunction in cats with cardiac diseases by analyzing the reduction of segmental radial strain and strain rate (Takano et al., 2015). Studies using 2D-STE in cats with HCM focus only on the ventricular function (Sugimoto et al., 2015; Takano et al., 2015). No study has been used 2D-STE to assess left atrial function in feline HCM.

The evaluation of changes in left atrial function in feline HCM may be helpful to indicate the severity and cardiac event outcomes. The more accurate left atrial function assessment could have clinical values for management cats with HCM.

CHAPTER III

MATERIALS AND METHODS

Conceptual framework

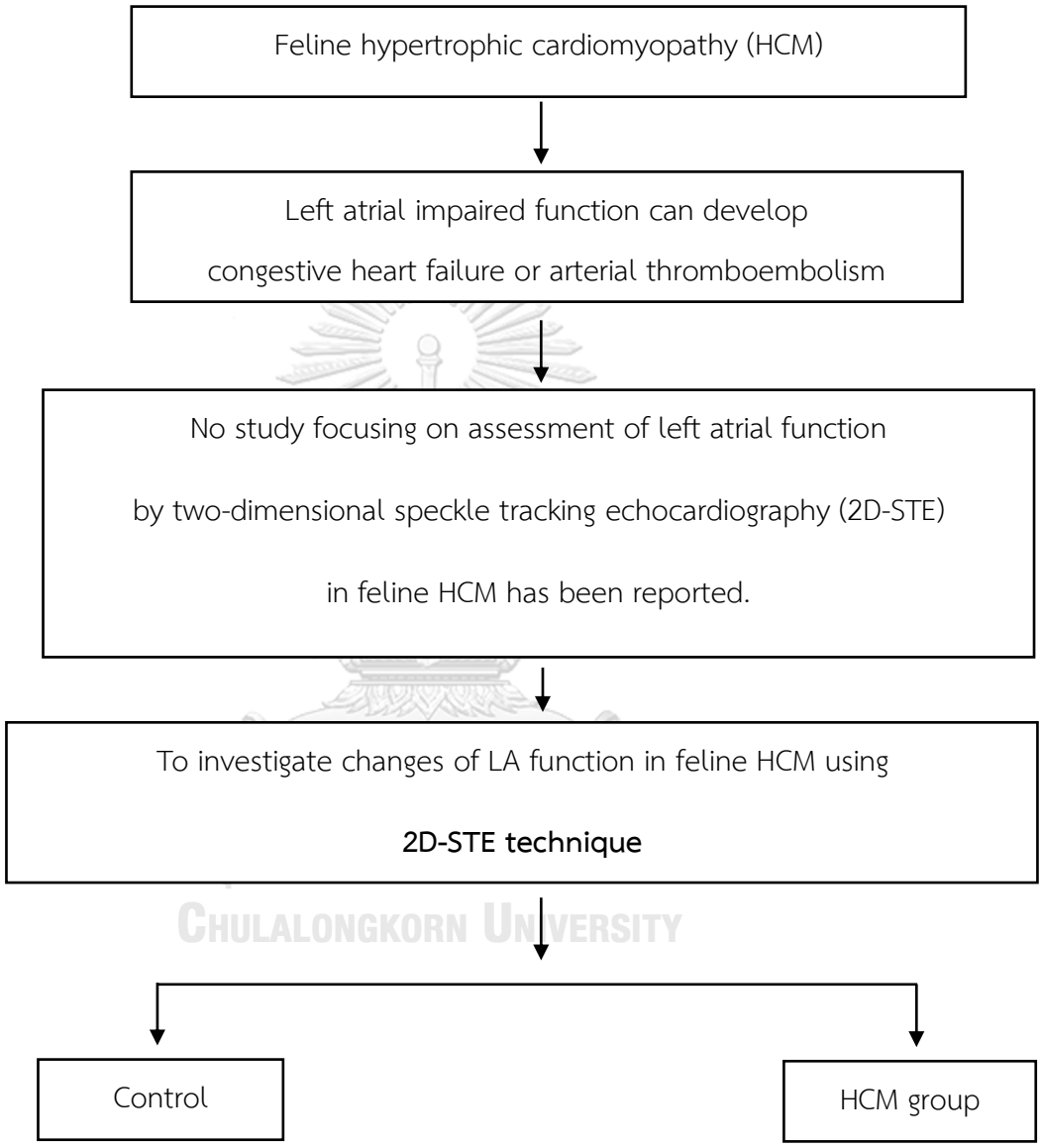


Figure 1 Conceptual framework of this study

Animals

Adult cats (>1 year old) with body weight 2-6 kilograms, any sex and breed were enrolled in the study. The population consisted of twenty healthy control cats and seventeen client-owned cats with hypertrophic cardiomyopathy (HCM). All cats recruited to the study presented at Small Animal Teaching Hospital, Faculty of Veterinary Science, Chulalongkorn University during August 2018 – June 2019.

Information of all cats, including breed, sex, age, weight, body condition score (BCS), and clinical signs were recorded. Complete physical examination, systolic blood pressure measurement, electrocardiography, radiography, and blood collection for complete blood count, blood chemistry, and total T4 measurements were performed. The cardiac structure and function were assessed by transthoracic echocardiography.

Inclusion and exclusion criteria

For inclusion criteria, the control group consisted of cats with unremarkable cardiac structural and functional abnormalities evaluated by conventional echocardiography. Cats with left ventricular wall thickness during diastole ≥ 6 mm in at least one region were recruited into the HCM group (Nelson and Couto, 2009). HCM cats with and without congestive heart failure were included. All cats did not receive cardiac medication before enrolled in the study.

For exclusion criteria, cats with renal disease (creatinine > 2.0 mg/dL) (Ettinger and Feldman, 2009), systolic blood pressure (Doppler or oscillometric method) > 160 mmHg (Linney et al., 2014), and hyperthyroidism (serum total T4 concentration > 4 µg/dl) (Nelson and Couto, 2009; Macintire et al., 2012) were excluded from the study.

Conventional echocardiography

Two-dimensional (2D) and m-mode echocardiography were performed by an investigator. The ultrasound machine (Samsung Madison, Eko7, Seoul, South Korea) with a 4-12 MHz phased array transducer was used.

M-mode echocardiography was performed on the right parasternal long-axis four-chamber view to measure the chamber size and wall thickness. Left ventricular internal dimension at end-diastole (LVIDd) and end-systole (LVIDs), interventricular septum thickness at end-diastole (IVSd) and end-systole (IVSs), and left ventricular posterior wall thickness at end-diastole (LVPWd) and end-systole (LVPWs) were recorded (Boon, 2011).

Pulsed-wave Doppler and tissue Doppler imaging were used for assessing the LV diastolic function. Transmitral flow velocities were obtained in the left apical four-chamber view at the mitral annulus level. The gate was placed at the tips of the mitral valve leaflets when they were wide open (Disatian et al., 2008). Peak velocity of early diastolic transmitral flow (E), peak velocity of late transmitral flow (A), and the ratio of E to A (E:A) was recorded. Isovolumic (or isovolumetric) relaxation time (IVRT) was measured from the left apical five-chamber view by locating the gate in the left ventricular outflow tract near the anterior mitral valve leaflet to reveal both aortic ejection flow and left ventricular inflow (Schober and Maerz, 2006; Boon, 2011). Pulmonary vein flow velocities were measured in the right parasternal short-axis view (Santilli and Bussadori, 1998). Peak velocity of systolic pulmonary vein flow (S), peak velocity of diastolic pulmonary vein flow (D), peak velocity of pulmonary vein flow reversal at atrial contraction (AR), and the ratio of S to D (S:D) were recorded. The myocardial motion along the longitudinal axis of the heart was investigated by placing one mm sample volume gate on the subendocardial portions of the lateral corner of the mitral annulus (Koffas et al., 2008). Peak velocity of early diastolic mitral annular motion as determined by pulsed-wave Doppler (E'), peak velocity of diastolic mitral annular motion as determined by pulsed-wave Doppler (A'), peak velocity of diastolic

mitral annular motion as determined by pulsed-wave Doppler (S'), the ratio of E' to A' (E':A') and the ratio of E to E'(E:E') were recorded (Koffas et al., 2006).

The diastolic filling pattern was classified by transmitral flow patterns. An E:A ratio of <1 was classified as delayed relaxation pattern, an E:A ratio of 1-2 was classified as normal or a pseudonormal filling pattern and an E:A ratio of >2 was classified as restrictive filling pattern. For differentiation of pseudonormal filling from normal pattern was considered from E':A'<1 (Payne et al., 2013).

