www.cardiol.br

www.dicsbc.org

ABC Imagem Cardiovascular

Sociedade Brasileira de Cardiologia • ISSN 2318-8219 • Volume 33, N° 1, January/February/March 2020

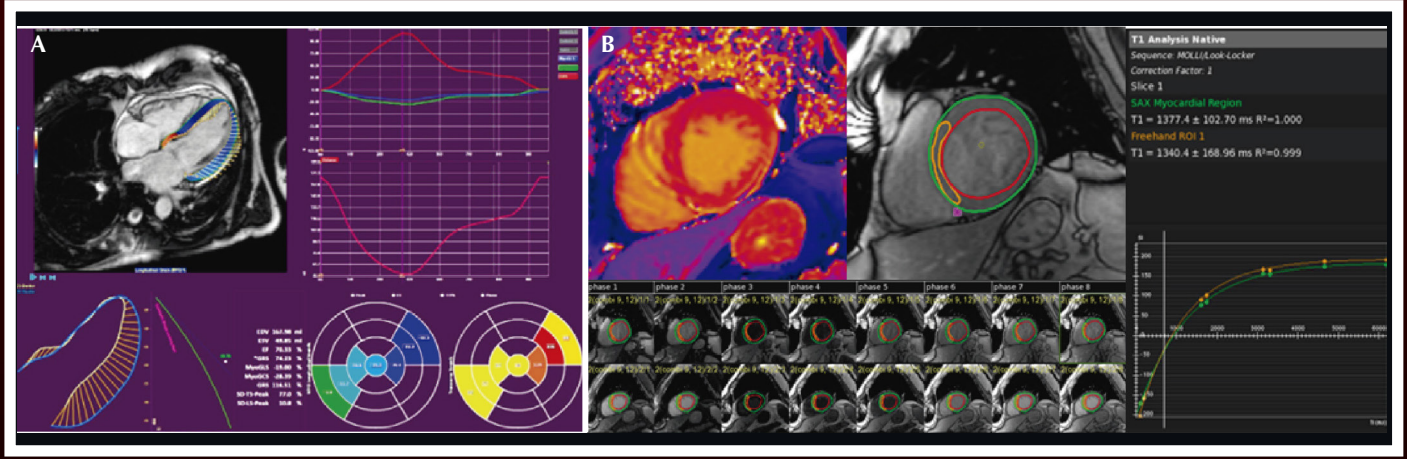


Figure 1 – *Advanced techniques in cardiac magnetic resonance imaging: (a) left ventricular myocardial strain by normal (global and segmental) strain; (b) abnormal left ventricular T1 mapping (high T1 values and increased extracellular volume in the septum of a patient with myocarditis).*

www.cardiol.br
www.dicsbc.org
ABC Imagem Cardiovascular

Department of Cardiovascular Imaging

SBC Directors

National Editorial Board

International Editorial Board

Arquivos Brasileiros de Cardiologia - Imagem Cardiovascular

Volume 33, Nº 1, January/February/March 2020

Indexing source: LILACS - Literatura Latino-Americana e do Caribe em Ciências da Saúde - www.bireme.br, LATINDEX - Sistema Regional de Información en Línea para Revistas Científicas de América Latina, El Caribe, España y Portugal - www.latindex.unam.mx

Department of Cardiovascular Imaging/ Brazilian Society of Cardiology
Rua Barata Ribeiro nº 380 cj.54
01308-000 - São Paulo - SP - Brasil
Fone/Fax: +55 (11) 3259-2988
Fones: +55 (11) 3120-3363
+55 (11) 3259-2988 / +55 (11) 2589-4168

Editorial Coordination
Atha Comunicação e Editora
Rua Machado Bittencourt, 190 - conj. 410
São Paulo, SP, Brasil
Tel.: (11) 50879502

Editorial Support
revista@dicsbc.com

The journal Arquivos Brasileiros de Cardiologia — Imagem Cardiovascular is the official body of the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology.

www.cardiol.br
www.dicsbc.org
ABC Imagem Cardiovascular

Contents - *Sumário*

Click on the title to read the article

www.cardiol.br
www.dicsbc.org
ABC Imagem Cardiovascular

Brief Communication - *Comunicação Breve*

Case Reports - *Relatos de Caso*

Image - *Imagem*

Message from the President

Carlos Eduardo Rochitte
DIC President for the years 2020–2021

Dear DIC colleagues and associates,

I would like to wish everyone, on behalf of the Department of Cardiovascular Imaging (DIC) of the Brazilian Society of Cardiology (SBC), a great start to the year 2020. The Department's new board, for the years 2020–2021, starts its administration focusing on its educational and scientific mission.

Works for the DIC Conference, to be held from April 2nd to 4th in Brasília (Federal District), are in full swing. It will be the largest conference solely dedicated to cardiovascular imaging in Latin America. In a concerted effort with the conference president Dr. Marcos Valério Coimbra Resende and the president of the scientific committee Dr. Adenalva Lima de Souza Beck, and Dr. Guilherme Urpia Monte in the cardiovascular imaging program, and supported by our former president Dr. Marcelo Vieira, we are preparing a conference of the highest scientific level with 16 international guest speakers, 7 of whom are in the field of cardiovascular imaging and the leading specialists in echocardiography and cardiovascular imaging from our country. For the first time, we are holding the conference together with the SBC-DF Conference, which will further enrich both events, at one venue and with even broader themes in Cardiology and Cardiovascular Imaging. It will be a fantastic and unforgettable conference!

We intend to provide our associates increasingly better and to get closer to those we represent. The Department's smartphone app is being prepared so we can all be united by our inseparable mobile phones. This will allow a more direct relationship with the associates, who will then be able to communicate, receive notifications from the department and make financial transactions in our digital store.

The new DIC committees that cover the department's main lines of activity now have their new coordinators, with their e-mails informed to all DIC associates (published simultaneously with this letter from the president on our website and soon on the app). Here, it is worth highlighting the committees' new approach. All associates who have paid their annual fees may ask the coordinator to participate in the committees and give their opinion on matters that are important to their local reality and their daily lives. We want to encourage everyone to participate as member of committees that they think they can help. The participation of all is very important. The Department belongs to all associates and we want to democratize it as much as possible.

The successful activities that were started by the previous administration, with Dr. Marcelo Vieira as president, will continue to be carried out, such as the Regional Symposia.

Many activities are planned and we will promote them throughout our administration for the purposes of improving our Department and getting closer to our associates, providing actual opportunities for learning, updating and professional and scientific growth.

I would like to thank the trust placed in this board. We will work hard with the support of everyone. We will always be available to listen to our associates and raise the Department to ever higher levels.

Thank you all very much. You will all hear from us soon in the future.

Message from the Editor

Silvio Henrique Barberato
Editor-in-Chief, Arquivos Brasileiros de Cardiologia - Imagem Cardiovascular

I am very pleased to take over as an editor-in-chief of Arquivos Brasileiros de Cardiologia (ABC) Imagem Cardiovascular for the years 2020–2021, following the exceptional job done by the previous editor, Dr. Viviane Hotta. The journal is currently indexed in the LILACS and LATINDEX databases. The first mission ahead is indexing it to Scielo, so we can aim PubMed in the future. It is important that the journal be appreciated and recognized as one of the main platforms of national scientific production in the field of Cardiovascular Imaging. We invite all the members and the academic community of the Department of Cardiovascular Imaging (DIC) to support us in this process by sending their work to ABC Imagem Cardiovascular, particularly original articles and reviews.

In order to increase the number of articles published and make them interesting for the readers, we are proposing, in this administration, the writing of manuscripts in new formats, with succinct approaches targeted at the discussion of practical topics concerning the daily work of cardiovascular imaging. These new features include the article series "My style of doing" (written by an author who works on Cardiovascular Imaging) and "What cardiologists expect from echocardiography" (written by a clinical cardiologist requesting and making use of imaging information). In addition, two new sections were created to foster debate on key traditional and emerging topics: professional advocacy and qualification of echocardiographers, artificial intelligence, and technological innovations on imaging. Other activities are underway, such as getting closer and more integrated with Arquivos Brasileiros de Cardiologia (whose editor-in-chief is our current President, Professor Carlos Rochitte, to whom I am much grateful for his trust and cooperation) and the pursuit of greater international collaboration, to increase the visibility of our articles in the global scientific community. Our prestigious team of associate editors includes: Bruna Morhy Borges Leal Assunção - SP (Adult Echocardiography); Marcia Ferreira Alves Barberato - PR (Pediatric Echocardiography); Rodrigo Julio Cerci - PR (Tomography); Otavio Rizzi Coelho Filho - SP (Magnetic Resonance Imaging); Ana Cristina Lopes Albricker - MG (Vascular Imaging); Simone Cristina Soares Brandão - PE (Nuclear Medicine); Marcelo Haertel Miglioranza - RS (Professional Advocacy and Qualification of Echocardiographers), José de Arimateia Batista Araujo-Filho - USA (Innovation and Artificial Intelligence). I invite all members to contribute to our esteemed cardiovascular imaging journal!

Sincerely Yours.

Cardiotoxicity in Cancer Treatment: New Frontiers in the Multimodality Diagnostic Approach

Cardiotoxicidade no Tratamento Oncológico: Novas Fronteiras na Abordagem Diagnóstica Multimodalidade

José de Arimateia Batista Araujo Filho[1,2], Marcelo Dantas Tavares de Melo[3], Roberto Vitor Almeida Torres[1,3], Cesar Higa Nomura[1,3]

Hospital Sírio-Libanês,[1] São Paulo, SP, Brazil; Memorial Sloan-Kettering Cancer Center,[2] Nova Iorque, Estados Unidos; Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo,[3] São Paulo, SP, Brazil.

Continued improvements in the effectiveness of cancer treatment have led to the current existence of millions of survivors of different types of pediatric and adult cancer worldwide. However, a parallel increase in the incidence of toxicity-related morbidity and mortality of many of the drugs used has created a new epidemiological challenge in this population. With a wide spectrum of involvement, cardiovascular toxicity is one of the most aggressive side effects of cancer therapy and is currently one of the leading causes of mortality in cancer survivors worldwide.[1] Different mechanisms are associated with this, including: direct damage to cardiomyocytes, endothelial injuries, hemodynamic or metabolic disorders, conduction disorders and thrombotic events. This cascade of involvement is potentially associated with different cytotoxic and immunotherapeutic chemotherapies or radiation therapies, and may have an acute onset or take years to be consolidated.[2]

The recent discovery and increasing use of new molecular targeted drugs (targeted therapies) in cancer treatment, as well as multimodal and multi-drug treatment regimens, have created new challenges and increased the special interest of cardiologists and oncologists in the subject. The main focus of the professionals involved today is the early detection of myocardial involvement and the early prediction and treatment of associated cardiac dysfunction. The current American Society of Clinical Oncology guidelines recommend risk stratification for cardiac dysfunction prior to the initiation of any potentially cardiotoxic drug.[3]

Despite the growing interest of the scientific community, there is no universal definition of cardiotoxicity and multiple controversies still persist on the topic. Cardiotoxicity is a generic term that can range from coronary artery disease (CAD), peripheral vascular disease, systemic or pulmonary hypertension, arrhythmias and heart failure, to valvular or pericardial involvement. Regarding cardiac involvement, the most widely recognized diagnosis of cardiotoxicity is based on abnormalities in left ventricular systolic function (LV) measured by a single method, usually LV ejection fraction (LVEF), sometimes on a single occasion.[4] A significant absolute (below a certain level) or relative (relative to pretreatment values) change in LVEF should be considered for diagnosis, but thresholds considered relevant for clinical decision-making vary within the different guidelines available. According to the 1st Brazilian Guideline for Cardio-oncology of the Brazilian Society of Cardiology published in 2011, in line with the American National Institute of Health (NIH), cardiotoxicity is defined as the asymptomatic reduction of LVEF between 10% and 20% (grade I), reduction in LVEF below 20% or below normal (grade II) or the onset of symptomatic heart failure (grade III).[5] A number of more recent studies contest these criteria, especially because they select only patients with established dysfunction (late phase) and because they do not consider subclinical myocardial involvement, when other parameters (especially myocardial strain) are known to be more sensitive. Notwithstanding such controversies, the most widespread definition of cardiotoxicity currently considers an LVEF drop ≥10% to <53% (suggesting confirmation upon further examination after 2–3 weeks), according to the Consensus of the American Society of Echocardiography.[6] We also know that LVEF measurement is subject to considerable intra- and inter-observer variability, as well as frequent discrepancies between different imaging modalities.[4] Therefore, limiting cardiotoxicity detection to a single LVEF measurement underestimates the clinical significance of other manifestations associated. These shortcomings and controversies may contribute to the current understanding that cardiotoxicity may be an underdiagnosed clinical condition.

In this context, the use of serum biomarkers — especially troponins and natriuretic peptides — is a commonly adopted strategy for early identification of subclinical myocardial damage and intensive follow-up of these patients,[5] often requiring complementation of workup. Echocardiography is still the mainstay of cardiac toxicity imaging,[7] especially with advanced 3D, strain and tissue Doppler techniques. Other imaging modalities such as computed tomography (CT) and cardiac magnetic resonance imaging (MRI) may add important information in a multimodality approach, often for the purposes of complementing it and in specific clinical situations[8]. For example, the high sensitivity of cardiac CT to detect pericardial effusion and thickening is known to be superior to echocardiography.[8] However, the role of cardiac CT in cardio-oncology is mainly restricted to the evaluation of coronary or valvular calcium and obstructive CAD.[8]

The high precision in ventricular functional analysis, as well as in the characterization of myocardial edema, inflammation and fibrosis have made cardiac MRI (CMRI) a method of great versatility and potentiality in the assessment of cardiotoxicity. In cardio-oncology, CMRI had its first recommendations in the complementary evaluation of LVEF in patients with limited echocardiographic window or in the presence of borderline

Keywords

Cardiotoxicity; Drug Therapy; Echocardiography.

