

## Mitral flow propagation velocity in non-sedated healthy cats

[*Velocidade de propagação do fluxo mitral em gatos saudáveis e não sedados*]

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### ABSTRACT

Mitral flow propagation velocity (Vp) is an index used to evaluate the left ventricular diastolic function. Its influence on human and small animal cardiopathies has been studied; however there are few reports evaluating this variable in domestic felines. In addition, there is a lack of studies in non-sedated healthy cats. Therefore, the purpose of this study was to establish values for Vp and its correlation with other echocardiographic indexes in non-sedated healthy cats in order to provide new perspectives related to diastolic function in this species. Twenty-six clinically healthy cats were submitted to echocardiography to assess the animals' cardiac conditions. Variables such as age, heart rate (HR), body surface area (BSA), initial (E mitral) and late (A mitral) ventricular filling waves, isovolumic relaxation time (IVRT) and E/IVRT relation were correlated to Vp. No proven relation between any of these variables and Vp was observed in this present study, except for HR and BSA. In the variability analysis, higher values were verified for inter-observer analysis. This study concludes that Vp proved to be an useful index for estimating left ventricular relaxation in non-sedated healthy domestic cats and provides reference ranges for this variable.

Keywords: feline, cardiopathies, echocardiography, diastolic function

### RESUMO

A velocidade de propagação do fluxo mitral (Vp) é um índice utilizado para avaliação da função diastólica do ventrículo esquerdo. Sua importância nas cardiopatias em humanos e pequenos animais vem sendo estudada; porém, há poucos trabalhos avaliando essa variável em gatos domésticos. Nessa espécie, estudos utilizando animais saudáveis e não sedados não foram encontrados na literatura. Dessa forma, objetivou-se estabelecer os valores da Vp e sua correlação com outros índices ecocardiográficos em gatos domésticos saudáveis e não sedados, de forma a fornecer novas perspectivas relacionadas à função diastólica nessa espécie. Foram utilizados 26 gatos domésticos clinicamente saudáveis, submetidos à ecocardiografia para se avaliar a condição cardíaca dos animais. As variáveis idade, frequência cardíaca (FC), área de superfície corporal (SAC), onda de enchimento ventricular inicial (E mitral) e tardio (A mitral), tempo de relaxamento isovolumétrico (TRIV) e a relação E/TRIV foram correlacionadas com a Vp. No presente estudo não foi observada correlação da Vp com nenhuma das variáveis estudadas, exceto com a FC e o SAC. Quanto à análise de variabilidade, foi observado um maior valor para a análise inter-observador. O estudo permite concluir que a Vp demonstrou ser um índice útil para se estimar o relaxamento ventricular esquerdo em gatos domésticos saudáveis e não sedados, além de fornecer valores de referência para essa variável.

Palavras-chave: felino, cardiopatias, ecocardiografia, função diastólica

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## INTRODUCTION

Echocardiography is the non-invasive tool of choice for cardiac function assessment in cats, once it enables an observation of the heart in real-time as well as flows and valve morphology achievement, besides being an evaluation of the cardiac chambers size (Bonagura, 2000).

Many echocardiographic techniques such as Doppler and two dimensional speckle tracking have been used in veterinary medicine in order to better understand the physiopathology of cardiac abnormalities in cats, as well as obtain their diagnoses (Chetboul *et al.*, 2006; Koffas *et al.*, 2006; Adin and Diley-Poston, 2007; Wess *et al.*, 2010).

Left ventricular (LV) diastolic dysfunction is an important cause of clinical symptoms and is considered one of the first functional abnormalities detected in a large number of cardiopathies (Schober *et al.*, 2003; 2010). In this context, hypertrophic cardiomyopathy (HCM) is considered one of the most common cardiac abnormalities in domestic cats and it often leads to the onset of cardiac heart failure (CHF) symptoms or even sudden death of asymptomatic animals (Ferasin, 2009; Silva *et al.*, 2013). The physiopathological mechanism is primarily related to diastolic dysfunction which is responsible for HCM clinical symptoms, since an abnormal relaxation pattern can cause abnormal rise of ventricular filling pressure, hence an atrial enlargement (Côté *et al.*, 2011).

Mitral flow propagation velocity (Vp) is an echocardiographic variable used to determine left ventricular diastolic function. This index has been studied in medicine with the aim to characterize its influence in either healthy or sick individuals in different hemodynamic conditions (Rivas-Gotz *et al.*, 2003; Kidawa *et al.*, 2005; Khalaf, 2012). In veterinary medicine, Vp has been mainly evaluated in dogs with degenerative myxomatous mitral valve disease (DMVD) to obtain its true importance and influence over other variables (Schober *et al.*, 2010). Other studies evaluated Vp in dogs with induced CHF (Schober *et al.*, 2008), and with dilated cardiomyopathy (O'Sullivan *et al.*, 2007). According to the study of Cavalcanti *et al.* (2007), Vp is a relatively independent index in boxer breed dogs. Furthermore, they verified in

their study that Vp is inversely proportional to the animals' age.