The LA diameter (LAD) was measured on the right parasternal short-axis view parallel with the mitral annulus both the maximal and minimal LAD (LADmax and LADmin) (Abbott and MacLean, 2006) (Swedish method). The percentage of fractional shortening of the left atrium (LA-FS) was calculated by the formula (LADmax-LADmin/LADmax)x100 (Abbott and MacLean, 2006). For measurement of the maximal and minimal volume were measured from the left apical four-chamber view. The percentage of LA ejection fraction (LA-EF) were computed by automated software from ultrasound machine software (Abbott and MacLean, 2006). The LA area changes (FAC) were measured by tracing along the LA endocardial border during LA end-diastole and systole phases (Figure1). The LA fractional area change (FAC) was be calculated with the formula FAC = [(LAAmax – LAAmin)/LAAmax] ×100 (Cameli et al., 2012; Baron et al., 2017)

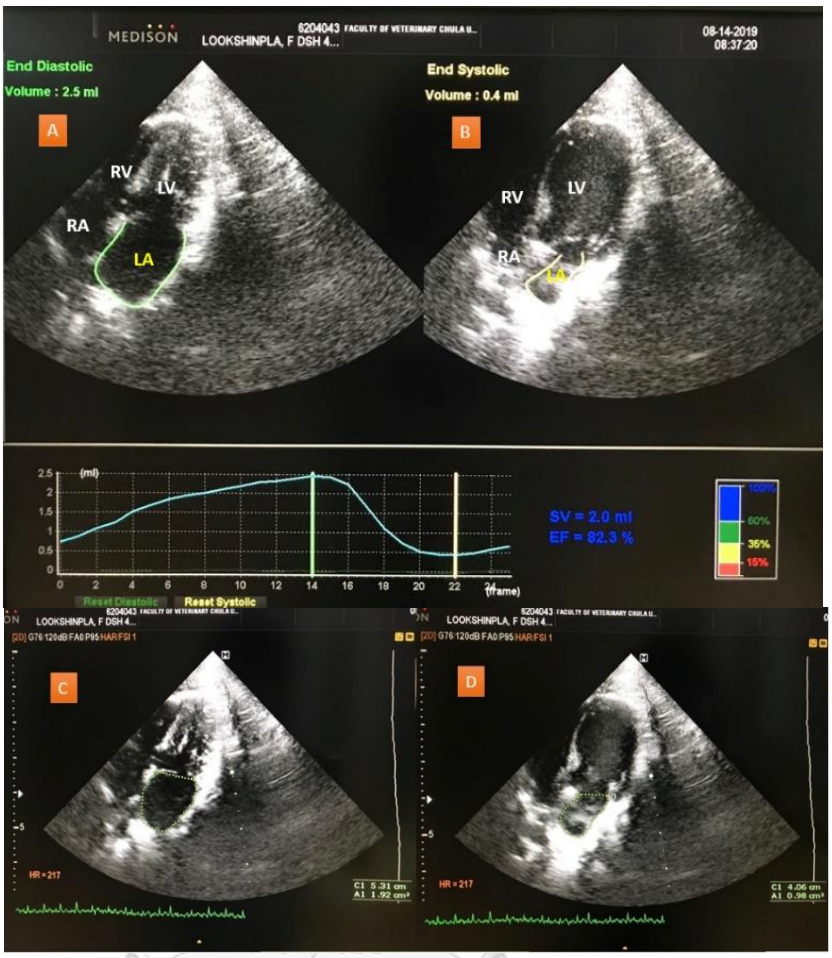


Figure 2 A and B are maximal and minimal volume of LA assessed by automated software; C and D are left atrial maximal area and minimal left atrial area by tracing the LA endocardial border, respectively.

Two-dimensional speckle tracking echocardiography (2D-STE)

2D-STE was performed on the left apical 4-chamber view to analyze the left atrial longitudinal deformation. Two-dimensional echocardiographic images were recorded for 3 cardiac cycles and 3 sceneries, and stored in DICOM format. The good quality images were selected for offline analysis. The LA wall, including the interatrial septum, lateral wall, and the atrial roof were tracked along the endocardium border during end-diastole. After automatic tracking, manual editing was performed to correct software system errors in the region of interest. The ultrasound machine computer software calculated the LA strain. The mean values of the measurement from three consecutive cardiac cycles were used in all analyses. The number of speckle segments of each cat was recorded. The strain of each segment (as percentages) was plotted on the *y*-axis versus time (in seconds) on the *x*-axis over an entire cardiac cycle (figure 2). The different color graphs represent strain from different segments. The white dotted line is the average strain. The peak atrial longitudinal strain [PALS] is the peak strain value during LV contraction (reservoir phase) (Cameli et al., 2012).

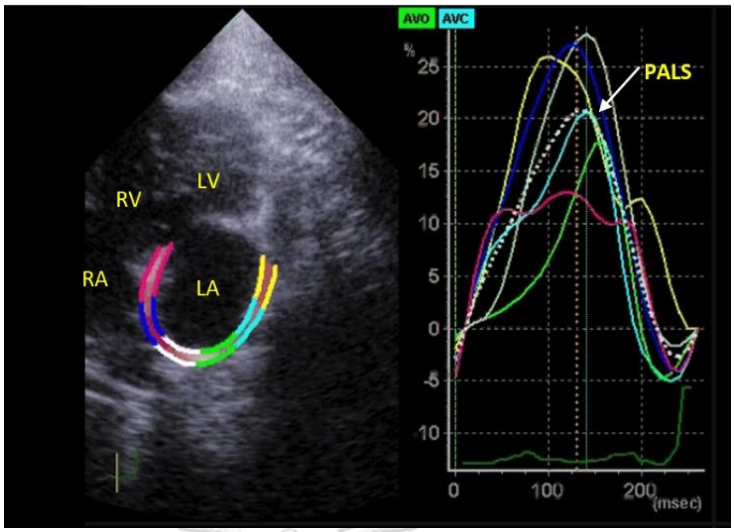


Figure 3 The image of the left apical 4-chamber view of the left atrial strain profile of a cat. A region of interest is manually drawn to include the left atrial wall. The automatic software system divided the left atrial wall into 6 different segments with different colors. A white dotted line is presented as the mean of strain value of the left atrium. LA: left atrium; LV: left ventricle; PALS: peak atrial longitudinal strain (white arrow); RA: right atrium; RV: right ventricle.

Measurement variability

Data from randomly selected six cats recruited into the study were used for assessing measurement repeatability of PALS in the same cardiac cycle from the same cine loop. Intra-observer coefficient of variation (CV) was calculated from data obtained from different examinations of each cat in two different days (seven days apart) by the same investigator. Inter-observer variable was calculated from the data that were measured by two different operators with different levels of experience in echocardiography. The variability was quantified as the coefficient of variation (CV) by the formula. %CV=standard deviation (SD)/mean x 100. The degree of repeatability was determined as follows: CV <5%, very low variability; 5-15%, low variability; 16-25%, moderate variability; or >25% high variability (Bland, 2000).

Sample size calculation

This study used mean and standard deviation (SD) of the left atrial fractional shortening (LA-FS) from a previous study (Linney et al., 2014) to estimate sample size calculation. A minimum difference of LA-FS between HCM cats and healthy cats is about 10%. For the calculation, the estimated SD was set at 10, power was set at 0.8, and α (confidence level or type I error rate) was set at 0.05. The calculation was performed with a freeware program (G Power 3.1). The result for the sample size calculation is 34 cats (i.e., 17 HCM cats and 17 control cats).

Statistical Analysis

The statistical analyses were performed by using a commercial software (SPSS version 22, IBM, Chicago, IL, *USA*.). The descriptive statistical analyses were used to describe cat characteristics including sex and breed. For age, weight, body condition score, systolic blood pressure, and heart rate, the results were reported as mean and standard deviation (SD). The analytical statistics were performed to compare the significant difference of the data between two groups (the control and HCM groups). Normality was assessed with the Shapiro-Wilk normality test. For normal distribution quantitative data, the independent Student t-test was used. For non-normal distribution data, the Mann-Whitney test was applied. The comparison of three subgroups including the control, the HCM cats with LAD <16 mm, and the HCM cats with LAD >16 mm was performed by using the one-way ANOVA. An ANCOVA model was used to test the fixed effects of sex, breed, and age as covariates on conventional and 2D-STE derived echocardiographic variables. The correlation (r) between PALS and LA-FS, LA-EF, and FAC assessed by conventional echocardiography was tested by Pearson's correlation coefficient. The degree of the Pearson's correlation coefficient was determined as follow: r = >0.7 indicate strong correlation; 0.4-0.6 indicate moderate correlation; <0.4 indicate weak correlation (Akoglu, 2018). The $p<0.05$ was considered significant.

