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Figure 3 of the article: Using Three-Dimensional Printing in Surgical Mitral Valve Repairs

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Editor-in-Chief's Acknowledgments

Daniela do Carmo Rassi Frota
Editor in chief (2022-2023)

Dear colleagues,

We have reached the end of the 2022-2023 administration with great joy and fulfillment regarding our journal, ABC Imagem Cardiovascular. Over the past two years, there has been a significant effort by the directors of the Cardiovascular Imaging Department (DIC) to constantly grow our journal and make progress with indexations. This required everyone involved, including editors, reviewers, and especially authors who submitted incredible papers on all subjects, to demonstrate unwavering commitment to this cause.

Of note is the increase in the number of papers published yearly, allowing our journal to remain internationally relevant. Another notable development last year was the introduction of Clarivate's ScholarOne submission and review system. This tool played a key role in improving our submission processes and facilitating the integration between journals of the Brazilian Society of Cardiology's ABC family.

As for indexations, we managed to join the Directory of Open Access Journals (DOAJ) in August 2022. The journal was then submitted to SciELO Brazil in September 2023, and we are currently still under their analysis process. Nonetheless, all this progress is a reflection of prior administrations, as well as the current one, all of whom paid special attention to the scientific segment of our department and prioritized quality across all of our publications.

I would like to list the names of past editors-in-chief and the dates of their tenures, as they were essential to bringing our journal to its current standards:

– Fernando Santana Machado, April 1988 to April 1992
– Rogério Tasca, April 1992 to April 1994
– Vera Márcia Lopes Gimenez and José Carlos Ferreira da Silva Filho, May 1994 to April 1996
– Caio César Jorge Medeiros, May 1998 to April 2000
– Carlos Eduardo Suaide Silva, January 2001 to December 2002
– Cláudia Gianini Monaco, January 2003 to December 2004
– Valdir Ambrósio Moisés, January 2005 to December 2007
– Vera Márcia Lopes Gimenez, January 2008 to December 2009
– Marcelo Luiz Campos Vieira, January 2010 to December 2011
– Carlos Eduardo Suaide Silva, January 2012 to December 2013
– Ana Clara Tude Rodrigues, January 2014 to December 2015
– José Maria Del Castillo, January 2016 to December 2017
– Viviane Tiemi Hotta, January 2018 to December 2019
– Silvio Henrique Barberato, January 2020 to December 2021

I would like to offer special thanks to André Almeida, president of the Department of Cardiovascular Imaging, who prioritized our journal throughout his entire tenure and contributed to its growth and advancement. I would also like to thank Silvio Henrique Barberato, chief officer of the current administration, for his support during the initial transition and during the challenges we faced down this journey. I wish him success during the next tenure as president of the DIC.

Important people like Marcelo Vieira and Ana Cristina Camarozano were indispensable during our efforts to make our journal go global, actively contributing to international invitations. Finally, I would like to thank the team of associate editors with whom I had the honor and joy of working. They are highly skilled people who dedicated themselves immensely to our journal and DIC. Without them, none of this would have been possible. I would also like to thank Simone Nascimento dos Santos, Viviane Tiemi Hotta, Leonardo Sara da Silva, Karen Saori Shiraishi Sawamura, Marco Stephan Lofrano Alves, Tiago Senra Garcia dos Santos, Rafael Willian Lopes, Alexandre Costa Souza, Laura Mercer-Rosa, Rhanderson Miller Nascimento Cardoso, and Cristiane Singulane.

Thank you for this opportunity and all your support over these last two years, during which I had the chance to meet and work with wonderful and skilled people, not to mention all the friendships we have forged over this time. I wish the next editor-in-chief Marcelo Dantas Tavares all the best, and I hope they accomplish all of their goals.

Thank you very much,

Daniela do Carmo Rassi Frota

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Our Acknowledgment to DIC's Members and Partners

The experience as president of the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology (DIC/SBC) for the 2022/23 administration was enriching. I am immensely thankful and have no complaints.

I had the opportunity to meet amazing people, visit spectacular places, participate in brilliant discussions, and so much more...

Our initial goal in this administration was to create expansiveness and breathe life into our Department. And I believe we've achieved that. Today, DIC is made up of brilliant, experienced people, as well as many young adults filled with energy and vigor. And they're spread all across the country.

These are young men and women who made significant contributions in these past two years, setting DIC towards a promising future.

There are plenty of people to thank. We're talking about professionals like Dr. Andrea Vilela, who brilliantly coordinated our Qualification Commission, which I believe is the most important at DIC. She had plenty of support from incredibly talented young men and women, as well as other experienced colleagues who did an amazing job.

And we can't forget about Dr. Daniela Rassi, another rising star who, together with her excellent co-editors, is helping our magazine grow in leaps and bounds towards a new level within the world's medical literature.

We built an executive commission made up of myself and three colleagues: VP of adult echocardiography Dr. Alex Felix, CFO Dr. Mohamed Saleh, and administrative officer Dr. Sílvio Barberato. Together with our incredible colleague Margareth Lima, secretary/manager at DIC, we met every Wednesday over these past two years, from 8 p.m. to 10 p.m., in addition to other meetings outside our regular schedule. Although we operate under a presidential regime, in which the president's orders are final, we managed to create a coalition parliament to help us find the best pathways for DIC through joint decision-making. Dr. Alex Felix is a brilliant professional whose work skills and altruism are second to none. Dr. Mohamed Saleh's financial management skills are a sight to behold, not to mention he's a reliable friend who's always ready to help. Dr. Sílvio Barberato's enviable sense of balance was a huge help, and he's ready to be an excellent president of our Department throughout his 2024/25 tenure.

We wouldn't be able to achieve so much without the outstanding support from other brilliant doctors, like our colleagues Marcelo Vieira, Fábio Villaça, Marcelo Tavares, Edgar Lira, Simone Brandão, Adriana Mello, José Aldo Teodoro, Ana Camarozano, José Roberto Souza (a.k.a. Beto), Wagner Pires, Marcelo Miglioranza, Márcio Bittencourt, Otávio Rizzi Filho, Marcos Lofrano, and so many more... Not to mention those I consider my advisors: our friends Samira Saady Morhy, José Luiz Barros Pena, Fábio Villaça, and Marcelo Vieira, to whom I reached out for help in the most difficult times of this administration.

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We held two unforgettable congresses: in 2022, in São Paulo, under the presidency of the vibrant Marly Uellendahl, with Márcio Lima as president of the scientific commission, and the DIC/2023 congress in Brasília, with the help of our dear friend Adenalva Beck and Dr. Marias Estefânia Otto, president of the scientific commission. Thank you for these incredible, unforgettable events.

DIC has produced plenty of projects in these past two years. This includes countless webinars, symposiums, podcasts, miscellaneous projects (most notably the *Memórias do DIC* project), investments in quality to improve safety in the creation and application of the qualification exam, maintaining the Clinical Key (which has a high financial cost for DIC, but still provides great benefits for our members), DIC's new physical headquarters (to be inaugurated on Dec. 9th, 2023), a number of publications (articles, books, documents...), but, above all, we produced a genuine union between the people who contributed to this process.

It's worth noting the highly positive contributions of our legal department under the coordination of Dr. Breno Garcia, a competent lawyer who provided us with legal security during our most tense and delicate moments.

I believe that thanks to this fantastic group of people, we left DIC/SBC in an even better position than we found it. Could we have done more? That's certainly possible. But believe me, we did the best we could do, thinking primarily of DIC's growth and the well-being of our members.

There is still plenty to do... One of the most important projects in DIC's near future will be the greater participation of our members inside SBC's board of directors. This will be possible by electing a significant number of our representatives to be delegated associates at SBC in the upcoming elections. Another major strategy will be improving DIC's engagement in correlated associations, such as AMB and CFM.

I have no doubt that our next president, Dr. Sílvio Barberato, together with his directors, will continue to forge a path to maintain DIC as one of the best, if not the best, and most productive departments of the Brazilian Society of Cardiology.

I thank God and all our partners and members at DIC, who were always with us throughout this journey and helped us create a project that benefitted everyone involved.

Merry Christmas, and may God bless us with health and peace in 2024.

Kind regards,

André Almeida

President of DIC (2022/23 administration)

Editorial

Women Representation in Scientific Publications

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In 2015, the United Nations General Assembly named February 11 the International Day of Women and Girls in Science. This date has been celebrated since 2016, with the aims of raising awareness of women's excellence in science and reminding the international community that science and gender equality must advance hand in hand.[1]

Data from the United Nations and UNESCO indicate that women represent less than 30% of researchers worldwide and demonstrate how barriers and underrepresentation of women and girls still persist, especially in areas such as science, technology, engineering, and mathematics.[1]

To this day, the overload of domestic work and family care leaves women at a disadvantage in academia, generating disparities not only in the development of studies and the publication of articles, but also in representation among researchers, which is crucial for a more comprehensive discussion and for the diversity of the topics chosen for study. Cultural, social, and economic factors and beliefs can limit the educational opportunities available to women, further discouraging their participation in scientific research.

Notwithstanding some actions, gender inequality is still predominant in science. Although men and women hold approximately the same number of bachelor's and master's degrees, at the highest academic ranks, the balance is tipped in favor of male scientists. In the European Union and the United States, only 20% and 21% of full professors are women, respectively. This number is even lower for natural science professors.[2]

Regarding representativeness in clinical trials, a study conducted by Denby et al. demonstrated that women constituted only 10.1% of clinical trial leadership committees. This number was substantially lower than the already low proportion of women doctors or researchers in the cardiovascular therapeutic area. In 55.5% of leadership committees, there was no female representation, and publications of cardiovascular clinical trials had women in only 9.3% of the first or 10.0% of the last author position.[3]

Keywords

Women; Scientific and Technical Activities; Scientific Communication and Diffusion.

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Prior studies suggest that gender diversity in research teams can produce higher quality research. Greater visibility of women in clinical trial leadership roles could increase recruitment of female participants and attract more women investigators to cardiovascular clinical research. A vicious cycle has been observed for women in academic medicine, with the exclusion of women leading to further exclusion, lack of recognition, and slow rates of promotion.[3]

When bringing this analysis and discussion to the Cardiovascular Imaging Department of the Brazilian Society of Cardiology, we observed a different scenario from the one reported regarding the number of women as first or last authors of articles published between 2017 and 2022 in *ABC Cardiovascular Imaging*. Women were the majority during this period, with the exception of 2018 (Figure 1).

In relation to the position of women as editor-in-chief, a study conducted by Pinho Gomes et al. examined the representation of women and men. The analysis included 41 medical categories and used data from the 2019 Clarivate Analytics Web of Science Journal Citation Reports. The results indicated a significant underrepresentation of women, corresponding to only 1 in 5 editors-in-chief of the leading medical journals. Some categories had no female editors-in-chief (dentistry, oral surgery, and medicine; allergy; psychiatry; anesthesiology; and ophthalmology), while others had a greater presence of women as editors-in-chief (primary health care, microbiology, and genetics and heredity). In 27 of the 41 categories, women represented less than a third of editors-in-chief, for example, 1 in 10 for critical care medicine, 2 in 10 for gastroenterology and hepatology, and 3 in 10 for endocrinology and metabolism.[4]

The journal *ABC Cardiovascular Imaging* has had 17 editors since 1988, and 5 of them were women (Figure 2): Vera Marcia Lopes Gimenes (1994 to 1996; 2008 to 2009), Cláudia Gianini Monaco (2003 to 2004), Ana Clara Tude Rodrigues (2014 to 2015), Viviane Tiemi Hotta (2018 to 2019), and Daniela do Carmo Rassi Frota (2022 to 2023). Women currently represent 45% of the journal's associate editor positions.

Increasing representation of women on editorial boards, especially in editor-in-chief positions, is crucial to combating the inequalities present in academic publishing and academia in general. The underrepresentation of women in these positions is the result of several factors. First, women tend to decline invitations to editorial positions due to the expectation that these positions could interfere with family and/or professional commitments. This is related to the unequal distribution of responsibilities, where women often have more unpaid obligations and bear greater burdens or even the sole responsibility for

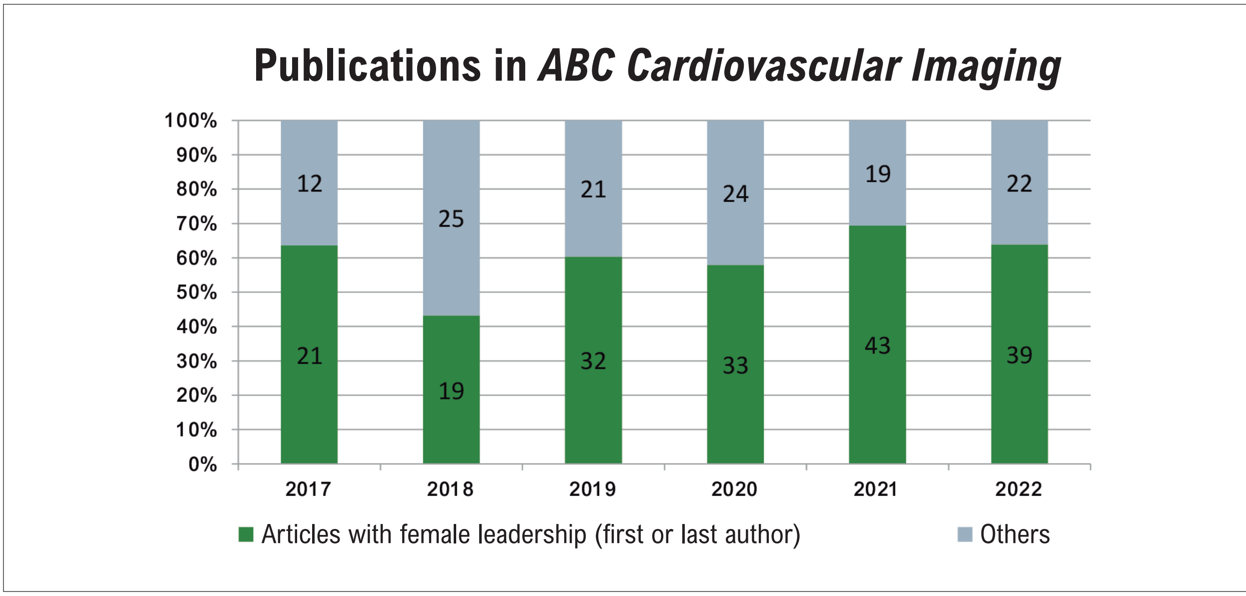

Figure 1 – *Number of articles published in ABC Cardiovascular Imaging with women as first and/or last authors, from 2017 to 2022.*

Figure 2 – *2023 Congress of the Cardiovascular Imaging Department with the editors-in-chief of ABC Cardiovascular Imaging*

mental work in domestic and family care. This uneven load can limit the time available for research and leadership. Furthermore, career interruptions, such as maternity leave, and gender bias contribute to hindering women's professional progression.[4]

Unconscious gender bias also devalues women's academic performance and perpetuates stereotypes that exclude women from leadership positions, including editor-in-chief. The lack of mentoring and appropriate female role models also negatively impacts women's advancement in academic careers. It is essential to increase the presence of women on editorial boards, especially as editors-in-chief, in order to address these deeply rooted inequalities. The presence of a female editor-in-chief is linked to greater representation of women on editorial and advisory boards, as well as in peer review. Given that editors-in-chief are often chosen from editorial boards, addressing the underrepresentation of women on these boards is a priority for achieving gender parity in leadership positions.

To achieve gender equality, it is necessary to act early, showing young girls how important it is to have a profession and providing good examples of scientifically successful women. The lack of female mentors and role models in cardiology has been repeatedly cited as a potential deterrent to the recruitment and retention of women in the field. The phrase "You cannot be what you cannot see" has often been cited in the context of academic cardiology.

Thus, despite the increasing representation of women in science and academic activities, as well as the greater awareness of gender inequality in these contexts, it is essential to promote public policies that encourage women in leadership positions, in addition to a sociocultural change that values the achievements and merit of women, respecting their role at the heart of the household.

Finally, it is also important to highlight the value of sisterhood among women and rich and of prolific partnerships that further enhance women's roles in the world of science so that, in the near future, more girls and women will achieve gender equality in all settings.

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Editorial

Assessment of Myocardial Fibrosis by Myocardial Deformation Analysis via Echocardiography

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Abstract

Myocardial fibrosis (MF) is a pathological condition common to several primary and secondary heart diseases. Diffuse MF is a common feature in nearly all heart diseases, playing a crucial role in the progression of heart failure (HF). Several studies have indicated that the existence of MF serves as a prognostic factor for adverse outcomes across a range of heart conditions, underscoring the significance of this factor in clinical settings. Consequently, diagnostic approaches for MF, whether in subclinical phases or within established heart diseases, emerge as valuable instruments for early detection, risk stratification, and/or ongoing monitoring of disease developments. Despite being the most accurate non-invasive test for MF research, cardiovascular magnetic resonance (CMR) imaging is a test that is not widely available and is expensive. An alternative method with increased accessibility and cost-effectiveness for assessing heart diseases and researching MF involves echocardiography with the Speckle Tracking (STE) technique to evaluate myocardial deformation ("strain"). Studies show that diminished strain values (both global and segmental) in various heart conditions are associated with the presence and extent of MF, as determined by CMR or histological analysis. MF research using echocardiographic myocardial deformation analysis with STE has gained more space in clinical and research routines as it is an easy-to-perform and low-cost test. The results found by this technique can have a relevant diagnostic, therapeutic, and prognostic impact on clinical practice.

MF is a pathological condition common to several chronic heart diseases, whether primary ones or secondary to systemic diseases with cardiac involvement. Diffuse MF is a common feature in nearly all heart diseases, playing a crucial role in the progression of HF.[1] MF is commonly found after an ischemic insult, but other causes, such as pathologies leading to volume or pressure overload, diabetes mellitus, hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy, non-compacted myocardium, arrhythmogenic right ventricular dysplasia, and systemic diseases such as sarcoidosis, can also contribute to MF.[2] Several studies have demonstrated that MF serves as a prognostic factor for adverse outcomes across a range of heart conditions and HF, underscoring the significance of this factor in clinical settings.[1-3]

Keywords

Endomyocardial Fibrosis; Global Longitudinal Strain; Echocardiography; Cardiomyopathies.

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MF occurs from the deposition of extracellular matrix (ECM) in the myocardial tissue, leading to excess collagen in relation to cardiomyocytes.[2] Following an aggressive event, the activation of inflammatory cells and cytokines triggers the proliferation of cardiac fibroblasts, which is a pivotal process in enhancing the production of collagen and other ECM proteins. The disproportionate ECM increase prompts an adaptive response within the myocardium, progressively distorting the architecture of muscle fibers, affecting the physiology of cardiomyocytes, and ultimately resulting in the gradual dysfunction of the heart muscle, characterized by the loss of compliance and/or myocardial contractility.[1,3-4] The MF process is the final stage of cardiomyopathies, resulting in irreversible damage to myocardium structure and to cellular and electrical functions, with consequent remodeling of the cavities. The degree of MF is related to the severity of ventricular dysfunction.[5]

The diagnosis of MF is increasingly important in the context of cardiomyopathies, as it reflects the pathological structural evolution related to HF in heart diseases and corroborates the need to integrate its diagnosis into the clinical management of patients.[3] Consequently, diagnostic approaches for MF, whether in subclinical phases or within established heart diseases, emerge as valuable instruments for early detection, risk stratification, and/or ongoing monitoring of disease developments.

The gold standard for diagnosing MF is endomyocardial biopsy.[3] Nevertheless, due to its invasive nature and the potential for complications, the use of this test is limited to situations where there is recent-onset HF with unsatisfactory evolution, evolving with progressive hemodynamic instability and/or ventricular arrhythmias or second-degree atrioventricular blocks Mobitz II or third degree that do not respond adequately to conventional measures.[4] Therefore, alternative non-invasive MF diagnostic methods are necessary for daily clinical practice.[3]

Non-invasive diagnostic techniques for MF include CMR with gadolinium for late enhancement investigation, heart tomography with iodinated contrast, PET CT, cardiac SPECT, and echocardiography with the assessment of myocardial deformation using the STE technique.[2,4]

Among non-invasive MF diagnosis methods, CMR is considered the most accurate as it better characterizes the myocardial tissue.[4] By using gadolinium-based contrast and late enhancement investigation, it is possible to define areas of focal scar/fibrosis in the different segments of the heart. Still through T1 sequence mapping, the method can detect signs of increased extracellular volume compatible with diffuse fibrosis of the myocardium.[2,3] However, due to its lower availability in peripheral centers and high cost, it has been limited to selected cases.

Echocardiography presents itself as a cost-effective and widely available alternative for assessing heart diseases. The integration of two-dimensional echocardiography with the evaluation of myocardial deformation using STE has become increasingly significant in clinical applications as both a diagnostic and prognostic tool across various heart diseases.[6]

STE uses dedicated software to identify Speckles in the two-dimensional image of the heart muscle. Speckles are a group of points in the two-dimensional image that occur due to the interaction of ultrasound waves with the myocardial tissue. These grouped points are selected by the software and monitored during the myocardial contraction and relaxation process. Through displacement and speed, it is possible to estimate the strain values and strain rate of the myocardial segments. Myocardial deformation analysis can be performed in the longitudinal, circumferential, and radial axes.[6-8]

STE has become a valuable tool for both the diagnosis and management of various myocardial diseases, including primary or systemic conditions, valvular heart disease, ischemic heart disease, HF, myocardial dyssynchrony, and those associated with diabetes mellitus and arterial hypertension. Additionally, STE is instrumental in diagnosing and monitoring cardiotoxicity resulting from chemotherapy, which is a prevalent application of this technique.[6]

Several studies have demonstrated that reduced strain values (both global and segmental) in different heart conditions are related to the presence and degree of MF, as determined by CMR or histological analysis. The assessment of myocardial deformation through STE allows for a comprehensive understanding of how the underlying disease impacts myocardial function.[9]

In HCM, studies demonstrate that the reduced global and regional strain value is related to the detection of MF on CMR. Popovic et al.[10] demonstrated that individuals with HCM and fibrosis detected on CMR exhibit reduced longitudinal strain values. Their findings also revealed that fibrosis and end-diastolic thickness of the myocardial wall are predictors of lower values of segmental longitudinal strain. Kobayashi et al.[11] compared the strain rate values of the septal segment of patients with HCM undergoing myomectomy due to dynamic obstruction of the left ventricular outflow tract with histopathological analysis and identified that lower strain rate values were correlated with the magnitude of myocyte hypertrophy, degree of fibrosis, dysplasia of intramural coronary arterioles, and disarray of myocardial fibers.

Gjesdal et al.[12] compared the post-infarction scar tissue mass in chronic ischemic heart disease assessed by CMR with the values found in the analysis of myocardial deformation by STE. In this study, reduced global longitudinal strain (GLS) values showed a significant inverse correlation with the amount of scar tissue detected on CMR. The GLS was even superior to the measurement of left ventricular ejection fraction in identifying smaller infarcts.

Recently, Nagata et al.[13] published a study evaluating the association between abnormal myocardial mechanics related to mitral valve prolapse (MVP), the presence of MF, and the association with arrhythmias. The study revealed that individuals with MVP and MF predominantly located in the basal and middle segments of the inferolateral wall, as observed through CMR, exhibited reduced strain values in the inferoposterior basal segment. Moreover, these patients demonstrated an abnormal strain pattern in the lower lateral wall, characterized by two distinct peaks—pre- and post-systolic—which occurred less frequently in the group without MF. Notably, the presence of MF and the abnormal double-peak strain pattern assessed through STE showed an association with ventricular arrhythmia.

In a separate study by Slimani et al.,[14] investigating the relation between post-load, MF, and left ventricular strain in the pre- and postoperative phases of patients with aortic stenosis undergoing valve replacement, it was revealed that reduced values of GLS and global circumferential strain (GCS) were linked to higher values of end-systolic stress in the left ventricular wall. Histopathological analysis of MF indicated that individuals with increased end-systolic stress in the left ventricular wall bore a greater burden of MF, leading to a more adverse outcome after aortic valve replacement. Fabiani et al.[15] also demonstrated the association between reduced GLS and ventricular septum longitudinal strain values and the presence of MF in patients undergoing aortic valve replacement for aortic stenosis and myocardial biopsy.

In patients with HF undergoing heart transplantation, analysis of GLS by STE of the recipient's heart before the procedure showed a correlation with the degree of MF, as assessed by histopathological evaluation of the diseased heart, showing lower GLS values in hearts with MF greater than 50%. Analysis of the GCS and left ventricular torsion also showed a correlation with the presence of MF, but to a lesser extent.[16]

Kostakou et al.[17] and Leitman et al.,[18] when evaluating patients diagnosed with myocarditis, observed that these individuals had reduced GLS values despite preserved ejection fraction on conventional echocardiography, in addition to reduced myocardial deformation values in segments that showed fibrosis or edema on CMR.

Reduced strain values by STE of the left atrium and right ventricle are also associated with the histopathological finding of MF with prognostic impacts. In their review on MF detection using STE, Lisi et al.[5] highlight their study revealing a correlation between the GLS of the right ventricular free wall and the presence of MF, as observed in histological analyses. The review also discusses research indicating an association between reduced right ventricle GLS and a poorer prognosis in conditions such as pulmonary hypertension and left HF. Furthermore, this review mentions their group's work on left atrium analysis using STE, demonstrating a connection between reduced values of peak GLS (PGLS) in the left atrium and the presence of MF in patients with significant mitral insufficiency undergoing valve repair due to MVP. They also mention that reduced PGLS values in the left atrium were predictors of a worse prognosis (HF and mortality) in two years.

Although uncommon in the literature, some studies have also shown a correlation between reduced strain values using the STE technique and the presence of fibrosis on CMR in chagasic patients. Gomes et al.[19] demonstrated that, in patients with stage A chagasic heart disease (asymptomatic, with positive serology, without changes on the electrocardiogram and chest x-ray) with MF on CMR, the analysis of deformation using STE detected reduced global, longitudinal, circumferential, and radial strain values when compared with patients who did not have fibrosis. A recently published meta-analysis found that patients with indeterminate-form Chagas disease (CD) did not show different GLS values when compared to healthy controls. However, in the segmental analysis, CD patients presented reduced myocardial deformation values in the basal and middle segments of the lower septal wall.[20] STE application could perhaps be an additional tool for early diagnosis of myocardial changes not detected by conventional methods, possibly with clinical and prognostic implications.

The Cardiomyopathy Unit at Instituto do Coração/HC-MFUSP has initiated a study involving chagasic patients lacking ventricular dysfunction but exhibiting fibrosis or edema on CMR, who underwent a one-year treatment with colchicine. Before and after the treatment, all participants underwent transthoracic echocardiography with an analysis of myocardial deformation through STE. The results of this analysis hold the potential for STE to identify segments affected by fibrosis/edema as observed on CMR.

MF research using echocardiographic myocardial deformation analysis with STE has gained more space in clinical and research routines as it is an easy-to-perform and low-cost test. The results found by this technique can have a relevant diagnostic, therapeutic, and prognostic impact on clinical practice.

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Original Article

Use of Echocardiography as a Supplementary Tool in Teaching Cardiac Anatomy and Physiology to Medical Students

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Abstract

Background: Ultrasonography has been increasingly used in teaching basic medicine. The simultaneous observation of the echocardiographic image and the electrocardiogram allows students to understand the physiological process of the heart and its function within the cardiovascular system.

Objective: Evaluate the acquisition and retention of knowledge among medical students during the study of cardiac anatomy and physiology through the use of echocardiography.

Methods: Thirty-four (34) students in the third semester took a pre-test (assessment 1) consisting of 20 multiple-choice questions, 15 of which were related to cardiac anatomy and physiology and 5 were "confusion-inducing questions." The test was designed by one of the authors, blind to the others. After the theoretical meeting, assessment 2 was carried out with the same questions. The following week, a practical echocardiography meeting was held, aimed at evaluating anatomy and physiology. A post-test (assessment 3) was carried out 30 days after the first meeting to assess knowledge retention. The variables were analyzed by the Kolmogorov-Smirnov, Student's T, and Wilcoxon tests, with a statistical significance level of $p < 0.05$.

Results: The average number of correct answers in assessment 1 was 6.37 ± 2.0 (42.4%), 9.8 ± 2.2 (65.3%) in the second assessment, and 10.3 ± 2.5 (68.6%) in assessment 3. There was a statistical difference between assessment 1 and the other assessments ($p = 0.01$).

Conclusion: Early introduction of echocardiography in the medical curriculum proves beneficial for imparting knowledge in cardiac physiology and anatomy, reinforcing theoretical understanding.

Keywords: Echocardiography; Education, Medical; Students, Medical; Anatomy; Cardiovascular Physiological Phenomena.

Introduction

Medical education has changed drastically in recent decades. Technological advances have allowed ultrasound techniques to be increasingly used for teaching medicine, particularly for anatomy[1] and physiology[2] subjects. Studies have shown that students' perception of the use of ultrasound in teaching anatomy is positive[3,4] and it has already been demonstrated that the use of echocardiography was as effective as the dissection of cadavers in teaching cardiac anatomy.[5]

Echocardiography provides a visual representation of cardiac cycle events, facilitating the correlation between anatomical structures and their physiological functions. The simultaneous examination of the ultrasound image of the heart, the phonocardiogram, and the electrocardiogram enables students to grasp the physiological processes of the heart and its role within the cardiovascular system,[6] thereby enhancing diagnostic accuracy at the bedside.[7] Published articles indicate that instructing cardiac physiology through ultrasound methods aids students in learning and retaining knowledge about the events of the cardiac cycle.[4]

While computer programs exist to simulate cardiac cycle mechanisms,[8,9] echocardiography provides the added benefit of teaching an imaging method widely employed in diagnosing various cardiovascular pathologies, concurrently providing an understanding of physiological mechanisms and cardiac circulation.[4]

Since 2016, Indiana University in the United States has integrated echocardiography into its curriculum. It is introduced for students in the second-year pre-clinical cycle in order to assist in understanding the practice and teaching of cardiology.[10]

Similarly, our university incorporates echocardiography into the curriculum during the third semester, serving as a tool

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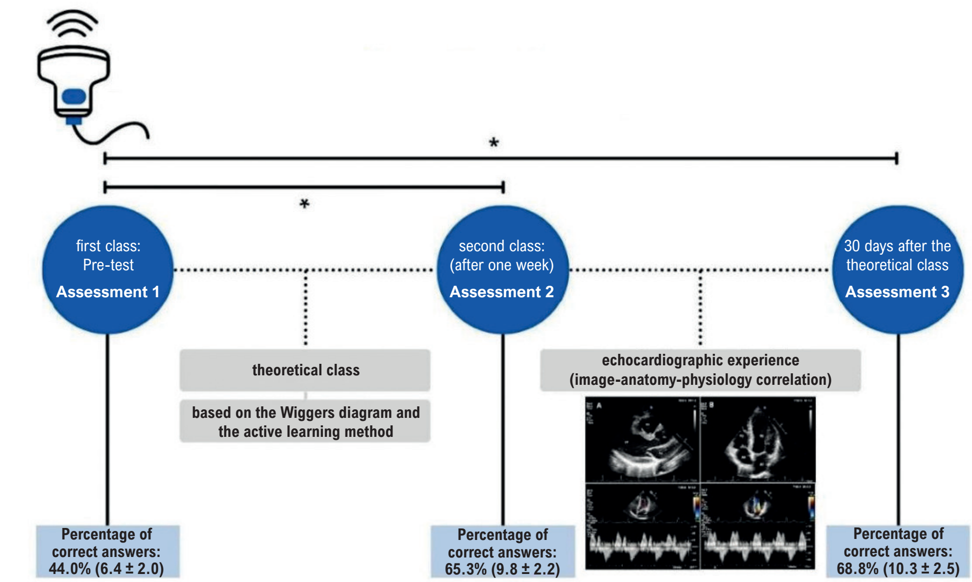
Central Illustration: Targeted use of Echocardiography as a supplementary tool in teaching cardiac anatomy and physiology to medical students



Key: *p < 0.05; % (mean ± SD)

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to facilitate the teaching of cardiac physiology and enhance understanding of cardiac anatomy and the phases of the cardiac cycle. This study aims to assess the actual knowledge gain resulting from the integration of current medical teaching methods (active methodologies and Problem-Based Learning – PBL) with echocardiography practice.

Materials and methods

Study design

Prospective, single-arm study, with 34 students in the third semester of the Medical school program at UNIDAVI - *Centro Universitário para o Desenvolvimento do Alto Vale do Itajaí*, in Rio do Sul, state of Santa Catarina, Brazil.

Students were asked to answer a pre-test (assessment 1), with a duration of 20 minutes, consisting of 20 multiple-choice questions, 15 of them related to anatomy and physiology, and 5 "confusion-inducing questions" (see next topic). The assessment was prepared by the coordinating professor of the phase, maintaining blindness to the practice of echocardiography.

Subsequently, the group was divided into three groups for theoretical discussions involving the Wiggers Diagram (Figure 1).[11] Each sub-class had twenty (20) minutes to research atrial, ventricular, and arterial pressure curves, as well as ventricular volume, electrocardiogram, and phonocardiogram. For three hours, students delved into the theoretical part and were questioned by the professors, aligning with the course's active methodology. Following the theoretical discussion, a new assessment (assessment 2) was conducted, comprising the same questions as the pre-test and allowing the same time for resolution.

After a one-week interval, the students proceeded to the echocardiography laboratory. The practical meeting spanned 60 minutes and was conducted on the Affinity 70@ (Philips@) device. Initially, the formation of an ultrasonic image and the visualization of cardiac chambers in the transthoracic echocardiogram (ECHO) were discussed. Divided into four groups, they were prompted to correlate cardiac anatomy with the echocardiographic image in the parasternal longitudinal and apical four-chamber views (Figure 2).

Within cardiac physiology, the pressure and volume curves of the left atrium (LA) and left ventricle (LV) were discussed, utilizing pulsed Doppler of the LV inflow and outflow tract obtained in the apical 4th and 5th chamber views, respectively. Discussion was encouraged regarding diastole and ventricular filling times based on heart rate (Figure 3).

Finally, at the fifth time point and with a thirty (30)-day interval, the students undertook the last test (assessment 3) as a surprise test, featuring the same questions as the previous tests and providing the same time to answer.

Evaluation

The assessment was developed by the coordinating professor of the phase using the Google Forms® platform, administered as a surprise test on electronic devices with

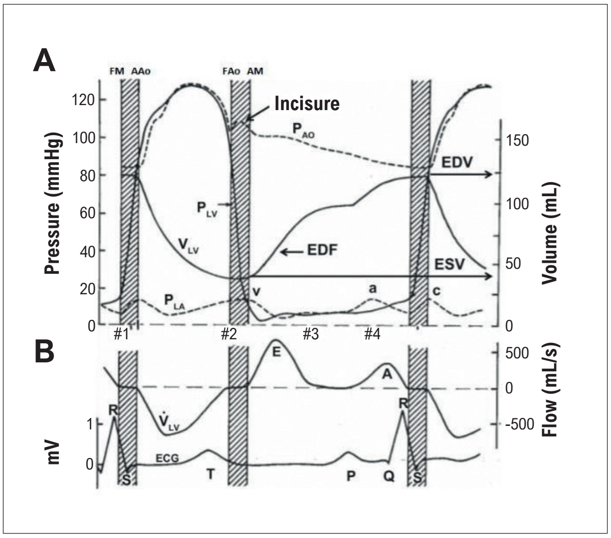

Figure 1 – *Wiggers Diagram. Key: A) Temporal correlation between ventricular pressure (VP), ventricular volume (VV), atrial pressure (AP) and aortic pressure (AoP). MVC: mitral valve closure; MVO: mitral valve opening; AVO: aortic valve opening; AVC: aortic valve closure; EDV: End diastolic volume; ESV: End systolic volume. #1 - B1 (mitral and tricuspid valves closure). #2 - B2 (aortic and pulmonary valves closure). #3 - B3 (third heart sound). #4 - B4 (fourth heart sound). B - Temporal correlation between blood flow during ventricular systolic ejection (VV) and diastolic filling waves (E and A waves of mitral inflow), in conjunction with the electrical impulses of atrial depolarization waves (P wave), ventricular depolarization (QRS complex), and ventricular repolarization (T wave) observed in the electrocardiogram (ECG). Adapted from Mitchell, 2014*[11]

restricted internet access. The questions were blinded to the practical instructor, and the content was covered in the echocardiography laboratory program. It was composed of twenty (20) multiple-choice questions (appendix 1), with fifteen (15) questions related to anatomy and physiology (the so-called "valid questions") and another five (5) "confusion-inducing questions" related to cardiology, but without addressing the topics discussed in theory and practice.

Confusion-inducing questions were introduced in the assessment to prolong the test, confuse students regarding the topic covered, and serve as control questions, since they do not explore the subject discussed in theory and practice. If assessment 1 solely focused on cardiac anatomy and physiology, the student would readily discern the designated topic and could engage in targeted study, artificially enhancing their performance in subsequent assessments. Consequently, these confusion-inducing questions showcase the student's capacity to enhance their knowledge and study without any didactic intervention.

Statistical analysis

The results of the three assessments were calculated in the SPSS@ (Statistical Package for the Social Sciences) software version 26.0, using the Kolmogorov-Smirnov normality test.

Given the distribution of the sample, a normal distribution of these findings was found in the first and second assessments using the parametric Student's t test for paired samples. For the analysis of the third assessment, given the non-normal distribution, the non-parametric Wilcoxon t test was used.

The results were expressed as mean and standard deviation (SD), with the analysis considered statistically significant when p value < 0.05 ($\alpha < 0.05$).

Results

The sample was made up of 34 students from the third semester (basic cycle) of the Medical School program, 25 of whom were female and 9 male, with a mean age of 20.9 years (SD ± 3.5 years).

In the first assessment, the average number of correct answers to valid questions was 6.7 (SD ± 2.0), corresponding to 44.6%. The average number of correct answers to the confusion-inducing topics was 2.5. The question with the lowest percentage of correct answers was "During which phase of the cardiac cycle are the values of aortic diastolic (DBP) and systolic (SBP) pressure observed?" with only five correct answers (14.3%).

In the second assessment, the average number of correct answers to valid questions was 9.8 (SD ± 2.2), totaling 65.3%, and 2.6 correct answers to confusion-inducing questions. In this assessment, the question with the lowest number of correct answers was a confusion-inducing question: "The definition of sinus rhythm is based on the following findings, EXCEPT for," with only eight correct answers (21.1%).

In the last assessment, the average number of correct answers was 10.3 (SD ± 2.5), correlating with 68.8% of the total, and 2.45 correct answers to the confusion-inducing questions. Again, the question correlated with fewer correct answers was a confusion-inducing question: "During a heart attack, what electrocardiogram change determines the need for emergency coronary angiography (cardiac catheterization)?" with only seven correct answers (20.6%).