Mailing Address: José de Arimateia Batista Araujo-Filho •

E-mail: ariaraujocg@hotmail.com

DOI: 10.5935/2318-8219.20200002

Editorial

functional parameters, especially when more reliable and accurate LVEF measurements were necessary to justify discontinuation of chemotherapy. In the age of targeted therapy, myocarditis became the most feared cardiac complication of cancer treatment (especially associated with a class of overwhelmingly successful immunotherapy known as immune checkpoint inhibitors) and CMRI was then raised to a new level due to its high sensitivity and specificity in this diagnosis through a combination of delayed enhancement techniques, and T1 and T2 mapping.[9] Advanced CMRI techniques (Figure 1) are still extremely valuable in the evaluation of fibrosis classically related to radiotherapy and some anthracyclics, as well as in the detection of myocardial deposits of amyloid material (causing increased extracellular volume on T1 mapping) or iron (with T2* time reduction) potentially associated with the use of some chemotherapeutic agents. In addition, CMRI plays a central role in the diagnosis of intracavitary thrombi, assessment of vascular complications (MR angiography) and may be an alternative in the evaluation of ischemia (stress CMRI) in patients receiving therapies potentially associated with vasospasm or accelerated atherosclerosis.[7] More recently, CMRI myocardial strain analysis in chemotherapy patients has demonstrated the ability of the method to detect important subclinical abnormalities.[9]

Although recent studies have shown a potential use of PET-CT in the early detection of cardiotoxicity,[10] the role of nuclear medicine in cardiotoxicity screening is limited by the high cost and limited availability of these methods. Scintigraphy techniques are currently in disuse in this context; however, the high precision in PET/SPECT myocardial perfusion analysis plays a role in the risk stratification of CAD in some patients. Recent evidence suggests that cardiac MRI may have an incremental value in the evaluation of myocarditis compared to PET-CT or CMRI alone.[11]

In the future, the role of imaging in cardio-oncology will depend on how we will be able to better and earlier predict subclinical cardiac involvement in an attempt to prevent or interfere in the progression of this process.[12] New tools with artificial intelligence are promising, especially in the identification and understanding of new parameters beyond conventional visual analysis.[13] It is known that the population of patients at risk for cardiotoxicity differs in many respects from those with primary cardiovascular risk, corroborating the need for collaboration among all members of the multidisciplinary team involved in developing individualized workup strategies and therapies. The correct indication and interpretation of the different diagnostic methods available - with their specific advantages and limitations (Chart 1), in a cost-efficient multimodality approach - is central in this process.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

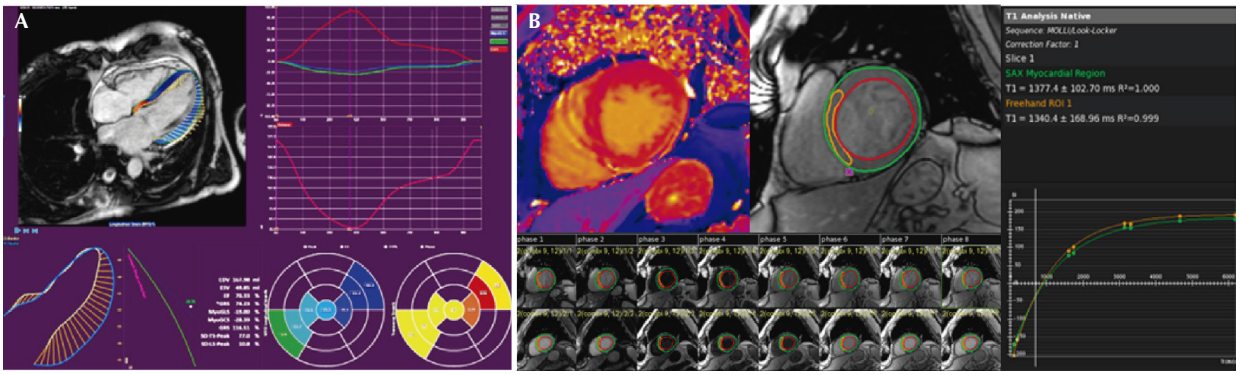


Figure 1 – *Advanced techniques in cardiac magnetic resonance imaging: (a) left ventricular myocardial strain by normal (global and segmental) strain; (b) abnormal left ventricular T1 mapping (high T1 values and increased extracellular volume in the septum of a patient with myocarditis).*

Chart 1 - Main aspects in the multimodality diagnostic approach of cardiotoxicity.

Diagnostic modality	Advantages	Disadvantages
Echocardiography	Low cost and wide availability (2D) Good time resolution (3D) Ability to detect subclinical strain	Operator-dependent Patients with limited acoustic window Variable spatial resolution
Cardiac computed tomography	Noninvasive Excellent sensitivity and specificity to confirm/rule out coronary artery disease	Radiation Limited role in myocardial tissue characterization
Cardiac magnetic resonance imaging	Gold standard in volumetric/functional evaluation and tissue characterization	High cost and limited availability in small centers
Nuclear Medicine	Functional and metabolic assessment with relative accuracy and reproducibility High precision in myocardial perfusion analysis (PET/SPECT)	Radiation High cost and limited availability in small centers (PET-CT)

PET/SPECT: Positron Emission Tomography/ Single Photon Emission Computed Tomography; PET-CT: Positron Emission Tomography-Computed Tomography.

References

1. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin. 2016;66(4):271-89.

2. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, Aboyans V, Asteggiano R, Galderisi M, et al.; Task Force Members; ESC Committee for Practice Guidelines (CPG); Document Reviewers. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). Eur J Heart Fail. 2017;19(1):9-42.

3. Armenian SH, Lacchetti C, Barac A, Carver J, Constine LS, Denduluri N, et al. Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2017;35(8):893-911.

4. Chung R, Ghosh AK, Banerjee A. Cardiotoxicity: precision medicine with imprecise definitions. Open Heart. 2018;5(2):e000774.

5. Kalil Filho R, Hajjar LA, Bacal F, Hoff PM, Diz Mdel P, Galas FR, et al. [I Brazilian Guideline for Cardio-Oncology from Sociedade Brasileira de Cardiologia]. Arq Bras Cardiol. 2011;96(2 Suppl 1):1-52.

7. Plana JC, Galderisi M, Barac A, Ewer MS, Ky B, Scherrer-Crosbie M, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2014;27:911-39.

7. Plana JC, Thavendiranathan P, Bucciarelli-Ducci C, Lancellotti P. Multi-Modality Imaging in the Assessment of Cardiovascular Toxicity in the Cancer Patient. JACC Cardiovasc Imaging. 2018;11(8):1173-86.

8. Lancellotti P, Nkomo VT, Badano LP, Bergler-Klein J, Bogaert J, Davin L, et al.; EuropeanSociety of Cardiology Working Groups on Nuclear Cardiology and Cardiac Computed Tomography and Cardiovascular Magnetic Resonance; American Society of Nuclear Cardiology, Society for Cardiovascular Magnetic Resonance, and Society of Cardiovascular Computed Tomography. Expert consensus for multi-modality imaging evaluation of cardiovascular complications of radiotherapy in adults: a report from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. J Am Soc Echocardiogr. 2013;26(9):1013-32. Erratum in: J Am Soc Echocardiogr. 2013;26(11):1305. Bergler, Jutta [corrected to Bergler-Klein, Jutta].

9. Jordan JH, Todd RM, Vasu S, Hundley WG. Cardiovascular Magnetic Resonance in the Oncology Patient. JACC Cardiovasc Imaging. 2018;11(8):1150-72.

10. Seraphim A, Westwood M, Bhuva AN, Crake T, Moon JC, Menezes LJ, et al. Advanced Imaging Modalities to Monitor for Cardiotoxicity. Current treatment options in oncology. Curr Treat Options Oncol. 2019;20(9):73.

11. Chen W, Jeudy J. Assessment of Myocarditis: Cardiac MR, PET/CT, or PET/MR? Curr Cardiol Rep. 2019;21(8):76.

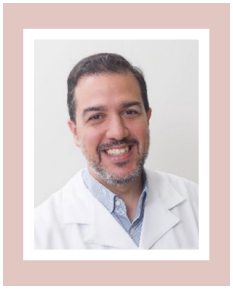
12. Steingart RM, Chandrashekhar Y, Marwick TH. Imaging in Cardio-Oncology. Where Are We and Where Should We Be Going? JACC Cardiovasc Imaging. 2018;11(8):1209-11.

13. Araujo-Filho JAB, Nascimento-Jr A, Gutierrez MA, Nomura CH. Inteligência Artificial e Imagem Cardíaca: Precisamos Falar sobre Isso. Arq Bras Cardiol: Imagem Cardiovasc. 2019;32(3):154-6.

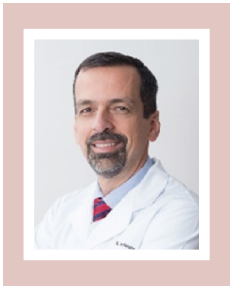
What does the Cardiologist expect from Echocardiography in Heart Failure with Preserved Ejection Fraction?

O que o Cardiologista Espera do Ecocardiograma na Insuficiência Cardíaca com Fração de Ejeção Preservada?

[1]Quanta Diagnóstico por Imagem, Curitiba-PR. [2]Universidade Federal do Paraná, Curitiba-PR. [3]CardioEco-Centro de Diagnóstico Cardiovascular, Curitiba, PR, Brazil.



Miguel Morita Fernandes-Silva[1,2]



Silvio Henrique Barberato[1,3]

Heart Failure (HF) with Preserved Ejection Fraction (HFpEF) has become increasingly prevalent, and currently accounts for about half of HF cases.[1] HFpEF is a heterogeneous syndrome characterized by multiple phenotypes, frequent presence of multiple comorbidities, high mortality, and for which no treatment has been shown to be effective in improving survival in randomized controlled trials.[2–6] This is partly due to its difficult diagnosis, for which there is no single biomarker or gold standard.Diagnosis of HFpEF is based on a set of clinical data and complementary tests, in which echocardiography plays a central role.[7,8]

Traditionally, echocardiography allows to classify diastolic dysfunction and to estimate the filling pressures from an integrated analysis of different parameters, where the transvalvular mitral flow pattern (E and A waves) is the main reference. Three patterns of diastolic dysfunction are defined in increasing order of severity: grade I (impaired ventricular relaxation without increased filling pressures), grade II (impaired ventricular relaxation coexisting with increased filling pressures, usually demonstrating "pseudonormal mitral flow pattern") and grade III (very high filling pressures accompanied by restrictive mitral flow pattern).[7]

Although useful, the application of echocardiography in HFpEF is not restricted to the assessment of diastolic function. In a patient with suspected HFpEF, echocardiography should assist in diagnostic management, providing information that corroborates (or not) HFpEF, and identifying the presence of other cardiac causes of exercise intolerance. The Heart Failure Association of the European Society of Cardiology has recently proposed the diagnostic algorithm HPA-PEFF, which involves a four-step approach: Step 1 (P) — "pretest" evaluation, identifying the patient with signs and symptoms suggestive of HF, preserved ejection fraction and ruling out other causes; Step 2 (E) — applying a diagnostic score with echocardiography and natriuretic peptides data; Step 3 (F1) — functional test; and Step 4 (F2) — "final" etiology of HF.[9] This algorithm comprehensively describes the required echocardiographic measurements in patients with suspected HFpEF. Although HFA-PEFF undertakes a full diagnostic approach,[9] including clinical examination and sequential use of other complementary tests, we will only focus on echocardiographic measurements in this editorial.

Firstly, the echocardiogram should report left ventricular ejection fraction (LVEF) measured using a biplanar method, diastolic function, ventricular volumes, left ventricular mass (LV) indexed to body surface area, and left atrial size. Besides, other cardiac causes of exercise intolerance must be ruled out, such as valve disease, pericardial effusion, constrictive pericarditis and pulmonary hypertension. In a patient with signs and symptoms of HF, the presence of LVEF $\geq$ 50% in an undilated ventricle with hypertrophy or concentric remodeling and enlarged left atrium is highly suggestive of HFpEF.

In patients with suspected HFpEF, the HFA-PEFF algorithm proposes the use of a score that includes biomarkers (serum natriuretic peptide levels) and a more detailed echocardiogram analysis, with functional and morphological criteria evaluated using well-defined cutoff values. These include tissue Doppler-derived parameters (septal and lateral e' velocities, mean E/e' ratio), peak velocity of tricuspid valve regurgitation and/or pulmonary artery systolic pressure estimation, left atrial volume index, left atrial mass (indexed to body surface area) and relative wall thickness. LV global longitudinal strain may also be helpful, if available. These measures define the presence of major and minor criteria, which are incorporated into a scoring system that derives the score. Table 1 describes the echocardiographic criteria that make up the proposed score and their cutoff values.

Mailing Address: Miguel Morita Fernandes-Silva •
E-mail: mim247@mail.harvard.edu

DOI: 10.5935/2318-8219.20200003

Diagnosis of HFpEF is challenging, and proper evaluation of patients with suspected HFpEF relies on a well-performed anamnesis and physical examination, along with rational and integrated use of complementary tests, among which echocardiography is essential.[10] Echocardiography is crucial to confirm the diagnosis of HFpEF, to rule out other causes of exercise intolerance and to suggest a specific etiology. Therefore, the clinician and the echocardiographer should be aligned in order to get the most out of this tool, increasing the accuracy of diagnosis and the chances of successful treatment.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

Table 1 - Echocardiographic criteria used in the diagnosis of heart failure with preserved ejection fraction.

Parameter	Major criterion for diagnosis of HFpEF	Comment
LVEF	≥ 50%	Measured by biplanar or three-dimensional method
Left atrial volume	> 34 ml/m² if sinus rhythm (or > 40 ml/m² if AF)	Minor criteria: 29–34 ml/m2 if sinus rhythm or 34–40ml/m2 if AF
LV mass and relative wall thickness	≥ 149 (men) or ≥ 122 (women) g/m² + relative wall thickness > 0.42	Minor criteria: ≥ 115 (men) or ≥ 95 (women) g/m² or septum ≥ 12 mm or relative wall thickness > 0.42 alone
e'	< 7 cm/s (septal) or < 10 cm/s (lateral) if age < 75 years; < 5 cm/s (septal) or < 7 cm/s (lateral) if ≥ 75 years	
Mean E/e' ratio	≥ 15	Minor criteria: 9–14
TR peak speed	> 2.8 m/s	
PASP	> 35 mmHg	
Global longitudinal strain	< 16% (absolute value)	Considered a minor criterion

LVEF - ejection fraction, AF - atrial fibrillation, LV - left ventricle, e' - mitral annulus early diastolic velocity on tissue Doppler; E - mitral flow early diastolic velocity on pulsed Doppler; TR - tricuspid regurgitation, PASP - pulmonary artery systolic pressure.

