PREVALENCE OF FELINE CARDIOMYOPATHIES AT THE CLINIC FOR INTERNAL DISEASES OF THE VETERINARY FACULTY OF ZAGREB FROM 2017 TO 2022

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Prevalence of feline cardiomyopathies at the Clinic for internal diseases of the Veterinary Faculty of Zagreb from 2017 to 2022

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ABBREVIATIONS

IVS – interventricular septum

VC – vena cava

RA – right atrium

RV – right ventricle

LA – left atrium

LV – left ventricle

AV – atrioventricular

SA – sinoatrial

HR – heart rate

ECG – electrocardiogram

EDV – end diastolic volume

ESV – end systolic volume

CO – cardiac output

SV – stroke volume

bpm – beats per minute

ACVIM – American College of Veterinary Internal Medicine

CM – cardiomyopathy

WHO – World Health Organization

HCM – hypertrophic cardiomyopathy

RCM – restrictive cardiomyopathy

DCM – dilated cardiomyopathy

ARVCM – arrhythmogenic right ventricular cardiomyopathy

UCM – undetermined cardiomyopathy

NCM – nonspecific phenotype cardiomyopathy

MyBPC3 – myosin binding protein

CHF – congestive heart failure

TE – thromboembolism

SAM – systolic anterior movement

DLVOTO – dynamic left ventricular outflow tract obstruction

VPC – ventricular premature complex

POC – point-of-care

NT-proBNP – amino pro-brain natriuretic peptide

cTnI – cardiac troponin I

tDi – tissue Doppler imaging

LA:Ao – left atrium diameter to aortic diameter ratio

PO – per os

ACEi – angiotensin converting enzyme inhibitor

ATE – arterial thromboembolism

PE – pulmonary oedema

PLE – pleural effusion

LVH – left ventricular hypertrophy

TMT – transient myocardial thickening

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1. INTRODUCTION

A cardiomyopathy is a primary disorder of the heart muscle, involving an abnormal structure and functionality. As defined by the American College of Veterinary Internal Medicine consensus, there are five types of cardiomyopathies, classified according to the phenotype: hypertrophic, restrictive, dilated, right ventricular arrhythmogenic, and non-specific (FUENTES et al., 2020). Cardiomyopathies represent the most common cardiac disease in cats, and more specifically hypertrophic cardiomyopathies, being the most prevalent type, may affect up to 15% of the cat population (KITTLESON and COTE, 2021a; KITTLESON and COTE, 2021b).

The purpose of this retrospective study is to get a better insight on this disease at the Clinic for Internal Diseases in the Veterinary Faculty of Zagreb, Croatia. By collecting data and extracting statistics about epizootiology, clinical findings, and treatment protocol, only to name a few, the tendencies associated with cardiomyopathies in cats will be inspected and, ultimately, compared with the results of previous studies. As this condition is quite common among our pet cats, diving deeper into this topic is valuable. This paper aspires to be of service to practising and future veterinarians, in their approach to diagnosing and handling cardiomyopathy patients.

2. REVIEW OF THE RESULTS OF PREVIOUS RESEARCH

2.1. Feline heart anatomy and physiology

The heart is the central organ of the cardiovascular system, serving as a pump. It is located in the mediastinum and extends from the third and seventh ribs (KÖNIG and LIEBICH, 2014). The weight of the heart varies from 9 to 12 grams in adult female cat and 11 to 18 grams in adult male cat (HUDSON and HAMILTON, 2010). According to KÖNIG and LIEBICH (2014), the heart represents approximately 0.75% of the body weight.

The heart is covered by the pericardium, which is a fibroserous membrane. The pericardium consists of a fibrous part and a serous part. The fibrous layer represents the outer part and is made of a tough connective tissue. It is covered by the pericardial mediastinal pleura. The fibrous layer extends caudally and attaches with the muscular diaphragm, forming the sternopericardial ligament. The heart is invaginated within the serous layer, which is like a sac. The serous membrane has two layers itself: the visceral pericardium, or epicardium, which is directly in contact with the heart muscle, and the parietal pericardium, in contact with the fibrous pericardium. The serous layers secrete a small amount of fluid, which is contained in the pericardial cavity. This cleft is located between the visceral and the parietal pericardium. It facilitates movement of the heart. The pericardium can be removed surgically, so it is not an essential organ. However, its function is to stabilize the heart, maintain its shape, and protect it from external friction and inflammation (HUDSON and HAMILTON, 2010; KÖNIG and LIEBICH, 2014).

The cat's heart is pear-shaped. Its base is directed dorsocranially, and its apex is directed caudoventrally, with a slight deviation to the left. On the surface of the heart muscle, three grooves are visible, which reveal the borders of the internal compartments. Cranially, at the base, there is the coronary groove, separating atria from ventricles. This groove contains a lot of fat (Figure 2). On the left craniolateral and the right caudolateral surfaces, two interventricular grooves are formed by the junction of the interventricular septum (IVS) with the external wall, respectively the paraconal groove (Figure 1) and the subsinosal groove. Both longitudinal grooves originate from the coronary groove, and they meet at the heart apex. All three grooves remain even if the heart goes through enlargement. At the base of the heart, the auricles of the atria are visible (Figure 1 and 2) and surround the blood vessels entering and exiting the heart. On the left side of the base of the heart, the pulmonary trunk emerges from the right ventricle and bends dorsally and caudally (Figure 1). It then divides into left and right

pulmonary arteries. In the middle of the heart base, the aorta emerges from the left ventricle (Figure 1). It continues cranially and dorsally until it rotates caudally and to the left, creating the aortic arch and then the descending aorta. The ligamentum arteriosum is a remnant of the ductus arteriosus from the foetal stage. It is found where the two large blood vessels exiting the heart are in closest proximity, connecting the dorsomedial surface of the pulmonary trunk with the ventrolateral surface of the ascending aorta. The cranial and caudal vena cava (VC) enter the right atrium at the cranial and right portion of the heart base. On the other hand, the pulmonary veins enter the left atrium at the caudal and left base of the heart. There are between 5 and 7 pulmonary veins (HUDSON and HAMILTON, 2010).

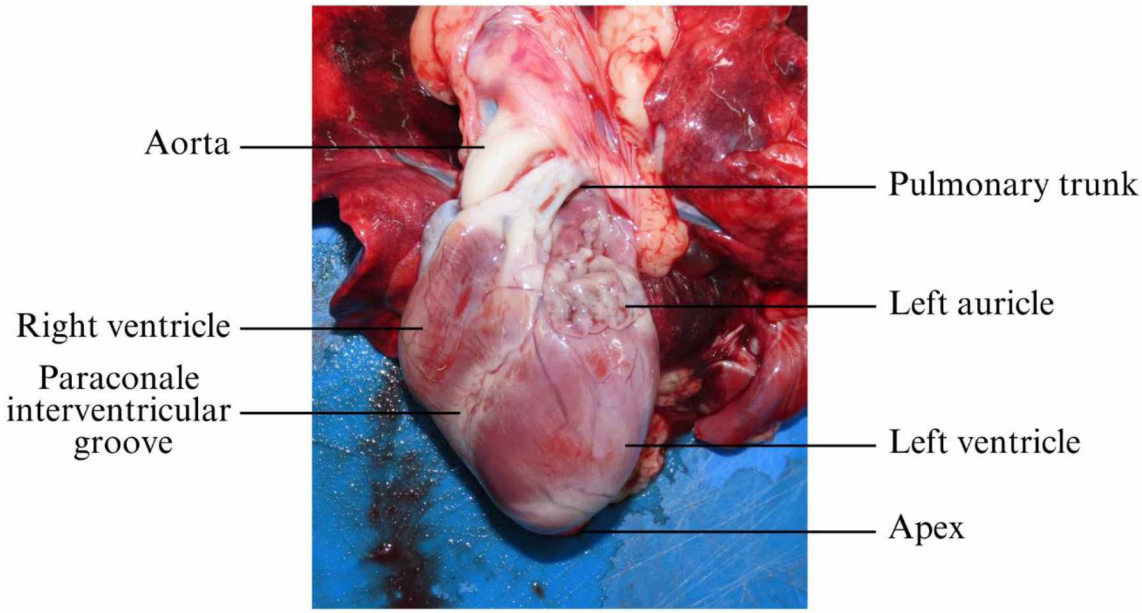

Figure 1. Left side of a cat's heart (courtesy of the Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Zagreb).

The heart is made of three layers: the epicardium, the outermost layer and part of the pericardium, the endocardium, the innermost layer, lining the cavities, and in between those two layers, the myocardium (FOX et al., 1999). This latter is the heart muscle, which forms four chambers: the right atrium (RA), the right ventricle (RV), the left atrium (LA), and the left ventricle (LV). The RA receives venous blood from the cranial VC, the caudal VC, and the coronary sinus. This later collects the blood from the heart itself and opens in the RA ventrally to the caudal VC. The opening of the cranial VC is located dorsocranially. The intervenous tubercle, a ridge between the openings of both VC, directs the blood flow towards the RV. The interatrial septum separates the right and the left atria. It also holds a small depression, which is the remnant of the foramen ovale from embryonic development. The RA extends into a blind-

end projection cranially and ventrally, called the right auricle (Figure 2). The surface of the right auricle is covered with the pectinate muscles, while the rest of the RA wall is smooth (HUDSON and HAMILTON, 2010). The wall of the RA is relatively thin (FOX et al., 1999). The blood from the RA transits to the RV via the atrioventricular (AV) valve, also called the tricuspid valve (Figure 2). This valve is composed of three cusps. Each of them is reinforced by the chorda tendineae, connective tissue on the free border of the cusps bound by the papillary muscles to the ventricular wall (Figure 2) (KÖNIG and LIEBICH, 2014). The RV is U-shaped and formed by an inflow tract from the tricuspid valve to the apex, and an outflow tract from the apex towards the outflow tract, called the conus arteriosus (Figure 2). At the end of this structure, the pulmonic valve is the gateway from the RV to the pulmonic trunk. It is composed of three semilunar cusps, with hallow sacs on the arterial side, called the pulmonary sinuses. The RV is separated from the LV by the IVS. The free wall and the IVS are covered with some muscle prominence called trabeculae carneae (Figure 2). Besides, they are connected by the trabeculae septomarginalis (Figure 2), near the apex. This muscle strand contains the Purkinje fibres. There may be more than one trabecula septomarginalis (HUDSON and HAMILTON, 2010). The LA is similar in shape and composition to the RA. However, the LA receives the openings of multiple pulmonary veins. Besides, the blood is projected to the LV via the left AV valve, also called mitral or bicuspid valve. Contrary to the right AV, the mitral valve is composed of only two cusps. But likewise, they are stabilized by the chordae tendineae and the papillary muscles. The LV has a conical shape, and its wall is approximately three times thicker than the RV wall (HUDSON and HAMILTON, 2010). According to HUDSON and HAMILTON (2010), there may be trabeculae carneae and trabecula septomarginalis, while KÖNIG and LIEBICH (2014) states that there are two trabeculae septomarginalis, and FOX et al. (1999) claims that there can be a great variation in the number and morphology of trabecula septomarginalis in the LV of cats. The blood exits the LV into the aorta via the aortic valve, which is made of 3 cusps. They are more developed than the pulmonic valve and each of them are backed with the aortic sinuses (HUDSON and HAMILTON, 2010).