Experimental design

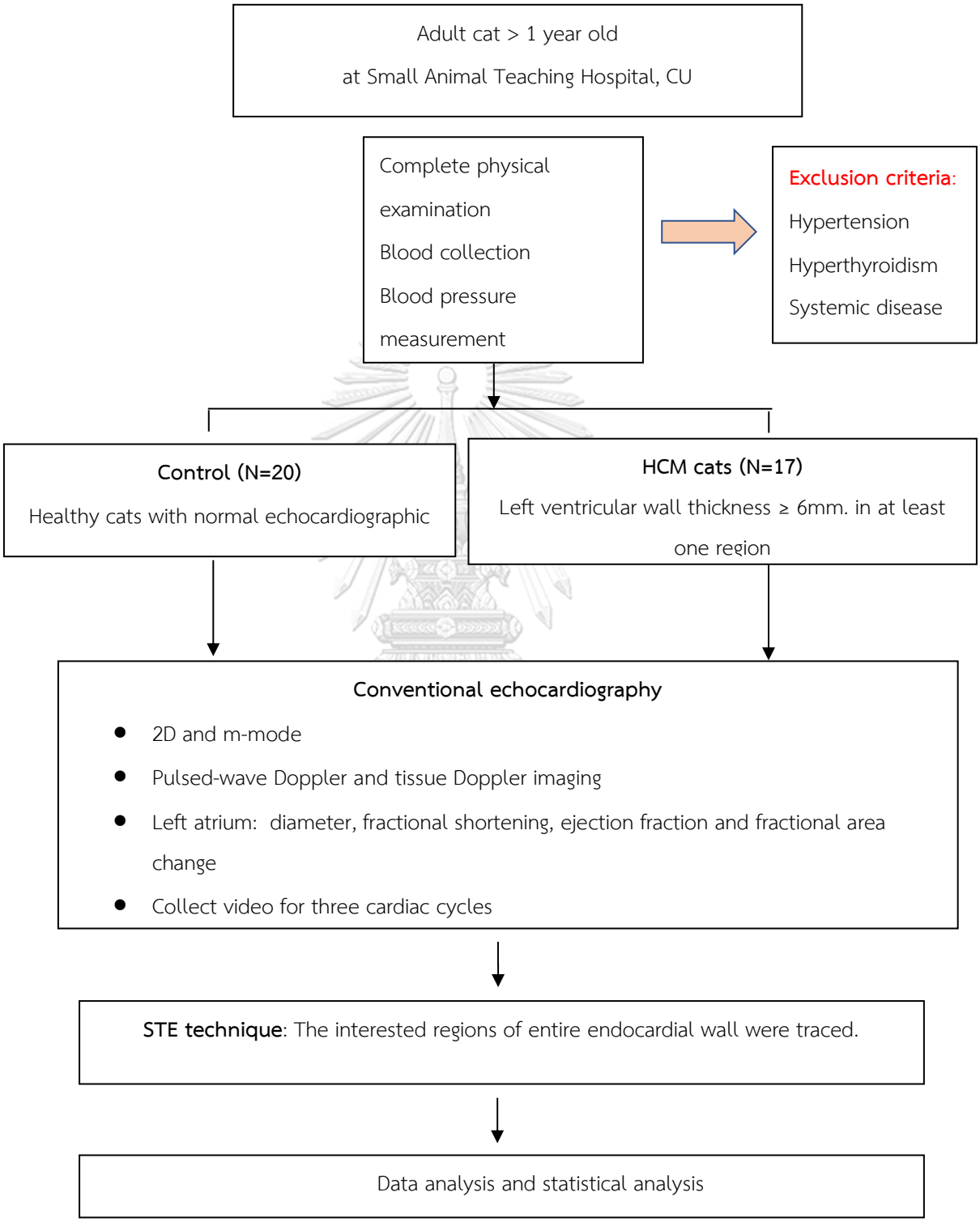


Figure 4 Experimental design of this study

CHAPTER IV

RESULT

Part I: General information

1.1 Signalment and physical examination findings

Thirty-seven cats presented at the Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University were included in the study: twenty control cats and seventeen hypertrophic cardiomyopathy (HCM) cats. The general characteristics of the control and HCM groups are summarized (Table 1). Age, body weight, heart rate, and systolic blood pressure did not differ significantly between the control and HCM groups. The vertebral heart score (VHS) of HCM cats was significantly higher than the control group (p=0.007). Male and domestic shorthair cats were overrepresented in the control and HCM groups. Eight out of seventeen HCM cats (47.1%) affected with arterial thromboembolism (ATE), and three out of eight HCM cats with ATE had congestive heart failure. None of HCM cats without ATE had congestive heart failure.

Table 1 The general characteristics of cats in the control and hypertrophic cardiomyopathy groups

Variable	Control	HCM	*p*-value
Number of cats	20	17	
Age (year)	5.05 ± 3.03	5 ± 3.43	0.963
Body weight (kg.)	4.47 ± 0.92	4.25 ± 1.04	0.497
Sex			
Male	14	10	
Female	6	7	
Heart rate(bpm)	206.90 ± 20.21	209.12 ± 31.64	0.798
Systolic blood pressure (mmHg)	128.35 ± 20.41	116 ± 20	0.073
Breed (no. of cats)			
Domestic shorthair	10	10	
American shorthair	5	-	
Sphinx	1	-	
Scottish fold	2	-	
Siamese	1	-	
Exotic shorthair	1	1	
Persian	-	5	
Khao Manee	-	1	
Vertebral heart score (VHS)	7.58 ± 0.41	7.99 ± 0.49	0.007*
HCM+ATE (% of HCM cats)	-	8 (47.1%)	
With CHF	-	3	
Without CHF	-	5	

Abbreviations: ATE: arterial thromboembolism; bpm: beat per minute; CHF: congestive heart failure.

Age, body weight, heart rate and systolic blood pressure and vertebral heart score (VHS) are expressed as mean± standard deviation.

*indicate statistical significance at $p<0.05$.

1.2 Complete blood count and blood chemistry profile values

Complete blood count

The mean complete blood count of the control and HCM groups is shown in Table 2. Neutrophil numbers were significantly higher in the HCM group than those in the control group, but values were within the normal limit. There was no significant difference in the red blood cell, hemoglobin, hematocrit, platelet and white blood cell numbers between the control and HCM groups. All complete blood count values were within the normal limit. Neutrophil numbers of HCM cats with ATE (13.83 ± 7.32 $x10^3$ cell/ µL) were significantly higher than those of HCM cats without ATE (7.09 ± 5.14 $x10^3$ cell/ µL) (p=0.042).

Blood chemistry profile value

The mean blood chemistry profile values of the control and HCM groups are presented in Table 2. Plasma alanine aminotransferase (ALT) was significantly higher in the HCM group than the control group. There was no significant difference in plasma alkaline phosphatase (ALP), blood urea nitrogen (BUN) and creatinine between the control and HCM groups. All values of blood chemistry profile were within the normal limit, except the plasma ALT level in the HCM group. The concentration of plasma ALT level was significantly higher in HCM with ATE (356.5 ± 220 U/L) than that in HCM without ATE (64.33 ± 39.69 U/L) (p=0.007).

Table 2 Complete blood count and blood chemistry profile values of the control and hypertrophic cardiomyopathy groups

Variable	Unit	Normal value [a]	Control (N=20)	HCM (N=17)	*p* value
CBC					
RBC	$x10^6$ cell/mm^3	6-10	9.09 ± 1.49	8.8 ± 1.59	0.572
Hemoglobin	g/dl	9.5-15	13.85 ± 1.91	13.62 ± 1.64	0.697
Hematocrit	%	29-45	38.97 ± 5.03	38.33 ± 3.82	0.668
Platelets	$x10^3$ cell/ µL	150-600	148.7 ± 72.19	150.59 ± 50.37	0.928
WBC	$x10^3$ cell/ µL	5.5-19.5	10.86 ± 8.88	13.41 ± 6.27	0.33
Neutrophils	$x10^3$ cell/ µL	2.5-12.5	5.10 ± 2.18	10.26 ± 6.98	0.009*
Lymphocytes	$x10^3$ cell/ µL	1.5-7	2.9 ± 1.46	2.34 ± 1.36	0.241
Monocytes	$x10^3$ cell/ µL	0-0.85	0.42 ± 0.7	0.31 ± 0.26	0.535
Eosinophils	$x10^3$ cell/ µL	0-1.5	0.91 ± 1.56	0.47 ± 0.48	0.275
Basophils	$x10^3$ cell/ µL	0-0.1	0.004 ± 0.005	0.01 ± 0.02	0.053
Blood chemistry					
ALT	(U/L)	28-76	42.95 ± 15.40	176.37 ± 189.17	0.013*
ALP	(U/L)	0-62	29.05 ± 8.61	37.93 ± 25.23	0.209
BUN	mg/dl	15-34	27.03 ± 3.97	28.13 ± 9.88	0.67
Creatinine	mg/dl	0.8-2.3	1.47 ± 0.25	1.54 ± 0.43	0.519
Total T4	µg/dl	1-4	2.77 ± 0.65	2.14 ± 1.14	0.057

Abbreviations: ALT: alanine amino transferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen, CBC: complete blood count, HCM: hypertrophic cardiomyopathy; RBC: red blood cell; WBC: White blood cell

*Indicate statistical difference at $p < 0.05$ between the control and HCM groups.

Data are expressed as mean± standard deviation.

The significant difference was assessed by independent student t-test.

[a] Normal reference value from: Douglass KM, Kenneth JD, Steven CH and William DS. 2012. Normal value of oxygen and hemodynamic parameters. In: Manual of Small Animal Emergency and Critical Care Medicine. 2nd ed. BT David(ed.). Philadelphia: Lippincott William and Wilkins. 514-515.

Part II: Echocardiography

2.1 Conventional echocardiography

The conventional echocardiography results showed an increase in IVSd, LVPWd, IVSs, LVPWs, LA and LA:Ao in the HCM group compared to the control group, while LVIDd were significantly lower in the HCM group than that in the control group. The pulsed-wave Doppler echocardiography demonstrated that E, S and D were significantly lower in the HCM group than those in the control group. The others pulsed-wave echocardiography and tissue Doppler imaging were not significantly different between the two groups. The LA-FS, LA-EF, and FAC were significantly lower in the HCM group (Table 3).

Left ventricular diastolic dysfunction was detected in 64.7% of the HCM group (29.4% of the HCM group had impaired ventricular relaxation pattern (E:A<1), 17.6% of the HCM group had increased LA pressure or pseudonormal filling pattern (E:A >1<2 and E':A'<1), and 17.6% of the HCM group had restrictive filling pattern (E:A >2)). All cats that had left ventricular restrictive filling pattern developed ATE.

Table 3 Comparison of conventional echocardiographic values in the control and hypertrophic cardiomyopathy groups

Variable	Control (N=20)	HCM (N=17)	*p* value
Size and structure			
IVSd (mm)	4.24 ± 0.89	7.12 ± 1.14	<0.001*
LVIDd (mm)	14.31 ± 1.65	12.38 ± 3.03	0.027*
LVPWd (mm)	3.5 ± 0.59	5.56 ± 1.64	<0.001*
IVSs (mm)	7.18 ± 1.40	8.63 ± 1.86	0.01*
LVIDs (mm)	6.35 ± 1.63	6.06 ± 2.38	0.669
LVPWs (mm)	7.01 ± 0.92	8.24 ± 1.94	0.026*
LA (mm)	12.22 ± 1.42	15.55 ± 2.81	<0.001*
Ao (mm)	8.66 ± 1.3	8.3 ± 1.73	0.476
LA:Ao	1.44 ± 0.28	1.92 ± 0.44	<0.001*
LV function			
FS%	55.58 ± 10.22	51.38 ± 10.79	0.233
E (m/s)	0.83 ± 0.19	0.62 ± 0.18	0.002*
A (m/s)	0.61 ± 0.12	0.53 ± 0.29	0.346
E:A	1.34 ± 0.31	1.46 ± 0.74	0.09
IVRT (m/s)	45.7 ± 6.64	47.4 ± 9.12	0.504
S (cm/s)	0.46 ± 0.09	0.31 ± 0.13	0.001*
D (cm/s)	0.35 ± 0.06	0.26 ± 0.12	0.006*
AR (cm/s)	0.14 ± 0.03	0.16 ± 0.05	0.367
S:D ratio	1.25 ± 0.2	1.2 ± 0.22	0.464
E’ (m/s)	0.11 ± 0.03	0.08 ± 0.04	0.056
A’ (m/s)	0.08 ± 0.03	0.07 ± 0.04	0.54
S’ (m/s)	0.07 ± 0.02	0.07 ± 0.03	0.625
E’:A’ ratio	1.33 ± 0.31	1.15 ± 0.39	0.16
E:E’ ratio	7.8 ± 2.92	9.7 ± 6.8	0.265