REFERENCES

1. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Card Fail Rev. 2017;3(1):7-11.
2. Massie BM, Carson PE, McMurray JJ, Komajda M, McKelvie R, Zile MR, et al.; I-PRESERVE Investigators. Irbesartan in patients with heart failure and preserved ejection fraction. N Engl J Med. 2008;359(23):2456-67.
3. Yusuf S, Pfeffer MA, Swedberg K, Granger CB, Held P, McMurray JJ, et al.; CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: The CHARM-Preserved Trial. Lancet. 2003;362(9386):777-81.
4. Cleland JGF, Tendera M, Adamus J, Freemantle N, Polonski L, Taylor J, et al. The perindopril in elderly people with chronic heart failure (PEP-CHF) study. Eur Heart J. 2006;27(19):2338-45.
5. Pitt B, Pfeffer MA, Assmann SF, Boineau R, Anand IS, Claggett B, et al.; TOPCAT Investigators. Spironolactone for heart failure with preserved ejection fraction. N Engl J Med. 2014;370(15):1383-92.
6. Solomon SD, McMurray JJV, Anand IS, Ge J, Lam CSP, Maggioni AP, et al.; PARAGON-HF Investigators and Committees. Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. N Engl J Med. 2019 Oct 24;381(17):1609-20.
7. Rohde LEP, Montera MW, Bocchi EA, Clausell NO, de Albuquerque DC, Rassi S, et al. Diretriz brasileira de insuficiência cardíaca crônica e aguda. Arq Bras Cardiol. 2018;111(3):436-539.
8. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al.; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution. Eur Heart J. 2016;37(27):2129-2200.
9. Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J. 2019;40(40):3297-317.
10. Barberato SH, Romano MM, Beck AL, Rodrigues AC, Almeida AL, Assunção BM, et al. Position Statement on Indications of Echocardiography in Adults - 2019. Arq Bras Cardiol. 2019;113(1):135-81.

Chronic Coronary Syndrome: What to Expect from Investigation and Management After ISCHEMIA?

Síndrome Coronariana Crônica: O que Esperar da Investigação e da Conduta após o ISCHEMIA?

Lucas Cronemberger Maia Mendes[1], Rafael Willain Lopes[2], Rodrigo Julio Cerci[3], Simone Cristina Soares Brandão[4]

[1]Hospital do Coração do Brasil / Rede D´Or - Brasília - DF Instituto Hospital de Base - Brasília – DF. [2]Hospital do Coração - HCOR, São Paulo-SP. [3]Quanta Diagnóstico por Imagem, Curitiba PR. [4]Hospital das Clínicas da Universidade Federal de Pernambuco, Recife, PE e Clínica Diagson, João Pessoa, PB.

Several clinical trials have questioned the best approach in Chronic Coronary Syndrome (CCS). Perhaps the greatest example was the COURAGE (Optimal Medical Therapy with or without PCI for Stable Coronary Disease) study in stable patients with obstructive coronary disease documented by invasive angiography, in which optimized clinical treatment (OCT) associated with percutaneous coronary intervention (PCI) were not better than OCT alone.[1] In the same direction, the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) was presented at the American Heart Association Congress in November 2019, and has not been published yet. It was conducted on a higher risk CCS patient profile compared to COURAGE, an obstructive coronary disease and at least moderate ischemia. In the study, the comparison of OCT alone and OCT associated with coronary revascularization showed no differences in terms of major cardiovascular outcomes[2] suggesting that in CCS, investing in cardiometabolic profile improvement seems to be the treatment key point.

The focus of this editorial was to discuss the design and results presented by ISCHEMIA so far, contributing to the debate. First of all, it is necessary to remember the importance of of the accumulated knowledge, which supports guidelines and should not be ignored. Considering a patient with chronic chest pain or an equivalent condition, the traditional clinical rational has taught us for many years that we should first consider coronary artery disease (CAD) diagnosis and risk stratification before defining management. Investigation can be initiated by identifying epicardial coronary atherosclerosis (and, for moderate to severe lesions, functional methods can be used to determine whether these symptoms are actually due to the obstructions detected); or by initially investigating the presence of significant myocardial ischemia, and then determining whether there is obstructive CAD or not and, if positive, its location, atherosclerotic burden and severity. Both information are useful and support clinical rational. Based on the pretest probability of CAD, the recently CCS guideline released at the European Cardiology Congress of 2019 defined the best strategy for the initial assessment in each case — whether anatomy or ischemia.[3]

Noninvasive diagnosis of coronary atherosclerosis has improved in the past 10 years, facilitated by the great accuracy of coronary computed tomography angiography (CCTA) compared to invasive angiography. Considering its great negative predictive value, ruling out obstructive CAD has become simple and safe. Besides, the detection of mild nonobstructive atherosclerosis has shown to impact drug treatment optimization, as shown at the SCOT-HEART study.[4] Coronary stenosis between 50% and 90%, on other hand, do not necessarily have functional repercussion.[3] In addition, the problem may not only be restricted to the epicardial arteries, but also includes the large myocardial capillary bed. Often, microcirculation has been shown to be even more important than epicardial atherosclerosis to justify ischemic symptoms, because, despite the presence of significant obstructions in the epicardial arteries, a healthy microcirculation could handle the myocardium demand, and the opposite is not possible.[5]

Before examining the findings of the study, it is essential to point out that the intention of ISCHEMIA was not to investigate the best initial diagnostic strategy for CCS, whether functional methods or CCTA. This specific question has been addressed in other clinical trials in patients without known CAD and with another risk profile.[4,6] ISCHEMIA was designed to answer the following question: in the setting of a CCS patient with at least moderate myocardial ischemia and significant coronary obstruction (≥50% luminal obstruction), both documented, is there really any benefit in adding invasive angiography and coronary revascularization when possible, to current OCT? [7]

That was a randomized "non-blinded" study involving 320 centers and 37 countries around the world. It included 5,179 patients with the initial assumption that there was moderate to severe ischemia identified by a functional examination (using myocardial perfusion scintigraphy, stress echocardiography, exercise treadmill testing or cardiac magnetic resonance imaging), after which a CCTA was performed to exclude patients with non-significant epicardial obstructive lesions (<50% luminal obstruction) or severe left main coronary artery disease. Patients with this inclusion profile were divided into two groups: "conservative", treated with OCT alone; and "invasive," which in addition to OCT according to current guidelines, would be submitted to an intended complete coronary revascularization with PCI or surgery, with on-site specialist decision for each case.[7,8]

Of the included patients, 90% reported angina; 75% of

Keywords

Coronary Artery Disease; Clinical Trial; Therapeutics.

Mailing Address: Lucas Cronemberger Maia Mendes •
SHLS 716 Bloco F Lote 6 - Asa Sul, Brasília - DF, 70390-700
E-mail: lucascmm@yahoo.com.br

DOI: 10.5935/2318-8219.20200004

Editorial

them were submitted to functional imaging exams and 25% to exercise treadmill testing only. In case of less than 60 mL/min creatinine clearance, CCTA was not performed to avoid contrast nephropathy, but most patients (73%) were able to do it. The groups were analyzed by intention-to-treat, with median follow-up of 3.3 years, more than 99% followed-up, and the chosen primary outcome was cardiovascular death, acute myocardial infarction (AMI), hospitalization for unstable angina or heart failure and resuscitated cardiac arrest.[2,7,8]

Still regarding the inclusion criteria in the ISCHEMIA study, patients were 21 years-old or older; moderate to severe ischemia was defined as ischemic burden greater than 10% on myocardial perfusion scintigraphy; stress echocardiogram showing at least three segments with moderate to severe hypocontractility or akinesia during the stress phase; ≥12% or ≥3 segments with severe hypocontractility or akinesia on cardiac magnetic resonance imaging; and exercise treadmill stress test demonstrating ST-segment depression on exertion ≥1.5 mm in ≥2 leads, or ≥2.0 mm in a single lead, in a low load (<7 METs), and angina. In addition to the rigorous and clear exercise test definitions, these patients needed to have a more severe lesion on CCTA (>70% luminal obstruction) to be included in order to avoid false positives as much as possible. The inclusion of exercise treadmill testing was important to bring the study closer to the reality of several places that still does not have access to more sophisticated imaging methods. [7,8]

The ISCHEMIA exclusion criteria were: NYHA functional class III–IV; unacceptable angina despite OCT; left ventricular ejection fraction (LVEF) ≤35%; acute coronary syndrome (ACS) in the last 2 months; PCI or coronary artery bypass grafting (CABG) in the last 12 months. Patients with glomerular filtration rate <30 mL/min or on dialysis were reallocated to an ancillary study (ISCHEMIA CKD); and those with ischemia detected on functional examination without significant lesions on CCTA were referred for the CIAO-ISCHEMIA study. [7,8]

It was difficult to recruit patients for the study, and the lower than expected rate of hard endpoints would decrease the statistical power to less than 60%. This led to modifications suggested by an independent panel in May 2017. The following were approved: expansion of primary outcome, initially death and AMI only; sample size reducing from 8,000 patients to about 5,000 randomized patients, and extension of follow-up. This produced a statistical power of >80% to detect a relative reduction of 18.5% in primary outcome in favor of the invasive group.[7] It is important to note that the primary outcome changing was pre-specified in the original protocol description and, therefore, did not compromise the results analysis. In another fact that may raise questions, 23% of the patients in the group initially proposed for OCT alone required coronary intervention throughout follow-up.[2] From a statistical point of view, there is no concern with this crossover, since the "intention-to-treat" analysis objective is to compare the initial strategies, and thus avoid multiple biases.

Baseline characteristics were very similar in the two study groups ("conservative" and "invasive"). It is remarkable the small proportion of women, only 23% of patients, and the high prevalence of hypertension (73%) and diabetes (42%); 33% had moderate ischemia, and 54% had severe ischemia; almost half of the patients included were triple vessel disease, with 87% affecting the anterior descending coronary artery (about 47% located at the proximal third).[2] This is, therefore, a population of greater severity than previous clinical trials.

Another interesting point was the management of risk factors: at the end of the described follow-up, despite all the rigor of a controlled study, 34% were not on high potency statins; 30% did not use angiotensin converting enzyme inhibitors (ACEI); 41% did not reach the established LDL cholesterol target <70 mg/dL; 3% did not use aspirin or a substitute; and, most impressive, 59% did not meet criteria for "high-level OCT," defined by the achievement of all established clinical goals.[2] This shows how difficult it is to put the OCT into practice.

Functional imaging exams were performed at the beginning of the study, in a phase in which when only 20% of the patients were optimized for therapeutic goals for stable angina.[2] It would be interesting to obtain data from the same exams after initiation of treatment (whether the "conservative" group or the "invasive" group) to assess if there was a significant reduction in stress-induced ischemia and, moreover, if patients who attended this improvement had less outcomes than those who did not, as observed in the COURAGE nuclear substudy.[9] This analysis may never be possible, as imaging stress testing for CCS monitoring was discouraged in the description of ISCHEMIA.[8]

About the reported results, there was no statistically significant difference in the primary outcome between the groups during an average follow-up of 3.3 years: 15.5% in the "conservative" group and 13.3% in the "invasive" group (HR 0.93 — 0.80 to 1.08; p=NS). The same was true for secondary outcomes, which included separated assessment of each of the primary outcome components, and the addition of stroke in some scenarios. Both the curves of primary outcome and those of certain secondary outcomes intersect around the two-year follow-up, and there is a supposed propensity for more outcomes in the OCT-only group.[2] The secondary outcome in which a difference was found was related to angina control and quality of life, improved in the invasive strategy group significantly and longstanding.[10] Another curious observation is that when analyzing "spontaneous AMI" only, a significant difference was found, being smaller in the invasive group (HR = 0.67; 0.53 to 0.83; p<0.01). Nonetheless, perioperative infarction episodes also happen in the real world and must be taken into account. When these were included in the subanalysis (obviously larger in the invasive treatment group), the AMI outcome was the same in both groups.[2]

Thus, so far, the main message of the ISCHEMIA study is that in patients with CCS and moderate to severe ischemia, generally speaking, adding coronary revascularization to OCT was not better than OCT alone, in terms of major cardiovascular outcomes (death, AMI, hospitalization for angina or heart failure, and resuscitated cardiac arrest), and any other conclusions are speculative.[2] It is not known whether the effect of coronary revascularization may become important in a longer-term follow-up, as observed in coronary heart disease patients with reduced LVEF from the STICH

study.[11] In the ISCHEMIA protocol, follow-up time was pre-specified, the consent term included the possibility of contact for up to 20 years, and more data may be available in the future. [8]

Some final messages about the initial presentation of the ISCHEMIA study findings:

1. It was designed to confront different treatment strategies in CCS;

2. It does not only reinforce but amplify COURAGE's concept of adding value to OCT: even in patients with moderate to severe ischemia, OCT can be as powerful as the interventions, and should more often be considered as an initial option for these patients too, and not just for those with little or no ischemia;

3. Learning about the functional consequence was the starting point in the study to establish a causal relationship between symptoms and the obstructive coronary lesions later seen or not on CCTA (14% had no obstructive disease greater than 50%);

4. The coronary anatomy knowledge of patients with suspected CCS was not questioned: the presence, location of the lesions and their degree of obstruction remain as relevant information, noting that 5% of the patients were excluded from the study due to the presence of significant left main coronary artery disease;

5. The study results do not apply to patients with acute coronary syndrome;

6. The study results do not apply to patients with CCS, ischemia and LVEF <35%, or with NYHA III–IV;

7. The study results do not apply to patients with CCS, ischemia and epicardial coronary lesion <50% or with significant left main coronary artery disease;

8. The study results do not apply to patients with CCS, ischemia and limiting symptoms despite OCT;

9. It is likely to impact future guidelines, decreasing the grade of recommendation of invasive treatment in certain CCS scenarios, such as, no longer suggesting coronary revascularization solely based on information on the degree of ischemia;

10. The best approach for patients with suspected chronic coronary syndrome is bring the patient to the center of the decision, providing as many information as possible — clinical, functional and anatomical data — and then decide the best management.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007;356(15):1503-16.