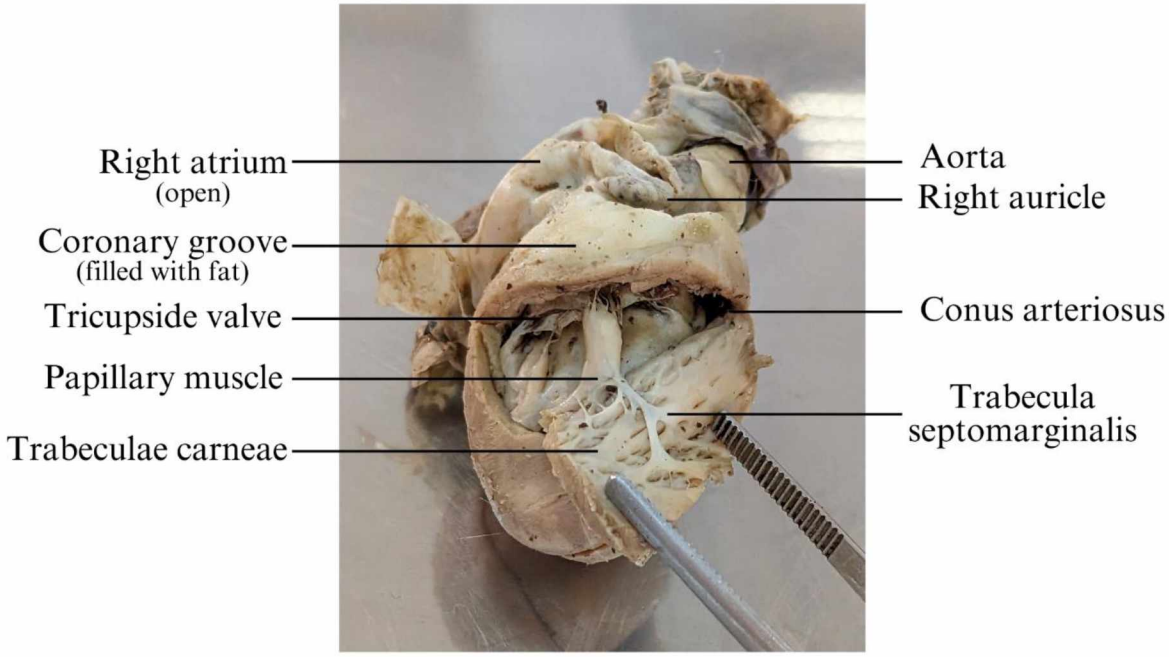

Figure 2. Right ventricle (open) of a cat's heart (fixed in formalin) (courtesy of the Department of Anatomy, Histology and Embriology, Faculty of Veterinary Medicine, University of Zagreb).

The myocardium holds two types of muscle cells: mostly contractile cells and, in a smaller amount, specialized excitatory and conductive fibres. The cardiac muscle cells are quite specific as they form gap junctions at each intercalated disc, allowing "communication" and free diffusion of ions. Thus, the action potential travels with ease between muscle fibres. Consequently, the heart muscle is called a syncytium, and it is composed of two distinct syncytia: the atrial one and the ventricular one. The conduction throughout the syncytia is achieved by the specialized excitatory and conductive fibres. Those muscle fibres have weak contractibility. They include: the sinoatrial (SA) node, the AV node, the bundle of His, and the Purkinje fibres.

The SA node is in the wall of the RA below the opening of the cranial VC. The SA is the pacemaker of the heart and controls the heart rate (HR). Indeed, it has the ability of self-excitation, produces action potentials, and has the fastest rate of spontaneous depolarization. Its fibres connect directly with the atrial muscle, so any action potential produced by the SA node is spread instantly to the wall of both atria. The internodal pathways lead the impulse from the SA node to the AV node. The AV node is situated in the ventral right side of the interatrial septum. The AV node causes a delay in the conduction to the ventricles, allowing atrial contraction first. In addition, there is no other pathway to the ventricles from the atria, thus this

node is referred to as the "gatekeeper". The impulse is then transmitted to the bundle of His, located within the IVS. The conduction is rapid, and splits into the right and left bundle branches. The right bundle branch leads the impulse into the free wall of the RV, while the left bundle branch splits again in two to cover the thicker wall of the LV. The final specialized fibres are the Purkinje fibres, which form an extensive network and conduct the electrical impulse into the ventricular myocardium. Due to the rapid conduction through the bundle of His and Purkinje fibres, the contraction of the whole ventricle is almost simultaneous (WARE, 2011).

The propagation of the action potentials and the impulse conduction throughout those specialized fibres generates cardiac cyclic activity and allows the heart to act as a pump. As explained by KLEIN (2013), the blood returning from the circulation enters the atria and leads to an increase in the atrial pressure. As the pressure becomes higher than the one in the ventricles, the AV valves open. This allows for most of the blood to flow passively into the ventricles. Then, once the atria contract, shown as P wave on the electrocardiogram (ECG) (FOX et al., 1999), the rest of the blood is pushed into the ventricles. This active flow of the blood represents only 20 to 30% of the ventricular filling. This phase is the mid to late ventricular diastole and, as mentioned previously, represents the ventricular filling. The next phase is the isovolumetric contraction. As the conduction of the impulse goes on, the ventricles start contracting. The semilunar valves are still closed, and due to a momentary backflow of blood from the ventricles towards the atria, the AV valves close. From this interaction, the first heart sound "S1" is heard. In this phase, the atrial pressure is back to low. Next, as the contraction becomes stronger, the pressure in the ventricles increases, until being higher than the arterial pressure. Thus, the semilunar valves open and blood is ejected into the arteries. This stage is called mid to late ventricular systole. It is shown on the ECG as the QRS complex, with the isovolumetric contraction step too. The last phase, called isovolumetric relaxation, consists of the beginning of the ventricles' diastole. The arterial pressure rises, and the ventricular pressure decreases as the blood left the ventricle into the arteries, and experienced a momentary backflow which closes the semilunar valves. This causes the second heart sound "S2" and appears as the T wave on the ECG (KLEIN, 2013).

The function of the heart as a pump for the cardiovascular system is based on the interconnection between multiple factors. Firstly, the preload of the heart represents the degree of myocardial stretch in diastole. It is proportional to the end diastolic volume (EDV). The EDV is the amount of blood present in the ventricles at the end of the filling. Thus, if the systemic veins are dilated for example, blood is pooling within the veins instead of returning to the heart,

making the EDV smaller and ergo the preload lesser. On the other hand, if the venous return increases, more blood will fill the ventricles and stretch the myocardium further. Consequently, there is an inverse relationship between the preload and the blood volume within the systemic veins (FOX et al., 1999). Another factor influencing the preload is the duration of the ventricular diastole, also called the filling time. If the filling time is shorter, the heart does not have the span to stretch. Increased HR decreases filling time and therefore EDV and preload. In contrast to EDV, the end systolic volume (ESV) is the amount of blood remaining in the ventricles right after the contraction phase. Next, the afterload is the amount of resistance the myocardium must overcome in order to eject blood from the ventricles to the aorta and the pulmonary trunk. This resistance is mainly made up of the arterial blood pressure. If the blood pressure increases, the resistance is stronger, and the afterload will be bigger. Another term is contractility. It represents the intrinsic strength of contraction. Inotropic agents can influence this factor. If the contractility increases, the ESV reduces (WARE, 2011).

The pumping activity of the heart is mainly expressed by the cardiac output (CO). According to WARE, (2011), CO is the volume of blood pumped from the ventricles over time. It is equal to the HR multiplied by the stroke volume (SV) and is expressed in ml/min. The SV is the volume ejected at each contraction and is expressed as ml/beat. Moreover, SV can be calculated by subtracting EDV and ESV. Generally, its value is approximately 65% of the EDV. The SV is directly proportional to the contractility and the preload, while it is inversely proportional to the afterload. As stated earlier, HR is determined by the SA node, and according to REECE (2015), the average HR of a cat is between 120 to 140 beats per minute (bpm).

However, many other factors can influence the HR, and those are called positive or negative chronotropic agents. First, the sympathetic nervous system, via the adrenergic receptors on the heart, can increase the HR, but it also enhances myocardial contractility and relaxation, and conduction velocity. Agents acting on the conduction velocity are called dromotropic, and the ones influencing the contractility force are called inotropic. Opposite to the sympathetic nervous system, the parasympathetic stimulation, via the muscarinic cholinergic receptors, slows down the SA node rate. It also causes slower conduction at the AV node and weaker contraction. In general, the vagal effect is stronger, compared to the sympathetic action (WARE, 2011). Moreover, ions also have a big impact on the HR. An increase in potassium levels will decrease the HR. On the other hand, calcium levels have a proportional effect on the HR. Thus, if calcium concentration increases, so will the HR, and inversely. Other positive chronotropic agents are T3 and T4 hormones, due to faster metabolism rate. As for the chemoreceptors,

located at the level of the aortic arch, they can behave as a weak positive chronotropic agent, when they detect hypoxia, hypercapnia, and blood acidosis. Indeed, its main role is actually to increase the respiratory rate (REECE, 2015). Finally, the arterial blood pressure also influences the HR. This reflex depends on the baroreceptors located with the chemoreceptors. If the arterial pressure is elevated, the HR will slow down, and conversely, if the pressure decreases, the HR will accelerate (FOX et al., 1999). According to REECE (2015), the mean arterial blood pressure of a cat is 105 mmHg. It is also important to mention the autoregulation of the heart's function, which is based on the Frank-Starling law. According to FOX et al. (1999), this law states that the greater the volume of blood in the ventricle is right before contraction, the stronger the force of contraction will be. So, the heart can adapt to changes in the blood flow, by modifying the strength of contraction and its frequency.

2.2. Classification and prevalence

According to the American College of Veterinary Internal Medicine (ACVIM) consensus (FUENTES et al., 2020), cardiomyopathy (CM) is defined as a diverse group of disorders of the heart muscle, with abnormal structure and functionality, in the absence of other cardiovascular diseases which could cause such abnormalities. The classification of CM is diversified and often subject to changes. First, CM were classified as primary and secondary, according to aetiology. Primary CM was idiopathic, and secondary was CM with an identifiable cause (FOX et al., 1999). Then, in 1995, the World Health Organization (WHO) proposed the following general categorisation according to dominant pathophysiology: hypertrophic CM (HCM), restrictive CM (RCM), dilated CM (DCM), arrhythmogenic right ventricular CM (ARVCM) and undetermined CM (UCM). Undetermined CM represents all CM that cannot be categorised in any of the four others. This classification is still widely used. Moreover, in 2006, the American Heart Association redefined the primary and secondary classification. Primary CM now refers to disorders confined to the myocardium, while secondary CM also involves different organs, as part of some generalised disturbances. From there, the primary CM are then divided into the five main categories from WHO (ETTINGER et al., 2017). Finally, the ACVIM consensus from 2020 recommends a classification according to the phenotype, with a focus on the clinical aspect, rather than the genetic or etiologic ones. Indeed, contrary to humans, most cases of CM in cats are idiopathic, making a classification based on aetiology meaningless. Overall, the ACVIM consensus kept the five main categories from WHO, except for UCM, and referred to them as phenotypic groups. Undetermined CM is replaced by CM of nonspecific

phenotype (NCM). Yet, one should be aware of the limitations of such categorization since the phenotype in the same cat can change over time, due to the progression of the disease (FUENTES et al., 2020).

Cardiomyopathies are the most common cardiac diseases in cats, and primary CM are more common than secondary ones. The most prevalent type of CM in cats is HCM. Indeed, HCM can affect up to approximately 15% of the cat population, and it represents approximately 60% of all CM cases. The second most common type in cats are RCM, accounting for 20% of cases on average, followed by NCM, whereas DCM (less than 5% of cases) and ARVCM are rare (KITTLESON and COTE, 2021a; KITTLESON and COTE, 2021b; KITTLESON and COTE, 2021c).

2.3. Aetiology and predisposing factors

According to FUENTES et al. (2020), HCM is more likely to be found in older and male cats. Indeed, the prevalence of HCM in older cats, even without hypertension or hyperthyroidism, is 29%, compared to 15% in the general population. However, as stated in ETTINGER et al. (2017), HCM is mostly first diagnosed around 5 to 7 years old. Male cats represent 70% of cases. Besides, as stated by FUENTES et al. (2020), most cats with HCM are mixed breeds, but some breeds such as Maine Coon, Ragdoll, British Shorthair, Persian, Bengal, Sphynx, Norwegian Forest cat, and Birman, are at higher risk of developing HCM.

In fact, while most cases of HCM are idiopathic, two mutations have been identified in cats, precisely in Maine Coon and Ragdoll cats. Both mutations affect the myosin binding protein C (MyBPC3) gene (FUENTES et al., 2020). According to KITTLESON and COTE (2021b), those mutations cause the sarcomere to be more responsive to calcium, making the myocardium hypercontractile. In Ragdoll cats, the mutation R820W leads to this sarcomeric dysfunction, while the mutation affecting Maine Coon cats is MyBPC3-A31P. The ACVIM consensus by FUENTES et al. (2020) reports that the prevalence of the mutation in Maine Coon cats reaches 35 to 42%, while KITTLESON and COTE (2021b) report it at 34 to 41%. KITTLESON and COTE (2021b) also add that 10% of the Maine Coon cats with this A31P mutation are homozygous, and only those cats will develop HCM, while the cats that are heterozygous for the mutation are subclinical and do not develop wall thickening. In those Maine Coon cats homozygous with the MyBPC3-A31P mutation, the disease develops at 2 to 3 years of age, sometimes as early as 6 months of age, which is much earlier than in other

nonpedigree cats. Additionally, another mutation affecting cardiac troponin T has been found in a Maine Coon cat with HCM (KITTLESON and COTE, 2021b). In short, as concluded by FUENTES et al. (2020), Maine Coon cats homozygous for MyBPC3-A31P mutation, Ragdoll cats homozygous for MyBPC3-R820W mutation, and the first-degree relatives of affected cats are at higher risk of developing HCM, because HCM is likely to be heritable (KITTLESON and COTE, 2021b).

