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Heart rate variability in dogs with myxomatous mitral valve disease: a contemporary review

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Abstract: Heart rate variability (HRV) is the fluctuation in the interval between heartbeats, reflecting the activity of the autonomic nervous system and serving as a prognostic indicator in canine cardiovascular diseases. Myxomatous mitral valve disease (MMVD) is the leading chronic cardiac condition in small and elderly dogs, often leading to congestive heart failure (CHF). MMVD alters the balance of autonomic regulation of the heart, resulting in increased sympathetic activity and decreased vagal tone, which can aggravate venous congestion and accelerate disease progression. HRV analysis, using linear and non-linear methods, allows the assessment of the autonomic function of the heart and the identification of early dysfunctions. Studies show reduced HRV in dogs with CHF is associated with disease severity, highlighting the importance of monitoring HRV to predict mortality and guide therapeutic interventions. The literature reveals that SDNN and rMSSD indicate parasympathetic tone, while the LF/HF ratio reflects autonomic balance. Pharmacological and non-pharmacological treatments, such as moderate exercise, have been shown to improve autonomic modulation in dogs with MMVD. Understanding the pathophysiological mechanisms of MMVD and CHF is crucial for clinical management. HRV assessment, despite its limitations, is a valuable tool for understanding disease progression and optimizing therapeutic interventions. Therefore, this literature review aims to provide methods for assessing HRV and relevant studies covering HRV and dogs with MMVD.

Keywords: autonomic balance; chronic valve degeneration; congestive heart failure; prognosis; treatment.

1. Introduction

Heart rate variability (HRV) is the fluctuation in the time interval between heartbeats, influenced by the activity of the autonomic nervous system (ANS) on the heart. This variation can provide valuable insights into prognosis and help predict mortality risk from animal cardiovascular diseases. HRV indices are calculated indirectly and non-invasively by analyzing electrocardiographic recordings, which can vary from short (5 to 30 minutes) to long (24 hours). The measurement of HRV can be performed using both linear methods, the most commonly utilized, and non-linear approaches. Variations in these indices are regarded as early and sensitive markers of autonomic dysfunction, suggesting a poorer prognosis in various medical conditions (Champéroux et al., 2018).

In small and elderly dogs, myxomatous mitral valve disease (MMVD) is recognized as the leading chronic acquired heart condition, accounting for approximately 75% of heart disease cases in this species. The highest prevalence of MMVD occurs in small breed dogs aged between 10 and 19 years (Pascon et al., 2021). The disease progresses slowly, and many dogs may remain asymptomatic for several years, or even throughout their lives. However, serious complications can arise as the disease advances, leading to the development of congestive heart failure (CHF) (Petrus et al., 2020).

MMVD can disrupt the balance of cardiac autonomic regulation by chronically activating neurohumoral mechanisms to restore cardiac output (CO). This activation involves compensatory neurohumoral systems, such as the autonomic nervous system (ANS) and the renin-angiotensin-aldosterone system (RAAS), which results in decreased vagal tone and increased sympathetic tone to maintain CO (Baisan et al., 2021). However, the prolonged activation of these mechanisms worsens venous congestion, eventually leading to CHF. Additionally, the chronic increase in sympathetic nervous system (SNS) activity accelerates the progression of the disease through various pathways (Marin-Neto & Simões, 2014).

Therefore, acknowledging the presence of cardiac autonomic imbalance is essential to providing a more precise prognosis concerning the disease and evaluating the risk of mortality. In dogs, there is no scientific consensus regarding the impact of primary conditions on heart rate variability (HRV), with most information stemming from limited studies or findings extrapolated from human heart disease. This literature review outlines the primary methods for assessing HRV and the studies conducted on HRV in dogs with MMVD, the most prevalent heart condition in veterinary cardiology.

2. Development

2.1. Cardiac autonomic control and congestive heart failure

The ANS regulates the body's physiological processes under normal and pathological conditions (Vanderlei et al., 2009). It consists of extrinsic and intrinsic ganglion cells, forming sympathetic endings in the myocardium and parasympathetic endings in the sinus node, atrial myocardium, and atrioventricular node (Pfenniger, 2019) (Figure 1). In terms of cardiac regulation, the ANS is responsible for controlling the pumping frequency and function of the heart, adapting these functions to the metabolic and tissue demands encountered by animals during their daily activities. This system relies on information from pressure baroreceptors, chemoreceptors, atrial receptors, ventricular receptors, modifications in the renin-angiotensin-aldosterone system (RAAS), and the thermoregulatory system. Through afferent details and complex interactions between stimulation and inhibition, sympathetic and parasympathetic tone responses are modulated, influencing heart rate and adjusting to immediate needs (Brandão et al., 2014).

