Sveriges lantbruksuniversitet
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Department of Anatomy, Physiology and
Biochemistry

Congenital heart defects in cats – prevalence and survival

A retrospective study of 60 cats

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Kongenitala hjärtfel hos katt – förekomst och överlevnad

En retrospektiv studie av 60 katter

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SUMMARY

Congenital heart disease (CHD) is defined as an anatomic defect of the heart or the associated great vessels present at birth. Depending on the severity of the defect, it may lead to heart failure, which generally results in a decreased quality of life and/or shortened life span. The prevalence of CHDs in cats in Sweden is not known and little is generally known about the expected lifespan of cats diagnosed with CHD. The purpose of this study was, therefore, to investigate the prevalence and distribution of CHD in a large group of cats presented at the University Animal Hospital in Uppsala, Sweden, between the years 1996 and 2013.

In the first part of the study, case records of cats presented and diagnosed with CHD at the University Animal Hospital, Uppsala, between 1996 and 2013, were retrospectively reviewed. In total, 60 cats had been diagnosed with CHD during the study period. The prevalence of CHD was 0.2 % of the total number of visiting cats (n = 32 919), and 7.3 % of cats diagnosed with heart disease (n = 824). Ventricular septal defect (VSD) was the most common CHD accounting for 46.7% of cases, followed by tricuspid/mitral valve dysplasia (8.3%), aorta stenosis (8.3%), pulmonic stenosis (6.7%), Tetralogy of Fallot (6.7%), atrial septal defect (5 %) and mitral valve dysplasia, endocardial fibrosis, patent ductus arteriosus each accounting for approximately 1.7% of CHD cases. In 13.3% of the cats, more than one congenital heart defect was present. There was no sex predilection ($P = 0.20$). Because of the nature of the material for this study, namely too few individuals of the same breed, no breed predilection could be established. However, the group of domestic shorthair, which accounted for 46.7 % of all the cats, were more likely to have VSD than all purebred cats together ($P = 0.008$).

For the second part of the study, follow-up telephone interviews with a standardised questionnaire, were conducted between the 24th of September and 8th of October in 2014. The aim was to reach all owners of cats that had been diagnosed with a CHD during the study period. However, 16 cats were lost to follow up because the owners could not be reached. Of the remaining cats, 31 had died and 13 were still alive, giving an estimated median survival time of 40 months. In total, 52 % of the cats had died from cardiac related disease. Their median survival time was 16 months, which was significantly shorter ($P = 0.032$) than cats that died from non-cardiac related disease with a median survival time of 35 months. Cats diagnosed with VSD had a median survival time of 123 months, which was significantly higher ($P = 0.013$) than cats diagnosed with other CHDs with a median survival time of 32 months.

In conclusion, the prevalence and distribution of CHDs was shown to be consistent with findings in American and European literature on the subject, with VSD being the most common CHD, followed by tricuspid/mitral valve dysplasia and aortic stenosis. The result that domestic shorthair was more likely to have VSD than purebred cats may be true for the whole cat population but can also be an reflection of the nature of the study population, hence more studies are needed. The fact that cats diagnosed with VSD had a markedly longer expected survival time than cats diagnosed with other CHDs is interesting from a clinical point of view, especially when considering that only one cat, out of nine dead cats with VSD, died because of cardiac related disease. This confirms the general empirically based idea that cats diagnosed with VSD have a relatively good long-term prognosis.

SAMMANFATTNING

Kongenitala hjärtfel definieras som närvaron av en anatomisk defekt i hjärtat eller dess stora kärl vid födseln. Beroende av defekternas svårighetsgrad kan de leda till hjärtsvikt med försämrad livskvalitet och/eller förkortad livslängd. Kännedomen kring prevalens och förväntad livslängd hos katter diagnostiserade med kongenitala hjärtfel är mycket begränsad varför syftet med denna studie var att undersöka detta hos en grupp katter vilka besökt Universitetsdjursjukhuset i Uppsala under perioden 1996 till 2013.

I den första delen av studien granskades journaler från de 60 katter som diagnosticerats med kongenitala hjärtdefekter vid Universitetsdjursjukhuset, Uppsala, mellan 1996 och 2013. Av det totala antalet besökande katter (n = 32 919) under studieperioden var prevalensen kongenitala hjärtdefekter 0.2 % medan prevalensen var 7.3 % av de katter som diagnostiseras med hjärtsjukdom (n = 824). Ventrikulär septumdefekt (VSD), även kallad kammarseptumdefekt, utgjorde 46.7 % av fallen och var den vanligast förekommande defekten. Därefter följde tricuspidalis/mitralis dysplasi (8.3 %), aortastenos (8.3 %), pulmonalisstenos (6.7 %), Fallots tetralogi (6.7 %) och förmaksseptumdefekt (5 %). Mitralisdysplasi, endokardiell fibros och persisterande ductus arteriosus stod för vardera 1.7 % av fallen. Totalt 13.3 % av katterna hade mer än en kongenital hjärtdefekt. Det fanns ingen könspredisposition ($P = 0.20$). På grund av materialets sammansättning med få individer av vardera ras kunde inget samband mellan ras och diagnos undersökas. Resultaten visade dock att gruppen huskatt, som stod för 46.7 % av alla katter, var mer benägna att ha VSD än de renrasiga katterna tillsammans ($P = 0.008$).

I den andra delen av studien genomfördes uppföljande telefonintervjuer utifrån ett standardiserat frågeformulär mellan den 24 sep och 8 okt 2014. Syftet var att kontakta alla kattägare vars journaler granskats i del I, men 16 katter utgick då ägarna inte kunde nås. Av de återstående 44 katterna hade 31 avlidit och 13 var fortfarande vid liv. Deras gemensamma median för överlevnad skattades till 40 månader. 52 % av katterna dog av hjärtrelaterad sjukdom med en medianöverlevnad på 16 månader. Detta var signifikant kortare ($P = 0.032$) än katter som dött av icke hjärtrelaterade skäl, vilka hade en medianöverlevnad på 35 månader. Katter som diagnostiseras med VSD hade en medianöverlevnad på 123 månader, vilket var signifikant högre ($P = 0.013$) än katter som diagnostiserats med andra kongenitala hjärtfel vilka hade en medianöverlevnad på 32 månader.

Sammanfattningsvis visade sig förekomst samt fördelning av kongenitala hjärtdefekter vara överensstämmande med europeisk och amerikansk litteratur publicerad i ämnet. Ventrikulär septumdefekt var den vanligaste defekten följt av mitralis/tricuspidalis dysplasi och aortastenos. Att huskatter hade en högre prevalens av VSD än raskatter kan vara representativt för kattpopulationen, men kan även bero på den utvalda populationens sammansättning varför fler studier behövs. Det faktum att katter diagnostiserade med VSD hade en markant längre överlevnad än katter diagnosticerade med andra kongenitala hjärtfel samt att bara en av nio döda katter med VSD hade dött i en hjärtrelaterad sjukdom är intressant ur klinisk synpunkt. Detta styrker den allmänna uppfattningen om att katter med VSD har en generellt god prognos för överlevnad.

CONTENTS

Abbreviations

AS   aortic stenosis

ASD   atrial septal defect

AVSD   atrioventricular septal defect

AVD   atrioventricular valve defects

CHD   congenital heart defects

MD   mitral valve dysplasia

MS   mitral valve stenosis

PDA   patent ductus arteriosus

PS   pulmonic stenosis

TD   tricuspid valve dysplasia

TS   tricuspid valve stenosis

TOF   Tetralogy of Fallot

VSD   ventricular septal defect

INTRODUCTION

The heart is the first functional organ in vertebrate embryos, and beats spontaneously in cats by week 3 of life (Verstegen *et al.*, 1993). The development of the heart is a complex, yet beautiful process. It begins with the formation of a primary endothelial tube that with time extends asymmetrically. By following an intricate mix of signals it loops and septates, forming the four chambers we know as the heart, and its paired arterial trunks (Dyce *et al.*, 2002).

Congenital heart disease (CHD) is defined as a morphologic defect of the heart or the associated great vessels present at birth. The abnormalities associated with the conditions occur during early embryologic development and are caused by pathological alterations or arrests during specific phases (MacDonald, 2006). The aetiology of CHD varies; they may develop as a result of toxicological (Khera, 1975), environmental, genetic, infectious, nutritional, and drug-related factors (Bonagura & Lehmkuhl, 1999).

Congenital heart disease can lead to heart failure, defined as a state of body function when the cardiovascular system is no longer able to circulate enough blood to meet the metabolic needs of the body. The condition is characterized by decreased cardiac output and a tendency towards decreased arterial pressure, which will activate compensatory mechanisms leading to vasoconstriction. The fluid retention and increased venous and capillary pressures can lead to congestive heart failure, which is a life-threatening condition, necessitating medical treatment (Hamlin, 1999).