Some other causes of HCM mentioned by FUENTES et al. (2020) are hypertension, neoplastic infiltration, acromegaly, decreased preload, transient myocardial thickening, and hyperthyroidism. KITTLESON and COTE (2021b) also mention lymphoma as a rare cause of HCM. Such cases of HCM are considered secondary.

As indicated by KITTLESON and COTE (2021c), the other types of CM in cats are by far mainly idiopathic. Before 1987, DCM was for the most part caused by a taurine deficiency. However, since then, taurine was added to commercial cat feed, making DCM due to taurine deficiency almost non-existent, but it can still occur in cats fed on home-made diets. According to WARE (2011) DCM might be the end-stage of some myocardial metabolic abnormality, toxicity, or infection. FUENTES et al. (2020) also report that DCM can be tachycardia mediated. Finally, per KITTLESON and COTE (2021c), no mutation has been found to be associated with DCM in cats. As for RCM, it may be the consequence of endomyocarditis, either infectious or immune mediated (WARE, 2011). Some studies reported by KITTLESON and COTE (2021c) link it to infection with *Bartonella* species. WARE (2011) adds that RCM can be the end-stage of myocardial failure and infraction from HCM. And according to FUENTES et al. (2020), like HCM, RCM can also be the consequence of hyperthyroidism. As mentioned by KITTLESON and COTE (2021c), both DCM and RCM affect mainly mixed breed cats. Furthermore, RCM shows no sex predilection and can occur between 4 months to 19 years of age. As for ARVC, it affects mainly mixed-breed cats, aged between 1 and 20 years (KITTLESON and COTE, 2021c).

2.4. Phenotype and pathophysiology

KITTLESON and COTE (2021b) define HCM as the concentric left ventricular hypertrophy, in the absence of another cardiac or systemic disease capable of producing the magnitude of hypertrophy evident.

According to NELSON and COUTO (2014), an abnormal sarcomere function associated with inappropriate cell signalling is believed to lead to myocytes hypertrophy and disarray, as well as increased collagen synthesis. This results in the typical thickening of the LV wall and/or IVS, with a smaller LV lumen. Therefore, the LV wall becomes stiffer, creating diastolic dysfunction. WARE (2011) states that when the ventricular distensibility is reduced, filling of the LV is impaired and higher diastolic pressures are required. As a result, the diastolic pressures of the LA and LV are progressively increasing. Besides, per NELSON and COUTO (2014), another important factor impairing diastole is the myocardial ischemia. This phenomenon is due to multiple factors: narrowing of the intramural coronary arteries, decreased coronary artery perfusion pressure, and insufficient myocardial capillary density for the degree of myocyte hypertrophy. As the early ventricular relaxation is active, the ischemia disturbs this function, and overtime, it leads to myocardial fibrosis, which reinforces the LV wall stiffness.

As a result of the pressure increase, the LA enlarges in order to create a buffer (WARE, 2011). However, this is not without any repercussions. First, as mentioned in NELSON and COUTO (2014), the increase of pressure in LA is followed by a growing pressure in the pulmonary veins as well, and consequently, pulmonary congestion and oedema. Eventually, pleural effusion will develop. Those are signs of congestive heart failure (CHF). The second repercussion explained in WARE (2011) is the risk of thromboembolism (TE): the blood accumulation and stasis mainly in the enlarged LA can form intracardiac thrombi, and if it were to be dislodged, it could cause systemic TE, which is a major complication of HCM (NELSON and COUTO, 2014).

As stated in NELSON and COUTO (2014), the LV papillary muscle hypertrophy and the consequent abnormal movement of the mitral valve cause systolic anterior movement (SAM) of the anterior leaflet of the mitral valve. KITTLESON and COTE (2021b) describe SAM as the pulling of the anterior leaflet of the mitral valve into the LV outflow tract. This phenomenon has two consequences that are interconnected, explained in KITTLESON and COTE (2021b). As the mitral valve leaflet is misshapen, mitral valve regurgitation ensues, and as stated in WARE (2011), worsens the LA enlargement and the increase of pressure. The other consequence mentioned in KITTLESON and COTE (2021b) is the dynamic left ventricular outflow tract obstruction (DLVOTO), which is a form of subaortic stenosis. This is also known as obstructive HCM (NELSON and COUTO, 2014). The narrowed outflow tract is also reinforced by the hypertrophy of the IVS. The DLVOTO further increases the LV pressure, wall

stress and myocardial oxygen demand, which advances the myocardial ischemia (WARE, 2011).

Finally, the LV volume may be decreased, because of the impaired LV filling and the reduced size of the lumen, and which results in reduced SV, also reinforced by the narrowed outflow tract. Thus, in order to maintain CO and BP, there may be activation of the neurohormonal system which increases the HR. However, the higher HR further impedes LV filling, promotes myocardial ischemia, decreases diastolic filling time leading to the worsening of the pulmonary vein congestion (NELSON and COUTO, 2014).

According to WARE (2011), the second most common CM of cats, RCM, is characterised by extensive endocardial, subendocardial, or myocardial fibrosis, with enlargement of both atrial chambers, while the LV may have some wall hypertrophy, a normal or slightly reduced chamber size, and possibly mild dilation. Due to the fibrosis, the LV becomes abnormally stiff, leading to diastolic dysfunction and impaired LV filling. Therefore, as explained in KITTLESON and COTE (2021c), both HCM and RCM are affected by diastolic dysfunction due to cardiac fibrosis. However, HCM shows myocardial thickening as a primary lesion, with secondary fibrosis, while in RCM, fibrosis is the primary lesion and there is no concentric hypertrophy of the myocardium. Thus, per WARE (2011), the enlargement of the LA is caused by the increased pressure needed to fill the LV. The same consequences as HCM can be found in RCM: myocardial ischemia, blood stasis in the LA with higher risk of thrombus formation, and left-sided CHF.

Dilated CM is defined as an inherent myocardial disease, causing myocytes death and/or weakness, that results in a decrease in contractility with consequent ventricular eccentric hypertrophy (KITTLESON and COTE, 2021c). Therefore, DCM is a heart condition with systolic dysfunction (NELSON and COUTO, 2014). Characteristically, as explained in NELSON and COUTO (2014), all heart chambers become dilated and secondary AV valve insufficiency develops, due to the chamber's enlargement and papillary muscle atrophy. Pulmonary oedema, pleural effusion, CHF, and low SV and CO are common consequences, as well as arrhythmias.

According to KITTLESON and COTE (2021c), ARVCM is characterised by a diffuse or regional thinning of the RV free wall, and with a severely enlarged RA. As of 2024, this disease lacks research and studies.

Lastly, all the non-congenital structural cardiac diseases that do not fit in the categories mentioned above are grouped within NCM. One example of abnormalities described in KITTLESON and COTE (2021c) is a normal LV with a large LA but normal LV diastolic function. Probably, cases of transition phases between two different CM types or cases of two CM in the same heart are classified in NCM.

2.5. Staging, clinical presentation, and physical examination

In order to provide guidance for therapy and prognosis, the ACVIM consensus established a staging system, based on clinical findings, as shown on Figure 3 (FUENTES et al, 2020). All cats predisposed to CM, without evidence of disease, are grouped in stage A. Stage B includes cats with CM but with no overt clinical manifestation. Furthermore, mainly according to the atrial size, cats are subcategorized in stage B1 or B2 (FUENTES et al., 2020). As explained in KITTLESON and COTE (2021a), no to mild atrial enlargement falls into stage B1, while moderate to severe atrial enlargement in stage B2. FUENTES et al. (2020) added stage C to include all cats that have or had clinical signs of CHF or TE, which can be controlled by therapy. Indeed, once a cat enters stage C, it does not move back to stage B, even if the treatment is successful (KITTLESON and COTE, 2021a). Finally, all cats with clinical signs refractory to treatment are grouped in stage D (FUENTES et al., 2020).

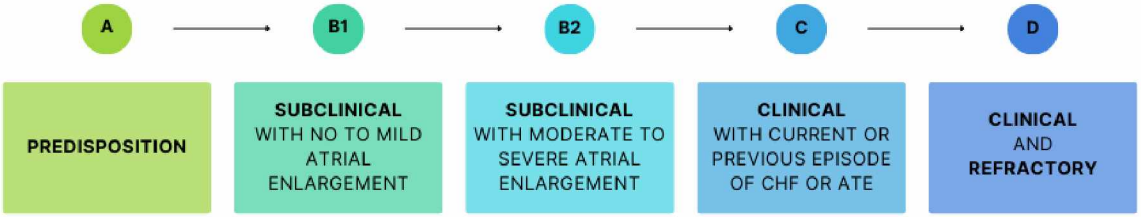

Figure 3. Stages of feline cardiomyopathy (Fuentes et al., 2020).

As cats in stage B are subclinical, most of them go undetected. So, according to KITTLESON and COTE (2021a), most cats with subclinical CM are presented due to incidental finding of a heart murmur, during a routine examination or a checkup for other health issues. However, a heart murmur is not a reliable indicator, as many cats with subclinical CM do not exhibit one and 25-33% of cats with a heart murmur do not have a CM. Arrhythmias are another possible presentation for cats in stage B, most commonly ventricular premature complexes (VPC). Not to mention, some cats can be asymptomatic and still diagnosed with CM during screening for the disease. This is mainly the case in breeding programs, for cats typically placed

in stage A. Finally, sudden death is also one of the presentations of cats with undiagnosed CM. As a matter of fact, cardiac diseases represent the most common cause of unexpected death in cats (KITTLESON and COTE, 2021a). Overall, it should be noted that 33 to 55% of cats diagnosed with HCM are asymptomatic and do not have any abnormal history (RUSH et al., 2002; COTE et al., 2011).

As stated by COTE et al. (2011) and KITTLESON and COTE (2021a), in clinical CM, the most common clinical presentation is respiratory difficulty, as the consequence of pulmonary oedema or pleural effusion caused by the left heart failure. Indeed, this occurs in 32-46% of cats diagnosed with HCM, and there are some precipitating agents to this event of respiratory difficulty, such as: fluid therapy in 28% of cases, anaesthesia or surgery (25%), and recent treatment with corticosteroid (21%) (RUSH et al., 2002; COTE et al., 2011). Other complaints coherent with CHF are lethargy, anorexia, vomiting, and weight loss. According to RUSH et al. (2002) and COTE et al. (2011), on top of respiratory difficulty from heart failure, in 12-17% of cats diagnosed with HCM, relevant complaints are lameness, paresis, and pain. These clinical signs are connected to arterial TE. KITTLESON and COTE (2021a) find that the clinical presentation is similar for every type of CM in cats, except for ARVCM. In fact, cats with clinical ARVCM are presented with right heart failure, and the subsequent ascites and pleural effusion, thus lesser respiratory signs compared to the other types of CM.