2. ISCHEMIA Study Results. Disponível em: https://www.ischemiatrial.org/ischemia-study-results#slides

3. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al.; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). European Heart Journal. 2019 [cited 2019 Dec 13];ehz425. Available from: https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/09/06/11/01/2019-esc-guidelines-for-chronic-coronary-syndromes

4. SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open-label, parallel-group, multicentre trial. Lancet. 2015;385(9985):2383-91.

5. Gould KL, Johnson NP, Bateman TM, Beanlands RS, Bengel FM, Bober R, et al. Anatomic versus physiologic assessment of coronary artery disease. Role of coronary flow reserve, fractional flow reserve, and positron emission tomography imaging in revascularization decision-making. J Am Coll Cardiol. 2013;62(18):1639-53.

6. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372(14):1291-300.

7. ISCHEMIA Trial Research Group, Maron DJ, Hochman JS, O'Brien SM, Reynolds HR, Boden WE, et al. International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial: Rationale and design. Am Heart J. 2018;201:124-35.

8. ISCHEMIA. The ISCHEMIA and ISCHEMIA-CKD Study Reults ares available! [Internet]. [cited 2019 Dec 13]. Availalble from: https://www.ischemiatrial.org/sites/default/files/ischemiatrial/attachments/Protv2.pdf

9. Shaw LJ, Berman DS, Maron DJ, Mancini GB, Hayes SW, Hartigan PM, et al.; COURAGE Investigators. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. Circulation. 2008;117(10):1283-91.

10. ISCHEMIA. ISCHEMIA-CKD [Internet]. [cited 2019 Dec 13]. Availalble from: https://www.ischemiatrial.org/system/files/attachments/ISCHEMIA-CKD%20QoL%20LBCT%20AHA%2019%20-%20Spertus_0.pdf

11. Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, et al.; STICHES Investigators. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. N Engl J Med. 2016;374(16):1511-20.

My approach of Diastolic Stress Echocardiography

Como Eu Faço Ecocardiograma de Estresse Diastólico

Faculdade de Medicina de Marília;[1] Instituto do Coração de Marília,[2] Marília, SP, Brazil.

Fabio Villaça Guimarães Filho[1,2]

Alexandre Rodrigues[1,2]

Introduction

Doppler echocardiography (DE) plays an essential role in the evaluation at rest on all patients with symptoms of heart failure (HF).[1,2] However, patients with HF and preserved ejection fraction (HFpEF) may have dyspnea during exercise only, with hemodynamic profile, cardiac output (CO) and left ventricular filling pressure (LVFP) at rest similar to healthy individuals with normal diastolic function.[1,2] Evaluation at rest may be insufficient in these patients, justifying an exam that can also do an evaluation with exercise, confirming or ruling out increased LVFP.[3,4]

Diastolic stress echocardiography

Normal response to exercise is a several fold increase in CO without increasing LVFP, especially by improving relaxation with more efficient diastole suction. In the presence of diastolic dysfunction, myocardial relaxation is impaired, becoming more evident with exercise, with abnormal relaxation and early diastole suction not suitable for normal filling. The result is an inadequate increase in CO with increased LVFP.

Evaluation of diastolic function parameters using diastolic stress echocardiography (DSE) during exercise shows these hemodynamic abnormalities.[5,6] The most studied and validated parameters are the ratio of mitral flow E-wave velocity to early diastolic velocity (e') on mitral annulus tissue Doppler, and peak tricuspid regurgitation velocity (PTRV) for the estimation of pulmonary wedge pressure (PWP) and pulmonary artery systolic pressure (PASP), respectively, rest and exercise.[7] In the presence of normal relaxation, there is a proportional increase in E and e' velocities during exercise, maintaining the ratio unchanged.[8] In individuals with myocardial disease and abnormal relaxation, there is no e' increase such as in E velocity, which also goes up due to increased left atrial (LA) pressure, with an expected increase in E/e' ratio. Studies with invasive hemodynamic correlation have shown that evaluation of E/e' ratio in exercise is very useful when it is <10 (septal) to rule out increased LVFP and >14 (mean) to suggest increased LVFP.[5,6,7] Estimating PASP during exercise is also very useful, as the presence of exercise-induced pulmonary hypertension is associated with adverse cardiac events and higher mortality rates.[9]

Myocardial ischemia may cause diastolic dysfunction with increased LVFP and dyspnea. Patients with known or suspected coronary artery disease referred for stress echocardiography for ischemia investigation benefit from the addition of diastolic function evaluation, where prognostic information related to functional capacity, clinical outcomes and mortality can be obtained.[10,11]

With a larger number of publications demonstrating feasibility, hemodynamic validation and diagnostic implications, diastolic function and chronic HF evaluation guidelines have been recommending the use of DSE in the clinical suspicion of HFpEF due to unexplained dyspnea on exertion with grade I diastolic dysfunction at rest.[3,4,12]

Protocols used in the diagnosis of HF_PEF with DSE

DSE can be performed on the bicycle or treadmill, and the choice will depend on the site availability and service experience. Pharmacological stress echocardiography is not recommended.[3,4] Of the two types, supine bicycle exercise is the most recommended for evaluations during stages and at peak, with hemodynamic validation.[7,13] Treadmill test is a good alternative, as abnormal findings in diastole persist after cessation of exercise.[3,4,14]

At our service, we use the treadmill with the Bruce protocol, and for patients with less mobility and for the elderly, modified Bruce protocol is used. Chart 1 shows the protocols, advantages and limitations, and Chart 2 shows the parameters of diastolic function and PASP.[3,4]

Keywords

Heart Failure; Echocardiography; Stress.

Mailing Address: Fabio Villaça Guimarães Filho •
Avenida Vicente Ferreira, 780. CEP: 17.515-000, Marília, SP, Brazil.
E-mail: fabio.icm@icm.com.br

DOI: 10.5935/2318-8219.20200006

Editorial

The treadmill is placed next to the echocardiographic unit to allow the patient to move to the stretcher right after the exercise, and is performed as follows:

1. Diastolic function and PASP variables are taken.

2. Left ventricular (LV) images are acquired: longitudinal and cross-sectional parasternal views, apical 4 and 2 chamber view for the evaluation of segmental contractility.

3. Patients go to the treadmill with continuous 3-lead ECG monitoring and blood pressure evaluation every 3 minutes.

4. They are encouraged to reach the age-predicted maximum heart rate (HR) (220-age) or to observe when any symptoms are felt.

5. As soon as the exercise is finished, they quickly move to the

Chart 1 – Protocols, advantages and limitations.

Modality	Protocols	Advantages	Limitations
Bicycle (upright, semi-supine or supine position)	Default: initial load 25 W, 60 rpm, 25 W increments every 2 minutes	Physiological Best recommended as it allows an evaluation at each stage More time for peak exercise acquisition More sensitive to detect ischemia than treadmill (peak images) Hemodynamic validation with invasive studies	Little availability Patient moving during exercise may impair image acquisition Lower workload achieved compared to treadmill
Treadmill	Bruce: 10% initial inclination and 2% increments at each 3-minute stage, up to the 7th stage Modified Bruce protocol: 0% initial inclination, each stage lasting 3 minutes and inclination increments to 5, 10, 12 and 14% at the 5th stage	Physiological Fairly available Doctors and patients are more familiar Higher workloads Larger double product at the expense of higher HR It may be more specific for detecting ischemia than cycling	Technical difficulty acquiring images at peak exercise Possibility of normalization of abnormalities post-exercise Very short time to acquire images (60 to 90 seconds after exercise discontinuation) Wait for recovery HR to reach 100–110/min to avoid merging of mitral Doppler waves and mitral annulus tissue Doppler waves No hemodynamic validation with invasive measurements

W: Watts; rpm: revolutions per minute, HR = heart rate.

Chart 2 - Parameters acquired at TED at rest and during exercise (bicycle) or immediate post-exercise (treadmill).

Parameter	Acquisition	Advantages	Limitations
E	Apical 4-chamber view of LV Pulsed Doppler with 1 to 3 mm volume sample between the tips of the mitral valve cusps Optimize gain and filter Measure at peak early diastole velocity	Highly feasible and reproducible	Merger of E and A velocities with high HR Decreases with age Acquire when HR is between 100 and 110 beats/min
(lateral, middle) e'	Apical 4-chamber view of LV Mitral annulus tissue Doppler with 5 to 10 mm volume sample in the septal and lateral area Optimize gain and filter	Highly feasible and reproducible	Merger of e', a' velocities with high HR. Decreases with age. Limited accuracy in patients with segmental abnormality in the segment studied, mitral annulus calcification, prosthetic annulus, pericardial disease. Use septal e' preferably; use lateral e' if there is medial annulus calcification or septal segmental contraction abnormality. Different cutoff points depending on sample site.
E/e' ratio	Ratio of E and e' velocities	Highly feasible and reproducible Hemodynamic validation with bicycle exercise	Decreased accuracy in normal individuals, mitral annulus calcification, significant mitral and pericardial valve disease, segmental contraction abnormality in the segment studied. Results clash with hemodynamic validation in some studies. Different cutoff points depending on sample site.
PTRV	Apical 4-chamber view of LV or parasternal view of RV inflow tract Peak velocity obtained by continuous Doppler Optimize gain and filter to show complete flow curve	Indirect adjunct of LV filling pressure estimation	Increased exercise velocity may be due to pulmonary parenchymal disease or normal response to increased exercise flow in normal individuals. Complete signal of tricuspid regurgitation is not obtained in 1/3 of patients. Less reliable if there is severe tricuspid regurgitation.

LV: left ventricle; RV: right ventricle; HR: heart rate; beats/min: beats/minute; E: Mitral peak early filling velocity; e': Early diastolic filling velocity on septal and lateral mitral annulus tissue Doppler; E/e' ratio: Mitral E velocity divided by e' velocity; PTRV: Peak tricuspid regurgitation velocity.

stretcher in the left lateral decubitus position, with LV imaging taken as at rest, at 60 to 90 seconds, avoiding normalization of any segmental contraction abnormality.

6. Acquisition of tricuspid Doppler, as PASP tends to normalize rapidly after exercise ceases. Contrast infusion may improve Doppler tracing and endocardial borders, but it is not useful for tissue Doppler. Right atrial pressure is estimated to be between 5 and 10 mm Hg due to the difficulty in assessing inferior vena cava diameters during exercise.

7. Mitral and tissue mitral annulus Doppler when HR is 100–110 beats/min.

Interpretation of DSE

Patient's exercise capacity should be compared with age and gender nomograms, determining whether dyspnea is the main limitation for test discontinuation.

Chronotropic response of patients with HFpEF may present incompetence, i.e. they cannot reach 85% of the HR expected.[15]

We evaluated LV segmental contractility: images at rest and after immediate exertion side by side, aiming to rule out segmental contractility abnormalities as a cause of ischemia.

Interpretation of diastolic function:[3,4]

The test is normal if septal E/e' <10 at rest and exercise, and PTRV <2.8 cm/sec. at rest and exercise. (Figure 1)

The test is abnormal when septal e' <7 cm/sec. or lateral e' <10 cm/sec. at rest and, with exercise, septal E/e' is >15, mean E/e' >14, PTRV > 2.8 m/sec. (Figure 2).

Isolated PTRV increase should not be used as a diagnostic criterion for HFpEF, as it may be caused by normal hemodynamic response to exercise in the absence of PVFP elevation or pulmonary parenchymal disease.[12]

New perspectives

The incorporation of new techniques should include: longitudinal systolic function by global longitudinal strain, diastolic function by strain rate, LA strain and measurement of early LV suction with torsion parameters.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

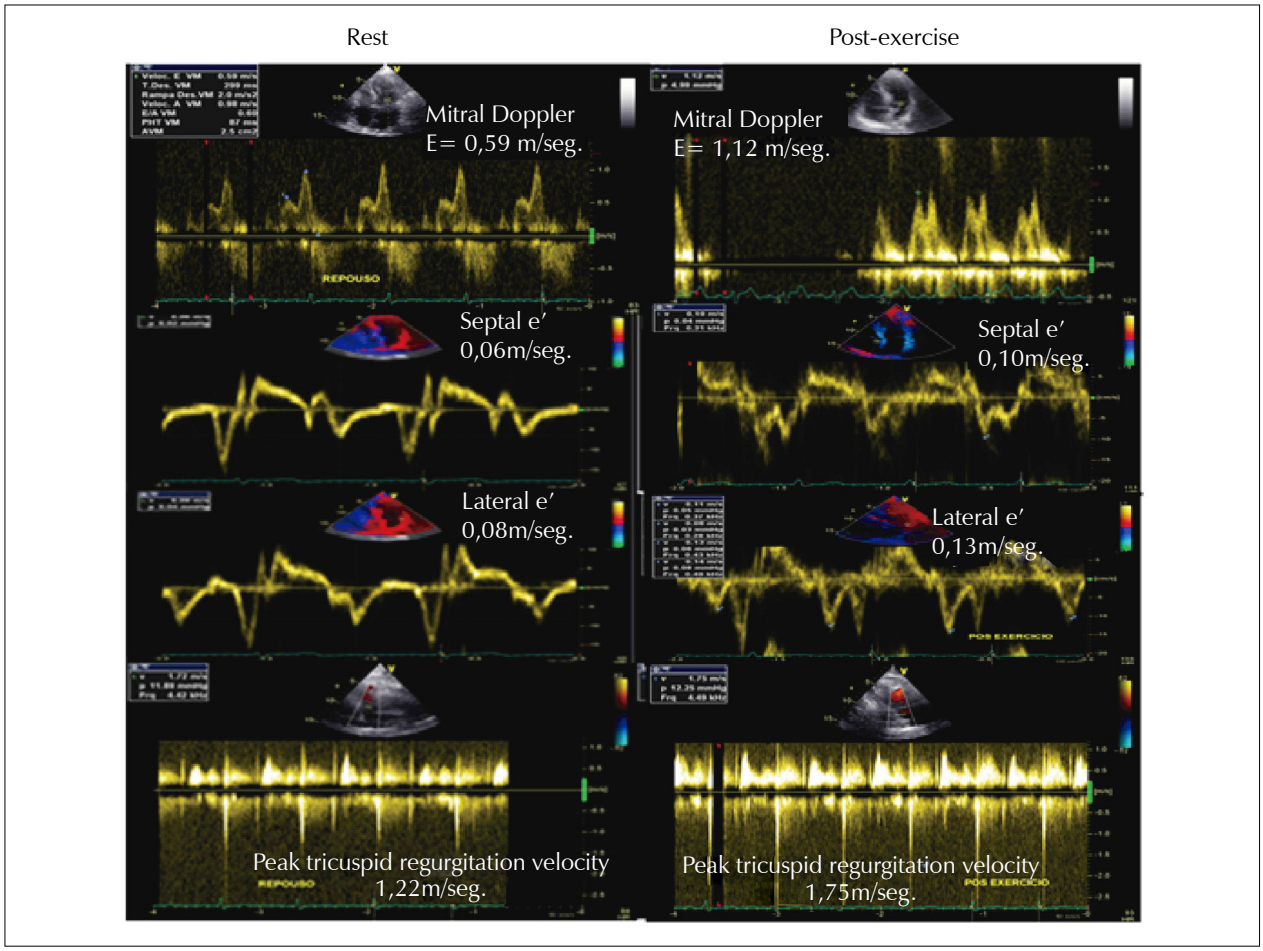


Figure 1 - *Female patient, 75 years old, hypertension and dyslipidemia, with dyspnea on exertion, submitted to modified Bruce protocol TED, with no LV segmental contractility abnormalities. Duration of 9 minutes, interrupted by fatigue, electrocardiogram with no abnormal findings. Submaximal HR was achieved with no abnormalities in segmental contraction after exercise. Medium E/e' at rest = 8.4 and PASP estimated at 16 mmHg. After exercise, medium E/e' = 9.7 and PASP estimated at 17 mmHg. Normal TED.*