Left sided heart failure is normally manifested by hypertension in the pulmonary veins and a decreased cardiac output on the left side. It often leads to pulmonary oedema and varying degrees of lethargy, dyspnoea and exercise intolerance. Right sided heart failure is characterized by congestion of the abdominal organs, ascites, pericardial effusion and pleural effusion (Kittleson, 1998a; Strickland, 2007). In cats, the latter is also thought to be caused by left heart failure because the pleura is partly supplied by the venous system (Johns *et al.*, 2012). The classification into left and right sided heart failure is not always well defined because the left and right circulatory systems are dependent of and affect each other in several ways. Some diseases and lesions therefore end up affecting both sides, immediately or in the long run (Strickland, 2007).

Heart failure generally results in a decreased quality of life and/or shortened life span. With that said though, it is important to understand that not all CHDs lead to heart failure and death. It is the severity and localisation of the lesion that determines the degree of its subsequent impact on the individual (Côté *et al.*, 2011).

LITERATURE REVIEW

Classifications of congenital heart defects

Ventricular septal defects

Ventricular septum defects (VSD) are characterized by communication between the two ventricles owing to an orifice caused by incomplete closure of the interventricular septa. The aetiology of VSD has been described to usually be unknown with no family history of the defect to be present (Kittleson, 1998b) and according to Côté *et al.* (2011) there are no known breed predispositions.

Lesions

The size and location of the defect can vary and is defined by the region in which it resides. The interventricular septum is made up of the inlet septum; the outlet septum (or infundibular); the trabecular septum; and the membranous septum. The latter is small and lies immediately below the aortic valve on the left side and between the tricuspid valve and the pulmonic valve on the right side. Most VSDs are perimembranous (Kittleson, 1998b; Côté *et al.,* 2011) and the most common one in cats occurs just below the aortic valve (Liu, 1977; Côté *et al.,* 2011) One third of the isolated VSDs in cats has been reported to be associated with dysplasia of the tricuspid valve (Liu, 1977). Defects in the muscular part of septum may occur but are rare in cats (Kittleson, 1998b). If the lesions weaken the supporting structures of the aortic valve, insufficiency may develop (Côté *et al.*, 2011).

Pathophysiology

In an uncomplicated VSD the pressure difference between the ventricles typically causes the blood to shunt across the defect from left-to-right in systole. Most of the blood will shunt directly into the right ventricular outflow tract and pulmonary artery (Bonagura & Lehmkuhl, 1999). It will then proceed to the lungs and return to the left atrium again via the pulmonary veins. Thus, it is the pulmonary arteries and veins, and the left side of the heart, which will experience the majority of the volume overload (Côté *et al.*, 2011). The size of the lesion and the pulmonary and systemic vascular resistance determines the outcome of the defect (MacDonald, 2006).

A small defect may be of no hemodynamic significance, as it provides a greater resistance to the blood flow than the pulmonary and systemic circulation. Thus, the flow through the pulmonary circulation is not greatly increased, and so the relative pressure of the heart remains within a normal functional range (Kittleson, 1998b). In some cases, small defects close spontaneously during growth (Côté *et al.*, 2011).

A moderate-sized defect present a lesser resistance to systolic flow and may therefore be large enough to increase pulmonary artery pressure and right ventricular systolic pressure by enabling a left-to-right shunt (Kittleson, 1998b). If clinical signs develop, they will be signs of left heart failure (Côté *et al.*, 2011).

A moderate to large VSD may cause the two ventricles to function as one common unit. Due to increased blood volume on pulmonary vasculature some patients may develop elevated pulmonary artery pressure (Côté *et al*., 2011). The increased pulmonary resistance results in an elevated right ventricular pressure that may reverse the shunted blood to the point of lesser resistance, and a right-to-left shunt may consequently develop (MacDonald, 2006). In this case the venous blood does not pass the lungs before entering the systemic circulation and severe signs of cyanosis and right heart failure may be seen (Côté *et al*., 2011). This is also referred to as Eisenmengers syndrome (MacDonald, 2006), for further description see page 12.

Clinical findings

Clinical signs are depending primarily on the size of the lesion. The most common clinical finding is a holosystolic murmur with puncta maxima at the right 4th or 5th intercostal space near the sternal border, although it may be heard on the left side as well if loud enough (Bolton & Liu, 1977; Kittleson, 1998b). In small to moderate-sized defects the murmur is typically harsh, loud and detected during auscultation of an asymptomatic kitten or adult cat at the time of routine evaluation. In moderate to large-sized defects the murmur is softer and often presented together with signs consistent with congestive left-sided heart failure (Bonagura & Lehmkuhl, 1999) . The murmur may be absent in cases with very large defects and/or severe pulmonary hypertension, because of the lack of a pressure differential across the septum. If pulmonary hypertension develops, signs of right sided failure and cyanosis will predominate (Strickland, 2007).

If the defect is causing destabilization of the aortic valve cusp, a non-continuous diastolic murmur of aortic insufficiency may also be present; this combination is then referred to as a to-and-fro murmur (Strickland, 2007). Due to the extra volume of blood that passes through the pulmonary valves a sound of functional pulmonic stenosis (PS) may also occur (Côté *et al.,* 2011).

Electrocardiogram and thoracic radiographs may show abnormalities, depending on hemodynamic consequences of the shunt. They may be normal or show evidence of left, right, or biventricular enlargement. On electrocardiogram, a right bundle branch block may also be seen (Strickland, 2007). Radiographs may correspondingly show signs of left congestive heart failure with patchy pulmonary oedema and pulmonary venous congestion (Côté *et al.,* 2011). In cases with pulmonary hypertension and right-to-left shunting a pattern of prominent tortuous pulmonary arteries may be seen on the radiographs (Strickland, 2007).

The diagnosis is made by echocardiography with colour-flow and continuous-wave Doppler. The defect can usually be identified by 2D echocardiography but if too small colour-flow Doppler may assist the examiner identifying it (Côté *et al*., 2011). Continuous-wave Doppler should be used to determine the velocity of the shunt (MacDonald, 2006). A high-velocity flow, greater than 4.5 m/s, and normal transpulmonic valvular velocities is associated with smaller "restrictive" shunts with none or small hemodynamic significance. These patients rarely present clinical signs. Low-velocity flow, less than 4.5 m/s, and increased

transpulmonic valvular velocities is associated with moderate- to larger "unrestrictive" defects that are hemodynamically significant and likely to result in clinical signs (Strickland, 2007).

Therapy and Prognosis

Most small, restricted VSDs are well tolerated and most of the cats do not develop clinical signs for years, if at all (Côté *et al.,* 2011). Potential treatments for moderate- to large defects include surgical and/or medical therapy. However, because there are currently very limited surgical interventions feasible in cats with large defects (particularly small cats), most animals that develop clinical signs are managed with heart failure medication. The prognosis is therefore largely dependent on the size of the defect (Côté *et al.,* 2011).

Atrioventricular valve dysplasia

Tricuspid valve dysplasia (TD) and mitral valve dysplasia (MD) generally lead to functional disturbances associated with their respective pathophysiologies. Great similarities can be seen between congenital and acquired degenerative valvular defects (MacDonald, 2006).

Lesions

There is no exact definition of the word dysplasia, but it is normally used as a term that describes abnormal growth within organs and tissues. The morphology of reported mitral and tricuspid defects varies extensively, including shortened, rugged, rolled or thickened valves, intergrowth and thickening or extension in *chordae tendinae* or valves attaching directly to the papillar muscles. Other findings comprise atrophy or hypertrophy of the papillar muscles, and papillar muscles located too high relative the valves (Liu & Tilley, 1976). Tricuspid valve dysplasia and mitral valve dysplasia may occur as isolated defects as well as together or in combination with other CHDs (Liu & Tilley, 1976; Kornreich & Moïse, 1997; Côté *et al.,* 2011).

Pathophysiology

Tricuspid valve dysplasia causes regurgitation in systole with subsequent atrial volume overload followed by atrial dilatation. This leads to increased diastolic venous return to the ventricle, which has to accommodate the volume overload as well as manage normal stroke volume to the pulmonary system despite the continuous leakage during systole. It does so by dilation of the volume space and thickening of the myocardial wall, also referred to as eccentric hypertrophy. The enlargement of the ventricle causes the atriovalvular orifice to expand, causing further regurgitation to the atria, because the valvular cusps cannot elongate. This creates a vicious cycle of increasing volume overload of the right side of the heart, which eventually will not be able to keep up the stroke volume, and congestive right heart failure may develop. In the long run the decreased pulmonary flow, and hence the decreased venous return to the left side, will make the left ventricle under loaded resulting in a decreased systemic blood flow (cardiac output). Right heart failure due to TD has ben described to be one of the most common reasons for ascites in cats (Kittleson, 1998c). Also signs of hepatomegaly, jugular vein distension and occasionally pleural effusion may be identified (Liu & Tilley, 1976; Kittleson, 1998c).