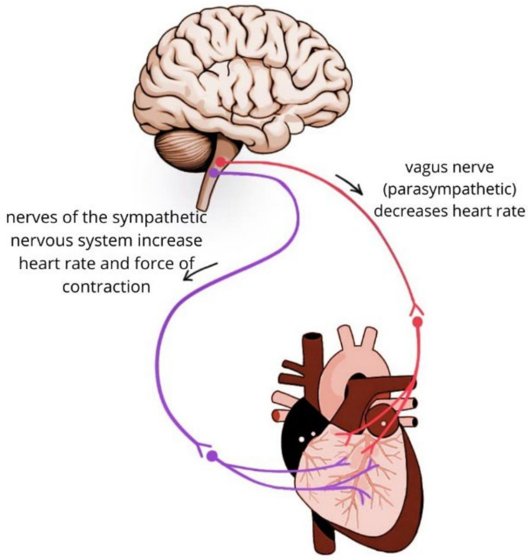

Figure 1 – Sympathetic and parasympathetic innervation of the heart.

Sympathetic nerves have a positive chronotropic (contractile frequency) and inotropic (contractile force) effect, while vagal fibers produce opposing effects. The chemical mediators responsible for these autonomic actions—norepinephrine and acetylcholine—act on specific adrenergic (sympathetic) and cholinergic (parasympathetic) receptors on effector cells. This interaction results in an irregular physiological heart rhythm, reflecting the autonomic balance within the sinus node (Champéroux et al., 2018). This balance fluctuates based on various factors, including wakefulness and sleep, body posture, physical training, stress, respiration, fluctuations in blood pressure, the renin-angiotensin-aldosterone system (RAAS), and pathological conditions (Billman, 2011).

CHF is characterized by the ongoing interaction between cardiac muscle dysfunction and neurohumoral mechanisms that become activated as a compensatory response. These mechanisms, such as the activation of the SNS, can help maintain blood flow despite decreased cardiac function. However, prolonged sympathetic hyperactivity leads to numerous functional adaptations of sympathetic receptors and direct toxic effects on cardiomyocytes, contributing to adverse remodeling of the cardiac chambers and a gradual decline in ventricular systolic function (Florea & Cohn, 2014). The hyperactivity of the SNS observed in heart failure patients arises from increased sympathetic nerve discharge and more significant catecholamine release from the adrenal medulla. Understanding these mechanisms is crucial for improving the treatment and monitoring of patients with CHF (Marin-Neto & Simões, 2014).

The proper functioning of the autonomic nervous system (ANS), in synchrony with all other systems, is essential to ensure that the organism can restore normal functions after periods of stress and respond to new events. This is why all information regarding autonomic behavior is fundamental for understanding other potential pathophysiological processes. In this context HRV has been used to measure heart rate variations influenced by the ANS. This allows for evaluating the body's ability to respond to both external and internal stimuli and identifying possible ANS dysfunctions that could lead to cardiovascular diseases and other clinical conditions (Champéroux et al., 2018).

Many studies recognize the significant relationship between the ANS and cardiovascular mortality, including sudden death. HRV helps assess the balance between sympathetic and parasympathetic influences on heart rhythm, enabling a non-invasive evaluation of autonomic modulation on the heart, and can therefore serve as a prognostic indicator for certain cardiac and systemic diseases. Changes in HRV patterns provide an early and sensitive indicator of compromised health. High heart rate variability indicates good adaptability, indicating a healthy individual with well-functioning autonomic control mechanisms. Conversely, lower variability often indicates abnormal and insufficient adaptability of the autonomic nervous system, suggesting the presence of a physiological malfunction in the individual (Taralov et al., 2015).

2.2. Analysis of heart rate variability

HRV is assessed using the electrocardiogram (ECG) and involves the analysis of periodic and non-periodic oscillations between consecutive heartbeats (NN intervals) (Figure 2), influenced by the interaction between the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). Changes in HRV patterns serve as sensitive and early indicators of potential cardiovascular health issues, as well as helping to stratify the risk of mortality in patients with heart disease. It is a significant and valuable technique for preventing and early diagnosing cardiovascular diseases (Tiwari et al., 2021). With the implementation of computer-aided HRV analysis, it has become a relatively straightforward and non-invasive test for examining autonomic function of the heart (Boguchi & Noszczyk-Nowak, 2017).