Variable	Control (N=20)	HCM (N=17)	*p* value
LA function			
LA-FS (%)	27.27 ± 6.94	14.95 ± 8.23	<0.001*
LA-EF (%)	69.10 ± 13.64	46.09 ± 21.48	0.001*
FAC (%)	63.73 ± 11.30	35.54 ± 18.07	<0.001*

Abbreviations: A : peak velocity of early diastolic transmitral flow; A': peak velocity of diastolic mitral annular motion as determined by pulsed wave Doppler; Ao: Aorta; AR : peak velocity of pulmonary vein flow reversal at atrial contraction; D: peak velocity of diastolic pulmonary vein flow; E : peak velocity of early diastolic transmitral flow; E' : peak velocity of early diastolic mitral annular motion as determined by pulsed wave Doppler; E:A : ratio of E to A; E'A' : ratio of E' to A'; E:E' : ratio of E to E'; FAC: left atrial fractional area change; FS : left ventricular fractional shortening; HCM: hypertrophic cardiomyopathy ;IVRT: isovolumic (or isovolumetric) relaxation time; IVSd : interventricular septum thickness at end-diastole; IVSs : interventricular septum thickness at end-systole; LA: left atrium, LA:Ao : left atrial and aorta ratio; LA-EF : left atrial ejection fraction; LA-FS: left atrial fractional shortening; LV: left ventricle; LVIDd: left ventricular internal dimension at end -diastole; LVIDs: left ventricular internal dimension at end -systole; LVPWd: left ventricular posterior wall thickness at end-diastole; LVPWs: left ventricular posterior wall thickness at end-systole; S : peak velocity of systolic pulmonary vein ; S' : peak velocity of systolic mitral annular motion as determined by pulsed wave Doppler; S:D :ratio of S to D.

Data are expressed as mean± standard deviation.

* indicate statistical significance at $p<0.05$

2.2 Two-dimensional speckle tracking echocardiographic

The median of peak atrial longitudinal strain (PALS) was significantly lower in the HCM group than that in the control group (p<0.001). The longitudinal strain of all LA regions was reduced significantly in the HCM group compared to the normal group except at the septal-roof and the lateral-roof of the LA wall (Table 4) (Figure 2).

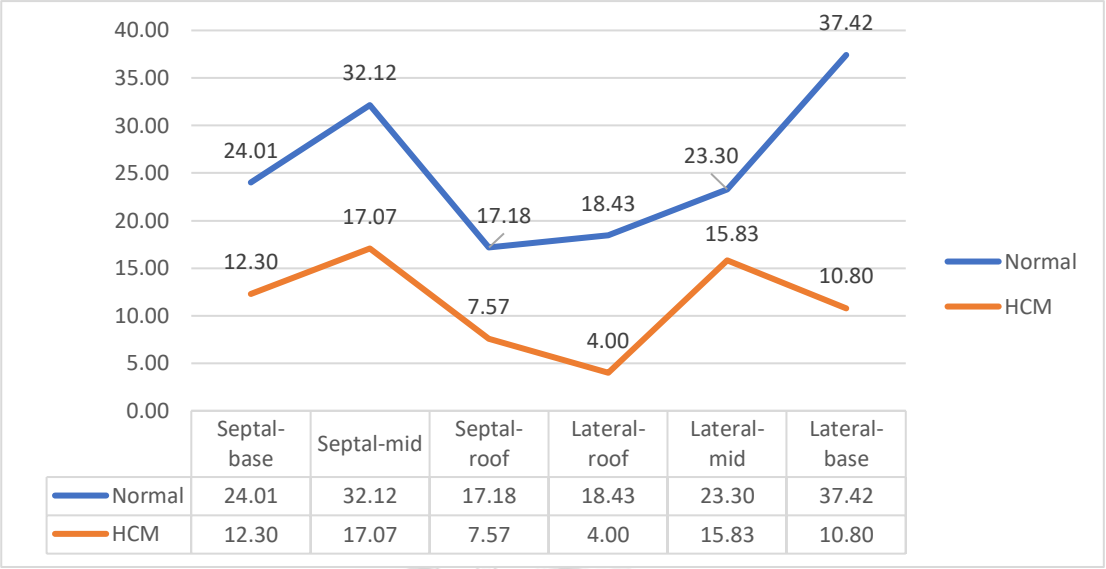
Table 4 Two-dimensional speckle tracking echocardiographic data of cats in the control and hypertrophic cardiomyopathy groups

Variable	Control (N=20)	HCM (N=17)	*p* value
PALS (%)	**27.25 [21.18,32.97]**	**13.33 [5.53,17.32]**	**<0.001***
Longitudinal strain of each LA region			
Septal - base	24.01 [15.84,40.74]	12.30 [5.22,19.01]	0.006*
Septal - mid	32.12 [25.67,54.54]	17.07 [6.48,24.82]	<0.001*
Septal - roof	17.18 [6.22,29.59]	7.57 [3.23,13.13]	0.063
Lateral - roof	18.43 [6.86,32.19]	4.00 [-0.22,28.47]	0.067
Lateral -mid	23.30 [18.17,35.77]	15.83 [1.97,25.42]	0.038*
Lateral- base	37.42 [13.60,46.80]	10.8 [7.22,17.23]	0.002*

Abbreviations: HCM: hypertrophic cardiomyopathy; LA: left atrium; PALS: peak atrial longitudinal strain

Data are expressed as median and 25th,75th percentiles.

* indicate statistical significance at p<0.05 by the Mann-Whitney U Test.



	Septal-base	Septal-mid	Septal-roof	Lateral-roof	Lateral-mid	Lateral-base
Normal	24.01	32.12	17.18	18.43	23.30	37.42
HCM	12.30	17.07	7.57	4.00	15.83	10.80

Figure 5 The line graph shows the median value of the atrial longitudinal strain in each region (septal-base, septal-mid, septal-roof, lateral-roof, lateral-mid, and lateral-base of the left atrial wall) between the normal group (blue) and hypertrophic cardiomyopathy (HCM) groups (orange).

2.3 Left atrial function between three subgroups categorized by the left atrial diameter

An assessment of LA function between three subgroups [control group (n= 20), HCM cats with the LA diameter <16 mm. (n= 9), and HCM cats with the LA diameter ≥16 mm. (n= 8)] was compared (Table 5). The results showed that LA-FS, LA-EF, FAC, and PALS in both HCM cat subgroups were significantly lower than those in the control group. However, the values of these variables were not significantly different between the HCM cat subgroups.

Table 5 Assessment of left atrial function between 3 subgroups of cats categorized by the left atrial diameter

Variables	Control (N = 20)	HCM with LAD < 16 mm (N = 9)	HCM with LAD ≥ 16 mm (N = 8)	*p* value
LA-FS (%)	27.28 ± 6.94 [a]	15.22 ± 6.97 [b]	14.63 ± 9.94 [b]	<0.001*
LA-EF (%)	69.10 ± 13.64 [a]	48.89 ± 24.75 [b]	42.95 ± 18.26 [b]	0.002*
FAC (%)	63.73 ± 11.30 [a]	34.49 ± 19.27 [b]	36.73 ± 17.86 [b]	<0.001*
PALS (%)	28.54 ±10.31[a]	13.49 ± 10.87[b]	12.80 ± 5.94 [b]	<0.001*

Abbreviations: FAC: left atrial fractional area change; HCM: hypertrophic cardiomyopathy; LAD: left atrial diameter; LA-EF: left atrial ejection fraction; LA-FS: left atrial fractional shortening; PALS: peak atrial longitudinal strain.

Data are expressed as mean± standard deviation

*indicate statistical significance at $p<0.05$.

[a] and [b] indicate significant difference.

2.4 Left atrial function and size between two subgroups within HCM group categorized by comorbidity with arterial thromboembolism

An assessment of LA function between two subgroups of HCM cats [HCM cats without arterial thromboembolism (ATE) (n= 9) and HCM cats with ATE (n= 8)] was compared (Table 6). The results showed that LA-FS, LA-EF, FAC, and PALS in HCM cats with ATE were significantly lower than those in HCM cats without ATE. The left atrial size between HCM cats with and without ATE was not significantly different.

Table 6 Left atrial function and diameter between two subgroups of HCM cats categorized by comorbidity with arterial thromboembolism

Variable	HCM without ATE (N=9)	HCM with ATE (N=8)	*p* value
LA-FS (%)	19.91 ± 5.98	9.36 ± 6.81	0.004*
LA-EF (%)	60.81 ± 18.20	29.54 ± 9.12	0.001*
FAC (%)	45.61 ± 15.03	24.22 ± 14.54	0.009*
PALS (%)	18.15 ± 8.53	7.55 ± 4.42	0.007*
LAD (mm.)	15.27 ± 2.14	15.87 ± 3.56	0.671

Abbreviations: ATE: arterial thromboembolism; FAC: left atrial fractional area change; HCM: hypertrophic cardiomyopathy; LAD: left atrial diameter; LA-EF: left atrial ejection fraction; LA-FS: left atrial fractional shortening; PALS: peak atrial longitudinal strain.

Data are expressed as mean± standard deviation

*indicate statistical significance at $p<0.05$.

Part III: Correlation

3.1 The correlations between the peak atrial longitudinal strain and echocardiographic values assessed by conventional echocardiography in entire population

Table 7 shows weak positive correlations between PALS and LVIDd, IVSs, LVPWs, E, S, D and E'. Moderate negative correlations between PALS and IVSd and LVPWd were observed. There was no significant correlation between PALS and LA diameter.