According to COTE et al. (2011), during physical examination, two abnormalities can be detected on auscultation in cats with CM. The most common one is a systolic heart murmur. It actually occurs in 47 to 72% of cats with HCM and 36% of cats with RCM (RUSH et al., 2002; FERASIN et al., 2003). The second most common finding is a gallop heart sound, occurring in 79% of cats with DCM and 1/3 of cats with HCM (FERASIN et al., 2003). Moreover, cats with CM can also be tachycardic or arrhythmic on cardiac auscultation. Nevertheless, as stated in COTE et al. (2011) and KITTLESON and COTE (2021a), a heart murmur can be benign or associated with other cardiac conditions, and, similarly, a gallop heart sound is not specific to CM, but can be found in other cardiac diseases, or with anaemia, fluid overload, and hyperthyroidism. All those auscultatory findings may or may not be present, even if the cat is presented in clinical heart failure. Therefore, cardiac auscultation is not adequate for screening, confirming, or excluding CM. Moreover, as reported by COTE et al. (2011), cats with CHF can present respiratory abnormalities during physical examination due to pleural effusion or pulmonary oedema, such as tachypnoea, dyspnoea, orthopnoea, and increased adventitious lung sounds. Indeed, 36% of cats diagnosed with HCM present dyspnoea. However, only 8% had

abnormal findings on lung auscultation (FERASIN et al., 2003). Thus, pulmonary auscultation is also limited to diagnose CM (KITTLESON and COTE, 2021a). Finally, specifically for cats with ARVCM, physical examination can also reveal hepatosplenomegaly, and abnormal jugular distension and pulsation, due to the right heart failure (COTE et al., 2011).

2.6. Differential diagnoses and diagnosis

As per COTE et al. (2011), the main differential diagnoses for HCM are secondary and reversible causes of left ventricular concentric hypertrophy. A common cause of secondary concentric hypertrophy is hyperthyroidism. In fact, as explained by FUENTES et al. (2020), this is a common condition in older cats and it is known to lead to auscultatory abnormalities, cardiac remodelling, and even CHF, and ATE. This disorder should be excluded by measuring serum thyroxine concentration. COTE et al. (2011) also explains that systemic hypertension is another common cause of secondary concentric hypertrophy, as it results in increased LV afterload and systolic wall stress, triggering cardiomyocytes replication. Therefore, FUENTES et al. (2020) recommends blood pressure determination for all cats with increased LV wall thickness. Other secondary causes of HCM described by COTE et al. (2011) are aortic stenosis and acromegaly. Aortic stenosis is a congenital heart disease that also increases afterload. It generates SAM of the mitral valve as well. As for acromegaly, the growth hormone has a direct effect on the cardiomyocytes. Moreover, lymphomas and rhabdomyosarcomas may give rise to asymmetrical concentric hypertrophy. However, infiltrative neoplastic myocardial diseases are infrequent in cats. Finally, one should also consider mitral valve dysplasia as a differential diagnosis, as it also causes SAM. Catecholamine-driven cats can also show SAM on echocardiography. According to COTE et al. (2011), differential diagnosis of RCM, DCM, and ARVCM are respectively end-stage HCM, HCM with an infarct, and tricuspid valve dysplasia.

When cats are presented for screening, genetic testing is an option for Maine Coon and Ragdoll cats – breeds systematically placed in stage A. When cats are intended for breeding, it is recommended to test Maine Coon for the MyBPC3-A31P mutation and Ragdolls for the MyBPC3-R820W mutation. Any cats homozygous for the mutation should be removed from the breeding program. However, as the prevalence is quite high (34%) in asymptomatic Maine Coon cats, some of them can still be used for breeding with other negative cats, that is if they are heterozygous, echocardiographically normal, and have outstanding characteristics. In non-breeding Maine Coon and Ragdoll cats, the genetic test can be performed to assess the risk of

developing HCM. In any case, these high-risk cats in stage A should have regular echocardiographic screening, every 6 to 12 months. Genetic testing is not necessary for non-Maine Coon and non-Ragdoll cats (COTE et al., 2011; FUENTES et al., 2020).

In the case of a cat presented with dyspnoea, the first step of the diagnostic process of CM, as stated in KITTLESON and COTE (2021a), is to define whether the patient has a cardiac condition or a respiratory condition. Initially, without any further diagnostic tests, this can be quite challenging. Results of studies may help the veterinarian to lean towards one option or the other. Indeed, as reported by DICKSON et al. (2017), a gallop heart sound, a rectal temperature below 37,5°C, or a tachycardia above 200 bpm all make the heart condition more likely than the respiratory condition. Some tools for further differentiation later are thoracic radiographs, thoracocentesis, point-of-care (POC) ultrasound, and POC cardiac biomarkers (KITTLESON and COTE, 2021a).

A tool interesting for both screening and initial differentiation between a cardiac or noncardiac condition is amino pro-brain natriuretic peptide (NT-proBNP). In cats, BNP is produced by the atria in normal circumstances, and additionally by the ventricle in case of increased ventricular wall stress. Therefore, it appears to be a convenient biomarker to identify heart conditions. Two different tests exist to determine the concentration of NT-proBNP in plasma or pleural fluid: a quantitative test completed in a laboratory and a POC test. The quantitative test is prescribed as a screening method when there is no urgency. If the concentration is higher than 99 pmol/L, the cat should be examined by echocardiography. However, if the concentration is below 99 pmol/L, the test becomes less valuable. Actually, this test tends to miss 50% of positive cats and there is a real overlap of plasma concentration between normal cats and mildly abnormal cats. Therefore, this screening method should be used only when there is a high suspicion of CM and when echocardiography is not possible. Besides, it should never be used as the sole screening tool. On the other hand, the POC test provides immediate results and is applied to discern the cause of acute dyspnoea in a cat. It is quite reliable as the sensitivity is 90% and the specificity is 86-88%. However, POC ultrasound is still the preferred method in this situation, and the POC test for NT-proBNP should not be utilised for screening. Another biomarker for heart diseases in cats is cardiac troponin I (cTnI), secreted by damaged cardiomyocytes. As NT-proBNP, it is able to distinguish cardiac from noncardiac causes of dyspnoea, but with lower accuracy (COTE et al., 2011; BORGEAT et al., 2015; FUENTES et al., 2020; KITTLESON and COTE, 2021a).

Once the patient is stable and after the general clinical examination, the veterinarian should always start the diagnostic process with some general tests, including complete blood count, biochemistry, urinalysis, and, as mentioned earlier, serum thyroxine concentration and blood pressure measurement. Detecting anaemia is critical as it may worsen the condition, and it is essential to assess the renal function before starting the medical treatment of the heart disease (COTE et al., 2011).

Thoracic radiographs may be used in the diagnostic process of CM, but they do not provide a final diagnosis and always require further investigation. Indeed, one can suspect CM when the radiograph reveals cardiomegaly, dilation of the LA, or both. However, cats with mild HCM may have a normal radiograph, and even when the CM is severe enough to cause CHF, the heart size can appear physiological. Thus, a normal heart size on radiograph does not exclude CM. Besides, no differentiation between phenotypes of CM is possible with radiographs. Indeed, the "valentine-shape" heart (Figure 4.) is actually not specific for HCM. Some nuances can be established: in case of ARVCM, the radiograph can reveal enlargement of the right side of the heart, and, in RCM cases, it is possible to see biatrial enlargement. But this is still non-diagnostic and non-specific. Nevertheless, radiography is still considered the best option to detect pulmonary oedema and pleural effusion (Figure 5.), which are signs of CHF. But since this procedure is stressful and risky for cats in respiratory distress, it should be delayed and POC ultrasound should be favoured (COTE et al., 2011; FUENTES et al., 2020; KITTLESON and COTE, 2021b; KITTLESON and COTE, 2021c).

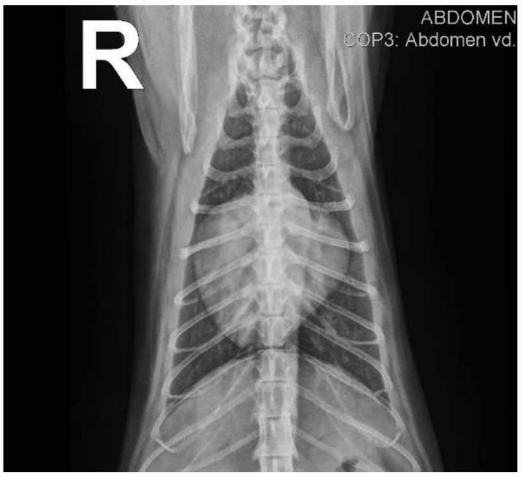

Figure 4. Ventrodorsal radiograph of cat, revealing an enlarged heart silhouette with the characteristic "valentine-shape" (source: Archive of the Department of Radiology, Ultrasound Diagnostics and Physical Therapy, Faculty of Veterinary Medicine, University of Zagreb).

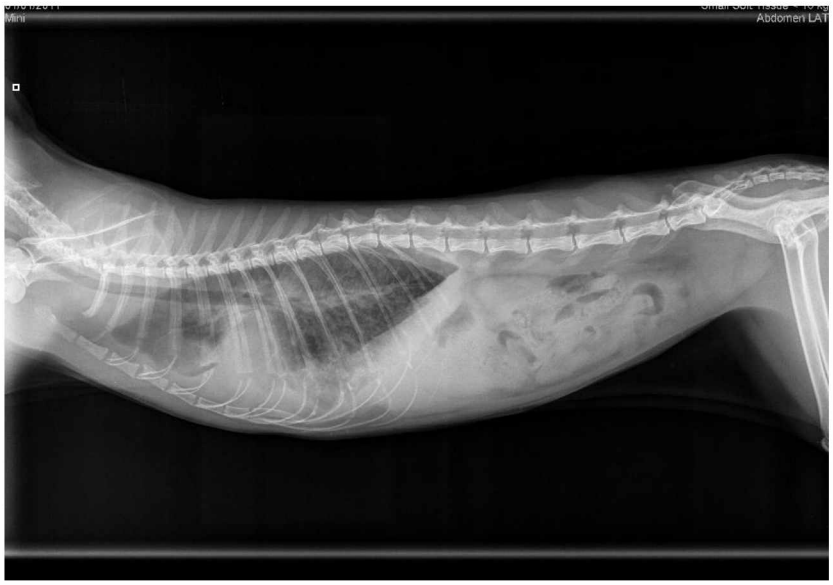

Figure 5. Laterolateral radiograph of a cat, revealing pleural effusion in the ventral part of the chest and pulmonary oedema in the diaphragmatic lung lobes (source: Archive of the Department of Radiology, Ultrasound Diagnostics and Physical Therapy, Faculty of Veterinary Medicine, University of Zagreb).

Electrocardiography is not a reliable tool for diagnosis of CM. In fact, in one study, only 25% of cats with HCM showed LV enlargement pattern on ECG. So, it cannot be used for screening. However, it remains the best approach to detect any arrhythmias associated with CM and should be performed when an abnormal heart rhythm is identified on cardiac auscultation. Arrhythmias are most common with ARVCM. They are frequent with HCM, and possible in RCM cases, while they are quite rare in DCM cases. The most common arrhythmias concomitant with CM are VPC, ventricular tachycardia, atrial premature complex, atrial tachycardia, atrial fibrillation, and AV blocks. These can be found alone or in combination (FERASIN et al., 2003; COTE et al., 2011; FUENTES et al., 2020; KITTLESON and COTE, 2021b: KITTLESON and COTE, 2021c).

As per FUENTES et al. (2020), the gold standard for diagnosis of CM in cats is echocardiography. Three categories of cardiac ultrasound exist: the focused POC, the standard, and the best practice. The POC echocardiography is performed for unstable cats in CHF. It allows assessment of the LA size and function and the LV systolic function, as well as visualisation of pleural or pericardial effusion and B-lines over the lungs. The standard cardiac ultrasound is recommended for cats suspected to have a CM, but also for older cats before

anaesthesia or fluid therapy, or if a prolonged treatment with corticosteroids is prescribed. This method examines the heart chambers dimensions and geometry, the LA and LV fractional shortening, and it searches for SAM. The best practice ultrasound is advocated for cats suspected to have a CM, especially if the LV wall thickness is in the grey zone (between 5 and 6 mm). In this case, the results should be interpreted according to the animal's body size, family history, LA and LV appearance and function. For this level of echocardiography, spectral Doppler and tissue Doppler imaging (tDi) are performed, as an addition to the standard practice (FUENTES et al., 2020).