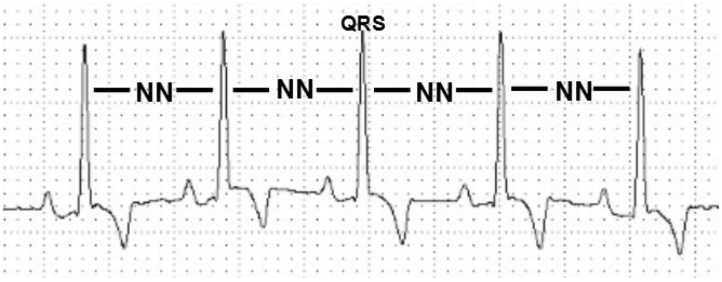

Figure 2 – ECG tracing demonstrating QRS complexes and NN intervals.

High HRV indicates good adaptability, suggesting a healthy individual with well-functioning autonomic control mechanisms. Conversely, lower variability often reflects abnormal and insufficient adaptability of the ANS, indicating a physiological malfunction in the individual that requires further investigation for a specific diagnosis (Pumprla et al., 2002). In patients with CHF, HRV is significantly reduced, which correlates with the severity of CHF and its prognosis. The underlying physiological mechanism for the decrease in HRV is likely an alteration in the cardiac sympathetic-parasympathetic balance, characterized by relative sympathetic dominance, probably due to reduced parasympathetic activity. HRV estimation provides prognostic information beyond traditional risk factors, being able to predict sudden cardiac death in patients with chronic CHF (Florea & Cohn, 2014).

Detailed HRV analysis can be conducted using linear and non-linear methods. Linear methods are the most commonly used, including time-domain analysis (statistical and geometric indices) and frequency-domain analysis (spectral analysis of ordered NN intervals). Non-linear methods involve analyzing fluctuations refined from trends, correlation functions, Hurst exponents, fractal dimensions, and Lyapunov exponents (Taralov et al., 2015; Tiwari et al., 2021).

Moreover, HRV can be assessed in both the long and short term (Pumprla et al., 2002; Shaffer & Ginsberg, 2017). Short-term HRV is typically calculated over 5 minutes, using the magnitude of frequency components obtained through spectral analysis to assess autonomic function. Long-term HRV is calculated using nominal 24-hour indices in the time domain, frequency domain, and non-linear index to predict mortality risk. However, there is a more significant difference between short-term and long-term HRV than just the length of data collection. Short-term HRV data is generally recorded under controlled monitoring conditions. At the same time, long-term HRV better represents processes with slower fluctuations (e.g., circadian rhythms) and the cardiovascular system's response to a broader range of environmental stimuli and workloads. Therefore, short- and ultra-short-term values are not interchangeable with 24-hour values (Shaffer & Ginsberg, 2017).

Time domain HRV analysis

Time domain techniques are the most straightforward methods for assessing HRV; however, they provide less information about the pathophysiological state of patients than frequency domain techniques. There are two approaches to evaluating HRV in the time domain: statistical methods and geometric methods (Shaffer & Ginsberg, 2017). Statistical methods involve calculating indices based on statistical operations of NN intervals over a specific period. These parameters are derived from direct measurements of regular NN intervals or the differences between these intervals, measured in milliseconds, which provide insights into fluctuations in cardiac cycles (Billman et al., 2015; Champéroux et al., 2018; Tiwari et al., 2021). On the other hand, geometric methods focus on the geometric characteristics of the graph generated by HRV analysis, such as the range of data observed in RR histograms (Hezzel et al., 2018).

These methods utilize mathematically straightforward techniques to measure the variability in a continuous electrocardiogram over a predefined period. After editing to remove non-sinus beats and artifacts, the remaining regular RR intervals are calculated and subjected to simple statistical analysis (Billman et al., 2015), meaning only the beats resulting from normal electrical activation (originating from depolarization of the sinus node) are included (Billman, 2011). Numerous variables can be directly calculated from the intervals and differences between intervals, with all variables in the time and frequency domains analyzed using specific software (Tiwari et al., 2021).

The statistical variables evaluated in the time domain include:

- Standard deviation of all NN intervals (SDNN): This represents the dispersion of cardiac cycle durations around their mean value, measured in milliseconds (ms) (Shaffer & Ginsberg, 2017), and is the most accurate time domain measure used. Approximately 30-40% of the SDNN magnitude is attributed to the difference between daytime and nighttime NN intervals (Billman, 2011). It is a crucial measure of HRV because, mathematically, the standard deviation of subsequent RR intervals relates to the variance of HRV, which in turn reflects the total power of HRV during the recording period (Shaffer & Ginsberg, 2017). Reduced SDNN values indicate diminished autonomic modulation of the heart, predominating either sympathetic or parasympathetic activity (Fuji & Wakao, 2003).
- Standard deviation of regular NN intervals obtained every 5 minutes (SDANN): This provides a smoothed version of SDNN, being less prone to editing errors than SDNN, as it reflects the average of several hundred NN intervals, minimizing the effects of unedited artifacts (Billman, 2011). Like SDNN, SDANN is also a global HRV index, so its values can be influenced by the length

of the ECG recording and the longest and shortest RR intervals, varying based on the duration of data acquisition (Boguchi & Noszczyk-Nowak, 2017; Pirintr et al., 2017).