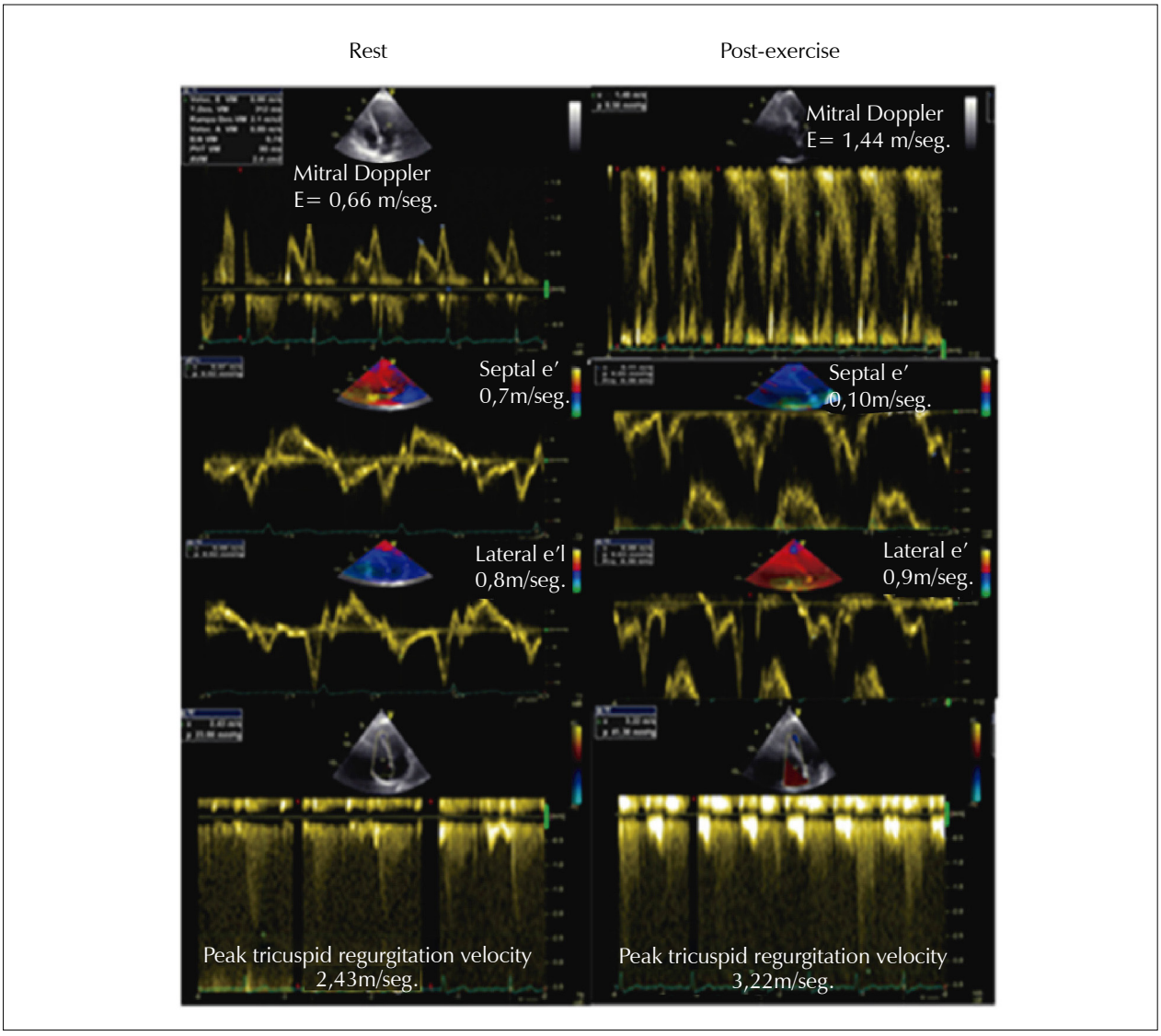


Figure 2 - *Female patient, 68 years old, arterial hypertension, diabetes and dyslipidemia, fatigue on medium exertion, submitted to Bruce protocol TED, with no abnormal findings in LV segmental contractility. The patient completed 7 minutes, presented moderate fatigue, reached 90% of the maximum expected HR. Electrocardiogram with no abnormal findings, no abnormalities in segmental contraction after exercise. Medium E/e' at rest = 8.8 and PASP estimated at 28 mmHg. After exercise, medium E/e' = 15 and PASP estimated at 46 mmHg. Abnormal TED.*

References

1. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Am Soc Echocardiogr. 2016;29(4):277-314.
2. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2016;17(12):1321-60.
3. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, et al. The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Eur Heart J Cardiovasc Imaging. 2016;17(11):1191-229.
4. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R, et al. The Clinical Use of Stress Echocardiography in Non-Ischaemic Heart Disease: Recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. J Am Soc Echocardiogr. 2017;30(2):101-38.
5. Ha JW, Oh JK, Pellikka PA, Ommen SR, Stussy VL, Bailey KR, et al. Diastolic stress echocardiography: a novel noninvasive diagnostic test for diastolic dysfunction using supine bicycle exercise Doppler echocardiography. J Am Soc Echocardiogr. 2005;18(1):63-8.
6. Borlaug BA, Nishimura RA, Sorajja P, Lam CS, Redfield MM. Exercise hemodynamics enhance diagnosis of early heart failure with preserved

ejection fraction. Circ Heart Fail. 2010;3(5):588-95.

7. Obokata M, Kane GC, Reddy YN, Olson TP, Melenovsky V, Borlaug BA. Role of Diastolic Stress Testing in the Evaluation for Heart Failure With Preserved Ejection Fraction: A Simultaneous Invasive-Echocardiographic Study. Circulation. 2017;135(9):825-38.

8. Ha JW, Lulic F, Bailey KR, Pellikka PA, Seward JB, Tajik AJ, et al. Effects of treadmill exercise on mitral inflow and annular velocities in healthy adults. Am J Cardiol. 2003;91(1):114-5.

9. Lam CS, Roger VL, Rodeheffer RJ, Borlaug BA, Enders FT, Redfield MM. Pulmonary hypertension in heart failure with preserved ejection fraction: a community-based study. J Am Coll Cardiol. 2009;53(13):1119-26.

10. Grewal J, McCully RB, Kane GC, Lam C, Pellikka PA. Left ventricular function and exercise capacity. JAMA. 2009;301(3):286-94.

11. Holland DJ, Prasad SB, Marwick TH. Prognostic implications of left ventricular filling pressure with exercise. Circ Cardiovasc Imaging. 2010;3(2):149-56.

12. Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J. 2019;40(40):3297-317.

13. Talreja DR, Nishimura RA, Oh JK. Estimation of left ventricular filling pressure with exercise by Doppler echocardiography in patients with normal systolic function: a simultaneous echocardiographic-cardiac catheterization study. J Am Soc Echocardiogr. 2007;20(5):477-9.

14. Ishii K, Imai M, Suyama T, Maenaka M, Nagai T, Kawanami M, et al. Exercise-induced post-ischemic left ventricular delayed relaxation or diastolic stunning: is it a reliable marker in detecting coronary artery disease? J Am Coll Cardiol. 2009;53(8):698-705.

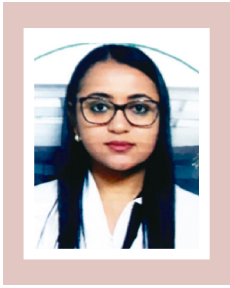
15. Borlaug BA, Melenovsky V, Russell SD, Kessler K, Pacak K, Becker LC, et al. Impaired chronotropic and vasodilator reserves limit exercise capacity in patients with heart failure and a preserved ejection fraction. Circulation. 2006;114(20):2138-47.

MY Approach to Echocardiographic Assessment of Cardiotoxicity in Cancer Therapy

Como eu Faço a Avaliação Ecocardiográfica da Cardiotoxicidade na Terapia do Câncer

1. Hospital 9 de Julho – São Paulo, Brazil

Marcelo Goulart Paiva[1]



Seliny Monteiro Campelo Lira[1]

Over the last three decades, we have seen a significant increase in cancer patients' survival and, as a result, the emergence of cardiovascular complications with the potential to offset the benefits obtained.[1,2]

Early diagnosis of cardiovascular impairment related to cancer treatment provides the opportunity for prevention and treatment, especially in myocardial dysfunction and, consequently, in the development of heart failure. [1,2]

Defining Cardiotoxicity

Several definitions of cardiotoxicity (CTX) regarding different therapeutic regimens and diagnostic criteria make it difficult to standardize it in the literature. We chose to follow the consensus of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI), defining CTX as left ventricular ejection fraction (LVEF) drop >10% (compared to pretreatment levels) to less than 53% or lower limit of normality.[3]

The role of echocardiography

echocardiography has established itself as the basis for CTX diagnosis and monitoring because it is a widely available, cost-effective and harmless method (free of risk, contrast and ionizing radiation), which makes it possible to repeat it numerous times. Whenever possible, the report should include: time interval from chemotherapy (CT) performed (how many days after the QT cycle, for example), which drugs were used, vital signs, and the data mentioned below.[2]

Simpson's method should be routinely used to calculate LVEF. However, its intra and interobserver variability can be as high as 10% (absolute value). Findings outside the expected parameters should be repeated and confirmed after 2–3 weeks of the initial finding.[4]

In the population of cancer patients, the 3D technique is preferable over 2D because it has shown greater reproducibility and accuracy in the recognition of borderline or slightly reduced LVEF. In patients undergoing chemotherapy, it presented the lowest intra and interobserver time variability (5.6%, absolute value).[5]

LVEF drop reflects a marker of late myocardial damage, accompanied by worse prognosis. Cardiac dysfunction only becomes evident when myocardial damage is significant. Therefore, its absence does not exclude cardiotoxicity.[5–7]

The application of strain by speckle tracking to analyze ventricular mechanics enables the detection of subclinical lesions with good reproducibility and accuracy. Multiple studies have demonstrated the value of global longitudinal strain (GLS) in the detection of subclinical myocardial dysfunction in patients during and after cancer treatment.[8–10] Its role seems to be more relevant in the association with borderline normal or slightly reduced LVEF (LVEF 50–59%).[3] Overall, although early detection of changes is conceptually important, the value of these actual abnormalities should be demonstrably correlated with clinical outcomes.[8]

In order to increase the accuracy of 2D echocardiography in detecting CTX signals, it is recommended to perform a combined LVEF analysis (Simpson's method), LV wall motion score calculation and longitudinal systolic function studies, especially where advanced methodologies are unavailable (3D echocardiography and myocardial strain study). Although there are no diagnostic reference values, the progressive decline in peak mitral annular systolic velocity using tissue Doppler (s'

Keywords

Cardiotoxicity; Drug Therapy; Echocardiography.

Mailing Address: Marcelo Goulart Paiva •
Avenida Brasil 678. 01430-000. São Paulo – Brazil.
E-mail: mgpaiva123@gmail.com

DOI: 10.5935/2318-8219.20200007

wave) and mitral annular plane systolic excursion (MAPSE) should be valued.[11–12]

Abnormalities in parameters related to diastolic function, such as E and A waves, E/A ratio, isovolumetric relaxation time and myocardial performance index, were described early after CT. However, longitudinal studies have not been able to reproduce the prognostic value of these findings and there is insufficient evidence to use this analysis in the diagnosis of CT-induced CTX.[12,13]

The prevalence of right ventricular involvement (assessed by anterior tricuspid annular excursion, s' wave and fractional area variation) and its prognostic value have not been properly studied yet. Data regarding the influence of CT on remodeling, ventricular function and mechanics are scarce and sometimes conflicting. Interestingly, the difference in RV longitudinal strain is more pronounced when the septal region is disregarded, suggesting greater RV myocardial sensitivity. [14]

Which patients are at high risk for cardiotoxicity?