The hemodynamic mechanism behind the pathophysiology for mitral valve dysplasia is the same as for TD regarding regurgitation to the atria and volume overload of the ventricle with its subsequent enlargement and decreased cardiac output. The difference is the final outcome, which is congestive left heart failure with elevated left atrial and pulmonary venous pressures (MacDonald, 2006). The latter will cause pulmonary oedema, as well as enlargement (due to elevated resistance in the pulmonary circulation) of the right ventricle in the long run. An MD is considered more severe than a similar size TD due to the nature of pressure differences between the left and right side of the heart. Because the pressure is much higher on the left side, a small MD can cause just as much, and even more, hemodynamic changes then a larger TD (Kittleson, 1998c).

Both of the congenital defects share many similarities with their corresponding chronic degenerative valvular diseases. Both of them also predispose for arrhythmias, primarily atrial fibrillation but also premature atrial contractions. Additionally, the atrial dilatation might present a small risk of developing secondary atrial thrombi when non-flowing blood coagulate (Kittleson, 1998c; Côté *et al.,* 2011).

Clinical findings

There is a wide spectrum of clinical presentations, from murmurs detected at routine evaluation to clinical signs of congestive left (MD) or right (TD) heart failure in severe cases (Côté *et al.,* 2011). During auscultation a regurgitating systolic murmur is usually detected over the affected area and rhythm disturbances may be present. Electrocardiography may show various supraventricular arrhythmias (Côté *et al*. 2011) and in cases of TD splintered QRS complexes are common (Kornreich & Moïse, 1997). Thoracic radiography may show dilatation of the atria and ventricles. Echocardiography including Doppler is necessary to diagnose the defect (MacDonald, 2006).

Therapy and prognosis

Symptomatic therapy is usually the only option and the prognosis is guarded to poor if clinical signs are present together with other concurrent cardiac malformations and/or severe cardiomegaly (Côté *et al*. 2011).

Atrioventricular valve stenosis

Congenital tricuspid valve stenosis (TS) and mitral valve stenosis (MS) are characterized by a narrowed annulus of the atrioventricular valves or subvalvular or supravalvular area (Liu & Fox, 1999; Campbell & Thomas, 2012). The defects are rarely seen in cats; if present, they usually occur in conjunction with valve dysplasia and regurgitation (MacDonald, 2006; Côté *et al*., 2011). Valvular dysplasias are more common than stenoses, but in cases where the atrium is dilated and the ventricle of normal size, obstruction should be suspected.

Pathophysiology

The stenotic area in the valvular region impedes normal diastolic filling function and results in elevated atrial pressure and consequently atrial enlargement. In MS it leads to increased

pulmonary venous congestion and pulmonary edema, much like in MD, and subsequently congestive left side heart failure. In cases of TS it can lead to enlargement of the right ventricle and congestive right heart failure (Liu & Fox, 1999). The clinical signs, diagnostics, therapy and prognosis are largely consistent with MD and TD (Côté *et al*. 2011).

Aortic stenosis

Aortic stenosis (AS) is characterized by an abnormal narrowing in the aortic outflow region. The defect is thought to be uncommon in cats but cases have been reported (Stepien & Bonagura 1991; Côté *et al*., 2011).

Lesions

The stenosis can be subvalvular, caused by a fibrous ring and hypertrophied muscle tissue distally of the valvular plane. It can also be valvular, caused by thickened and/or intergrown cusps; or supravalvular with an actual narrowing of the great vessel itself (Liu, 1977; Bonagura & Lehmkuhl, 1999; Margiocco & Zini, 2005).

Pathophysiology

The stenosis obstructs the outflow of blood from the left ventricle to the systemic circulation, which leads to increased pressure in the ventricle. Concentric left ventricular hypertrophy (thickened walls) occurs to reduce wall stress and compensate for the pressure overload (MacDonald, 2006). Because the ventricular wall becomes less elastic, and the filling more restrictive in nature, resulting in atrial dilatation. The latter can also be a result from volume overload. Systolic function is usually maintained, but diastolic dysfunction may develop in severe cases of hypertrophy and myocardial fibrosis (MacDonald, 2006). Due to the altered pressure and morphology of the ventricle, insufficiency in the mitral ostium may develop. A fast and turbulent blood flow in the stenotic area causes a murmur and potentially post stenotic dilatation of the vessels. Additionally, the continuous turbulent flow in the stenotic area can worsen the primary defect and over time make the stenosis more severe (Bonagura & Lehmkuhl, 1999).

Clinical findings

Clinical presentation is associated with cases of sudden death with no prior clinical signs, or with development of acute congestive left-sided heart failure including tachypnea, dyspnea, and crackles (Stepien & Bonagura 1991). Syncope has also been reported (Margiocco & Zini, 2005). The signs are corresponding to the severity of the defect; mild or moderate lesions may be asymptomatic. Severe cases may cause impaired growth, exercise intolerance, collapse and laboured breathing (Strickland, 2007). During auscultation a systolic ejection murmur at the left base may be heard, and in some cases a diastolic murmur of aortic regurgitation can be heard (even though these murmurs are generally very difficult to discern). Sometimes the murmur may radiate to the right base or be loudest at the sternum (Bonagura & Lehmkuhl, 1999). A gallop rhythm may be auscultated (Côté *et al*., 2011).

Electrocardiography and radiography may appear normal or may show evidence of atrial and/or ventricular enlargement (Margiocco & Zini, 2005). Radiographs may also show a post stenotic dilatation bulge of the aorta as well as pulmonary venous congestion and patchy pulmonary oedema. Echocardiography with Doppler is necessary to assess the severity of the defect as well as to differentiate it from other heart related diseases. Congenital subvalvular stenosis is for example very hard to differentiate from acquired aortic stenosis associated with for example hypertrophic cardiomyopathy or other cardiac conditions (Strickland, 2007).

Therapy and prognosis

Interventional therapy might be considered but like all surgical heart therapy it is difficult due to the cat being such a small animal. Furthermore, surgical intervention on AS in dogs has not been proven successful regarding long-time survival (Strickland., 2007). Medical therapy is therefore recommended in cases of congestive heart failure. The prognosis is generally poor for all cases that are considered to be worse than mild, with an increased risk of sudden death or developing congestive heart failure (Côté *et al*., 2011.).

Pulmonic stenosis/pulmonary artery stenosis

Pulmonic stenosis (PS) is characterized by an abnormal narrowing in the outflow region of the right ventricle, while pulmonary artery stenosis is referred to as stenosis in the main or branched pulmonary artery. Several cases have been reported but the defects are generally described as uncommon in cats (Hopper *et al*., 2004; Schrope & Kelch, 2007).

Lesions

Obstruction to right ventricular outflow can develop in the infundibular region (Schrope, 2008), or be subvalvular, valvular or supravalvular (Hopper *et al*., 2004; Schrope & Kelch, 2007).

Pathophysiology

As described for AS, the stenosis hampers the outflow of blood from the ventricle. This can lead to development of right ventricular concentric hypertrophy, thickened papillary muscles, flattening of the interventricular septa, tricuspid valve regurgitation, mild right atrial dilatation, post stenotic dilatation and a turbulent post stenotic jet. Flattening of the interventricular septum is attributed to decreased compliance and increased diastolic pressure in the right ventricle (Hopper *et al*., 2004). The hemodynamic changes can result in right-sided heart failure (Bonagura & Lehmkuhl, 1999; Strickland, 2007).

Clinical findings

Animals with mild to moderate pulmonic stenosis are usually asymptomatic, but if the severity of the lesion is large enough clinical signs of dyspnoea, fatigue and exercise-induced syncope secondary to low cardiac output may be seen (Strickland, 2007). Decompensation and signs of right-sided heart failure may occur. Murmurs are systolic and of ejection type with puncta maxima at the left heart base over the pulmonic valve but can radiate widely (Schrope & Kelch, 2007). Electrocardiography and radiography may appear normal or may

show evidence of right atrial and/or ventricular enlargement. Echocardiography and Doppler is necessary to diagnose and determine the severity of the lesion (MacDonald, 2006).

Therapy and prognosis

As for most of the congenital heart defects the prognosis depends upon the severity of the defect. Therapy is seldom required in cats with mild defects, most cats seem to remain asymptomatic, or presenting only mild clinical signs. But in more moderate cases, where therapy might be indicated, medical therapy is recommended. A few cases of balloon valvuloplasty in cats have also been reported (Schrope, 2008).

Tetralogy Of Fallot

Tetralogy of Fallot (TOF) is a combination of cardiac malformations including VSD, overriding dextropositioned aorta (ready communication of the aorta with both ventricles above the septal defect) and PS with a secondary hypertrophy of the right ventricle. The extent of the malformations may vary (MacDonald, 2006).