According to KITTLESON and COTE (2021b), the following criteria must be assessed in HCM: LV wall thickness, LA size and function, diastolic dysfunction, and RV free wall thickness. COTE et al. (2011) also adds SAM. As explained by KITTLESON and COTE (2021b), to characterise the LV wall thickness and find the thickest region, the entire LV should be checked, using multiple views. It is preferable to use 2D echocardiography, over M-mode. The latter can be used to measure a region of hypertrophy already identified. Besides, measures should be taken during diastole. The thickness measured should include the endocardium, but it should not comprise papillary muscles, regions of endocardium thickening, false tendons insertion sites or the pericardium. Most commonly, a general and symmetrical hypertrophy is detected, but it is possible to find only regional thickenings. In most normal-sized cats, LV hypertrophy is defined as end-diastolic LV wall thickness equal to or above 6 mm. A thickness below 5 mm is considered normal. But it should be noted that the body weight influences the LV wall thickness (KITTLESON and COTE, 2021b). Cats with end-diastolic LV wall thickness between these 2 cut-off values are in the grey zone, and are classified as equivocal, requiring further interpretation and tests (COTE et al., 2011; FUENTES et al., 2020). Another possible finding is a bulge at the base of the IVS. If this is the only abnormal finding, diagnosis can be problematic, and the veterinarian should question whether it is a case of slowly progressing HCM or a non-HCM ageing change (KITTLESON and COTE, 2021b).

The LA size is a crucial feature to check. Indeed, a severely enlarged LA signifies that the cat has CHF or is at high risk of developing it. It also represents an increased risk for blood stasis, and consequently thrombus formation and arterial TE. Measuring LA diameter to aortic diameter ratio (LA:Ao) is the mean of choice to determine LA enlargement and it should be obtained when the LA is at its largest. A finding of LA:Ao below 1,6 is normal, while LA:Ao above 1,8 to 2,0 implies that the LA is enlarged. Additionally, if the LA diameter is above 19

mm, it strengthens the conclusion that the LA is enlarged. Usually, the LA is globally enlarged, but it is not always the case (KITTLESON and COTE, 2021b).

Diastolic dysfunction is a characteristic trait of HCM and it is estimated with tDi (KITTLESON and COTE, 2021b). However, authors agree that it is not necessary to establish a diagnostic of HCM and it is not distinct to this condition (COTE et al., 2011; KITTLESON and COTE, 2021b). Moreover, KITTLESON and COTE (2021b) state that a mild thickening of the RV free wall occurs in half of HCM cases. Finally, according to COTE et al. (2011), another feature of HCM is SAM. Therefore, mitral regurgitation can be identified during the echocardiography, which can also be caused by mitral valve dysplasia. The main difference is that in case of mitral valve dysplasia, the valves have an abnormal structure, while the structure of the valves is not altered with SAM.

To conclude, diagnosis of severe HCM with echocardiography is quite straightforward, as hallmark signs can be recognised: marked LV wall thickening, enlarged papillary muscles, LA enlargement, SAM, and end-systolic cavity obliteration (**Figures 6. and 7.**). Nevertheless, the diagnosis is more challenging in case of moderate HCM, and even harder with mild forms, as there are intra- and interindividual variation with ultrasonography (KITTLESON and COTE, 2021b).

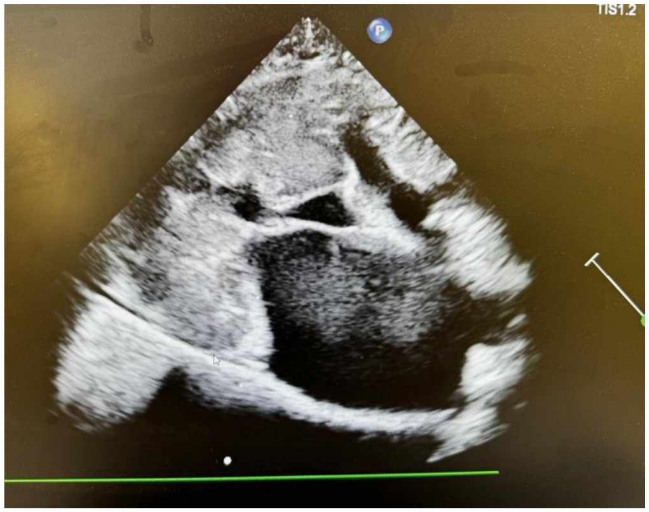

Figure 6. Right parasternal long axis view of feline heart. There is marked LV concentric hypertrophy with left atrial enlargement, consistent with phenotype of hypertrophic cardiomyopathy (source: Archive of the Clinic for Internal Diseases, Faculty of Veterinary Medicine, University of Zagreb).

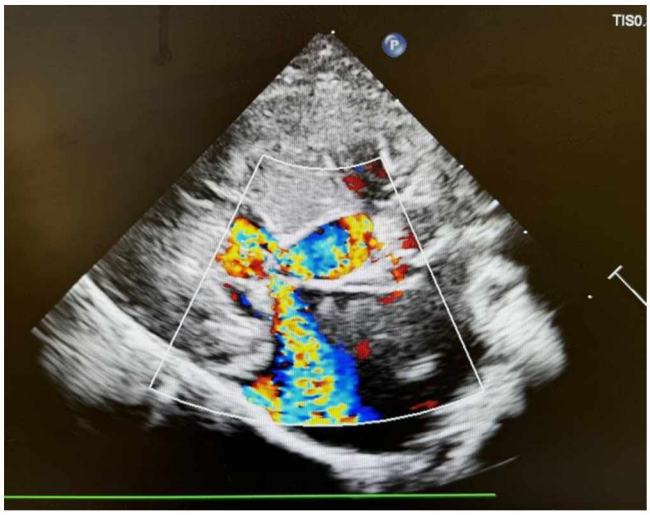

Figure 7. Right parasternal long axis view of feline heart with colour-Doppler window placed over a part of the left ventricle (left ventricular outflow tract) and left atrium. The still image shows a typical flow profiles of dynamic outflow tract obstruction due to systolic anterior motion of the mitral valve. Additionally, there is LV concentric hypertrophy. These findings are typical of obstructive form of hypertrophic cardiomyopathy (source: Archive of the Clinic for Internal Diseases, Faculty of Veterinary Medicine, University of Zagreb).

In RCM cases, the echocardiography will identify a normal LV with an enlarged LA, and occasionally, a larger RA (Figure 8.). Definite diagnosis is established by assessing diastolic dysfunction with tDi, which would show a tall E-wave (KITTLESON and COTE, 2021c). Besides, it is possible to discern pericardial effusion on occasion, irregular hyperechoic endocardial regions (caused by endomyocardial fibrosis), and mild mitral regurgitation (COTE et al, 2011). In DCM cases, the echocardiography will reveal a very poorly contractile and dilated LV (>11mm in systole and >16mm in diastole), a dilated LA, and functional mitral regurgitation. A LV systolic dysfunction is reported, with a fractional shortening <20% (COTE et al., 2011; KITTLESON and COTE, 2021c). Finally, in ARVCM cases, the two main characteristics are: enlarged RA and RV, and mild tricuspid regurgitation. Paradoxical movement of the IVS and aneurysmal akinesis (lack of movement) regions can occur. Usually, the LV is normal or smaller and the LA can sometimes be enlarged (COTE et al., 2011; KITTLESON and COTE, 2021c).

Other imaging methods, such as CT and MRI, are slowly developing for diagnosis of CM, and they will likely become more used, as the costs decrease, and the imaging time reduces (KITTLESON and COTE, 2021b). For now, even though MRI is the most accurate to determine LV mass, it is mainly used for research (COTE et al., 2011).

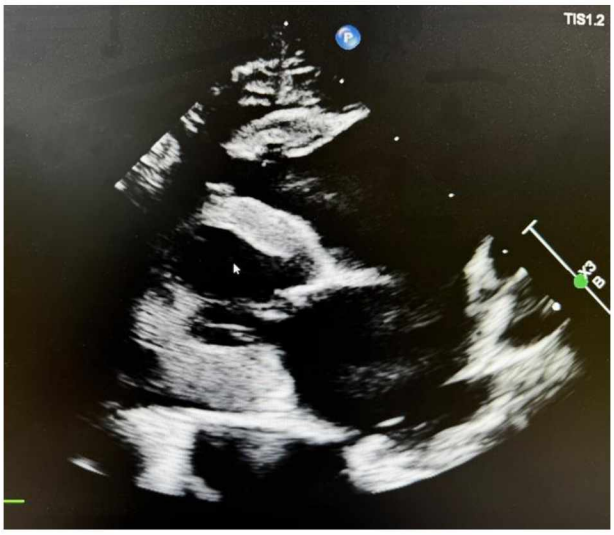

Figure 8. Right parasternal long axis view of feline heart. There is marked biatrial enlargement with non-hypertrophied LV, a phenotype typically seen in cases of restrictive cardiomyopathy (source: Archive of the Clinic for Internal Diseases, Faculty of Veterinary Medicine, University of Zagreb).

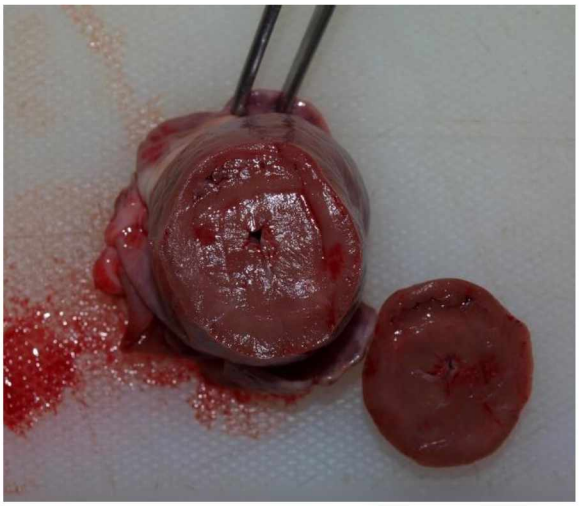

Figure 9. Hypertrophic heart at post-mortem examination of a Maine Coon cat. The cardiac mass is increased, as the heart weighs 38g. The LV wall is diffusely thickened, and the LV lumen is narrowed (courtesy of the Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Zagreb).

Finally, as indicated by COTE et al. (2011), the diagnosis can also be made by postmortem examination (Figure 9.) and histopathological study. HCM is characterised by myofiber disarray of the LV, concentric LV hypertrophy, and increased heart mass. Restrictive CM shows an increase in heart weight, biatrial dilation, and normal wall thickness, and, histologically, focal or diffuse fibrous tissue in the different heart layers. Pathological findings in DCM reveal

dilated LA and LV and, in severe cases, all four chambers may be dilated. In ARVCM, dilation of the RA and RV and focal or diffuse thinning of the walls are typical, and, histopathologically, there is myocardial atrophy with fibrofatty or fibrous replacement, and possibly lymphocytic infiltrates.

2.7. Management and therapy

As per FUENTES et al. (2020), the treatment and management of cats with CM is based on the staging (Figure 10.). For cats in stage B1, treatment is not recommended. Indeed, according to KITTLESON and COTE (2021b), in the case of HCM, no medication can lessen the hypertrophy or decelerate the progression of the condition. However, they should be monitored every year by veterinarians - to detect severe enlargement of the LA - and by the owners, by checking the cat's respiratory rate at rest or sleep occasionally and calling the veterinarian if the respiratory rate exceeds 30 breaths/min. Besides, treatments that can set off heart failure should be avoided, as well as breeding of sexually intact cats in stage B1. As mentioned by FUENTES et al. (2020) and KITTLESON and COTE (2021b), if the CM is associated with severe DLVOTO and severe SAM, a beta blocker can be prescribed to decrease its gradient, especially if the cat is exposed to higher stress levels. The treatment of choice is atenolol, with a dosage of 6.25 to 12.5 mg per os (PO) q12h. However, using a beta blocker should be considered only if it can be provided to the cat consistently and with minimum stress. This is not necessary in case of mild to moderate DLVOTO.

According to FUENTES et al. (2020) and KITTLESON and COTE (2021b), in stage B2, cats are at higher risk of developing CHF and arterial TE, due to a more pronounced LA enlargement. Therefore, if risk factors for TE are found, thromboprophylaxis treatment should be implemented. The best option for cats is clopidogrel, an antiplatelet drug, at a dose of 18.75 mg PO q24h. Clopidogrel can be used alone, but, as it is not 100% effective, it can also be combined with other drugs: aspirin (another antiplatelet drug) or anticoagulants, such as low molecular weight heparins (enoxaparin) and selective Xa inhibitors (rivaroxaban). As per FUENTES et al. (2020), monitoring is still key at this stage and owners should inspect their cat's respiratory rate more regularly. However, stress is more likely now to trigger a complication, so appropriate handling at the veterinary clinic becomes even more important. Similarly to stage B1 cats, the use of atenolol can be contemplated.

