

# **Blood pressure in the Cavalier King Charles Spaniel**

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## **SAMMANFATTNING**

Blodtryck kontrollerar blodflöde till kroppens organ och dess bibehållande är därför en av kroppens viktigaste funktioner. Blodtryck är ett resultat av hjärtminutvolym och total perifer resistens. Vid mitralisendokardos sker en förlust av slagvolym, och därmed hjärtminutvolym, för vilket kompensatoriska mekanismer sätts in. Veterinary Blood Pressure Society rekommenderar regelbunden kontroll av blodtryck hos hundar med hjärtsjukdom men trots detta utförs kontroller sällan. Cavalier king charles spaniel rasen har en hög prevalens av mitralisendokardos och syftet med studien var att dels beräkna referensvärden för normalt blodtryck, dels undersöka effekten på blodtrycket av ökande mitralisinsufficiens.

Totalt undersöktes 57 hundar i studien genom auskultation och gradering av eventuella blåsljud samt blodtrycksmätning med en oscillometrisk metod. Undersökningen utfördes i en stressfri hemmiljö men trots detta exkluderades sju hundar på grund av för höga stress nivåer.

För beräkning av referensvärden undersöktes 29 hundar utan blåsljud. Medelvärden  $\pm$  två standarddeviationer användes som referensvärden och gav ett normalt systoliskt blodtryck på  $126 \pm 18$  mmHg, diastoliskt blodtryck på  $76 \pm 18$  mmHg och en hjärtfrekvens på  $101 \pm 36$  slag/min.

För att undersöka effekten av ökande mitralisinsufficiens på systoliskt och diastoliskt blodtryck undersöktes 31 hundar som delades in i fyra grupper beroende på grad av blåsljud. En signifikant stegring av systoliskt blodtryck konstaterades vid ökande läckage i mitralisklaffen. Det systoliska trycket ökade inte till sådan grad att hypertension uppkom. Systoliskt blodtryck är den mest variabla blodtrycksparametern och påverkas även av ålder, kön och temperament så dessa faktorer togs hänsyn till vid bedömning av resultaten. Det diastoliska blodtrycket påverkades inte signifikant av ökande läckage. Hjärtfrekvens ökade också signifikant med ökad insufficiens vilket överensstämmer väl med resultat från tidigare studier.

Studien konstaterar att det sker en påverkan på framför allt systoliskt blodtryck vid progression av mitralisendokardos men inte till sådan grad att hypertension uppkommer. Ytterligare studier bör göras för att undersöka effekten på blodtryck under pågående hjärtsvikt samt under långtidsbehandling då blodtryckssänkande läkemedel används. Beräknade referensvärden underlättar tolkning av blodtrycksresultat från cavalier king charles spaniel.

## **INTRODUCTION**

Maintenance of blood pressure is one of the body's main priorities as it controls blood supply to vital organs. Blood pressure is a result of cardiac output and total peripheral resistance (Egner et al., 2003). Cardiac output in particular is affected by systolic dysfunction such as myxomatous mitral valve disease and the resulting compensatory mechanisms (Miller et al., 1995). The Veterinary Blood Pressure Society recommends regular monitoring of blood pressure in patients with heart disease both with and without therapy (Egner et al., 2003). Despite these

recommendations this is rarely performed and very limited literature exists on effects of heart disease on blood pressure. The Cavalier King Charles spaniel breed has a high prevalence of myxomatous mitral valve disease (Häggström, 1996) and this study was designed partly to investigate the effect of increasing mitral regurgitation on blood pressure.

Blood pressure reference values are breed specific (Bodey et al., 1996a) yet few reference values for individual breeds exist. This study was also aimed at obtaining such values for the Cavalier King Charles spaniel.

## **LITERATURE STUDY**

### **Myxomatous Mitral Valve Disease**

Myxomatous mitral valve disease (MMVD) is the most common cardiovascular disease in dogs, especially in small to medium sized breeds (Häggström et al., 1992; Häggström et al., 1995). Male dogs develop MMVD earlier than females and MMVD increases in prevalence with age (Häggström, 1996; Häggström et al., 2004).

#### ***Etiology***

MMVD is caused by a progressive myxomatous degeneration of the mitral valve (Häggström et al., 2004). During early stages of the disease, small nodules form along the free margin of the leaflets. As the disease progresses an enlargement of the nodules occurs and the leaflet becomes thick and irregular. Chordae tendineae thicken and elongate which can result in mitral prolapse or rupture (Häggström, 1996).

Reasons behind this degeneration and thickening of the mitral valve are not known for definite. Theories suggest the repeated impact on the leaflets may cause damage to which the thickening is a response. Abnormalities of collagen and other components of the extracellular matrix are believed to increase this response, therefore predisposing for MMVD, and result in an abnormal movement of the valves. The apposition of the leaflets and the regurgitant flow that follows increases the impact on the valves thus increasing the damage and thickening further (Häggström et al., 2004).

