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Association Between Ventricular Trabeculation and Cardiovascular Diseases: A Systematic Review

Asociación entre Trabeculación Ventricular y Enfermedades Cardiovasculares: Revisión Sistemática

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SUMMARY: The limited understanding of the anatomical variations of the trabeculae carneae and their impact on cardiac function reveals a gap in current knowledge. Therefore, this study presents a systematic review that identifies and analyzes variations in the trabeculae carneae and evaluates their relationship with cardiac diseases. We conducted a systematic review following the guidelines of the Cochrane Collaboration Handbook. The databases reviewed were Web of Science, PubMed, Scopus, and BVS. Observational human studies investigating the morphology or morphometric characteristics of trabeculae carneae were considered for inclusion. A total of 314 articles were found, of which eight were selected. The selected studies used imaging tools that allowed visualization of the trabeculae carneae. However, none provided a morphometric description of the trabeculae carneae in healthy populations or those with cardiovascular pathologies. Although some studies suggest that trabeculae carneae play a significant role in cardiac structure and that their distribution pattern could constitute a risk factor in developing cardiac pathologies, other investigations did not find evidence of a clear pathological relationship. It is essential to accurately define ventricular trabeculation through dissection studies, which, together with imaging tools, could be sufficient to establish quantitative and qualitative parameters that allow the identification of its role in myocardial pathophysiology

KEYWORDS: Heart; Trabeculae carneae; Cardiomyopathies; Diagnostic Imaging.

INTRODUCTION

Trabeculae carneae develop during the early stages of embryonic heart formation (Dong *et al*., 2021) and consist of intricate septa or clusters of muscle fibers within the heart's ventricles. These structures increase the contact area between blood and heart tissue, facilitating effective contraction and adequate blood pumping. In addition, they perform a critical function by preventing the walls of the ventricles from sticking together, allowing blood to enter the heart's interior fluidly during the filling phase or diastole, thus influencing ventricular end-diastolic volume (Del Monte-Nieto *et al*., 2018; Olejnickova *et al*., 2024). In this same sense, the areas between the trabeculae carneae, called intertrabecular spaces, also facilitate blood flow through the heart during the cardiac cycle (Fatemifar *et al*., 2019). Therefore, the morphology and arrangement of the trabeculae carneae, along with the intertrabecular spaces, play a key role in normal cardiac function, and their significant variability between individuals can influence the diagnosis and management of various cardiovascular pathologies (Meyer *et al*., 2020).

Genetic, environmental, and pathological factors may influence the variability of the trabeculae carneae among individuals, making it difficult to identify relevant diagnostic patterns, such as indicators of heart disease. This is particularly true in non-compaction cardiomyopathy, a condition characterized by an altered ventricular wall with prominent trabeculae and deep intertrabecular recesses, where imaging modalities such as echocardiography and magnetic resonance imaging serve as primary tools for assessing trabeculae characteristics. However, these diagnoses are highly observer-dependent, which can lead to inconsistencies in interpretation (Gati *et al*., 2013; Captur *et al*., 2014). Therefore, non-compaction cardiomyopathy, also known as trabeculae disease, remains a clinical

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challenge due to the lack of widely accepted diagnostic criteria and limitations in determining how many trabeculations can be considered excessive (Stöllberger *et al*., 2015; Riekerk *et al*., 2022). Diagnostic difficulty highlights the need for detailed morphometric studies since morphometry, together with imaging tools such as computed tomography, magnetic resonance imaging, or more accessible resources such as ultrasound, contribute to more precise diagnoses and effective surgical planning (Duque-Colorado *et al*., 2024).

A lack of understanding of the anatomical variations of the trabeculae carneae and how these affect cardiac function represents a knowledge gap. Thus, in the present study, a systematic review is carried out in order to identify and analyze the variations in the trabeculae carneae, evaluating how they are associated with heart diseases.

MATERIAL AND METHOD

Study protocol. This systematic review was conducted according to the guidelines of the Cochrane Collaboration Handbook (Higgins *et al*., 2019) and reported following the PRISMA statement recommendations (Page *et al*., 2021) for systematic reviews and meta-analyses. The research design was structured based on the PICO strategy, which clearly defines the key elements of the study: the Population of Interest, the Intervention analyzed, the Comparison established, and the Outcomes.