There are few studies available on Vp in non-sedated healthy felines as well as in cardiopathic ones. A study conducted with sedated cats showed that Vp was not influenced by preload values and nor by heart rate (Schober *et al.*, 2003). The study conducted by Ward *et al.* (2012) showed that Vp suffers small variation in animals which were anesthetized with acepromazine + butorphanol or acepromazine + butorphanol + ketamine.

Despite the different echocardiographic techniques used in veterinary medicine that became recently available, there is still much to study on cardiac function in cats as well as on cardiovascular variations that may develop in this species. Thus, to better understand the clinical significance of variations in feline echocardiography, it is essential to obtain reference values from non-sedated healthy subjects, since such knowledge can aid in early diagnosis of cardiac diseases. Therefore, the aim of this study was to evaluate the values obtained for Vp as well as its correlation with variables such as age, heart rate (HR), body surface area (BSA), initial (E mitral) and late (A mitral) ventricular filling waves, isovolumic relaxation time (IVRT) and E/IVRT ratio since there is little information available about the influence of Vp on these variables in non-sedated healthy cats.

## MATERIALS AND METHODS

In order to conduct this study, twenty-six domestic cats from the small animal service of the institution were examined. A prior consent from the owners was obtained and the project was approved by the Ethics on Animals Use Committee under the number 052/11. All the animals were clinically examined. Systolic blood pressure (Doppler indirect method), thoracic radiography (right lateral and ventrodorsal recumbency), electrocardiography (ECG) and echocardiography were performed for assessing whether the animals were healthy.

An Esaote<sup>®</sup> (Mylab 40) ultrasound machine with a 4-10MHz sectorial scanning transducer and a simultaneous ECG monitor were used in order to perform the echocardiography. The animals were gently positioned on the left and right

lateral recumbence without sedation while the exam was being processed. The images and echocardiographic measurements were obtained in the right parasternal short axis view, right longitudinal parasternal and left apical 4-chambers view. The assessment of systolic and diastolic left ventricular dimensions were made through the M-mode echocardiography, and the ratio between the left atrium (LA) and aorta dimensions were evaluated through two dimensional mode. Moreover, valve flows were measured by pulsed Doppler as well as early (E) and late (A) mitral valve ventricular filling waves and isovolumic relaxation time (IVRT) of the LV. The ratio among E/A, E/Vp and E/IVRT were calculated subsequently. All echocardiographic indices and variables achieved were accomplished following the criteria recommended by Boon (2011).

In order to assess Vp, the M-mode was accomplished with the cursor positioned over the mitral valve, while the color Doppler was activated. Thus, with an enlarged image it was possible to visualize mitral flow being spread into LV. According to recommendations by Schober *et al.* (2003), Vp was measured from the opening of the mitral valve leaflet through 1.5 cm distance inside the LV with the aid of a line drawn in the color change zone (blue-red) of wave E (Fig. 1).

All results from continuous variables were clearly investigated and the test for normality (*Kolmogorov-Smirnov*) was performed. A descriptive analysis was done as well as the frequency analysis for categorical variables (gender and breed) and also for continuous variables with the purpose of obtaining median (age) and mean (weight, BSA and echocardiographic variables). The correlation between Vp and other echocardiographic parameters was enabled by the use of *Sperman's* correlation test. The Vp variability was observed (intra and interobserver variability) and assessed through the coefficient of variation (CV - %) from duplicate measurements (Schober *et al.*, 2010; Ward *et al.*, 2012). In order to evaluate intraobserver variability, six animals were randomly selected and Vp was measured on the first and fifteenth day. For the assessment of interobserver variability, Vp was measured in these six animals by two examiners that were unaware of previous results. For measuring

variability coefficient, the difference between the CV achieved on both analysis dates was calculated. For all analysis performed a  $P < 0.05$  was considered statistically significant.