Cats in stage C have or have had an episode of CHF. Therefore, the first step is to stabilise and treat cats presented with acute decompensated heart failure. As the protocol is the same for all types of CM, identifying the phenotype is unnecessary at first. Veterinarians may manage heart failure by means of empirical diuretic therapy, oxygen supplementation, sedation with anxiolytics, while ensuring gentle handling, a quiet environment, and providing a hiding box to decrease stress levels of the patient. The diuretic of choice is furosemide, administered intravenously at a constant rate infusion (0.5-1 mg/kg/h) or by boluses (3-6 mg/kg). Furthermore, if pleural effusion is noticed, thoracocentesis should be performed. If signs such as hypotension, hypothermia and bradycardia are identified, low cardiac output can be suspected. Then, an additional treatment option is pimobendan PO, preferably only if DLVOTO is not present. However, its use is controversial in stage C, since its benefits (improving diastolic function and systolic LA function) have not been proven in cats. Intravenous fluid therapy is contraindicated and angiotensin converting enzyme inhibitors (ACEi) are not necessary. Discharging the patient as soon as possible once it is stable is crucial and the cat should be reevaluated after 3 to 7 days (FUENTES et al., 2020; KITTLESON and COTE, 2021a; KITTLESON and COTE, 2021b).

Once the episode of acute CHF is controlled, therapy must be adjusted and adapted to maintain a stable state in the patient. Treatment with a loop diuretic should usually be kept for life and is the most important drug for cats in stage C. A dose of 1-2 mg/kg PO q8-12h is usually recommended to start. It can be raised to 4 mg/kg PO q8h, or more if needed. The goal is to keep the sleeping respiratory rate below 30 breaths/min. Clopidogrel, as a prophylactic antithrombotic, is required for every cat in stage C, with the same dosage as cats in stage B2. Once more, ACEi are not indicated and pimobendan may be considered, but is not crucial. Re-examination should be performed every 2 to 4 months if it is not too stressful for the cat (FUENTES et al., 2020; KITTLESON and COTE, 2021b).

According to BORGEAT et al. (2014), FUENTES et al. (2020), and KITTLESON and COTE (2021a), if a cat is presented with arterial TE, the first option and most common solution is euthanasia. Nonetheless, as long as the owner is well informed, 48 to 72h can be provided for the cat to naturally lyse the thrombus. Therefore, if euthanasia was not opted for, the main objective is to minimise pain. Methadone intravenously or fentanyl by constant rate infusion are the best two options. Anticoagulant treatment should be started as soon as possible to prevent formation of a new thrombus. The drugs of choice are unfractionated heparin or low molecular weight heparin. A loading dose of clopidogrel (75mg) should be administered PO,

followed by the standard dose. If CHF is also detected, it should be treated as mentioned above. Finally, once stabilisation is achieved, supportive care should be maintained until reperfusion occurs, or for up to 72h. In case of survival until discharge, the cat must be brought back to the clinic for regular checkups.

In a cat with refractory CHF despite treatment (stage D), furosemide can be switched to torsemide PO. The starting dose is 0.2 mg/kg q24h or more depending on the needs. Usually, the dose of torsemide corresponds to 1/10 to 1/20 of the dose of furosemide. At this stage, it may be advisable to add pimobendan and diet changes should be contemplated. Indeed, a low sodium diet might help, whereas adding any kind of sodium to the feed is proscribed (KITTLESON and COTE, 2021b). Still, as cardiac cachexia may arise, it is more important that the cat keeps eating. Hence, it is more useful to increase the calorie intake than to focus on lowering sodium (FUENTES et al., 2020).

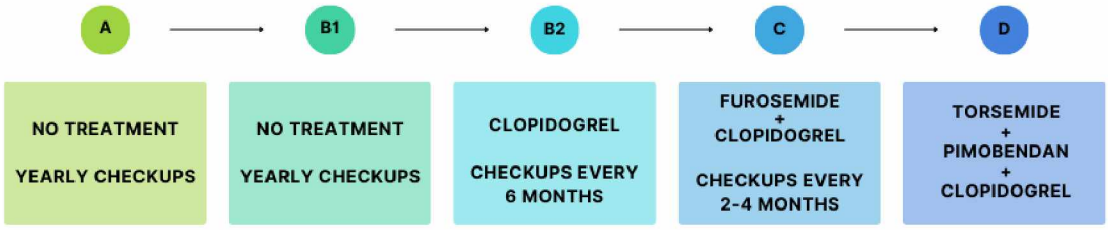

Figure 10. Simplified scheme of the treatment protocol for cats with cardiomyopathy according to the staging (Fuentes et al., 2020).

As stated by KITTLESON and COTE (2021c), management and treatment for all CM is overall the same as the protocol for HCM mentioned above. Specifically, for ARCVM cases, the only additions are to perform abdominocentesis in the event of severe ascites, to prescribe sotalol if ventricular tachycardia occurs and diltiazem, possibly combined with digoxin, or sotalol if atrial fibrillation happens.

2.8. Prognosis

In HCM patients, the prognosis depends largely on the staging. According to FOX et al. (2018), cats with mild to moderate disease may never progress to a severe condition. Therefore, B1 cats have a good to excellent short-term prognosis and a fair to guarded long-term prognosis, and, as stated by PAYNE et al. (2013), B2 cats have a guarded short and long-term prognosis. Finally, cats in stage C and D have a poor prognosis and are indeed more likely to die from the

heart condition than anything else (PAYNE et al., 2013). As reported by RUSH et al. (2002), an exception to these prognoses are cats with secondary HCM and cats with a CHF set off by a trigger, such as stress, fluid therapy, anaesthesia, or surgery. Indeed, if they survive the first episode and the underlying cause is treated, their odds of survival are significantly higher.

Usually, 7% of cats in stage B1 and B2 develop CHF within the first year, 20% within 5 years, and 25% within 10 years (FOX et al., 2018), and some factors can help veterinarians to determine the risk of CHF and TE, namely: a gallop heart sound or arrhythmia detected during auscultation, a moderate to severe LA enlargement, a reduced LA fractional shortening, a severe LV hypertrophy, a diminished LV systolic function, a regional wall thinning with hypokinesis, and a restrictive diastolic LV filling pattern (PAYNE et al., 2013: PAYNE et al., 2015). Based on RUSH et al. (2002) and FOX et al. (2018), once the patient develops CHF, it passes away within a couple of months. On the other hand, factors that predict a higher risk of sudden death are a history of syncope, a ventricular arrhythmia, a LA enlargement, and a regional LV wall hypokinesis (PAYNE et al., 2015). It should be noted that DLVOTO is not an indicator of a poor prognosis, contrary to human medicine (PAYNE et al., 2013; FOX et al., 2018; KITTLESON and COTE, 2021b), while a younger age forecasts a chance of longer survival (PAYNE et al., 2013). Of course, the owner's compliance to the veterinarian's recommendations also plays an important part in determining survival of the patient (KITTLESON and COTE, 2021b). Finally, PAYNE et al. (2013) reported that a concentration of NT-proBNP above 1500 pmol/L is indicative of a poorer prognosis. However, a study by BORGEAT et al. (2015) revealed that cTnI might be a better prognostic tool compared to NT-proBNP. Overall, cardiac biomarkers should be studied further in order to be able to evaluate their value as prognostic indicators.

For cats that develop arterial TE, the prognosis is grave. In fact, the one-year survival rate approximates 10% (BORGEAT et al., 2014). Survival rate may increase if only one limb is affected, no severe heart condition is detected, and no CHF is associated with the TE (KITTLESON and COTE 2021a).

Cats with DCM, RCM, or ARVCM are attributed a poor to grave prognosis. According to HAMBROOK and BENNET (2012), cats with DCM will die within weeks to months after the initial diagnosis. The exception is for cats with DCM caused by taurine deficiency. Indeed, if they survive the initial phase, they have a better long-term prognosis (PION et al., 1987).

3. MATERIALS AND METHODS

For the purpose of this study, all cats with an echocardiography examination in their medical record between January 1st, 2017, and December 31st, 2022, were collected. This was done by retrospectively searching within the database of the Clinic of Internal Medicine at the Faculty of Veterinary Medicine in Zagreb, Croatia, within this 5-year period. A total of 282 cases were gathered. Each of their reports were downloaded and translated from Croatian to English with Google Translate.

For every case, the following data was collected on an Excel sheet: the complaint and reason for presentation for cardiological examination, the presence of a heart murmur, the presence of an arrhythmia, and finally the diagnosis. Specifically for cats with a CM phenotype, the following additional information were taken: the age at the time of diagnosis, the gender, the breed, whether the animal is or has been symptomatic at any point until the diagnosis, the presentation at the first medical visit leading to the first cardiological examination, the ECG findings, the radiography findings, and the echocardiography results including the eventual presence of DLVOTO and SAM. The ECG and radiography findings of interest are the ones closest to the diagnostic echocardiography.

The complaints were categorised as follows: “finding of a heart murmur”, “finding of an arrhythmia or gallop rhythm”, “dyspnoea”, “hindlimb paresis”, “screening and control”, and “other”. Here, dyspnoea represents any kind of respiratory disturbances, such as tachypnoea, respiratory distress, abdominal breathing, open-mouth breathing, and cough. “Screening and control” as a complaint includes cats with a breed predisposition, pre-anaesthesia check-ups, referred cases, abnormal radiography findings, suspicious cardiac biomarkers results, and more.

Four groups were established for the presentation: “CHF”, “arterial TE” (ATE), “respiratory difficulties”, and “asymptomatic”. If a cat is presented with dyspnoea, LA enlargement, and pulmonary oedema (PE) and/or pleural effusion (PLE), it is grouped as a CHF case. Cats placed in the ATE group have hindlimb paresis or weakness as the primary complaint and, on the echocardiography, an enlarged LA associated with a dilated left auricle, spontaneous echo-contrast or formed thrombus. Finally, respiratory difficulties as a group refers to cats with dyspnoea but without other signs of CHF.

The diagnosis is established as reported on the medical record and the cases are grouped as follow: “no cardiological problem”, “other cardiological problems”, “secondary CM”, “HCM”,

"NCM", "ARVCM", "RCM", and "DCM". "Secondary CM" comprises hypertensive CM, thyrotoxic CM, transient myocardial thickening (TMT), pseudohypertrophy, and others.

All the statistical analyses were performed using Microsoft Excel (Version 2404 Build 16.0.17531.20140).

4. RESULTS

4.1. Diagnosis and prevalence

Out of the 282 cases collected, 115 cats (40.8%) were diagnosed with a CM between 2017 and 2022. The details of the different diagnosis are presented in Table 1. As reported, most cases had no cardiac problem (93). However, this number is closely followed by cases of HCM (89). Secondary CM (41) comes next as the third most common diagnosis, followed by other cardiac problems (33). The two most prevalent secondary CMs were thyrotoxic CM and hypertensive CM, with 17 and 14 cases respectively. Mitral valve dysplasia, ventricular septal defect, pericardial mass, pulmonary and aortic stenosis are all examples of other cardiac problems diagnosed in the 282 studied cases. Finally, the four other phenotypes of CM proceed, with fairly small numbers of cases.

Table 1. Count of cases for each diagnosis group, with the percentage equivalent, from 2017 to 2022 at the Clinic for Internal Diseases.

Diagnosis	Count of cases	Percentage
No cardiac problem	93	32.98%
HCM	**89**	**31.56%**
Secondary CM	41	14.54%
Other cardiac problem	33	11.70%
NCM	**12**	**4.26%**
RCM	**9**	**3.19%**
DCM	**4**	**1.42%**
ARVCM	**1**	**0.35%**
Total	*282*	*100%*

4.2. Epizootiology

The breed, gender, and age at diagnosis of CM cases were studied, with a focus on HCM cases. Mixed breed cats represent 80% of CM cases (93 out of 115). However, 22 cats diagnosed with a CM were pure breeds. Persian cats (5) and Maine Coon cats (4) were the most common. The other represented breeds were: British shorthair (3), Bengal (3), Siamese (2), Exotic (2), Oriental shorthair (2), and Russian blue (1).

Male cats amount to 74 cases out of 115 CM cases (65%), and 60 cases out of 89 cases of HCM (69%); whereas female cats constitute 39 cases of CM (35%) and 27 cases of HCM (31%). Two cases were excluded for the study of this data since the gender was not indicated.