Pathophysiology

The pathophysiology differs depending on the severity of the lesions. Cases with a mild VSD and mild PS may develop a typical left-to-right shunt. In severe cases of TOF however, the stenosis in the pulmonic artery causes pressure in the right ventricle to increase and most of the venous blood returning from the systemic circulation will shunt directly through the VSD and out the overriding aorta. This right-to-left shunt (Bolton *et al.*, 1972) consequently leads to severe hypoxia. Because of the poorly oxygenated blood the kidneys will be stimulated to produce erythropoietin, and secondary polycythaemia may develop (Bush *et al.*, 1972). Hypertrophy of the right ventricle is secondary to the PS and is thus not a CHD in itself (MacDonald, 2006).

Clinical findings

A kitten with significant TOF is usually identified at an early age due to severe clinical signs of hypoxia; including weakness, lethargy, cyanosis, fatigue on exercise, dyspnoea, tachypnoea and syncope. TOF is typically associated with stunted growth, arrhythmias and/or hyper viscosity of the blood as well as sudden death due to hypoxia, (Bolton *et al.*, 1972). On auscultation a murmur associated with PS and/or VSD is usually detected, but in severe cases murmurs may be absent due to total equilibration of the ventricles (Bush *et al.*, 1972). Diagnosis of TOF is made by echocardiography including Doppler.

Therapy and prognosis

Surgical therapies, including creation of a systemic-to-pulmonic shunt have been described. They are in most cases very difficult to perform however, partly because of cats being such minuscule animals (Côté *et al.*, 2011). Most cats die at a very young age due to rapid development of congestive heart failure and its complications. The prognosis is poor in most cases (Bolton *et al.*, 1972). However, the extent of the primary lesions and their effects must be considered in order to provide an accurate prognosis (Côté *et al.*, 2011).

Atrial septal defects

Atrial septal defect (ASD) is characterized by communication between the two atria owing to a defect in the interatrial septum (MacDonald, 2006).

Lesions

Three types of primary defects have been defined and they are currently being classified according to location of the septal malformation (Bonagura & Lehmkuhl, 1999; Kittleson, 1998b). Defects in the most apical part of septum, near the atrioventricular valves, are called *ostium primum* defects. ASDs located in the fossa ovalis, caudal to the intervenous tubercle, are called *ostium secundum defects*. Finally, ASDs located dorsocranial to the fossa ovale are named *sinus venosus defects* (MacDonald, 2006). Atrioventricular canal defects are endocardial cushion defects that include an *ostium primum* ASD and a VSD (MacDonald, 2006; Schrope, 2013).

Pathophysiology

Typically an ASD causes blood to shunt from left-to-right and the severity of the shunt depends on (1) the size of the orifice, and (2) the relative resistances in the systemic and pulmonary circulations. If the defect is small, differential pressures between the two chambers may still be maintained and the defect is called *restrictive*. If the ASD is large, blood from the left atrium will shunt freely in to the lower-pressured right atrium and consequently an enlargement of both the right chambers, pulmonary artery, and the pulmonary veins follow from the volume overload. As a result, advanced cases might develop right ventricular failure with high pulmonary resistance leading to pulmonary hypertension (Bonagura & Lehmkuhl, 1999). Conditions that increase right atrial or ventricular pressures will retard left-to-right shunting and may lead to reversed (right-to-left) shunting. Severe atrioventricular canal defects with mitral regurgitation may lead to left-sided or bilateral congestive heart failure (Bonagura & Lehmkuhl, 1999; Schrope, 2013).

Clinical findings

Animals with small, uncomplicated, restrictive lesions are usually asymptomatic (Bonagura & Lehmkuhl, 1999). Cats with moderate ASDs reveals a grade II to III/VI left holosystolic murmur at physical evaluation, which is created as a result of the functional PS due to the large right ventricular stroke volume. There might also be a split S2 heart sound (MacDonald, 2006). In advanced cases with severe lesions, signs of congestive heart failure may be present (Bonagura & Lehmkuhl, 1999).

Thoracic radiographs might reveal right- and left-sided cardiomegaly and pulmonary over circulation. In cases of large shunts pulmonary oedema may be present (MacDonald, 2006). Electrocardiogram can be normal, or may demonstrate signs of right atrial or right ventricular enlargement. Intraventricular conduction disturbances or arrhythmias can occur as well as left cranial axis deviation or right bundle branch block (Bonagura & Lehmkuhl, 1999). Echocardiography with colour-Doppler and continuous-wave Doppler is necessary to determine the diagnosis and severity of the left-to-right shunt (MacDonald, 2006).

Therapy and prognosis

Therapies and prognosis for ASD are very similar to the ones for VSD, see above.

Patent ductus arteriosus

Patent ductus arteriosus (PDA) is characterized by persistence of the embryologic ductus arteriosus, which connects the pulmonary trunk and the aorta during fetal life (MacDonald, 2006).

Lesions

When the young cat starts to breath at birth, elevated oxygen tension in the arterial blood flowing through the ductus will inhibit vasodilatory prostaglandin release. This normally results in contraction of the circumferentially oriented smooth muscle cells. Eventually the ductus is permanently closed by fibrous contracture, resulting in the *ligamentum arteriosus* (MacDonald, 2006; Strickland, 2007; Côté *et al.,* 2011). Failure of the ductus to close will result in PDA. The morphology of the PDA is divided into six grades depending on the volume of muscle cells within the wall of the ductus. A grade one ductus has practically a normal amount of muscle cells, whereas the sixth grade ductus almost lack smooth muscle cells completely (MacDonald, 2006; Kittleson, 1998d).

Pathophysiology

Because of the differential pressures of flow in the aorta (120/80 mmHg) and the pulmonary artery (25/12 mmHg) blood will shunt from the descending aorta to the pulmonary artery via the open ductus in both systole and diastole in a left-to-right direction. This leakage of blood creates a circuit of volume overload through the pulmonary system and the left side of the heart, as well as a decrease of cardiac output into the systemic circulation. The overload itself leads to stretching and thickening of the left ventricular myocardium, so called eccentric hypertrophy (Kittleson, 1998d). The condition may eventually progress into left sided congestive heart failure. In severe cases a right-to-left shunt might develop, due to increased hypertension of the lungs, see Eisenmenger´s syndrome (Strickland, 2007).

Clinical findings

Hitchcock *et al*. (2000) found in a study including 21 cases of PDA, that abnormal respiration, exercise intolerance, and poor growth were the most common clinical complaints presented. During physical evaluation, a bounding femoral pulse and a continuous-type, so called "machinery" murmur with puncta maxima at the cranial left-heart base is typical for PDA. However, the murmur may be totally absent in a right-to-left shunt (Côté *et al*., 2011). Likewise, Hitchcock *et al*. (2000) found both murmur and bounding pulse to be missing in one third of their cases. Signs of cyanosis accompanying severe cases of PDA presented with Eisenmenger's syndrome are usually limited to the caudal parts of the body. This is due to the ductus anatomically being located caudal to the cranial outputs from the aorta. Thus the cranial parts of the body receive more of the oxygenated blood before it shunts back to the lungs via the PDA (Jones & Buchanan, 1981; Strickland, 2007).

Thoracic radiographs most commonly show signs of cardiomegaly, left-sided enlargement, and increased pulmonary circulation. Electrocardiography may or may not indicate left ventricular enlargement with a normal sinus rhythm. Echocardiography is necessary to confirm the diagnosis and might show signs related to the haemodynamic changes and the PDA itself. Colour-Doppler and continuous-wave Doppler is necessary to determine the direction and severity of the shunt (MacDonald, 2006; Côté *et al.,* 2011).

Therapy and prognosis

Today surgical closures of the ductus or catheter-based occlusion with coils are the only therapeutically options, however the latter is rarely done in cats because of the difficulties operating on such a small heart. However, if the procedure is performed successfully on a young individual, the cat is considered cured and the prognosis turns from poor to excellent (Côté *et al.*, 2011.).

Eisenmenger´s syndrome

Eisenmenger´s syndrome is considered a CHD in itself. It is associated with large non-resistive defects (PDA, VSD, ASD or atrioventricular canal defect) and a large left-to-right shunt causing pulmonary arterial hypertension, which ultimately proceeds into right-to-left shunting. Initially, the pulmonic blood flow is greatly increased because of the large left-to-right shunt. Over time, the pulmonary arterioles develop irreversible pathological changes, which result in severely elevated and fixed pulmonary vascular resistance. Systemic vascular resistance thus becomes lower than the pulmonary vascular resistance, and blood flow consequently reverses to shunt from right to left instead. This results in arterial hypoxemia, cyanosis, and secondary polycythaemia as described above (MacDonald, 2006). The prognosis in these cases is poor (Kittleson, 1998b).