There is a polygenetic inheritance of MMVD meaning that several genes influence the trait. Due to the strong degree of inheritance, breeding programmes have been set in action in breeds such as the Cavalier King Charles spaniel (Häggström et al., 2004).

Very little is known how other factors, such as diet, weight and exercise, affect progression of the disease (Häggström et al., 2004).

#### ***Pathophysiology***

A low degree of mitral regurgitation does not lead to any significant cardiac changes (Häggström et al., 2004) but as the thickening and contraction of the mitral valves progresses the regurgitation increases (Häggström et al., 1995). A loss of forward stroke volume occurs for which compensation is necessary (Häggström et al., 2004). Total stroke volume increases due to an increase in preload which, according to the

Frank-Starling mechanism, results in an increased force of contraction (Häggström et al., 2004; Häggström, 1996). Heart rate also rises (Häggström et al., 2004). The left atrium is remodelled in response to the increasing regurgitant volume with hypertrophy and dilation of the myocardium (Häggström et al., 2004; Häggström, 1996). Dogs are able to compensate for the insufficiency for years (Häggström et al., 1992, Häggström et al., 2004). When compensation is no longer possible congestive heart failure, usually left sided with pulmonary oedema, develops (Häggström et al., 1995, Häggström et al., 2004).

### ***Clinical signs***

Clinical signs of decompensated mitral regurgitation and congestive heart failure begin mild then gradually increase over days or weeks. Pulmonary oedema, due to increased left atrial and pulmonary venous pressure, and bronchial compression result in dyspnoea and cough. Exercise intolerance and weakness is seen due to reduced ventricular forward flow. Right sided heart failure can occur with resulting ascites and pleural effusion (Häggström, 1996, Häggström et al., 2004). Other diseases with similar clinical signs occur so it is important to evaluate all clinical findings (Häggström et al., 2004).

### ***Diagnostics***

During early stages of the disease a soft systolic mitral murmur of low intensity is heard during auscultation (Häggström et al., 2004; Pedersen, 1999). A systolic click is heard in some dogs. Stress or exercise increases the intensity of the murmur (Häggström et al., 2004). During progression of the disease the intensity of the murmur increases and an estimation of the severity of the disease can be made (Häggström, 1996). Presence of sinus arrhythmia during auscultation rules out the possibility of decompensated mitral regurgitation (Häggström, 1996). An echocardiogram is useful to confirm diagnosis as it shows site and degree of valve leakage and morphology of the valves (Häggström et al., 2004).

### ***Therapy***

No therapy inhibiting or preventing the progression of MMVD exists so therapy is aimed at relieving clinical signs caused (Häggström et al., 2004; Häggström et al., 2005). There is no evidence showing that therapy started before clinical signs of heart failure delays progression of the disease (Häggström et al., 2004).

Drugs used are mainly diuretics such as furosemide often combined with an ACE inhibitor. Use of diuretics in combination with pimobendan for treatment of congestive heart failure due to mitral insufficiency has been proven efficient and the use of this is increasing in clinical practice (C. Kwart personal communication).

### ***Myxomatous mitral valve disease in the Cavalier King Charles spaniel***

Cavalier King Charles spaniels (CKCS) develop MMVD at an earlier age and with higher prevalence than other breeds (Malik et al., 1992; Häggström, 1996). Insufficiency of the mitral valve increases over a period of three to four years (Häggström et al., 1995). The early onset of MMVD is more prevalent in males than females (Häggström, 1996) but there seems to be no relation to coat colour (Malik et al., 1992).

Since Cavaliers are affected at an earlier age they are also at greater risk for developing congestive heart failure (Häggström et al., 1992). It is not uncommon that heart failure occurs from five years of age, whilst in other breeds dogs tend to be over the age of 10 years (Darke, 1987).

One study has shown that at the age of approximately six to seven years, 50% of Cavaliers in Sweden have a heart murmur (Häggström et al., 1992). Studies done in the USA show a 56% prevalence of heart murmurs in CKCS over the age of four years (Beardow et al., 1993), and studies from the UK show a 59% prevalence at that age (Darke, 1987). Studies also show the frequency of insurance claims for veterinary care, death or euthanasia related to heart disease is significantly higher in the CKCS compared to other breeds (Egenvall et al., 2006).

The etiology behind the problem of MMVD in the Cavalier is believed to be polygenetic (Häggström et al., 2004) and parental cardiac status has a major effect on the development of MMVD in offspring (Häggström, 1996). The CKCS breed was almost lost in favour of the King Charles spaniel early in the 20<sup>th</sup> century. However during the late 1920's the breed was restored using only a handful of dogs (Östergren et al., 2005). One can imagine that this very limited breeding material may have played an important part in the high prevalence of MMVD in the Cavalier that we see today.