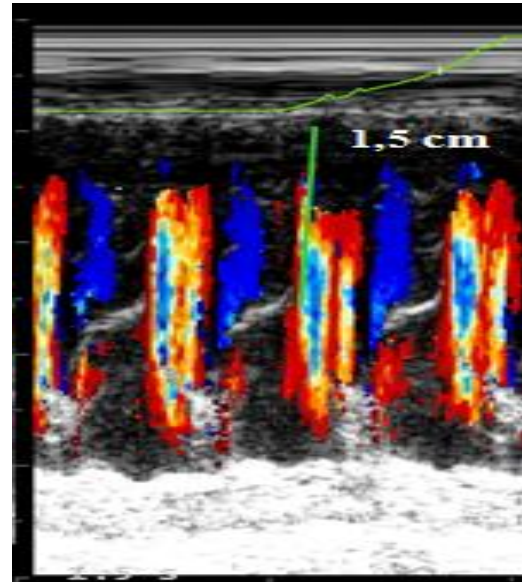


Figure 1. Mitral flow propagation velocity (Vp) determined by the slope ramp (green line) positioned in the transitional color zone (red-blue) from the opening of mitral valve leaflet through 1.5cm distance inside LV in a non-sedated healthy cat

All statistical analyses were performed using *SPSS for Windows* version 17.0 (SPSS, 2008).

## RESULTS

The animals presented mean values of systolic blood pressure within the normal range ( $129.50 \pm 15.03$  mmHg). No relevant variations were verified in the thoracic radiography and ECG did not show any myocardial electrical disturbance or arrhythmia.

The weight variations and BSA presented normal distribution data ( $P > 0.05$ ), since the average was  $3.99 \pm 0.99$  kg (2.5–6.8) and  $0.25 \pm 0.04$  (0.18–0.36), respectively. Regarding the animals' age, the distribution was not normal ( $P < 0.05$ ) and the median obtained was 24 months (7–84). Furthermore, regarding the gender variable, it was verified that 61.5% of the animals were males and 38.5% were females. Among these animals' sorts of breeding, there was one

Siamese (3.8%), six Persians (23.1%) and 19 mixed breed animals (73.1%).

In Table 1 the values (mean±standard deviation) are displayed for echocardiographic variables in this study, and all values are within the normal range (Schober *et al.*, 2003; Boon, 2011). The mean value calculated for Vp in this present

study was 0.71 m/s and it was also observed a HR mean value with 162.63 beats per minute.

Table 2 shows the existing correlation between Vp and other variables in this study. A significant correlation of Vp could only be verified between HR and BSA.

Table 1. Values for echocardiographic and heart rate in non-sedated healthy cats (n = 26)

| Variable analyzed | Mean±standard deviation | Minimum | Maximum |
|-------------------|-------------------------|---------|---------|
| Vp (m/s)          | 0.71±0.11               | 0.39    | 1.05    |
| A mitral (m/s)    | 0.62±0.13               | 0.40    | 0.93    |
| E mitral (m/s)    | 0.89±0.14               | 0.50    | 1.27    |
| E:A Ratio         | 1.47±0.21               | 1.04    | 2.15    |
| E:Vp Ratio        | 1.28±0.31               | 0.80    | 2.49    |
| IVRT (ms)         | 41.50±9.31              | 19      | 67      |
| E:TRIV Ratio      | 0.0225±0.0067           | 0.01    | 0.04    |
| Heart Rate (bpm)  | 162.63±43.38            | 55      | 239     |

Vp: mitral flow propagation velocity; A mitral: late mitral valve ventricular filling wave; E mitral: early mitral valve ventricular filling wave; IVRT: isovolumic relaxation time.

Table 2. *Sperman's* coefficient for correlation between mitral valve flow propagation velocity (Vp) and echocardiographic parameters in non-sedated healthy cats (n = 26)

| Compared Variables | Age (months) | BSA         | A mitral (m/s) | E mitral (m/s) | E:A Ratio | IVRT (ms) | E:IVRT Ratio | Heart Rate |
|--------------------|--------------|-------------|----------------|----------------|-----------|-----------|--------------|------------|
| Vp (m/s)           | r = -0.268   | r = -0.490* | r = -0.014     | r = 0.010      | r = 0.021 | r = 0.159 | r = -0.134   | r = 0.276* |
|                    | P = 0.185    | P = 0.013   | P = 0.882      | P = 0.912      | P = 0.819 | P = 0.076 | P = 0.136    | P = 0.05   |

Vp: mitral flow propagation velocity; BSA: Body surface area; A mitral: late mitral valve ventricular filling wave; E mitral: early mitral valve ventricular filling wave; IVRT: isovolumic relaxation time.

\*Significant correlation at level 0,05.

Regarding intra and interobserver variabilities, Vp achieved higher values (P<0.05) for interobserver analysis (9.90%) when compared with intraobserver variability (7.57%).

## DISCUSSION

The greater number of males, as well as the fact that most of the animals were young adults, may be explained by the random selection of animals examined in this study. Moreover, regional characteristics explain the fact of having a greater representation of mixed breed animals compared to other breeds.