Table 7 The correlation of the peak atrial longitudinal strain and echocardiographic values assessed by conventional echocardiography in entire population

Variable	r	*p* value
Size and structure		
IVSd (mm)	-0.563	<0.001*
LVIDd (mm)	0.362	0.028*
LVPWd (mm)	-0.516	0.001*
IVSs (mm)	-0.393	0.016*
LVIDs (mm)	0.256	0.126
LVPWs (mm)	-0.379	0.021*
LA (mm)	-0.248	0.139
Ao (mm)	0.17	0.314
LA:Ao	-0.315	0.058
LV function		
FS%	-0.061	0.721
E (m/s)	0.41	0.012*
A (m/s)	0.277	0.107
E:A	-0.191	0.271
IVRT (m/s)	-0.204	0.24
S (cm/s)	0.41	0.013*
D (cm/s)	0.341	0.042*

AR (cm/s)	0.164	0.353
S:D ratio	0.164	0.338
E’ (cm/s)	0.459	0.004*
A’ (cm/s)	0.117	0.523
S’ (cm/s)	0.078	0.651
E’:A’ ratio	0.132	0.435
E:E’ ratio	-0.21	0.212

Abbreviations: A : peak velocity of early diastolic transmitral flow; A’: peak velocity of diastolic mitral annular motion as determined by pulsed wave Doppler; Ao: Aorta; AR : peak velocity of pulmonary vein flow reversal at atrial contraction; D: peak velocity of diastolic pulmonary vein flow; E : peak velocity of early diastolic transmitral flow; E’ : peak velocity of early diastolic mitral annular motion as determined by pulsed wave Doppler; E:A : ratio of E to A; E’A’ : ratio of E’ to A’; E:E’ : ratio of E to E’; FAC: left atrial fractional area change; FS : left ventricular fractional shortening; HCM: hypertrophic cardiomyopathy ;IVRT: isovolumic (or isovolumetric) relaxation time; IVSd : interventricular septum thickness at end-diastole; IVSs : interventricular septum thickness at end-systole; LA: left atrium, LA:Ao : left atrial and aorta ratio; LV: left ventricle; LVIDd: left ventricular internal dimension at end -diastole; LVIDs: left ventricular internal dimension at end -systole; LVPWd: left ventricular posterior wall thickness at end-diastole; LVPWs: left ventricular posterior wall thickness at end-systole; S : peak velocity of systolic pulmonary vein ; S’ : peak velocity of systolic mitral annular motion as determined by pulsed wave Doppler; S:D :ratio of S to D.

The significant correlation was assessed by Pearson’s correlation coefficient.

*indicate statistical significance at p <0.05

3.2 The correlation of the peak atrial longitudinal strain and left atrial function parameters assessed by conventional echocardiography in entire population

The correlation analysis from data of all cats demonstrated a strongly positive correlation between PALS and LA-EF as well as PALS and FAC. The peak atrial longitudinal strain moderately positive correlated with LA-FS (Table 8, Figure 6).

Table 8 The correlation between the peak atrial longitudinal strain and left atrial function parameters assessed by conventional echocardiography in entire population

Variable	r	*p* value
LA-FS (%)	0.538	0.001*
LA-EF (%)	0.797	<0.001*
FAC (%)	0.746	<0.001*

Abbreviations: FAC: left atrial fractional area change; HCM: hypertrophic cardiomyopathy; LA-EF: left atrial ejection fraction; LA-FS: left atrial fractional shortening

The significant correlation was assessed by Pearson's correlation coefficient.

*indicate statistical correlation at $p < 0.05$

The ANCOVA demonstrated that age, sex, and breeds had no effect on values of PALS, LA-FS, and LA-EF. However, FAC was affected by breeds (domestic shorthair or pure breeds) (p=0.04).

Part IV: The measurement variability

The intra-observer and inter-observer measurement variability of PALS were 4.17% and 14%, respectively.

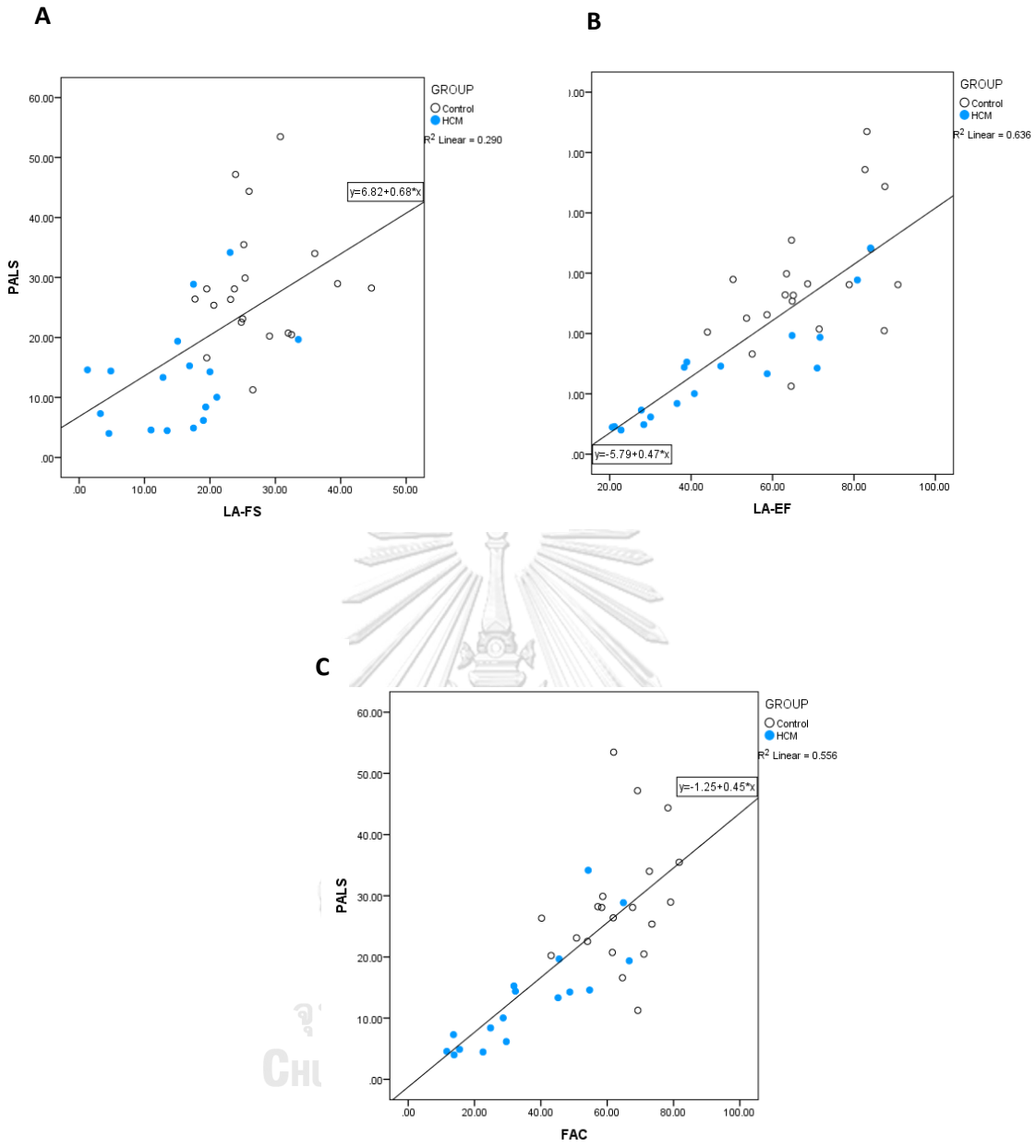


Figure 6 The scatter plots show the correlation between (A) peak atrial longitudinal strain (PALS) and left atrial fractional shortening (LA-FS) (r=0.538, *p*=0.001)
(B) peak atrial longitudinal strain (PALS) and left atrial ejection fraction (LA-EF) (r=0.797, *p*<0.001) and (C) peak atrial longitudinal strain (PALS) and left atrial fractional area change (FAC) (r=0.746, *p*<0.001) in the control (white) and hypertrophic cardiomyopathy groups (blue).

CHAPTER V

DISCUSSION

Part I: General information

1.1 Signalment and physical examination findings

Thirty-seven cats were included in the study: Twenty control cats and seventeen HCM cats. The general characteristics of the control and HCM groups are summarized in Table 1. Age, body weight, heart rate, and systolic blood pressure did not significantly difference between the control and HCM groups. Male and domestic shorthair cats were overrepresented in the control and HCM groups. The mean age of the HCM group in this study was five years old. This result is in agreement with a previous study suggesting that HCM usually develops in male middle-age cats (Nelson and Couto, 2009; Visser et al., 2017; Fox et al., 2018). The vertebral heart score (VHS) of the HCM group was significantly higher than that of control group. Nearly 50 % of the HCM group in this study had arterial thromboembolism (ATE) suggesting that HCM cats had a high risk to develop ATE. This result is in agreement with previous studies reporting that 24% of HCM cats had developed ATE. Those studies suggested that HCM cats may develop ATE secondary to left atrial dilation and left auricular dysfunction. When the left atrium function decreases, the blood stasis within the left atrium may be occurred resulting in thrombus formation. Eventually arterial thromboembolism may develop (Hogan, 2017; Fox et al., 2018).

1.2 Complete blood count and blood chemistry profile values

Complete blood count

The means of all complete blood count values in the control and HCM groups were within the normal range. However, the number of neutrophils was significantly higher in the HCM group compared to that in the control group. An increase in neutrophil numbers may be secondary to stress reaction in HCM cats (Fincel and Hill, 1983). Interestingly, the number of neutrophils was increased in HCM cats affected with ATE suggesting that not only stress but also inflammation secondary to ischemic injury from ATE (Hogan, 2017) may be the cause of an increase in neutrophil numbers in HCM cats in this study.