Before starting cancer treatment, all patients should be evaluated for the risk of CTX. Factors related to the treatment proposed (which drugs are used and association with radiotherapy) and the presence of comorbidities, cardiovascular risk factors, age and gender should be considered. The presence of basal LVEF of 50–55% increases the risk of cardiac complications, especially when anthracycline is involved.[1-3,15]

Echocardiographic evaluation before therapy

The ASE/EACVI recommends evaluation of LVEF and SLG in all patients expected to undergo any therapy associated with the risk of CTX in order to assess any potentially underlying heart disease.[12] In the presence of structural abnormalities, systolic dysfunction (LVEF <50–55%) with or without SLG <16%, cardiac evaluation and control of associated cardiovascular risk factors is recommended.[3,12,15] (Figure 1)

Echocardiographic evaluation during therapy

Echocardiographic monitoring in asymptomatic patients during cancer treatment is recommended for all patients considered at high risk. The ASE/EACVI and the American Society of Clinical Oncology have different guidelines on how often it should be performed, reflecting the lack of literature data to support either of those guidelines.[1,2]

Monitoring during anthracyclic therapy should be performed after cumulative dose of 240 mg/m² and thereafter, at every 50 mg/m². During therapy with trastuzumab, the US FDA's recommendation is to repeat the echocardiography every 3 months, although asymptomatic LVEF drop in asymptomatic patients should not necessarily determine discontinuation of therapy, as found in the SAFE-HEARt study.[16] An evaluation at every 3 months is also recommended while tyrosine kinase inhibitors are used.[1–3,15]

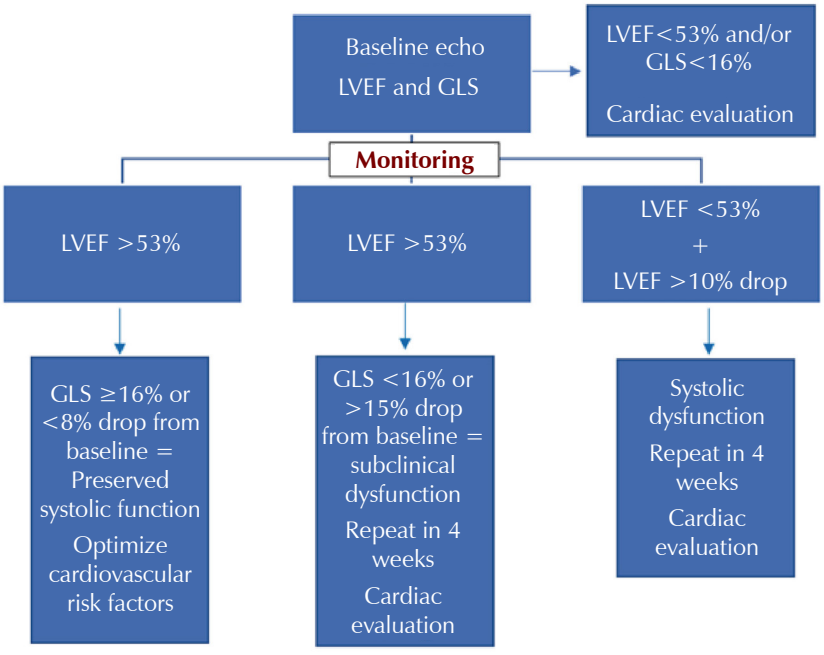


Figure 1 – *Flowchart for prior evaluation and monitoring during cancer treatment. LVEF (left ventricular ejection fraction), GLS (global longitudinal strain). In addition to echocardiographic evaluation, we suggest ECG (electrocardiogram) and biomarkers (natriuretic peptide and troponin). Monitoring depends on the associated risk factors and the drug used.*[3,15]

The presence of symptoms suggestive of CHF and alterations in biomarkers, such as natriuretic peptides and troponin, help in risk stratification and in determining the need for echocardiographic reassessment, including for other drugs, such as cyclophosphamide and carfilzomib.[1–3,15,17–18] (Figure 1)

Echocardiographic evaluation after therapy

Again, we have observed a lack of consensus regarding late follow-up.[1,2] We recommend echocardiography in the first 6 to 12 months after completion of anthracyclic treatment, since the study by Cardinale et al. demonstrated the prognostic value of LVEF after completion of CT and the prevalence of myocardial dysfunction (98% of cases) in the first 12 months.[1-3,15,19]

Radiotherapy

Radiotherapy, especially when the total dose exceeds 30 Gy (or more than 2 Gy per day) is related to various cardiovascular complications. Pericardial disease is described as the most common manifestation, usually occurring a few weeks after treatment. Acute pericarditis is usually self-limited. However, 10% to 20% of patients develop chronic or constrictive pericarditis after 5 to 10 years. Late-onset conditions occurring years or decades after exposure include: chronic pericarditis, mitral and aortic valve diseases, large and medium vessel vasculopathy (porcelain aorta and carotid stenosis), cardiomyopathies (dilated and restrictive forms), conduction disorders and coronary atherosclerotic disease (acute and chronic coronary insufficiency). Patients should be reevaluated after 5 years in high-risk cases and, thereafter, at every 5 years, including provocative tests for ischemia such as stress echocardiography.[15–20]

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Armenian SH, Lacchetti C, Barac A, Carver J, Constine LS, Denduluri N, et al. Prevention and monitoring of cardiac dysfunction in survivors of adult cancers: American society of clinical oncology clinical practice guideline. J Clin Oncol. 2017;35(8):893-911.
2. Zamorano JL, Lancellotti P, Rodriguez Muñoz D, Aboyans V, Asteggiano R, Galderisi M, et al.; ESC Scientific Document Group. 2016 ESC position paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC committee for practice guidelines: The task force for cancer treatments and cardiovascular toxicity of the european society of cardiology (ESC). Eur Heart J. 2016;37(36):2768-2801
3. Liu J, Banchs J, Mousavi N, Plana JC, Scherrer-Crosbie M, Thavendiranatan P, et al. Contemporary Role of Echocardiography for Clinical Decision Making in Patients During and After Cancer Therapy. JACC Cardiovasc Imaging. 2018;11(8):1122-31.
4. Otterstad JE, Froeland G, St John Sutton M, Holme I. Accuracy and reproducibility of biplane two-dimensional echocardiographic measurements of left ventricular dimensions and function. Eur Heart J. 1997;18(3):507-13.
5. Thavendiranathan P, Grant AD, Negishi T, Plana JC, Popović ZB, Marwick TH. Reproducibility of echocardiographic techniques for sequential assessment of left ventricular ejection fraction and volumes: application to patients undergoing cancer chemotherapy. J Am Coll Cardiol. 2013;61(1):77-84.
6. Ewer MS, Lenihan DJ. Left ventricular ejection fraction and cardiotoxicity: is our ear really to the ground? J Clin Oncol. 2008;26(8):1201-3.
7. Eidem BW. Identification of anthracycline cardiotoxicity: left ventricular ejection fraction is not enough. J Am Soc Echocardiogr. 2008;21:1290-2.
8. Thavendiranathan P, Poulin F, Lim K, Plana, JC, Woo A, Marwick T. Use of Myocardial Strain Imaging by Echocardiography for the Early Detection of Cardiotoxicity in Patients During and After Cancer Chemotherapy– A Systematic Review. J Am Coll Cardiol. 2014;63(25 Pt A):2751-68.
9. Sawaya H, Sebag I, Plana JC, Januzzi JL, Ky B, Cohen V, et al. Early Detection and Prediction of Cardiotoxicity in Chemotherapy-Treated Patients. Am J Cardiol. 2011;107(9):1375-80.
10. Negeshi K, Negeshi T, Hare JL, Haluska BA, Plana JC, Marwick TH, et al. Independent and Incremental Value of Deformation Indices for Prediction of Trastuzumab-Induced Cardiotoxicity. J Am Soc Echocardiogr. 2013;26:493-8.
11. Tassan-Mangina S, Codorean D, Metivier M, Costa B, Himberlin C, Jouannaud C, et al. Tissue Doppler imaging and conventional echocardiography after anthracycline treatment in adults: early and late alterations of left ventricular function during a prospective study. Eur J Echocardiogr. 2006;7(2):141-6.
12. Plana JC, Galderisi M, Barac A, Ewer MS, Ky B, Scherrer-Crosbie M, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: A report from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr. 2014;27(9):911-39.
13. Dorup I, Levitt G, Sullivan I, Sorensen K. Prospective longitudinal assessment of late anthracycline cardiotoxicity after childhood cancer: the role of diastolic function. Heart. 2004;90(10):1214-6.
14. Calleja A, Poulin F, Khorolsky C, Shariat M, Bedard PL, Amir E, et al. Right ventricular dysfunction in patients experiencing cardiotoxicity during breast cancer therapy. J Oncol. 2015;2015:609194.
15. López-Fernández T, Martín García A, Santaballa Beltrán A, Montero Luis Á, García Sanz R, Mazón Ramos P, et al. Cardio-Onco-Hematology in Clinica Practice. Position Paper and Recommendation. Rev Esp Cardiol. 2017;70(6):474-68.
16. Lynce F, Barac A, Geng X, Dang C, Yu AF, Smith KL, et al. Prospective evaluation of the cardiac safety of HER2-targeted therapies in patients with HER2-positive breast cancer and compromised heart function: the SAFE-HEaRt study. Breast Cancer Res Treat. 2019;175(3):595-603.
17. Peres E, Levine JE, Khaled YA, Ibrahim RB, Braum TM, Krijanovski OI, et al. Cardiac complications in patients undergoing a reduced-intensity condition hematopoietic stem cell transplantation. Bone Marrow Transplantation. 2010;45(1):149-52.
18. Sethi TK, Basdag B, Bathia N, Moslehi J, Reddy NM. Beyond Anthraciclines: Preemptive Management of Cardiovascular Toxicity in the Era of Targeted Agents for Hematologic Malignancies. Curr Hematol Malig Rep. 2017;12(3):257-67.
19. Cardinale D, Colombo A, Bacchiani G, Tedeschi I, Meroni CA, Veglia F, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation. 2015;131(22):1981-8.
20. Herrman J, Finch W, Lee SM, Yang EH. Clinical Cardio-Oncology. In: Radiation-Induced Heart Disease Long-Term Manifestations, Diagnosis, and Management. Philadelphia: Elsevier; 2017. cap.14. p. 272-5.

Echocardiographic Assessment of Right Chambers by Gender and Body Surface Area

Análise Ecocardiográfica das Câmaras Direitas segundo Sexo e Superfície Corporal

Rafael Yared Forte, Ana Cristina Camarozano, Daniela de Castro Carmo, Jerônimo Antonio Fortunato, Rubens Zenóbio Darwich, Júlia Ventura Niclewicz, Liz Andréa Villela Baroncini

Hospital da Cruz Vermelha, Cruz Vermelha Brasileira, Filial do Estado do Paraná, Curitiba, PR; Curso de Especialização em Ecocardiografia Transtorácica, Instituto Saber e Aprender, Curitiba, PR, Brazil

Abstract

Introduction: Assessment of right chambers dimensions and function according to gender, age, body surface area and body mass index is not uniformly performed.

Objective: To evaluate, by transthoracic echocardiography dimensions and function of right chambers, according to gender, body surface area and body mass index in an outpatient population.

Method: Cross-sectional study. Eighty-one patients were selected, 60.4 ± 13.5 years (57 women, 70%). Parameters assessed were the following: proximal, basal, medium and longitudinal, right ventricle diameter; right atrium area and right atrium volume; right ventricle wall thickness; tricuspid annular plane systolic excursion; and tricuspid annulus tissue Doppler and S' wave.

Results: Female sex presented lower diameters (Student's t-test) of proximal right ventricle diameter (20.6 mm ± 2.4 vs. 22.7 mm ± 2.2; p = 0.001), basal right ventricle diameter (34,4 mm ± 3,5 vs. 38,2 mm ± 4,8; p <0.001), medium right ventricle diameter (27 mm ± 3.3 vs. 32.4 mm ± 4.9; p <0.001), right atrium area (13.7 cm^2 ± 2.7 vs. 16.6 cm^2 ± 3.9; p = 0.002) and right atrium volume (37 mL ± 10.6 vs. 50.7 mL ± 15.6 ; p = 0.002). Body mass index and body surface area correlated with proximal right ventricle diameter (correlation coefficient - CC 0.24; p = 0.03), basal right ventricle diameter (CC 0.22; p = 0.04), medium right ventricle diameter (CC 0.23; p = 0.04), longitudinal right ventricle diameter (CC 0.28; p = 0.01), right atrium area (CC 0.40; p = 0.001), and right atrium volume (CC 0.24; p = 0.0006).

Conclusion: Right ventricular diameters, right atrial area and volume were lower in females. A correlation was found with body mass index and body surface area. Tricuspid annular plane systolic excursion and S' were not influenced by sex, body mass index and body surface area.

Keywords: Heart Ventricles; Organ Size; Echocardiography.

Resumo

Introdução: *A avaliação sistemática das dimensões e da função das câmaras direitas, de acordo com sexo, idade, superfície corporal e índice de massa corporal, não é uniformemente realizada.*

Objetivo: *Avaliar, ao ecocardiograma transtorácico, as dimensões e a função das câmaras direitas de acordo com o sexo, superfície corporal e índice de massa corporal em uma população ambulatorial.*

Métodos: *Estudo observacional, transversal. Foram selecionados 81 pacientes, 60,4 ± 13,5 anos, de ambos os sexos (57 mulheres, 70%). Foram avaliados: diâmetro proximal do ventrículo direito, basal do ventrículo direito, médio e longitudinal; área do átrio direito e volume do átrio direito; espessura da parede livre do ventrículo direito; excursão sistólica do anel valvar tricúspide; e Doppler tecidual do anel tricúspide, onda S'.*

Resultados: *O sexo feminino apresentou menores diâmetros em relação ao sexo masculino (teste t de Student) de diâmetro proximal do ventrículo direito (20,6 mm ± 2,4 vs. 22,7 mm ± 2,2; p = 0,001), basal do ventrículo direito (34,4 mm ± 3,5 vs. 38,2 mm ± 4,8; p < 0,001), diâmetro médio do ventrículo direito (27 mm ± 3,3 vs. 32,4 mm ± 4,9; p < 0,001), área do átrio direito (13,7 cm^2 ± 2,7 vs. 16,6 cm^2 ± 3,9; p = 0,002) e volume do átrio direito (37 mL ± 10,6 vs. 50,7 mL ± 15,6 ; p = 0,002). O índice de massa corporal e a superfície corporal se correlacionaram positivamente com o diâmetro proximal do ventrículo direito (coeficiente de correlação - CC 0,24; p = 0,03), diâmetro basal*

Mailing Address: Liz Andréa Villela Baroncini •
DEP-CVB-PR - Departamento de Ensino e Pesquisa, Avenida Vicente Machado, 1.310, Batel, CEP: 80420-011, Curitiba, PR, Brazil
E-mail: lizandreabaroncini@hotmail.com
Manuscript received 21/10/2019; revised 12/11/2019; accepted 13/11/2019

DOI: 10.5935/2318-8219.20200008

do ventrículo direito (CC 0,22; p = 0,04), diâmetro médio do ventrículo direito (CC 0,23; p = 0,04), diâmetro longitudinal do ventrículo direito (CC 0,28; p = 0,01), área do átrio direito (CC 0,40; p = 0,001) e volume do átrio direito (CC 0,24; p = 0,0006).