Review question. In patients with cardiac disease (P), what variations in the trabeculae carneae (I) have researchers reported, and how are these variations associated with such diseases, including a possible differentiation by sex (O), ¿compared to the general population (C)?

Inclusion criteria.

- Observational studies in humans with no limit on publication dates
- Studies published in all languages.
- Studies investigating the morphology or morphometric characteristics of the trabeculae carneae.
- Studies investigating the association between trabeculae carneae and heart disease.

Exclusion criteria

- Systematic reviews, narrative reviews, letters to the editor, or other documents that did not provide primary information.
- Studies in preprint or editorial form.
- Studies that are not available in an accessible format.
- Studies investigating diseases or conditions other than cardiac diseases.
- Studies that do not include data on the relationship between variables.
- Studies that include pregnant patients.

Databases and Search Strategy. The researchers conducted the research using the Web of Science, PubMed, Scopus, and BVS databases. No language or publication year filters were applied. Three researchers independently designed and executed the search strategy in October and November 2024. The following keywords were employed: trabeculation, trabeculae, trabeculated, trabecular, cardiomyopathy, heart failure, myocardial dysfunction, fractal analysis, descriptive, analytical, observational, cohort, case-control, and cross-sectional. Boolean operators such as AND and OR were used to combine search terms. Appendix 1 details the search strategy in each database.

Selection and data extraction. Three researchers independently identified eligible studies. In the first stage, they reviewed the articles' titles and abstracts, followed by a detailed analysis of the full texts. The researchers discussed any study of questionable relevance and decided on its inclusion through consensus. A first reviewer extracted information from the primary studies, considering the authors, population, study design, objective, parameter analyzed, methods used, and main outcomes. Subsequently, a second reviewer verified the integrity and accuracy of the recorded information.

Assessment of methodological quality of studies. The researchers assessed the methodological quality of the studies included in the systematic review using the Newcastle-Ottawa Scale (Wells *et al*., 2000) for cohort and case-control studies. This scale focuses on three key areas: 1) selection or representativeness of the study groups and the clarity of their definitions; 2) comparability or control of confounding factors between groups; and 3) outcome or follow-up, which involves evaluating outcomes/exposure and ensuring adequate follow-up. Each aspect is given a score, with a maximum of 9 indicating a lower risk of bias. The researchers assessed cross-sectional studies using the STROBE scale (von Elm *et al*., 2008), a tool comprising a 22-item checklist. The implementation of this scale allowed a systematic assessment of the methodological quality of the studies analyzed, enhancing the robustness of the review's conclusions. To assess the level of agreement between reviewers in the study selection process, we used Cohen's kappa index (Cohen, 1960) for both the title and abstract selection phase and the full-text evaluation.

Ethical Considerations. No interventions were carried out throughout this study. Therefore, this research presents a minimal risk, per the Declaration of Helsinki (World Medical Association, 2013).

RESULTS

Study Selection. The search and selection process for articles is summarized in Figure 1. A total of 314 articles were found in the databases, of which 30 documents were duplicates. After an initial screening by title and abstract, we discarded 233 articles because they did not pertain to the review topic. After reviewing 51 full-text articles, we excluded 43 documents for not being observational studies or for including pregnant females in the population.

Cohen's kappa index of 0.92 was obtained for records excluded based on the title and abstract, indicating a high agreement between reviewers. Similarly, a kappa index of 0.82 for reports excluded after full-text assessment indicated substantial agreement, although slightly lower than in the first stage, as expected due to the complexity and subjectivity of decisions at this stage.