Blood chemistry profile values

The mean of plasma alanine transferase (ALT) concentration was significantly higher in the HCM group than that in the control group. The mean of plasma ALT concentration of the HCM group was higher than the normal range approximately 2.3 folds. The result of this study showed that the plasma ALT concentration was increased in HCM cats affected with ATE compared to those without ATE. An increase of plasma ALT concentration in the HCM group may be secondary to muscle damage or liver injury in cats affected with ATE (Kang et al., 2015).

Part II: Echocardiography

2.1 Conventional echocardiography

Left ventricular diastolic function is known to be associated with HCM cats. Left ventricular diastolic function can be assessed by pulsed-wave spectral Doppler echocardiography and tissue Doppler imaging including transmitral flow, isovolumic relaxation time, pulmonary venous flow, and myocardial motion (Boon, 2011). According to the result of pulsed-wave Doppler echocardiography in the present study, peak velocity of early diastolic transmitral flow (E), peak velocity of systolic pulmonary vein (S) and peak velocity of diastolic pulmonary vein flow (D) in the HCM group were decreased suggesting changes in diastolic function in HCM cats.

Left atrial dilatation and dysfunction in myocardial disease have been previously reported in humans (Leung et al., 2008), dogs (Baron et al., 2017), and cats (Smith and Dukes-McEwan, 2012; Linney et al., 2014). The present study showed that fractional shortening of the left atrium (LA-FS) and left atrial ejection fraction (LA-EF) were lower in the HCM group compared to the control group. These findings were consistent with a previous study in HCM cats (Linney et al., 2014). Percentage of left atrial fractional area change (FAC) was reduced in HCM cats compared to normal cats in the present study. A similar result was found in cats with myocardial disease (Schober and Maerz, 2006). These results suggest that HCM cats have not only left ventricular diastolic dysfunction but also impaired LA function.

2.2 Two-dimensional speckle tracking echocardiography

Two-dimensional speckle tracking echocardiography (2D-STE) is a novel echocardiographic technique that can be used to assess the LA longitudinal strain in dogs (Baron et al., 2017; Caivano et al., 2018; Dermlim et al., 2019) and humans (Cianciulli et al., 2010; Cameli et al., 2012; Todaro et al., 2012; Ahmed et al., 2015). This technique has been used to evaluate the left ventricular myocardial function in cats with adequate repeatability (Sugimoto et al., 2015; Takano et al., 2015; Suzuki et al., 2017). To our knowledge, no study focusing on assessment of the LA function in feline HCM by using 2D-STE has been reported.

The peak atrial longitudinal strain (PALS) assessed by 2D-STE provides the longitudinal deformation of the left atrium during the reservoir phase (Cianciulli et al., 2010; Cameli et al., 2012). The result of this study showed that PALS was lower in the HCM group than in the control group. The lowest atrial longitudinal strain was found at the LA roof. It is possible that the LA roof is closed to the mediastinum which may be limited the movement of this region (Rimbaş et al., 2015). The longitudinal strain of all LA regions were reduced in the HCM group suggesting the global LA functional changes in cats affected with HCM.

2.3 Left atrial function between 3 subgroups categorized by left atrial diameter

Interestingly, the present study showed that changes in PALS, LA-FS, LA-EF, and FAC were found in HCM cats with both normal LA size and enlarged LA. This finding suggests that the poor performance of the LA function in HCM cats does not depend on the LA size. Moreover, the change in the LA function may occur before the LA structural change.

2.4 Left atrial function between two subgroups within HCM group categorized by comorbidity with arterial thromboembolism

Arterial thromboembolism (ATE) is known to be associated with underlying myocardial disease. This study found that almost 50% in the HCM group had ATE. HCM cats with ATE had poorer LA function than those without ATE. The LA diameter was not different between HCM cats with and without ATE. These results suggest that the

development of ATE may depend on LA function but not LA size. It is possible that an impairment of LA function may increase the risk of blood stasis and ATE development.

Part III: Correlation

3.1 The correlation of the peak atrial longitudinal strain and echocardiographic values assessed by conventional echocardiography in entire population

There was moderate negative correlation between the peak atrial longitudinal strain (PALS) and thickness of left ventricular wall at diastole. This finding suggests that left ventricular wall thickness relate to left atrial function. In humans, a more impaired LA function was found in subjects with overt HCM and a greater extent of LV fibrosis (Farhad et al., 2017). The present study found that there was no correlation between PALS and LA diameter suggesting that reservoir function of LA is not related to LA size.

3.2 The correlation of the peak atrial longitudinal strain and LA function parameters assessed by conventional echocardiography in entire population

The peak atrial longitudinal strain (PALS) assessed by two-dimensional speckle tracking (2D-STE) correlated with LA function parameters assessed by conventional echocardiography. This result suggests that PALS is another method that can be used to evaluate the LA function. Previous studies suggested that 2D-STE is less load-dependent and high repeatability method than conventional echocardiography (Roşca et al., 2011; Cameli et al., 2012; Rimbaş et al., 2015).

Based on ANCOVA, PALS was not affected by age, breeds, and sex. However, breeds effected FAC assessed by conventional echocardiography. These findings suggest that PALS may be a more suitable parameter to evaluate the LA function in cats than parameters assessed by conventional echocardiography.

Part IV: The measurement variability

The present study demonstrated that 2D-STE can be used to evaluate changes in the LA function in HCM cats with high repeatability and reproducibility. Intra- and inter-observer variability of PALS were clinically acceptable (CV ≤ 15%). Similar results have been reported in humans (Ahmed et al., 2015) and dogs (Baron et al., 2017; Dermlim et al., 2019).

In this present study has some limitations that should be considered. First, 2D-STE software was created for analyzing the left ventricular function in humans; therefore, it may have some limitations in the LA function assessment in cats. Second, it was challenged to trace the thin feline LA wall. Increasing size by increasing depth and increasing gain of images may help to visualize the LA wall. Finally, 2D-STE requires high quality images that are difficult to obtain in cats with very fast heart rate. Cats should be handled in a less stressful condition to reduce the heart rate.

In conclusions, the peak longitudinal strain of LA assess by 2D-STE can be used to evaluate changes in the LA function in HCM cats. This method is repeatability and reproducibility and may be useful for diagnosis and management cats affected with HCM.

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APPENDIX

Appendix A: Data of the control group

No.	NAME	AGE (year)	BREED	SEX	WEIGHT (kg.)	HR (bpm)	VHS	SBP (mmHg)
1	Tiger	3	American Shorthair	Mc	5.2	227	7.8	146
2	บราวนี่	5	American Shorthair	M	3.5	212	8	143
3	แสนดี	3	American Shorthair	F	2.8	200	7.5	133
4	Leo	3	American Shorthair	M	5	200	8	158
5	แม่	10	Siamese	Fs	3.14	180	7.8	152
6	โล้น	4	Sphinx	Mc	4.95	220	7.8	118
7	บักเขียบ	4	American Shorthair	M	5.5	220	7.8	97
8	ฟ้าวกราร์	2	Scottish fold	Mc	5.9	192	7	160
9	ปังเย็น	2	Exotic Shorthair	M	3.2	180	7.7	133
10	แก่เฒ่า	8	DSH	Mc	4.06	192	7.8	147
11	Lovely may	9	DSH	Fs	4.14	245	7	92
12	เชสเตอร์	12	DSH	Mc	4.12	212	7.2	145
13	Creamy	7	DSH	Mc	4.4	234	7	91
14	Elvis	9	DSH	Mc	5.24	228	7.2	113
15	แกสบี้	5	Scottish fold	M	4.1	192	8.4	130
16	ลูกชิ้นปลา	4	DSH	Mc	5.96	204	7.3	125
17	ถังเงิน	2	DSH	Mc	5.6	200	7	121
18	ถังทอง	2	DSH	Fs	4.3	235	7.5	123
19	มุมิ	3	DSH	F	3.8	176	7.8	119
20	Pauline	4	DSH	F	4.5	189	7.9	121

Abbreviations: bpm: beat per minute; DSH: domestic shorthair; F: intact female; Fs: spayed female; HR: heart rate; M: intact male; Mc: castrated male SBP: systolic blood pressure; VHS: vertebral heart score

Appendix B: Data of the hypertrophic cardiomyopathy group

No.	NAME	AGE (year)	BREED	SEX	WEIGHT (kg.)	HR (bpm)	VHS	SBP (mmHg)	CHF	ATE	SEC
1	อั่งเปา	11	Persia	Mc	4.3	208	7.6	121	no	no	no
2	เพชร	5	DSH	Fs	4.8	200	7.8	none	yes	Yes	no
3	มาเฟีย	2	DSH	Mc	5.4	250	8.5	130	yes	yes	yes
4	สามสี	14	DSH	Fs	2.8	220	7.5	110	no	no	no
5	มีมี่	3	Persian	F	2	220	8.2	123	no	yes	no
6	แบล็คแมน	2	Persian	M	4.1	180	9.1	90	no	yes	no
7	Feeling	4	Exotic Shorthair	Mc	6	212	7.5	120	no	no	no
8	เหมียว	7	DSH	F	3.3	225	8	100	no	no	yes
9	กะทิ	9	ขาวมณี	Mc	5.6	200	8.1	120	no	no	no
10	ดวงดี	2	DSH	M	4.35	250	7.3	122	no	yes	no
11	ขาว	3	DSH	Fs	3.1	190	7.2	117	yes	yes	yes
12	น้องสี่	3	DSH	F	5.2	164	7.8	120	no	yes	no
13	ช็อกโก้	6	Persian	Mc	3.8	169	8.5	148	no	no	no
14	อัปป้า	3	DSH	Mc	4.74	171	8.1	138	no	no	no
15	ถุงทอง	4	DSH	M	4.5	284	8.2	104	no	no	yes
16	บิ๊ก	4	Persian	Mc	4.32	212	8.1	133	no	no	no
17	มะขาม	3	DSH	F	3.9	200	8.4	60	no	yes	yes