Other defects

Besides the defects listed above, there are many others, all of which are very uncommon. Two examples of those are endocardial fibroelastosis and right-sided aortic arch.

Endocardial fibroelastosis is characterised by fibroelastic thickening of the endocardium, and often leads to dilatation of the left atrium and ventricle. The mitral valves may be affected and there is a risk of developing left or double-sided congestive heart failure. The defect can be hard to differ from neonatal myocarditis and atrioventricular valve dysplasia (Liu, 1977).

A right-sided aortic arch is characterised by a persisting fourth right aortic arch, which results in obstruction of the oesophagus, typically causing the animal to regurgitate undigested feed at the time of weaning. Radiographs may support the diagnosis, and surgery with parting of the persisting ligament is the recommended therapy (Bolton & Liu, 1977).

Prevalence of congenital heart defects

When compared to acquired heart diseases in cats, congenital heart malformations are much more uncommon (Côté *et al*. 2011). Kittleson *et al* (1998e) at the University of California, Davis, Veterinary teaching hospital, USA, reported that 5 % of the cats with heart disease (n = 927) during a 10 year period (1986 - 1996), were diagnosed with a CHD. And in Switzerland Riesen *et al*. (2007) reported the prevalence of CHDs to represent 12 % of 408 cats diagnosed with heart disease over a period between 1998 and 2001. The occurrence of different congenital heart malformations varies between studies, but VSD, TD and MD seems to be the most commonly diagnosed in both Europe and the United States (Kittleson, 1998e; Riesen *et al.,* 2007). The prevalence of ASD among the cat population seems to vary depending on the studies made. Overall however, most seem to agree on ASD to be one of the more common CHDs in cats with a percentage between 9 - 15 % (Kittleson, 1998e; Bonagura & Lehmkuhl, 1999; Riesen *et al*., 2007). Less commonly reported are pulmonic stenosis, aortic stenosis, patent ductus arteriosus, Tetralogy of Fallot, common atrioventricular canal, double chamber right ventricle, double outlet right ventricle, cor triatriatum sinister and dexter, and vascular ring abnormalities (Kittleson, 1998e; MacDonald, 2006; Riesen *et al*., 2007). The prevalence of CHDs in cats in Sweden is not known. Furthermore, little is known about the expected lifespan of cats diagnosed with CHD.

OBJECTIVE

The first aim of the study was to investigate the prevalence and distribution of congenital heart defects in a large group of cats presented at the University Animal Hospital in Uppsala, Sweden, between the years 1996 and 2013. The second aim of the study was to investigate the expected lifespan of cats diagnosed with CHDs.

MATERIALS AND METHODS

Study population and follow-up

Case records of cats presented and diagnosed with congenital heart disease at the University Animal Hospital, Uppsala, between 1996 and 2013, were reviewed retrospectively. Information regarding breed, sex and age at presentation as well as findings on echocardiographic and Doppler examination or post mortem examination was obtained. For the second part of the study, follow-up telephone interviews with a standardised questionnaire, were conducted between the 24th of September and 8th of October in 2014. If the cat was still alive, questions focused on its general condition, any signs of cardiovascular disease, other diseases and medication. If the cat was deceased, information about time and cause of death was obtained together with autopsy reports, if available. In some cases, cause of death was not determined by a veterinarian or was for other reasons uncertain. The owners were then asked about the cat's clinical status prior to the time of death, and whether the cat had received any treatment for a diagnosed cardiac related condition during its lifetime. Two cats, diagnosed with subvalvular AS, were excluded from the present study, due to difficulties differentiating the diagnosis from hypertrophic cardiomyopathy.

Compilation of information

Based on obtained answers, deceased cats were sorted into two main groups depending on the cause of death being cardiac related or not. Material from case records and the interviews regarding the cats in the first group, was evaluated to assess the likelihood of the cats dying from a cardiac related disease. The assessment was based on a four-levelled probability scale with one (1) owning the strongest evidence and four (4) the weakest:

1) Pathological anatomic diagnosis (PAD) where a cardiac related cause of death that could be associated to findings of the PAD
2) Euthanasia, due to CHD diagnosis alone or in combination with clinical signs
3) Sudden death during transport to clinic, judged as cardiac related by veterinarian
4) Sudden death with clinical signs of cardiac related disease or acute congestive heart failure prior to time of death, described by the owner

Statistical methods

All statistical analyses were performed using the statistical program JMP Pro v 11.0.0 (SAS Institute Inc., Cary, NC, USA). Logistic Fit was used to assess association between diagnosis and age at the time of diagnosis. The association between sex, breed and diagnosis was investigated using the Pearson Chi^2 test. Date of birth, date and cause of death, or age at the time of the follow-up, was compiled to calculate median survival time.

The Kaplan-Meier method was used to estimate median survival times and plot time to event curves for the whole study population, for cats with VSDs versus other CHDs and for cats with cardiac-related and non-cardiac related death. In addition, the Wilcoxon-signed rank test was used to determine whether a significant difference existed between cats with VSDs versus other CHDs, and between cats with cardiac-related and non-cardiac related death. Data is presented as medians and interquartile ranges (IQR). A value of $P < 0.05$ was considered significant for the analyses. When comparing cats with VSD to other CHDs, only cats with isolated VSDs were included.

RESULTS

Part I: Prevalence and distribution of congenital heart disease

A total of sixty (60) cats were diagnosed with congenital heart disease during the study period. The prevalence of congenital heart disease was 60/32919 (0.2 %) of the total number of patient cats, and 60/824 (7.3 %) of cats with heart disease. The diagnoses were based on echocardiographic and Doppler findings in 59 cats and on post mortem examination in 1 cat. In 8/60 (13.3 %) of the cats, more than one congenital heart defect was present. In the whole study population a total of 69 cardiac malformations were found (TOF and MD/TD being counted as isolated defects). In total, 14 breeds were represented, Domestic Shorthair (46.7 %) being the most common one. VSD (48.7 %) was the predominating type of CHD. Distribution of breeds and frequencies of the different cardiac malformations are presented in Table 1.

There were 31 (51.7 %) female cats and 29 (48.3 %) male cats. No sex predilection ($P = 0.20$) could be established. Age at presentation ranged from 2 months to 11.2 years with a median of 10 months (IQR 6.0-17.8 months). There was no association between age at presentation and type of congenital defect ($P = 0.71$, $R^2 = 0.06$). There was no breed disposition, except for domestic shorthair being more likely than pure breed cats to have VSD ($P = 0.0008$), Figure 1.
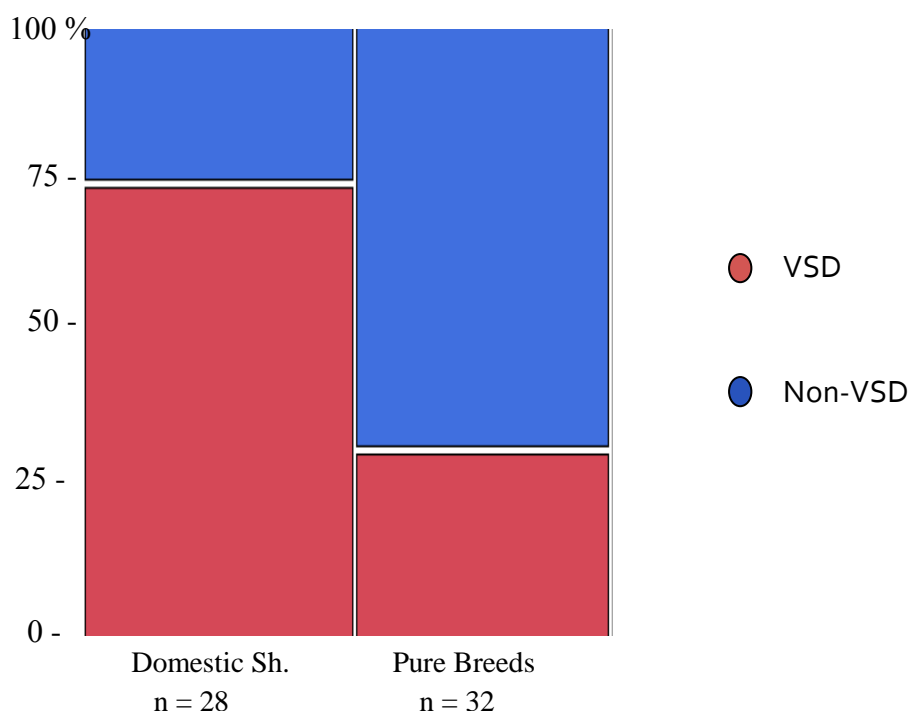

Figure 1. *There was a significant predilection for ventricular septal defect (VSD) within domestic shorthair (P = 0.008) compared to cats of pure breed. 28 out of 60 cats with congenital heart defects were diagnosed with VSD, 19 being domestic shorthair and 9 being of pure breeds.*