Due to the genetic disposition of MMVD, breeding programmes have been initiated in Sweden with the aim to reduce the prevalence of MMVD in CKCS (Häggström et al., 2004). Before mating both dogs have to be at least two years of age and have a heart certificate from a specially qualified veterinarian certifying the absence of a heart murmur. This certificate only has a validity of eight months. If dogs are under the age of four years, their parents have to be certified free of heart murmurs up to four years of age. Males with a heart certificate from the age of seven years but who later develop a murmur can be used in breeding. Only offspring bred by this standard can be registered in Sweden (Cavaliersällskapet, 2005).

## **Blood Pressure**

One of the body's main priorities is to maintain blood pressure so there is sufficient blood supply to vital organs. Blood is required to supply oxygen and nutrients to the organs and to remove metabolic waste. Certain diseases and drugs result in changes in blood pressure, which can have negative effects on the body (Egner et al., 2003).

Blood pressure is a result of cardiac output and total peripheral resistance. Cardiac output is the volume of blood leaving the heart per minute and is defined as the product of heart rate and stroke volume. Blood pressure can therefore be defined as:

Blood Pressure = (Heart Rate x Stroke Volume) x Total Peripheral Resistance



Any factors affecting the above parameters lead to a change in blood pressure. Total peripheral resistance is affected by width of blood vessels and blood viscosity (Egner et al., 2003).

Blood pressure changes during different stages of the cardiac cycle and the different pressures are called systolic arterial pressure and diastolic arterial pressure. Systolic pressure occurs when the heart contracts during systole and diastolic pressure during diastole when the heart refills (Egner et al., 2003).

### ***Regulation of blood pressure***

Several interrelated systems help regulate and maintain blood pressure. Some of these mechanisms have a rapid, immediate effect whilst other effects are for long term regulation of blood pressure. These mechanisms can be divided into three groups (Guyton et al., 2000).

#### ***Rapid regulation***

Rapid regulation of blood pressure is achieved in less than a minute with the help of reflexes controlled by baroreceptors and chemoreceptors. These reflexes are effective during short term fluctuations in blood pressure (Guyton et al., 2000; Egner et al., 2003).

Baroreceptors are located in the walls of most large arteries in the thoracic and neck region, especially in the aortic arch and carotid arteries. During a change in blood pressure the baroreceptors stretch, sending signals activating the autonomic nervous system (Guyton et al., 2000). If a fall in pressure occurs there is a sympathetic stimulation and catecholamines (adrenaline and noradrenaline) are released. Catecholamines stimulate a vasoconstriction, increased heart rate and contractility resulting in a rise in blood pressure (Guyton et al., 2000; Egner et al., 2003). The opposite response occurs if blood pressure is too high. This mechanism is not of importance in long term regulation since the receptors reset to the new pressure level after one to two days (Guyton et al., 2000)

Carotid and aortic chemoreceptors are sensitive to decreases in oxygen and increases in carbon dioxide and hydrogen ions. During a fall in blood pressure oxygen concentration decreases and a build up of carbon dioxide occurs. This initiates a release of catecholamines and a rise in blood pressure (Guyton et al., 2000).

#### ***Intermediate regulation***

Intermediate regulation sets in after about 30 minutes and can last for hours up to days. The three main mechanisms are 1) renin-angiotensin-aldosterone system (RAAS) vasoconstriction 2) stress-relaxation mechanism 3) capillary fluid shift mechanism (Guyton et al., 2000).

When blood pressure decreases, renin is released from the kidneys activating RAAS. Angiotensin II is a product of the RAAS system and it affects blood pressure through a variety of different mechanisms. Vasoconstriction occurs during this intermediate phase. RAAS also play a part in the long term regulation of blood pressure (Guyton et al., 2000).

The stress-relaxation mechanism functions in such a way that when blood pressure increases the walls of the blood vessels stretch. This decreases the peripheral resistance, thus decreasing blood pressure (Guyton et al., 2000).

In the capillary shift mechanism, fluid is shifted through capillary walls in and out of circulation to readjust blood volume to maintain normal blood pressure (Guyton et al., 2000).

#### *Long term regulation*

Long term regulation is mainly controlled by the kidneys with the renal blood volume control mechanism. The kidneys regulate excretion of urine to control blood volume and thus also blood pressure. Decreased blood volume decreases blood pressure. Different factors are involved in regulating this mechanism (Guyton et al., 2000).

Angiotensin II from RAAS causes release of aldosterone. This results in stimulation of thirst and causes retention of water and sodium, increasing blood volume and, in turn, blood pressure (Egner et al., 2003).

Atrial natriuretic peptide (ANP) release is stimulated by atrial stretch during increased pressure. It results in an increased glomerular filtration rate and decreased reabsorption of sodium. This increases excretion of salt and water, reducing blood volume. ANP also inhibits production of aldosterone, renin and ADH. (Guyton et al., 2000; Egner et al., 2003)

Decreased pressure stimulates secretion of antidiuretic hormone (ADH). Release of ADH results in increased fluid reabsorption by the kidneys, thus restoring blood pressure (Guyton et al., 2000).