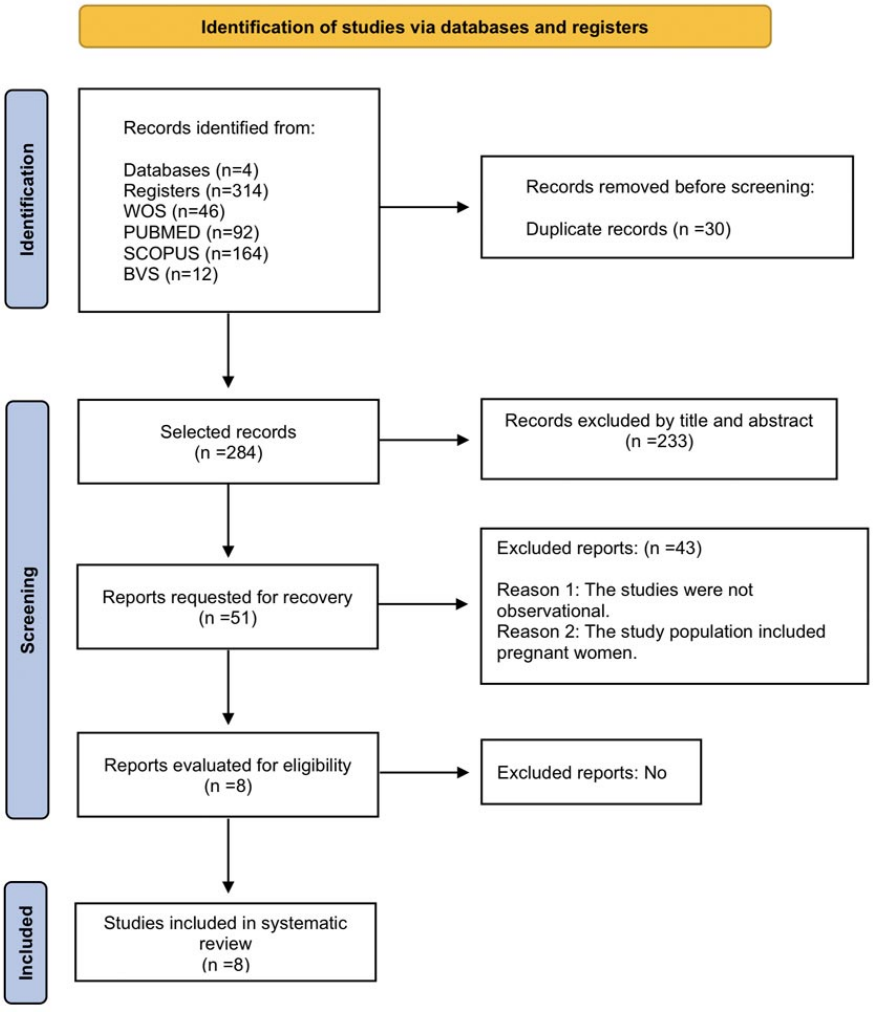

Fig. 1. Systematic search flow diagram.

Findings of the study. Table I presents the characteristics of the articles selected for this systematic review. Although all studies used imaging tools to visualize the trabeculae carneae, none provided a morphometric description of the trabeculae carneae in healthy populations or those with cardiovascular pathologies.

Assessment of methodological quality. The assessment of all studies using the Newcastle-Ottawa scale indicated high quality. Table II includes the evaluation of cohort studies, while Table III details the rating of case-control studies. The cross-sectional studies obtained a score higher than 85% (n = 19 items), highlighting their adequate methodological quality.

DISCUSSION

Trabeculae carneae plays a significant role in cardiac structure. Their distribution pattern could represent a risk factor in the development of cardiac pathologies, as determined by Xie *et al*. (2024) in 403 participants of Chinese origin, showing that the maximum apical fractal dimension of the left ventricle is an independent predictor of adverse events in patients with dilated cardiomyopathy, suggesting that greater complexity in trabeculation is associated with pathological remodeling of the myocardium. This finding is consistent with that observed by Jiang *et al*. (2023), who reported that fractal dimension is associated with outcomes in hypertrophic cardiomyopathy. Similarly, Sigvardsen *et al*. (2020) found that a higher trabeculated mass was associated with a higher risk of heart failure and sudden cardiac death, suggesting that hypertrabeculation could represent a pathological phenotype within the spectrum of ventricular remodeling. Results reinforce the hypothesis that increased trabeculation is not a simple morphological trait but could reflect structural alterations that compromise cardiac function. In this sense, trabecular organization may serve as a clinically relevant marker for risk stratification in these patients.

Table I. Characteristics of included studies.