Abbreviations: ATE: arterial thromboembolism; bpm: beat per minute; CHF: congestive heart failure.; DSH: domestic shorthair; F : intact female; Fs : spayed female ; HR: heart rate; M: intact male ;Mc: castrated male; SBP: systolic blood pressure; SEC: spontaneous echo contrast; VHS : vertebral heart score

Appendix C: M-mode echocardiographic values of the control group

No.	NAME	IVSd (mm.)	LVIDd (mm.)	LVPWd (mm.)	IVSs (mm.)	LVIDs (mm.)	LVPWs (mm.)	LA (mm.)	Ao (mm.)	LA:AO	FS (%)
1	Tiger	5.5	14.9	4.1	11.1	5.5	7.5	12.4	11.5	1.08	63.09
2	บราวนี่	5.3	14.5	3.2	8.5	4.9	7.3	10.7	9.8	1.09	66.21
3	แสนดี	5	14	3.7	6.4	8.6	5.9	12.7	6.8	1.87	38.57
4	Leo	4.9	13.9	3.9	8.7	7	6.4	9.8	10.3	0.95	49.64
5	แม่	3.9	11.3	3.2	6	6.4	6.6	12.2	7.7	1.58	43.36
6	โล้น	5.4	13.2	4.8	7.2	6.6	8.8	15	7.9	1.90	50.00
7	บักเขียบ	3.4	15	2.8	8.1	4.5	7.5	10.5	8.8	1.19	70.00
8	ฟ้วกราร์	3.1	14.5	3.1	7.2	6.1	7.2	11.8	9	1.31	57.93
9	ปังเย็น	3.2	17.3	2.8	6	10	5.5	13.2	10.3	1.28	42.20
10	แก่เฒ่า	3.9	12	3.4	6.8	3.8	7.3	13.7	8.3	1.65	68.33
11	Lovely may	3.4	13.4	2.6	7.1	3.8	6.8	11.8	7.7	1.53	71.64
12	เชสเตอร์	4.5	14.7	3.2	8.1	5.5	7.5	13.9	9.2	1.51	62.59
13	Creamy	3	12.2	3.8	7.9	5.1	7	11.5	7.7	1.49	58.20
14	Elvis	3.9	15.6	3.2	5.8	6.8	5.8	10.2	10	1.02	56.41
15	แกสบี้	5.3	15.8	4.2	7.7	7.2	9	13.4	10.1	1.33	54.43
16	ลูกชิ้นปลา	4.3	16.7	3	7.7	6	7.1	12.2	8.3	1.47	64.07
17	ถังเงิน	3.4	15.6	3.4	5.3	8.3	7	12.3	7.5	1.64	46.79
18	ถังทอง	5.6	14.5	4.5	5.6	5.8	7.9	13.6	7.9	1.72	60.00
19	มุมิ	4.1	11.5	3.9	7	6.6	6	10.2	7.1	1.44	42.61
20	Pauline	3.6	15.6	3.2	5.3	8.5	6.2	13.3	7.3	1.82	45.51

Abbreviations: Ao: aorta; FS : left ventricular fractional shortening; IVRT: isovolumic (or isovolumetric) relaxation time; IVSd : interventricular septum thickness at end-diastole; IVSs : interventricular septum thickness at end-systole; LA: left atrium, LA:Ao : left atrial and aorta ratio; LVIDd: left ventricular internal dimension at end -diastole; LVIDs: left ventricular internal dimension at end -systole; LVPWd: left ventricular posterior wall thickness at end-diastole; LVPWs: left ventricular posterior wall thickness at end-systole

Appendix D: Spectral Doppler echocardiographic and tissue Doppler imaging values of the control group

No.	NAME	E	A	E/A	IVRT	S	D	Ar	S/D	E'	A'	S'	E'/A'	E/E'
1	Tiger	0.81	0.8	1.01	44	0.48	0.36	0.17	1.09	0.14	0.08	0.09	1.75	5.79
2	บราวนี่	0.76	0.65	1.17	44	0.46	0.38	0.14	1.21	0.08	0.1	0.06	0.80	9.50
3	แสนดี	0.86	0.84	1.02	39	0.35	0.3	0.14	1.17	0.1	0.09	0.06	1.11	8.60
4	Leo	0.75	0.58	1.29	44	0.32	0.27	0.18	1.19	0.1	0.09	0.08	1.11	7.50
5	แม่	0.71	0.38	1.87	56	0.39	0.42	0.11	0.93	0.07	0.06	0.06	1.17	10.14
6	โล้น	1.28			38	0.53	0.32	0.1	1.66	0.19	0.12	0.08	1.58	6.74
7	บักเขียบ	0.86	0.78	1.10	44	0.43	0.31	0.16	1.39	0.05	0.04	0.03	1.25	17.20
8	ฟ้วกราร์	0.64	0.6	1.07	44	0.47	0.4	0.14	1.18	0.13	0.1	0.08	1.30	4.92
9	ปังเย็น	0.62	0.52	1.19	39	0.53	0.38	0.12	1.18	0.14	0.08	0.07	1.75	4.43
10	แก่เฒ่า	0.96	0.61	1.57	56	0.59	0.46	0.15	1.18	0.09	0.09	0.07	1.00	10.67
11	Lovely may	0.94	0.69	1.36	37	0.58	0.41	0.1	1.18	0.12				7.83
12	เชสเตอร์	0.89	0.52	1.71	43	0.44	0.36	0.14	1.18	0.12		0.08		7.42
13	Creamy	1.22	0.78	1.56	47	0.54	0.32	0.23	1.18	0.19		0.07		6.42
14	Elvis	0.46	0.68	0.68	47	0.54	0.38	0.12	1.18	0.16		0.11		2.88
15	แกสบี้	0.82	0.59	1.39	46	0.36	0.31	0.12	1.16	0.1	0.08	0.07	1.250	8.20
16	ลูกชิ้นปลา	0.79	0.5	1.58	64	0.38	0.35	0.1	1.09	0.13	0.13	0.09	1.000	6.08
17	ถังเงิน	0.76	0.5	1.52	50	0.58	0.48	0.17	1.21	0.09	0.05	0.07	1.800	8.44
18	ถังทอง	1.04			47	0.56	0.36	0.18	1.56	0.13		0.1		8.000
19	มุมิ	0.8	0.45	1.78	42	0.41	0.23	0.11	1.78	0.09	0.06	0.06	1.500	8.89
20	Pauline	0.7	0.55	1.27	43	0.32	0.23	50	1.39	0.1	0.06	0.06	1.667	7.0

Abbreviations: A : peak velocity of early diastolic transmitral flow; A': peak velocity of diastolic mitral annular motion as determined by pulsed wave Doppler; Ao: Aorta; AR : peak velocity of pulmonary vein flow reversal at atrial contraction; D: peak velocity of diastolic pulmonary vein flow; E : peak velocity of early diastolic transmitral flow; E' : peak velocity of early diastolic mitral annular motion as determined by pulsed wave Doppler; E:A : ratio of E to A; E'A' : ratio of E' to A'; E:E' : ratio of E to E'; S : peak velocity of systolic pulmonary vein ; S' : peak velocity of systolic mitral annular motion as determined by pulsed wave Doppler; S:D :ratio of S to D

Appendix E: The left atrial functional values assessed by conventional echocardiography and two-dimensional speckle tracking echocardiography of the control group

No.	NAME	LA-FS(%)	LA-EF(%)	LAAmax (cm^2)	LAAmin (cm^2)	FAC (%)	Septal			Lateral			PALS (%)
							Base	Mid	Roof	Base	Mid	Roof	
1	Tiger	39.52	50.3	1.15	0.24	79.11	66.57	44.87	13.90	8.13	19.73	22.37	28.97
2	บราวนี่	26.55	64.57	1.03	0.32	69.24	7.47	28.80	4.00	6.50	13.33	9.60	11.27
3	แสนดี	25.98	87.6	1.39	0.31	78.31	35.73	34.07	7.70	20.17	86.03	84.10	44.37
4	Leo	20.59	64.84	1.59	0.42	73.48	-26.90	-36.47	0.60	72.90	31.87	85.37	25.37
5	แม่	36.04	84.17	0.79	0.22	72.72	49.53	58.30	26.23	14.23	31.00	30.17	34.00
6	โล้น	23.91	82.7	1.84	0.57	69.14	38.97	55.10	27.27	29.07	63.23	77.03	47.17
7	บักเขียบ	24.79	53.6	1.30	0.59	54.06	19.17	30.17	35.53	25.07	18.43	12.37	22.53
8	ฟ้วกราร์	19.51	55	1.61	0.57	64.61	15.50	24.83	30.37	33.23	4.13	-17.03	16.60
9	ปังเย็น	19.51	78.84	1.33	0.43	67.67	28.43	23.93	39.43	24.23	37.07	21.93	28.10
10	แก่เฒ่า	25.37	63.44	1.04	0.43	58.65	85.30	54.77	-50.03	-11.87	39.33	41.53	29.90
11	Lovely may	23.73	90.8	1.20	0.50	58.33	14.30	18.20	66.10	56.30	18.20	-14.10	28.10
12	เชสเตอร์	25.17	64.67	0.97	0.17	81.71	10.43	60.27	32.83	48.40	28.53	37.47	35.47
13	Creamy	32.48	87.43	1.33	0.38	71.07	23.87	29.07	5.73	35.77	21.90	9.87	20.47
14	Elvis	17.71	63.1	1.06	0.40	61.81	23.47	40.10	-2.53	-13.90	3.90	47.47	26.40
15	แกสบี้	29.11	44	1.87	1.06	43.10	16.87	24.70	20.97	4.23	18.17	37.37	20.23
16	ลูกชิ้นปลา	44.70	68.63	1.69	0.72	57.16	36.67	40.87	10.50	16.70	27.60	43.77	28.23
17	ถังเงิน	25.00	58.63	1.08	0.51	50.75	24.17	29.90	7.80	7.93	24.70	44.80	23.10
18	ถังทอง	31.97	71.47	1.02	0.39	61.55	22.50	28.20	17.77	15.67	18.87	17.30	20.73
19	มุมิ	23.15	65.1	0.96	0.57	40.23	41.33	53.87	20.27	-14.20	13.67	37.73	26.33
20	Pauline	30.77	83.17	1.25	0.47	61.95	64.23	58.07	16.60	28.73	68.60	87.53	53.47