#### ***Blood pressure in the dog***

Normal blood pressure values in dogs are breed-specific (Bodey et al., 1996a). Despite this, very few breed specific studies have been done and no reference values are available for the Cavalier King Charles spaniel. There are large variations between breeds, for example 118/66 mmHg for the Labrador and 149/87 mmHg for the Greyhound (Egner et al., 2003), so it is important to use correct reference values.

Non-breed specific reference values for dogs using an oscillometric method are (Egner et al., 2003):

- average blood pressure: 133/75 mmHg
- mild hypertension: >150/95 (+20) mmHg
- moderate hypertension: >160/100 (+20) mmHg
- severe hypertension: >180/120 (+50) mmHg
- mild hypotension: <100/60 mmHg
- moderate hypotension: <90/50 mmHg
- severe hypotension: <60/40 mmHg

Reference values for spaniel breeds obtained in a study (Bodey et al., 1996a):

- systolic pressure: 131.8 mmHg
- diastolic pressure: 74.4 mmHg
- heart rate: 124 bpm

Factors such as age, sex, temperament and stress also affect blood pressure, systolic pressure being the most variable parameter. Males have higher pressures than females, intact males having the highest and intact females the lowest pressures (Bodey et al., 1996a). Pressures also increase with age until reaching advanced age when they once again decrease (Bodey et al., 1996a; Bodey et al., 1997).

## **AIM OF THE STUDY**

### **Study One**

Normal blood pressure values for dogs are breed-specific and reference values for the CKCS have not been found in the literature. One aim of the study is to calculate normal blood pressure reference values for the Cavalier King Charles spaniel.

### **Study Two**

During MMVD cardiac output decreases resulting in compensatory mechanisms being activated. This study also aims at investigating effects on systolic and diastolic blood pressures as MMVD progresses and mitral regurgitation increases.

## **MATERIAL AND METHODS**

An application concerning the study method ethics was sent to and approved by the Swedish Animal Welfare Agency (reference number C 322/5).

### **Choice of dogs**

A total of 57 pure bred Cavalier King Charles spaniels (20 males and 37 females) were examined in this study (table 2). Dogs were recruited through contact with breeders and through journals from the university veterinary hospital and examined between September and October 2006. All dog owners signed an agreement allowing their dogs to take part in the study.

Seven dogs were excluded from the study due to high stress levels making blood pressure measurements difficult to interpret.

The dogs were split into five categories; 19 dogs under five years of age without heart murmur, 10 dogs five years and above with no heart murmur, six dogs with a low degree murmur, nine dogs with a moderate degree murmur and six dogs with a high degree murmur. None of the studied dogs were on medication.

The 29 dogs with no heart murmur were used in study one. They were between the ages of one to 11 years and included 20 females and nine males.

For study two, dogs were grouped in no heart murmur and over the age of five years, low degree murmur, moderate degree murmur and high degree murmur. Dogs examined were between the ages of five to 14 years and included 10 males and 21 females.

### **Auscultation and grading of intensity of heart murmurs**

Auscultation was performed using a Littman Classic II S.E. stethoscope over all puncta maxima of the heart, with special attention paid to the mitral area. The heart rate was counted and the intensity of an eventual heart murmur graded on a scale of zero to six. Dogs were divided into five groups as follows:

- 1) *Under the age of 5 years without heart murmur*
- 2) *5 years and above without heart murmur*
- 3) *Low degree heart murmur (grade 1-2)*  
Grade 1 - low intensity and localised murmur heard only in a quiet environment  
Grade 2 - low intensity murmur heard clearly over the puncta maxima
- 4) *Moderate degree heart murmur (grade 3-4)*  
Grade 3 - moderate intensity murmur  
Grade 4 - high intensity murmur but no precordial thrill can be palpated
- 5) *High degree heart murmur (grade 5-6)*  
Grade 5 - high intensity murmur and a precordial thrill can be palpated  
Grade 6 - high intensity murmur, a precordial thrill can be felt and the murmur can be heard even when the stethoscope is not in direct contact with the chest wall

(Kvart et al., 2002; Häggström et al., 1995).

### **Measuring blood pressure using an oscillometric method**

There are several different methods for measuring blood pressure, both invasive and non-invasive. During daily clinical practice non-invasive methods are more suitable. The Veterinary Blood Pressure Society recommends either the Doppler or oscillometric methods for measuring blood pressure in the dog and cat (Egner et al., 2003). During this study blood pressure measuring using a non-invasive oscillometric method was used. This method gives both systolic and diastolic blood pressures. The instrument is quiet, automatic and quick, resulting in a minimum amount of stress for the dog (Coulter et al., 1984).

The instrument used was an oscillometric Krutech VET420A. This instrument was originally designed for use in human medicine but has been tested for its reliability for use in veterinary practice by technicians at Kruuse Denmark.

Blood pressure measurements can be taken with a cuff placed around the foreleg, hind leg or tail. At the start of the study the foreleg was used. However, it was found that the measurements fluctuated greatly and the dogs were stressed making the results difficult to interpret. Several studies have shown that the tail site gives the most accurate indirect systolic and diastolic readings compared to direct readings (Bodey et al., 1996b; Bodey et al., 1994).