Using the parametric test, significant relevance was observed between assessments 1 and 2 ($p < 0.001$). There was also statistical significance using the non-parametric test to compare assessments 1 and 3 ($p < 0.001$). No difference between assessments 2 and 3 ($p = 0.14$) was observed (Chart 1), as well as in the rate of correct answers to confusion-inducing questions ($p > 0.3$).

In the comparative analysis of the correct answers to the valid questions by the students in the three assessments (Chart 2), a tendency for students to have a higher number of correct answers after the theoretical meeting was observed (assessment 2) and, mainly, after the practical meeting (assessment 3). Although there is no statistical significance in relation to assessments 2 and 3, the chart shows the student's knowledge retention tendency, given that the last assessment was applied thirty (30) days later.

Discussion

This study assessed the influence of incorporating echocardiography into the learning process of cardiology for students in the foundational stage of medical education. Our findings demonstrate that the early introduction

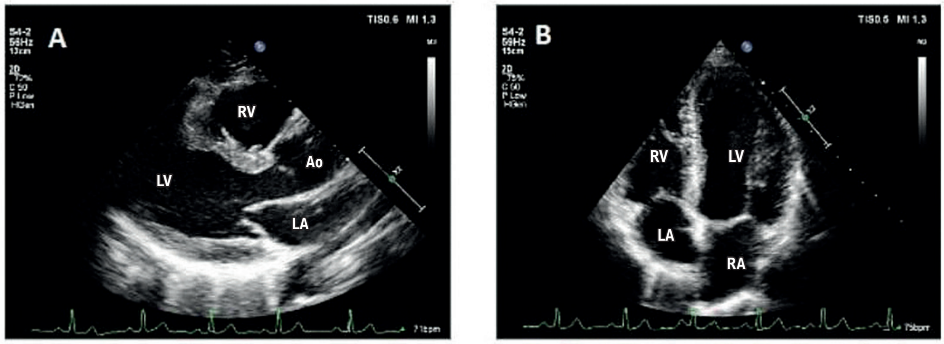

Figure 2 – Echocardiographic images in sections: A) Parasternal longitudinal; B) Apical four-chamber view. Key: LV: left ventricle; LA: left atrium; RV: right ventricle; RA: right atrium.

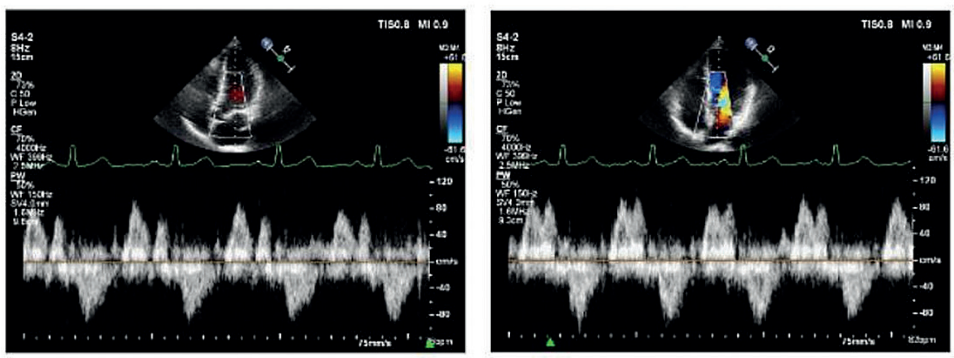

Figure 3 – Echocardiographic images in the Apical 4-chamber view of the inflow tract and outflow tract of the left ventricle with pulsed Doppler.

of echocardiography in medical education is not only feasible but also enhances the acquisition and retention of knowledge concerning cardiac anatomy and physiology among medical students.

Echocardiography bridges the gap between fundamental concepts and clinical applications, fostering student interest in the subject by emphasizing the need for a solid understanding of physiology for effective utilization of the method in clinical practice.[6] Teaching cardiac anatomy and physiology through ultrasound proves to be viable and beneficial for medical students, elevating their performance and fostering a greater enthusiasm for expanding their knowledge.[2] Educational activities that integrate echocardiography are well-received by students as they provide a tangible representation of the physiological processes within the heart.[12]

In certain studies, experimental anatomical models, echocardiography simulators, comparisons with anatomical practice, and cadaver dissection were employed to assess the knowledge gained by medical students. Torabi and colleagues, using a teaching software model, demonstrated the positive impact of introducing echocardiography to medical students during cardiology classes, both subjectively through student evaluations and objectively in practical tests.[10] Studies by Griksaitis, Sawdon, and Finn suggest that both anatomical dissection of cadavers and echocardiography are equally effective methods for teaching cardiac anatomy, with no significant superiority of one over the other.[5] This observation is supported by Canty *et al.*, who devised a three-hour practical session incorporating an ultrasound simulator as a supplementary tool for learning cardiac anatomy, and revealed that the knowledge acquired by students in this session was comparable to that obtained through the use of plastic models and cadaver dissection.[13]

Currently, some universities have used echocardiography to teach anatomy, clinical examination, and image acquisition to recognize some cardiac pathologies.[14] In our study, a notable knowledge gain was observed between the pre-theoretical assessment (assessment 1) and the post-echocardiography practice evaluation (assessment 3), with the percentage of correct answers rising from 44.6% to 68.6%. This result is comparatively lower than the study conducted by Bell *et al.*, where students' average correct score increased from 53.3% in the pre-test assessment to 81.7% in the post-test assessment.[4] In the work of Varadharaju and colleagues, 89.6% of students showed a better understanding of cardiac anatomy and physiology through real-time echocardiography.[15] Both studies performed the post-test assessment immediately after the practical class, and participants were voluntary.

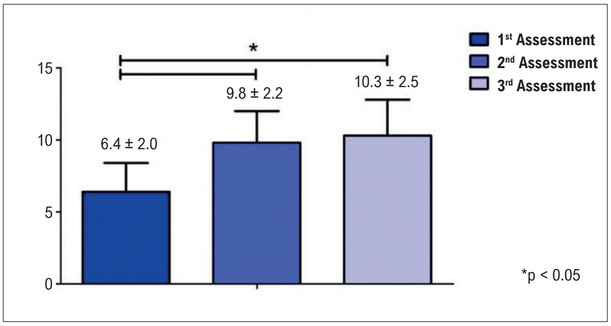

Chart 1 – *Average number of correct answers in assessments and standard deviation.*

Regarding knowledge retention, our study observed the maintenance and even enhancement of correct answers, correlating assessment 2, with 65.3% (after theory), and assessment 3, with 68.6% (30 days after practice). Numerous studies illustrating knowledge retention through the application of echocardiography are lacking in the literature. However, the research conducted by Jujo and colleagues revealed that, although there was a notable decline in the student's capability to capture Point of Care Ultrasound (POCUS) images after eight weeks, knowledge retention during this period remained consistent, with a slight reduction from 23.1 points to 19.6 points in comparison to the assessment conducted after the presentations, which was not statistically significant.[16]

Limitations and strengths of the study

Our work has certain limitations, such as the absence of a control group, preventing a direct comparison between the theory and practice of echocardiography. While it was initially suggested to create a control group when devising the study protocol, the lack of a standardized curriculum for teaching echocardiography in medical schools hindered this comparison. We encourage future comparative studies using our teaching methodology to pave the way for an appropriate curriculum.

Despite being the first study in Brazil to evaluate the effectiveness of an echocardiography laboratory for teaching cardiology, it was conducted in a single center using a methodology developed by the authors.

The investigation into knowledge retention occurred only four weeks after educational activities, due to the sequencing of the academic curriculum, which consists of Practical Skills III covering cardiology and pulmonology sessions. These sequential activities complement the study of cardiac anatomy and physiology and could interfere with the results of the assessments. Future studies should be carried out so that longer-term knowledge can be assessed.

The effective number of research participants aligns with sample calculations for educational interventions, recommending the inclusion of 25 or more participants in such studies.[17] Finally, the compulsory analysis of all students in the phase, without relying on volunteers, minimizes the risk of overestimation bias in the evaluation of medical education, as indicated by Callahan, Hojat, and Gonnella.[18]

Conclusion

Using transthoracic echocardiography as an instructional tool in cardiology education is viable within the medical curriculum, providing students in the foundational cycle with enhanced knowledge of cardiac anatomy and physiology.

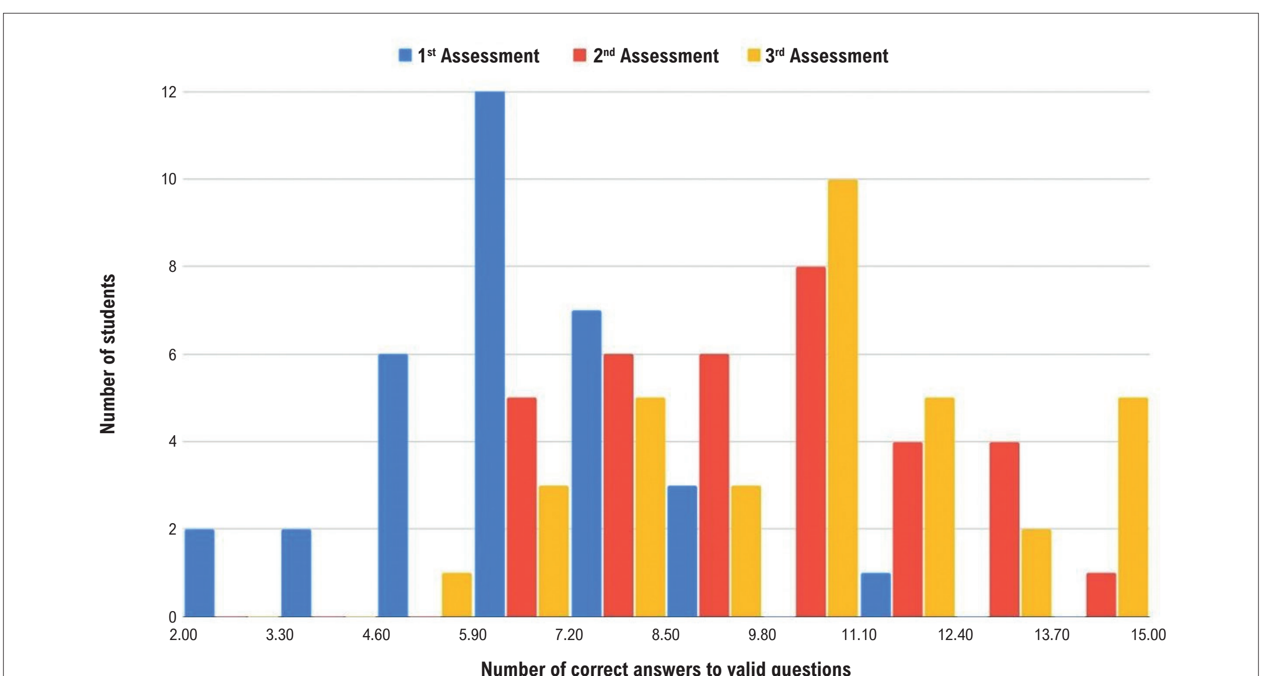

Chart 2 – *Comparative analysis of medical students' performance in evaluations.*

In addition to instructing on the acquisition of specific echocardiographic images for diagnosing particular cardiac pathologies, the incorporation of echocardiography into medical programs enhances students' capacity to assess the appropriateness of requested exams, along with their indications and proper interpretation.

Author Contributions

Conception and design of the research: Bacca COF, Toniazzo SRF, Matias LF, Kuhl ALN, Mees TN, Gambetta MV; acquisition of data: Bacca COF, Kuhl ALN, Mees TN, Gambetta MV; analysis and interpretation of the data: Bacca COF, Rocha FR; statistical analysis: Rocha FR; writing of the manuscript: Bacca COF, Toniazzo SRF, Rocha FR, Matias LF, Kuhl ALN, Mees TN, Ramos N, Gambetta MV; critical revision of the manuscript for intellectual content: Bacca COF, Toniazzo SRF, Ramos N, Gambetta MV.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Original Article

Use of Artificial Intelligence to Assess Cardiac Function by Echocardiography: Systematic Review of the State of the Art

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Abstract

Background: Echocardiography is part of the routine investigation of most heart diseases. However, its operator-dependent nature and the quality of the image obtained can cause significant variability in measurements and impair their interpretation. The method has advanced on its path of standardization and incorporation of new technologies in an attempt to reduce its deficiencies. Recently, part of this advancement was due to the incorporation of artificial intelligence (AI).

Objectives: The objective of this work was to investigate the use of AI in the assessment of cardiac function through echocardiography, discussing its potential to improve the method.

Methods: We conducted a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), searching for articles within the period of 2000 to 2023.

Results: A total of 31 articles were included, classified into four categories of studies that used AI: 1) for image analysis and echocardiographic parameters (N = 14); 2) in the image acquisition process (N = 11); 3) for integration with clinical data (N = 3); and 4) for application to the exam flow (N = 3).

Conclusion: AI provides automation and standardization of images and respective measurements that result in more accurate diagnoses, overcoming the limitations encountered by the conventional method. However, the use of AI is still an evolving reality within echocardiography.

Keywords: Echocardiography; Artificial Intelligence; Machine Learning; Deep Learning; Global Longitudinal Strain.

Introduction

Echocardiography is the most requested imaging method and is part of the routine investigation of most heart diseases. Due to its non-invasive, non-ionizing nature, high availability, and portability, the method is present in various clinical scenarios - outpatient, hospital, urgency and emergency units, intensive care units, and as a guide for interventional and surgical procedures - and normally is the first option to access cardiac anatomy and function. However, its operator-dependent nature and image quality can influence echocardiographic measurements. Since its development, the method has advanced in its path of standardization and incorporation of new technologies in an attempt to reduce its variability.

This advance is partly due to the incorporation of artificial intelligence (AI) into the method. “AI” is a broad term coined by Arthur Samuel in the 1960s. It applies to any computer program, such as algorithms and models, which imitate human logic and intelligence.[1] In echocardiography, the first use was in the 70s, when Fourier analysis was used to evaluate the mitral valve with the aid of M-mode.[2] Semi-automated measurements are already part of today’s echocardiography laboratory practice. In their workflow, modern devices come equipped with software packages that assist in measurements and calculations, such as left ventricular ejection fraction (LVEF), myocardial deformation (strain), and the Doppler study for hemodynamic assessment.[1]

Machine learning is one of the subfields of AI. The computer receives the data, learns from it, predicts a result, and, using statistical methods, can even improve its performance the next time it is presented with similar data. This allows, for example, a trained machine to identify structures within a new image and label them accurately. Another subfield, known as deep learning, later emerged. This is applied when a large amount of data must be processed. In this case, the data is processed as large subsets. Just like in a biological neural network, the processing is organized in a hidden chain made up of thousands of consecutive artificial neural layers until a final result is reached.[1] An artificial neural network can use convolution operations, which allow a third to be generated from two input data called Convolutional Neural Networks.[3]

In this sense, AI in echocardiography can be extremely advantageous for identifying, quantifying, and interpreting images while minimizing the variance between assessments

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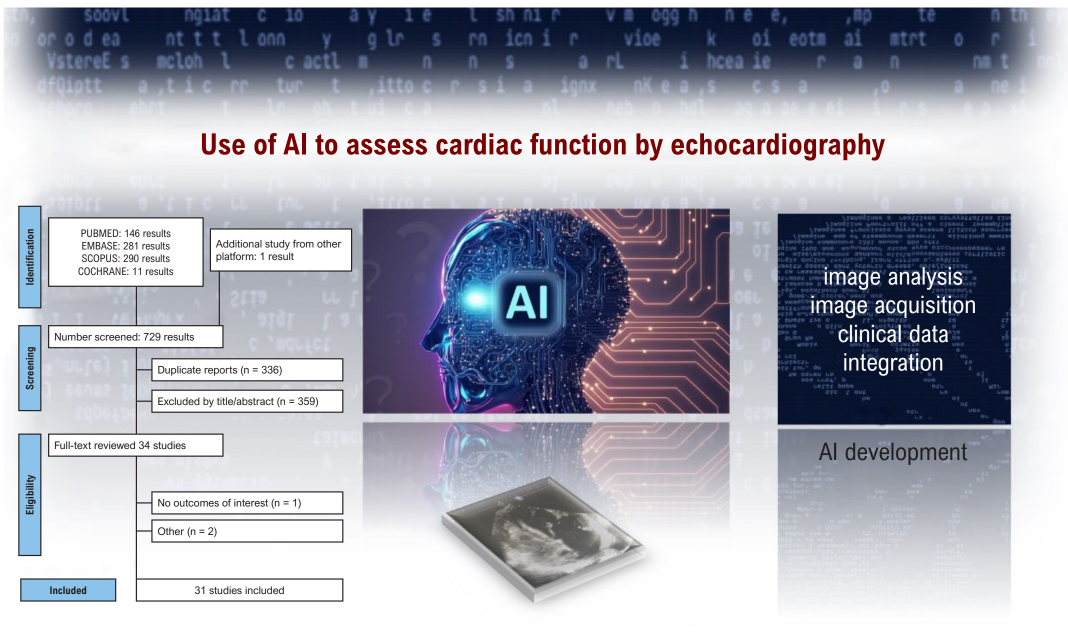
Central Illustration: Use of Artificial Intelligence to Assess Cardiac Function by Echocardiography: Systematic Review of the State of the Art



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Flowchart of search and selection of studies on the use of AI in echocardiography. AI: artificial intelligence.

and providing reproducible measurements and an accurate diagnosis. The examiner may find significant support in this technology, which would enable a reduction in time spent on data extraction and integration and, in turn, present the potential to make the healthcare system more sustainable.[4] Furthermore, AI-driven echocardiographic practice would not only streamline clinical decision-making but also provide learning methods with interactive feedback for training less-experienced examiners.[5]

Thus, the use of AI in echocardiography can be divided into four main scenarios: education, image acquisition, image analysis, and integration with clinical data.[6] Although there is evidence that positively affirms the role of AI technology in echocardiography diagnosis, there are still challenges to be overcome, such as insufficient standardization of echocardiography protocols and insufficient generalization of models in clinical applications.[6]

Given the limitations of the technique and the need to investigate future trends, this systematic review was conducted based on several studies to externally validate the performance of AI technology in echocardiography. Although similar works are found in the literature that investigated the application of AI in the automated analysis of echocardiographic images, this study sought to conduct a survey over the last five years on innovations in the area, with the aim of exploring the use of AI in echocardiography, analyzing current evidence for its effectiveness and discussing its potential to improve cardiac care.

Methods

This is a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[7] We searched for articles within the MEDLINE, EMBASE, SCOPUS, and Cochrane Central databases from January 2000 to March 2023, without language restrictions, with our target method being echocardiography, whose intervention is the use of AI during some stage of the exam, with full texts and descriptors present in the title or summary of the article. The following descriptors in English were used for the research: (“AI”) AND (“Echocardiography”) AND (“Function” OR “Strain”). We also checked these databases for the presence of previous or ongoing systematic reviews on the subject. We combined results from different databases and discarded repeated results using Zotero software. Two investigators (H.A.F.N and B.S.Y) performed the search independently and five investigators reached an agreement on study eligibility (H.A.F.N, B.S.Y, T.H.L.P.C, I.E.S, Y.M.R.B). Initially, a first screening was conducted to identify studies that evaluated the use of any type of AI during the echocardiography exam. In a second step, we selected the articles to be read in full through the Rayyan platform and assessed the relevance of the data, as well as whether there was more than one article evaluating the same cohort of patients. A third step consisted of reviewing the references of these selected articles to obtain other sources not revealed in the digital search. We classified the studies according to their design (case-control, randomized, retrospective cohort, prospective cohort, and case report), regarding the primary objective of using AI and the main result found with the study. For each study, we extracted the following information: first author; study institution; start and end date; year of publication; single center or multicenter; characteristics of the studied population (average age and distribution by sex); echocardiographic parameters evaluated; methods and windows used to assess cardiac function; AI model; study design; and study conclusions.

Results

We identified 729 references in searches of electronic databases, discarding 336 duplicates and another 359 excluded by title and/or abstract. We obtained 33 articles for full reading, of which three were discarded because they did not fit the scope of the review according to the authors. Only one additional article was included after manually searching the references (Figure 1). A total of 31 articles were included in the qualitative analysis of this review, being classified into four main categories: 1) studies that use AI for image analysis and echocardiographic parameters (N = 14, Table 1); 2) studies that use AI in the image acquisition process (N = 11, Table 2); 3) studies that use AI to integrate with clinical data (N = 3, Table 3); and 4) studies that trained AI software for application to the exam flow (N = 3, Table 4); All articles were published in English. Twenty-six articles are from a single center, with 7 (%) from the United States, 2 (%) from Israel, 2 (%) from Norway, 2 (%) from Italy, 2 (%) from England, 1 (%) from Germany, 1 (%) from Greece, 1 (%) from France, 1 (%) from Uganda, 1 (%) from Portugal, 1 (%) from Ireland, 1 (%) from Austria, 1 (%) from Netherlands, 1 (%) from China, 1 (%) from Canada, and 1 (%) from Japan. A single article was developed in several centers (13 different centers). Four articles did not inform of the country where the study took place.

Discussion

The implementation of AI tools in echocardiographic study has the potential to improve patient care and optimize diagnosis and treatment. The studies present in this systematic review are favorable to the application of automated technology in the examination routine, due to its similarity, feasibility, usefulness, precision, accuracy, and reproducibility comparable to manual assessment. Although the use of AI in the examination is still limited and, therefore, prone to modifications aimed

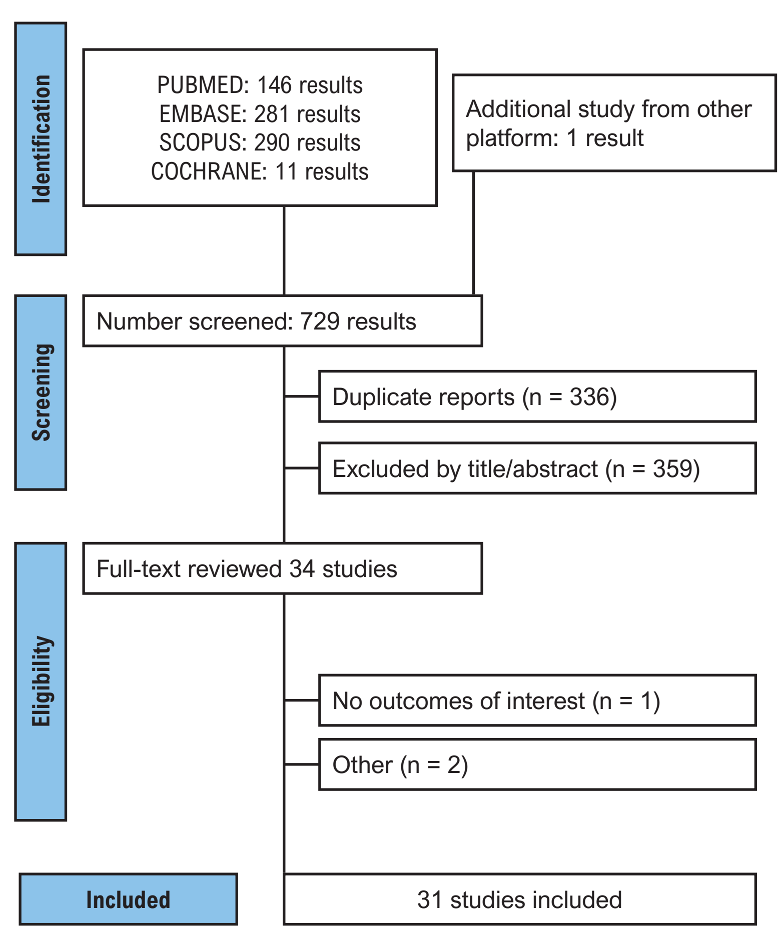

Figure 1 – *PRISMA flow diagram of study screening and selection*

Table 1 – Studies that use AI for image analysis

Author/year	Country	Design and objective	N	Evaluated parameters	AI model	Main results
Cottela *et al.*, 2023[8]		Retrospective cohort Evaluate AI calculation of LVEF and GLS in patients with amyloidosis	51	LVEF, GLS	EchoGo Core 2.0, Ultromics	Fully automated AI-calculated LVEF and GLS are comparable to manual measurements in patients with cardiac amyloidosis.
Sveric *et al.*, 2023[9]	Germany	Prospective cohort Investigate AI viability for the calculation of LVEF in the workflow	889	LVEF	LVivo Seamless™	The AI-based application automatically identified standard apical LV views and measured LVEF. It yielded equivalent results to the currently used MBS method and has the potential to improve LVEF quantification.
He *et al.*, 2023[10]	USA	Randomized clinical trial Compare AI with the sonographer's initial assessment of LVEF	3495	LVEF	EchoNet-Dynamic	Cardiologists were not able to distinguish between the initial assessments by AI versus the sonographer. The initial assessment of LVEF by AI was non-inferior to the assessment by sonographers.
Wang *et al.*, 2022[11]	USA	Retrospective cohort Evaluate AI software usability in patients with COVID-19	50	LVEF, GLS, EDV, ESF	EchoGo, Ultromics	EchoGo software output had high correlations with left ventricular volumes and moderate correlations with LVEF and GLS compared with standard TTE measurements.
Liel-Cohen *et al.*, 2022[12]	Israel	Retrospective cohort Evaluate AI's capability of identifying views and compare GLS results with conventional methods	100	GLS	LVivo Seamless™	The results provided by the AI-based LVivo Seamless solution showed excellent capability to automatically identify 4CH, 2CH, and 3CH views, along with excellent GLS results compared to automated functional imaging.
Sachpekidis *et al.*, 2022[13]	-	Retrospective cohort Evaluate the accuracy of a novel HUD with AI-assisted algorithm to automatically calculate LVEF	100	LVEF	Auto EF, Vivid™	The AI-assisted autoEF algorithm in a novel HUD can accurately calculate LVEF in real-time as compared to the recommended manual biplane Simpson's method on cart-based systems in an "all-comers" patient population.
Salte *et al.*, 2021[14]	Norway	Retrospective cohort Examine automated measurements of GLS using deep learning and AI compared with conventional methods	200	GLS	EchoPAC v.202, GE Ultrasound	Fully automated measurements of GLS using a novel deep learning AI-based technology for motion estimation are feasible and fast and they yield results comparable with the most widely used semiautomatic software.
Hanif *et al.*, 2021[15]	-	Transversal Test whether AI measurement of strain can be more reliable compared to human interpretation	52	GLS	EchoGo, Ultromics	AI-based longitudinal strain analysis was feasible on most echocardiograms without any operator intervention. The bias between EchoGo's longitudinal strain and conventional software appears small.
Penso *et al.*, 2022[16]	Italy	Transversal Feasibility, comparison, and assessment of AI strain measurement compared with conventional methods	203	RVEF, RVFWLS	3D Auto RV, Philips Medical Systems	The rapid analysis and excellent reproducibility of AI-based 3DE RV analysis supported the routine adoption of the system.
Di Candia *et al.*, 2022[17]	Italy	Transversal Compare results of a fully automated analysis and manual tracing analysis using a new AI software	28	LVEF	AI Simpson e AI Wall Motion Tracking	AI fully automated analysis was found to be technically simple, less time-consuming, and highly reproducible. This reduces the variability of manual measurements between different sonographers and at various times.
Papadopoulou *et al.*, 2022[18]	Greece	Transversal Evaluate the reliability and diagnostic accuracy of a HUD-assisted AI to automatically calculate ejection fraction	100	LVEF	Kosmos autoEF	The use of a novel HUD with AI-enabled capabilities provided similar LVEF results to those derived by manual biplane Simpson's method on cart-based systems and shows clinical potential.
Salte *et al.*, 2020[19]	Norway	Multicentric Prospective Examine the feasibility of automated measurements of GLS using AI compared to conventional speckle-tracking application	100	GLS	-	Fully automated measurements of GLS using a novel deep learning AI-based technology for motion estimation are feasible and fast and they yield results comparable with the most widely used semiautomatic software.

Popoff *et al.*, 2020[20]	France	Transversal Evaluate the accuracy and reproducibility of AI tool to compute LV volumes and EF, in comparison with cardiac magnetic resonance as reference	114	LVEF	A deep convolutional neural networks model	Compared to manual contouring, LV volumes, and EF by AI showed comparable or improved accuracy and higher reproducibility. These findings demonstrate the value of AI-based tools, with the potential for full automation, for objective assessment and follow-up of cardiac function.
Asch *et al.*, 2021[21]	USA	Prospective cohort Determine whether AI-automated estimates could be used to accurately classify LV function	233	LVEF	A machine learning algorithm, Caption Health	The new machine-learning algorithm allows accurate automated evaluation of LV function from echocardiographic views commonly used in the POC setting. This approach will enable more POC personnel to accurately assess LV function.

EDV: left ventricular end-diastolic volume; ESF: left ventricular end-systolic volume; GLS: global longitudinal strain; HUD: handheld ultrasound device; LVEF: left ventricle ejection fraction; POC: point-of-care; RVEF: right ventricle ejection fraction; RVFWLS: right ventricular free wall longitudinal strain; AI: artificial intelligence; AI: artificial intelligence; TTE: transthoracic echocardiogram; AutoEF: automatic ejection fraction; EF: ejection fraction; LV: left ventricle; 4CH: four chamber view; 2CH: two chamber view; 3CH: three chamber view.

Table 2 – Studies that use AI for image acquisition.

Author/year	Country	Study design and objective	N	Evaluated parameters	AI model	Main results
Peck *et al.*, 2023[22]	Uganda	Cross-sectional. Evaluate the ability of nonexperts to obtain diagnostic-quality images in patients with RHD using AI guidance with color Doppler	50	Presence/ absence of RHD, abnormal mitral valve morphology, and mitral regurgitation	-	AI guidance with color Doppler is feasible to enable RHD screening by nonexperts, performing significantly better for assessment of the mitral than aortic valve.
Klempfner *et al.*, 2023[5]	USA	Prospective cohort. Determine the diagnostic acumen of echocardiographic studies obtained by inexperienced users guided by an AI algorithm	240	Left and right ventricular size and function, pericardial effusion, valve morphology, left atrial and inferior vena cava size	UltraSight algorithm	After minimal training with novel AI-guidance software, novice users can acquire images in ten standard cardiac echocardiographic views, with diagnostic quality approaching that of expert sonographers.
Dadon, Ziv *et al.*, 2022[23]	Israel	Randomized clinical trial Evaluate AI use as a didactic tool to improve noncardiologist clinicians' assessment of LVEF from the A4C view	-	LVEF	LVivo EF	The introduction of an AI-based tool to clinicians working in the emergency department improved the assessment accuracy of LVEF as compared to the control group.
Varudo *et al.*, 2022[24]	Portugal	Prospective cohort. To compare real-time measurements taken by novices and experts with LVEF reference measurements taken manually by echo experts	95	LVEF	Real-Time EF algorithm	Machine learning-enabled real-time measurements of LVEF were strongly correlated with manual measurements obtained by experts.
Burke *et al.*, 2022[25]	Ireland	Cross-sectional. Evaluate study quality by novice scanners with AI guidance	120	Image quality to determine LVEF, pericardial effusion	Caption AI System	The Caption AI technology safely allows novice users to provide efficient and accurate point-of-care echo in differing clinical settings to a standard comparable to expert scanners.
Narang *et al.*, 2021[26]	USA	Prospective cohort. Test whether novice users could obtain 10-view transthoracic echocardiographic studies of diagnostic quality using a DL-based software	240	Left ventricular size, function, pericardial effusion, and right ventricular size	Software Caption Guidance	The DL algorithm allows novices without experience in ultrasonography to obtain diagnostic transthoracic echocardiographic studies for evaluation of left ventricular size and function, right ventricular size, and the presence of a nontrivial pericardial effusion.

Surette *et al.*, 2020[27]	USA	Prospective multicentric clinical trial. Evaluate whether novice-acquired images guided by the software were of diagnostic quality in patients with and without implanted electrophysiological devices	240	Right ventricular size and function	-	New DL software can guide novices to obtain TTEs that enable qualitative assessment of RV size even in the presence of implanted EP devices.
Schneider *et al.*, 2020[28]	Austria	Cross-sectional. Evaluate if the new machine learning algorithm can help novice operators to acquire diagnostic image loops	14	LVEF	-	Machine-learning algorithms can guide ultrasound novices to acquire diagnostic echo loops and provide an automated LVEF calculation that agrees with a human expert.
Motazedian *et al.*, 2022[29]	Netherlands	Prospective cohort. Determine the accuracy of POCUS bedside AI-assisted LVEF compared to formal TTE	449	LVEF	EchoNous Kosmos	AI assisted POCUS performed by both novice and experienced scanners can accurately determine LVEF compared to a comprehensive TTE.
Zhai *et al.*, 2022[30]	China	Cross-sectional. Identify the degree of correlation between auto LVOT-VTI and the manual LVOT-VTI acquired by POCUS-trained doctors	46	LVOT-VTI	AI software tool	AI might provide real-time guidance among novice operators who lack the expertise to acquire the ideal standard view.
Fung *et al.*, 2019[31]	Canada	Prospective cohort. Evaluate the accuracy of the AI system for assessing image quality, as compared to subjective expert analysis	53	PLAX, PSAX, A2C, A4C and subcostal IVC	-	AI systems can assess image quality with modest accuracy.

A2C: apical two-chamber; A4C: apical four-chamber; DL: deep learning; IVC: inferior vena cava; LVEF: left ventricle ejection fraction; LVOT-VTI: left ventricular outflow tract velocity time integral; PLAX: parasternal long-axis; POCUS: point-of-care ultrasound; PSAX: parasternal short-axis; RHD: rheumatic heart disease; RV: right ventricle; TTE: transthoracic echocardiogram; AI: artificial intelligence; EP: electrophysiological.

at advancing and improving the method, the benefit that the technology represents for echocardiography seems to outweigh any fears or disadvantages.

Image analysis and echocardiographic parameters

AI-automated measurement of parameters such as LVEF and global longitudinal strain (GLS) can be comparable to manual measurement by experienced sonographers and incorporations of these tools have reliably maintained measurement accuracy.[8-13] This fact is relevant due to the additional benefits they offer: they increase the operational effectiveness of the exam and the consistency quality of the analysis;[6] allowing the reduction of variability between different examiners,[14-18] overcoming human limitations such as tiredness or distraction; and increasing the reproducibility of the exam.[1]

Image Acquisition

Much of the literature focuses on AI interpretation or analysis of already acquired images, but there is growing evidence regarding the use of AI technology for image acquisition by non-experts.[5,19-24] Automated technology can guide a non-expert examiner by recognizing incorrect images and the need for additional views or enhancements. It can also help standardize image acquisition and measurements.[1,6] In this way, it would be a tool used to optimize training and echocardiographic studies,[5,25,26] with the possibility of acquiring images of diagnostic quality comparable to those acquired manually by experts.[5,19,20,22-24] The technology is applicable in clinical practice, in emergencies, and in remote areas with scarce resources and few experienced professionals.[5,21,25,27]

Integration with clinical data

In the field of echocardiography, interpretation of exam findings is necessary to improve patient care and monitoring. Thus, training AI software to associate image data with patient clinical data allows the retention of relevant diagnostic information without the need for advanced analysis skills by an expert and without the expenditure of time and resources. Correlation with functional abnormalities, pathological states, prediction of outcomes, and risk stratification are examples of the usefulness of integrating algorithms with clinical data. The results presented by the study by Kusunose *et al*. support the possibility of using AI software for automated diagnosis of functional abnormalities, and the study by O'Driscoll *et al*. to calculate LVEF and GLS.[28,29] From a future perspective, the integration of AI software with clinical data could allow the creation of personalized therapies for each patient.

AI development

Databases of echocardiographic studies were used to train protocols and deep learning algorithms to detect cardiac dysfunction, identify anatomical abnormalities, and define workflows.[30-32] After training, the accuracy found was similar to the accuracies using conventional methodologies. This validation is essential since, in the development of AI software, both software and images come from external suppliers. The quality of the images used is a relevant point because, if the data entered is of low quality, biased, or restricted, the interpretation by the algorithm will be as well. A future challenge will be to develop deep learning algorithms that run on different equipment, have uniform naming standards, and store and retrieve data in a vendor-independent manner.[1]

Table 3 – Studies that use AI for integration with clinical data

Author/ year	Country	Study design and objective	N	Evaluated parameters	AI model	Main results
Kusunose *et al.*, 2019[32]	Japan	Prospective cohort. Investigate whether a DCNN could provide improved detection of RWMAs	300	Presence of wall motion abnormalities	ResNet, DenseNet, Inception-ResNet, Inception, and Xception	The results support the possibility of using DCNN for automated diagnosis of RWMAs in the field of echocardiography.
O'Driscoll *et al.*, 2022[33]	England	Retrospective cohort. Evaluate whether LVEF and GLS, automatically calculated by AI, increases the diagnostic performance of SE for CAD detection	512	LVEF and GLS at rest and stress	EchoGo Core 1.0, Ultromics	AI calculation of LVEF and GLS by contouring of contrast-enhanced and unenhanced SEs at rest and stress is feasible and independently improves the identification of obstructive CAD beyond conventional methods.
Asch, F.M. *et al.*, 2022[34]	Multicentric	Prospective cohort. Assess the hypothesis that AI-based analysis of echocardiographic images could predict mortality more accurately than conventional analysis by a human expert	870	LVEF, LVLS	EchoGo Core, Ultromics	AI-based analysis of LVEF and LVLS had similar feasibility as manual analysis and AI-based, but not manual, analyses were a significant predictor of in-hospital and follow-up mortality.

CAD: coronary artery disease; DCNN: deep convolutional neural network; GLS: global longitudinal strain; LVEF: left ventricle ejection fraction; LVLS: left ventricle longitudinal strain; RWMAs: regional wall motion abnormalities; SE: stress echocardiography.

Table 4 – Studies that developed an AI

Author and year	Country	Study design and objective	Number of patients	Evaluated parameters	AI Model	Main results
Asch *et al.*, 2019[38]	USA	Transversal Develop an algorithm and assess its feasibility and accuracy for automated quantification of LV EF by a well-trained expert computer against reference	99	LVEF	AutoEF (BayLabs)	A machine learning algorithm for the estimation of LV EF that avoids image segmentation and volume measurements is highly feasible and can yield results that are in close agreement with what experienced readers measure using conventional methodology.
Stowell *et al.*, 2021[35]	England	Transversal Develop a method based on machine learning, trained and validated with accredited experts from AI Echocardiography Collaborative	-	Left ventricle longitudinal tension	-	The open-source, vendor-independent AI-based strain measurement automatically produces values that agree with expert consensus as strongly as individual experts.
Tromp *et al.*, 2021[36]	Singapore	Transversal Develop a fully automated deep-learning workflow to classify, segment, and annotate two-dimensional videos and Doppler modalities in echocardiograms	-	-	-	Deep learning algorithms can automatically annotate 2D videos and Doppler modalities with similar accuracy to manual measurements by expert sonographers.