Table 1. *The distribution of congenital heart defects amongst different breeds in Part I of the study (n = 60)*

Diagnosis / Breed	VSD	MD/TD	AS	TOF	PS	ASD	MD	PDA	EFE	PS+VSD	AS+PS	VALV AS+PS	VALV AS+MS	ASD+RAA	PDA+ECD	DORV+PA+VSD	RA+VSD	Sum	%
Bengalese	1		1															2	**3.3**
Birman			2		1			1										4	**6.7**
British Sh.	1		1															2	**3.3**
Cornish Rex					1													1	**1.7**
Devon Rex		1		1				1								1		4	**6.7**
Domestic Sh.	19	1		3	1	2									1		1	28	**46.7**
European Sh.	1																	1	**1.7**
Maine Coone	2											1						3	**6.4**
Mixed Race	1																	1	**1.7**
Norwegian FC.	2	1											1					4	**6.7**
Ocicat					1													1	**1.7**
Oriental Sh.						1						1						2	**3.3**
Persian	1	1					1								1			4	**6.7**
Ragdoll		1	1															2	**3.3**
Siamese														1				1	**1.7**
Sum	28	5	5	4	4	3	1	1	1	1	1	1	1	1	1	1	1	60	
%	**46.7**	**8.3**	**8.3**	**6.7**	**6.7**	**5**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**	**1.7**		**100**

Sh. = Shorthair, FC. = Forest Cat, EFE = endocardial fibroelastosis, RAA = right aortic arch, ECD = endocardial cushion defect, DORV = double right ventricle outflow, PA = pulmonic atresia, RA = riding aorta. For other abbreviations see abbreviation list.

Part II: Cause of death and survival

16 out of the 60 cats from the first part of the study were excluded from the second part of the study due to inability to reach the owners at the time of the follow-up. Of the remaining 44 cats, 13 (29.5 %) were still alive, and 31 (70.5 %) had died.

Out of the deceased cats, 16 (52 %) were judged to have died from cardiac related disease. 18,8 % was diagnosed with either MD/TD (3), ASD (3) or more than 1 CHD (3), 12.5 % had AS (2), 12.5 % had TOF and one cat each (6.3 %) was diagnosed with PDA, PS or VSD. See table 2 for distribution of probability levels and table 3 for breed and frequencies of CHDs.

15 cats (48 %) had died from other reasons, with trauma (23 %) being the most common cause of non-cardiac related death, see figure 2.
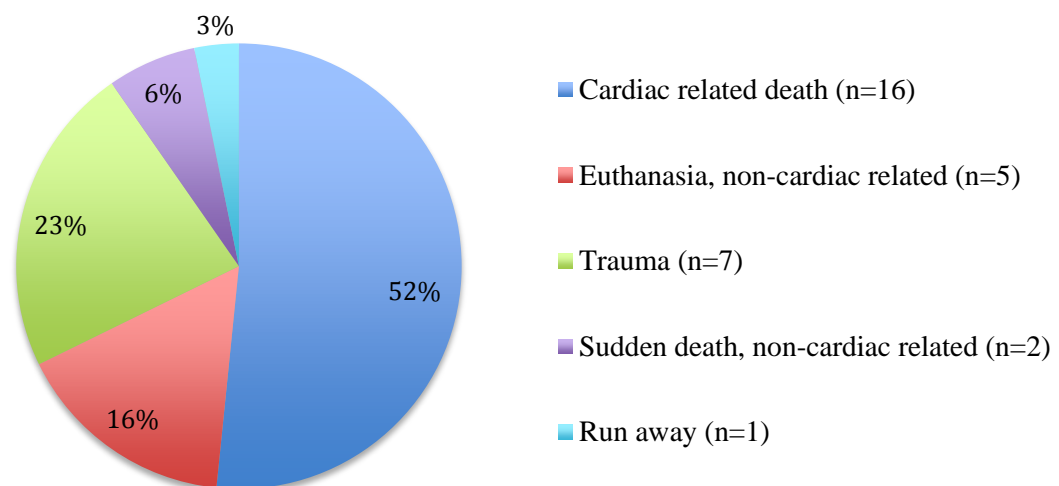

Figure 2. *Causes of death. Information about cardiac related deaths are listed in Table 2. Non-cardiac related reasons for euthanasia include: behavioural changes (2), undiagnosed disease (2), (chronic) kidney disease (1). Traumas include: hit by car (4), unidentified trauma (2), drowned (1). Sudden deaths, non-cardio related, include one (1) kitten dying from tooth related problems and one (1) cat dying from unidentified disease*

Table 2. *Distribution of cats dead due to heart related disease (level 1 owning the strongest of evidence and level 4 the weakest).*

Probability level	Sum (n = 16)	%
1. PAD	1	6.3
2. Euthanasia, due to CHD diagnosis alone or in combination with clinical signs	11	68.8
3. Sudden death during transport to clinic, judged as cardiac related by veterinarian	3	18.8
4. Sudden death with anamnestic signs of heart disese	1	6.3

Table 3. *Distribution of congenital heart defects and breeds among cats dead from cardiac related disease (n = 16). Sh. = Shorthair, FC. = Forest Cat, MIX = > 1 CHD, n = number of individuals included in part II for each diagnosis. For other abbreviations see abbreviation list*

Breed	MIX n = 5	MD/TD n = 5	ASD n = 3	AS n = 3	TOF n = 3	PDA n = 1	PS n = 3	VSD n = 19	Sum	%
Birman	-	-	-	1	-	1	-	-	2	12.5
Brittish Sh.	-	-	-	1	-	-	-	-	1	6.3
Cornish Rex	-	-	-	-	-	-	1	-	1	6.3
Devon Rex	1	1	-	-	1	-	-	-	3	18.8
Domestic Sh.	1	1	2	-	1	-	-	1	6	37.5
Norwegian FC	1	-	-	-	-	-	-	-	1	6.3
Oriental Sh.	-	-	1	-	-	-	-	-	1	6.3
Persian	-	1	-	-	-	-	-	-	1	6.3
Sum	3	3	3	2	2	1	1	1	16	
%	18.8	18.8	18.8	12.5	12.5	6.3	6.3	6.3		100

The estimated probability for surviving when diagnosed with a CHD, within this study population (n = 44), is presented in figure 4, showing an estimated median survival time of 40 months with IQR 19 - 159 months.
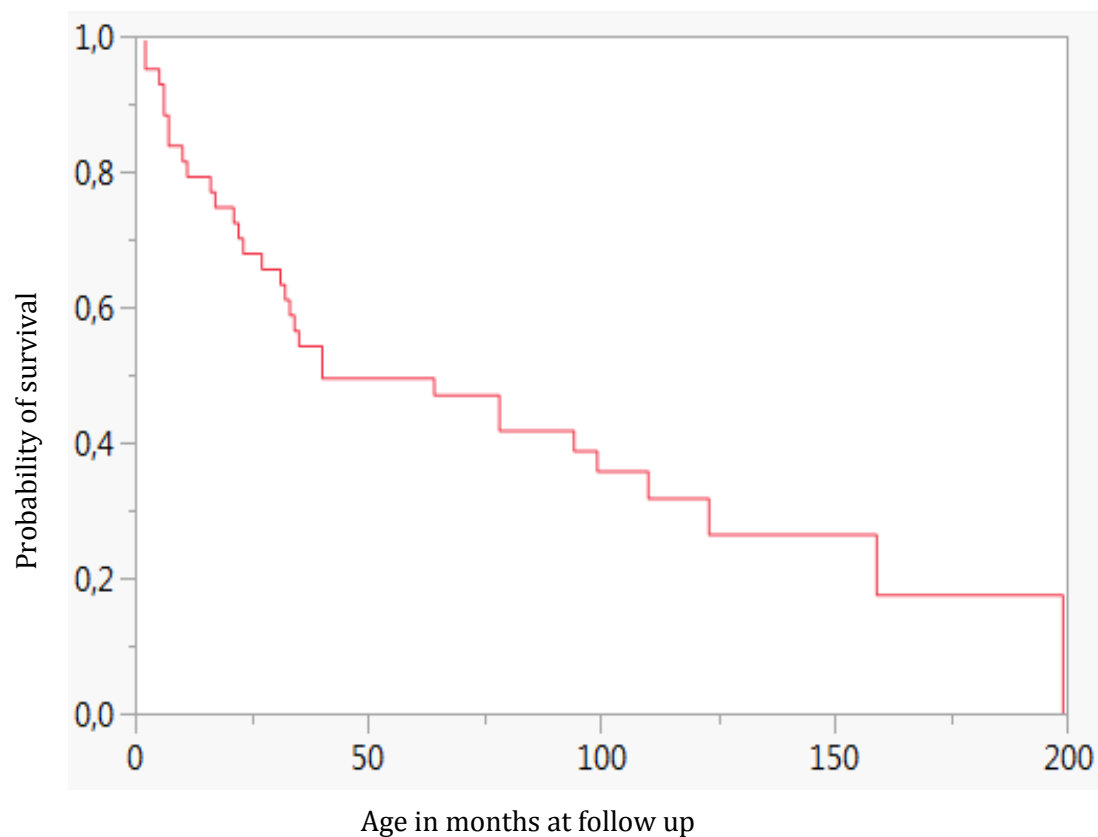