- Average standard deviations of regular NN intervals every 5 minutes (SDNNi): This reflects the average changes between NN intervals occurring within five minutes, significantly correlating with SDNN and SDANN, as low and high HRV are global phenomena that affect all measures (Shaffer & Ginsberg, 2017).
- Square root of the squared mean of consecutive NN intervals (rMSSD): This measures the average variation of the interval between beats. NN50 is the absolute count of differences between successive intervals more significant than 50 ms, and pNN50 is the proportion of disagreements exceeding 50 ms (Billman, 2011). RMSSD strongly correlates with the High Frequency (HF) variable and, thus, with parasympathetic modulation (Shaffer & Ginsberg, 2017).
- % of regular consecutive NN intervals with a difference greater than 50 ms (pNN50): Each RR interval is compared to the adjacent one, and the difference is calculated. The number of adjoining interval comparisons with differences >50 ms (NN50) is then observed. This number is divided by the number of comparisons to obtain a percentage. Like RMSSD, pNN50 estimates high-frequency variations in heart rate and may relate to parasympathetic regulation of the heart (Billman, 2011).

Another index indicating HRV in the time domain is vasovagal tone (VVTI), a useful unconventional HRV index that can be easily calculated in clinical settings (Pereira et al., 2008). It quantifies high-frequency variations in heart rate and can be derived from ECG recordings using a simple mathematical formula, typically employing the natural logarithm of the variance of 20 consecutive RR intervals acquired in a brief recording period. In resting dogs, it can provide reliable information regarding HRV, serving as an excellent prognostic indicator alongside HRV assessment, as it can indicate the probability of developing CHF, primarily influenced by parasympathetic tone (Bruller et al., 2017; Doxey & Boswood, 2004; Traufler et al., 2019).

The main geometric methods used in veterinary medicine include the triangular index and the Lorenz graph (also known as the Poincaré graph). The triangular index is calculated by constructing a density histogram of regular RR intervals, which displays the length of the RR intervals on the horizontal axis (x-axis) and the frequency of each interval on the vertical axis (y-axis). The union of the histogram column points forms a triangular shape, with the width of the triangle's base representing the variability of the RR intervals. The triangular index (corresponding to the base of the triangle) is calculated by dividing the area (total number of RR intervals used to construct the figure) by the height (number of RR intervals with modal frequency) of the triangle. It closely correlates with the standard deviation of all RR intervals and is not influenced by ectopic beats and artifacts, as they fall outside the triangle. The Poincaré graph analyzes the dynamics of HRV, representing a time series within a Cartesian plane where each RR interval correlates with the preceding interval, defining a point on the graph. Its analysis can be qualitative (visual) by evaluating the attractor's shape, which helps show the complexity of the RR intervals, or quantitative by adjusting the ellipse formed by the attractor, yielding three indices: SD1 (dispersion of points perpendicular to the line of identity, representing instantaneous HRV), SD2 (dispersion of points along the line of identity, representing long-term HRV), and the SD1/SD2 ratio (the ratio between short and long variations of the RR intervals) (Shaffer & Ginsberg, 2017; Vanderlei et al., 2009).

Frequency domain HRV analysis

Frequency domain measurements estimate absolute or relative power distribution across four frequency bands. The Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) categorized HR oscillations into ultra-low frequency (ULF), very low frequency (VLF), low frequency (LF), and high frequency (HF) bands (Shaffer & Ginsberg, 2017).

Total power (TP) represents the total energy in the power spectrum above 0.4 Hz and is divided into four distinct frequency bands: 1 - high frequency (HF), ranging from 0.15 to 0.4 Hz, corresponds to respiratory modulation and indicates the performance of the vagus nerve in the heart; 2 - low frequency (LF), ranging from 0.04 to 0.15 Hz, is influenced by the actions of both the vagus nerve and sympathetic components in the heart, with a predominance of sympathetic activity, and has been associated with the baroreceptor and thermoregulatory systems, vasomotor activity, and the RAAS; 3 - very low frequency (VLF), ranging from 0.01 to 0.04 Hz, is considered a marker of sympathetic activity; and 4 - ultra-low frequency (ULF), ranging from 10^-5 to 10^-2 Hz, which does not have a clear physiological correspondence. The LF/HF ratio reflects relative and absolute changes between the sympathetic and parasympathetic components of the autonomic nervous system (ANS), characterizing the autonomic balance of the heart (Billman et al., 2015; Vanderlei et al., 2009).