AutoEF: automatic ejection fraction; LVEF: left ventricle ejection fraction.

The incorporation of AI into clinical practice raises ethical concerns, primarily about responsibility, as care becomes more indirect, and transparency as the extent to which the patient needs to know and agree is called into question. It is worth remembering that the use of AI is already part of people's routine, and this type of technology is increasingly available to society. This interaction tends to be irreversible and, certainly, in medical practice - and in echocardiography - it will be no different. Even so, this is not a man versus machine competition. We cannot imagine a scenario in which one replaces the other. On the contrary, AI is in favor of the doctor and against the obscurity of human and systemic limitations, such as high demand, lack of specialists, ergonomics, and service exhaustion. Especially because, by increasing the operational effectiveness of the exam, there can be better use and direction of the specialist doctors' skills. It is expected that this incorporation will contribute to the democratization of access to the exam, representing an advance in health care.

However, this systematic review has its limitations. First, the vast majority of studies have a cross-sectional design. However, as our objective was diagnostic validation, studies with this design are sufficient to show the non-inferiority of their methods. Designs that study long-term association measures may better clarify the benefits of AI for the quality of longitudinal patient follow-up. Second, AI software usually requires a minimum image quality. Sometimes, patients with poor windows were excluded.[10,14,15] In several of the studies, the images analyzed were collected in ideal scenarios, by experienced specialists, or were packages from supplier centers. Therefore, larger studies with low-quality images, especially in patients with poor windows, hemodynamically unstable, or in non-ideal settings (ICU, emergency) should be encouraged. Third, most softwares are capable of measuring a limited number of parameters. Thus, further studies can validate the benefits of using AI beyond the parameters studied in this review.

Conclusion

The application of AI in the area of echocardiography has proven to be a highly effective and accurate method in four main domains (Central Illustration). AI provides the automation and standardization of images and respective measurements, which results in more accurate diagnoses, overcoming the limitations found in manipulation by a human sonographer. Furthermore, AI has also proven to be a facilitating tool in obtaining satisfactory results even when used by non-experts. The advantages offered by AI make the exam much faster and more accessible, as the duration of training for a specialist professional is one of the challenges of exam availability in public health. Therefore, as a result of the facts presented, AI is a beneficial resource that can be widely implemented in echocardiography services, as the advantages presented by the method cover a wide range of dimensions, from the accuracy of results and data integration for clinical correlation to the prevention of ergonomic diseases related to the sonographer's work.

Author Contributions

Conception and design of the research, acquisition of data and analysis and interpretation of the data: Neves HAF, Yuasa BS, Costa THLP, Santos IE, Benavides YMR, Lofrano-Alves MS; writing of the manuscript: Neves HAF, Yuasa BS, Costa THLP, Santos IE, Benavides YMR; critical revision of the manuscript for intellectual content: Lofrano-Alves MS.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Original Article

Clinical and Echocardiographic Aspects of Patient-Prosthesis Mismatch in Patients With Prosthetic Aortic Valves

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Abstract

Introduction: Patient-prosthesis mismatch (PPM) is considered to occur if a prosthetic heart valve has a high transvalvular pressure gradient and a reduced indexed valve area, despite normally functioning discs. PPM may have clinical and hemodynamic repercussions for patients.

Objective: To analyze the clinical and echocardiographic characteristics of PPM in patients with prosthetic aortic valves.

Methods: Patients aged 18 years or over with a biological or mechanical aortic valve undergoing follow-up since February 2010 were included. PPM was considered mild if the indexed valve area was ≥ 0.85 cm²/m² and severe if ≤ 0.65 cm²/m². Variables were compared between groups with moderate or severe PPM (PPMAO2) and mild PPM (PPMAO1); significant if p<0.05.

Results: Sixty patients (36 women) with prosthetic aortic valves (29 biological and 31 mechanical) were included. PPMAO2 was diagnosed in 12 patients (20%), who had a mean valve area of 0.66 cm²/m² and mean gradient of 24 mm Hg. Functional class II or III was more frequent in the PPMAO2 group (66.7%) than in the PPMAO1 group (20.8%); p<0.001. Left atrial volume (51 ± 16 mL/m² x 40 ± 12 mL/m²; p=0.002) and left ventricular septal and wall thicknesses (10.83 mm x 10 mm; p=0.018) were higher in the PPMAO2 group.

Conclusions: Moderate or severe PPM occurred in 20% of patients. These patients were more symptomatic and had higher left atrial volumes and left ventricular myocardial wall thickness.

Keywords: Aortic Valve; Heart Valve Prosthesis Implantation; Echocardiography.

Introduction

Approximately 90,000 prosthetic valves are implanted each year in the United States, with biological valves predominating over mechanical valves, but a marked increase has been recently observed in percutaneous bioprosthesis implantation worldwide.[1,2] In Brazil, according to the Information Technology Department of the Brazilian Unified Health System (DATASUS for short, in Portuguese), 17.4% of major cardiovascular operations include prosthetic valve implantation.[3] It is known that, after prosthetic valve implantation, patients with significant aortic stenosis progress with clinical and ventricular function improvement and increased survival.[4,5]

Despite improvements in hemodynamic performance, durability, and surgical implantation techniques and reduction in thrombogenicity, prosthetic heart valves are still subject to complications or dysfunctions.[6] Another condition that can occur with prosthetic heart valves is patient-prosthesis mismatch (PPM), which is characterized by high transvalvular pressure gradients and a reduced valve area indexed to the patient's body surface area, despite normally functioning discs.[1,7] The diagnosis considers both the expected valve hemodynamic performance and the patient's cardiac output needs, largely related to body surface area.[8] An imbalance between these two variables determines the high transvalvular pressure gradients that correspond to the initial expression of PPM.[6,9]

PPM was first described and characterized in 1978 by Rahimtoola.[10] Several studies have been developed with the purpose of better understanding hemodynamics and clinical consequences.[11-13] Currently, for the diagnosis of PPM in aortic valves, it is recommended that the effective valve area be calculated using Doppler echocardiography with the continuity equation.[14,15] PPM has been associated with increased short- and long-term mortality after aortic valve replacement, reduced functional capacity, increased hospitalization for heart failure, and decreased prosthetic valve durability.[16] In a meta-analysis of 34 studies including 27,186 patients and 133,141 patient-years with prosthetic

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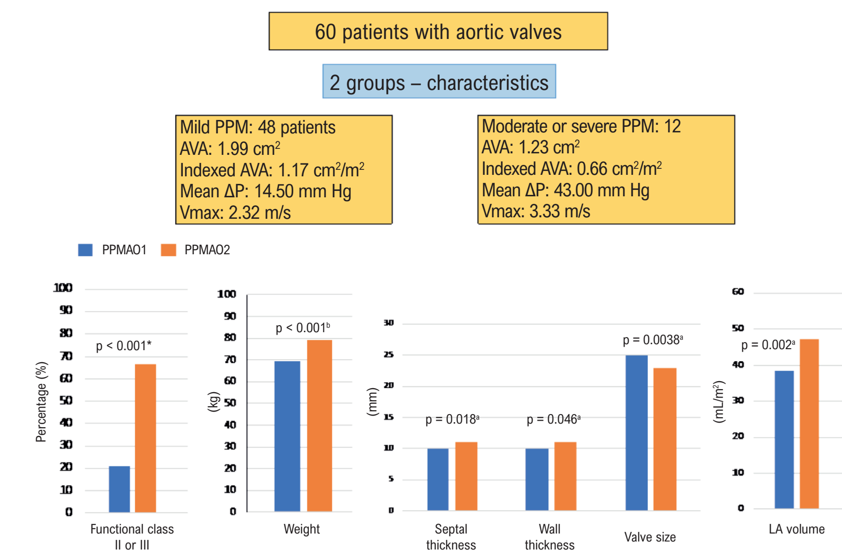
Central Illustration: Clinical and Echocardiographic Aspects of Patient-Prosthesis Mismatch in Patients With Prosthetic Aortic Valves



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*The figure summarizes the hemodynamic characteristics of the patients' prosthetic valves (text boxes) and the main results of the study (bar graphs). The 60 patients were divided into two groups according to the hemodynamic pattern of the prosthetic aortic valves. One group with mild patient-prosthesis mismatch (PPMAO1) and the other with moderate or severe patient-prosthesis mismatch (PPMAO2); AVA: aortic valve area; ΔP: transvalvular systolic pressure gradient; Vmax: maximal transvalvular systolic velocity; LA: left atrium; p: statistical significance of the test; a: Mann-Whitney test; b: Student's t-test; *: Fisher's exact test. The values of the variables correspond to the mean or median depending on the normal or non-normal distribution of the variable and the test performed.*

aortic valves, moderate and severe PPM increased all-cause mortality (hazard ratio, 1.19 and 1.84, respectively) and overall cardiovascular mortality (hazard ratio, 1.32 and 6.46, respectively).[17]

In Brazil, several valve types and designs are used in patients with severe valvular disease requiring surgery. There are imported prostheses, but there are also national prostheses, mainly biological valves. However, few studies in Brazil have addressed PPM.[18] The 2020 guidelines for valvular heart diseases of the Brazilian Society of Cardiology[19] mention PPM as a cause of prosthetic valve dysfunction, but they do not reliably and objectively describe the diagnostic aspects and possible measures to reduce or avoid its incidence.[19] Conversely, a document published by the European Society of Cardiovascular Imaging, in collaboration with the Brazilian Department of Cardiovascular Imaging, suggests a flowchart similar to that of other international associations but does not detail the method to obtain the valve area for the diagnosis of PPM.[20]

Therefore, the present study aimed to analyze the clinical and echocardiographic characteristics of PPM in a cohort of patients with prosthetic aortic valves.

Methods

Patients of either sex aged 18 years or over with a biological or mechanical aortic valve undergoing outpatient follow-up since February 2010 were included, regardless of the number of previous operations. These patients had high transvalvular gradients previously defined by postoperative echocardiogram and had been attending regular outpatient follow-up visits with clinical and valve data available. Patients with previously confirmed prosthetic valve dysfunction or whose previous clinical and echocardiographic data did not allow the assessment of valve hemodynamics were excluded. The study was approved by the institution's Research Ethics Committee (CAAE: 65219317.4.0000.5505).

Clinical evaluation was performed during an outpatient visit along with a review of the patient's electronic or paper medical records if available. The following data were collected and recorded: sex; age; body surface area; body mass index (BMI); medical history, such as valvular disease leading to prosthetic valve implantation, hypertension, diabetes mellitus, and atrial fibrillation; and New York Heart Association (NYHA) functional class. The predicted effective valve area was obtained based on the type, brand, and size of the prosthetic valve reported in the patients' medical records, according to data from the literature or the manufacturer.

Doppler echocardiography

Echocardiography was performed using a Vivid 7 device (General Electric) equipped with 1- to 5-MHz transducers.

Simultaneous electrocardiogram derivation was used. The imaging planes used and the assessment of all 4 cardiac chambers, including left ventricular septal and posterior wall thickness, as well as the analysis of the systolic function parameters of the ventricles and native valves followed the recent recommendations of the American Society of Echocardiography.[21]

The prosthetic valves were analyzed based on morphological characteristics and leaflet or disc motion. The prosthetic valve area was calculated using the continuity equation and expressed as absolute values (cm^2) and indexed values (cm^2/m^2). Maximal and mean pressure gradients and maximal flow velocity across the prosthetic valve were determined with continuous-wave Doppler. If present, prosthetic valve regurgitation was analyzed using the methods recommended in the guidelines of the American Society of Echocardiography.[22] Inferior vena cava diameter (cm) and maximal tricuspid regurgitation velocity (m/s) were also analyzed.

PPM was suspected if the mean pressure gradient across the aortic valve on prior routine Doppler echocardiography was greater than 20 mm Hg in the absence of structural abnormalities or leaflet or disc motion and more than mild regurgitation. In patients with suspected PPM, another echocardiogram was performed to determine all the parameters needed to confirm or exclude the diagnosis. The diagnosis of PPM was based on the determination of the valve area indexed to the patient's body surface area (cm^2/m^2). PPM was considered mild if the indexed valve area was above 0.85 cm^2/m^2, moderate if between 0.65 and 0.85 cm^2/m^2, and severe if less than or equal to 0.65 cm^2/m^2. For comparison purposes, patients were divided into two groups: PPMAO1 group, patients with mild PPM; and PPMAO2 group, patients with moderate or severe PPM.

Statistical analysis

The data were presented with descriptive analysis according to the normal or non-normal distribution of the variables. Statistical analysis was initially performed using summary measures: mean, median, minimum and maximum values, standard deviation (SD), and absolute and relative frequencies (percentage). Normally distributed continuous variables were presented as mean (SD), whereas non-normally distributed continuous variables were presented as median and interquartile range (IQR). The Shapiro-Wilk test was used to assess the normality of the data. The Mann-Whitney test, Student's t-test for independent samples, Pearson's chi-square test, and extension of Fisher's exact test were used for inferential analyses to compare the data according to the PPM classification.[23] The significance level was set at 5% for all comparisons. Statistical analyses were performed in SPSS version 24 and R version 3.6.3.[23]

Results

Sixty patients with prosthetic aortic valves were included, 36 of whom were women (60%); 21 patients (35%) were older than 60 years, 54 (90%) had hypertension, 12 (20%) had diabetes mellitus, and 8 (13%) had chronic kidney disease. According to the adopted criteria, moderate or severe PPM was diagnosed in 12 patients (20%) (PPMAO2 group). As expected, patients in the PPMAO2 group had significantly smaller absolute valve area and indexed valve area and significantly higher maximal transvalvular systolic velocity and maximal and mean transvalvular pressure gradients than those in the PPMAO1 group (Table 1).

At the time of the echocardiogram, the 12 patients in the PPMAO2 group had significantly higher weight, height, and BMI than those in the PPMAO1 group, but the two groups did not differ significantly in age or body surface area (Table 2).

The valve dysfunction before surgery or implantation underlying the indication for surgery was aortic stenosis in 46 (76,6%) patients, aortic insufficiency in 10 (16,7%), and double aortic valve dysfunction in 4 (6,6%). The cause of aortic valve dysfunction was degenerative (calcification) in 36 patients (60%), sequelae of rheumatic fever in 18 (30%), infective endocarditis in 4 (6.7%), and bicuspid aortic valve in 2 (3.3%). Among associated valvular diseases, 14 (23.3%) were mild mitral insufficiency, 4 (6.7%) were moderate mitral insufficiency (2 in the PPMAO2 group), and 18 (30%) were mild tricuspid insufficiency; 2 patients also had an ascending aorta tube graft that was implanted at the time of valve replacement surgery. There was no significant difference in the proportion of pure aortic stenosis before surgery between the PPMAO1 group (37 patients, 77.1%) and the PPMAO2 group (9 patients, 75.0%) ($p=0.856$; Fisher's exact test). Seven patients (11.7%) had a prosthetic valve in the mitral position; 2 of them were in the PPMAO2 group.

Of the 60 prosthetic aortic valves, 31 were mechanical and 29 were biological, 1 of which was implanted percutaneously. There was no significant difference in the proportion of mechanical valves between the groups; there were 27 mechanical valves (56.3%) in the PPMAO1 group and 8 (66%) in the PPMAO2 group ($p=0.552$; Fisher's exact test). There was also no significant difference in the proportion of biological valves between the PPMAO1 (41.4%) and PPMAO2 (33.3%) groups ($p=0.651$; Fisher's exact test). Regardless of prosthetic valve type, the size of the valves implanted in patients in the PPMAO2 group (median: 23 mm; IQR: 23.4-26.7 mm) was significantly smaller ($p=0.0038$; Mann-Whitney test) than that in patients in the PPMAO1 group (median: 25 mm; IQR: 22.2-24.7 mm). The median predicted effective valve area was 1.68 cm^2 (IQR: 1.79-2.08 cm^2) in the PPMAO2 group and 2.03 cm^2 (IQR: 1.54-1.89 cm^2) in the PPMAO1 group ($p=0.0013$; Mann-Whitney test).

NYHA functional class was I in 42 patients (70%), II in 13 (21.7%), and III in 5 (8.3%); no patient was in functional class IV. The proportion of patients with NYHA functional class II or III in the PPMAO2 group (8 patients; 66.7%) was significantly higher than that in the PPMAO1 group (10 patients; 20.8%) ($p<0.001$; Fisher's exact test). Atrial fibrillation was present in 7 patients (14.6%) in the PPMAO1 group and in 2 patients (16.7%) in the PPMAO2 group ($p=0.562$; Fisher's exact test).

Table 1 – Comparison of hemodynamic measurements in prosthetic aortic valves between patients with patient-prosthesis mismatch (PPM) classified as mild (PPMAO1) and moderate or severe (PPMAO2)

MEASUREMENT		PPMAO1	PPMAO2	p
	N	48	12	
PAV area (cm^2)	Mean ± SD	1.99 ± 0.32	1.23 ± 0.34	<0.001[b]
Indexed PAV area (cm^2/m^2)	Mean ± SD	1.17 ± 0.21	0.66 ± 0.18	<0.001[b]
Maximal ΔP (mm Hg)	Median	27.00	43.00	
	IQR	23.4 – 47.2	23.6 – 51.1	0.001[a]
Mean ΔP (mm Hg)	Median	14.50	23.50	0.002[a]
	IQR	9.4 – 31.2	16.4 – 31.4	
PAV Vmax (m/s)	Median	2.32	3.33	<0.001[a]
	IQR	1.46 – 2.53	1.46–3.84	

[a]Mann-Whitney test; [b]Student's t-test for independent samples; ΔP: pressure gradient; N: number of patients (the same for all measurements); IQR: interquartile range; p: p-value of statistical comparison between groups; PAV: prosthetic aortic valve; Vmax: maximal flow velocity.

Table 2 – Anthropometric characteristics of patients with patient-prosthesis mismatch (PPM) classified as mild (PPMAO1) and moderate or severe (PPMAO2) in prosthetic aortic valves

Variable		PPMAO1	PPMAO2	p
	N	48	12	
Age (years)	Median	60.23	66.51	0.456[a]
	IQR	40 – 74.5	47.4–82.4	
Weight (kg)	Mean ± SD	69.45 ± 4.78	79.23 ± 8.91	<0.001[b]
BMI (kg/m^2)	Median	26.71	31.45	<0.001[a]
	IQR	30.14 – 32.8	31.4 – 35.6	
BSA (m^2)	Median	1.75	1.89	0.056[a]
	IQR	1.73 – 1.91	1.98 – 2.08	
Height (cm)	Mean ± SD	176 ± 6.45	181 ± 5.78	0.049[b]

Mann-Whitney test, [b]Student's t-test for independent samples, BSA: body surface area; BMI: body mass index; IQR: interquartile range; N: number of patients (the same for all variables); p: p-value of statistical comparison; SD: standard deviation.

The indexed left atrial volume was significantly higher in patients with moderate or severe PPM than in those with mild PPM. There was no significant difference in the values of end-diastolic and end-systolic diameters and of left ventricular mass index and ejection fraction between the two groups, but myocardial wall thickness was significantly higher in patients in the PPMAO2 group than in the PPMAO1 group (Table 3). Measurements of the right chambers were not significantly different between the two groups (Table 3). Maximal tricuspid regurgitation velocity was not significantly different between patients in the PPMAO1 group (mean: 2.61 m/s; SD: 0.48 m/s) and those in the PPMAO2 group (mean: 2.38 m/s; SD: 0.48 m/s). The Central Figure summarizes the main results of the study.

Discussion

The present study analyzed PPM, clinical impairment, and structural and functional features on echocardiography in patients with prosthetic aortic valves. As expected, due to the division of patients, there was a significant difference in valve area, indexed valve area, transvalvular gradients, and maximal systolic velocity between the two groups. The values of these variables in the present study are consistent with those reported in previous studies. The mean maximal transvalvular systolic velocity in the present study was 3.21 m/s, higher than that in the study conducted by Zorn et al, who found a value of 2.88 m/s in their sample.[24] The mean gradient of patients with moderate or severe PPM in the present study was 24.2 mm Hg, similar to that found by Echahidi et al, who described a mean of 25 mm Hg in patients with severe PPM; in the same study, in patients with moderate PPM, the mean gradient was 19 mm Hg.[25] In the study by Otto et al, the mean gradient was 28 mm Hg in patients with severe aortic PPM and 21 mm Hg in patients with moderate PPM.[18]

PPM was observed in 20% of the prosthetic aortic valves in the present study. Similar findings were observed in previous studies, such as those by Dayan et al and

Bonderman et al, who also observed 20% of PPM in patients with prosthetic aortic valves.[26,27] Kohsaka et al found 11% of severe PPM in a sample of 469 patients; it is worth noting that PPM was mainly found in mechanical aortic valves of sizes 19 to 23.[28] The rate of PPM diagnoses could decrease with reclassification based on patients' BMI, but this has not been observed in most published studies.[20] It is worth noting that 8 patients in the PPMAO2 group had a BMI greater than 30 mg/kg^2. This variable was significantly higher in the PPMAO2 group, but the aim of the study was not to analyze this other classification, but rather the preestablished criteria for determining PPM and its severity.

In the present study, PPM was diagnosed based on the measurement of the effective valve area by Doppler echocardiography corrected for body surface area in patients with prosthetic aortic valves without evidence of dysfunction. Although the absolute value of the valve area can be used, the valve area indexed to the patient's body surface area appears to have greater sensitivity and specificity as reported by Hanyama et al.[29]

The mean indexed valve area in patients with moderate or severe aortic PPM was 0.66 cm^2/m^2. Echahidi et al found an indexed valve area of 0.53 cm^2/m^2 in patients with severe PPM and 0.73 cm^2/m^2 in patients with moderate PPM.[25] Zorn et al identified a mean valve area of 0.42 cm^2/m^2 in patients with severe PPM.[24] Otto et al identified a mean of 0.51 cm^2/m^2 in patients with severe PPM and 0.73 cm^2/m^2 in patients with moderate PPM.[18] The indexed valve area in the present study was, therefore, slightly higher than that reported in previous studies, possibly due to the inclusion of moderate and severe PPM in the same group.

The main parameters that determine PPM are the effective valve area and the patient's need for greater cardiac output, usually related to the patient's size. In the present study, there was no difference in the proportion of mechanical and biological valves between the two groups. However, both the size of the valves used and the effective valve area predicted before surgery were significantly smaller in patients with moderate or severe PPM than in those with mild PPM. Body surface area was not significantly different between the groups. Considering that the diagnosis of PPM is based on the effective valve area indexed to the patient's body surface area, this finding differs from that of previous studies reporting that patients with severe PPM have a greater body surface area.[30,31]

Table 3 – Comparison of echocardiographic measurements in left and right chambers between patients with patient-prosthesis mismatch (PPM) classified as mild (PPMAO1) and moderate or severe (PPMAO2) in prosthetic aortic valves

MEASUREMENT		PPMAO1	PPMAO2	p
	N	48	12	
iLAV (mL/m^2)	Median	38.40	47.40	0.002[a]
	IQR	29.6 – 84.5	43.4 – 87.6	
LVDd (mm)	Mean ± SD	50.42 ± 5.95	52.08 ± 5.16	0.378[b]
LVDs (mm)	Median	32.00	34.00	0.394[a]
	IQR	29.5 – 51.4	29.4 – 41.4	
IVST (mm)	Median	10.00	11.00	0.018[a]
	IQR	9 – 14	9 – 13	
WT (mm)	Median	10.00	11.00	0.046[a]
	IQR	10 – 12	8 – 12	
MI (g/m^2)	Mean ± SD	103.98 ± 24.89	121.33 ± 37.91	0.058[b]
LVEF (%)	Median	60.00	56.00	0.111[a]
	IQR	35 – 61.4	41.4 – 58.7	
iRAV (mL/m^2)	Median	20.00	22.00	0.236[a]
	IQR	19.8 – 31.7	17.8 – 33.2	
RVDd (mm)	Median	23.00	25.50	0.009[a]
	IQR	21.2 – 30.6	24.5 – 31.4	
PCRVA (%)	Mean ± SD	42.96 ± 8.42	46.57 ± 6.72	0.175[b]
TAPSE (mm)	Mean ± SD	19.50 ± 2.90	20.17 ± 2.66	0.472[b]
TAV (cm/s)	Mean ± SD	11.16 ± 1.57	11.26 ± 1.49	0.846[b]

[a]Mann-Whitney test, [b]Student's t-test for independent samples. Dd: end-diastolic diameter; Ds: end-systolic diameter; WT: wall thickness; IVST: interventricular septal thickness; TAPSE: tricuspid annular plane systolic excursion; EF: ejection fraction; MI: mass index; IQR: interquartile range; N: number of patients (the same for all analyses); p: p-value of statistical comparison; iRAV: indexed right atrial volume; iLAV: indexed left atrial volume; RV: right ventricle; LV: left ventricle; TAV: tricuspid annular velocity; PCRVA: percentage change in right ventricular area; LVEF: Left ventricular ejection fraction.

It is possible that the smaller size of the valves implanted in patients with moderate or severe PPM may have had a greater impact on the diagnosis of PPM. However, as the comparison of body surface area had a p-value of 0.056 and weight, height and BMI were significantly higher in the group with moderate or severe PPM, a possible impact of this variable on the rate of diagnoses cannot be ruled out.

Rheumatic disease as the cause of native valve disease leading to valve replacement had a considerable proportion of 30%, but less than that of degenerative cause. In the study by Otto et al, the prevalence of rheumatic disease in patients with severe PPM was 43.1%, while in the Brazilian study by Oliveira et al it was 29.7%.[3,18] The incidence of rheumatic disease remains high in Brazil, so a high proportion in relation to degenerative disease was expected compared with studies conducted in high-income countries, as shown by Mothy et al.[32]

The proportion of NYHA functional class II or III was significantly higher in patients with moderate or severe PPM than in those with mild PPM. These data contrast with those described by Vicchio et al, who administered a questionnaire to patients with PPM but did not identify a significant difference in functional class in those with severe PPM.[33] Atrial fibrillation was uncommon in the present study, with no significant difference in its proportion between the groups.

Patients with moderate or severe PPM had significantly higher left ventricular septal and myocardial wall thicknesses than those with mild PPM. However, this was not accompanied by a significant difference in the left ventricular mass index. The left ventricular mass index is the mass calculated based on left ventricular wall thicknesses and end-diastolic diameter. The value is corrected for body surface area and defines the existence of ventricular hypertrophy on echocardiogram. Although we cannot state that patients with moderate to severe PPM had left ventricular hypertrophy, the greater myocardial wall thickness suggests a possible consequence.

The absence of a difference in left ventricular end-diastolic and end-systolic diameters between the two patient groups in the present study was similar to that of the study by Zorn et al.[24] The indexed left atrial volume was higher in patients with moderate or severe PPM. A contributing factor could be the association of mitral valve disease prior to aortic valve surgery. However, 3 of the 7 patients with a prosthetic valve in the mitral position due to significant previous mitral valve disease were in the PPMAO2 group, whereas 2 of the 4 patients with moderate mitral insufficiency were in the PPMAO2 group. Another contributing factor could be left ventricular diastolic dysfunction as a result of the greater pressure gradient in the prosthetic aortic valve and the greater myocardial wall thickness. However, left ventricular diastolic function was not analyzed in the present study.

This study has limitations that need to be addressed. As it was a retrospective cohort analysis, the echocardiograms that defined PPM were performed late in relation to the time of surgery. To better characterize PPM, echocardiograms should have been performed a few weeks after patients were discharged from the hospital. Some patients in the study had transvalvular systolic velocity greater than 3.0 m/s. The criteria recommended by the 2009 American Society of Echocardiography guidelines could have been applied to this group,[23] which include measurement of acceleration time and analysis of the contour of the velocity curve of continuous-wave Doppler. This analysis was not included in the present study, because patients with a possible diagnosis of prosthetic valve dysfunction had already been excluded from the study. The relatively small sample size was also a limitation.

Conclusion

The rate of moderate or severe PPM in aortic valves was 20%. There was no impact of valve type (biological or mechanical) on the proportion of PPM, but valve size and the effective valve area predicted before surgery were smaller in patients with moderate or severe PPM and may have been determining factors.

Patients with moderate or severe PPM were more symptomatic than those with mild PPM, despite no significant differences in the proportion of atrial fibrillation or left ventricular ejection fraction. The indexed left atrial volume and left ventricular myocardial wall thickness were the echocardiographic variables with significantly higher values in patients with moderate or severe PPM.

Author Contributions

Conception and design of the research: Bispo IGA, Hemerly DFA, Kyiose AT, Moises VA; Acquisition of data, analysis and interpretation of the data, statistical analysis and writing of the manuscript: Bispo IGA, Moises VA; critical revision of the manuscript for intellectual content: Bispo IGA, Hemerly DFA, Fischer CH, Moises VA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Universidade Federal de São Paulo under the protocol number 20/4820 CAAE 65211317400005505. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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Review Article

Coronary CT Angiography in Asymptomatic Patients: Is There Evidence For Using It?

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Abstract

Cardiovascular diseases are the leading cause of death worldwide, and their clinical management is complicated by 3 main pathophysiological factors: a) a long onset period, often decades before a clinical event; b) a silent clinical course; and c) a multifactorial and heterogeneous pathogenesis among different population subgroups. Coronary CT angiography is the best available tool for diagnosing and phenotyping coronary artery disease, whether obstructive or non-obstructive. This allows early diagnosis and monitoring of the disease, which is essential for deciding who should be treated, determining the therapeutic approach, and for better patient adherence to clinical treatment. Early and accurate diagnosis generally results in better clinical outcomes.

"A straight path never leads anywhere other than the goal."

Andre Gide

Clinical case

A 48-year-old woman arrived for a routine check-up with no clinical complaints, but reported being worried because her mother (who was a smoker) had had a myocardial infarction at the age of 63. She had controlled hypertension (using 1 medication), was overweight (body mass index = 27), and was sedentary (but could climb 4 flights of stairs without stopping). The results of the physical examination were normal, as were those of a resting electrocardiogram. Her blood pressure was 118/64 mmHg. Her laboratory tests were all within normal limits. Her total cholesterol was 192 mg/dl; LDL-c: 125 mg/dl; HDL-c: 51 mg/dl; triglycerides: 80 mg/dl. The patient's Framingham score indicated a 2% risk of events in 10 years.

After discussion with the patient, the doctor requested coronary CT angiography (CCTA), which revealed non-calcified plaque with positive remodeling, resulting in 30-40% stenosis of the proximal anterior descending artery. There were no coronary calcifications (calcium score = 0).

In this case, should clinical treatment be initiated considering that the patient's clinical scores indicated low risk? Would CCTA findings help the patient make necessary lifestyle changes? Moreover, should a statin be introduced? If so, for which LDL-c target?

Keywords

Coronary Artery Disease; Computed Tomography Angiography; Asymptomatic Diseases.

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Introduction

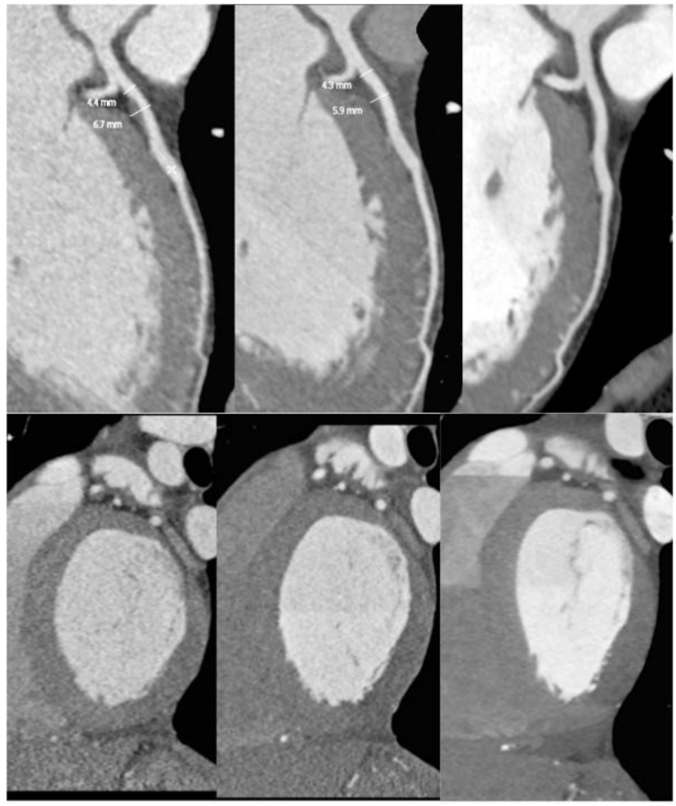
Cardiovascular disease is the leading cause of death worldwide. Although this fact is often repeated, far fewer people are aware that it kills more than the second, third, fourth, fifth, sixth, and seventh leading causes of death combined,[1] having great social and economic impact. Cardiovascular disease involves 3 pathophysiological factors that require more complex management: a) a long onset period, often decades before a clinical event; b) a silent clinical course; and c) a multifactorial and heterogeneous pathogenesis among different population subgroups.

Long onset period, often decades before a clinical event

Coronary artery disease (CAD) has a very early onset, often before the fourth decade of life. Pathology analyses in young adults < 35 years of age who died from trauma have found a > 70% prevalence of subclinical CAD, with a large proportion being obstructive CAD.[2,3] CAD is even present in 1 in 6 adolescents.[4]

Because its onset is so early and it has such a long clinical course, the most effective interventions are changes in patient lifestyle. Specific interventions, which are often expensive or have side effects, are not as effective. For example, consider carriers of PCSK9 gain-of-function mutations. Because it is a gain-of-function mutation in an enzyme that helps eliminate cholesterol, the cholesterol levels of these patients are on average 30% lower than matched controls, a reduction similar to that found in large studies on statins. However, unlike statins, these people are born with the mutation, ie, they spend their entire lives with lower levels of plasma cholesterol, while statins only reduce it after beginning therapy, and this reduction is subject to dosage irregularities inherent to all drugs. As a result, while statins reduce cardiovascular events by up to 30%, mutation carriers have a staggering 90% fewer events than matched controls.[5] This illustrates long-term power to reduce risk factors, in contrast to specific interventions. Graphing an imaginary patient's life, in which time is the abscissa and exposure to modifiable risk factors is the ordinate, the objective would be to reduce the area under the curve as much as possible, as shown in Figure 1.

Central Illustration: Coronary CT Angiography in Asymptomatic Patients: Is There Evidence For Using It?



Arq Bras Cardiol: Imagem cardiovasc. 2023;36(4):e20230091

Serial coronary CT angiography images (from left to right: baseline, 30 months, and 60 months) showing progressive plaque regression in the proximal left anterior descending artery. The upper images are multiplanar reconstructions and the lower images show transverse sections (arrows). The reference luminal diameter remained constant, but the tunica intima diameter decreased between baseline and 30 months, indicating decreased positive remodeling. There was also a progressive reduction in the degree of stenosis and total plaque volume.

Silent clinical course

Non-obstructive CAD causes no symptoms and has no warning signs. Even obstructive lesions (ie, > 50%) are, for the most part, asymptomatic. In addition, the fact that half of myocardial infarction patients never have suggestive symptoms before the event shows that a lack of symptoms does not indicate an absence of disease. On the contrary, when symptoms appear, they are a late sign, indicating an advanced stage of the disease. Between 50%–70% of young adults who have myocardial infarctions did not meet recommendations for statin use before the event.[6] In addition to a lack of symptoms, remaining undiagnosed also prevents therapy before an infarction.

Multifactorial and heterogeneous pathogenesis occurs among different population subgroups

Diseases such as mesothelioma, in which there is a strong association between exposure to agent (ie, asbestos) and the disease, allow for simple and emphatic recommendations. But this is definitely not the case with cardiovascular diseases, which have an extremely varied pathophysiology, a variety of risk factors with weak causal association, as well as heterogeneous heredity.

A study revealed that more than 400 genetic polymorphisms are associated with CAD,[7] possibly due to different degrees of penetrance for each variation, as well as epigenetic variations. More than 200 risk factors for CAD have been reported in the literature, although for the vast majority, despite being associated, the causal relationship is weak, ie, their relative importance in the development of CAD is low, except in rare conditions, such as some variants of familial hypercholesterolemia or specific genes of great penetration and pathogenicity. Additionally, different population groups are exposed to different environmental factors, and genotype/phenotype interactions vary. This is one reason why clinical scores have limited performance and high measurement variability, both for diagnosing obstructive CAD and predicting events.[8,9]

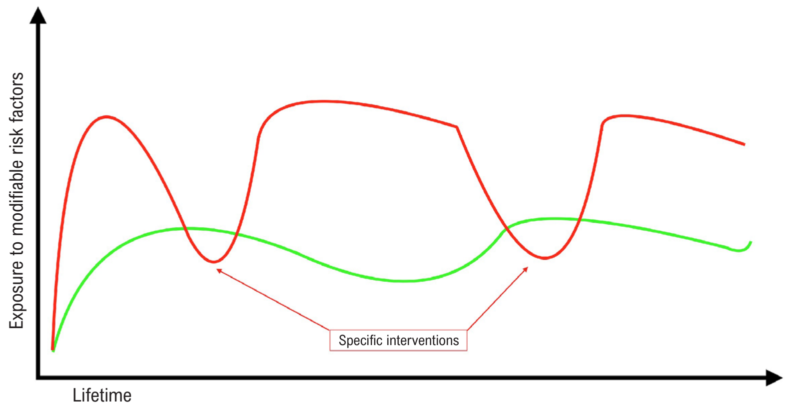


Figure 1 – *Model illustrating exposure to modifiable risk factors throughout life in 2 imaginary cases. The green line represents an individual who successfully minimizes exposure to risk factors, while the red line represents an individual with greater exposure who, at certain points, undergoes specific interventions. The objective is to obtain the smallest possible area under the curve, which is generally achieved in long-term rather than short-term interventions*

Furthermore, scores place great weight on age, since most events occur in older adults. However, as a result we lose the opportunity to diagnose atherosclerosis, change habits, and begin therapy in young people. If the goal is to reduce the area under the curve for risk factors throughout life, early diagnosis is essential.