The dog was therefore placed in a standing position. Since this is not a stressful position for the dog it helps to obtain an accurate reading (Bodey et al., 1994). A cuff was placed around the root of the tail. The cuff was automatically inflated to compress the medial caudal artery and then the pressure was slowly released until the artery reopened and sensors detected systolic and diastolic blood pressures (Egner et al., 2003). Results were recorded in a protocol.

To obtain reliable results it is important the dog is calm since nervous or excitable dogs have higher blood pressures (Bodey et al., 1996a; Bodey et al., 1997). Therefore, acclimatisation to the surroundings is important before taking the readings (Stepien, 2005). Measurements were taken in the dogs' home environment to minimise stress. Heart rate was used as an indication of stress. Studies have shown that pressure readings should be discarded when a high heart rate is present or the dog is clearly stressed (Bodey et al., 1997). Dogs with a heart rate above 140 bpm were excluded from the study. Studies have also shown that the precision of pressure readings is improved if a series of readings are taken and the mean value calculated. Six to ten readings are recommended and the first readings and obvious deviations should be discarded (Stepien, 2005; Bodey et al., 1996b). Due to this, six blood pressure measurements were taken and a mean value calculated. The recommendations above for which readings to discard were followed.

Size of cuff used is also important and a cuff width of about 40% of the tail's circumference should be used (Stepien, 2005; Bodey et al., 1996a). I used a neonatal cuff 3cm wide.

### **Statistics**

Statistics were calculated using JMP version 3.0.2. Mean values and standard deviations were calculated within the individual groups; no heart murmur under five years of age, no heart murmur five years and above, low degree murmur, moderate degree murmur and high degree murmur. Further tests and analyses performed to investigate significant differences were an analysis of variance (ANOVA), post hoc tests (Tukey-Kramer), linear regression analyses and multiple regression analyses.

## **RESULTS AND DISCUSSION**

### **Study One – blood pressure reference values for the CKCS**

Using 29 dogs within the age span of one to 11 years (dogs 1-29, table 2) without heart murmur, a normal heart rate, systolic and diastolic pressure was calculated. These dogs had a mean systolic blood pressure of 126 mmHg, a mean diastolic blood pressure of 76 mmHg and a mean heart rate of 101 bpm. Normal blood pressures and heart rate for CKCS were calculated using the mean value  $\pm$  2 standard deviations giving the following results:

Normal systolic blood pressure:  $126 \pm 18$  mmHg

Normal diastolic blood pressure:  $76 \pm 18$  mmHg

Normal heart rate:  $101 \pm 36$  bpm

Systolic pressure and heart rate were slightly lower than average values found in literature for dogs in general and spaniel breeds in specific. Diastolic pressure results are similar to existing reference values. As measurements were taken in a stress free, home environment and most other studies are performed in clinical environments this

is not surprising. Systolic pressure and heart rate both increase with stress whereas diastolic pressure is more stable (Bodey et al., 1996a).

## Study Two – effect of MMVD on blood pressure

Using 31 dogs between the ages of five to 14 years of age (dogs 20-30, table 2) the effect of MMVD on blood pressure and heart rate was investigated. A summary of mean values calculated for heart rate, systolic and diastolic pressures are seen in table 1.

Table 1. Mean blood pressures and heart rate for different degrees of heart murmur

| Degree of heart murmur | Systolic bp (mmHg) | Diastolic bp (mmHg) | Heart rate (bpm) |
|------------------------|--------------------|---------------------|------------------|
| None (n=10)            | 125.2              | 76.8                | 97.2             |
| Low (n=6)              | 131.8              | 79.0                | 92.7             |
| Moderate (n=9)         | 136.4              | 84.6                | 101.6            |
| High (n=6)             | 144.0*             | 84.7                | 115.7**          |

\*Significantly higher than the value for dogs with no heart murmur

\*\*Significantly higher than the value for dogs with a low degree murmur

### Systolic blood pressure

Mean systolic blood pressures for the different groups were as seen in table 1 and figure 1. A significant difference was observed between the groups no heart murmur and high degree murmur suggesting an increase in systolic blood pressure when a high degree of mitral regurgitation occurs. Systolic pressure did not, however, rise to such a degree that hypertension occurred.