Low-frequency variables indicate changes related to baroreceptors and the RAAS. High frequencies are modulated by breathing and controlled by the parasympathetic nervous system (Billman, 2011; Oliveira et al., 2014). The high- and low-frequency components are named as such because the vagus nerve and sympathetic system send a higher or lower frequency of impulses to the ANS (Kleiger et al., 2005).

2.3. Limitations of using HRV analysis

Autonomic cardiovascular control is not merely the dominance of the SNS or PNS. It involves a complex interaction through various circulatory reflexes such as baroreceptors, chemoreceptors, and the ANS. Additionally, various molecular and hormonal factors and central oscillations can influence HRV and contribute to the overall complexity of signals. Under different physiological or pathological conditions, any of these mechanisms may become dominant, inhibiting others, which can reduce the complexity of HRV and lead to a “simplification” of cardiovascular control (Hayano & Yuda, 2019; Taralov et al., 2015).

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HRV analysis, regardless of the method used, does not provide a direct measure of autonomic cardiac activity but rather an indirect one. Consequently, interpretations should be made qualitative rather than quantitatively (Billman, 2011). One limitation of time-domain HRV is that recordings of different durations cannot be compared, as such recordings yield very different measurements. Additionally, all heartbeats evaluated must be “normal” (i.e., all ectopic beats must be excluded from the time series) to accurately reflect the effects of regulatory mechanisms on the sinoatrial node. Furthermore, it is crucial to obtain high-quality recordings; otherwise, the automatic identification of RR intervals by analysis software may be flawed (Shaffer & Ginsberg, 2017).

Regarding the VVTI, it is a variable that may be considered inadequate due to its short recording period, which does not assess the effects of circadian rhythms, thermoregulation, blood pressure regulation, exercise, or the RAAS (Brüller et al., 2017; Doxey & Boswood, 2004; Trauffler et al., 2019) and primarily responds to respiratory variations. Therefore, its prognostic and diagnostic power may not be comparable to other HRV indices (Pereira et al., 2008).

In the frequency domain, the value measured for each frequency band depends on the duration of the recording; thus, selecting an appropriate recording duration is essential to ensure comparability of results (Li et al., 2019; Shaffer & Ginsberg, 2017). It is important to note that although the LF frequency component has been widely used to estimate sympathetic modulation of the heart, this frequency band also contains parasympathetic information and data from other regulatory components. Therefore, some authors suggest that the LF component should not be used as an index of sympathetic regulation (Billman, 2011).

2.4. Analysis of HRV in myxomatous valve disease in dogs

It is well established that heart diseases lead to changes in the autonomic control of the heart, evidenced by an increase in HR and a decrease in HRV (Oliveira et al., 2014). The development of CHF secondary to MMVD is associated with a reduction in HRV (Baisan et al., 2021; Oliveira et al., 2012; Oliveira et al., 2014; Rasmussen et al., 2012), as neurohumoral activation begins in animals with MMVD when clinical signs of CHF appear (Borgarelli & Häggström, 2010). In veterinary medicine, no established parameters exist for each HRV assessment method, making it difficult to compare different methodologies, as recordings of varying durations yield different measurements (Fernandes & Seara, 2021). Since 1996, numerous studies have been conducted in different research centers worldwide (Figure 3), exploring HRV and MMVD using various assessment methods (Figure 4).

Figure 3 – World map showing the locations (marked with green flag) where the main studies on HRV in patients with MMVD were carried out. Image: Google® Maps, 2025.