Calcium score

The calcium score is a useful way of stratifying the risk of cardiovascular events and determining the therapeutic approach. The examination is simple to perform (although it requires specific tomography with ECG synchronization) and involves simple image reading and interpretation. Moreover, it does not require intravenous contrast or beta-blockers. The calcium score can independently predict cardiovascular events better than clinical risk factors or carotid intima-media thickness.[10] However, since it only detects the calcified part of the atherosclerotic plaque, positive results (above a discretionary cut-off point, most often 100 Agatston units) can only indicate preventive therapies. However, low calcium scores do not exclude coronary atherosclerosis, since non-calcified plaque is prevalent, especially in younger patients, who could derive the greatest long-term benefit from preventive measures. Perhaps because it does not exclude CAD, the Multi-Ethnic Study of Atherosclerosis cohort found that one-third of cardiovascular events occurred in patients with a calcium score of 0.[11] In the Coronary Artery Calcium Consortium cohort, 43% of cardiovascular deaths occurred in people without coronary calcium.[12] Aside from calcification being linked to age and the fact that its absence does not exclude CAD, the calcium score is not useful in longitudinal CAD assessment, since statin use may increase scores by increasing the calcified portion and decreasing the non-calcified portion of plaque.[13] The approximate 15% variability in measurements across 2 scans makes analysis of the clinical course problematic.[14,15]

CCTA

CCTA allows non-invasive detection of coronary atherosclerosis, accurately quantifying the degree of stenosis and identifying morphological markers of higher risk, such as positive remodeling, lipid content, punctate calcifications, and the "napkin ring" sign.[16] Currently CCTA is the first test performed when investigating symptoms suggestive of obstructive CAD. Since its sensitivity is > 95%, it is increasingly seen as a gatekeeper for invasive catheterization, which is especially relevant, considering that two-thirds of catheterizations do not involve obstructive CAD.[17] Symptoms suggestive of obstructive CAD do not interfere with the prognostic power of CCTA, with symptomatic and asymptomatic patients having the same event rate according to test results.[18]

CCTA is superior to the calcium score for determining prognosis in asymptomatic patients,[19] even in a subgroup of older adults[20] and people with diabetes.[21] In approximately one-third of asymptomatic patients without coronary calcification, CAD is confirmed by CCTA.[22]

Although investigating obstructive CAD is the main use of CCTA, being recommended by national and international guidelines, this may not be its most important role. CCTA is revolutionizing cardiology due to its ability to detect non-obstructive CAD, or in earlier stages of the disease, when long-term therapeutic results are more favorable, it can motivate patients to make difficult lifestyle changes.

CCTA in non-obstructive CAD.

CCTA is highly sensitive for detecting non-obstructive CAD, having good correlation with invasive measurements such as intravascular ultrasound and optical coherence tomography.[23] Plaque composition can be inferred non-invasively, identifying markers of cardiovascular event risk, such as positive remodeling (plaque growth towards the tunica externa is related to greater plaque inflammation), foci of hypodensity (fat has a low density in CT, therefore, foci with a density < 30 HU are correlated with a higher lipid load).[24] Furthermore, the atherosclerotic burden can be assessed subjectively by visual analysis and reported using indices, such as the segment involvement score or the segment stenosis score, which are associated with cardiovascular events independently of calcium score or risk factors. More recently, semi-automated tools have been developed for coronary segmentation and atherosclerosis quantification, determining the percentage of calcified and non-calcified plaque, and identifying plaque with low density and positive remodeling.[25] Such tools are promising, although still little used in clinical practice due to the laboriousness of editing coronary contours.

Disease monitoring

Returning to the initially-described patient case, the physician decided to prescribe a statin (targeting LDL-c < 70 mg/dl) and outlined an intensive weight loss and exercise program, to which the patient adhered. The central figure details this patient's case, including 3 serial CCTAs (T = 0 [baseline]; T = 30 months, and T = 60 months) that showed progressive reduction of the arterial lesion. By the third examination (at 60 months), the lesion was virtually undetectable. Early detection of the disease allowed aggressive clinical intervention, which resulted in atherosclerosis regression.

Likewise, if subsequent CCTAs had shown disease progression, a frank conversation would have been necessary with the patient to show the therapeutic failure of current measures and the need for new course of action.

Since the disease is insidious and its clinical course is long, asymptomatic, and has a heterogeneous pathophysiology, the ability to monitoring atherosclerosis would be a powerful weapon for both doctors and patients.

Longitudinal studies involving CCTA have shown that cholesterol and glucose control result in low or no progression of the total coronary atherosclerotic burden, in addition to beneficial changes in plaque morphology, with a larger calcified component and an unchanged or reduced non-calcified component.[26,27]

When CCTA is normal

Normal CCTA results show an absence of plaque (calcified or non-calcified). This is valuable information, since the rate of cardiovascular events in people with normal CCTA results is extremely low (less than 0.1%/year), and remains low for ≥ 5 years (most likely for 10 years). Few therapies are cost-effective in this group of people. Obviously, healthy lifestyles should be encouraged, but statins should probably not be used, since to prevent a cardiovascular event the number needed to treat is prohibitively high.[28] Thus, an examination every 10 years might save the high long-term cost of continuous drug therapy.

Risks of CCTA

With current technology, the radiation dose from CCTA is similar to that of a chest CT (2–5 mSv). The biological risks arising from exposure to this type of radiation are uncertain, being based on theoretical calculations rather than empirical data. Further discussion is beyond the scope of this article, but, if there is a risk, it is very low.

The rate of severe allergic reactions to the intravenous iodinated contrast media used in CCTA is 1 in 17,000 injections. Contrast nephrotoxicity has been re-examined in light of new evidence: CT with intravenous contrast media was compared to CT without it. Rather than comparing renal function before and after applying contrast media, large new studies of more than 20,000 patients have compared those who underwent CT scans who did received contrast media with controls who did not. These studies found no post-examination differences in renal function between the groups, ie, nephrotoxicity could not be attributed to the contrast medium.[29,30]

Conclusion

Imaging screening for breast cancer, colon cancer, lung cancer, etc. is performed routinely and is recommended by large international societies. However, these diseases kill only a small fraction of those who die from coronary heart disease. The purpose of screening is early disease detection so that therapy can begin sooner, more assertively, and more effectively. Screening programs for any disease involve challenges related to selecting the population for screening, determining how to use the results, and documenting that the treatment strategy is associated with fewer events and improved prognosis, in addition to the program's costs and a number of other important issues. CAD, the leading cause of death worldwide, has an early onset, a long clinical course, and involves great pathophysiological heterogeneity. However, there are effective therapies for CAD. Thus, screening should be considered in light of these facts. CCTA is currently the best available tool for this purpose.

Author Contributions

Conception and design of the research; acquisition of data; analysis and interpretation of the data; statistical analysis; writing of the manuscript; critical revision of the manuscript for intellectual content: Gottlieb I.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Review Article

Use of Three-Dimensional Echocardiography in the Analysis of Ventricular Function in Chagas Disease

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Abstract

Chagas disease is recognized as a global public health issue, capable of causing cardiac, digestive, and neurological manifestations. The echocardiogram is a fundamental complementary exam in assessing patients with cardiac involvement, evaluating various parameters of cardiac structure and function. This review aims to discuss the use of three-dimensional echocardiography in analyzing ventricular function in patients with Chagas disease.

Introduction

Chagas disease, caused by the protozoan *T. cruzi*, is mainly transmitted by vectors, through the inoculation into the skin from feces of triatomines that have been previously infected after sucking the blood of contaminated people or animals. It can also be transmitted orally, transplacentally, by transfusion of blood and blood products, by solid organ transplantation, or by accidents with biological material.[1-3]

It is estimated that approximately 6 to 7 million people are infected worldwide, mainly in Latin American countries. However, in recent years, with the increase in migratory flow from rural to urban areas and from endemic countries to non-endemic countries, this pathology has been recognized as a global public health problem.[3]

Its natural history involves an acute phase, which is not always symptomatic and may last from a few weeks to a few months, and a chronic phase, which can manifest with cardiac, digestive, or neurological impairment. Cardiac involvement represents the most feared manifestation, characterized by complications with high morbidity and mortality, such as heart failure, arrhythmias, and stroke.[1,2,4]

In this scenario, echocardiography is the most commonly used complementary exam for assessment and follow-up of patients with Chagas disease, making it possible to analyze cardiac structure and function, detect intracavitary thrombi, and assess secondary valve involvement.[1,5] In recent years, new techniques, such as three-dimensional (3D) echocardiography and the assessment of myocardial strain using the speckle-tracking method have shown to be promising in the assessment of cardiac mechanics in various clinical scenarios.[6-14]

The objective of this review is to discuss the use of 3D echocardiography in the analysis of ventricular function in patients with Chagas disease.

Keywords

Echocardiography, Three-Dimensional; Chagas Cardiomyopathy; Ventricular Function.

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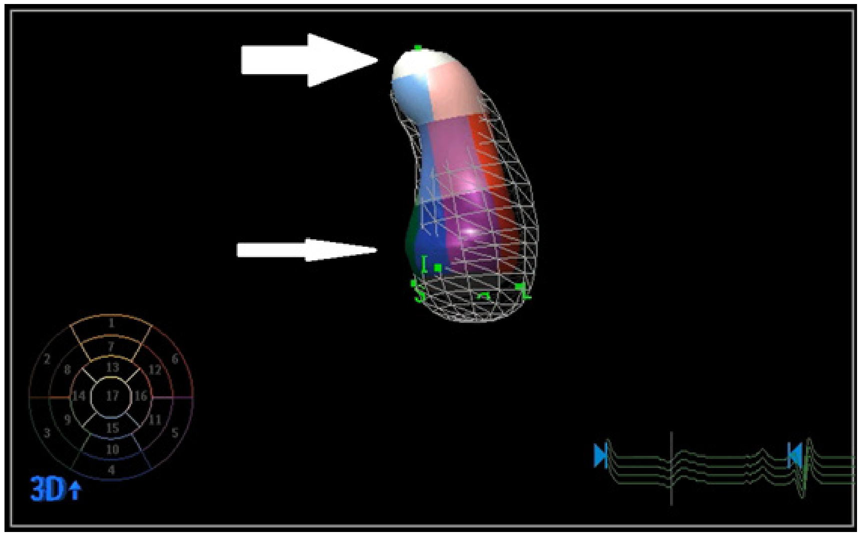
Assessment of left ventricular function by 3D echocardiography

In patients with Chagas disease, segmental involvement is a marker of unfavorable prognosis, which has already been demonstrated in diverse studies. The most characteristic segmental changes occur in the inferior, inferolateral, and apical segments of the left ventricle (LV).[4,6,15-17] These segments are not always adequately assessed on two-dimensional (2D) studies, due to image shortening (which can exclude the apical segments from analysis) or to not including segments in the quantification of global function of Simpson's biplane method (which does not encompass the inferolateral segments).[6] Assessment of left ventricular ejection fraction (LVEF) is one of the main parameters for classification and staging of patients with Chagas disease; therefore, it is recommended to use methods that show high accuracy and reproducibility for estimating LVEF.[1,5,6]

3D echocardiography allows the calculation of ventricular volumes, without requiring estimation using geometric formulas, as is the case with 2D echocardiography.[13] Furthermore, it has demonstrated greater reproducibility and accuracy in calculating volumes compared to cardiac magnetic resonance, and the method is increasingly used in diverse cardiomyopathies.[11,13,18,19] Regarding advantages in relation to other modalities, we can highlight that it the method is less cumbersome, non-invasive, more portable, not related to radiation exposure, and capable of obtaining images with shorter acquisition time and better temporal resolution. However, compared to 2D echocardiography, 3D echocardiography has some limitations related to cost, availability, spatial resolution, and technical difficulties, especially in patients with irregular heart rhythm, such as atrial fibrillation.[10,13,19]

In spite of the greater accuracy of 3D echocardiography in comparison to 2D for analysis of ventricular volumes and LVEF in different clinical scenarios, its prognostic superiority still remains uncertain.[6] In a single-center observational study conducted with 172 patients with ischemic and non-ischemic dilated cardiomyopathy who were candidates for therapy with an implantable cardioverter defibrillator (ICD), 3D LVEF

Central Illustration: Use of Three-Dimensional Echocardiography in the Analysis of Ventricular Function in Chagas Disease



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3D rendering of left ventricular volume during systole in a patient with Chagas disease, showing large apical aneurysm formation (thick arrow), as well as minor basal inferior septal dyskinesia (thin arrow).

proved to be an independent predictor of major arrhythmic events, suggesting that 3D LVEF could change the decision to implant an ICD in this scenario, where up to 20% of patients could be reclassified below the indication threshold for ICD implantation when using the 3D method.[20] A recent single-center study with 725 patients referred for routine echocardiographic evaluation also found that 3D LVEF had an incremental value for predicting composite outcomes, in relation to 2D LVEF. Furthermore, the partition values for mild, moderate, and severe reduction in LV systolic function on the 3D method demonstrated greater discriminatory power for cardiac death than the 2D values, and LV dilation defined by 3D volume showed a greater association with mortality.[21]

In addition to the absolute assessment of ventricular volumes and 3D LVEF, it is also possible to obtain a volume-time curve corresponding to the dynamic changes in LV volume during the cardiac cycle.[22] Analysis of this curve makes it possible to assess new non-invasive parameters of ventricular performance, such as maximum systolic flow, peak flow during early LV filling, and peak flow during left atrial contraction.[23,24] A recently published cross-sectional study, involving 20 patients with Chagas disease and 15 healthy individuals, aimed to characterize these parameters in patients with Chagas disease. In that study, patients with Chagas disease had maximum systolic flow, peak flow during early LV filling, and peak flow during atrial contraction similar to patients in the control group, thus demonstrating, in a non-invasive manner, that the increase in LV end-diastolic volume was the main adaptive mechanism that made it possible to maintain flow and stroke volume in patients with severe LV systolic dysfunction.[25]

Notwithstanding the increasing use of 3D echocardiography to estimate volumes and LVEF in various pathologies, to our knowledge, there are no studies that have specifically evaluated the superiority of 3D echocardiography in relation to 2D echocardiography in patients with Chagas disease, in relation to diagnostic capacity, classification in degrees of left ventricular systolic dysfunction, or in terms of prognosis of major cardiac outcomes, such as ventricular arrhythmias or mortality.

Assessment of right ventricular function by 3D echocardiography

In patients with Chagas disease, involvement of the right ventricle (RV) may occur early in the natural history of the disease, affecting patients with the indeterminate and digestive form of Chagas disease.[1,5,26-29]

Assessment of the RV by 2D echocardiography poses a series of challenges. [13,30,31] The RV has a more complex geometric formation than the LV, with at least 6 distinct morphological regions: inflow tract, outflow tract, apex (septal and free wall regions), and body (septal and free wall regions).[32] Furthermore, the RV has other characteristics that make it difficult to assess using the 2D method, for example, a very thin myocardial wall, the presence of prominent trabeculations, and a greater arrangement of endocardial fibers in the longitudinal direction. For these reasons, 2D echocardiography analysis is performed in an integrated manner, obtaining various geometry and function parameters.[13,30,31,33]

Accordingly, 3D echocardiography has been increasingly used to analyze RV systolic function. By means of specific

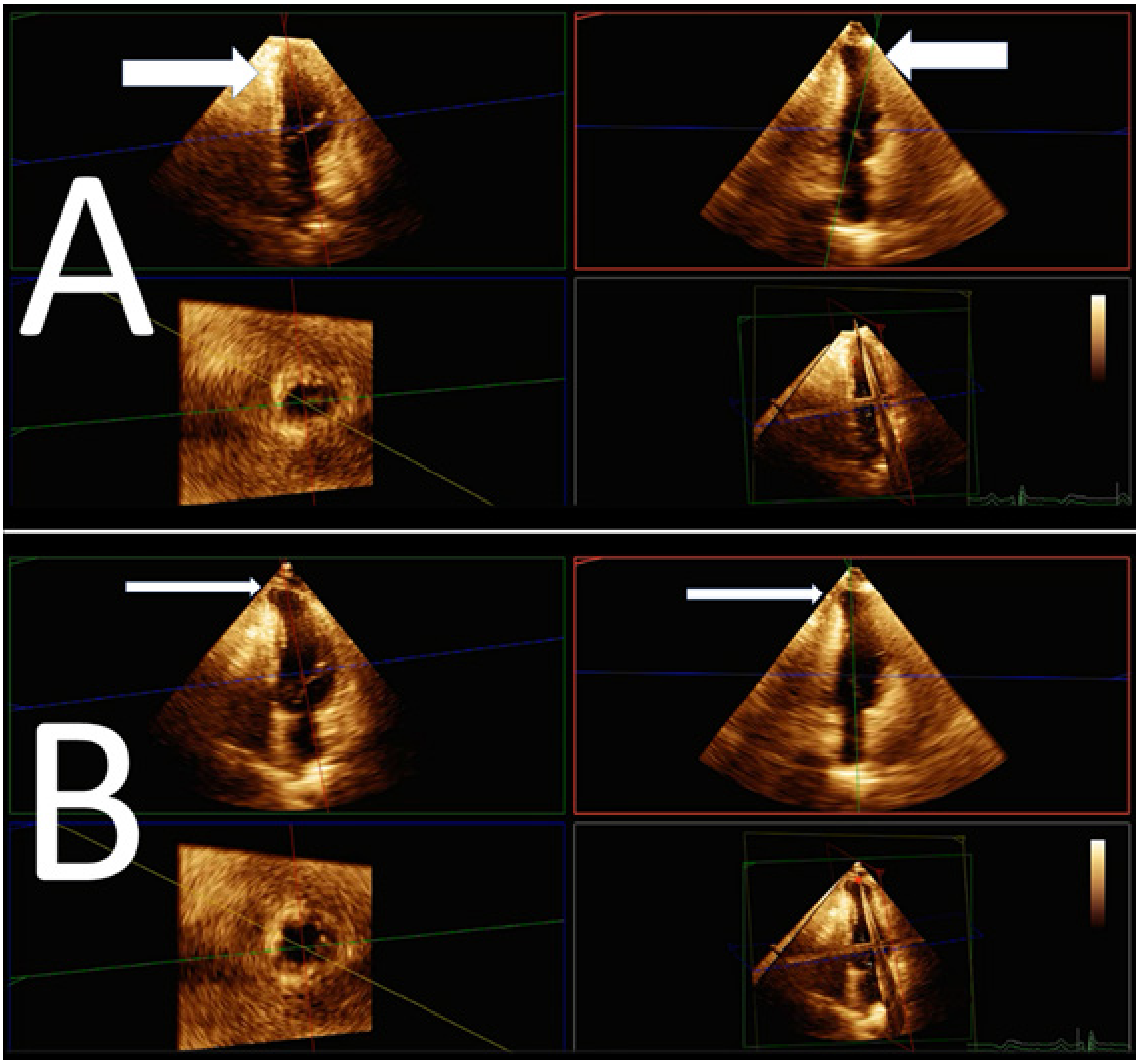

Figure 1 – *Multiplanar images derived from 3-dimensional acquisition in a patient with Chagas disease. Panel A – Notable shortening of the left ventricular apex (thick arrows). In this case, the assessment of ventricular volumes may be inaccurate. Panel B – After adjusting the planes, it was possible to identify the true apex with the inclusion of a large apical aneurysm in the analysis of ventricular volumes (thin arrows).*

software designed to evaluate the RV, it is possible to assess right ventricular ejection fraction (RVEF) and volumes, showing good correlation with cardiac magnetic resonance.[12,34,35]

3D echocardiography can also be used to characterize RV geometry, and it is a promising method for assessing RV remodeling.[32] Previous studies conducted in patients with pulmonary hypertension and tetralogy of Fallot have demonstrated differences in RV remodeling according to the etiology of RV overload.[36,37]

In recent years, some studies have demonstrated the additional prognostic value of analyzing RV systolic function with the use of 2D echocardiography. Nagata et al. found that 3D echocardiography showed high accuracy in relation to cardiac magnetic resonance in the assessment of RVEF and volumes. It was also demonstrated that 3D RVEF was independently associated with cardiac outcomes in diverse etiologies of RV dysfunction.[6] In an observational study including 394 patients with heart disease, Surkova et al. demonstrated that 3D RVEF was associated with mortality ($p < 0.0001$).[38] Kitano et al. published a meta-analysis that demonstrated that RVEF < 45% was associated with worse cardiovascular outcomes, both in individuals with normal LVEF and in those with reduced LVEF. In the same study, subgroup analysis revealed that RVEF had prognostic value both in patients with pulmonary hypertension and in those with cardiovascular disease. Univariable Cox proportional analysis revealed that 3D RVEF was associated with both cardiac death ($p < 0.0001$) and major adverse cardiovascular events ($p < 0.0001$). 3D RVEF remained an independent predictor of cardiac death ($p < 0.0001$) and

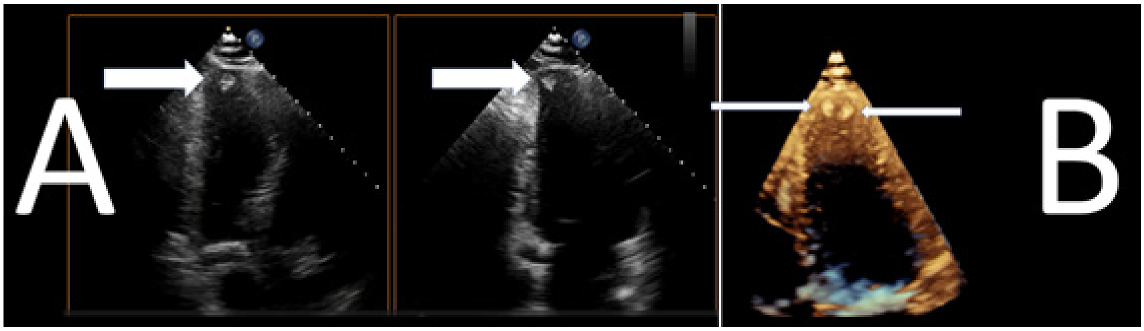

Figure 2 – *Assessment of intracavitary thrombi in a patient with Chagas disease. Panel A – Orthogonal images obtained through simultaneous biplanar evaluation. Panel B – 3D image showing 2 apical thrombi.*

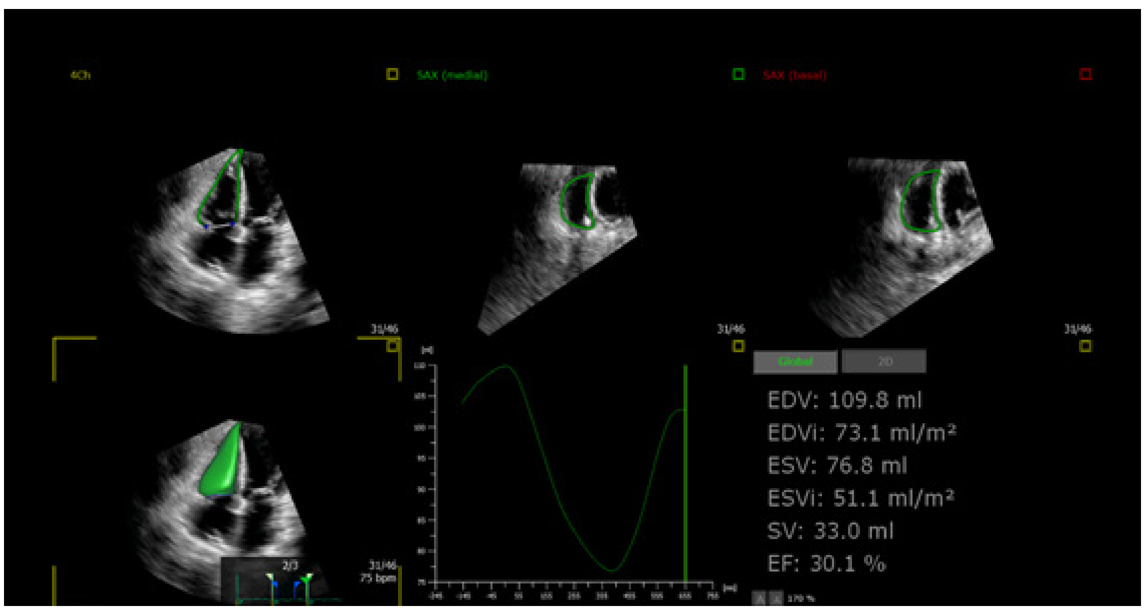

Figure 3 – *3D assessment of right ventricular function in a patient with Chagas disease. The RVEF was calculated to be 30%. EDV: End-Diastolic Volume; EDVi: Indexed End-Diastolic Volume; ESV: End-Systolic Volume; ESVi: Indexed End-Systolic Volume; SV: Stroke Volume; EF: Ejection Fraction.*

major adverse cardiovascular events ($p < 0.0001$), even after multivariable Cox proportional hazard analysis.[39]

In spite of initial evidence of the additional value of 3D echocardiography in some clinical conditions, to date there are no studies characterizing changes in RV size, geometry, and function using this method in patients with Chagas disease.

Assessment of 3D myocardial strain

In recent years, the assessment of cardiac mechanics using the speckle-tracking method has proven to be a promising tool in the assessment of myocardial dysfunction. There are several studies demonstrating the ability of global longitudinal strain analysis to predict severe events, such as mortality and composite outcomes.[40,41]

Even though the role of speckle-tracking echocardiography in detecting regional changes in patients with Chagas disease, even in more subtle forms, has already been demonstrated, it is not possible to confirm that the changes are correlated with the presence of myocardial fibrosis,[42,43] as they may be manifestations of altered strain even before fibrotic replacement. More recently, it has been proposed that 3D myocardial strain analysis would have additional prognostic value, and several indices can be obtained using this tool.[41,44]

A recent study including 72 patients with Chagas disease aimed to characterize new echocardiographic variables according to LVEF and to evaluate their role in predicting clinical outcomes in patients with Chagas disease.[45] In this study, the feasibility of acquiring LV strain was high (91.5% in patients with LVEF < 40%; 89.4% in patients with LVEF ≥ 40% and < 50%; 88% in patients with LVEF ≥ 50%), even though it was inferior to the feasibility of 2D strain (99.3%, 98.9%, and 100%, respectively). After regression analysis using the Cox model, the parameters derived from 3D strain that proved to be predictors of composite outcomes (hospitalization for heart failure, complex ventricular arrhythmias, heart transplantation, and death) were 3D global longitudinal strain and 3D LV area strain.[45] In particular, 3D LV area strain is a very promising index that quantifies change in the endocardial area, integrating longitudinal and circumferential deformation, allowing more detailed assessment of the different types of myocardial fibers and making it possible to better understand the pathophysiology of cardiomyopathies.[41] However, a recent study of patients with ischemic and non-ischemic cardiomyopathy did not find an incremental value for 3D strain in comparison with analysis of LVEF.[46]

Conclusion

Chagas disease is a global public health problem with elevated morbidity and mortality, mainly due to cardiac involvement of the disease. There are several theoretical advantages to the use of 3D echocardiography in patients with Chagas disease due to characteristics that are intrinsic to the method and to the pathology. However, in patients with Chagas disease, the additional value of 3D echocardiography in relation to 2D echocardiography still needs to be better clarified, by means of studies that also take into consideration the cost-effectiveness of the method.

Additional considerations

The data for this review were identified through database searches in the PubMed, Medline, Lilacs, and Scielo platforms. Articles published in Portuguese, English, and Spanish were accepted.

Author Contributions

Conception and design of the research, acquisition of data and writing of the manuscript: Barros-Filho ACL; analysis and interpretation of the data and critical revision of the manuscript for intellectual content: Barros-Filho ACL, Romano MMD.

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Study Association

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Review Article

What Is Important in the Echocardiographic Evaluation of Patients With Cardiac Sarcoidosis?

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Abstract

Sarcoidosis is a systemic condition, of unclear etiology, associated with the formation of non-necrotizing granulomas in several organs, and thoracic involvement in 90% of the cases. Cardiac impairment is detected in approximately 10% of the patients, reaching 25% in autopsy studies. It is in charge of about half the deaths in patients with sarcoidosis, and an important prognostic factor. Interventricular septum and the left ventricle free wall are the most affected regions, especially in the subepicardial portion. The development of changes in conduction (including atrioventricular block and ventricular arrhythmia) and heart failure are the most common manifestations. Diagnosis is challenging and often requires more advanced imaging examinations, such as positron emission tomography or late-enhancement cardiac magnetic resonance imaging. However, these examinations have high cost and are not so available. The conventional transthoracic echocardiography, on the other hand, is widely accessible, but presents later and little specific findings. The most important ones are the reduction of the left ventricle ejection fraction < 50% and the presence of abnormal tapering of the basal interventricular septum. Other segmental changes, especially when not correspondent to coronary territories, and aneurisms, are also relevant. Besides, there may be diastolic dysfunction, pericardial effusion and right ventricular dysfunction, both due to impairment primary or secondary to pulmonary hypertension. The most advanced ultrasound techniques, such as myocardial strain, myocardial work and elastography, are promising in the search of an earlier diagnosis at a lower cost.

Introduction

Sarcoidosis is a systemic condition, of unclear etiology, with a probable autoimmune component, associated with the formation of non-necrotizing granulomas in several organs and tissues.[1] Its prevalence is about 0.05%[2] and, in about 70% of the cases, it affects individuals aged between 25 and 40 years, with a second peak of incidence in women aged more than 50 years.[3]

Clinical manifestations are diverse, as well as the clinical course of the disease, which can be self-limited or chronic. Thoracic involvement occurs in 90% of the cases, with hilar adenopathy and/or diffuse pulmonary micronodules, especially along lymphatic structures.[1]

Cardiac impairment is clinically detected in about 10% of the patients; however, prevalence reaches 25% in autopsy studies.[4] The interventricular septum and the left ventricle free wall are the most affected regions, especially in the subepicardial portion. The most common clinical manifestations are the development of conduction changes (including atrioventricular blocks and potentially fatal ventricular arrhythmias) and cardiomyopathy, leading to heart failure.[4] Patients may be asymptomatic or present with palpitation, dyspnea, syncope or even sudden cardiac death as a first manifestation.[4]

Cardiac impairment is associated with granulomatous infiltration, and progressive evolution to cicatricial fibrosis. It is responsible for about 50% of the deaths in patients with sarcoidosis,[5] being an important factor for poor prognosis in the disease. Therefore, all patients diagnosed with sarcoidosis should be actively questioned about cardiovascular symptoms and undergo a resting electrocardiogram, with individualized indication for transthoracic echocardiography and a 24-hour Holter test.[6]

There are specific criteria for the diagnosis of cardiac sarcoidosis, both in its isolated form and associated with systemic impairment.[7,8] Such criteria require, in most cases, the performance of advanced imaging examinations, such as gallium[6,7] scintigraphy, ^{18}F-FDG PET/CT (^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography) or late-enhancement cardiac magnetic resonance (CMR) (Figure 1). However, these are expensive and less available examinations, rarely used as initial diagnostic methods. Transthoracic echocardiography, on the other hand, is widely available and has low cost. In this article, we will discuss the main diagnostic and prognostic ultrasound findings associated with cardiac sarcoidosis, as well as the use of more advanced techniques as way to increase diagnostic sensitivity.

Conventional echocardiography evaluation

From the diagnostic point of view, the most important findings are reduced left ventricle ejection fraction (LVEF) < 50% and the presence of abnormal tapering of the basal interventricular septum. Other segmental changes, especially if not correspondent to coronary territories, including the presence of aneurisms, are also relevant. Such findings, despite being associated with more advanced impairment,

Keywords

Echocardiography; Sprains and Strains; Sarcoidosis.

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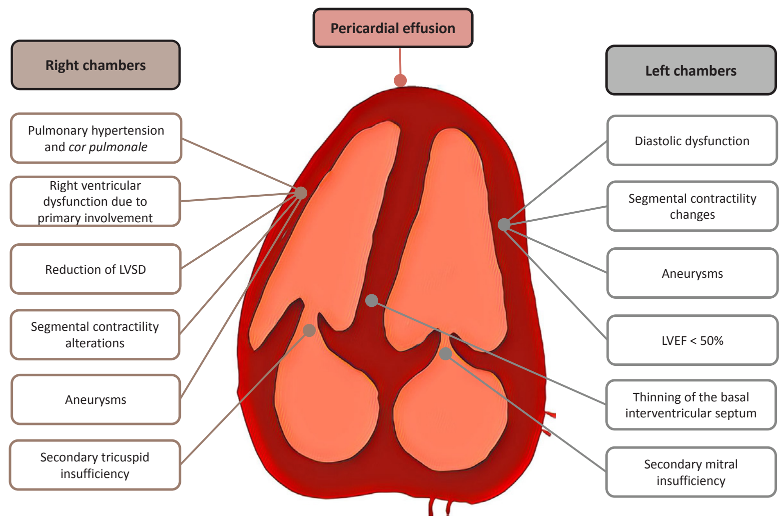
Central Illustration: What Is Important in the Echocardiographic Evaluation of Patients With Cardiac Sarcoidosis?



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Main echocardiographic findings in sarcoidosis. RV: right ventricle; RV GLS: right ventricle global longitudinal strain; LVEF: left ventricle ejection fraction.

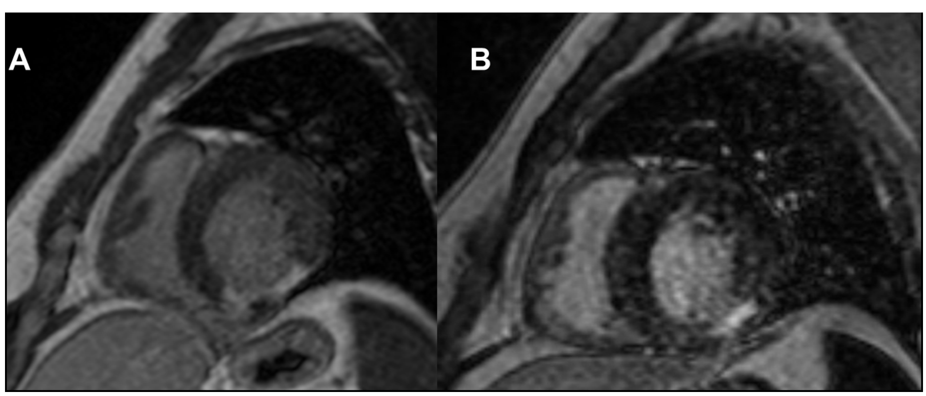

Figure 1 – *Images of a cardiac magnetic resonance of a patient with cardiac sarcoidosis showing akinesia (A) and fibrosis using transmural late enhancement (B) in the inferior lateral and inferior walls, cross-sectional view.*

are contemplated as larger criteria by the main diagnostic algorithm used nowadays.[8] Figures 2 to 4 show these changes in examinations of patients diagnosed with cardiac sarcoidosis.

Diastolic dysfunction, despite not being specific for diagnosis, appears in earlier stages in comparison to the previously mentioned findings, and may suggest an additional investigation in patients with an established systemic diagnosis, or at the presence of suggestive clinical condition. According to a study published in 2019, diastolic dysfunction of the left ventricle was present in 26% of the 77 patients with confirmed diagnosis of systemic sarcoidosis.[9] Therefore, routine echocardiography, according to previously established criteria for other diseases, is essential.

Another important aspect is the analysis of the pericardium, once its direct involvement, after primary myocardial dysfunction, is described in 20% of the patients with cardiac sarcoidosis.[10] The most frequent finding is the presence of small-volume pericardial effusion, but evolution is also described for constrictive pericarditis and cardiac tamponade.