Authors	Population	Study design	Objective	Parameter analyzed	Methods Used	Main outcomes
Grebur *et al*. (2024)	Hungarians	Cross-sectional	Analyze cardiac rotation parameters in subjects with LV noncompaction morphology and preserved ejection fraction, comparing genotypes and healthy controls.	Mass of ventricular trabeculae	MRI and ultrasound	In comparison with controls, LVNC subjects had reduced apical rotational degree and one-third had negative apical rotation.
Xi *et al*. (2024)	Chinese	Cohort	Evaluate the prognostic value of LV myocardial trabecular complexity using fractal analysis in patients with DCM.	Mass of ventricular trabeculae	MRI and fractal analysis	LV maximal apical FD was an independent predictor of the adverse clinical outcomes in patients with DCM.
Laissy & Ben-Driss (2024)	French	Case-control	Evaluate whether measurement of LV volume, mass, and ejection fraction, with and without including trabeculations on cine MRI, can help diagnose LVNC versus normal individuals with excess trabeculations.	Volume and mass of ventricular trabeculae	cineMR	When excluding the trabeculations, LV ejection fraction was within normal ranges both in patients and controls, while it increased by 9.8 % in LVNC and decreased by 10.9 % in controls when trabeculae were included.
Jiang *et al*. (2023)	Chinese	Cross-sectional	Investigate the prognostic value of biventricular FD in patients with HCM.	Volume and mass of ventricular trabeculae	MRI and fractal analysis	LV maximal apical FD and RV global FD were independent predictors of sudden cardiac death events and rehospitalization due to heart failure in patients with HCM.
Sigvardsen *et al*. (2020)	Danes	Cohort	Determine whether increased LV trabeculation is associated with an increased rate of major adverse cardiovascular events in individuals from the general population.	Mass of ventricular trabeculae	Computed Tomography	Increased LV trabeculation is independently associated with an increased rate of major adverse cardiovascular events in the general population.
Mazurkiewicz *et al*. (2017)	Poles	Cross-sectional	Evaluate the impact of trabeculations on outcomes in patients with DCM.	Mass of ventricular trabeculae	MRI and ultrasound	DCM patients had more trabeculation than controls.
Captur *et al*. (2015)	Diverse	Cross-sectional	To quantitatively determine the population variation and relationship of LV trabeculation to LV function, structure, and clinical variables.	Volume and mass of ventricular trabeculae	MRI and fractal analysis	Positive association between trabeculation and male. Furthermore, trabeculation was influenced by ethnicity and/or racial background, Hispanic > African >Caucasian > Chinese.
Kawel *et al*. (2012)	Diverse	Cross-sectional	Determine the normal range of the trabeculated to compact myocardium ratio in a large population-based study and to examine the relationship to demographic and clinical parameters.	Trabeculations thickness	cineMR	Thicker maximum trabeculation was significantly associated with Chinese and black ethnicities. Trabeculated to compact myocardium ratio was a robust and reproducible measure that is independent of age, sex, ethnicity, height, and weight in participants without cardiac disease or hypertension.

LV: left ventricular; LVNC: left ventricular noncompaction; DCM: dilated cardiomyopathy; MRI: magnetic resonance imaging; FD: fractal dimensión; HCM: hypertrophic cardiomyopathy

Table II. Quality analysis of cohort studies: Newcastle-Ottawa scale.

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of Interest was not present at start of study	Comparability of cohorts based on the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Punctuation
Xie *et al.* (2024)	*		*	**	*	*	*	*	8
Sigvardsen *et al.* (2020)	*		*	**		*		*	6

Table III. Quality analysis of case-control studies: Newcastle-Ottawa scale.

Study	Is the case definition adequate?	Representativeness of the cases	Selection of Controls	Definition of Controls	Comparability of cases and controls on the basis of the design or analysis	Ascertainment of exposure	Same method of ascertainment for case s and controls	Non-Response rate	Punctuation
Laissy *et al.* (2024)	*		*	*	**	*	*	*	8

On the other hand, studies have identified that including or excluding the trabeculae carneae in the measurement of the left ventricular ejection fraction introduces variability in the results (Laissy *et al*., 2024), posing a challenge in clinical diagnosis. In left ventricular noncompaction cardiomyopathy, excluding the trabeculae carneae may result in an underestimation of compacted myocardial mass, leading to false negatives (Yang *et al*., 2022), which would cause an overestimation of left ventricular ejection fraction, potentially delaying treatment in patients with underlying ventricular dysfunction. Along the same lines, Grebur *et al*. (2024) evaluated the relationship between left ventricular noncompaction cardiomyopathy and cardiac rotation parameters in 108 Hungarian individuals, finding that the reduction in apical rotation in these patients suggests that the trabecular alteration affects ventricular mechanics. These events underscore the necessity of assessing the functionality of the trabeculae carneae beyond their mere presence or absence. These reviewed studies established associations between increased trabecular mass and cardiac diseases such as dilated cardiomyopathy, ventricular hypertrophy, and heart failure, although they did not determine causality.