Conclusão: *As médias dos diâmetros ventriculares, área e volume atriais direitos foram menores no sexo feminino. Foi encontrada correlação positiva destes parâmetros com o índice de massa corporal e a superfície corporal. Os valores da excursão sistólica do anel valvar tricúspide e S' não foram influenciados por sexo, índice de massa corporal e superfície corporal.*

Palavras-chave: Ventrículos do Coração; Tamanho do Órgão; Ecocardiografia.

Introduction

The right ventricle (RV) plays an important role in the morbidity and mortality of patients with cardiopulmonary diseases.[1–3] However, its systematic evaluation is not uniformly performed. This is partly due to the enormous attention given to left heart evaluation, the scarcity of studies providing normal reference values for right ventricular size and function, and because right ventricular echocardiographic examination has many limitations.[1] Much of the chamber is located behind the sternum, has an irregular shape, trabeculated walls and a variable location within the chest, depending on the patient's position. Besides, RV is known to be functionally different from LV, as its contraction is mainly determined by longitudinal shortening due to the structural organization of its myocardial fibers.[2] Despite these problems, echocardiography may provide useful information about RV, including the determination of its dimensions and function.[4]

Current RV reference values are based on large populations or grouped values from various studies; most are not indexed for body surface area (BSA) and only cite lower reference values for women. As a result, patients with near-normal values may be erroneously classified as being outside the reference average. The available data are insufficient to classify mild, moderate and severe abnormalities. When interpreting an examination, common sense should be used to determine the extent of abnormality for any given parameter.[5]

In light of the above, the purpose of this study was to evaluate, by transthoracic echocardiography, the dimensions and function of the right chambers according to gender, age, BSA and body mass index (BMI) in a varied outpatient population.

METHODS

Population studied

Cross-sectional observational study. The study included 81 patients, aged 60.4±13.5 (24 to 88 years old, with a median of 61 years), of both genders (57 women, 70%), older than 18, from the cardiology outpatient clinic of Hospital da Cruz Vermelha de Curitiba, of any ethnicity, referred by the attending physician for transthoracic echocardiography for any clinical indication. The choice of patients was not established by any statistical criteria, but by convenience, according to the individual's availability to participate in the study. For each patient, a protocol form including clinical and echocardiographic parameters was filled out. The following clinical data were collected: age, gender, weight, height, body surface (BSA), body mass index (BMI), presence of systemic arterial hypertension (SAH), diabetes mellitus (DM), coronary artery disease (CAD), smoking (current or past) and dyslipidemia. The diagnoses of SAH, DM, dyslipidemia and smoking were found in the patients' medical records and/or were reported by them (self-reported information). The presence of CAD was confirmed by medical and patient records, including: nonfatal myocardial infarction and surgical or percutaneous coronary artery bypass grafting. The medications regularly used by the patient were also noted.

Exclusion criteria were: a) patients with significant valve diseases (moderate and severe); b) patients with valve prostheses; c) patient with LV contraction segmental abnormalities due to ischemic heart disease or other cardiomyopathies; and d) patients with pulmonary emphysema or self-reported chronic obstructive pulmonary disease; e) patients with moderate to severe pulmonary arterial hypertension (pulmonary artery systolic pressure, PSAP >50 mmHg); f) patients with left ventricular contractile dysfunction (ejection fraction <52% for men and <54% for women); g) patients with infiltrative diseases and periocardiopathies; h) patients with congenital heart disease with pulmonary hyperflow with or without surgical correction; and i) patients with pacemaker.

The patients underwent a complete two-dimensional transthoracic echocardiography scan by one of either Phillips IE 33, Envisor or Vivid E General Electric echocardiography equipment. All acoustic windows with all standard echocardiographic measurements and analyzes were performed on each patient. Ultrasound scans were performed by two experienced echocardiographers with echocardiography qualification from the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology (DIC-SBC).

All patients signed two copies of an informed consent form, one copy of which was retained by the study participant. The study was approved by the local Research Ethics Committee.

Main echocardiographic parameters analyzed in this study

Diameters: proximal RV diameter from the longitudinal parasternal window ((RVP; normal up to 28 mm), basal RV diameter from the 4-chamber apical window (RVB; normal up to 41 mm), médium RV diameter from the 4-chamber apical window (RVM; normal up to 35 mm) and longitudinal diameter (RVL; normal up to 83 mm) from the 4-chamber apical window. All linear RV measurements were performed at the final diastole (Figure 1).

Right atrial area (RAA; normal up to 8.5 cm^2) and right atrial volume index (RAV; normal up to 27 ml/m^2 in women and up to 32 ml/m^2 in men) measured from the 4-chamber apical window (Figure 1).

RV free wall thickness measured in diastole at the subcostal

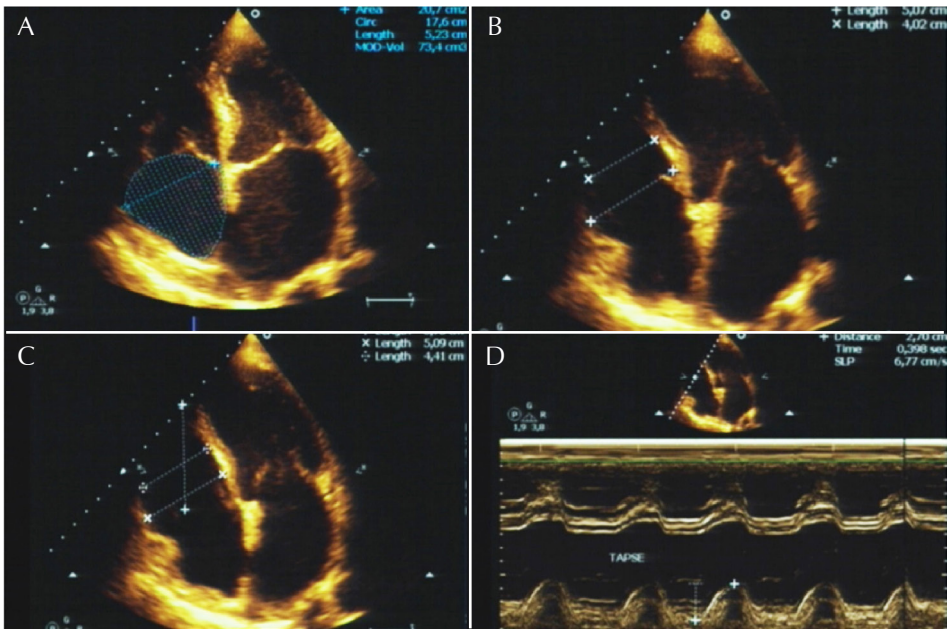


Figure 1 – *Echocardiogram showing on (A) Left top panel Four-chamber view of right atrial volume. (B) Right top panel: Two-dimensional measurements of basal and middle right ventricular diameters at end diastole. (C) Left bottom panel: Four-chamber view of two-dimensional measurements of basal, middle and longitudinal right ventricular diameters at end diastole. (D) Right bottom panel: Four-chamber apical view of unidimensional measure of tricuspid annular plane systolic excursion.*

section by M-mode or two-dimensional echo. Thickness >5 mm indicates RV hypertrophy (RVH).

Tricuspid annular plane systolic excursion (TAPSE) measured from the 4-chamber apical window (normal ≥17 mm). Evaluates RV systolic longitudinal function (Figure 1).

Tissue Doppler of the tricuspid annulus, S' wave measured from the 4-chamber apical section at the tricuspid annulus level (normal >9.5 cm/s) and on the RV free wall. Evaluates RV systolic longitudinal function.

All quantifications and values considered in this study were based on the guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging. [1,4–7]

Statistical analysis

The results obtained in the study were described by means, medians, minimum values, maximum values and standard deviations (quantitative variables) or by frequencies and percentages (categorical variables). To evaluate the association between two quantitative variables, Pearson's or Spearman's correlation coefficient was estimated. A comparison of two groups regarding quantitative variables was performed using Student's t-test for independent samples or Mann-Whitney's non-parametric test. More than two groups were compared considering the one-way analysis of variance (ANOVA) and the least significant difference (LSD) test for multiple comparisons or Kruskal-Wallis' non-parametric test. The normality condition of the variables was evaluated using the Kolmogorov–Smirnov test. In this study, p values <0.05 were considered statistically significant.

Data were analyzed using the IBM SPSS Statistics v.20.0 computer program. Armonk, NY: IBM Corp.

Results

Table 1 shows the clinical characteristics of the study population. There was a predominance of females (70%), 60% hypertensive, 35% diabetics, 29% dyslipidemics, 3% smokers, most of them overweight and obesity. Table 2 shows the baseline echocardiographic parameters of the study population. A positive correlation was found between age and proximal RV diameter (correlation coefficient [CC] 0.25; p = 0.02) and a negative correlation between RAA (CC -0.25; p=0.04) and RAV (CC -0.26; p = 0.03). The other variables did not correlate with age (Table 3). Females had smaller RVP diameters than males (20.6±2.4 mm versus 22.7±2.2 mm; p=0.001), RVB (34.4±3.5 mm versus 38.2±4.8 mm; p<0.001), RVM (27±3.3 mm versus 32.4±4.9 mm; p<0.001), RVA (13.7±2.7 cm² versus 16.6±3.9 cm²; p=0.002) and RVV (37±10.6 ml versus 50.7±15.6 ml; p=0.002) (Table 4). BMI and BSA correlated positively and significantly with the RVP diameters (p=0.03), RVB (p=0.04), RVM (p=0.04), RVL (p=0.01), RAA (p=0.001) and RAV (p=0.0006), (Table 5). The parameters of right ventricular function (TAPSE and S') did not vary significantly with age and between genders (Tables 3 and 4). The presence of SAH, DM, dyslipidemia and smoking did not influence the variables analyzed (data not shown).

Discussion

In this study, the absolute values of the echocardiographic parameters of the right chambers presented mean within normality limits[4] for both genders, with smaller diameters, area and volume in females, and this difference decreased

Table 1 - Baseline characteristics of the study population.

Variable		n (%)
Age (years)	60.4 ± 13.5	81
Gender		
Male		24 (30)
Female		57 (70)
Systemic Arterial hypertension		
No		30 (37)
Yes		51 (63)
Diabetes mellitus		
No		53 (65)
Yes		28 (35)
Dyslipidemia		
No		57 (70)
Yes		24 (30)
Smoking		
No		77 (96)
Yes		4 (4)
Body mass index (kg/m²)	28.2 ± 5.5	81
Body surface area (m²)	1.84 ± 0.24	81

Table 2 - Basal echocadiographic parameters in the study population.

Variable	n	Mean ± standard deviation
TAPSE (mm)	79	24.4 ± 3.2
RVB (mm)	80	35.5 ± 4.3
RVM (mm)	80	28.6 ± 4.5
RVL (mm)	78	59.2 ± 6.7
RVP (mm)	79	21.2 ± 2.5
RAA (cm²)	66	14.6 ± 3.3
RAV (ml)	66	40.9 ± 13.6
S'B. cm/s	75	13 ± 0.03
S'L. cm/s	76	11 ± 0.03
RV thickness. cm	75	0.38 ± 0.07
AAD/SC. cm²/m²	66	8.0 ± 1.4
VAD/SC. mL/m²	66	22.3 ± 6.1

TAPSE = tricuspid annular plane systolic excursion; RVD = right ventricular (RV) proximal diameter; RVB = basal LV diameter; RVM = mean RV diameter; RVL = RV longitudinal diameter; RAA = right atrial area; RAV = right atrial volume; S'B = lateral tricuspid annular tissue Doppler; S'L = RV free wall tissue Doppler; BSA = body surface area.

Table 3 - Correlation between echocardiographic parameters and age (years).

Variables	n	Correlation coefficient	p
Age x TAPSE (mm)	78	-0.06	0.584
Age x RVB (mm)	79	-0.08	0.465
Age x RVM (mm)	79	-0.10	0.375
Age x RVL (mm)	77	0.02	0.872
Age x RVP (mm)	78	0.25	0.028
Age x RAA (cm²)	66	-0.25	0.043
Age x RAV (ml)	66	-0.26	0.038
Age x S'B (cm/s)	75	0.13	0.250
Age x S'L (cm/s)	76	-0.07	0.538
Age x RV Thickness (cm)	74	0.17	0.151
Age x RAA/BSA (cm²/m²)	66	-0.13	0.299
Age x RAV/BSA (ml/m²)	66	-0.22	0.077

Pearson's correlation coefficients (TAPSE, RVB, RVM, RVL, RV, RAV, RAA/BSA and RAV/BSA) and Spearman's correlation coefficient (RAA, S'B, S'L and TV Thickness). TAPSE = tricuspid annular plane systolic excursion; RVD = right ventricular (RV) proximal diameter; RVB = basal LV diameter; RVM = mean RV diameter; RVL = RV longitudinal diameter; RAA = right atrial area; RAV = right atrial volume; S'B = lateral tricuspid annular tissue Doppler; S'L = RV free wall tissue Doppler; BSA = body surface area.

when indexed by body surface. The current recommendations for quantifying the cardiac chambers define higher values for men and lower values for women.[4] These differences become smaller after indexation by body surface, a finding observed in this study for right atrial volume and area. However, most values cited in the literature regarding RV diameters are not indexed for gender and BSA.[8] This also occurs regarding LV measurements. Considering that there was a significant predominance of females (70%) in the population studied here, these data become relevant and should be taken into consideration in the evaluation of the right chambers, including for the right atrium as, for the left atrium, the reference values are the same for men and women.[4]

There was also a positive and significant correlation between BMI and BSA with the dimensions of the right chambers. This finding is corroborated by Lang R et al.[4] and Grunig et al.,[7] who determine a standard deviation of normality between the genders in all parameters of diameter, area and volume.