Left ventricular impairment may be primary, due to granulomatous myocardial infiltration, or secondary, due to pulmonary hypertension associated with lung impairment; its analysis is essential using quantitative parameters. The estimated systolic pressure of the pulmonary artery, in echocardiography, showed correlation with the measurements shown by the right catheterization in patients with pulmonary sarcoidosis.[11] Peak

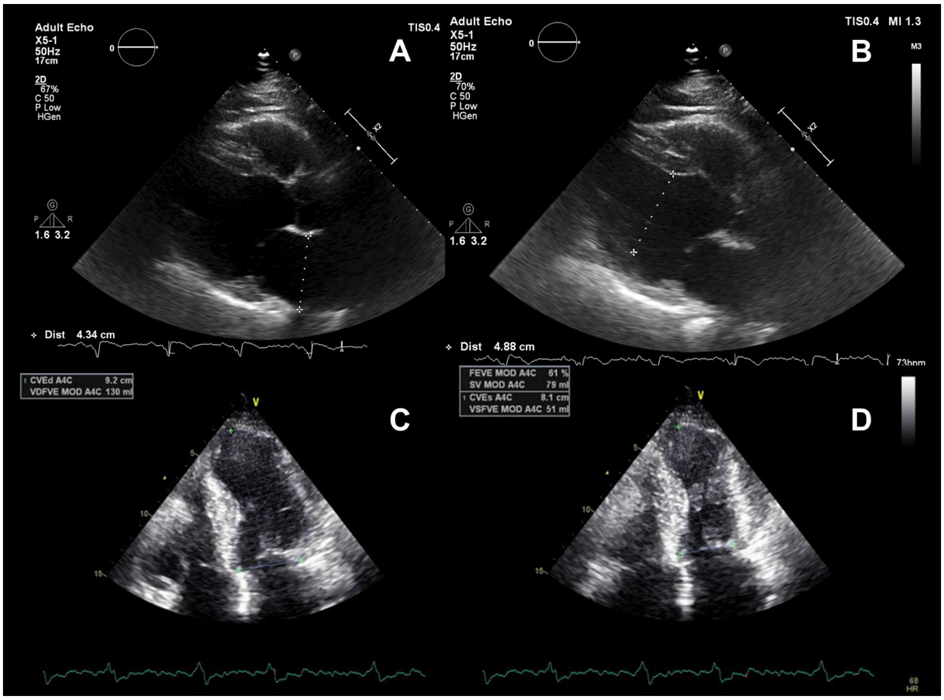

Figure 2 – *Images in transthoracic echocardiography in patient with cardiac sarcoidosis. It is possible to see tapering and akinesia of the basal interventricular septum in the longitudinal parasternal view (A and B). Another patient with cardiac sarcoidosis and dyskinesia of the apical region in apical 4 chamber view (C and D).*

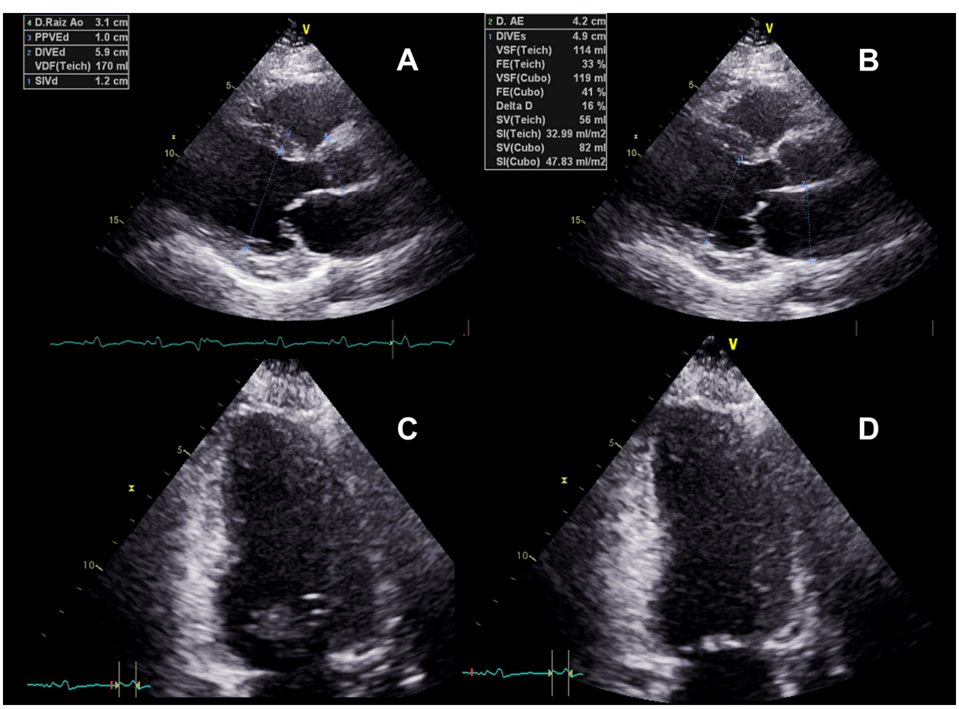

Figura 3 – *Images in transthoracic echocardiography in patient with cardiac sarcoidosis. There is increased refringency and akinesia of the basal segment of the interior lateral wall in the longitudinal parasternal view (A, diastole; and B, systole). The same patient presents akinesia of the basal segment of the inferior wall in apical 2 chamber view (C, diastole; and D, systole).*

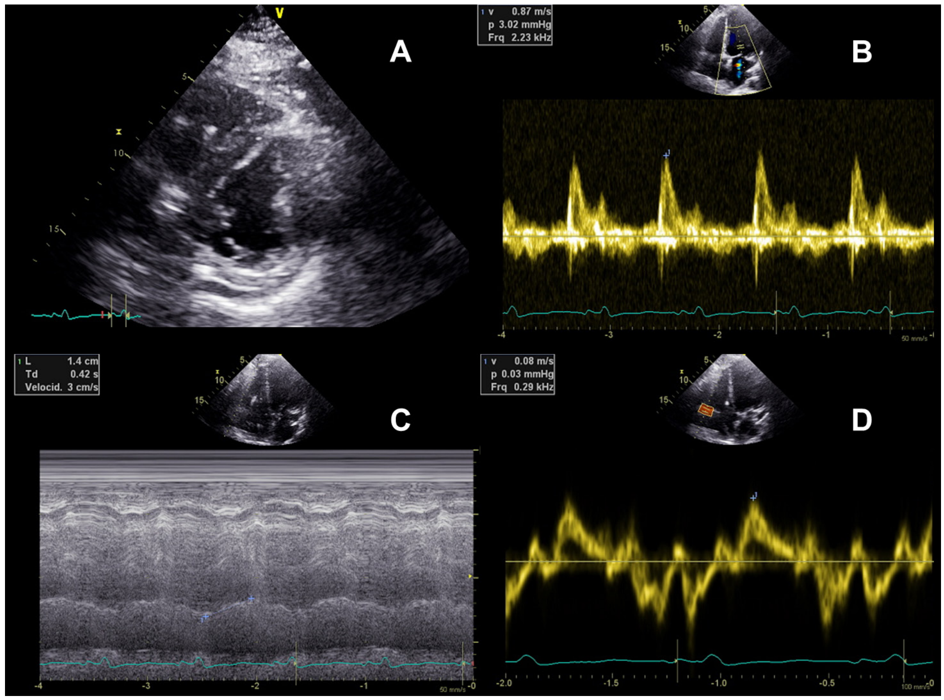

Figure 4 – *Images in the transthoracic echocardiography of patient with cardiac sarcoidosis. There is rectification of the ventricular septum, in the cross-sectional parasternal view, due to pressure overload and pulmonary hypertension, besides mild pericardial effusion in cross-sectional parasternal view (A). There are signs of diastolic function in mitral Doppler, with E/A ratio > 2, and shortened time of deceleration (B), besides systolic dysfunction of the right ventricle, assessed by the reduced tricuspid annular plane systolic excursion (TAPSE = 14 mm; abnormal if < 16 mm), and reduced s' wave of the right ventricular free wall (s' wave = 8 mm/s; abnormal if < 9,5 mm/s).*

tricuspid regurgitation velocity < 2.9 m/s was verified to rule out pulmonary hypertension in these patients, whereas values > 3,4 m/s considerably increase the chances of pulmonary hypertension by invasive measurement.[12]

The central illustration represents the main echocardiography findings associated with cardiac sarcoidosis.

Despite theoretically affecting any portion of the heart, endocardial and valve impairment is less reported. However, a recently published study demonstrated that 68% of the patients with cardiac sarcoidosis and moderate or major mitral insufficiency, presented hypercaptation of some level in papillary muscles, usually both, even when mitral insufficiency was classified as functional.[13] Besides, 61% of the patients presented improvement of at least one grade of mitral insufficiency after treatment with immunosuppressants,[13] raising the hypothesis that inflammation can be more relevant than considered before.

Advanced echocardiography techniques

Among the advanced echocardiography techniques, the evaluation of myocardial strain using the speckle tracking technique is the most analyzed one. Absolute left ventricular global longitudinal strain (LV GLS) lower than 16.3% showed 82.2% sensitivity and 81.2% specificity for the diagnosis of cardiac sarcoidosis in patients with confirmed systemic diagnosis, whereas absolute right ventricular global longitudinal strain (RV GLS) lower than 19.9% showed 88.1% sensitivity and 86.7% specificity.[14]

A meta-analysis published in 2020 assessed 589 patients with confirmed extracardiac sarcoidosis and 378 controls, showing consistent reduction of longitudinal and circumferential global strain in this group of patients, associated with cardiovascular outcomes, such as all-cause mortality, hospitalization due to heart failure, implantable cardioverter defibrillator (ICD) or appropriate therapy with that device.[15]

Myocardial strain was also compared with other imaging methods, and had correlation with the late enhancement findings in CMR.[16] When compared to ^{18}F-FDG PET/CT,[16] there was also an association with the number of myocardial segments with perfusion changes, and both methods had prognostic value.[17]

These data strengthen the use of the strain as a diagnostic and prognostic evaluation tool in these patients, with potential for earlier detection in relation to conventional echocardiographic findings.

Other advanced techniques are currently being analyzed by the Cardiomyopathy Group at Instituto do Coração (InCor). The evaluation of myocardial work and myocardial elastography in patients with confirmed cardiac sarcoidosis and sarcoidosis with no cardiac involvement is ongoing.

Myocardial elastography is an ultrasound modality that allows non-invasive assessment of myocardial stiffness by measuring the speed of propagation of shear waves naturally generated by the closure of the mitral valve. In media with a known density, it is known that this speed is directly proportional to the tissue stiffness.[18] This technique has already been shown to be feasible in the evaluation of patients with cardiac amyloidosis.[19]

Myocardial work is an approach deriving from myocardial strain, which represents the volume-pressure curve area of the left ventricle, built with data from LV GLS and the non-invasive blood pressure verification. Thus, it incorporates the effects of load variation, not contemplated by other methods, such as LVEF and LV GLS,[18] also being a promising technique for diagnostic and prognostic purposes.

Tridimensional echocardiography (3D Echo) is still little available in transthoracic studies due to the learning curve to perform the examination, besides the costs associated with the specific transducer. The 3D Echo provides more accurate measurements of heart chambers and LVEF, with numbers that are comparable with those obtained in the CMR. This technique was used in patients with sarcoidosis and no diagnosed cardiac impairment, and showed reduction in the left atrial emptying fraction,[20] and increased systolic dissinchrony index (SDI)[21] when compared to control individuals, generating the hypothesis of other possible early markers for cardiac impairment.

Prognostic evaluation by the echocardiography

The most important prognostic factor is the presence of left ventricular dysfunction, related to the extension of cardiac impairment. Besides reduced LVEF, the extension of late myocardial enhancement through CMR and the number of segments with changes in perfusion in PET follow the same reasoning and are associated with negative cardiovascular outcomes.[22]

Another prognostic data that is easy to verify is the thickness measurement of the interventricular septum basal portion $\leq$ 4 mm, which was considered as an independent predictor of adverse events (all-cause mortality, heart failure leading to hospitalization and severe symptomatic arrhythmias).[23]

As previously discussed, myocardial strain presents prognostic value in many studies. LVEF lower than 14% was significantly related to hospitalization and heart failure.[14]

Challenges in echocardiography assessment

Conventional echocardiography findings are often unspecific or late. Besides, the differential diagnosis with other cardiomyopathies, or even with coronary artery disease, can be challenging. Therefore, the development of advanced techniques that can be incorporated to conventional examination, without substantial increase in cost, is very relevant.

Some technical aspects related to the method also made evaluation difficult, such as limitation in the acoustic window of patients with excess weight, often associated with the chronic use of corticoids, or extensive lung impairment. In these situations, the use of ultrasound enhancement agents can facilitate the evaluation of segmental dysfunction, tapering and aneurism, and should be used when available.

Conclusion

Despite the limitations, transthoracic echocardiography has several benefits and is indispensable in the clinical practice of the cardiologist, including to evaluate patients with cardiac sarcoidosis.

The detailed evaluation of biventricular function, searching for the findings that are most suggestive of cardiac impairment caused by sarcoidosis, is essential, especially in cases of clinical suspicion or patients that have already been diagnosed with the systemic form of the disease, leading it to more specific imaging examinations. In this context, the use of myocardial strain with speckle tracking should be encouraged and performed whenever technically possible.

In the future, the domain of advanced ultrasound techniques by the echocardiographer promises to increment the diagnostic and prognostic evaluation of these patients, allowing earlier treatment and better clinical outcomes.

Author Contributions

Conception and design of the research: Santorio NC; acquisition of data and writing of the manuscript: Santorio NC, Santorio PT, Hotta VT; critical revision of the manuscript for intellectual content: Fernandes F, Hotta VT.

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This article does not contain any studies with human participants or animals performed by any of the authors.

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Review Article

Using Three-Dimensional Printing in Surgical Mitral Valve Repairs

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Central Illustration: Using three-dimensional printing in surgical mitral valve repairs

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Abstract

Mitral regurgitation is an important cause of morbidity and mortality, and surgical mitral valve repair continues to be the treatment of choice when feasible. We use three-dimensional echocardiography associated with three-dimensional printing to create surgical models that allow trainees to practice or improve surgical techniques in order to improve the outcomes of surgical repairs, contributing to more advanced medical training.

Keywords

Three-Dimensional Printing;Echocardiography; Mitral Valve Insufficiency; Thoracic Surgery; Mitral Valve Annuloplasty

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Introduction

Mitral regurgitation is an important cause of morbidity and mortality, progressively leading to a decline in cardiac function, enlargement of the left cavities, and development of pulmonary arterial hypertension, being a prevalent cause of heart failure with a major social and public health impact.[1] Its causes include congenital, inflammatory, infectious, degenerative factors, secondary functional changes such as ventricular dilation, dysfunction and displacement of the papillary muscles, and, less commonly, increased atrial volume.[2]

As shown in several studies, mitral repair has numerous benefits when it comes to valve replacement in terms of prognosis, early and late mortality, morbidity, and durability, being considered the gold standard treatment for mitral regurgitation.[3,4] However, this approach is technically challenging, compromising outcome predictability and often resulting in increased surgery duration, increased extracorporeal circulation time, and significant residual mitral insufficiency, which may lead to the need for valve replacement with implantation of prosthesis.[3-5]

Valvular dysfunction does not occur symmetrically. It may involve isolated segments or affect the valve more comprehensively (Figure 1). Echocardiography can identify numerous parameters that help determine the mechanism of dysfunction. The method determines anatomical details such as the segments involved, measurements of the leaflets and their ratios, shape and dimensions of the mitral annulus, involvement of the subvalvular apparatus, distance between the papillary muscles and the valve tissue or adjacent structures involved, as well as the degree of regurgitation. The mechanism and anatomical information will be key to determining the possibility of surgical repair and the surgical technique to be used. Degenerative valve disease with mitral prolapse is the most commonly found dysfunction, and its surgical repair outcome is known to be beneficial when feasible. Three large groups can be differentiated . The degree of involvement of the leaflets can be divided into two groups: grades 1 and 2, known as fibroelastic degeneration (FED), being the mildest form with involvement of few valve segments and less excess tissue, mainly from the posterior leaflet, with a greater possibility of performing a successful repair; and grades 3 and 4, known as Barlow’s syndrome (BS), a multi-segmental condition consisting of a myxomatous infiltration with greater involvement of both leaflets, showing a marked alteration, with significant deformation of the valve complex, restricting its repair to highly specialized centers with extensive experience. Therefore, valve replacement is the treatment of choice in most cases. The frustum form (FF), or Barlow frustum, would be grade 3 and refers to an intermediate change whose approach must be evaluated on a case-by-case basis. Analyzing the most affected leaflet is of great importance for the final outcome. Surgery on the posterior leaflet, especially when the involvement is located at the level of scallop P2, is considered simpler, with better success rates. Injuries to scallops P1 and P3 and commissural lesions are technically more difficult, but still have a good possibility of repair. Involvement of the anterior leaflet requires more challenging techniques and must be performed by experienced surgeons. The most currently used techniques in repairs include triangular or quadrangular resection of the involved segment, patch placement, cleft closure, chord transfer, the use of neochords, and annuloplasty with ring placement.[6-10]

Divergent results can be observed in repairs performed on valves with similar involvement, which may be related to the surgeon’s degree of proficiency, the patient’s own factors, or an inadequate preoperative assessment.[11] Currently, echocardiography, especially with three-dimensional evaluation, allows a better analysis of the valve anatomy with more precise measurements and a good visualization of the mechanism involved. However, these data are often not adequately presented to the surgeon, resulting in a poorly planned procedure.

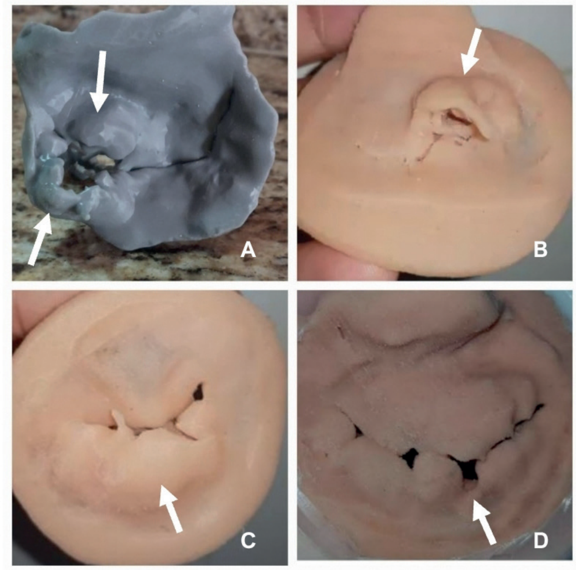

Figure 1 – *Printed models showing different forms of mitral disease with prolapse and flail affecting the lateral commissure and A1/P1 (A), anterior leaflet flail at the level of A2/A3 (B), prolapse with flail of P2 (C), and Barlow's syndrome with posterior cleft (D).*

New technologies allow the printing of realistic models from images obtained from 3D TEE with scale accuracy proven in studies, enabling physical measurements and allowing prior visualization of the operating field. From the three-dimensional image acquired in DICOM format, a three-dimensional model is obtained, which is converted into a file that can be printed on different materials with different physical characteristics and resistances using a three-dimensional printer. Furthermore, molds can be printed using materials that mimic the resistance of the valve tissue. A simulated surgery can then be performed pre-operatively with the same dimensions and characteristics that would be found during the actual procedure.[12-16]

This study aims to allow more effective planning for mitral valve repair surgeries by creating models that mimic the patient’s anatomy. These models are useful when deciding on the surgical treatment and verifying and testing pre-operatively the best surgical approach to be adopted.

It is intended to make cardiac images more tangible and may allow greater predictability of the surgical outcome without harming the patient. Another potential effect is to train a greater number of professionals to perform these techniques, reducing the learning curve and allowing the development of new approaches or alternative techniques in a controlled and close-to-real environment, impacting medical training.

Methods

The study involves the creation of three-dimensional models through 3D printing, which are then submitted to a cardiac surgeon specialized in surgical mitral valve repair, who will assess whether it is possible to perform the usual surgical techniques on the printed models to simulate an actual surgical procedure.

Advanced models were created, which include mitral annulus, leaflets, papillary muscles, and tendon chordae of different mitral diseases, using silicone with resistance characteristics similar to those of the human valve tissue. These models were based on images obtained by three-dimensional transesophageal echocardiographic examinations. The diseases were selected considering varying degrees of surgical difficulty and the need to use different surgical techniques.

The exams were performed using a Phillips Epic Cvx device with an X8 esophageal probe. The images were submitted to the QStation software to evaluate valve measurements using a semi-automatic method and, subsequently, the images were exported to an open-source software (3DSlicer) to create three-dimensional models (Figure 2) and recorded in stl (stereolithography) format. Then, the file was exported to a three-dimensional printer (Flashforge Inventor) for printing a mold which must be printed in a soluble filament (PVA) and then filled with specific silicone (Ecoflex), thus generating a model with elastic characteristics that supports simulated surgery (Figure 3).

To aid the applicability of the surgical technique, ring models for annuloplasty were constructed by three-dimensional printing using elastic material from computer models generated using measurements and shapes of annuloplasty rings already available on the market.

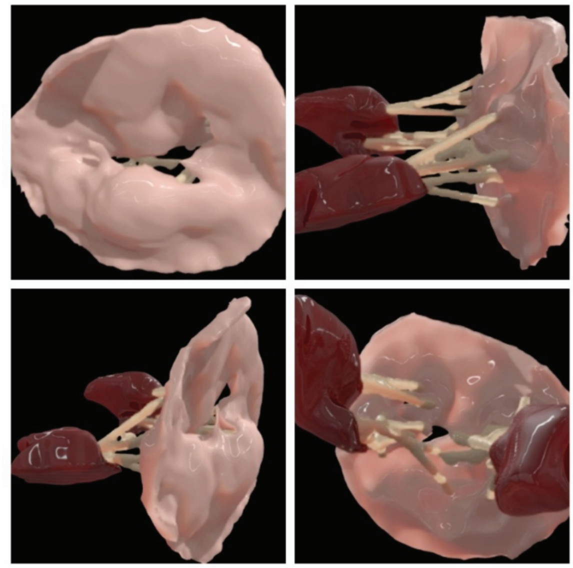

Figure 2 – *Virtual three-dimensional model.*

Results

Advanced valve models were created featuring diseases involving the anterior leaflet, the posterior leaflet in its three scallops, and Barlow's syndrome with diffuse involvement. The chordae are 1.5 mm thick, which is the smallest thickness accepted for the methods used, to allow their integrity after the manufacturing process. A silicone dye was used to facilitate visualization during handling and to allow more accurate placement.

Specimens created were measured using a caliper. The measurements were compared with those obtained from the three-dimensional transesophageal echocardiogram using an automated software (Philips MVQ) with a good correlation between the measurements (Figure 4).

From the printed models, it was possible to apply different techniques using regular surgical material and common surgical threads (Figure 5). Techniques such as annuloplasty, triangular and quadrangular resection, and neochord implantation were performed with good correlation with tissue resistance, texture, and behavior when compared to the actual patient when assessed by a cardiac surgeon specialized in mitral valve repair (Figure 6).

Conclusion

Although this is an experimental work with limited scope, we tried to demonstrate that it is possible to use three-dimensional echocardiography associated with three-dimensional printing for the planning and training of surgical mitral valve repairs. Currently, a large number of surgeons in Brazil perform few surgical repairs, which impacts their ability to perform more advanced techniques, leading to unnecessary valve replacement in some cases. Investments and more research in this field could induce a more advanced medical training program, which could lead to more qualified surgeons and train new ones. In addition, it is also possible to develop new techniques, such as minimally invasive surgery and robotics, without negative impacts on patients. Therefore, we could improve surgical repair statistics with impacts on the general population.

Author Contributions

Conception and design of the research, acquisition of data, analysis and interpretation of the data and writing of the manuscript: Visconti RB; critical revision of the manuscript for intellectual content: Visconti RB, Belem LHJ, Cornélio MCL, Nogueira ACS, Weitzel LH.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

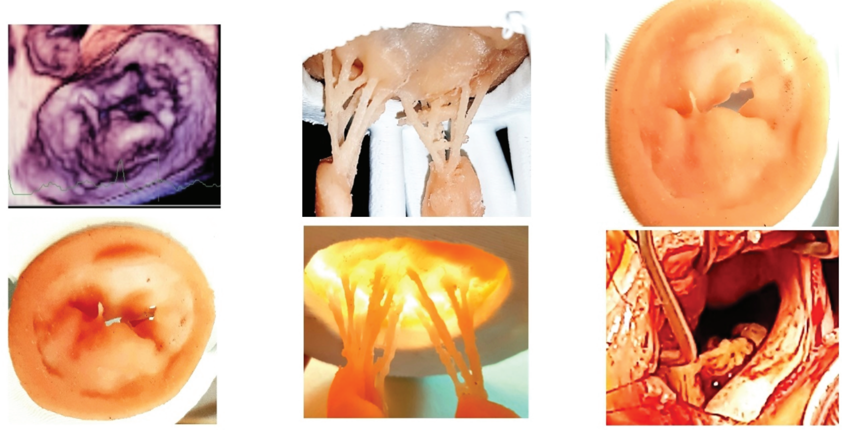

Figure 3 – *Image on the upper left corner obtained by three-dimensional echocardiography. Advanced three-dimensional model printed in silicone containing leaflets, subvalvular apparatus, and papillary muscles. Picture of the surgical specimen on the lower right corner.*

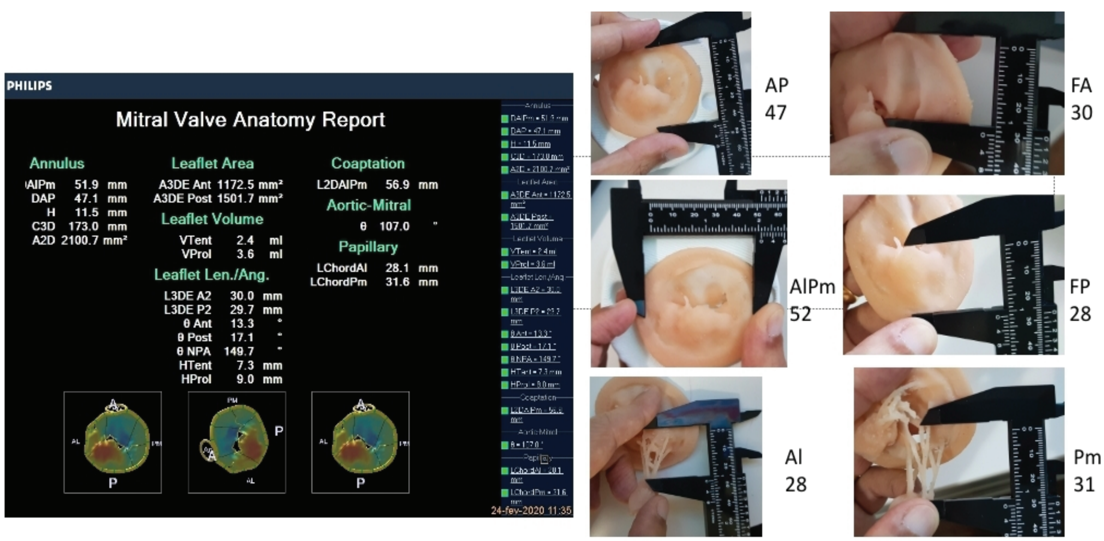

Figure 4 – *Comparison between mitral valve measurements obtained using specific software (Philips MVQ) and measurements found on the printed model. AP: anteroposterior diameter, AlPm: laterolateral diameter, FA: anterior leaflet, FP: posterior leaflet, Al: chordae of the anterolateral papillary muscle, Pm: chordae of the posteromedial papillary muscle.*

Figure 5 – *Before and after simulated surgery on a printed specimen.*

Figure 6 – *Surgical techniques applied to printed model.*

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Three-Dimensional Model Printing in Congenital Heart Disease

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Abstract

Introduction: Three-dimensional (3D) printing refers to a set of methods used to create solid 3D objects, based on digital files. The use of 3D models can improve understanding and knowledge about congenital heart diseases. Their usefulness has been demonstrated in preoperative planning, simulation of interventional procedures, and in surgical decision-making. The objective of this study is to offer a review of the literature on the various rapid prototyping methods and their applicability in medical practice, especially in congenital heart diseases.

Methods: This is a literature review study. Data for discussion were collected by consulting the following electronic database: LILACS, MEDLINE, SCOPUS, and the Scientific Electronic Library Online.

Results: During the period evaluated by the study, a total of 480 articles were published addressing the topic of 3D printing (TDP) for heart disease, with 196 articles related to TDP for congenital heart disease. Of these, 22 were included in this study.

Conclusion: TDP is a technology that is still under construction. It has the potential to assist physicians and surgical teams in therapeutic decision-making, to promote learning for students in specialization and postgraduate studies, to contribute to surgical skills training, and to clarify information for family members.

Keywords: Cardiology; Thoracic Surgery; Congenital Heart Defects; Three-Dimensional Printing.

Introduction

Three-dimensional (3D) printing or rapid prototyping refers to a set of methods used to create solid 3D objects (models or prototypes), based on digital files. There are different forms of 3D printing (TDP); one of the most popular is the one that uses the technique of additive processing, in which the object is created layer by layer, by successive depositions of a highly resistant plastic polymer. The images are acquired from the patient's exams, such as 3D echocardiography, computed tomography (CT), or magnetic resonance imaging (MRI). It is possible to create highly complex customized parts that would not be feasible using conventional manufacturing techniques. Although the use of 3D technology has been a recurring topic in the medical literature since 1988, 95% of studies on TDP were published since 2012.[1]

In recent decades, the use of this technology in the medical field has shown exponential growth due to the reduced production costs, the breaking of patents, the fact that health professionals have mastered the creative process, and investments in research. 3D modeling and printing is currently used in diverse scenarios, such as dentistry, tissue engineering, manufacturing of medical devices, formulating new drugs, and creating anatomical models for education, training, and surgical planning.[2]

For cardiovascular diseases, the use of 3D models can improve understanding and knowledge about congenital heart diseases. Studies have demonstrated their usefulness in preoperative planning, in the simulation of interventional procedures, and in individualized intraoperative surgical decision-making.[3,4]

The majority of 3D images for diagnosing congenital heart diseases currently used in clinical practice are derived from high-resolution methods, such as CT, MRI, and, to a lesser extent, 3D echocardiography.[5] For the pediatric population and for the mother-fetus dyad, imaging modalities that use radiation, contrast, and sedation, such as CT and MRI, constitute limiting factors. The development of ultrasound scanning images, in both 3D and 4D, has expanded the capacity to achieve a complete assessment of the fetal heart, generally between 24 and 28 weeks of gestation, making it possible to create excellent 3D models.[6,7]

The objective of this study is to offer a review of the literature on the various rapid prototyping methods and their applicability in medical practice, opening new horizons and perspectives in medicine.

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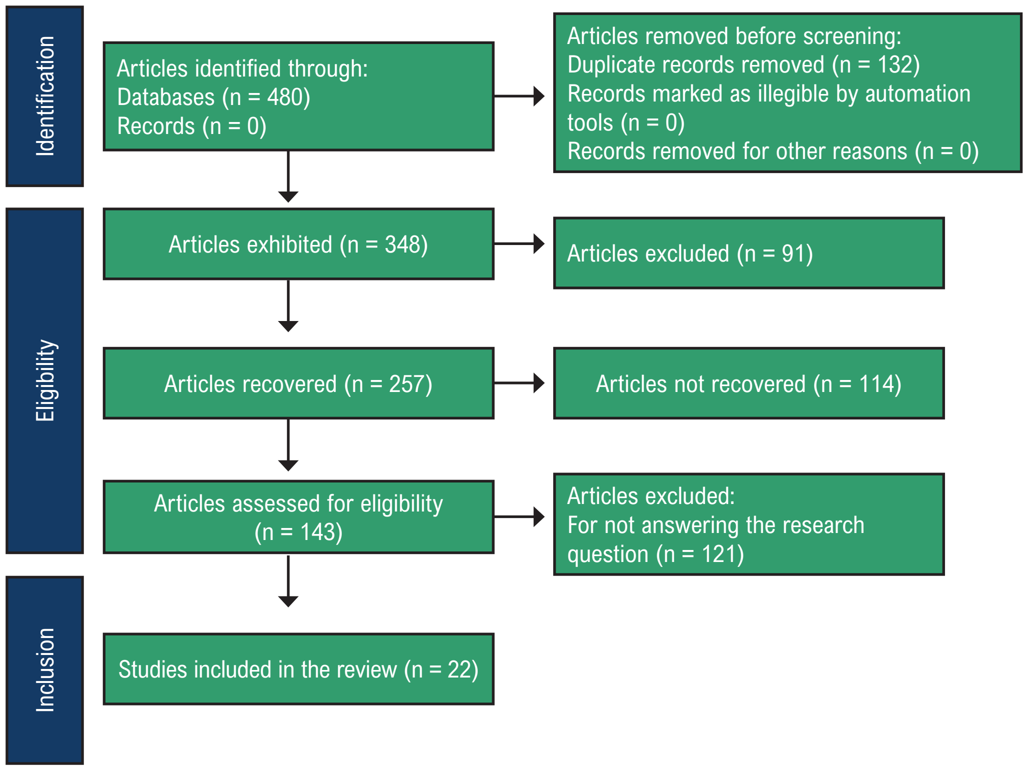
Central Illustration: Three-Dimensional Model Printing in Congenital Heart Disease



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Flowchart of the article selection process, adapted from PRISMA

Methods

This is a literature review study. The following inclusion criteria were determined for article selection: addressing 3D prototyping; congenital heart disease in the title and/or abstract; being an original work; available for full-text reading; and published in Portuguese, English, or Spanish. The following were excluded: editorials, letters to the reader, studies whose full texts were not available, and case reports. The search period was defined as 2014 to 2022, making it possible to highlight scientific evolution on this topic.

The following online databases were used in the literature search: Latin American and Caribbean Literature in Health Sciences (LILACS); Medical Literature Analysis and Retrieval System Online (MEDLINE), SCOPUS, and the Scientific Electronic Library Online (SciELO).

The search for indexed articles was based on the following Health Sciences Descriptors (DeCS): "children," "heart surgery," "congenital heart disease," and "3D prototyping." The following terms from the Medical Subject Headings (MeSH) were also adopted: "cardiac surgery," "congenital heart diseases," and "TDP." The planning was guided based on the combination of the Boolean operators AND and OR, carrying out a joint and individual search so that there would be no possible divergences.

Two researchers independently selected the studies to be used, and there was no disagreement. Initially, duplicate studies were eliminated through the use of the Zotero data and reference formulator. Rayyan® software was then used to organize and consult the titles and abstracts of articles by peers, aiming to verify the inclusion/exclusion criteria. Subsequently, the 22 articles included in the study were read in full.

Analysis was subsequently conducted based on the level of evidence, in accordance with the methodological approach of the Agency for Healthcare Research and Quality (AHRQ) and the GRADE system. The selected studies were ordered in a Microsoft® Excel table, including the following data: database, author, year of publication, location and language, methodological design, and level and quality of evidence. The investigation was based on a meticulous reading of the selected studies, prioritizing qualitative analysis.

Results

During the period evaluated by the study, a total of 480 articles were published addressing the topic of TDP for heart disease, with 196 articles related to congenital heart disease. Of these, 22 were selected to be part of this review (Table 1).

Table 1 – Summary of the articles included in the study

Author	Type of study	Results	Conclusions
Oliveira et al.[1]	Systematic review	A total of 9,253 publications on TDP and 497 on 3D heart printing were included in the study.	Prints of 3D models are helping surgeons in surgical planning and promoting a greater understanding of the pathologies for patients and family members.
Liaw et al.[2]	Systematic review	The main applications of TDP are in dentistry, tissue engineering, anatomical models, medical devices, and drug formulations. Currently, more than 85 medical devices are 3D printed.	New TDP technologies are expanding their use in medical areas and reducing their production costs.
Lau et al.[3]	Systematic review	A total of 28 studies were included in the review: 61% case reports and 36% expert opinions	The use of TDP in models of congenital heart disease has applications in teaching, preoperative planning, and simulations.
Han et al.[4]	Clinical study	The use of 3D prototypes reduces surgical time, without impact on hospital stay or complications.	The use of 3D prototypes facilitates surgical planning and reduces operation time.
Chen et al.[5]	Descriptive study	Image acquisition with Voluson E10 (ultrasonography) and use of Mimics and Meshmixer software for segmentation and modeling of 3D prototypes.	First publication demonstrating the method of TDP of a fetal heart with images derived from echocardiography.
Byrne et al.[6]	Systematic review	A total of 136 studies were included in the review: 1 clinical study, 80 journal articles, and 55 case reports.	Image segmentation methods require a high degree of software knowledge and operator time.
Olivieri et al.[7]	Cohort study	Nine patients underwent 3D echocardiography to study their pathologies, and 3D prototypes were produced based on the images.	It is technically feasible to produce 3D prototypes, and they accurately reflect pathologies.
Alves et al.[8]	Cohort study	Based on patients' CT image, after segmentation and processing, a 3D model was produced using the SLA technique.	The use of rapid prototyping is an extremely valuable tool in supporting medical activities. Based on 2D medical images from CT and MRI, it is possible to obtain 3D models.
Gou et al.[9]	Descriptive study	Image acquisition by Voluson (ultrasonography) and use of Mimics software for segmentation and 3D prototype modeling. The 3D objects were then generated, smoothed, and exported as STL files and subsequently printed in resin.	3D prototypes of tetralogy of Fallot are technically feasible to produce and can be printed in multicolored resin.
Shui et al.[10]	Cohort study	Based on CT, MRI, and echocardiography images, it is possible to produce 3D prototypes.	The accuracy of 3D prototypes is mainly determined by the quality of the images obtained.
Bagaria et al.[11]	Multi-center cohort study	Fifty 3D prototypes were produced to assist surgical cases.	All surgeons reported that the prototypes were useful for planning, simulation, and reference in the surgical field.
Marro et al.[12]	Systematic review	The study details the stages of preparing 3D prototypes and the most used forms of printing.	3D prototypes are expanding their use in diverse medical areas to the extent that new technologies emerge.
Bagaria et al.[13]	Systematic review	The study details the evolution of prototyping and applications in the medical field.	The use of TDP, with technological advances, will allow the production of bioprototypes, tissues, and organs.
Rayan et al.[14]	Cohort study	The study compared surgical variables in 79 cases of congenital heart diseases with the production of prototypes in relation to cases without 3D models.	The use of 3D models reduced surgical time in the operating room by favoring better planning and anatomical references.

Rankin et al.[15]	Systematic review	A total of 261 studies were included in the review: 5% used DICOM, 38% CT, 20% MRI, 28% ultrasound, and 9% bioprint.	3D prototyping is widely used in the planning, simulation, and manufacture of prostheses. The simplification of software will favor greater application of this technology.
Fadero et al.[16]	Descriptive study	The study describes the stages of 3D image processing based on CT and its applications in medicine.	The processing of 3D images needs to be simplified in order to expand the use of this technology.
Bizzotto et al.[17]	Cohort study	In the study, 40 prototypes were produced, and their impact on surgical planning and providing information for patients was analyzed.	The use of 3D prototypes facilitates surgical planning and increases patients' understanding of the procedures performed.
Karsenty et al.[18]	Clinical trial	The study assessed the understanding of heart conditions by dividing them into two groups: one with 3D models and another without	The use of 3D models improved students' understanding and satisfaction with the learning process.
Preece et al.[19]	Clinical trial	The study assessed students' understanding of heart disease by dividing them into 3 groups: 3D models, text books, and computer models.	The group of students with 3D prototypes showed a better understanding of anatomy.
Biglino et al.[20]	Cross-sectional study	The use of 3D prototypes facilitated students' understanding: in relation to anatomy (86%), spatial orientation (70%), and anatomical complexity (66%).	3D prototypes are important tools for understanding congenital heart disease.
White et al.[21]	Cross-sectional study	The use of 3D prototypes facilitates the understanding of complex congenital heart diseases (tetralogy of Fallot), but there was no difference in pathologies such as atrial septal defect and ventricular septal defect.	3D prototypes facilitate students' understanding, but the biggest impact is on complex heart diseases.
Su W et al.[22]	Cross-sectional study	Students who had contact with 3D prototypes had a better understanding of congenital heart disease.	The use of 3D prototypes increases student interest and learning about heart diseases.

CT: computed tomography; DICOM: digital imaging and communications in medicine; MRI: magnetic resonance imaging; STL: standard triangle language; 3D: three-dimensional; SLA: stereolithography.

Steps of TDP

Rapid prototyping comprises 2 production stages: first, the virtual stage and second, the physical stage. The virtual stage can use solid modeling computer-aided design (CAD) software to obtain the virtual geometry of the biomodel. Alternatively, files obtained by 3D scanners, CT, or MRI can be converted to obtain the virtual geometry of the prototype.[8,9]

There are multiple steps in the printing process for the production of 3D prototypes, namely: image acquisition, segmentation, creation of a 3D mesh, post-processing of the 3D mesh, and printing of the 3D model (Figure 1). 3D prototypes are basically created by reading a numerical code (G Code) developed through CAD and computer-aided manufacturing (CAM) programs, which are capable of segmenting and modeling structures.

The initial step in printing 3D objects is image acquisition. This is considered the most important step, seeing that the quality of the printed models directly depends on the quality of the data acquired (image resolution).[10] This file is obtained by acquiring sectional images using digital equipment, such as MRI, CT, or even 3D/4D ultrasound.[11] The digital imaging and communications in medicine (DICOM) format is currently a standard in the medical equipment industry; as it is globally accepted, it is the format that provides the greatest interoperability between computer systems and medical equipment.