The variable Vp showed slightly higher values when compared to those obtained by Schober *et al.* (2003), and lower values than the those obtained by Ward *et al.* (2012). In this last reference it was proved that Vp does not change

in a clinically significant way after sedation. However, the number of animals tested in both studies was small (n=7), which may have influenced the mean values observed and explains the differences obtained compared with the present study (n=26).

The IVRT showed relevant value within the standard established by Boon (2011), which was similar to value obtained by Ward *et al.* (2012). However, this variable presented numerically lower than those achieved by Schober *et al.* (2003). The study performed by Ward *et al.* (2012) verified that a small variation of this variable exists when comparing non-sedated and sedated animals. Thus, the variation observed in relation to the study developed by Schober *et al.* (2003) may be attributed to the sedation procedure adopted in both studies. Furthermore, in dogs with DMVD, the cutoff-value for IVRT

is 46 m/s, and lower values indicate worsening symptoms of their conditions and onset of CHF (Schober *et al.*, 2010).

Concerning mitral flow, E and A waves showed higher mean values than those described in literature (Bright *et al.*, 1999; Schober *et al.*, 2003; Ward *et al.*, 2012), and this fact can be explained by HR influence on mitral flow, once a higher HR can increase the values of waves E and A. However in the study of Santilli and Bussadori (1998) in non-sedated cats, lower values than those in our study were observed. On the other hand, the study mentioned was conducted over 10 years ago, so differences on ultrasound machine and its accuracy could be an explanation. In addition, E/A relation with values verified in this present study are higher than those reported by Ward *et al.* (2012) and lower than the values obtained by Schober *et al.* (2003), and identical to the value obtained by Soares *et al.* (2005); such variation can be a consequence of the sedation process, heart rate, and from the difference in the number of animals tested.

Vp did not correlate with A mitral, E mitral, E/A and IVRT ratio variables, and these findings are similar to what is described in literature, whether for studies in cats or in dogs (Schober *et al.*, 2003; Cavalcanti *et al.*, 2007; Schober *et al.*, 2010). However, in the present study, Vp correlated significantly with BSA and HR, although the correlation coefficient is low ( $r = 0.276$ ). This fact differs from that observed in the study developed by Schober *et al.* (2003), in which Vp was not affected by HR. This can be justified by the influence of sedation on variables evaluated in the study. According to Cavalcanti *et al.* (2007), in which Vp was evaluated in Boxer breed dogs, there were no significant correlation of this variable with other echocardiographic indices, it only was verified an inverse relation with age. Thus, Vp was considered a relatively independent index. However, a correlation between Vp and the animals' age in the present study was not verified, there was only a relation between Vp and BSA, in which the correlation was negative. These differences may have occurred due to the difference between the species (cats and dogs) and the fact that the cats were not sedated in this present work.

Regarding intra and interobserver variabilities, a higher percentage of interobserver analysis was shown. However, all values were considered low, since they are below 15%, just like the value achieved in other studies of this same variable (Schober *et al.*, 2010; Ward *et al.*, 2012). Additionally, interobserver variability was lower than that observed by Ward *et al.* (2012). Thus, Vp can be considered as an index with good reproducibility.

Some limitations found in this study should be clarified. Such limitations include problems in obtaining quality images of non-sedated cats, since the high heart rate of these animals makes the appropriate achievement of mitral flow and images for measuring Vp difficult. In addition, the study was conducted on 26 non-sedated cats with mixed breed animals being over represented and there were only few Persians and Siameses. Thus, developing a study involving a larger number of animals is essential in order to determine the influence of breed and gender on Vp.

Another limitation that should be considered is the manual method of measuring Vp flow ramp, especially when this ramp looks nearly vertical, may raise the values of this variable (Schober *et al.*, 2003). However, aiming to minimize these factors and increase the analysis reliability, a 1.5 m/s sweep speed and five measurements of Vp per animal were adopted and performed as recommended by Schober *et al.* (2003). Furthermore, the present study was conducted in pet animals, so no invasive analysis for obtaining hemodynamic data was performed, in order to collaborate with the clinical conditions of the animals.

## CONCLUSIONS

The present study provided information about Vp and its relevance for determining diastolic function in non-sedated healthy felines. Vp proved to be a useful index to estimate left ventricular relaxation in non-sedated healthy domestic cats, which contributed to the achievement of values that can be used as reference indexes in healthcare routine. Vp demonstrated to be a relatively independent index, and it can be used to obtain diastolic function in domestic cats. However, developing studies in cats with heart diseases to obtain Vp values and comparing them with ones obtained

in healthy animals are essential to evaluate the role of this variable in the diagnosis of cardiac abnormalities in cats.

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