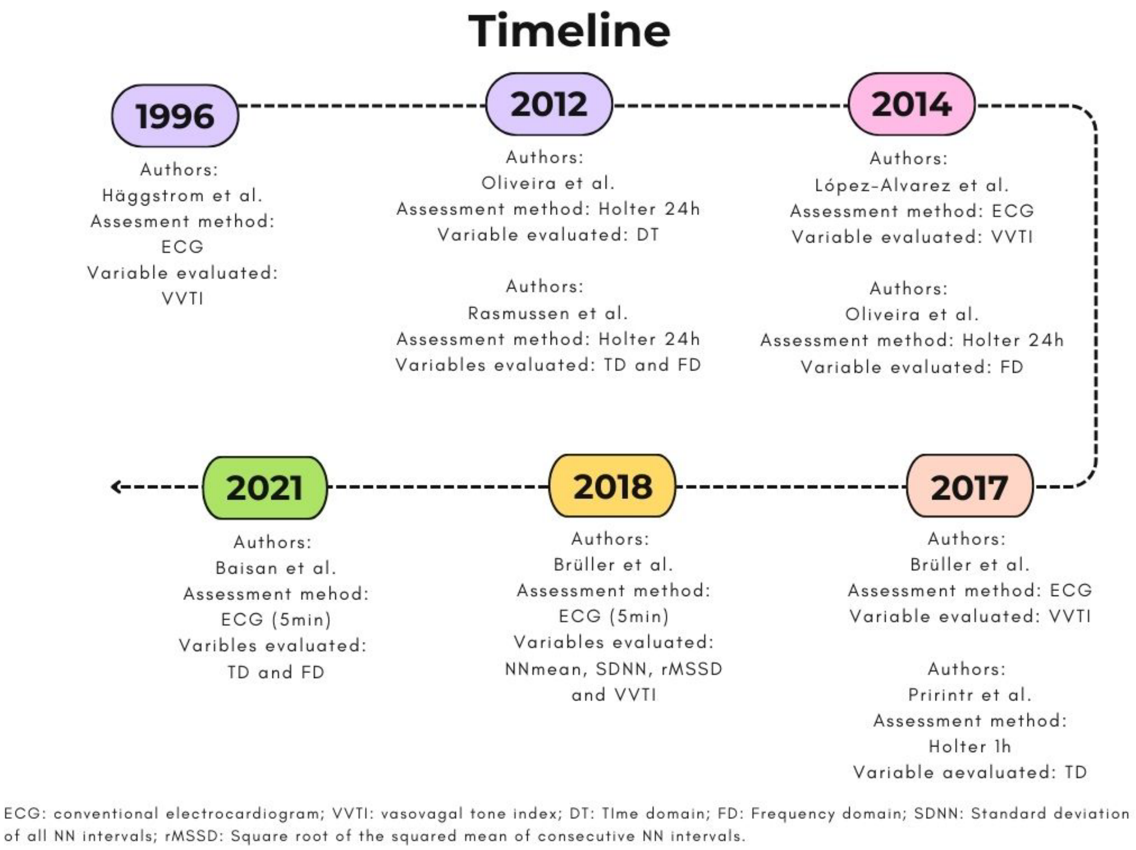

Figure 4 – Main studies reviewed, since 1996, involving the assessment of HRV in patients with MMVD.

A pioneering study by Häggström et al. (1996) evaluated HRV in dogs with MMVD and found a decrease in variability in Cavalier King Charles Spaniel (CKCS) dogs with CHF symptoms compared to healthy dogs of the same breed, using the VVTI as an evaluation tool. This study noted that animals with more advanced CHF had significantly lower VVTI values ($p<0.001$), with the index decreasing as CHF severity worsened, although without statistical differences. A significant correlation was found between VVTI and HR. Another important observation was that VVTI assessments must consider the dog's stress during the examination, as highly stressed dogs may show reduced VVTI, highlighting the need for careful handling during electrocardiogram procedures. It was also noted that decompensated MMVD consistently reduces VVTI, concluding that this technique is more sensitive than specific.

Using VVTI as an index for HRV evaluation, Brüler et al. (2017) also found significant differences in dogs with MMVD showing clinical signs of CHF, presenting lower VVTI values compared to asymptomatic patients. It was observed that lower VVTI suggests that asymptomatic patients may progress to CHF. This study also found that patients with greater left atrial enlargement (left atrium/aorta ratio >1.8, as seen on echocardiogram) had lower VVTI values than those with smaller atria. Such findings are crucial for clinical decision-making, as they relate VVTI to other prognostic indices and suggest a reduction in parasympathetic tone during CHF development. Another study assessed how NNmean, SDNN, rMSSD, and VVTI respond to vagal stimulation through digital ocular compression. Unlike the asymptomatic groups with and without cardiac remodeling, the group of dogs with symptomatic MMVD showed no response to the stimulus, indicated by the absence of changes in all variables. This finding suggests not a lack of vagal activity but rather a diminished response to parasympathetic stimuli in these patients. The absence of difference between the asymptomatic groups supports the theory that some degree of autonomic imbalance precedes clinical evidence of cardiovascular disorders (Brüler et al., 2018).