The second step is image segmentation, which consists of delimiting the area of interest for the study, thus making it possible to determine which region will be studied. To determine the region of interest, some aspects must be taken into consideration, such as anatomical area and types of tissues to be studied. The objective of segmentation is to isolate the area of interest, within the set of volumetric data that was collected, extracting a segmented data surface, which makes it possible to generate the surface mesh. There are several free open-source programs that contain a variety of manual

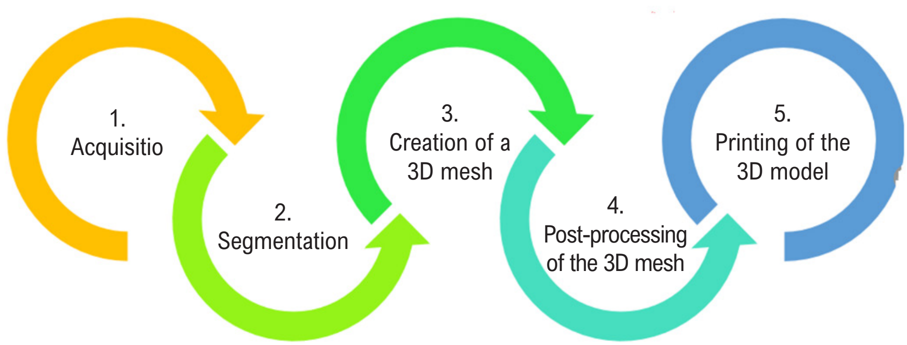

Figure 1 – *Required steps to create anatomical models based on imaging exams and TDP*

and automatic tools, thus making it possible to manipulate DICOM data in print-ready files.

Among the tools available for image segmentation, the threshold is widely used in CT and is based on the definition of density intervals that express, for example, only the voxels that correspond to the tissue studied. In segmentation based on 3D ultrasound, not all software can open volumetric blocks such as that performed by 3D Slicer (open-source software) and Mimics (paid software), which, at the end of the process, generate a virtual model in wavefront object format (WFO) and standard triangle language (STL), the latter geared toward TDP. In some cases, manual editing of images is necessary, with tools such as cropping, erasing, and selecting.

After segmentation, the creation of the mesh begins, which consists of reconstructing individual 2D segments in a 3D volume interface. The reconstruction process basically consists of obtaining a 3D model of the objects of interest, making it possible not only to visualize them, but also to better understand their structure through the extraction and analysis of the objects' geometric parameters.

The rapid prototyping machine cannot directly process the acquired images due to 2 main reasons: the image format provided and the thickness of the images which is in the range of 1 to 5 mm, whereas the image slices used in the rapid prototyping processes are around 0.25 mm. There are numerous methods for reconstructing and visualizing 3D objects based on their cross sections. The main methods can be classified into the following 2 categories, volume-based and surface-based methods.[12]

After acquiring the 3D object, post-processing of the 3D object mesh is carried out. This consists of making it visually pleasing and highlighting the characteristics necessary to understand the part. At this stage, 3 steps must be strictly followed to carry out the process in the best way possible: repairing, cleaning, and smoothening. When repairing, it is fundamental to locate the places where there are flaws in the image and thus correct them, making the surface of the object as regular as possible. One of the most used software programs for this step is currently Meshmixer, free software from Autodesk; however, there are others with additional tools such as Mimics. During cleaning, an algorithm is used to reduce noise without losing anatomical information. Smoothening regularizes and smooths the image surface to improve the quality and definition of the 3D image to be printed.[11]

In TDP, several technologies are used to manufacture 3D models, including the following: fused deposition modeling (FDM), stereolithography (SLA), selective laser sintering (SLS), TDP, laminated object manufacturing (LOM), among others of greater specificity, and inkjet. The most used in the medical field are FDM, SLA, and SLS.[13]

FDM constructs parts by depositing an extruded thermoplastic material. The injector head traces the perimeters of the transversal section and fills them, thus constructing each layer. On the other hand, SLS allows the construction of physical models using materials in powder form. The powder is processed in an inert, thermally controlled environment inside a chamber. It reaches the melting temperature (sintering) due to the action of a CO_2 laser. After a layer is sintered, a new one is deposited and so on, until the construction of the part is completed (Figures 2 and 3). The principle of the SLA technique is the photopolymerization of a liquid resin, where a laser beam traces a pattern on the surface of the liquid resin that solidifies and builds the part layer by layer. SLA has made TDP cheaper and popularized it, because it allows the production of various parts at once, with a high degree of precision.

The costs of producing prototypes or 3D models have reduced with the introduction of these new technologies and cheaper materials. FDM 3D printers cost approximately 1,000 Brazilian reais (BRL), while professional SLS printers cost around 25,000 BRL. The material for 3D printers costs 250 to 500 BRL per kg, while the SLS material costs 500 to 2,000 BRL per kg.

Discussion

In recent years, there has been progress in the application of rapid prototyping systems in diverse medical specialties. Therefore, it has become necessary to develop a literature review on the

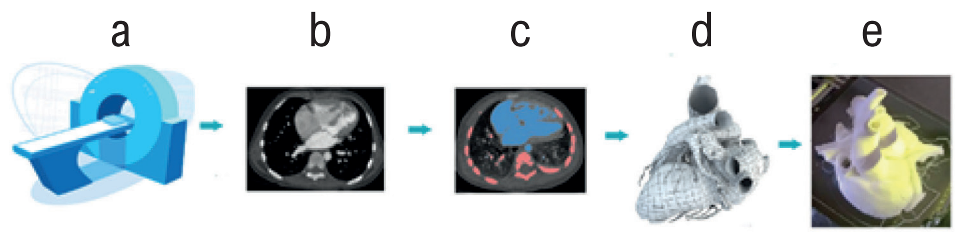

Figure 2 – *Stages of 3D model creation: a) use of image production equipment; b) image acquisition; c) image segmentation; d) reconstruction of a 3D model; e) printing of a computational model by the 3D printer (original figures).*

Figure 3 – *Construction of 3D models: a) cleaning and smoothening carried out using the software; b) estimated model for production by the printer; c) produced model (original figures).*

applicability of the technique in this area of health, considering the scarcity of studies in the literature that can, in a synthetic manner, assist in the production of 3D models.

Applications in medicine

Preoperative analysis can be considered one of the most useful applications of TDP technology. Surgical procedures in areas of complex anatomy with a high risk of injury to important structures benefit from rapid prototyping of 3D models.[15]

Various CAD programs currently allow virtual surgical planning (VSP) to be carried out with a better understanding of spatial geometry, anatomical relationships, and the possibility of programming less invasive surgical access.[16]

Some studies demonstrate that TDP technology in planning and carrying out surgical procedures leads to reduced surgical time, reduced intraoperative blood loss, reduced time of exposure to ionizing radiation during the surgical procedure, reduced complications, and probable improvement in surgical results.[13]

Another major benefit of applying this technology is also in the communication between the medical team and patients and family members. The use of anatomical models to provide information about the type of surgical treatment proposed promotes a better understanding of the patient's clinical condition, surgical programming, rehabilitation, and greater adherence to treatment, contributing to an improved doctor-patient relationship.[17]

Importance of 3D prototypes in congenital heart diseases

Congenital heart disease is the most common birth defect, occurring in approximately 9 out of every 1,000 live births. This corresponds annually to 1.35 million newborns with heart disease, 70% of whom will require treatment during the first year of life.[18] These patients require care and monitoring throughout their lives, from interdisciplinary management in primary care to specialized follow-up with clinical cardiology, interventional cardiology, and pediatric cardiac surgery.

Congenital heart defects are predominantly taught based on 2D representations of heart defects. Educational tools for teaching in this context include simple diagrams in books or texts and images from echocardiography, angiography, or even advanced imaging modalities such as CT or MRI. The ability to translate 2D images into 3D mental representations of injuries is a crucial point in learning. Tactile manipulation and the use of various senses are capable of promoting greater spatial appreciation and understanding of complex anatomies.[19]

Promising initiatives using 3D modeling and printing technology have been developed to better understand complex cardiac anatomies. Biglino et al.[20] cite the importance of this tool in the training of cardiology nursing professionals and reinforce the optimization of prototypes through stripes and colors that highlight important injuries and the use of complementary educational material. White et al.[21] describe that the incorporation of 3D printed models during didactic teaching sessions provided greater immediate understanding for pediatric and pediatric emergency residents. In a controlled study, Su et al.[22] used 3D prototypes of ventricular septal defects as an aid in teaching medical students. The post-test results showed better results in the domains of "knowledge acquisition" and "structural conceptualization" in the 3D group, reiterating the effectiveness of using this technology for medical education.

In a recent Brazilian systematic review, Oliveira et al.[1] compiled 9,253 publications on "TDP" and 497 publications on "heart TDP" and concluded that 3D printed models are helping fellows, residents, and surgeons in practice and surgical planning, even of rare cases; helping other health professionals to better understand diseases; and increasing parents' and family members' understanding of the child's pathology.

The limitations of this study include the heterogeneity of the selected studies, possible biases in individual studies, and the rapid evolution of rapid prototyping methods, leading to some methods being less used today.

The majority of 3D cardiac studies and models are obtained from CT angiography or MRI, which generally produce images with better resolution. However, thin mobile structures are better visualized by 3D echocardiography. TDP reproduces the differences between the imaging methods from which it was constructed; therefore, septal defects and valve diseases are better represented by 3D echocardiography, and the anatomy of large vessels and their relationships with the chambers are well represented by CT and MRI. In some cases, it is possible to use biomodels made by means of both methods.

Conclusion

Printing 3D prototypes is a technology that is under construction. It still presents limitations and challenges to ensure better product quality. Among them, we can highlight the precision of the assembly, the construction of models with the same mechanical properties as the tissues, the shorter preparation time, and the economic cost.

TDP models of congenital heart diseases are helping fellows, residents, and surgeons in surgical practice and planning, even in rare cases; helping other health professionals to better understand diseases; and increasing parents' and family members' understanding of the child's pathology.

Author Contributions

Conception and design of the research: Freitas MB; acquisition of data: Freitas MB, Lima RM; analysis and interpretation of the data: Freitas MB, Figueiredo JL, Cajueiro FC, Lima RM; statistical analysis: Cajueiro FC; writing of the manuscript: Freitas MB, Freitas MH; critical revision of the manuscript for intellectual content: Figueiredo JL, Freitas MH, Lima RM, Teixeira CM.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Review Article

Role of Shear Wave Elastography in the Assessment of Myocardial Stiffness in Various Cardiomyopathies

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Abstract

Echocardiography is essential for the diagnosis and treatment of cardiovascular disease. Assessing left ventricle diastolic function is a major challenge, and several well-known ultrasound techniques, such as pulsed Doppler for mitral flow, tissue Doppler, and myocardial strain, are used to non-invasively estimate left atrial filling pressure. Although widely available, this approach has several limitations and does not truly represent the intrinsic properties of the cardiac muscle. However, cardiac elastography can be studied non-invasively by estimating myocardial stiffness through shear wave propagation speed in cardiac tissue. Elastography is already widely used to assess stiffness in other tissue types, such as thyroid, liver, and breast. In the context of cardiological assessment, this technique has already been successfully used in diseases such as cardiac amyloidosis and hypertrophic cardiomyopathy. This article aims to review the main concepts of this promising technique and present the published experiences of national and international services.

Introduction

Heart failure is defined as the heart's inability to pump a sufficient quantity of blood to meet the body's metabolic needs, or to do so at the expense of increased filling pressures.[1] This concept is extremely important, since approximately 50% of heart failure cases are classified as having preserved left ventricular ejection fraction,[1] in which increased filling pressure appears to be the predominant mechanism.

Classically, cardiac catheterization, an invasive technique, is used to directly measure intracavitary filling pressures, allowing construction of the pressure-volume curve. This approach characterizes the intrinsic properties of ventricular pump function throughout the cardiac cycle, in addition to hemodynamic variables, which clarifies the pathophysiology of heart diseases and contributes to their diagnosis.

One important property, a concept applied to different materials, is stiffness, ie, the extent to which an object resists deformation in response to an applied force.[2] Compliance, the opposite of stiffness, quantifies a material's deformability.[2] Thus, myocardial stiffness represents resistance to stretching when the myocardium is subjected to stress, corresponding to the slope of the stress vs deformation curve.[3] Left ventricular compliance is the variation in pressure in relation to variation in volume, and left ventricular stiffness can be measured by the slope of the pressure-volume curve in final diastole.[4]

Normal diastolic function is characterized by a normal left ventricular relaxation rate, with myocardial and left ventricular stiffness parameters within normal limits, resulting in low filling pressures.[5] During diastole, both active relaxation and myocardial stiffness, an intrinsic property associated with sarcomere proteins (such as titin) and the extracellular matrix, simultaneously determine the filling pattern of the left ventricle.[6] However, active relaxation is more predominant in early diastole, while passive myocardial stiffness is more predominant at end-diastole.[6] This implies that myocardial stiffness has a greater influence on the slope of the pressure-volume curve during end-diastole[6].

In most cases, diastolic function is determined through routine echocardiographic techniques, such as pulsed Doppler analysis of mitral flow, tissue Doppler and, more recently, myocardial strain, which allows non-invasive estimation of left atrial filling pressure. Despite their wide availability, these techniques have several limitations and do not, in fact, represent the intrinsic properties of the cardiac muscle.

Shear wave elastography represents a paradigm shift in echocardiography by non-invasively measuring myocardial stiffness, which can add important information to diastolic function assessment. In this article, we will discuss the fundamentals of its use and its main clinical applications.

Physical properties and methodology of shear wave elastography

Shear wave elastography is widely used for non-invasive assessment of liver and breast nodules, in addition to other applications, such as the characterization of kidney, prostate, and thyroid lesions.[7]

This technique involves measuring shear wave propagation speed in different tissues, which is directly proportional to their stiffness. It is important to conceptually differentiate between shear waves and compressive waves, which are

Keywords:

Elasticity Imaging Techniques; Muscle Rigidity; Amyloidosis.

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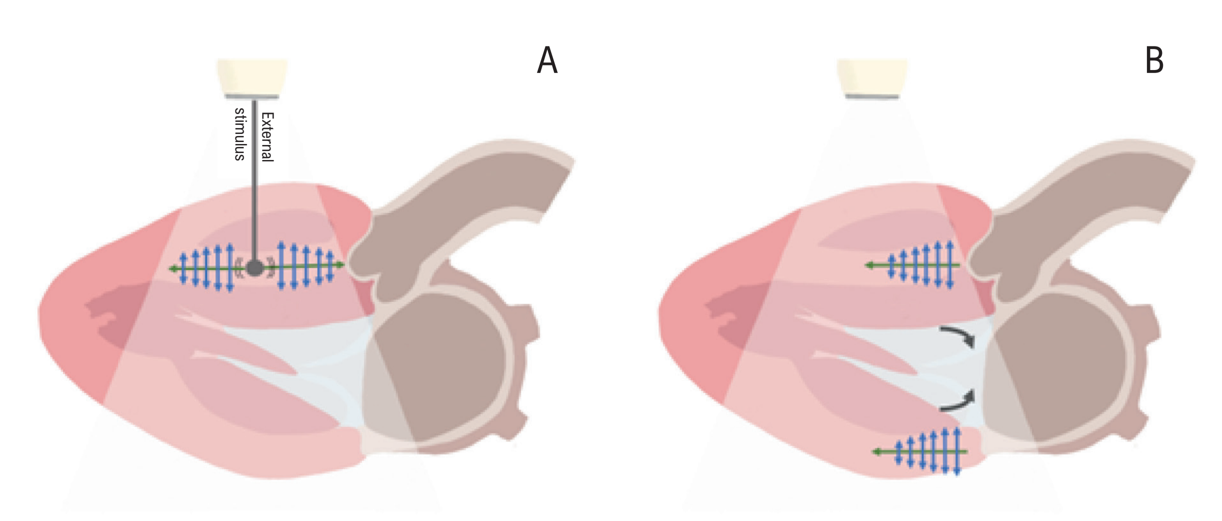
Central Illustration: Role of Shear Wave Elastography in the Assessment of Myocardial Stiffness in Various Cardiomyopathies



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Myocardial elastography methods. In A, shear waves are generated through impulses emitted by the transducer itself. In B, shear waves are generated naturally by mitral valve closure. The blue arrows represent tissue displacement, while the green arrows indicate the direction of shear wave propagation.

used in conventional ultrasound to produce images. In compressive waves, the particles move in parallel with the propagation direction, while in shear waves they move perpendicularly to it.[8] Additionally, shear waves have a propagation speed of around 1-10 m/s, which is much lower than compressive acoustic waves (around 1450-1550 m/s in soft tissue).[7] To evaluate shear waves with reasonable precision, specific transducers and equipment with a frame rate between 1000 and 10,000 frames/second are required.[9]

The lower propagation speed of shear waves make them essential for tissue characterization. It has been demonstrated that pathological tissue changes lead to increased propagation speed.[10] The evolution of ultrasound devices has made it possible to track such waves and differentiate small variations that occur during their journey through unhealthy tissue.

Cardiac elastography can be performed in different ways, depending on how the waves are generated, which is illustrated in the Central Figure. One way is through short, high intensity acoustic radiation pulses emitted by the transducer itself, which form shear waves that displace tissue (Central Figure A). To properly perform this technique, the targeted cardiac wall must be oriented parallel to the transducer, which emits the impulse and determines the speed at which the waves propagate through the tissue.[9]

In the context of cardiac physiology, the closing of the atrioventricular and semilunar valves generates shear waves of itself. Another technique is based on assessing the intrinsic movement of these naturally generated waves (Central Figure B). This analysis is more feasible and can be performed with more conventional equipment. Furthermore, such waves do not depend on an acoustic window for generation, allowing broader application in clinical practice. However, while transducer-generated waves can be controlled in time and space by an ultrasound device, naturally-generated waves appear at specific locations and periods during the cardiac cycle, requiring propagation velocity analysis at specific points.

Considering an isotropic medium with uniform density, stiffness can be estimated from the shear wave propagation speed according to the equation: $\mu = \rho c^2$, where "μ" represents myocardial stiffness (kPa), "ρ" tissue density, and "c" the shear wave propagation speed.[9]

A recently published Brazilian study was conducted at the Heart Institute of the University of São Paulo School of Medicine (InCor), in partnership with the Radiology Institute of the University of São Paulo University Hospital (InRad).[11] In this study, assessments were performed with a device already used by the service, an APLIO i800 (Canon Inc., Tokyo, Japan), with small adjustments made for the elastographic study and images obtained from a multifrequency convex probe (fundamental frequency 3.5 MHz). Shear wave propagation speed was measured at end-diastole, when the heart moves the least. Long-axis parasternal windows were used to assess the basal segment of the septum, while short-axis parasternal windows were used to assess the basal segment of the septum and the basal, middle and, apical segments of the septum, plus the right ventricle free wall, as shown in Figure 1.

Clinical applications of shear wave elastography

Several studies have shown promising results with this technique. In 2019, Petrescu et al. found higher propagation velocities in patients with cardiac amyloidosis and older adults, which suggested a correlation between propagation velocities and myocardial stiffness.[12] In 2020, the same group evaluated propagation speed in heart transplant patients, finding a good correlation with invasive measurement (right catheterization) of pulmonary capillary pressure and a diffuse pattern of myocardial injury assessed by cardiac magnetic resonance imaging.[13]

Based on shear wave propagation speed, Villemain et al. found greater myocardial stiffness in patients with hypertrophic cardiomyopathy than healthy controls, in addition to a significant correlation between fibrosis assessed by delayed enhancement cardiac magnetic resonance imaging and diastolic dysfunction parameters assessed by conventional echocardiography.[14]

Cvijic et al. used the method to evaluate hypertensive patients, finding that patients with advanced disease and concentric remodeling or concentric hypertrophy had greater stiffness than healthy controls.[15]

Alencar Neto et al. found greater myocardial stiffness in patients with transthyretin cardiac amyloidosis than healthy controls.[11] A decreasing pattern of stiffness towards the apex was described,[11] suggesting a pattern of apical sparing, which is compatible with the pathophysiology of the disease.

Although these are initial studies, they show that the technique is feasible and has potential clinical application. Considering that several diseases present with a hypertrophic phenotype, such as amyloidosis and hypertrophic cardiomyopathy, additional and more expensive diagnostic resources are required; a non-invasive technique associated with echocardiography can improve diagnosis and may add prognostic value for these diseases. Furthermore, it may revolutionize the assessment and understanding of diastolic function in general.

Challenges to using shear wave elastography

In addition to the difficulties inherent to new diagnostic techniques, such as different acquisition protocols and equipment, being an ultrasound technique, it is consequently operator-dependent and angle-dependent.[16]

Associated with such technical factors, cardiac tissue is essentially anisotropic, with different layers, thin walls, and its own movement patterns,[17] variables that can influence shear wave propagation speed. Furthermore, it has been shown that both geometric changes[18] and increased preload[17] affect

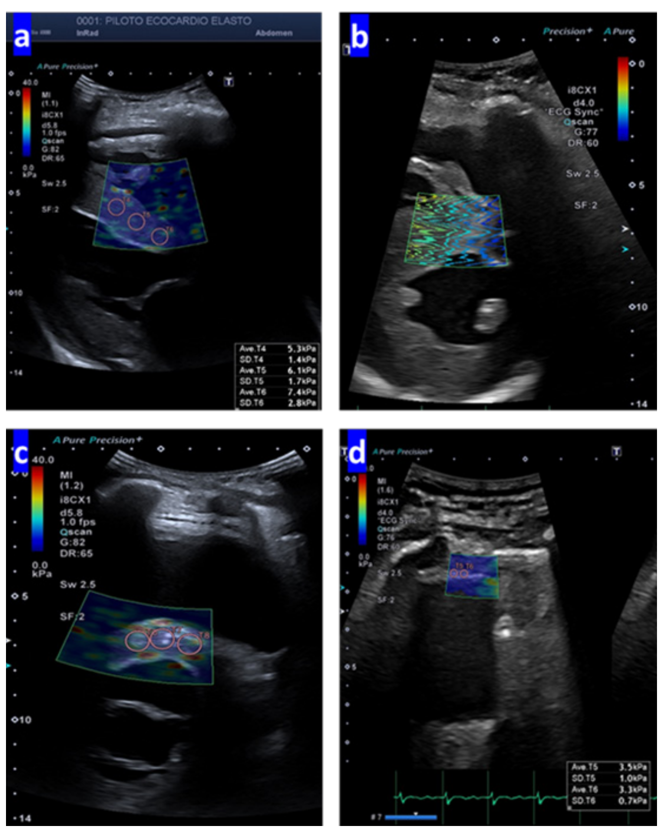

Figure 1 – *Myocardial elastography. In A, the basal segment of the interventricular septum is assessed in a long-axis parasternal window. In B and C, the middle and basal segments of the septum, respectively, are assessed in a short-axis parasternal window. In D, the right ventricle free wall is assessed in a short-axis parasternal window.*

these measurements. These mechanical factors limit the use of Young's modulus to determine myocardial stiffness, since they are not considered in this equation. Given that propagation speed is influenced by these variables, they should ideally be determined at the time of evaluation for correct interpretation of the results.

Other limitations include definitions of the ideal echocardiographic window and the number of myocardial segments to be analyzed. Significantly higher propagation velocities were obtained in an apical window than a parasternal window in healthy volunteers, with no significant correlation between the measured values.[19] It is worth mentioning that the directions in which the natural valve-generated shear waves propagate within the myocardium are unknown, which impairs accurate velocity estimation.[20]

It is also important to consider that elastography assessment depends on the phase of the cardiac cycle, with the impulse activated according to electrical heartbeat monitoring. However, there is no impediment to using the method in irregular heart rhythms, which limits conventional diastolic function assessment.

Future perspectives for shear wave elastography

Elastography may prove useful in other heart diseases, improving diagnostic and, possibly, prognostic and therapeutic response assessment. Since it is a non-invasive, accessible, and low-cost technique, it can be incorporated into traditional echocardiogram, a daily component of the clinical practice of cardiologists.

As interest in the technique has grown, the number of studies on cardiac elastography has increased. However, different impulse emission techniques, ultrasound devices, and configurations make it difficult to understand the data and standardize the results. The technique's standardization is fundamental and must be achieved in the future. Likewise, different result metrics can be found in the literature. There is a greater tendency to use wave propagation speed, rather than elasticity, thus avoiding equations that depend on mechanical factors inapplicable to the myocardium.

Tissue dispersion and anisotropy data can also be obtained through elastography, allowing for more advanced tissue characterization. Furthermore, most studies typically report shear wave speed in the interventricular septum using a long-axis parasternal window, due to the almost orthogonal relationship between the position of the ultrasound beam and the cardiac tissue required to induce the shear waves. However, other echocardiographic windows and regions of the myocardium may be used for other assessments, commensurate with advances in device quality.

Conclusions

Cardiac elastography has shown good accuracy in evaluating shear wave propagation speed, allowing myocardial stiffness estimation despite limitations, as well as a non-invasive and inexpensive detailed assessment of diastolic function. The method is still being tested and is the subject of growing interest in the national and international scientific community. The method may provide unique additional information to conventional echocardiography and add important diagnostic value for a variety of heart diseases.

Author Contributions

Conception and design of the research: Fernandes F; acquisition of data and analysis and interpretation of the data: Santorio NC, Pereira NM; writing of the manuscript: Santorio NC, Pereira NM, Cafezeiro CRF; critical revision of the manuscript for intellectual content: Fernandes F, Santorio NC, Cafezeiro CRF, Alencar Neto AC, Bueno BVK, Pereira FL, Chammas MC.

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Case Report

Exploring Complexities in Differential Diagnosis: Torn Chord Tendinea in the Aortic Valve

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Introduction

The prevalence of anomalous chordae in the aortic valve is rare in clinical practice.[1] These anomalies, although uncommon, can have significant clinical implications, including valve insufficiency, arrhythmias and/or embolic risk. Accurate diagnosis and understanding of its pathophysiology are essential for adequate patient management.

The uncommon nature of anomalous chordae in the aortic valve means that their presence can often go unnoticed or misdiagnosed. Medical literature presents few reports on these structures of probable embryonic origin, leaving gaps in clinical knowledge.[2] Furthermore, due to its ability to influence cardiac hemodynamics and potential to complicate clinical conditions, it is essential to expand the understanding of its incidence, clinical manifestations, and best management practices.

Case report

A 59-year-old female patient with a history of gastroesophageal reflux disease (GERD) attended an outpatient consultation with a cardiologist reporting dyspnea on exertion and unintentional weight loss (around 10 kilos) in 6 months. She denied other cardiovascular symptoms and fever, without infectious stigmata. Physical examination was unremarkable; however, during dental evaluation, impaired oral hygiene and the presence of signs of infection with abscess were noted in a dental unit. During the initial investigation, the transthoracic echocardiogram (TTE) revealed cardiac cavities with normal dimensions (left atrium volume: 25mL/m^2, diastolic diameter 48mm, systolic diameter 30mm, end-diastolic volume 107mL), mild mitral and tricuspid valve reflux, normal diastolic function (E/e': 06), myocardial contractility and preserved biventricular systolic function (LVEF: 67%, estimated using the Simpson method). Furthermore, a filamentary lesion was identified in the aortic valve on its ventricular surface. This lesion, characteristically mobile, had dimensions of approximately 11 mm. Given the clinical relevance of this observation and the potential implication of endocarditis or other cardiac pathologies, blood cultures were collected to identify possible infectious agents.

Transesophageal echocardiography (TEE) assessed the aortic valve lesion with greater precision, identifying incipient signs of degeneration with minimal reflux. Additionally, an image with a serpiginous appearance was detected, with a maximum diameter of up to 21 mm (Figures 1 and 2), adhered to the ventricular surface of the non-coronary valve, suggestive of vegetation.

In addition to evaluating inflammatory markers and searching for infectious foci, additional screening was conducted to investigate autoimmune diseases. The tests performed, which included lupus anticoagulant, rheumatoid factor, anti-Beta-2 glycoprotein antibodies, antinuclear antibodies (ANA), anti-Sm, anti-RNA, and anti-DNA, all returned within normal parameters, not indicating autoimmune disease activity. White blood cell count showed 5.82 thousand/mm^3, C-Reactive Protein (CRP) (5.2mg/L; RV: < 10mg/dL) and procalcitonin remained at normal levels (0.05ng/mL; RV : < 0 .5ng/mL). NT-proBNP was at a level that rules out acute heart failure – 136pg/mL; reference value (RV): < 450pg/mL. Hemoglobin and hematocrit were slightly reduced (12.0g/dL and 36.4%, respectively), indicating mild anemia, but renal function was confirmed as normal (Urea 30mg/dL, Creatinine 0.92mg/dL). In parallel to the infectious and immunological investigation, a complementary evaluation was carried out with a tomography of the chest, sinuses and abdomen, without significant changes, as well as an annual screening mammogram, carried out prior to hospitalization, without relevant findings.

The cardiovascular surgery team was consulted, and the therapeutic approach was discussed in the Heart Team: clinical *versus* surgical treatment. The patient remained afebrile and stable during the hospitalization period, with negative blood cultures. Empirical antibiotic therapy was started (1st set: ceftriaxone associated with oxacillin and gentamicin, later replaced by the 2nd set, with daptomycin associated with ceftriaxone).

After 6 weeks of clinical treatment, during which there was no reduction of the lesion or symptomatic improvement, and considering the significant extension of the lesion with a large mobile component in the left ventricular outflow tract, the medical team decided, together with the patient, to proceed with surgical intervention. This decision was based on the potential risk of embolization, given the mobility and location of the lesion, which substantially increased the possibility of serious embolic events. Prolonged clinical management,

Keywords

Aortic Valve; Heart Valve Diseases; Diagnostic Imaging; Cardiac Surgical Procedures

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without evidence of regression of the injury, reinforced the need for a more definitive resolution to mitigate the associated risks and promote a more effective recovery.

Intraoperatively, a 5-cm lesion suggestive of chorda tendineae was identified and removed (Figure 1). Anatomopathological evaluation confirmed valve tissue, and culture was negative. Seven days after surgery, the patient was discharged from the hospital, showing subsequent improvement in symptoms and, upon reassessment with TTE, maintained biventricular systolic function and minimal aortic insufficiency, without residual lesions.

Discussion

The chordae tendineae of the aortic valve, also called fibrous "strands", formed between the aortic valve and other cardiac structures, are embryonic remnants of the valve formation process.[3,4] In terms of diagnosis, there are descriptions of its association with embolic events or endocarditis, although its clinical relevance is still subject to debate. Therefore, careful evaluation and close clinical follow-up are recommended when such structures are identified.[5,6]

Although this congenital alteration is a rare observation on imaging exams, its identification is of fundamental importance, as, in some cases, it may be associated with complications.[3,4] Among these, we may consider the possibility of embolic events and progressive aortic regurgitation, including signs of ectasia of the proximal aortic segments and/or consequent eccentric left ventricular hypertrophy due to volumetric overload.

Anomalous aortic chordae tendineae can be associated with valve lesions and manifest itself both in chronic conditions, with an intact cord, and in acute cases of aortic insufficiency due to its rupture. This rupture, whether spontaneous or resulting from trauma, ischemia or senile degeneration, can give rise to a mobile filamentary image on exams, complicating the differential diagnosis with thrombi or vegetation, as demonstrated in the clinical case at hand.[5]

The change in flow generated by the presence of chorda tendineae in an anomalous position can alter the phenotypic expression of endocardial cells in the left ventricular outflow tract, resulting in fibroproliferative lesions that can increase the incidence of cardiac complications.[1] Furthermore, this tendon anomaly can also lead to the formation of a gradient in the left ventricular outflow tract, even resulting in subvalvular aortic stenosis.[4]

During the intraoperative surgical approach, it was possible to identify in detail the specific sites of insertion of the anomalous chorda tendineae (Figure 2), located in the interventricular septum, in the region of the mitral aortic window and, additionally, in the Arantius node belonging to the right coronary valve. Notably, the cord associated with this last site was broken, which determined the finding correlated with the TTE (Figures 3 and 4).

The detection of an anomalous chordae tendineae in the aortic valve, especially when considering the patient in question, highlights the complexity and diagnostic challenges faced in clinical practice. In the present case, the extremely mobile lesion observed in the left ventricular outflow tract introduced an ambiguous diagnostic scenario, where the possibility of endocarditis emerged as a differential diagnosis. This case highlights the importance of an in-depth understanding and a meticulous approach in evaluating such anomalies, thus ensuring diagnostic accuracy and appropriate clinical management.

Conclusion

The presence of chordae tendineae in the aortic valve, although often underdiagnosed, can have significant implications for cardiac hemodynamics. When this tendinous chord is ruptured with a large component of mobility, it can be confused with vegetation, commonly associated with endocarditis, introducing complexity to the differential diagnosis.

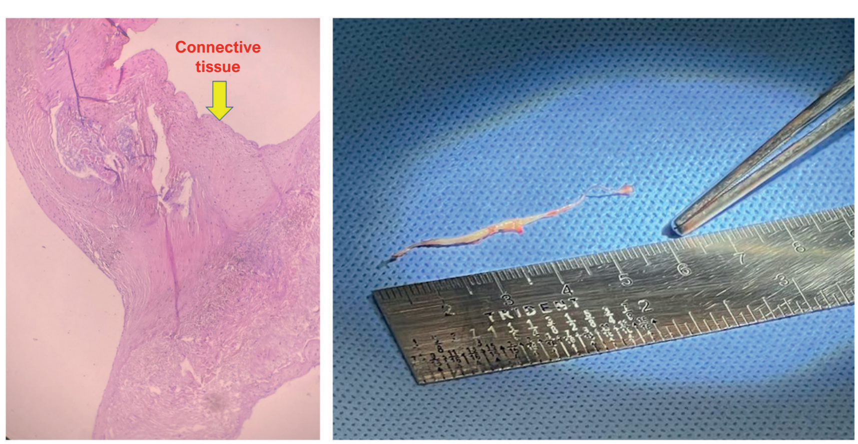

Figure 1 – *On the left, histological section with connective tissue characteristic of valve tissue with the presence of myxomatous areas in between. On the right, anatomical image of the specimen after excision of the lesion.*

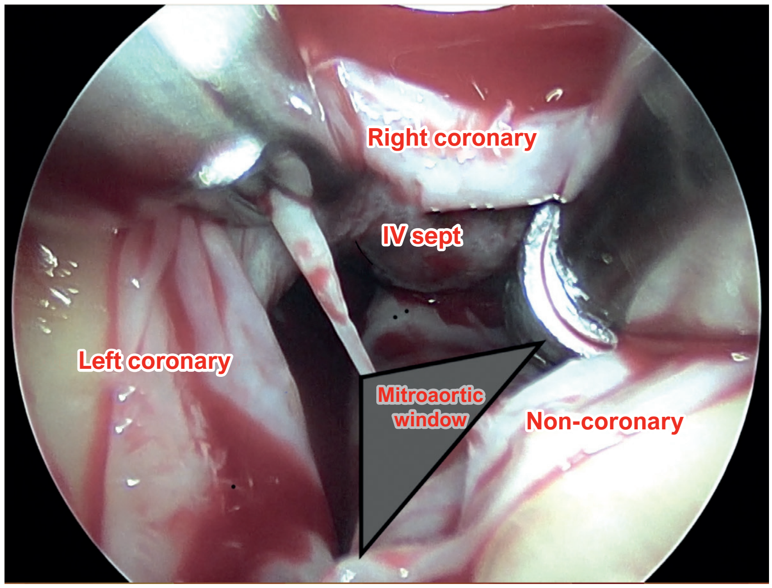

Figure 2 – *Surgeon's view through videothoracoscopy in minimally invasive surgery: after transverse aortotomy and suspension of the aortic valve leaflets. An anomalous cord is identified in the left ventricular outflow tract with fixed ends in the interventricular septum and Mitroaortic Fibrosa (FIMA).*

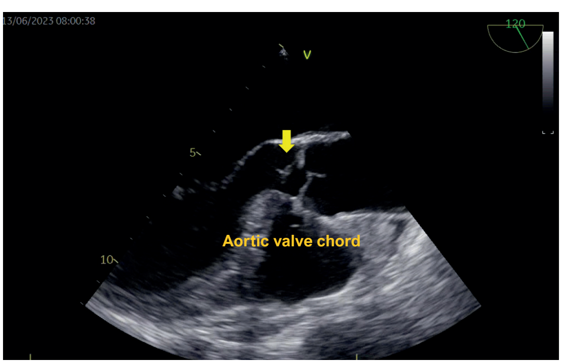

Figure 3 – *Transesophageal echocardiogram at 120°, showing a filamentary lesion related to the ventricular surface of the aortic valve, markedly mobile and measuring up to 21mm.*

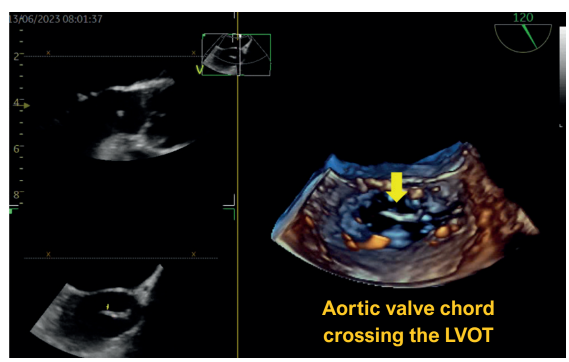

Figure 4 – *3D Transesophageal Echocardiogram, in 4D Zoom mode, with visualization from the ventricular view, showing a filamentary lesion crossing the left ventricular outflow tract.*

Author Contributions

Conception and design of the research: Costa A; acquisition of data:_Costa A, Alves ES, Pinheiro P, Flausino L; analysis and interpretation of the data:_Freire MV; writing of the manuscript: Costa A, Freire MV, Pinheiro P; critical revision of the manuscript for intellectual content: Morel RV.

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Ethics Approval and Consent to Participate

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Takotsubo Syndrome After Percutaneous Mitral Valve Repair With Mitraclip®: A Case Report

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Introduction

Takotsubo syndrome (TTS), also known as stress cardiomyopathy or broken heart syndrome, is a condition whose pathophysiology is not well established, but which results from multiple factors that act synergistically in a setting of stress perception and cardiocirculatory response.[1] It was first described in 1990, and the disproportionate and excessive increase in serum catecholamines is known to play a central role in its pathogenesis by favoring the occurrence of complications. Although rare, TTS deserves attention due to its inherent risk of decompensated heart function.[2,3]

Case report

An 83-year-old man was referred for elective mitral valve repair after multiple hospitalizations for cardiac decompensation, characterized mainly by dyspnea at rest (New York Heart Association [NYHA] functional class [FC] IV). He had significant mitral regurgitation (MR) due to partial rupture of pretendinous cords of the posterior leaflet (P2 segment) and mild myxomatous degeneration (Figure 1). After discussion with the Heart Team, percutaneous mitral valve repair with Mitraclip® was indicated.

The patient's past medical history included systemic arterial hypertension, diabetes, chronic atrial fibrillation with oral anticoagulant therapy, pulmonary hypertension with a pulmonary artery systolic pressure of 52 mmHg, and anxiety disorder. Furthermore, coronary artery disease was detected during preoperative catheterization, and percutaneous transluminal angioplasty of the proximal third of the left anterior descending (LAD) artery was performed after identification of a type A lesion (70%), followed by stenting (Figure 2).