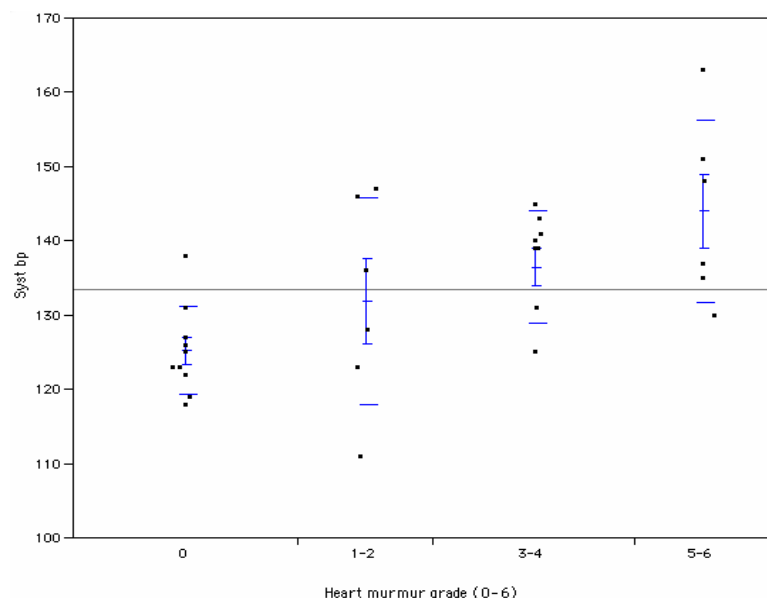


Figure 1. Systolic blood pressure in relation to heart murmur grade (0-6). A significant difference is observed between groups 0 and 5-6.

During a systolic dysfunction, such as MMVD, cardiac output decreases due to leakage in the mitral valve. This in turn leads to a decrease in arterial blood pressure. Since one of the body's first priorities is to maintain blood pressure, a variety of different compensatory mechanisms will set in (Miller et al., 1995). The rapid response is a release of catecholamines by stimulation of baroreceptors and chemoreceptors resulting in an increase in heart rate and force of contraction. Peripheral vasoconstriction also occurs giving an increased total peripheral resistance. This leads to blood pressure increasing to normal or slightly above normal (Guyton et al., 2000; Egner et al., 2003; Miller et al., 1995). The vasoconstriction however, leads to an increased afterload so that cardiac output once again decreases (Miller et al., 1995). To compensate for this, the intermediate regulation sets in with the vasoconstricting function of RAAS and capillary fluid shift (Guyton et al., 2000) once again bringing blood pressure up to normal or slightly above. Since MMVD is a chronic, progressive disease, these short term regulatory mechanisms are not enough. Long term regulatory mechanisms ought to play the most important role in regulating blood pressure in dogs with MMVD. The renal blood volume mechanism helps to increase blood volume, increasing cardiac output and also blood pressure (Guyton et al., 2000). A negative effect is the increased risk of pulmonary oedema (Miller et al., 1995). It has been suggested that hypertension occurs during early stages of heart disease and then develops to hypotension during later stages (Egner et al., 2003). From results obtained in this study one would draw the conclusion that with the mechanisms set in action, compensation towards a systolic pressure slightly above normal is achieved.

As mentioned earlier, systolic pressure is the most variable pressure parameter and is affected by numerous factors of which not all could be eliminated in this study. Studies have shown that increased age increases systolic pressure (Bodey et al., 1996a). Degree of murmur also intensifies with age as MMVD progresses (Hägström, 1996). One could therefore suspect that age is an important factor increasing systolic pressure and not the progression of MMVD. Temperament and stress affects systolic blood pressure and heart rate can be used as an indication. Stress has been reduced to a minimum by obtaining measurements in a home environment to not affect results. A multiple regression analysis was performed to compare the effects of degree of heart murmur, heart rate and age on systolic pressure. Although no single factor had a significant effect on its own, degree of heart murmur had a p-value of 0.07 whereas heart rate had 0.35 and age 0.86. The p-value for degree of heart murmur was very close to that of the cut off point of significance ( $p=0.05$ ) whereas heart rate and age were very far off. With a larger sample group this trend would probably be shown clearer. Sex is also an important factor to consider. Only 20% of dogs with no heart murmur were male whereas in the group with a high degree murmur 50% of dogs were male. Males have been reported to have higher pressures than females (Bodey et al., 1996a). In the group of dogs without a heart murmur, sex had no significant effect on systolic blood pressure. These analyses suggest that increased mitral insufficiency is the deciding factor increasing systolic pressure.

### **Diastolic blood pressure**

Results for mean diastolic pressures were as seen in table 1 and figure 2. There was no significant effect on diastolic pressure as a murmur occurred and increased.

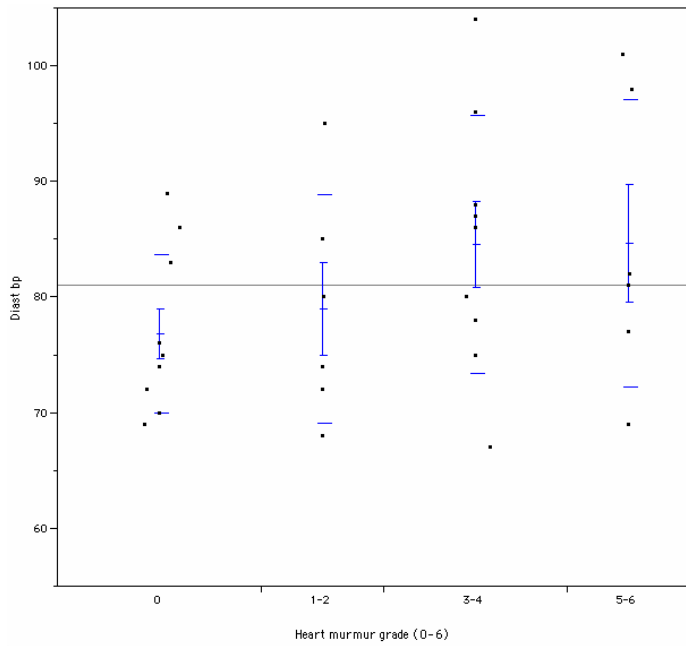


Figure 2. Diastolic pressure in relation to heart murmur grade (0-6).