In another study, Rasmussen et al. (2012) compared HRV at different stages of MMVD in CKCS and other breeds, finding no significant differences between them. However, it was noted that in more advanced stages of the disease, HRV decreases due to an increase in minimum and average heart rate. The study concluded that there is a reduction in SNS activity, as seen in the decrease of the HF variable, and the LF variable also decreased, indicating a change in cardiac autonomic balance in more advanced disease stages, regardless of breed.

In the study by Oliveira et al. (2012), dogs with CHF secondary to MMVD showed decreased values in HRV variables in the time domain, specifically pNN50 and SDANN, indicative of parasympathetic tone. This suggests that changes in HRV in these cases may result from parasympathetic withdrawal rather than an increase in sympathetic tone. These results underscore the importance of understanding the pathophysiological mechanisms involved in MMVD and CHF to develop new therapeutic strategies.

Animals with MMVD exhibited a significant reduction in total power, representing overall HRV, compared to controls. Only sick dogs and those with heart failure showed an increase in heart rate, prolonged tachycardia relative to bradycardia, a reduced high-frequency index (indicative of parasympathetic control), and an elevated low-frequency index (indicative of sympathetic and parasympathetic control) compared to controls ($p<0.05$) (Oliveira et al., 2014). However, it was impossible to confirm whether there is a reduction in the influence of the parasympathetic nervous system (PNS) or an increase in the impact of the SNS on the sinus node in CHF development, as the changes observed correlate with both sympathetic and parasympathetic control.

In assessing HRV in asymptomatic animals in stages B1 and B2, Pirintr et al. (2017) identified early preclinical changes in ANS activity and some initial changes in HRV in the frequency domain, such as the HF variable, which preceded changes in echocardiographic and radiographic examinations compared to healthy animals. The same study also found that symptomatic animals had significantly lower HRV values. After clinical signs appeared, the SDNN and rMSSD variables were lower, indicating vagal tone withdrawal. Animals in stage C exhibited SNS activation, as reflected by an increased LF/HF ratio (Baisan et al., 2021). These results suggest the importance of evaluating HRV in animals with MMVD, both in preclinical and symptomatic stages, to understand disease progression and therapeutic interventions better.

Another aspect studied in patients with MMVD related to HRV is its correlation with mortality. A study by López-Alvarez et al. (2014) found that dogs with MMVD show an increase in heart rate and a decrease in HRV in the year leading up to death. These changes were most pronounced in dogs that died or were euthanized due to heart disease. These findings suggest that HRV analysis may be a valuable tool for monitoring the progression of heart disease in dogs with MMVD, facilitating early intervention and improving prognosis.

Finally, it is essential to mention some studies correlating HRV in patients with MMVD who underwent various treatments, whether pharmacological or not (Figure 5). In one study, dogs in stages B1 and B2 treated with enalapril for 14 days showed increased cardiac autonomic modulation, evidenced by the rise in the SDNN index. Additionally, LF decreased while HF increased, suggesting an increase in parasympathetic tone relative to sympathetic tone during short-term therapy (Chompoosan et al., 2014). Another study found that dogs with stage B1 and B2 MMVD treated with sildenafil also exhibited increased cardiac autonomic modulation, indicating that the rise in parasympathetic activity surpassed sympathetic activity, supported by increases in NN, SDNN, pNN50, and rMSSD in time domain parameters, as well as LF, HF, and total power in the frequency domain (Pirintr et al., 2017). In research by Beluque et al. (2021), dogs with stage C MMVD treated with the beta-blocker metoprolol, combined with standard treatment for 30 days, showed an increase in the pNN50 variable assessed through 24-hour Holter monitoring, indicating more significant vagal predominance after treatment. However, other HRV variables in the time domain did not show significant changes.