Mitraclip® implantation was performed via the right femoral vein. After transseptal puncture guided by three-dimensional transesophageal echocardiography, the delivery catheter was advanced across the septum. Two clips were implanted: the first was placed at the A2-P2 segment, and the other was placed lateral to the first (Figure 3). After the procedure, mild MR was identified, with a mean transmitral gradient (TMG) of 5.8 mm Hg in the orifice with the greatest TMG. There were **no** complications during the procedure.

On postoperative day 3, the patient developed hyperactive delirium, dyspnea requiring oxygen therapy, and tight, continuous, intense chest pain (not radiating). On physical examination, the patient presented confusion, mucocutaneous pallor, diaphoresis, tachypnea, and an oxygen saturation of 98% on 2 lpm of oxygen by nasal cannula. No adventitious sounds were detected on respiratory auscultation. His blood pressure was 150/70 mm Hg and heart rate was 109 bpm, with an irregular heart rhythm. The peripheral pulses were palpable and symmetric.

Electrocardiography (ECG) revealed symmetrically inverted peaked T-waves in the anterolateral leads, and laboratory tests showed an elevated high-sensitivity cardiac troponin level (73.8 ng/mL; reference range < 14 ng/mL), suggesting non ST-elevation acute coronary syndrome (ACS).

A transthoracic echocardiogram (TTE) revealed significantly reduced left ventricular ejection fraction (LVEF) – from 51% to 25% (Simpson) – and significant apical hypokinesia as well as in the mid-anterior, mid-anteroseptal, and mid-anterolateral walls.

In view of the complementary exams, an emergency coronary cineangiography was performed, which ruled out significant coronary lesions and reveled a patent stent in the LAD artery, but with increased systolic volume due to extensive anterior, inferior, and apical akinesia (sparing only the base) on ventriculography (Figure 4).

Because of absence of thrombotic lesions on angiography, the patient remained hospitalized and receiving clinical treatment. On postoperative day 4, troponin levels were significantly reduced to 24.3 ng/mL. The patient was clinically improved and discharged from hospital.

One year after the intervention, the patient remained clinically stable (NYHA FC II). Control TTE showed LVEF recovery to 61% (Simpson), moderate MR, and mild stenosis (TMG 4.0 mm Hg and peak gradient (Gp) 17.0 mm Hg), with normal segmental LV contractility (Figure 5).

In view of the foregoing, a diagnostic hypothesis of TTS secondary to Mitraclip® implantation was made, based on dynamic changes in ECG and echocardiography, elevation of markers of myocardial necrosis, apical "ballooning", and hyperkinesia of basal segments on ventriculography, with no evidence of coronary artery obstruction on coronary cineangiography despite recent stent implantation at the LAD artery, in a setting of postoperative stress.

Keywords

Takotsubo Cardiomyopathy; Mitral Valve Insufficiency; Case Reports

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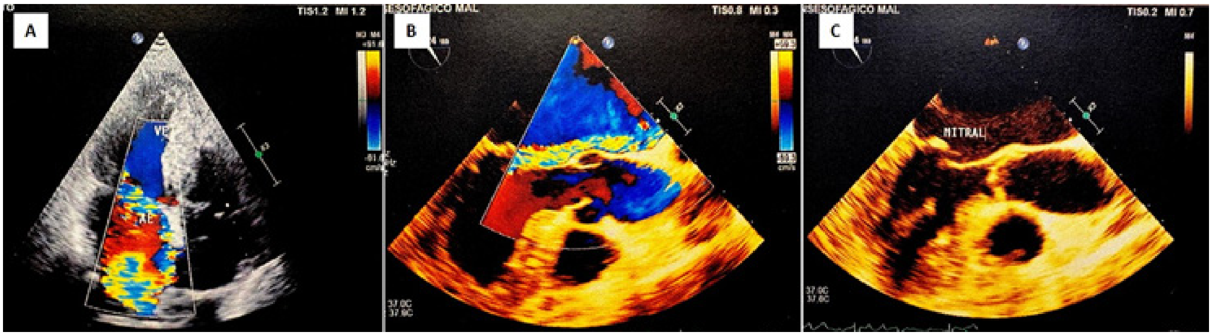

Figure 1 – *Preoperative transesophageal echocardiography. (A) and (B): Significant eccentric MR. (C): Mitral valve prolapse with myxomatous degeneration and partial rupture of pretendinous cords (flail) of the posterior leaflet (P2 segment).*

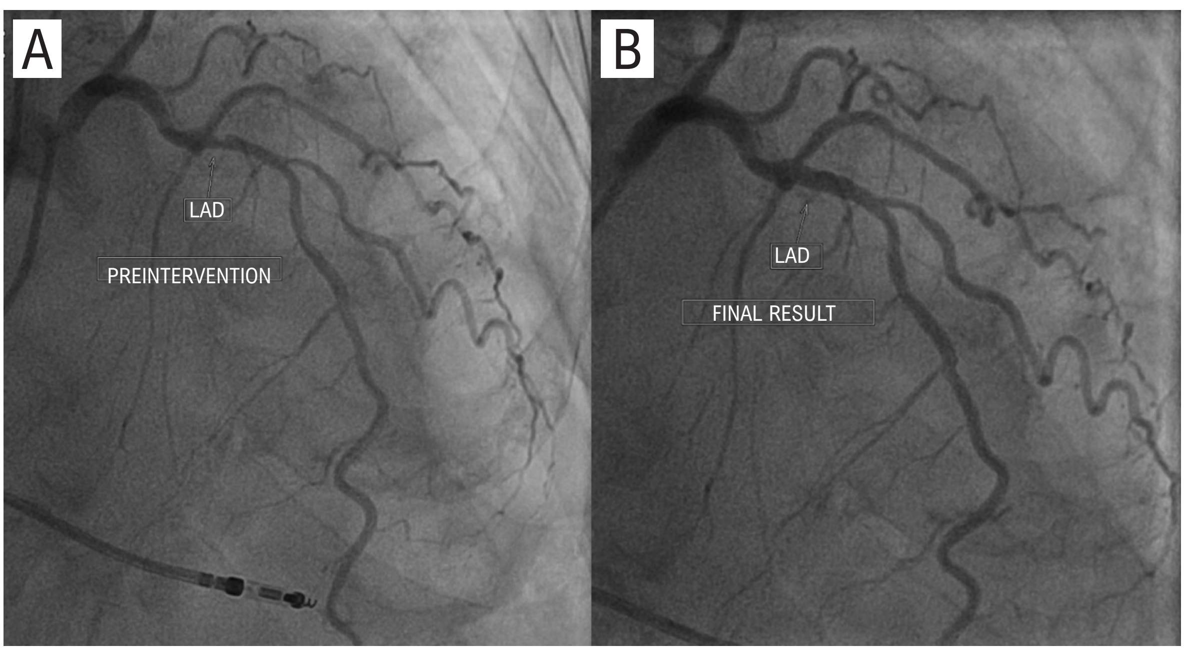

Figura 2 – *Coronary cineangiography. (A): Type A lesion (70%) of the proximal third of the LAD artery; (B): Angioplasty of the LAD artery with everolimus-eluting stent (3.0 x 8.0 mm).*

Discussion

This case report draws attention to the presumed correlation between TTS secondary to percutaneous Mitraclip® implantation and mitral valve repair in an older male patient at very high cardiovascular risk.

Studies have shown that catecholamines play a central role in the pathogenesis of TTS.[2] Other aspects that may be related to TTS include macro and microvascular endothelial dysfunction, vasospasm, and calcium overload in myocytes, which cause disorders of ventricular contraction and function, mostly affecting postmenopausal women.[1,3]

Clinical characteristics are usually similar to those of ACS. Patients present with chest pain, dyspnea, acute heart failure, abnormal ECG (such as ST segment elevation or depression or T wave inversion), and increased serum troponin. However, these ACS patients do not present troponin peaks , as would be expected in cases of acute myocardial infarction (AMI), nor obstructive lesions that justify the severe contractility deficit observed in TTS. Although rare, TTS is a differential diagnosis of ACS, which may be underdiagnosed given the higher prevalence of AMI due to obstructive coronary artery disease in the general population.[1-4]

Coronary angiography combined with ventriculography is considered the gold standard for TTS diagnosis. It shows apical akinesia of the LV with normal contractility of the base, which creates a "balloon" appearance in its apical

Case Report

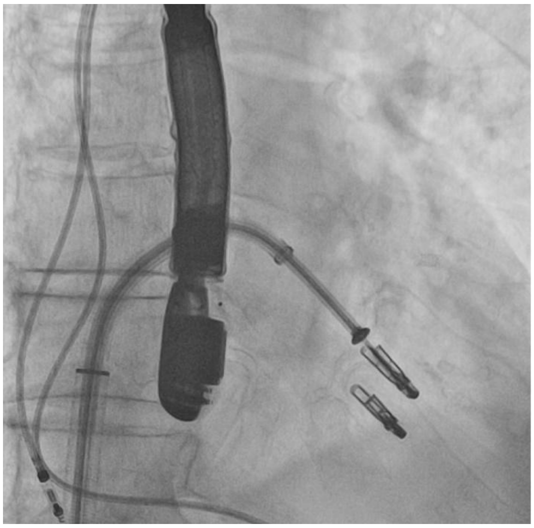

Figura 3 – *Percutaneous Mitraclip® NT implantation.*

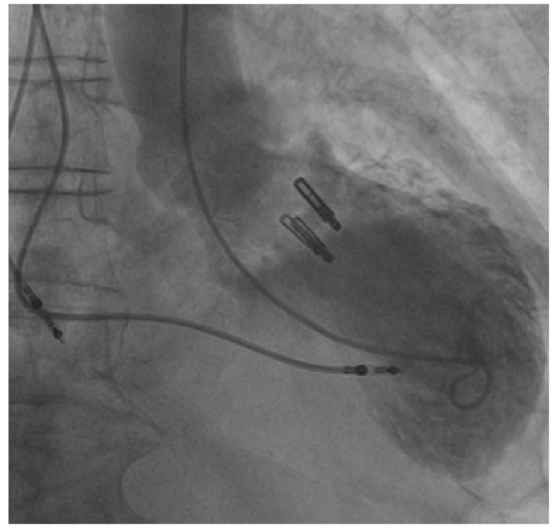

Figura 4 – *Ventriculography during systole on the third day after Mitraclip® implantation*

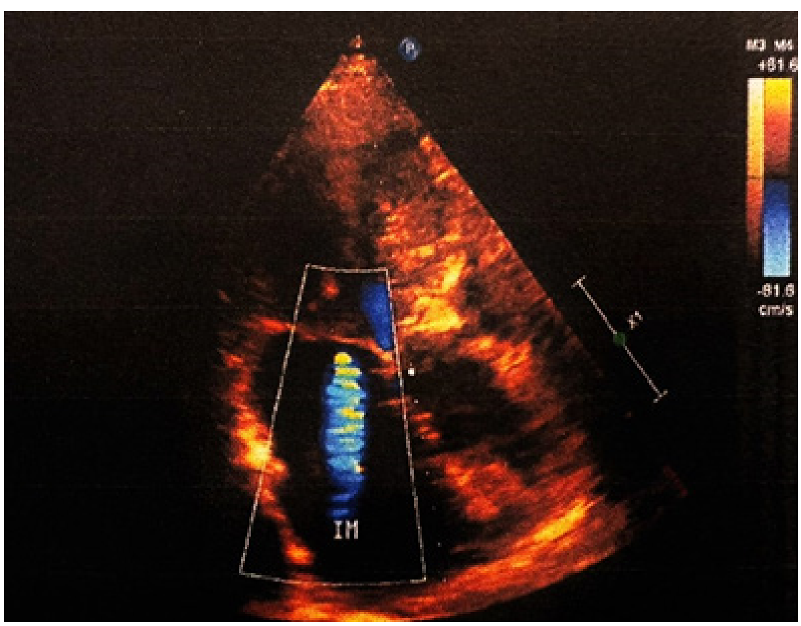

Figure 5 – *TTE 1 year after Mitraclip® implantation showing moderate MR.*

portion (“apical ballooning) , without evidence of obstructive coronary artery disease.[1]

TTS treatment involves clinical support measures. Most cases progress with spontaneous and complete remission within days or weeks. However, the acute phase, which results from complications such as cardiogenic shock, arrhythmias, and cardiac arrest, may be more severe, with high morbidity and mortality rates.[1,3]

From an epidemiological perspective, TTS is extremely rare. Despite conducting a comprehensive literature search, we found only one report of MitraClip®-related TTS, which occurred in 2020 in the United States. Similar to our case, it was observed in an older male patient and had a favorable clinical outcome.[5] Another study described the case of a woman with TTS who underwent open surgery to correct severe MR triggered by an adverse reaction to protamine.[6]

MitraClip® implantation is less invasive than thoracotomy valve replacement for the treatment of severe MR. It is considered effective and safe in patients refractory to clinical treatment, with excellent results reported by the COAPT study and its 5-year follow-up, in addition to being an alternative treatment for those at high surgical risk or with contraindications to surgery.[4,7,8] Despite being less invasive, the percutaneous technique may induce catecholamine release as a result of physical and emotional stress, as also happens in open surgery and hospitalization.[2] The case described in this report brings attention to the fact that TTS is a potential complication of percutaneous mitral valve repair with MitraClip®.

Author Contributions

Conception and design of the research: Souza AL, Prudente ML, Nogueira ACC, Gardenghi G; acquisition of data: Souza AL; analysis and interpretation of the data and writing of the manuscript: Souza AL, Prudente ML, Gardenghi G; critical revision of the manuscript for intellectual content: Souza AL, Prudente ML, Rodrigues D, Nogueira ACC, Gardenghi G.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the CEP/HUGO under the protocol number 85497418.2.0000.0033. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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The Importance of Imaging Multimodality in the Diagnosis of a Rare Case of Papillary Fibroelastoma in the Left Ventricular Apex

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Introduction

Papillary fibroelastoma (PF) is a rare, benign primary cardiac neoplasm, initially described as an incidental finding in autopsies or surgeries, and ranks third among the most common cardiac tumors. It mainly affects the heart valves, accounting for 75% of all tumors in this region and is often diagnosed incidentally.[1]

Its clinical presentation can vary widely, ranging from asymptomatic cases to situations in which systemic embolization occurs, caused by adherent thrombi as well as by fragmentation of the tumor itself. Currently, PF is no longer a tumor diagnosed only in autopsies and can now detected with new cardiovascular imaging modalities, thus enabling early treatment and preventing complications.[2]

Our study presents a clinical case report of a patient with PF located at the apex of the left ventricle, in which the diagnosis was suggested during a transthoracic echocardiogram. Hence, our work demonstrates the importance of the multimodality of cardiovascular imaging in identifying primary cardiac tumors, such as PF. Furthermore, the importance of differential diagnoses, propaedeutic aspects, and the therapeutic approach to PF was addressed.

Case Report

Our study presents the case of a 53-year-old female patient with a previous history of transient ischemic attack (TIA). The clinical examination was normal, and the electrocardiogram was in a proper sinus rhythm. In the preoperative assessment of lumbar denervation, a transthoracic echocardiogram (TTE) was requested, which revealed an oval mass, slightly more echogenic than the myocardium, homogeneous, with a smooth, mobile surface, located at the apex of the left ventricle, which could correspond to a thrombus or tumor (Figure 1). The TTE was complemented with ultrasound contrast to better characterize the mass, ruling out the possibility of a thrombus, confirming that it was an apical, pedunculated tumor, with homogeneous contrast distribution, measuring 0.9 cm x 1.0 cm, with a peduncle of 0.6 cm in length and 0.2 cm in thickness (Figure 2), suggestive of PF. Subsequently, a cardiac magnetic resonance imaging (CMRI) scan was performed, which identified a homogeneous pedunculated mass at the apex of the left ventricle, measuring 1.0 x 0.8 cm, isointense on T1 and T2, with no fat saturation, without first-pass perfusion, showing late peripheral enhancement "in a peripheral halo" (Figure 3), compatible with PF. The patient underwent heart surgery, and an oval, pedunculated tumor was identified at the apex of the left ventricle (Figure 4). After surgical excision of the tumor, the histopathological study revealed that it was a neoplasm comprised of avascular bundles with fibroelastic content and endocardial lining, consistent with the diagnosis of PF.

Keywords

Cardiac Papillary Fibroelastoma; Heart Neoplasms; Transient Ischemic Attack

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Discussion

The diagnosis and treatment of cardiac masses are a real challenge, although they are rarely found in clinical practice.[3] The incidence of primary cardiac tumors is approximately 0.017% to 0.20%, half of which are myxomas and nearly 75% are benign.[2] PF can be found in different regions of the heart, representing around 10% of all cardiac tumors. Typically, this type of tumor affects the heart valves, and is more common in the valves on the left side of the heart, especially the aortic valve (29%) and the mitral valve (25%), compared to the pulmonary valve (13%) and the tricuspid valve (17 %). However, it can appear on any endocardial surface, including non-valvular regions,[4] as observed in the case described above.

The occurrence of PF in the apex of the left ventricle is considered to be extremely rare. According to a study conducted by Sovic et al.,[5] from 1997 to 2018, only 13 cases of PF in the apical region were described in the medical literature.

In most cases, the tumor is single, pedunculated, and avascular, and has an average size of approximately 1 cm in diameter, but it can vary between 0.2 and 4.6 cm, and is attached to the endocardium by a short, thin rod. Microscopically, this pathology consists of avascular connective tissue covered by an endothelium, with an appearance similar to "sea anemone".[6]

In the study by Saleh et al.,[7] 14 patients were found with 18 lesions (mean age of 60.5 ± 12.3 years), resembling the age of the patient in this report. Eleven patients (79%) were symptomatic. Most lesions were solitary, with a diameter of ≤1.5 cm, half involving the left side of the heart.

Generally, PF is asymptomatic and, in most cases, is diagnosed incidentally during imaging tests or surgeries for other causes. The clinical manifestation occurs mainly due

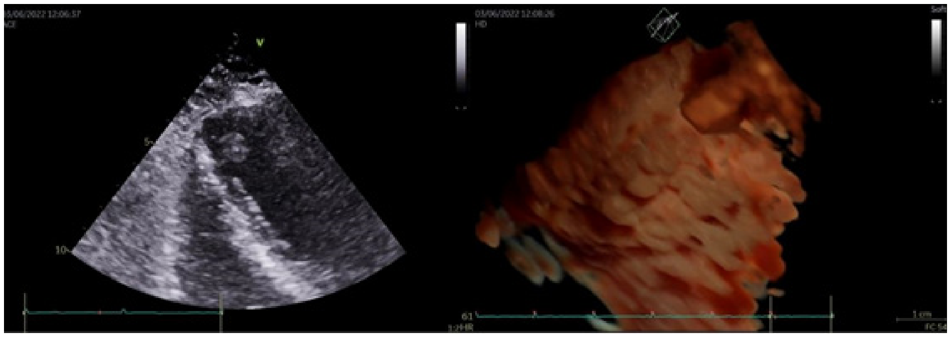

Figure 1 – *Two-dimensional and three-dimensional transthoracic echocardiogram (TTEcho): a rounded structure was identified, slightly more echogenic than the myocardium, homogeneous, measuring 1.2 x 1.2 cm, with a smooth, mobile surface, located at the apex of the left ventricle, with a velvety appearance, which may correspond to a thrombus or a tumor.*

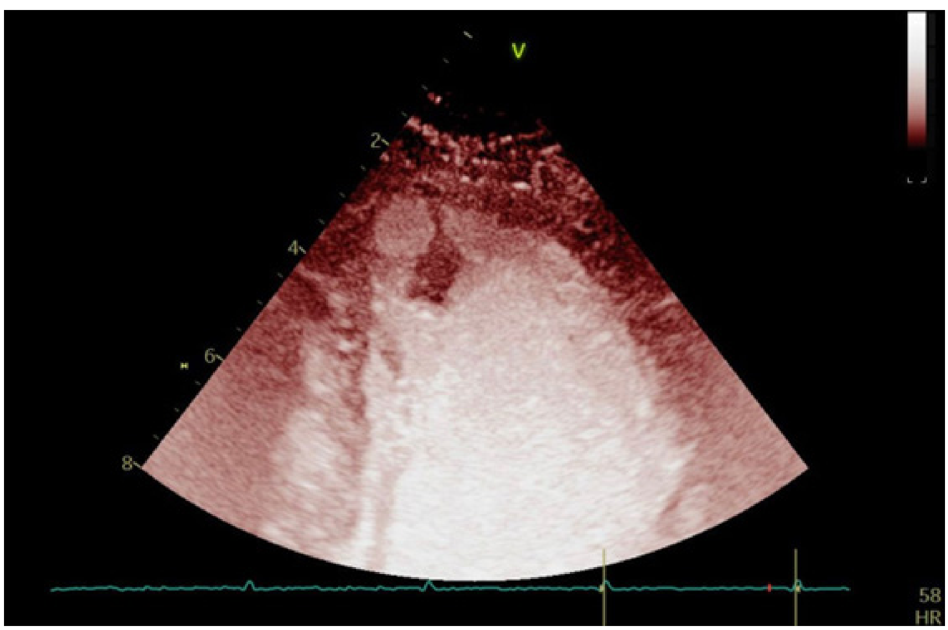

Figure 2 – *Contrast echocardiogram, showing the presence of a tumor at the apex of the left ventricle, with benign characteristics, suggestive of papillary fibroelastoma.*

to embolization, often cerebrovascular. In the case reported herein, the patient had a previous episode of TIA. PF can cause peripheral embolisms and an obstruction of the coronary ostia, which can begin as a myocardial infarction, especially in the aortic valve. Differential diagnosis must be made with clots, calcium, vegetation, or other foreign bodies.[8]

Symptomatic patients or those with pedunculated tumors should undergo surgical resection as the treatment of choice, aiming to prevent embolic phenomena. In asymptomatic individuals, surgery is controversial, with tumor mobility being the determining factor for surgical intervention. Therefore, asymptomatic patients with non-mobile tumors can be monitored in periodic clinical evaluations. Recurrence is rare, and has been only described in a few cases, highlighting the relevance of monitoring with TTE for identification.[2,9]

Advances in non-invasive diagnostic imaging techniques have played a key role in evaluating and identifying an increasing number of intracardiac tumors more quickly and more effectively, even in the case of those that are poorly defined and small in size. Among these techniques, TTE stands out as a non-invasive method with greater access and high accuracy in detecting cardiac tumors, presenting a specificity of 87.8% and a sensitivity of 88.9%.[2] Ultrasound contrast allows for a better visualization of the structures

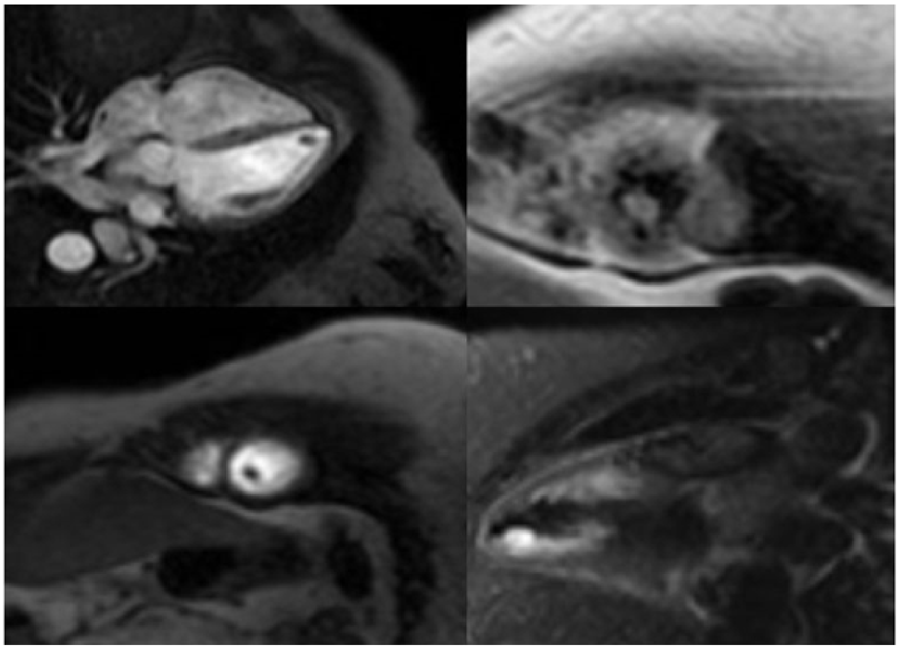

Figura 3 – *Cardiac magnetic resonance imaging (CMRI), showing a homogeneous pedunculated mass at the apex of the left ventricle, measuring 1.0 x 0.8 cm, isointense on T1 and T2, with no fat saturation and no first-pass perfusion, showing late peripheral enhancement "in a peripheral halo".*

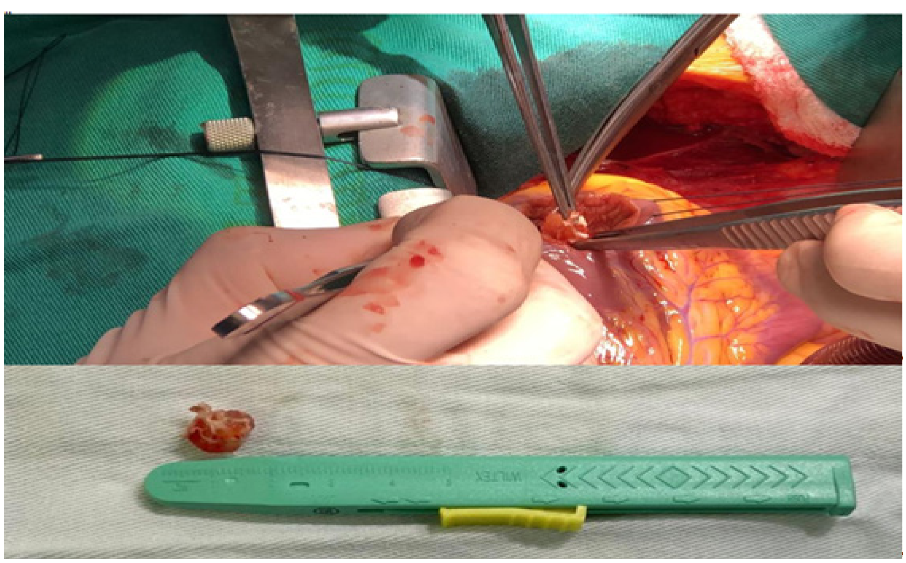

Figure 4 – *Oval tumor, measuring 1.0 x 0.8 cm, pedunculated at the apex of the left ventricle.*

within the cavity and the assessment of their vascularization. The difference in blood flow in cardiac masses can help distinguish between vascular or non-vascular thrombi or tumors through the contrast distribution pattern.[10] CMR evaluates key characteristics, including morphology, dimensions, location, extension, homogeneity, and presence of the infiltration of surrounding tissues. Furthermore, it also analyzes signal characteristics that can assist in histopathological characterization, such as fatty infiltration, necrosis, hemorrhage, calcification, and vascularization.[10]

Conclusion

This report shows that PF in the apex of the left ventricle is rare, as evidenced by the scarcity of reports in the medical literature. The diagnosis is generally made incidentally. Although it is benign and asymptomatic in most cases, it is important to perform differential diagnoses in order to choose the appropriate treatment and prevent complications, such as embolic events. Non-invasive cardiovascular imaging techniques have been very useful in diagnostic evaluations and play an important role in identifying PF. The present case highlights the importance of using different imaging modalities to diagnose and plan PF surgery.

Author Contributions

Conception and design of the research: Pereira MM, Pereira LSM, Melo Filho JX; acquisition of data: Pereira MM, Melo Filho JX, Juliano MTH; analysis and interpretation of the data and writing of the manuscript: Pereira MM, Pereira LSM; critical revision of the manuscript for intellectual content: Pereira MM, Melo Filho JX, Juliano MTH, Melo RJL, Nina VJS; patient management during hospitalization: Juliano MTH; cardiac MRI: Melo RJL; surgical treatment: Nina VJS.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Hospital e Maternidade São Domingos under the protocol number 6.482.701. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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Case Report

Asymptomatic Pericardial Cyst: A Case Report and Brief Review of its Management

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A 59-year-old female patient, with high blood pressure, *diabetes mellitus*, and dyslipidemia, was referred to a tertiary care service for investigation of an irritating, non-productive cough that had onset two months prior. She denied symptoms of reflux or postprandial stuffiness, as well as nasal congestion or signs of allergic rhinitis. She denied smoking, alcohol consumption, and contact with individuals with tuberculosis and did not report previous pneumonic events.

She was taking losartan (50mg 12/12h), atenolol (25mg 12/12h), metformin (850mg 2x/day), and simvastatin (20mg at night), in addition to 100mg of acetylsalicylic acid at lunch daily.

She was initially medicated with dexchlorpheniramine maleate 2 mg per day and additional biochemical tests and a simple chest x-ray were requested. Upon return, she reported complete improvement in respiratory symptoms, biochemical tests were within normal limits, but the x-ray revealed a mass in the right anterior region of the chest (Figure 1A), which began to be investigated.

Given the suspicion of a cyst or neoplasia, a chest computed tomography was requested, which revealed a cystic lesion with regular contours located in the right cardiodiaphragmatic sinus, in contact with the pericardial surface on the right (Figure 3A).

Upon consultation with cardiology, the patient was asymptomatic and had no abnormalities on clinical examination, and it was found that the comorbidities were under adequate laboratory control. An electrocardiogram and a transthoracic echocardiogram were then requested, with only the latter being performed, which revealed cavities with preserved dimensions and systolic function, but with a hypoechogenic image in the right atrioventricular sulcus of imprecise dimensions, apparently without causing cardiac compression (FIGURE 2). A review of old medical records indicated that a chest x-ray taken 10 years earlier showed a mass with the same topography and smaller dimensions (Figure 1B). A magnetic resonance imaging (MRI) examination of the heart was then requested, which revealed the presence of a pericardial cyst, located in the anterior mediastinum, measuring 8.8 x 3.6 x 7.4 cm (Figure 3B). No significant changes were observed in the cardiac chambers and in the functions of the left and right ventricles. The patient remains under semi-annual clinical follow-up, without symptoms, for a period of one year, under expectant management.

Keywords

Pericardium; Mediastinal Cyst; Case Reports.

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Discussion

Pericardial cyst is an uncommon clinical entity, with an estimated incidence of 1/100,000 to 1/10,000 autopsies. Its etiology is not yet completely understood, but it is believed to be due to an abnormal development of the pericardium during embryogenesis. It is necessary to differentiate the cyst from the pericardial diverticulum, which possibly have the same origin but, in the latter, there is communication with the pericardial cavity.[1] Most cases are asymptomatic, even with large dimensions, and the lesion is often discovered incidentally during imaging exams or heart surgery. When symptomatic, the clinical presentation is variable and may include cardiorespiratory symptoms, such as chest pain, dyspnea,[2] cough,[3] sudden cardiac death or signs of cardiac tamponade.[4]

The diagnosis of pericardial cyst is initially suspected by the incidental performance of a chest x-ray, which shows the mass attached to the cardiac silhouette. Doppler echocardiography, computed tomography and cardiac MRI allow the diagnosis to be confirmed, notably the last two.[5] Chest x-ray may reveal a mediastinal mass or an area of increased density. Computed tomography (CT) scans and cardiac MRIs provide more detailed information about the location, size, and characteristics of the cyst. Transthoracic echocardiography can be useful in evaluating cardiac function and the presence of cyst-related complications, such as cardiac compression. Differential diagnosis should include neoplasms and, more rarely, migratory hydatid cysts, which may be single.[6]

The approach to managing a pericardial cyst depends on presence or absence of symptoms, size of the cyst, impairment of cardiac function, and presence of complications, notably rupture and hemorrhage. In asymptomatic patients, an expectant approach with regular follow-up every one or two years is a safe and effective option, avoiding unnecessary invasive procedures. Recent data suggest that, in most cases, size may be maintained or even reduced, contrary to what was evidenced in this case.[7]

Surgical intervention is reserved for symptomatic patients or when there are significant complications such as cardiac compression or tamponade. Although open surgery is the most commonly used approach, punctures for drainage and relief and alcohol-based sclerosis thoracoscopy have been used.[8]

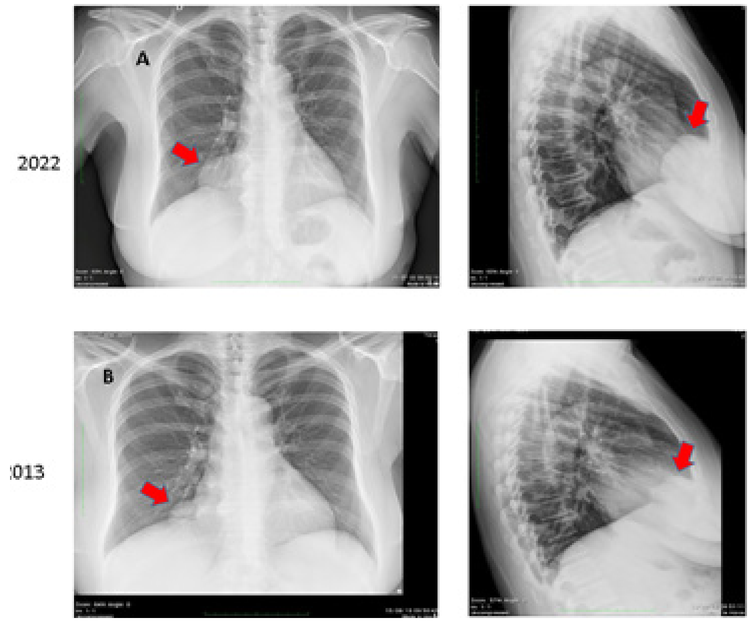

Figure 1 – *Postero-anterior and lateral chest radiographs, showing the pericardial cyst (arrows) in 2013 (lower image) and in 2022 (upper image).*

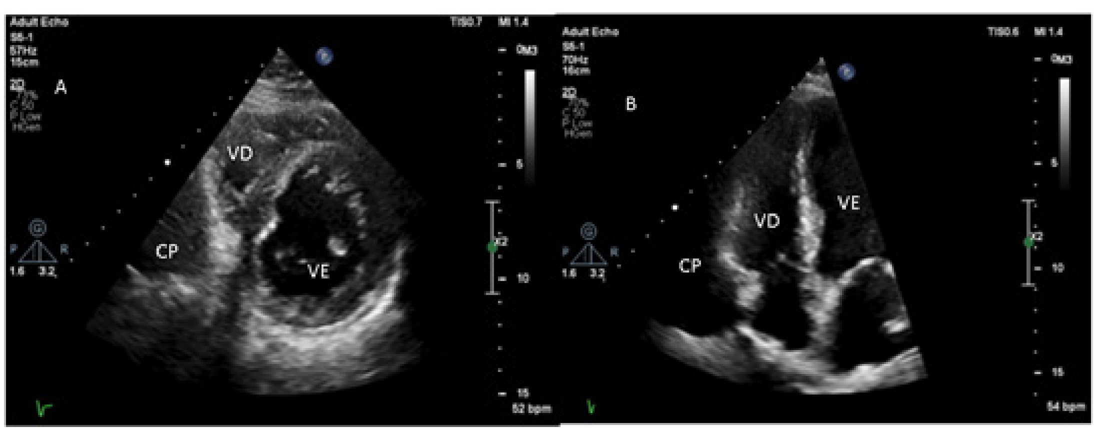

Figure 2 – *Short-axis (left image) and four-chamber (right image) Dopplerechocardiogram images showing the pericardial cyst (CP) as a luminescent area posterior to the right ventricle (VD). VE=Left ventricle.*

Conclusion

Pericardial cyst is a rare condition that can be asymptomatic and diagnosed incidentally. Expectant management is a valid option in asymptomatic cases, with regular monitoring to detect the development of symptoms or complications. Surgical intervention must be based on an individualized assessment, considering the presence of symptoms, the size and location of the cyst, cardiac function, and the risk of complications. It is paramount to increase awareness of this clinical condition to ensure proper diagnosis and management of patients. Additional studies are needed to improve our understanding of the etiology, pathophysiology, and treatment approaches of pericardial cyst.

Author Contributions

Conception and design of the research: Schmidt A; acquisition of data: Volpe GJ, Wada DT; analysis and interpretation of the data: Barbosa MR, Moreira HT, Volpe GJ, Wada DT; writing of the manuscript: Barbosa MR, Schmidt A; critical revision of the manuscript for intellectual content: Moreira HT, Volpe GJ, Wada DT, Romano MMD, Schmidt A.

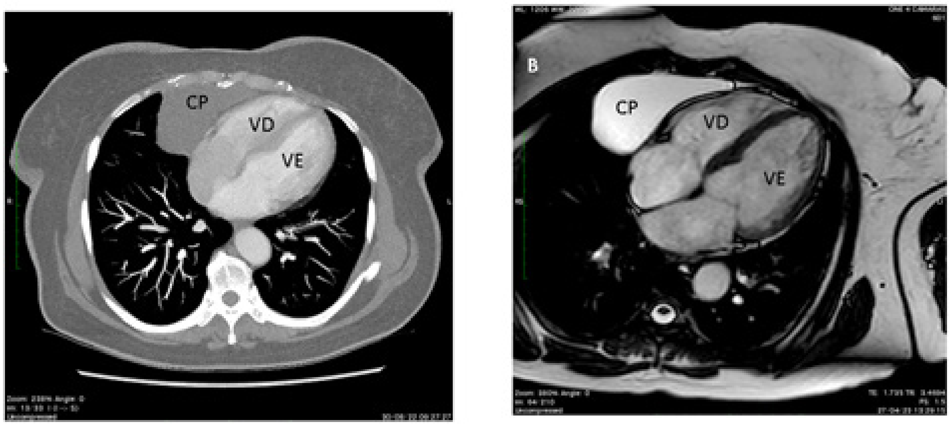

Figure 3 – *Chest computed tomography (left image) and cardiac magnetic resonance (right image) in four-chamber position, showing the well-defined and homogeneous pericardial cyst (CP).*

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Case Report

Anomalous Origin of the Coronary Artery from an Inappropriate Coronary Sinus

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Abstract

Congenital anomaly of the coronary arteries is a potentially lethal disease, especially in young people. Currently, non-invasive cardiovascular imaging tests have shown better definition of the origin and course of the coronary arteries. Surgical treatment should be indicated in symptomatic patients, while the ideal management of asymptomatic patients remains controversial. We report a case of anomalous origin of the left coronary artery from the right coronary sinus with an interarterial course, in an asymptomatic patient treated with revascularization surgery.