A previous study has shown that dogs with mitral regurgitation have a significantly lower diastolic pressure than healthy dogs (Coulter et al., 1984). The previous study by Coulter only included eight dogs of unknown breed, age and temperament with mitral regurgitation of unknown degree and can thus be considered inconclusive.

A multiple regression analysis was performed comparing the effects of degree of heart murmur, age and heart rate on diastolic pressure. Heart rate and degree of heart murmur were shown to have no significant effect on diastolic pressure. Interestingly it was shown that as age increases, diastolic pressure significantly increases ( $p=0.04$ ).

Diastolic pressure is determined by degree of arterial elasticity, circulating blood volume and duration of diastole (Egner et al., 2003). These parameters are not greatly affected by the dysfunction from MMVD and therefore a change in diastolic pressure is not to be expected.

Systolic pressure is affected by forward stroke volume of the left ventricle amongst other things. Mitral regurgitation and the compensatory mechanisms activated have a large effect on stroke volume and therefore it is reasonable to assume that systolic pressure can more easily be affected.

### **Heart rate**

Mean heart rates in the different groups were as seen in table 1 and figure 3. There was a significant difference between the groups with a low degree murmur and a high degree murmur suggesting heart rate increases with increased mitral regurgitation.



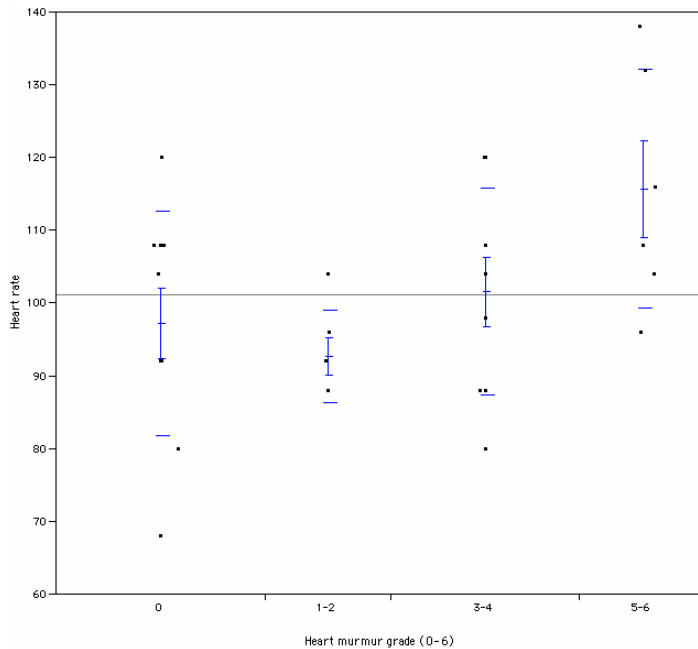


Figure 3. Heart rate in relation to heart murmur grade (0-6).  
Significant difference between groups 1-2 and 5-6.

This correlates well with previous results from other studies. During the progression of MMVD, cardiac output decreases and increased heart rate is the main compensatory factor to maintain adequate forward stroke volume (Hägström, 1996). With a larger sample group it would also be expected to see a significant difference between the group without heart murmur and the group with a high degree murmur.

### **Progression of MMVD**

As MMVD progresses further or during an acute systolic dysfunction, such as rupture of chordae tendineae (Egner et al., 2003), cardiac output decreases but the body is unable to compensate. This leads to hypotension and cardiogenic shock may develop (Miller et al., 1995). During cardiogenic shock arterial blood pressure decreases to less than 80 mmHg and the supply of blood to vital organs is drastically reduced (Egner et al., 2003).

### **Further studies**

For further studies it would be interesting to monitor blood pressure in patients during acute congestive heart failure, during the first 24 hours of therapy with diuretics and ACE-inhibitors or pimobendan and during continued therapy. Despite recommendations to monitor blood pressure in these patients, blood pressure measurements are rarely taken.

Investigating if the sympathetic stimulation in dogs with high degree murmurs and increased systolic pressure, affects the sinus arrhythmia would be an interesting future study. If that is the case, cardiac auscultation might be a useful simple diagnostic tool for evaluation of the sympathetic tone and possible basis for evaluation of the controversial need for therapy with beta blockers.