Figure 4. *Kaplan-Meier plot presenting the probability of surviving as a function of age within the group of cats diagnosed with congenital heart defects. At age = 0 the number of cats was 44.*

The estimated survival times within the groups of deceased cats are shown in figure 5. Cats that died from cardiac related disease had an estimated median survival time of 16 months (IQR 6 - 48), which was significantly shorter ($P = 0.032$) than the cats that died due to other causes. The latter had an estimated median survival time of 35 months (IQR 23 - 78).
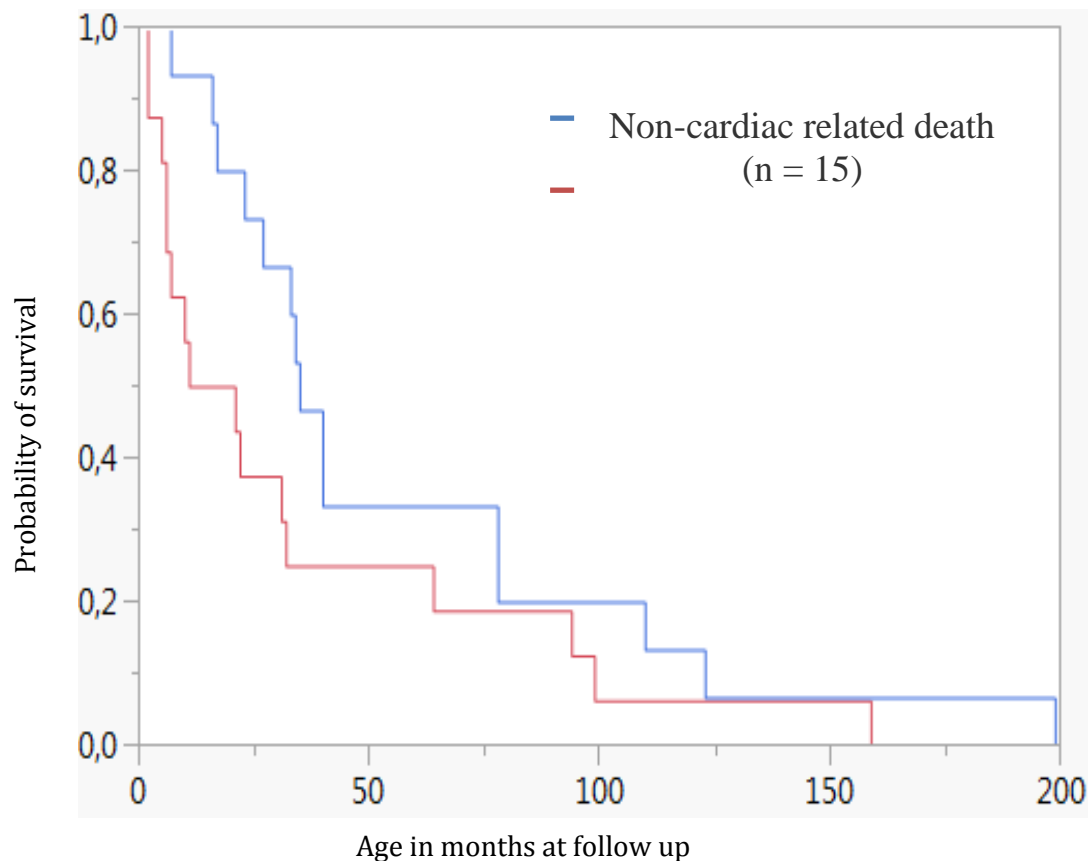

Figure 5. *Kaplan-Meier plot presenting survival probability for cats diagnosed with congenital heart defects deceased in a cardiac related death versus non-cardiac related death. Cats that died because of cardiac related disease had approximately a 37 % chance to reach the age of 2 years while cats that died from other reasons had approximately a 73 % chance to reach the same age.*

In total 19 (43.2 %) out of 44 cats were diagnosed with VSD and their estimated median survival time was 123 months (IQR 35 - 199). Median survival time in the group of cats diagnosed with CHDs other than VSD (56.8 %) was 32 months (IQR 11 - 94). In figure 6 a comparison between the two groups shows that a cat diagnosed with VSD is estimated to live significantly longer ($P = 0.013$) than a cat diagnosed with another CHD.
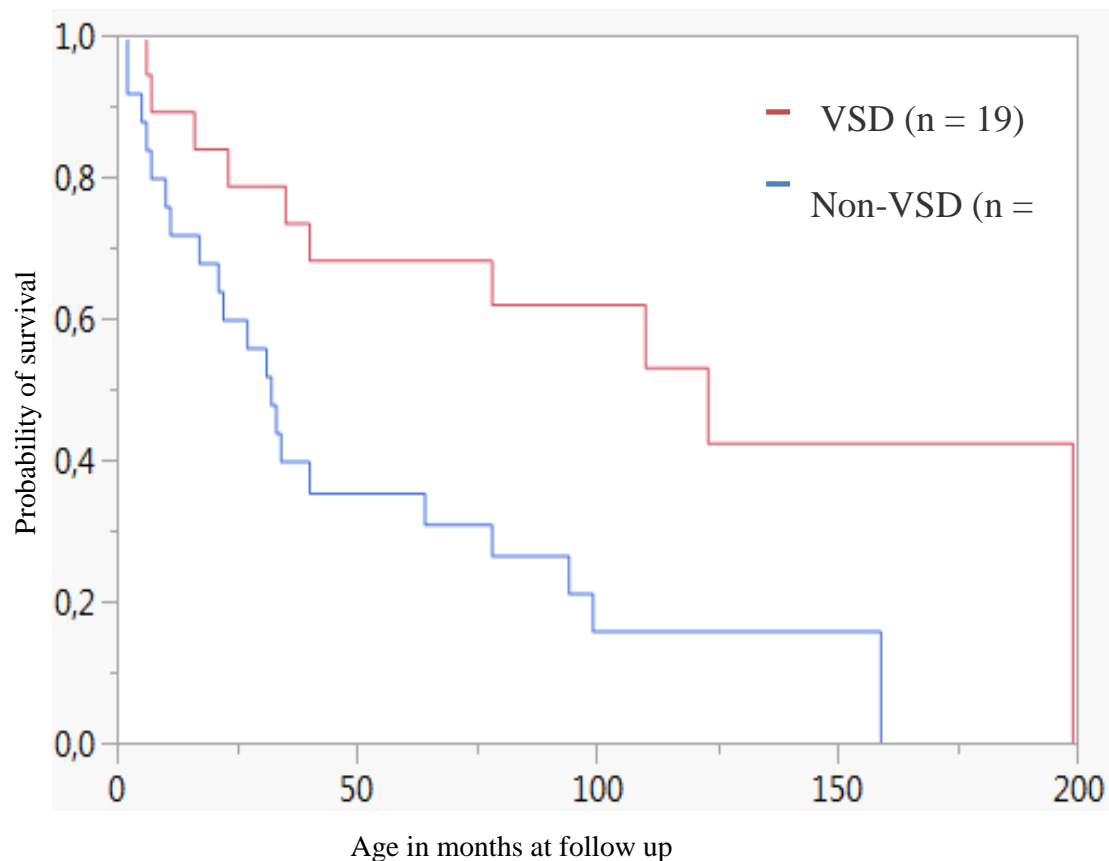

Figure 6. *Kaplan-Meier plot presenting the probability of surviving until a certain age within the group of cats diagnosed with ventricular septal defect (VSD) versus cats with other congenital heart diseases (CHDs). The VSD group included 10 dead (52.6 %) and 9 cats still alive at time for the follow-up, while the group diagnosed with other CHDs included 21 (84 %) dead and 4 cats still alive.*

A summary of survival probability data within the study population of part II is presented in table 4.