Introduction

Congenital anomaly of the coronary arteries can be benign or potentially severe, causing myocardial ischemia, infarction, and sudden death. The incidence varies between 0.3% and 1.5% in necropsy studies and coronary cineangiography.[1] The origin and proximal course of the anomalous coronary arteries are the main factors predicting severity.[2,3]

This anomaly represents the second most frequent cause of sudden death of cardiovascular origin in competitive athletes.[4] Its diagnosis is difficult, as the individual may be asymptomatic until before the lethal event.[5,3] The surgical techniques used to treat this pathology have evolved; however, there is no consensus regarding the most appropriate treatment for each type of patient.[5,6]

In the case of anomalous origin of the left coronary artery with an interarterial course, surgical revascularization is recommended, regardless of documented ischemia or symptoms.[7]

The objective of this study is to report an unusual case of anomalous origin of the left coronary artery from the right coronary sinus with an interarterial course in an asymptomatic patient.

Keywords

Coronary Vessel Anomalies; Sudden Death; Myocardial Revascularization.

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Case report

We report the case of a 47-year-old male patient, who walked and ran 3 times a week. The patient, who denied angina, dyspnea, syncope, or palpitations, sought his physician for routine exams. He denied systemic arterial hypertension, diabetes, or smoking. The physical examination was normal. Electrocardiogram was normal, and the patient had normal blood pressure. He underwent an exercise test that revealed electrocardiographic changes during exercise compatible with an ischemic response pattern, without complaints of angina, with a normal blood pressure response, without arrhythmia, and a good workload (10 METs).

Doppler echocardiography was normal. Given these exercise abnormalities, myocardial perfusion scintigraphy was requested to assess the presence of myocardial ischemia.

Myocardial perfusion scintigraphy was performed under the Bruce protocol reaching stage IV, lasting 10 minutes and 6 seconds, reaching 10 METs, and 97% of the age-predicted maximum heart rate. The blood pressure curve was normal; the patient did not report chest pain, and the electrocardiographic tracing during exercise revealed a descending ST depression of 2 mm in CM5 and 1 mm in CM5 during recovery (Figure 1).

The perfusion images, analyzed qualitatively and quantitatively using Wackers-Liu software (Yale University), were normal, and the circumferential profiles of the images showed normal distribution (Figure 2). Left ventricular ejection fraction was also normal, without segmental contractile dysfunction.

Due to the inability to clarify the electrocardiographic changes induced by exercise, coronary tomography angiography was requested (Figures 3, 5, 6, 7, 8, 9, 10 and 11). The coronary calcium score was zero. The dominance was right; the left coronary trunk was absent. The anterior descending artery was non-dominant, originating from the right coronary sinus in an independent ostium; following a course between the aorta and the pulmonary artery trunk toward the anterior wall of the left ventricle; subsequently, it followed the anterior interventricular sulcus along the usual course. The circumflex artery was very important, originating in the right coronary sinus in an independent ostium, following a retroaortic course, passing between the aorta and the left atrium and continuing through the left atrioventricular sulcus in the usual course. The right coronary artery was the dominant artery, reaching the posterior interventricular sulcus, where it gave rise to a posterior descending branch.

Preoperative coronary cineangiography was performed, which confirmed the tomography angiography findings, namely, proximal systolic narrowing of the anterior descending artery during its interarterial course; it did not reveal

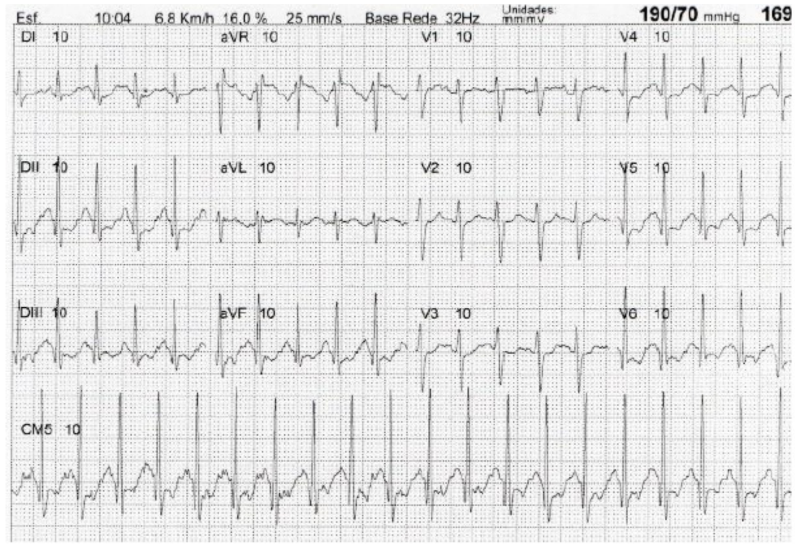

Figure 1 – *Electrocardiographic tracing obtained during Myocardial Perfusion Scintigraphy. A 2mm downsloping ST segment depression is observed at the J point in lead CM5, along with ventricular repolarization changes in the inferior and anterolateral walls. Image provided by Eduardo Lins Paixão.*

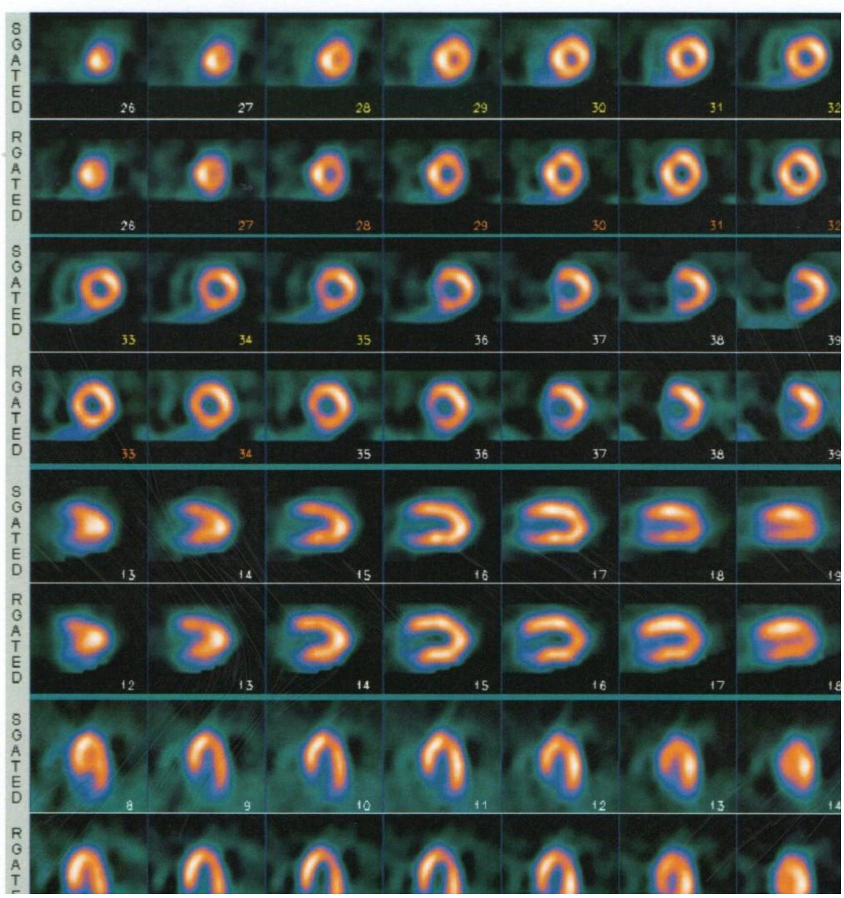

Figure 2 – *Images from the stress and rest Myocardial Perfusion Scintigraphy performed using the 1-day protocol with Tc99m-MIBI. Normal tracer distribution is observed in the walls of the left ventricle. There are no signs of post-stress transient left ventricular dilation. Image provided by Eduardo Lins Paixão*

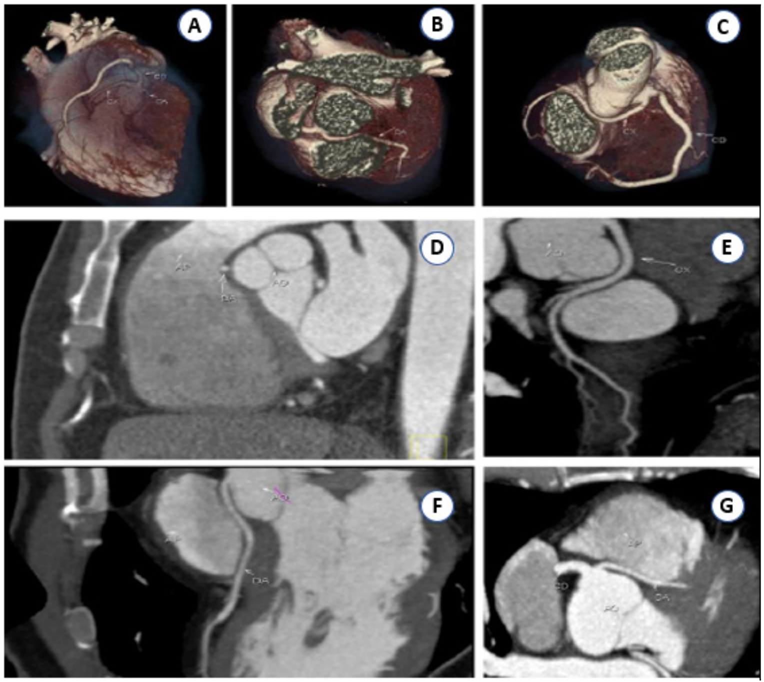

Figure 3 – *Image A: 3D reconstruction of a coronary angiography (AngioCT-3D), identifying the origin of the RCA, LAD, and LCx from the right coronary sinus; Image B: AngioCT-3D showing the interarterial course of the LAD; Image C: AngioCT-3D displaying the retroaortic course of the LCx; Image D: Interarterial course of the LAD; Image E: Retroaortic course of the LCx; Images F and G: Interarterial course of the LAD. RCA: Right Coronary Artery; LAD: Left Anterior Descending; LCx: Left Circumflex. Image provided by Eduardo Lins Paixão.*

obstructive arterial disease (Figure 4). The patient underwent surgical revascularization of the anterior descending artery through the anastomosis of the left internal mammary artery. The surgical procedure took place approximately 6 months after diagnosis, without complications. The patient resumed his physical activities and is asymptomatic.

Discussion

Anomalous origin of the coronary artery is a rare congenital heart disease. In cases of anomalous origin of the coronary artery, the coronary artery originates from the coronary sinus inappropriately, either through a separate or common ostium or through a sub-branch. There are several subtypes; in the interarterial subtype, the coronary artery follows a course between the aorta and the pulmonary artery, presenting a potential risk of sudden death. A comprehensive review published by Cheezum et al. suggests that the true prevalence of this abnormality is likely underestimated. In this series, 39% of the sample with some type of anomalous origin of the coronary artery had the interarterial subtype. There are few studies that have screened for anomalous origin of the coronary artery in the absence of clinical indications.[8]

In current guidelines, coronary tomography angiography and cardiac magnetic resonance angiography are the only methods with a class I indication. In many centers, tomography angiography is the preferred method for this diagnosis. Invasive angiography allows for greater spatial and temporal resolution, and it has a class IIa indication for diagnosing anomalous coronary artery. Functional tests, such as exercise testing and myocardial perfusion scintigraphy, analyze the functional significance of the anomalous origin on coronary flow.[9]

Grani et al. examined 46 adults (mean age of 56 years) diagnosed with anomalous origin of coronary arteries by tomography angiography, and they identified perfusion changes only in patients with concomitant coronary artery disease.[10]

Physical stress is preferable to assess myocardial perfusion, since most cases of sudden death attributed to anomalous origin of the coronary arteries occur with strenuous exercise. Several publications have reported a large number of false positives and negatives with these methods. Among 27 young athletes with anomalous origin of the coronary arteries described by Basso et al., 6 patients had a normal exercise test before presenting sudden death. Therefore, the absence of ischemia during stress testing cannot be seen as sufficient.[11]

This clinical case followed current recommendations. Even in the absence of documented ischemia, due to the interarterial course of the anterior descending coronary artery, revascularization was indicated.

The objective of this study is to report an unusual case of anomalous origin of the left coronary artery from the right coronary sinus with an interarterial course in an asymptomatic patient. It is necessary to reflect on this diagnosis in young patients with symptoms of angina and syncope on exertion.

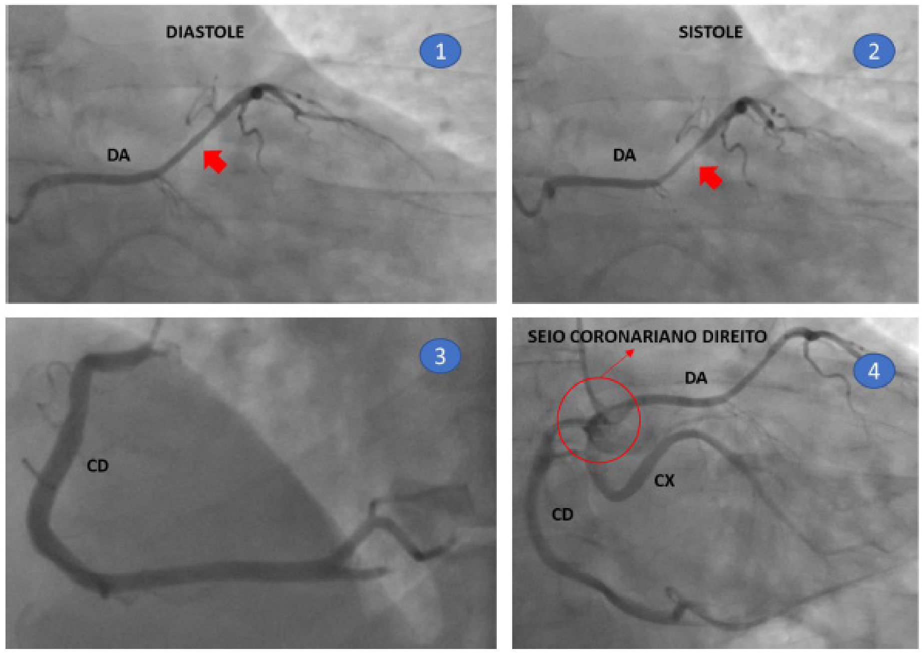

Figure 4 – *Cinecoronariography: In image 1, the left anterior descending coronary artery originating from the right coronary sinus with an interarterial course is evident; highlighted (arrow) is the vessel diameter in diastole, within the interarterial segment (between the aorta and pulmonary arteries). In image 2, the vessel diameter in systole is observed, showing extrinsic compression of the vessel. Image 3 displays the normal right coronary artery, while image 4 illustrates the origin of the right coronary, circumflex, and left anterior descending arteries, all arising from the right coronary sinus. Imagens cedidas por Eduardo Lins Paixão.*

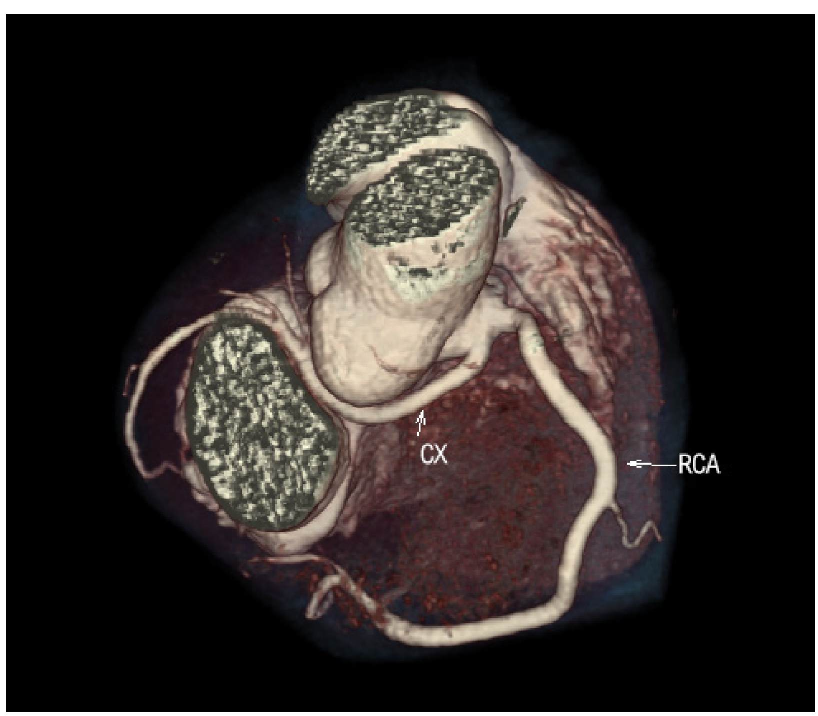

Figure 5 – *3D reconstruction, in a transverse section with a craniocaudal view, showing the right coronary sinus, from which the right coronary artery originates and follows its normal course, through the right atrioventricular sulcus. Note also the circumflex artery, which originates from the right coronary sinus, in an independent ostium; follows a retroaortic course, passing between the aorta and left atrium; and subsequently follows the left atrioventricular sulcus in the usual course. CX: circumflex artery; RCA: right coronary artery.*

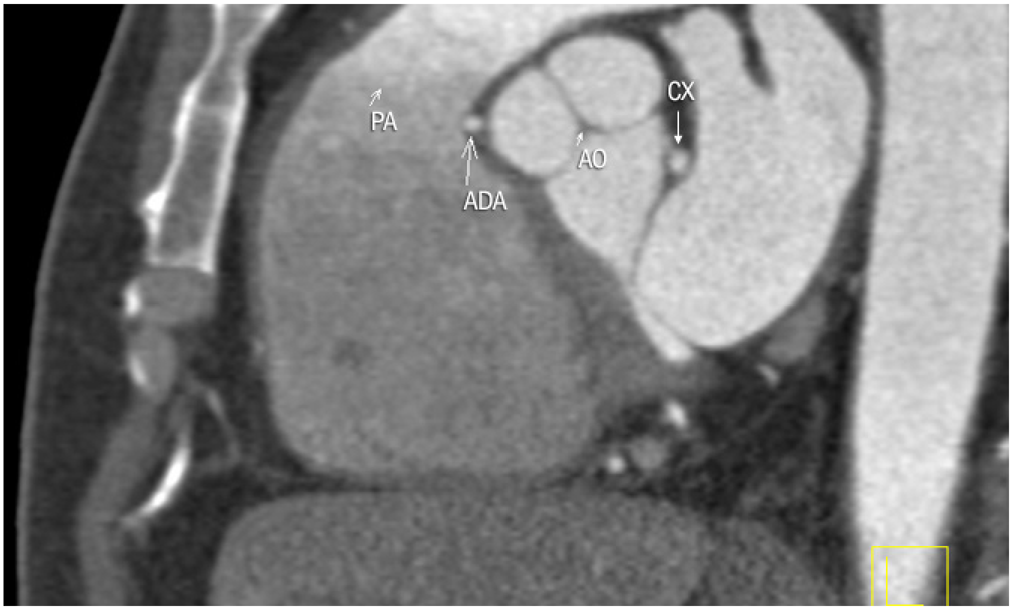

Figure 6 – *Coronary tomography angiography: 2D reconstruction, in a multiplanar section, showing the pulmonary artery, the aorta, and, between them, the image of the anterior descending coronary artery. Posterior to the aorta, the circumflex artery can be seen. ADA: anterior descending artery; AO: aorta; CX: circumflex artery; PA: pulmonary artery.*

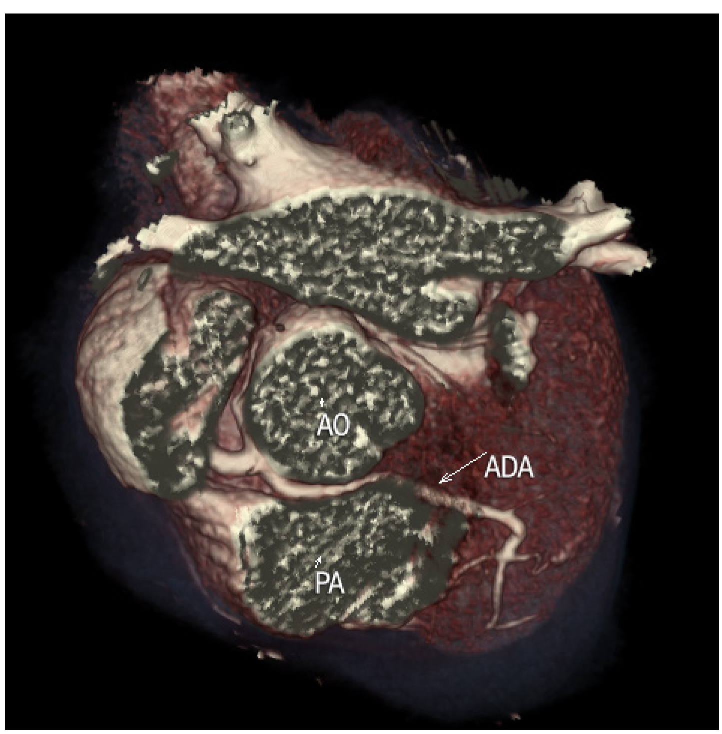

FigurE 7 – *Coronary tomography angiography: 3D reconstruction, in a transverse section with a craniocaudal view, showing the pulmonary artery, the aorta, and the anterior descending artery, which has an anomalous origin in the right coronary sinus, following an interarterial course and subsequently following the usual course through the anterior interventricular sulcus. ADA: anterior descending artery; AO: aorta; PA: pulmonary artery.*

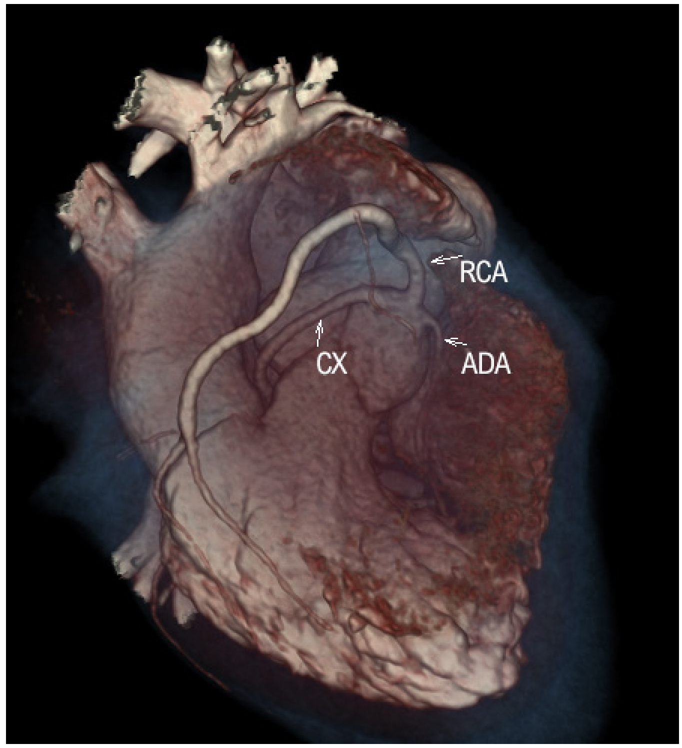

FigurE 8 – *Coronary tomography angiography: 3D reconstruction, showing the right coronary sinus and the common origin of the right coronary, circumflex, and anterior descending arteries in this sinus. ADA: anterior descending artery; CX: circumflex artery; RCA: right coronary artery.*

Figure 9 – *Coronary tomography angiography: 2D reconstruction, in a sagittal section, showing the pulmonary artery, the aorta, and, between them, the image of the anterior descending coronary artery. ADA: anterior descending artery; AO: aorta; PA: pulmonary artery.*

Figure 10 – *Coronary tomography angiography: 2D reconstruction, in a sagittal section, showing the circumflex artery in its retroaortic course, subsequently following the usual course. AO: aorta; CX: circumflex artery.*

Figure 11 – *Coronary tomography angiography: 2D reconstruction, in a transverse section with a craniocaudal view, showing the pulmonary artery, the aorta, and the anterior descending artery, which has an anomalous origin in the right coronary sinus and follows an interarterial course.*
ADA: anterior descending artery; AO: aorta; PA: pulmonary artery; RCA: right coronary artery.

Nonetheless, the diagnostic challenge is enormous, considering that a large portion of these patients do not have symptoms before sudden death; this fact requires more research to find a cost-effective means of assessment, particularly in individuals who practice intense competitive sports.

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Author Contributions

Conception and design of the research and statistical analysis: Paixão EL; acquisition of data: Couto MC, Lages DB, Paixão EL; analysis and interpretation of the data: Couto MC, Pacífico FA, Lages DB, Santos LS, Farias MA, Paixão EL; obtaining financing: Couto MC, Lages DB, Santos LS, Farias MA, Paixão EL; writing of the manuscript: Couto MC, Lages DB, Santos LS, Farias MA, Paixão EL; critical revision of the manuscript for intellectual content: Pacífico FA, Paixão EL.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Faculdade de Medicina de Olinda under the protocol number CAAE 63407522.3.000.8033. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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Case Report

Subaortic Stenosis in Association with Patent Ductus Arteriosus in a Young Woman from the Andes Region

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Background

Defects affecting the left ventricular outflow tract (LVOT) are considered major congenital heart defects accounting for 6 out of 10,000 live births.[1] Subaortic stenosis accounts for approximately 1% of all congenital heart defects and 15% to 20% of all LVOT obstruction defects.[2] Subaortic membrane stenosis (SMS) is the most common type of subaortic stenosis, although it is a rare condition scarcely reported in the medical literature.[2,3] Previous studies have reported its association in some cases with other congenital heart defects such as ventricular septal defects and patent ductus arteriosus (PDA).[3,4] Its association with PDA is particularly rare, to the extent that a case series published in 2020 mentioned only 3 previous cases.[3] The objective of this article is to report a case of SMS in association with PDA in a woman from the Andes region.

Case description

A 24-year-old female patient from the Andean region of Peru, who had previously been diagnosed with severe SMS and PDA at age 13, was evaluated by the cardiology service of our hospital because of dyspnea and pain in left upper limb on exertion. At age of 5, she was diagnosed with heart murmur and remained without further medical assessment until she was 13 years old. At baseline clinical assessment 10 years prior, physical examination revealed faint second heart sound (S2), systolic aortic heart murmur III/VI, apical impulse displaced toward the sixth intercostal space, and palpable liver 1 cm below the right costal margin. Echocardiogram showed SMS, PDA sized 13 mm in length with bidirectional flow in diastole, enlargement of the left ventricle and left atrium, preserved ejection fraction (60%), left ventricular hypertrophy, and severe pulmonary hypertension. At that time, the proposed management comprised subaortic membrane resection, PDA closure, and new atrial septal defect creation. However, the patient lost adherence to the management plan, and she sought a new medical approach 10 years after the first cardiovascular assessment.

In our hospital, her physical examination findings were dyspnea classified as NYHA II, systolic aortic heart murmur II/VI, along with systolic murmur in the pulmonary, tricuspid, and mitral valves. Electrocardiogram showed normal sinus rhythm, 75 bpm, and left ventricle systolic overload. Echocardiogram findings were consistent with enlargement of the left ventricle and left atrium, ejection fraction 57%, left ventricle diastolic dysfunction type III, preserved right ventricular function (tricuspid annular pulmonary systolic excursion = 25 mm), moderate mitral valve insufficiency, mild mitral valve stenosis, moderate aortic valve insufficiency, severe subaortic stenosis with mean transvalvular gradient 73.6 mmHg, peak aortic velocity 5.34 m/s, moderate tricuspid valve insufficiency, and pulmonary hypertension (pulmonary artery systolic pressure = 76 mmHg) (Figure 1A and 1B). It was not possible to characterize the PDA through the echocardiogram due to an inappropriate acoustic window. Therefore, the patient underwent computed tomography angiography (Figure 2A and 2B). The angiogram showed PDA, Krichenko angiographic classification type A (conical ductus) sized 28 × 29 mm at aortic opening and 18.7 × 23.3 mm at pulmonary opening (Figure 2B). Cardiac catheterization findings showed severe mixed pulmonary hypertension, right ventricle-to-pulmonary artery shunt, ratio of pulmonary blood flow (Qp) to systolic blood flow (Qs) of 3.5, resting left ventricular-aortic systolic gradient (ΔP) of 100 mmHg, and pulmonary vascular resistance (PVR) of 3.79 WU. The patient was transferred to a specialized cardiovascular health center in Lima in order to undergo surgical procedure.

Keywords

Subvalvar Aortic Stenosis; Ductus Arteriosus; Patent; Andean Ecosystem

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Discussion

SMS in association with PDA is a particularly rare pathological condition mostly diagnosed during childhood.[3] We have reported the case of a young female patient seeking care for this cardiovascular condition, who was diagnosed when she was 13 years old. Our patient was diagnosed later than other previous cases reported in the literature, in which the latest diagnosis age was 8 years old.[3] On the other hand, there is not a probable association between male or female sex and the presence of these heart defects. We found that Steinherz et al. reported that the majority of their cases of SMS and PDA were female, with a ratio of 5:1 in New York,[4] but Mofa et al. reported the predominance of male patients at a ratio of 4:3 in a city in Saudi Arabia.[3]

Aortic stenosis is frequently associated with other heart defects.[3-5] For instance, Xie et al. reported that 11 out of 213 children who underwent PDA closure also had aortic

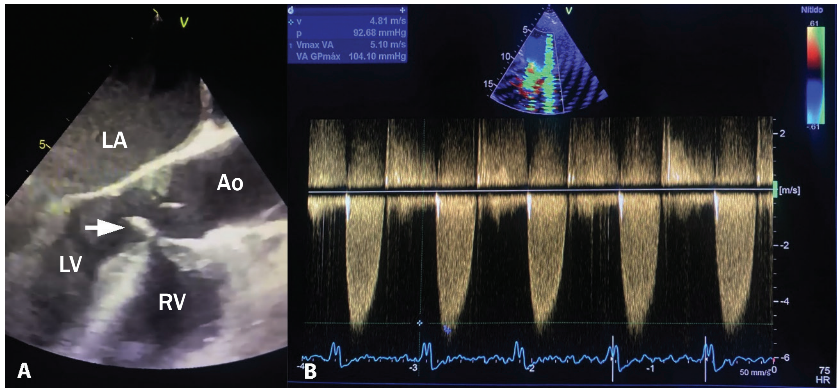

Figure 1 – *Transesophageal echocardiogram findings. (A) Subaortic membrane stenosis (arrow), fibromuscular ridge arising in the left ventricular outflow tract attached to the ventricular septum. (B) Doppler echocardiography shows aortic valve insufficiency and subvalvular stenosis. Ao: Aorta; LA: left atrium; LV: left ventricle; RV: right ventricle.*

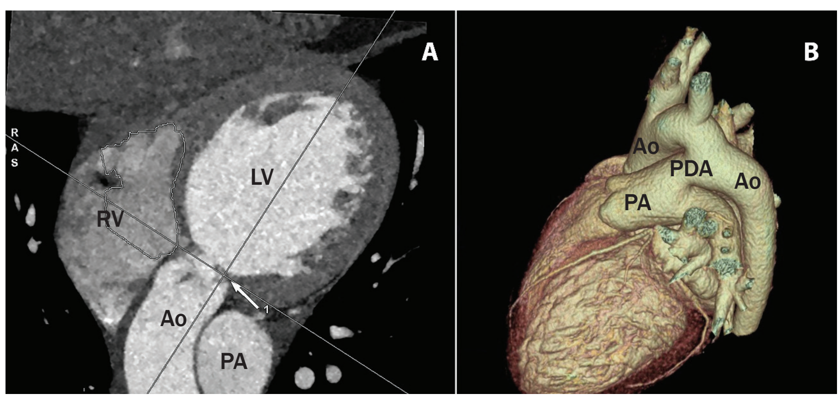

Figure 2 – *Computed tomography angiography findings. (A) White arrow showing subvalvular aortic stenosis, membranous type. (B) Patent ductus arteriosus type A (conical ductus) arising after the origin of left subclavian artery and running from the descending aorta to the pulmonary trunk. Ao: Aorta; LV: left ventricle; PA: pulmonary artery; PDA: patent ductus arteriosus; RV: right ventricle.*

stenosis during a 6-year follow-up in a Chinese cohort.[5] Other case series from Beijing Anzhen Hospital reported the concomitant finding of aortic stenosis and PDA in 20.6% of children initially diagnosed with aortic stenosis.[6] However, the previously mentioned Chinese case series did not mention the type of subaortic stenosis that their patients presented.[5,6] Few published reports focused only on the concomitant finding of SMS and PDA.[3,4]

Few epidemiological studies about the incidence or prevalence of concomitant SMS and PDA are available in the literature.[7,8] Moreover, the only epidemiological studies available were published in the late twentieth century. Therefore, we are able to recognize an important gap in our knowledge nowadays, which highlights the need for new studies on this topic.

Our patient presented Qp/Qs 3.5, ΔP 100 mmHg, and PVR 3.79 WU. These findings were similar to those reported in other studies where Qp/Qs ranged between 3.0 to 4.6, and ΔP ranged from 38 mmHg to 139 mmHg.[5,9] Due to the echocardiogram and angiogram parameters found in our patient, suitable surgical correction was a recommendation for her heart defects, according to the European Society of Cardiology guidelines for the management of cardiac defects in adults.[10]

Finally, the prompt intervention in these heart defects should be addressed as the primary objective, as soon as they are diagnosed, because of highly probable complications, such as pulmonary hypertension and further aortic valve damage leading to aortic insufficiency, as previously described in this case report and other previous studies.[3,9]

Conclusion

In conclusion, SMS and PDA is a very rare association of heart defects rarely reported in the literature that can progress to more complex cardiovascular pathology by adolescence or early adulthood. Therefore, it requires special consideration by cardiologists in order to preserve the functionality of the heart and lungs in patients affected by this pathological entity.

Author Contributions

Conception and design of the research, analysis and interpretation of the data, writing of the manuscript and critical revision of the manuscript for intellectual content: Sandoval RH, Cachicatari-Beltran A, Baltodano-Arellano R, Levano-Pachas G; acquisition of data: Sandoval RH.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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Warning and Recommendations from the Department of Cardiovascular Imaging Regarding Transesophageal Echocardiography in Patients Using GLP-1 Analogs

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Transesophageal echocardiography is a fundamental diagnostic method for evaluating complex heart diseases. It provides essential data for therapeutic definition and, in some cases, assists in evaluation of percutaneous or surgical interventions.[1]

Transesophageal echocardiography exams are performed on outpatients or inpatients, who might be in wards, intensive care units, or even in surgery, with heterogeneous scenarios that need to be individually assessed, not only regarding the exam routine, but also always following precise clinical indications, weighing the risks and benefits for the patient.

To obtain better exam results and facilitate tolerance to the discomfort caused by the presence of the transducer in the oropharynx, we use topical anesthesia with lidocaine in the oropharynx and sedation at varying degrees of intensity, taking into account the patient's age group, clinical conditions, comorbidities, the presence of support from a professional anesthetist, and the respiratory and hemodynamic monitoring resources available.

The incidence of complications related to the exam is quite low, provided that the presence of absolute and relative contraindications is carefully observed (Table 1),[2] and it must always be performed by a qualified and experienced echocardiography specialist, in order to guarantee maximum safety in the procedure.

We must not neglect the risk of vomiting and bronchoaspiration during the procedure. It is essential for patients to fast appropriately for each clinical situation, respecting the standardized practice of each institution, usually 6 to 8 hours for patients on an oral diet (with residues) in the absence of conditions that cause obstruction of the gastrointestinal tract or gastric stasis.[3]

Keywords

Transesophageal Echocardiography; Diagnosis; Glucagon-Like Peptide 1.

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Glucagon-like peptide-1 (GLP-1) analogs, for example, semaglutide, liraglutide, and dulaglutide, used for the treatment of type 2 diabetes and obesity, are medications that require greater care in preoperative assessment in general and specifically in transesophageal echocardiography procedures. Due to the gastric stasis (gastroparesis) caused by these medications, there is an increased risk of periprocedural bronchoaspiration and vomiting, even after the recommended fasting period. The fact that it is a relatively new topic, which still does not have robust evidence and extensive literature, means that there are somewhat conflicting recommendations in the publications issued by different medical societies.

The American Society of Anesthesiologists recommends the following:[4]

- If using GLP-1 analogs with a daily dose, such as liraglutide, continue using them until the day before the procedure.
- If using GLP-1 analogs with a weekly dose, such as semaglutide, continue using them up to 7 days before the procedure.

The Brazilian Society of Diabetes (SBD), on the other hand, recommends the following:[5]

- If using GLP-1 analogs such as lixisenatide, suspend 1 day before the procedure.
- If using GLP-1 analogs with a daily dose, such as liraglutide, suspend 2 days before the procedure.
- If using GLP-1 analogs with a weekly dose, such as semaglutide, suspend 21 days before the procedure.
- If using dulaglutide and tirzepatide, suspend 15 days before the procedure.
- In the event that the patient has not followed the above recommendations, it is possible to evaluate each case individually, preferably assessing the presence of gastric contents by means of ultrasound.

These SBD recommendations have been endorsed by the Brazilian Society of Anesthesia (SBA) under opinion C.SBA 2055/23, issued on July 4, 2023. In the event that the medications were suspended within the recommended timeframe, the fasting period remains as usual.

Table 1 – Relative and absolute contraindications to transesophageal echocardiography. Adapted from Hahn et al.[2]

Absolute contraindications	Relative contraindications
• Active upper GT bleeding	• History of radiation therapy in neck and mediastinum
• Esophageal stricture	• History of prior GT surgery
• Esophageal tumor	• Recent upper GT bleeding
• Esophageal perforation/laceration	• Barrett's esophagus
• Esophageal diverticulum	• History of dysphagia
• Intestinal perforation	• Restricted neck mobility (severe cervical arthritis, atlantoaxial joint disease)
	• Symptomatic hiatal hernia
	• Esophageal varices
	• Coagulopathy, thrombocytopenia
	• Acute esophagitis
	• Active peptic ulcer

GT: gastrointestinal tract.

Both guidelines warn that, if the patient has not followed the above recommendations, the assessment of the presence of gastric contents by means of ultrasound may assist in the decision whether or not to suspend the procedure.

While there is no robust evidence available regarding the duration of fasting and/or the duration of suspension of GLP-1 agonists, the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology recommends following the official SBD recommendations.

Author Contributions

Conception and design of the research, acquisition of data, analysis and interpretation of the data, writing of the manuscript and critical revision of the manuscript for intellectual content: Felix AS, Almeida ALC, Melo MDT, Barberato SH.

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This article does not contain any studies with human participants or animals performed by any of the authors.

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