The median age at diagnosis of CMs was 9 years old. For HCM cases specifically, the median was 8 years old, but the most common diagnostic age was 6 years old. Indeed, 10 cats were diagnosed with HCM at this age. The youngest cat was 2 years old and the oldest was 20 years old. It should be noted that a third of cats diagnosed with HCM were between 4 and 7 years old.

4.3. Complaints and presentation

The distribution of the reason for the cardiological examination is shown in Figure 11. It should be noted that some cats were presented with two problems combined. The most prevalent complaint was "dyspnoea", as it was reported in 108 cases. The second most common reason for arrival was "screening" (96). This included patients with a breed predisposition or incidental findings of abnormal X-ray or biomarker results, referred cases, and pre-anaesthesia controls. The four other categories of complaints were counted as follows: "finding of a heart murmur" (46), "hindlimb paresis" (23), "other" (12), and "finding of a gallop rhythm or other arrhythmia" (7). "Other" complaints consist of lethargy, weakness, cyanosis, weight loss and hypothermia.

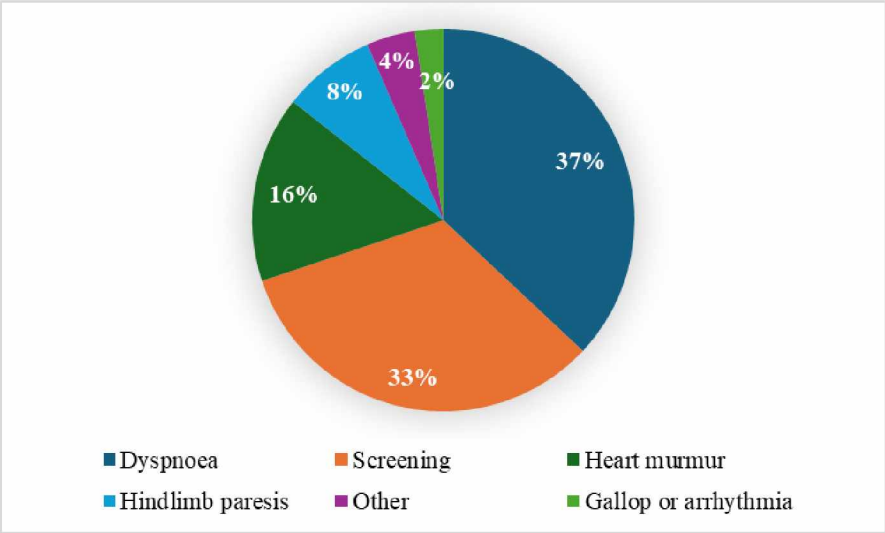

Figure 11. Distribution of complaints leading to a cardiological examination for all the 282 cases collected.

As shown on Figure 12, the distribution of complaints in HCM cases follows almost the same pattern as for all the 282 cases. Indeed, dyspnoea is still the leading complaint, with 42 cases. “Finding of a heart murmur” becomes slightly more prevalent than “screening”, with 18 and 17 cases respectively. “Hindlimb paresis” (16) is the fourth most common affection, while only 2 cases of “finding of a gallop rhythm or other arrhythmia” and 1 case with another complaint were reported.

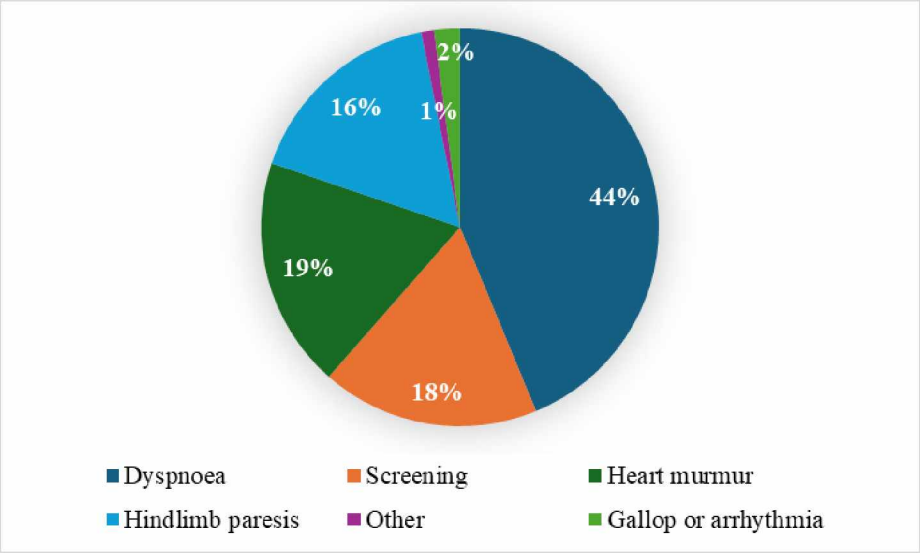

Figure 12. Distribution of complaints leading to a cardiological examination for all the 89 HCM cases.

The clinical presentation of CM cases was divided into asymptomatic and symptomatic, and the latter was additionally split into three groups. The count of cases for each clinical group and CM phenotype is presented in Table 2. Information about clinical presentation was lacking for 2 HCM cases, 1 NCM case, and 1 RCM case.

Table 2. Clinical presentation of CM cases, with a breakdown of the different symptomatic groups and calculated percentage.

	Count of cases					
Clinical presentation	**HCM**	**NCM**	**RCM**	**DCM**	**ARVCM**	**Total**
Asymptomatic:	**37** (42.5%)	**4** (33.4%)	**2** (25%)	**2** (50%)	**0**	**45** (40.5%)
Symptomatic:	**50** (57.5%)	**7** (63.6%)	**6** (75%)	**2** (50%)	**1** (100%)	**66** (59.5%)
CHF	*28*	*6*	*5*	*1*	*1*	
ATE	*8*	*0*	*0*	*0*	*0*	
CHF and ATE	*6*	*1*	*1*	*1*	*0*	
respiratory difficulty	*8*	*0*	*0*	*0*	*0*	
Total	**87**	**11**	**8**	**4**	**1**	**111**

4.4. Auscultatory findings: heart murmurs and arrhythmias

Table 3. Case count for the eventual presence of heart murmur, according to the diagnosis, with calculated percentage.

	Case count			
Presence of a heart murmur	**All cases**	**Cases without primary CM**	**Cases with primary CM**	**Cases with HCM**
NO	162 (63.3%)	103 (68.2%)	59 (56.2%)	40 (50%)
YES	94 (37.7%)	48 (31.8%)	46 (43.8%)	40 (50%)
Total	256	151	105	80
**Count of cases without data*	*26*	*16*	*10*	*9*

As presented in Table 3, the eventual presence of a heart murmur was recorded for each case and the percentage was calculated for each diagnosis category. Several cases lacked data about auscultation and were therefore excluded. It is interesting to add that out of the 94 cases with a heart murmur, 49% have a CM and 51% do not have a CM.

Arrhythmias were detected by auscultation in 32 cases of CM (30.2%), out of 106 cases, since 9 cases had no information about auscultatory findings. No arrhythmia was found in the other 74 cases (69.8%). When specific phenotypes of CM are considered, 22% of HCM cases and 75% of DCM cases had an arrhythmia. Besides, 15% of cases without a CM had an arrhythmia too.

4.5. Echocardiography findings: SAM and DLVOTO

For all cases with a primary CM, the echocardiography findings of SAM and DLVOTO were recorded. The echocardiography examination did not allow for the search of these two criteria in 9 cases out of 115 CM cases. Consequently, these 9 cases were excluded for this part of the analysis. Systolic anterior movement was detected in 32 cases of CM, amounting to 27.8%, while DLVOTO was found in 25 cases (21.7%). In most patients, SAM and DLVOTO were identified together in the same patients. However, in 9 cases, only SAM was present, and in 2 cases, DLVOTO was alone. Moreover, out of the 32 cats with SAM, 24 had a heart murmur too, while the 8 other cats did not. Besides, 19 cats with a heart murmur had no finding of SAM.

It is also noteworthy that 13 cases without a primary CM had SAM too. This includes cats with mitral valve dysplasia (6), secondary CM (4), or aortic stenosis (1) for example. Similarly, 14 cases without a primary CM had DLVOTO.

4.6. Radiography findings

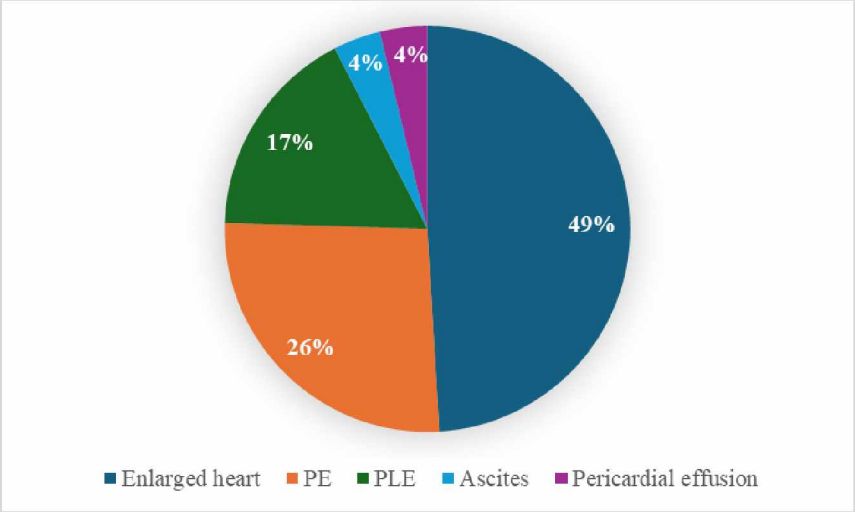

Figure 13. Distribution of radiography findings in 48 CM cases.

Radiography was performed in 48 cases out of the 115 cases of CM (42%). In 10 cats, the radiography did not reveal any abnormalities. The most prevalent finding was an enlarged heart (26), followed by PE (14) and PLE (9). Pericardial effusion and ascites were identified twice each. The distribution of the different radiography findings is shown in Figure 13.

4.7. Electrocardiography findings

Electrocardiography was carried on in 16 cats with a CM. The most common arrhythmia diagnosed was VPC (10). Atrial fibrillation (5) and third-degree AV block (2) were also detected. The ECG of a cat with DCM revealed both VPC and atrial fibrillation. Table 4 shows which arrhythmias were identified according to the cases' diagnosis.

Table 4. Count of each type of arrhythmias for each diagnosis category.

	Diagnosis category:					
Type of arrhythmia:	*HCM*	*NCM*	*RCM*	*DCM*	*ARVCM*	**Total**
VPC	4	4	0	1	1	**10**
Atrial fibrillation	3	1	0	1	0	**5**
Third-degree AV block	1	0	1	0	0	**2**
Normal	1	0	0	0	0	**1**

5. DISCUSSION

5.1. Diagnosis and prevalence

In a 5-year interval, 282 cats were presented for an echocardiography examination at the Clinic for Internal Diseases in the Veterinary Faculty of Zagreb. Cardiomyopathies were the most common diagnosis, with 115 cases, that is 40.8% prevalence. As reported in the literature, primary CMs are indeed the most important cardiac disease in cats. Secondary CMs and other cardiac diseases had a prevalence of 14.5% and 11.7% respectively. Besides, a total of 31 cats were diagnosed with thyrotoxic or hypertensive secondary CMs. These cases had hypertrophy of the left ventricle like in primary HCM. Therefore, as per FUENTES et al. (2020), hypertension and hyperthyroidism should be excluded in cats showing HCM signs on echocardiography.

Hypertrophic CM was the most common diagnosis with 89 cases, affecting 31.6% of the total population and representing 77.4% of CM cases. This follows trends noted in previous research where HCM was determined as the most important phenotype. However, it is reported that HCM can affect up to 15% of the cat population (KITTLESON and COTE, 2021a; KITTLESON and COTE 2021b). The result of this study shows a much higher prevalence. It should be noted that the Clinic for Internal Diseases at the Veterinary Faculty is a referral clinic. So, the studied cat population is at higher risk than the general population of cats in a first-opinion clinic. This could explain the disparity between the prevalences. Finally, in the literature, the two rarest phenotypes are DCM and ARVCM (KITTLESON and COTE, 2021a; KITTLESON and COTE 2021c). Here, DCM and ARVCM had in fact the smallest number of cases, making them less than 2% prevalent.