Abbreviations: FAC: left atrial fractional area change; LAA: left atrial area; LA-EF: left atrial ejection fraction; LA-FS: left atrial fractional shortening; PALS: peak atrial longitudinal strain

Appendix F: Conventional echocardiographic parameters of the hypertrophic cardiomyopathy group

No.	NAME	IVSd (mm.)	LVIDd (mm.)	LVPWd (mm.)	IVSs (mm.)	LVIDs (mm.)	LVPWs (mm.)	LA (mm.)	Ao (mm.)	LA:AO	FS (%)
1	อั่งเปา	6.1	14.5	3.8	7.7	7.5	7	15.4	10.9	1.41	48.28
2	เพชร	4.9	9.4	6.4	6	4.3	10.2	15.4	7	2.20	54.26
3	มาเฟีย	7.5	11	7.2	8.1	4.4	11.6	20.2	8.8	2.30	60.00
4	สามสี	6	11	4	7	4	8	11	6	1.83	63.64
5	มีมี่	7.5	8.1	5.5	8.8	3.9	5.8	10.4	7.2	1.44	51.85
6	แบล็คแมน	8.7	10.3	9.4	10	7.5	10.9	20.1	10.2	1.97	27.18
7	Feeling	6.6	13.6	5.3	8.8	5.3	7.7	15.1	11.4	1.32	61.03
8	เหมียว	8	19.1	2.4	4.4	13.6	4.6	17.1	6.1	2.80	28.80
9	กะทิ	6	16.2	4.6	9.7	6.8	7	17.6	9.4	1.87	58.02
10	ดวงดี	6.1	15.1	5.8	11.4	7.5	7.5	14.3	7.9	1.81	50.33
11	ขาว	6.4	9.6	4.8	7.1	5.3	6.4	16.4	6	2.73	44.79
12	น้องสี่	7.9	8.8	7.5	10.8	5	9.4	12.1	7	1.73	43.18
13	ช็อกโก้	8.1	10.9	6.2	11.3	4.9	7.9	17.1	9.4	1.82	55.05
14	อัปป้า	6.7	14.1	6.8	9.8	5.3	10.5	14.5	7	2.07	62.41
15	ถุงทอง	7.5	15	4.3	8.8	7.9	8.1	16.4	9.4	1.74	47.33
16	บิ๊ก	7.9	13.5	5.6	8.1	6	10.2	13.2	9.7	1.36	55.56
17	มะขาม	9.2	10.2	4.9	9	3.9	7.3	18.1	7.7	2.35	61.76

Abbreviations: Ao: aorta; FS : left ventricular fractional shortening; IVRT: isovolumic (or isovolumetric) relaxation time; IVSd : interventricular septum thickness at end-diastole; IVSs : interventricular septum thickness at end-systole; LA: left atrium, LA:Ao : left atrial and aorta ratio; LVIDd: left ventricular internal dimension at end -diastole; LVIDs: left ventricular internal dimension at end -systole; LVPWd: left ventricular posterior wall thickness at end-diastole; LVPWs: left ventricular posterior wall thickness at end-systole

Appendix G: Spectral Doppler echocardiographic and tissue Doppler imaging values of the hypertrophic cardiomyopathy group

No.	NAME	E	A	E/A	IVRT	S	D	Ar	S/D	E'	A'	S'	E'/A'	E/E'
1	อั่งเปา	0.51	1.04	0.49	43	0.42	0.43	0.2	0.98	0.09	0.07	0.05	1.29	5.67
2	เพชร	0.49	0.15	3.27	64	0.19	0.17	0.06	1.12	0.05	0.04	0.05	1.25	9.80
3	มาเฟีย	0.49	0.65	0.75	36	0.27	0.19	0.11	1.42	0.07	0.12	0.06	0.58	7.00
4	สามสี	0.73	0.48	1.52	46	0.62	0.54	0.2	1.15	0.13	0.12	0.17	1.08	5.62
5	มีมี่	0.58	0.23	2.52	44	0.22	0.2	0.14	1.1	0.03	0.03	0.04	1.00	19.33
6	แบล็คแมน	0.65	0.48	1.35	56	0.11	0.1	0.23	1.1	0.02	0.03	0.04	0.67	32.50
7	Feeling	0.61	0.33	1.85	39	0.38	0.29	0.1	1.31	0.16	0.09	0.09	1.78	3.81
8	เหมียว	0.99	0.54	1.83	38	0.32	0.37	0.25	0.86	0.1	0.07	0.07	1.43	9.90
9	กะทิ	0.7	0.44	1.59	56	0.32	0.23	0.12	1.39	0.09	0.05	0.06	1.80	7.78
10	ดวงดี	0.75	0.34	2.21	42	0.27	0.22	0.17	1.23	0.1	0.06	0.05	1.67	7.50
11	ขาว	0.94	0.54	1.74	36	0.19	0.18	0.16	1.06	0.08	0.05	0.04	1.60	11.75
12	น้องสี่	0.28	0.21	1.33		0.16	0.15	0.12	1.07	0.03	0.03	0.04	1.00	9.33
13	ช็อกโก้	0.48	0.47	1.02	44	0.42	0.23	0.14	1.83	0.06	0.05	0.05	1.20	8.00
14	อัปป้า	0.7	1.09	0.64	61	0.33	0.28		1.18	0.11	0.14	0.11	0.79	6.36
15	ถุงทอง	0.81	1.07	0.76						0.12	0.15	0.09	0.80	6.75
16	บิ๊ก	0.53	0.73	0.73	53	0.5	0.39	0.19	1.28	0.06	0.07	0.08	0.86	8.83
17	มะขาม	0.44	0.35	1.26	53	0.23	0.2	0.14	1.15	0.08	0.1	0.08	0.80	5.50

Abbreviations: A : peak velocity of early diastolic transmitral flow; A': peak velocity of diastolic mitral annular motion as determined by pulsed wave Doppler; Ao: Aorta; AR : peak velocity of pulmonary vein flow reversal at atrial contraction; D: peak velocity of diastolic pulmonary vein flow; E : peak velocity of early diastolic transmitral flow; E' : peak velocity of early diastolic mitral annular motion as determined by pulsed wave Doppler; E:A : ratio of E to A; E'A' : ratio of E' to A'; E:E' : ratio of E to E'; S : peak velocity of systolic pulmonary vein ; S' : peak velocity of systolic mitral annular motion as determined by pulsed wave Doppler; S:D :ratio of S to D

Appendix H: The left atrial functional values assessed by conventional echocardiography and two-dimensional speckle tracking echocardiography of the hypertrophic cardiomyopathy group

No.	NAME	LA-FS (%)	LA-EF (%)	LAAmax (cm^2)	LAAmin (cm^2)	FAC (%)	Septal			Lateral			PALS (%)
							Base	Mid	Roof	Base	Mid	Roof	
1	อั๋งเปา	23.08	84.07	1.37	0.62	54.27	34.40	62.73	26.40	28.13	47.10	30.77	34.17
2	เพชร	3.25	27.77	1.73	1.49	13.66	10.17	14.70	7.57	-0.47	-0.03	8.23	7.30
3	มาเฟีย	13.46	20.63	3.56	2.73	22.55	0.57	5.07	0.13	0.50	2.07	6.97	4.47
4	สามสี	20.00	70.97	0.80	0.41	48.73	15.47	23.93	20.43	21.53	18.73	-17.83	14.27
5	มีมี่	19.00	30.03	1.06	0.75	29.57	9.73	6.30	0.00	-2.20	9.07	5.07	6.17
6	แบล็คแมน	1.27	47.27	2.57	1.17	54.70	12.30	18.03	21.73	29.40	24.07	12.33	14.60
7	Feeling	17.48	80.83	1.51	0.53	64.89	15.90	24.70	7.33	28.23	84.23	10.80	28.87
8	เหมียว	21.05	40.8	2.18	1.53	28.63	-5.03	-5.70	7.90	13.50	15.83	17.93	10.03
9	กะทิ	33.52	64.8	2.14	1.16	45.49	14.47	22.00	15.03	19.70	26.77	28.50	19.67
10	ดวงดี	17.48	28.37	2.16	1.83	15.48	0.70	13.23	3.67	-10.97	1.40	14.47	4.90
11	ขาว	4.84	38.3	2.14	1.44	32.32	39.23	26.83	11.23	4.33	1.87	8.63	14.40
12	น้องสี่	4.55	22.77	1.18	1.02	13.84	10.80	3.07	2.80	0.60	-2.90	5.00	4.00
13	ช็อกโก้	16.88	38.93	2.23	1.51	31.87	22.13	17.07	7.83	17.37	22.30	12.07	15.27
14	อัปป้า	19.35	36.53	1.21	0.91	24.83	11.50	13.90	7.00	-4.50	6.67	16.53	8.40
15	ถุงทอง	15.06	71.67	2.45	0.81	66.65	24.47	27.43	-1.20	2.87	31.27	37.67	19.37
16	บิ๊ก	12.82	58.67	1.53	0.84	45.18	14.63	24.93	7.33	0.03	17.03	7.47	13.33
17	มะขาม	10.99	21.17	2.38	2.10	11.64	0.00	6.67	8.37	4.00	4.60	7.97	4.57

Abbreviations: FAC: left atrial fractional area change; LAA: left atrial area; LA-EF: left atrial ejection fraction; LA-FS: left atrial fractional shortening; PALS: peak atrial longitudinal strain

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