Despite the above, not all studies support a clear pathological relationship. Kawel *et al*. (2012) noted that a significant percentage of healthy subjects have an elevated compact/non-compact myocardium ratio. Furthermore, Mazurkiewicz *et al*. (2017) evaluated 276 Polish individuals using MRI and ultrasound, finding that trabeculation was not a predictor of adverse events in dilated cardiomyopathy, in contrast to left ventricular end-diastolic volume. Therefore, clinicians should assess left ventricular noncompaction cardiomyopathy by considering multiple functional parameters rather than focusing exclusively on trabeculation. There is probably a relationship between trabeculation and heart disease, but further studies are needed to confirm this. Furthermore, it is essential to explore screening methods beyond the ejection fraction to obtain a more accurate assessment of its impact on cardiovascular function.

In this context, studies have established that variability in trabeculation depends on genetic and metabolic factors. Consequently, increased trabeculation may represent an adaptive response in specific populations rather than an indicator of disease (Grebur *et al*., 2024). Although this systematic review included studies with different geographical distributions, covering Chinese, American, Polish, and Hungarian populations, among others, we consider it essential to develop future research that analyzes the morphometric characteristics of the trabeculae carneae in more populations since it will allow establishing more precise criteria to differentiate between normal anatomical variations in different groups and pathological patterns of trabeculation.

This study showed a lack of anatomical investigations that include detailed dissections on the morphometry of the trabeculae carneae, particularly in individuals with cardiac diseases. The

reviewed studies lacked precise morphometric measurements and sex-based analyses, limiting a comprehensive understanding of the role of trabecular variations in cardiac pathologies. Another limitation identified is the lack of unified criteria to define the amount and characteristics of ventricular trabeculation. Developing precise anatomical criteria could greatly influence clinical practice by establishing normal ranges for ventricular trabeculation and enhancing the diagnostic assessment of cardiac diseases.

In conclusion, additional studies are necessary to clarify the role of trabeculae carneae in myocardial pathophysiology. It is essential to define ventricular trabeculation accurately through dissection studies, which, together with imaging tools, could adequately characterize the trabeculae carneae. This approach would enable the establishment of quantitative and qualitative parameters, including the diameter and density of the fleshy trabeculae and the proportion of compact versus noncompact tissue in the left ventricle across sexes, with and without pathologies. This detailed anatomical information could provide a reliable basis for establishing normal ranges of trabeculation.

Notably, all studies have been performed mainly in the last decade, suggesting that ventricular trabeculation analysis is an emerging area of ??study, possibly driven by advances in imaging techniques.

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DÍAZ-VALLEJO, J. A.; DUQUE-PARRA, J. E.; GONZALEZ-CORREA, C. H. & DUQUE-COLORADO, J. Asociación entre trabeculación ventricular y enfermedades cardiovasculares: Revisión sistemática. *Int. J. Morphol., 43(3)*:1090-1096, 2025.

RESUMEN: Se llevó a cabo una revisión sistematica siguiendo las directrices del Cochrane Collaboration Handbook. Las bases de datos revisadas fueron Web of Science, PubMed, Scopus y BVS. Se incluyeron estudios observacionales en humano que investigaron la morfología o características morfométricas de las trabéculas carnosas. Se encontraron un total de 314 artículos, de los cuales se seleccionaron ocho. Los estudios seleccionados dieron uso a herramientas de imagen que permitieran visualizar las trabéculas carnosas, sin embargo, ninguno de ellos brindo una descripción morfométrica de las trabéculas carnosas en población sana o con patologías cardiovasculares. Aunque algunos estudios sugieren que las trabéculas carnosas desempeñan un papel significativo en la estructura cardíaca y que su patrón de distribución podría constituir un factor de riesgo en el desarrollo de patologías cardíacas, otras investigaciones no encontraron evidencia de una relación patológica clara. Resulta fundamental definir con precisión la trabeculación ventricular a través de estudios de disección, que de la mano de herramientas imagenológicas podrían ser suficientes para establecer parámetros cuantitativos y cualitativos que permitan identificar su rol en la fisiopatología miocárdica.

PALABRAS CLAVE: Corazón; Trabécula carnosa; Miocardiopatías; Diagnóstico por imágenes.

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