5.2. Epizootiology

Similarly, to the report by FUENTES et al. (2020), the vast majority of CM cases were mixed breed cats (80%), but high-risk breeds were also detected, such as Persian (5), Maine Coon (5), and British shorthair (3). Moreover, 65% of CM cases and 69% of HCM cases were male cats. This complies with the 70% male prevalence noted in ETTINGER et al. (2017). Finally, FUENTES et al. (2020) states that HCM is more likely a disease affecting older cats and ETTINGER et al. (2017) adds that most cats are diagnosed around 5 and 7 years old. Here, the median age of CM cats was 9 years old, with most diagnoses made in 6-year-old cats.

Besides, a third of cats diagnosed with HCM were between 4 and 7 years old. So, overall, all epizootiology data is in line with the literature.

5.3. Complaints and presentation

In HCM cases, dyspnoea was the most prevailing complaints in the owner's anamnesis, indicated in 44% of patients. This data seems appropriate since COTE et al. (2011) reports that dyspnoea is the chief complaint in 32-46% of cats diagnosed with HCM. The other main clinical complaints described in COTE et al. (2011) are signs associated with ATE, such as hindlimb paresis, found in 12-17% of cats diagnosed with HCM. Here, hindlimb paresis represented indeed 16% of the complaints in HCM cases. However, a large proportion of cats (39%) were diagnosed after the detection of a heart murmur (19%) or an arrhythmia (2%) or simply while performing controls (18%), so without any actual clinical complaint. This finding is also consistent with previous research, for example as stated in KITTLESON and COTE (2021a).

It is also worth mentioning that, out of all 282 cases, 108 cats were presented due to dyspnoea and 54 of them had a primary CM, so exactly 50%. Therefore, it would be interesting to study which would be the other main differential diagnosis for cats presented with dyspnoea in veterinary hospitals.

As for the clinical presentation, 42.5% of cats diagnosed with HCM were actually asymptomatic. This is coherent with the literature, which report that between 33 to 55% of cats diagnosed with HCM are subclinical (RUSH et al., 2002; COTE et al., 2011). So, at the Clinic for Internal Diseases, the disorder was mostly detected once clinical. Indeed, most presented cases had already signs of CHF mainly, but also ATE or both. It might be interesting to raise owners' awareness about monitoring their cat's respiratory rate to detect the onset of clinical CM earlier and start the treatment sooner with regular controls if necessary.

5.4. Auscultatory findings: hearts murmurs and arrhythmias

In this study, a heart murmur was detected by auscultation in 94 cats, and 51% did not have a CM. Indeed, heart murmurs were heard in cats with secondary CMs or with other cardiological disorders, and even in cats with no cardiac disturbance at all. Additionally, 32% of cats without a primary CM had a heart murmur, which is within the literature range of 25-33% (KITTLESON and COTE, 2021a). Therefore, as it is commonly agreed in theory, a heart

murmur is not specific to CM and can be benign (COTE et al., 2011; KITTLESON and COTE, 2021a). Moreover, in HCM cases, exactly 50% of cats had a heart murmur and 50% did not have one. The ratio is quite similar when considering all CM cases: 44% have a heart murmur and 56% do not have one. Consequently, the eventual presence of heart murmurs cannot be used to exclude or confirm a CM diagnosis.

As for arrhythmias, one was detected by auscultation in 22% of HCM and 75% of DCM. These findings are nearly the same as the ones reported in previous research: 79% of cats with DCM and 1/3 of cats with HCM have an arrhythmia on auscultation (FERASIN et al., 2003). However, comparably to heart murmurs, 15% of cases without a CM also had an arrhythmia. So, again, arrhythmias and gallop heart sounds are not specific to CMs.

Besides, one should not forget that cardiac auscultation is quite susceptible to human error, as the experience and the environment of the veterinarian can influence this process. Nonetheless, it is interesting to analyse this data since a few veterinarians still tend to over-associate abnormal auscultatory findings with cardiac pathologies.

5.5. Echocardiography findings: SAM and DLVOTO

KITTLESON and COTE (2021b) explains that DLVOTO is the consequence of SAM of the mitral valve. Therefore, it seems that SAM and DLVOTO should be found together in cats, or at least that SAM may be found without DLVOTO on a more frequent basis than the opposite. This was demonstrated in this retrospective study. Indeed, SAM was identified in 32 cases of CM, and it was accompanied by DLVOTO most times. From these 32 cases, SAM was revealed without DLVOTO on 9 occasions. However, 1 cat showed the presence of DLVOTO, but no signs of SAM. Further reading about these two echocardiographic findings would be required, as there are possibly other factors influencing DLVOTO, such as the IVS hypertrophy as it is stated in WARE (2011).

Apart from the correlation between SAM and DLVOTO, it is worth mentioning that SAM was also reported in 32 cats without a primary CM. As a matter of fact, SAM was identified in 6 cases of mitral valve dysplasia, 4 cases of secondary CM, and 1 case of aortic stenosis. COTE et al. (2011) mentions the three latter disorders as differential diagnoses to HCM, also leading to SAM of the mitral valve. Thus, it can be concluded that SAM is not a specific finding of CMs, even though it is a characteristic feature of HCM.

Lastly, while SAM of the mitral valve causes mitral regurgitation, not all cats with SAM had an audible heart murmur. Furthermore, some cats with a heart murmur did not exhibit SAM on echocardiography. There again, it is shown that relying on heart murmurs is not the best practice.

5.6. Radiography findings

Radiography was not performed routinely for cats suspected of CM. Indeed, a bit less than half (42%) of CM cases were sent for a radiography examination. This is a reasonable number as no final diagnosis can be drawn from this imaging technique. Besides, chest radiographs do not have the same sensitivity in diagnosing CM compared to echocardiography. Indeed, 10 cats with a CM had a normal radiograph. However, radiography was still useful to detect PE and PLE, and, according to previous research, it is indeed the best mean to visualise these CHF signs (COTE et al., 2011; FUENTES et al., 2020; KITTLESON and COTE, 2021b; KITTLESON and COTE, 2021c).

5.7. Electrocardiography findings

Electrocardiography examination was rarely conducted as it is not a diagnostic tool for CM in cats. The most common arrhythmia detected was VPC in 10 cases. This finding is consistent with the reports in KITTLESON and COTE (2021a). As there are only a small number of cases with ECG, it is difficult to draw any more reliable conclusions.

5.8. Management and prognosis

No specific data was recorded about management for the purpose of this study. Indeed, the management of the CM cases always complied with the protocol according to the staging, as presented by FUENTES et al. (2020). Besides, data about quality of life and survival was scarce as no follow-up was carried out. Therefore, it is not possible to conclude anything on that matter.

6. CONCLUSION

- Cardiomyopathies are the most important cardiac disease in cats, with HCM being the most prevalent phenotype and DCM and ARVCM the rarest.
- Primary CMs are more frequent than secondary CMs.
- The epizootiology study confirmed that CMs affect mainly mixed breed cats and male cats. The disease is more common in older cats, but it is most often diagnosed in middle-aged cats.
- Cardiomyopathies in cats are idiopathic, except in Maine Coon and Ragdoll cats in which mutations responsible for HCM were identified.
- A large proportion of cats diagnosed with a CM are subclinical. The rest of the cats are presented mainly with signs of CHF, namely dyspnoea, or occasionally signs of ATE, namely hindlimb paresis.
- Heart murmurs and arrhythmias may or may not be present in cats with a CM and can also be detected in cats without a CM. So, these auscultatory findings are not specific and should not be used to diagnose or exclude any cardiac conditions in the cat.
- Echocardiography is the gold standard for diagnosis of CMs in cats. It also allows differentiation between the different phenotypes.
- Radiography and ECG are not necessary for the diagnosis of CMs in cats. However, radiography allows for appropriate visualisation of CHF signs in the lungs, and ECG is used to identify any arrhythmia. The most prevalent type of arrhythmia in cats with CMs are VPC.
- Management and therapy are determined according to the staging of the cat. Thromboprophylaxis drugs are introduced at stage B2, and diuretics are added at stage C. Regular check-ups are essential.

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8. SAŽETAK

Elise Farah

Pretežitost pojave mačjih kardiomiopatija u Klinici za unutarnje bolesti Veterinarskog fakulteta Sveučilišta u Zagrebu u razdoblju od 2017. do 2022. godine

Kardiomiopatije predstavljaju najvažniju skupinu stečenih srčanih bolesti u mačaka. Hipertrofična kardiomiopatija najčešći je oblik kardiomiopatije u mačaka. Općenito govoreći, kardiomiopatije su idiopatske bolesti miokarda koje prvenstveno pogađaju starije i muške mačke. Opisane su i pasminske predispozicije, tako da se hipertrofična kardiomiopatija javlja u pashmina *Maine Coon* i *Ragdoll*, a povezana je sa specifičnom genskom mutacijom. Akutno popuštnje (kongestivno zatajivanje) srca i arterijska tromboembolija dva su tipična klinička scenarija kojima se kardiomiopatije očituju. Dijagnostički zlatni standard je ehokardiografija, koja dodatno omogućuje diferencijaciju između pet različitih fenotipova. Kliničko stupnjevanje kardiomiopatija korisno je u standardizaciji pristupa liječenju, ali i prognoziranju ishoda bolesti. Prikazano retrospektivno istraživanje ima za cilj analizirati pretežitost pojave kao i druge pokazatelje kardiomiopatija u populaciji mačaka zaprimljenih u Klinici za unutarnje bolesti Veterinarskog fakulteta u Zagrebu Sveučilišta u Zagrebu, tijekom petogodišnjeg razdoblja. Prikupljeni su te istraženi podatci o epizootiologiji, kliničkoj slici i dijagnostičkoj obradi.

Ključne riječi: hipertrofična kardiomiopatija, ehokardiografija, pretežitost, retrospektivno istraživanje, mačka

9. SUMMARY

Elise Farah

Prevalence of feline cardiomyopathies at the Clinic for internal diseases at the Faculty of Veterinary Medicine University of Zagreb from 2017 to 2022

Cardiomyopathies represent the most important cardiac disease in cats, and hypertrophic cardiomyopathy is by far the prevailing phenotype. This mainly idiopathic condition affects primarily older and male cats of mixed breed. However, some breeds, such as Maine Coon and Ragdoll, have a predisposition, linked to a mutation. Congestive heart failure and arterial thromboembolism are two fatal consequences, and are responsible for the presenting symptoms, when cats are not subclinical. The gold standard for diagnosis is echocardiography, which additionally allows for differentiation between the five different phenotypes. Clinical staging can guide veterinarians in establishing a management and treatment protocol, as well as assessing the prognosis. This retrospective study aims to analyse the prevalence and other trends associated to this feline disorder at the clinic for internal diseases in the Veterinary Faculty of Zagreb over a 5-year period. Data about epizootiology, presentation and diagnosis to name a few was collected and examined. Overall, most findings are coherent with results from previous research.

Keywords: hypertrophic cardiomyopathy, echocardiography, prevalence, retrospective study, cat

10. CURRICULUM VITAE

I was born and raised in France, by Lebanese parents. As I decided to become a veterinarian, I came across the Faculty of Veterinary Medicine in Zagreb, Croatia, and thus took the leap to go abroad and started my studies in 2017. Passionate about my path, I was fortunate to receive the Award for Best Academic Achievement every study year, and throughout my stay in Zagreb, I embraced several opportunities that enriched my experience.

Always eager to help my peers, I took the position of undergraduate assistant for two consecutive academic years in 2018, in multiple subjects for first and second-year students: Anatomy, Histology, Statistics, Breed characteristics, as well as Animal breeding and production. Additionally, I was nominated as class representative of my study year, and president of the student association *The Vet Society* for two consecutive years. I was able to speak on behalf of my colleagues and work on improving our overall student experience. For instance, in my role as president, I launched a couple of events that are now traditions, such as the *Freshers' Day* to help new students integrate better.

Motivated to learn and practise more, I started volunteering at the Reproduction and Obstetrics Clinic of the Faculty in 2021 for more than a year. I also did two externships in small animal practices: one month in Clinique Vétérinaire du Valvert in Écully, France, in 2022, and two months in Clontarf Veterinary Hospital in Dublin, Ireland, in 2023. Moreover, I attended the international symposium *SYMCO* in South Africa in 2019 to satisfy my curiosity about the work of wildlife veterinarians.