Table 4. *Summary of survival probability data within the study population of part II. Units are in months*

Group	Individuals	Deceased	Alive	Median survival	IQR
Total study population	44	31	13	40	19 - 159
Cardiac related death	16	16	-	16	6 - 48
Non-cardiac related death	15	15	-	35	23 – 78
VSD	19	10	9	123	35 – 199
Non-VSD	25	21	4	32	11 - 94

DISCUSSION

During the study period, a total of 60 cats were diagnosed with CHD. The overall prevalence of CHD in this study was 0.2 % of the total number of visiting cats and 7.3 % of cats diagnosed with heart disease. Ventricular septal defect was the most common congenital heart defect diagnosed, accounting for 46.7 % of cases, followed by TD/MD (8.3 %). In general, this seems to agree with literature from Switzerland and USA reporting a CHD prevalence of 8 - 12 % of cats with heart disease (Kittleson, 1998e; Riesen *et al*., 2007). The European study, including 48 cats with CHD, also reported VSD as the most common CHD (56 %) followed by MD (14.6 %) and TD (10.4 %) (Riesen *et al*., 2007). In the American literature, VSD and TD were most common, with an equal number of cases (n = 23) out of 100 diagnosed CHDs. In the same literature MD represented 11 % (Kittleson, 1998e). In the present study, all but one MD was diagnosed with a concurring TD, which is not commonly reported (MacDonald, 2006).

According to literature, prognosis and survival of cats diagnosed with CHDs depend on type and severity of the defect, but objective statistical data is lacking. In the present study, median survival probability for several different groups was estimated, Table 4.

The median survival time for the total study population was 40 months. The difference in median survival between cats that died from cardiac related disease (16 months) versus non-cardiac related disease (32 months) was 19 months. The explanation for this can partly be found in the severity of CHDs between the two groups. In the first group, 62 % (10/16) visited the clinic because of clinical signs and out of them 8 cats died within 1 year from diagnosis. In the second group, all CHDs were detected on a routine evaluation or when seeking veterinary advise for other reasons. Only 4 (n = 15) of these cats died within 1 year from diagnosis, 2 because of trauma and 2 because of other diseases. These findings seem to

agree with the literature that consistently says that defects accompanied by clinical signs have a poor prognosis and are more likely to cause congestive heart failure than defects with no signs. The distribution of CHDs does also play a part in the difference between the groups since the cats that died from non-cardiac related reasons mostly (9 out of 15) were diagnosed with VSD which in this study seems to have a better prognosis than other CHDs.

Cats diagnosed with VSD had a longer estimated median survival time than all the other groups, 123 months, which is interesting combined with information from table 3, showing that only one cat with VSD died from cardiac related disease (euthanasia by owners decision due to clinical signs). The results show that the most common CHD in cats had a relatively positive prognosis and that a cat with VSD was more likely to die from other causes than its CHD. This can partly be due to the fact that none but one of the cats diagnosed with VSD in the present study showed any clinical signs, but only had a heart murmur detected on routine evaluation. This indicates that at least most of them were of the restrictive type which usually does not give rise to hemodynamic changes and therefore does not hamper quality of life or lead to congestive heart failure in early life, if ever. The results are consistent with the dominating literature of today, suggesting that the smaller defects probably are of no significance for survival, while moderate to large defects may lead to clinical signs early in life (Kittleson, 1998b; Bonagura & Lehmkuhl., 1999; Côté *et al.,* 2011).

To the authors knowledge there have been no reports on association between VSD and breed, and according to published literature there is no known breed predisposition (Strickland, 2007; Côté *et al*., 2011). When we combined our data with prevalence data from Stockholm, neighbouring Uppsala, (1999 - 2013) in a recent study (Tidholm *et al*., 2015) we did not find any significant breed association. However, when comparing domestic shorthairs to all other breeds and VSD to all other diagnoses there was a significant difference (P = 0.0008) in the present study, with domestic shorthairs being more likely than pure breed cats to have VSD. Pure breeds and diagnoses are present in low numbers in both populations and the results need to be interpreted with caution. See further discussion in the limitations section.

In an earlier study, the prevalence of aortic stenosis was reported to be 12 % of CHDs, (Liu, 1977) while Kittleson (1998e) reports a more modest prevalence (3 %) over a period between 1986 - 1996. This discrepancy might be due to differences in study populations, but might also be a result of increased awareness of the diagnostic challenges that AS presents; such as differentiating it from hypertrophic cardiomyopathy, systemic hypertension of various aetiologies and hyperthyroidism, all of which can cause concentric hypertrophy of the left ventricle similar to that observed in aortic stenosis. For that reason two cats, diagnosed with subvalvular AS, were excluded from the present study. The remaining group included two valvular stenoses and three cats simply diagnosed with AS, the latter lacking more detailed information of the lesion in question. One cat was euthanatized, at the age of 8 weeks, on the day of diagnosis of AS because of clinical signs of congestive heart failure. The two other cats were diagnosed at an early age, 3 respectively 11 months, and stayed healthy with no clinical signs until they died. One died from trauma at the age of 40 months and the other from sudden death at the age of 99 months with no prior signs of disease. Sudden death

without previous clinical signs occurs in AS and therefore combined information from journals and follow-up lead to the conclusion that the cat died because of the diagnosed CHD.

Tetralogy of Fallot is uncommon but reported in cats (Bolton *et al.,* 1972; Bush *et al.,* 1972; Eyster *et al.,* 1977). Kittleson (1998e), found a prevalence of 4 % of diagnosed CHDs. In the present study the prevalence was slightly higher at 6.7 % (n = 4).

Pulmonic stenosis is considered an uncommon defect in cats with a reported prevalence between 2 - 8 % of isolated PS among diagnosed CHDs (Liu, 1977; Kittleson, 1998e). Pulmonic stenosis is reported to occur more often associated with other congenital heart defects than alone (Liu & Tilley, 1976; Bonagura & Lehmkuhl, 1999). The present study showed a prevalence of 6.7 % (n = 4) of isolated PS, which agrees with earlier studies. Three cats diagnosed with PS and other concurring CHDs were also found (table 1).

Reported prevalence of ASDs seems to vary substantially between reported studies. This could partly be due to the fact that different studies include different types of lesions under the ASD classification. One older study by Liu (1977), which is frequently referred to in the literature, separates between ASD (2 % in their material) and persistent common atrioventricular canal (10 % in their material), while in another study (McDonald 2006), the latter is seen as a part of the ASD complex. Bonagura & Lehmkuhl (1999) include both AVSD and endocardial cushion defects as ASD lesions and report a prevalence of 9 %, while Côté *et al.* (2011) sort them out as separate diagnoses. However, when combining the data, as in the present study, the reported prevalence is in the range of approximately 10 %. In our study, 5 % of the cats were diagnosed with ASD including one AVSD and two *ostium secundum* ASDs. It is worth noting that cats with a small or moderate ASD seldom show any clinical signs, or present with a heart murmur, and that small defects may be hard to diagnose with echocardiography. Because of this the defect might easily be missed and therefore its prevalence may be underestimated.

Patent ductus arteriosus is considered uncommon in cats (Côté *et al*., 2011.). PDA was diagnosed in 0.2 % cats per 1000 examined cats between 1968 - 1980 at the University of Pennsylvania (Jones & Buchanan, 1981) and Kittleson (1998e) found a prevalence of 7 % among their diagnosed CHDs between aug 1986 - aug 1996. The present study included one cat (1.7 %) with PDA.

Limitations of the study include its retrospective nature and the time between diagnosis and follow-up. Because the study period ranged over almost 20 years some of the owners might not accurately recall their cats' clinical signs prior to death. Postmortem examination was only performed in one cat. Possible geographic bias might also have influenced results as well as the fact that all cats were diagnosed at a specialised cardiology clinic, which frequently receives patients on referral. This might give the sample of the population a bias towards cardiac disease that might not correspond fully to the natural population of cats.

It is also important to mention that most kittens are not examined postnatally and do not see a veterinarian before the time of their first vaccination at approximately 8 weeks of age. Therefore it is likely that kittens with severe cases of CHD, such as transposition of the great

vessels, severe aortic stenosis and hypo-plastic left heart, die before it is even known that they are suffering from them. Therefore the present study, or any other study not including post-mortem examination of neonatal kittens, will likely not reflect the true prevalence of CHDs.

Another limitation is the low frequency of individuals of the same breed and the distribution of diagnoses amongst them. Because all pure breeds are only represented by less than five individuals it is not possible to make any assumptions or reliable statistics whether there might be any association between those breeds and different diagnoses.

Furthermore, because the groups are so small it is only possible to assess survival within the larger groups, such as VSD versus non-VSD; nothing can be said about prognosis or different survival probabilities within the other disease groups. Nor can the statistical analyse take degree of severity into consideration when analysing the survival data.

CONCLUSION

In conclusion, the prevalence and distribution of CHDs was shown to be consistent with findings in American and European literature on the subject, with VSD being the most common followed by MD/TD and AS. The result that domestic shorthair was more likely to have VSD than purebred cats may be true for the whole cat population but can also be an reflection of the nature of the study population, hence more studies are needed. The fact that cats diagnosed with VSD had a markedly longer expected survival time than cats diagnosed with other CHDs is interesting from a clinical point of view, especially when considering that only one cat, out of nine dead VSD cats, died because of cardiac related disease. This confirms the general empirically based idea that cats diagnosed with VSD have a relatively good prognosis for survival.

ACKNOWLEDGEMENTS

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