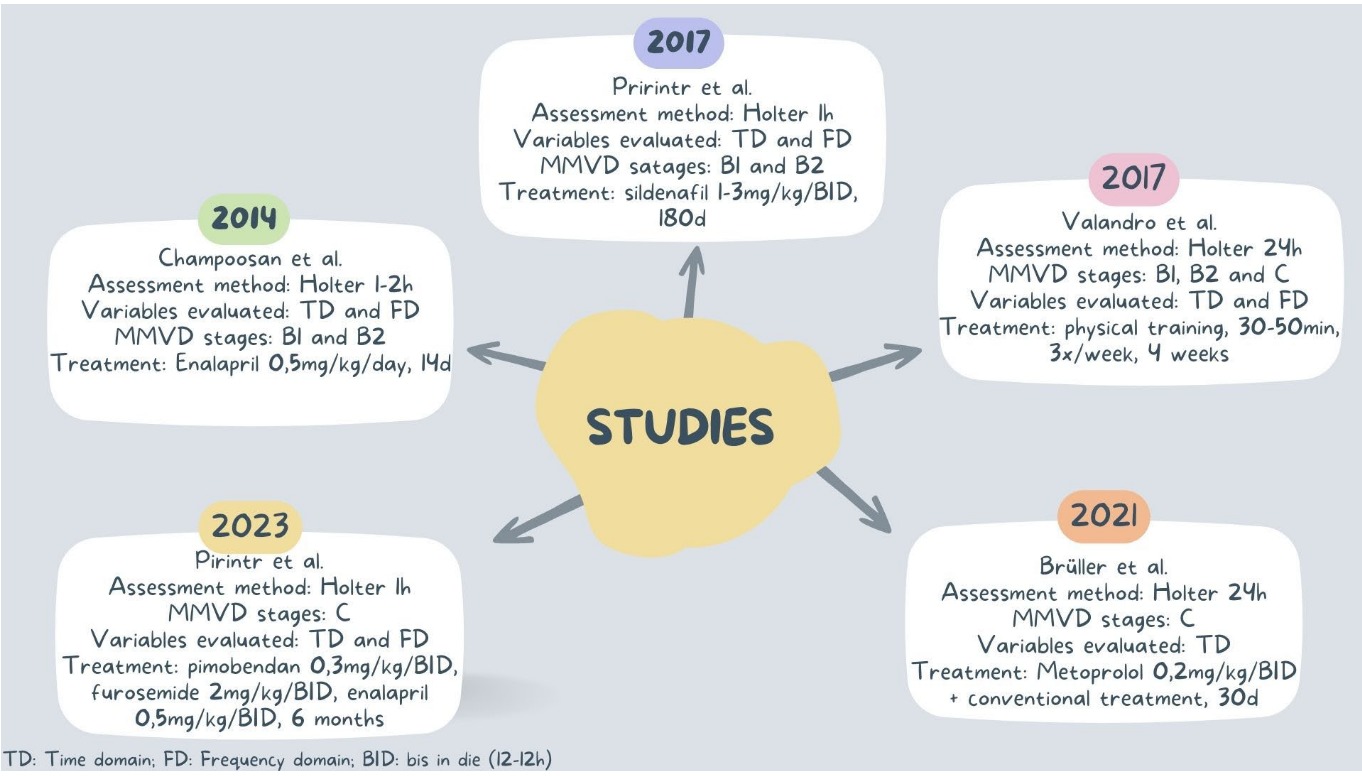

Figure 5 – Main studies reviewed involving the assessment of HRV in patients with MMVD undergoing different treatments.

The evaluation of HRV in symptomatic MMVD patients in response to therapy with pimobendan, furosemide, and enalapril for six months revealed that patients had lower values in time domain indices (SDNN, rMSSD, and pNN50), low frequency, high frequency, and total power, along with a higher LF/HF ratio after therapy, with these variables increasing significantly. Furthermore, the findings indicate that dogs with CHF secondary to MMVD exhibit low HRV due to parasympathetic tone withdrawal or increased sympathetic activation, and the instituted treatment can improve cardiac autonomic modulation (Pirintr et al., 2023).

Additionally, physical training involving moderate exercises (such as walking three times a week for 30 to 50 minutes over eight weeks) in dogs with asymptomatic MMVD restored the autonomic balance of these animals, as demonstrated by HRV variables in the time domain (rMSSD) and frequency domain (HF) compared to untrained dogs (Valandro et al., 2017), suggesting that this approach can be beneficial in the non-pharmacological treatment of MMVD in asymptomatic patients.

3. Conclusions

Heart rate variability (HRV) has been recognized as an essential marker of autonomic activity in dogs with chronic mitral valve disease (MMVD). Recent studies prove that HRV reduction occurs in patients with congestive heart failure (CHF), as demonstrated by various evaluated variables. It is increasingly clear that, in these stages, there is a reduction in the action of the parasympathetic nervous system (PNS) on cardiac autonomic balance. In the early stages, in asymptomatic dogs, there is still no scientific certainty regarding the occurrence of HRV reduction. Furthermore, pharmacological and non-pharmacological treatments, such as exercise training, can enhance cardiac autonomic modulation and increase parasympathetic activity in dogs with MMVD. Understanding the pathophysiological mechanisms involved in MMVD and CHF is essential. The assessment of HRV in animals with MMVD, despite its limitations, serves as a valuable tool for better understanding disease progression, determining prognosis, and initiating therapeutic interventions.

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