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## APPENDIX

**Table 2. List of examined Cavalier King Charles spaniels**

| Dog nr | Systolic<br>bp<br>(mmHg) | Diastolic<br>bp<br>(mmHg) | Heart<br>Rate<br>(bpm) | Age<br>(years) | Sex | Degree<br>murmur | Group     |
|--------|--------------------------|---------------------------|------------------------|----------------|-----|------------------|-----------|
| 1      | 141                      | 85                        | 124                    | 2              | M   | 0                | < 5 years |
| 2      | 123                      | 72                        | 92                     | 3              | M   | 0                | < 5 years |
| 3      | 136                      | 79                        | 136                    | 2              | M   | 0                | < 5 years |
| 4      | 134                      | 94                        | 136                    | 3              | M   | 0                | < 5 years |
| 5      | 115                      | 66                        | 76                     | 3              | F   | 0                | < 5 years |
| 6      | 128                      | 81                        | 100                    | 2              | F   | 0                | < 5 years |
| 7      | 128                      | 76                        | 96                     | 2              | F   | 0                | < 5 years |
| 8      | 118                      | 68                        | 80                     | 3              | F   | 0                | < 5 years |
| 9      | 139                      | 89                        | 96                     | 4              | F   | 0                | < 5 years |
| 10     | 148                      | 91                        | 108                    | 1              | F   | 0                | < 5 years |
| 11     | 122                      | 67                        | 104                    | 2              | F   | 0                | < 5 years |
| 12     | 122                      | 83                        | 84                     | 3              | F   | 0                | < 5 years |
| 13     | 127                      | 80                        | 80                     | 1              | F   | 0                | < 5 years |
| 14     | 113                      | 59                        | 88                     | 2              | F   | 0                | < 5 years |
| 15     | 132                      | 66                        | 116                    | 3              | M   | 0                | < 5 years |
| 16     | 128                      | 63                        | 88                     | 3              | M   | 0                | < 5 years |
| 17     | 118                      | 68                        | 120                    | 4              | F   | 0                | < 5 years |
| 18     | 110                      | 63                        | 116                    | 2              | F   | 0                | < 5 years |
| 19     | 132                      | 72                        | 128                    | 1              | M   | 0                | < 5 years |
| 20     | 127                      | 86                        | 108                    | 10             | M   | 0                | 0         |
| 21     | 123                      | 72                        | 92                     | 6              | F   | 0                | 0         |
| 22     | 126                      | 74                        | 92                     | 10             | F   | 0                | 0         |
| 23     | 131                      | 70                        | 120                    | 6              | F   | 0                | 0         |
| 24     | 138                      | 89                        | 108                    | 11             | F   | 0                | 0         |
| 25     | 122                      | 75                        | 104                    | 7              | F   | 0                | 0         |
| 26     | 119                      | 76                        | 108                    | 6              | F   | 0                | 0         |
| 27     | 123                      | 74                        | 92                     | 5              | F   | 0                | 0         |
| 28     | 118                      | 69                        | 80                     | 5              | M   | 0                | 0         |
| 29     | 125                      | 83                        | 68                     | 5              | F   | 0                | 0         |
| 30     | 123                      | 72                        | 88                     | 8              | F   | 1                | Low       |
| 31     | 111                      | 68                        | 88                     | 6              | F   | 1                | Low       |
| 32     | 136                      | 80                        | 104                    | 8              | M   | 1                | Low       |
| 33     | 128                      | 74                        | 92                     | 8              | F   | 1                | Low       |
| 34     | 146                      | 85                        | 96                     | 6              | F   | 2                | Low       |
| 35     | 147                      | 95                        | 88                     | 8              | M   | 2                | Low       |
| 36     | 141                      | 80                        | 88                     | 11             | F   | 3                | Moderate  |
| 37     | 140                      | 104                       | 98                     | 12             | F   | 3                | Moderate  |

|    |     |     |     |    |   |   |          |
|----|-----|-----|-----|----|---|---|----------|
| 38 | 139 | 88  | 104 | 7  | F | 3 | Moderate |
| 39 | 143 | 78  | 108 | 8  | M | 4 | Moderate |
| 40 | 145 | 96  | 80  | 8  | M | 4 | Moderate |
| 41 | 125 | 75  | 120 | 8  | F | 4 | Moderate |
| 42 | 125 | 67  | 88  | 11 | F | 4 | Moderate |
| 43 | 139 | 86  | 108 | 13 | F | 4 | Moderate |
| 44 | 131 | 87  | 120 | 9  | M | 4 | Moderate |
| 45 | 163 | 69  | 116 | 6  | M | 5 | High     |
| 46 | 137 | 82  | 96  | 12 | M | 5 | High     |
| 47 | 130 | 81  | 108 | 9  | F | 5 | High     |
| 48 | 148 | 98  | 138 | 14 | F | 6 | High     |
| 49 | 151 | 101 | 132 | 10 | M | 6 | High     |
| 50 | 135 | 77  | 104 | 9  | F | 6 | High     |

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