Regarding the assessment of right ventricular function, no significant differences were found between the genders or variation with age. These data are consistent with the study by Lindqvist P et al.[9] In this study, involving 255 healthy individuals, a RV diastolic function disorder was found, but not a systolic function disorder with increasing age. A plausible explanation for this finding is the fact that the population studied was relatively healthy, with no significant pulmonary arterial hypertension and no other cardiac pathologies that could alter the results. There is much discussion in the literature about the accurate assessment of RV function, since due to the anatomical particularities of this chamber, there is no single criterion, but several methods for its evaluation. Although RV function is noninvasively assessed by magnetic resonance imaging (considered the gold standard for RV volume), angiography or computed tomography, TTE is the most widely used technique due to its availability, safety, versatility, reproducibility and ability to capture real-time imaging with temporal and spatial resolution.[10–13] Echocardiographic indices of right ventricular function include:

Table 4 - Comparison of echocardiographic parameters between males and females.

Variable	n	Mean ± Standard deviation	p*
TAPSE, mm			
Female	56	24.7 ± 3.1	
Male	23	23.8 ± 3.6	0.268
RVB (mm)			
Female	57	34.4 ± 3.5	
Male	23	38.2 ± 4.8	< 0.001
RVM (mm)			
Female	57	27.0 ± 3.3	
Male	23	32.4 ± 4.9	< 0.001
RVL (mm)			
Female	55	58.9 ± 6.3	
Male	23	60.0 ± 7.6	0.514
RV (mm)			
Female	56	20.6 ± 2.4	
Male	23	22.7 ± 2.2	0.001
RAA (cm²)			
Female	47	13.7 ± 2.7	
Male	19	16.6 ± 3.9	0.002
RAV (ml)			
Female	47	37.0 ± 10.6	
Male	19	50.7 ± 15.6	0.002
S'B, cm/s			
Female	55	0.13 ± 0.03	
Male	20	0.12 ± 0.04	0.332
S'L, cm/s			
Female	56	0.11 ± 0.04	
Male	20	0.11 ± 0.03	0.739
RV thickness (cm)			
Female	55	0.38 ± 0.08	
Male	20	0.39 ± 0.06	0.250
RAA/BSA (cm²/m²)			
Female	47	7.87 ± 1.34	
Male	19	8.36 ± 1.49	0.199
RAV/BSA (ml/m²)			
Female	47	21.1 ± 5.2	
Male	19	25.4 ± 7.0	0.008

**Student's t test for independent samples or Mann-Whitney's non-parametric test, p<0.05. TAPSE = tricuspid annular plane systolic excursion; RVD = right ventricular (RV) proximal diameter; RVB = basal LV diameter; RVM = mean RV diameter; RVL = RV longitudinal diameter; RAA = right atrial area; RAV = right atrial volume; S'B = lateral tricuspid annulus tissue Doppler; S'L = RV free wall tissue Doppler; BSA = body surface area.*

Table 5 - Correlation between echocardiographic parameters and body mass index (BMI) and body surface area (BSA).

Variables	n	Correlation coefficient	p
BMI x TAPSE (mm)	78	0.16	0.173
BMI x RVB (mm)	79	0.22	0.046
BMI x RVM (mm)	79	0.23	0.043
BMI x RVL (mm)	77	0.28	0.015
BMI x RVP (mm)	78	0.24	0.032
BMI x RAA (cm²)	66	0.40	0.001
BMI x RAV (ml)	66	0.34	0.006
BMI x S'B (cm/s)	73	0.02	0.871
BMI x S'L (cm/s)	74	0.13	0.263
BMI x RV Thickness (cm)	74	0.04	0.759
BMI x RAA/BSA (cm²/m²)	66	0.03	0.806
BMI x RAV/BSA (ml/m²)	66	0.12	0.351
BMI x TAPSE (mm)	78	0.10	0.400
BSA x RVB (mm)	79	0.43	<0.001
BSA x RVM (mm)	79	0.47	<0.001
BSA x RVL (mm)	77	0.32	0.005
BSA x RV (mm)	78	0.40	<0.001
BSA x RAA (cm²)	66	0.60	<0.001
BSA x RAV (ml)	66	0.61	<0.001
BSA x S'B (cm/s)	73	-0.04	0.736
BSA x S'L (cm/s)	74	0.29	0.011
BSA x RV thickness (cm)	74	0.08	0.521
BSA x RAA/BSA (cm²/m²)	66	0.08	0.518
BSA x RAV/BSA (ml/m²)	66	0.27	0.031

TAPSE = tricuspid annular plane systolic excursion; RVP = right ventricular (RV) proximal diameter; RVB = RV basal diameter; RVM = mean RV diameter; RVL = RV longitudinal diameter; RAA = right atrial area; RAV = right atrial volume; S'B = lateral tricuspid annulus tissue Doppler; S'L = RV free wall tissue Doppler.

fractional area change (FAC), TAPSE, tricuspid annular tissue systolic velocity (tissue S'), tricuspid annulus isovolumetric acceleration and RV performance index. This study includes only TAPSE and tricuspid annular tissue Doppler because they are more widely used and have less inter and intraobserver variability, as the FAC analysis is limited due to the difficulty of defining endomyocardial border, with great variability in the literature.[12] Although TAPSE expresses a measure of longitudinal function only, it has shown good correlation with RV global systolic function estimation techniques, such as radionuclide-derived RV ejection fraction (EF) and two-dimensional variation of RV fractional area (FAC).[1] Previous studies have shown a decrease in TAPSE and tissue S' values with increasing age, although with values still considered within the normal range,[10–13] which was not reproduced in the data presented here. This fact can be explained by the

higher proportion of female patients, as D'Oronzio U et al.[14] and Henein et al.[15] suggested higher absolute values of TAPSE and FAC in women.

Regarding RA volume and area, there are few studies published in the literature and most of them include magnetic resonance imaging (MRI), considered the gold standard for atrial evaluation. The same studies cite a large inter and intraobserver variability and variability according to the ethnicity of the study population.[16,17] The data found here suggest an inverse variation in RA volume and area with age and a positive variation with gender, BMI and BSA. This finding regarding age is inconsistent with previous MRI studies that found no correlation with age and shows the great difficulty in correctly evaluating this chamber.[18,19] However, this study and those cited above were based on an older population that mostly included people older than 50. Studies involving younger healthy individuals found lower atrial reference values compared to older individuals.[20–22]

Similarly, the evaluation of RV hypertrophy lacks more consistent studies involving a larger number of individuals.[23–29] Cuspidi C. et al., [23] in a meta-analysis including 13 studies, with a limited number of participants, showed a mean difference of up to 1.3 mm in RV thickness in hypertensives compared to non-hypertensives with $P<0.001$. In this study, 51 participants were hypertensive (63%) and no significant differences in RV thickness were found regarding the non-hypertensive group.

Given the above, it is necessary to list the main limitations found here: small number of participants; failure to calculate intra and interobserver variability mainly regarding atrial measurement; analysis of RV TAPSE and S' only, without including the FAC calculation to evaluate RV systolic function; the non-inclusion of a larger number of individuals younger than 50 years of age and the inclusion of a larger and significant number of women compared to the number of men.

Conclusions

In this study, echocardiographic parameters of the right chambers presented mean ventricular diameters and lower atrial area and volume in females compared to males. A positive correlation of these parameters with BMI and BSA was also found. However, right ventricular function, TAPSE and S' values were not influenced by gender, BMI and BSA.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Voelkel NF, Quaife RA, Leinwand LA, Barst RJ, McGoon MD, Meldrum DR, et al; National Heart, Lung, and Blood Institute Working Group on Cellular and Molecular Mechanisms of Right Heart Failure. Right Ventricular Function and Failure: Report of a National Heart, Lung, and Blood Institute Working Group on Cellular and Molecular Mechanisms of Right Heart Failure. Circulation. 2006;114(17):1883-91.
2. Polak JF, Holman BL, Wynne J, Colucci WS. Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. J Am Coll Cardiol. 1983;2(2):217-24.
3. Di Salvo TG, Mathier M, Semigran MJ, Dec GW. Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. J Am Coll Cardiol. 1995;25(5):1143-53.
4. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1-39 e14.
5. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K. Diretrizes para Avaliação Ecocardiográfica do Coração Direito em Adultos: um Informe da Sociedade Americana de Ecocardiografia. J Am Soc Echocardiogr. 2010;23:685-713.
6. DiLorenzo MP, Bahtt SM, Mercer-Rosa L. How best to assess right ventricular function by echocardiography. Cardiol Young. 2015;25(8):1473-81.
7. Grünig E, Biskupek J, D'Andrea A, Ehlken N, Egenlauf B, Weidenhammer J, et al. Reference ranges for and determinants of right ventricular area in healthy adults by two-dimensional echocardiography. Respiration. 2015;89(4):284-93.
8. Kossaif A. Echocardiographic assessment of the right ventricle, from the conventional approach to speckle tracking and three-dimensional imaging, and insights into the "right way" to explore the forgotten chamber. Clin Med Insights Cardiol. 2015;9:65-75.
9. Lindqvist P, Waldenström A, Henein M, Mörner S, Kazzam E. Regional and global right ventricular function in healthy individuals aged 20-90 years: a pulsed Doppler tissue imaging study: Umea General Population Heart Study. Echocardiography. 2005;22(4):305-14.
10. Hoit BD. Right ventricular strain comes of age. Circ Cardiovas Imaging 2018;11:e008382.
11. Innelli P, Esposito R, Olibet M, Nistri S, Galderisi M. The impact of ageing on right ventricular longitudinal function in healthy subjects: a pulsed tissue Doppler study. Eur J Echocardiogr. 2009;10(4):491-8.
12. Chia EM, Hsieh H, Boyd A, Pham P, Vidaic J, Leung D, et al. RV geometry and function. Effects of age and gender on right ventricular systolic and diastolic function using two-dimensional speckel-tracking strain. J Am Soc Echocardiogr. 2014;27(10):1079-86.
13. Kukulski T, Hübbert L, Arnold M, Wranne B, Hatle L, Sutherland GR. Normal regional right ventricular function and its change with age: a Doppler myocardial imging study. J Am Soc Echocardiogr. 2000;13(3):194-204.
14. D'Oronzio U, Senn O, Biaggi P, Gruner C, Jenni R, Tanner FC, et al. Right heart assessment by echocardiography: gender and body size matters. J Am Soc Echocardiogr. 2012;25(12):1251-8.
15. Henein M, Waldenström A, Mörner S, Lindqvist P. The normal impact of age and gender on right heart structure and function. Echocardiography. 2014;31(1):5-11.
16. Li W, Wan K, Han Y, Liu H, Cheng W, Sun J, et al. Reference value of left and right atrial size and phasic function by SSFP CMR at 3.0T in healthy Chinese adults. Sci Rep. 2017;7(1):3196.
17. Karki DB, Pant S, Yadava SK, Vaidya A, Neupane DK, Joshi S. Measurement of right atrial volume and diameters in healthy Nepalese with normal echocardiogram. Kathmandu Univ Med J. 2014;46(46):110-12.
18. Maceira AM, Cosín-Sales J, Roughton M, Prasad SK, Pennell DJ. Reference right atrial dimensions and volume estimation by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Res. 2013;15:29.

19. Maceira AM, Cosín-Sales J, Roughton M, Prasad SK Pennell DJ. Reference left atrial dimensions and volume estimation by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Res. 2010;12:65.

20. Grünig E, Henn P, D'Andrea A, Claussen M, Ehlken N, Maier F, et al. Reference values for and determinants of right atrial area in healthy adults by 2-dimensional echocardiography. Circ Cardiovasc Imaging. 2013;6(1):117-24.

21. Le Ven F, Bibeau K, De Larochelliére E, Tizón-Marcos H, Deneault-Bissonnette S, et al. Cardiac morphology and function reference values derived from a large subset of healthy young Caucasian adults by magnetic resonance imaging. Eur Heart J Cardiovasc Imaging. 2016;17(9):981-90.

22. Henein M, Waldenström A, Mörner S, Lindqvist P. The normal impact of age and gender on right heart structure and function. Echocardiography. 2014;31(1):5-11.

23. Cuspidi C, Sala C, Muiesan ML, De Luca N. Right ventricular hypertrophy in systemic hypertension: an updated review of clinical studies. J Hypertens. 2013;31(5):858-65.

24. Matsukubo H, Matsuura T, Endo N, Asayama J, Watanabe T. Echocardiographic measurement of right ventricular wall thickness. A new application of subxiphoid echocardiography. Circulation. 1977;56(2):278-84.

25. Prakash R, Matsukubo H. Usefulness of echocardiographic right ventricular measurements in estimating right ventricular hypertrophy and right ventricular systolic pressure. Am J Cardiol. 1983;51(6):1036-40.

26. Gottdiener JS, Gay JA, Maron BJ, Fletcher RD. Increased right ventricular wall thickness in left ventricular pressure overload: echocardiographic determination of hypertrophic response of the ''nonstressed'' ventricle. J Am Coll Cardiol. 1985;6(3):550-5.

27. Nunes BD, Messerli FH, Amodeo C, Garavaglia GE, Scmieder RE, Frolich ED. Biventricular cardiac hypertrophy in essential hypertension. Am Heart J. 1987;114:813-8.

28. Cohn JN, Limas CJ, Guiha MD. Hypertension and the heart. Arch Intern Med. 1974;133(6):969-79.

29. Louie EK, Lin SS, Reynertson SI, Brundage BH, Levitsky S, Rich S. Pressure and volume loading of the right ventricle have opposite effects on left ventricular ejection fraction. Circulation. 1995;92(4):819-24.

Longitudinal Strain and Cardiac Amyloidosis: Case Reports

Strain Longitudinal Bidimensional e Amiloidose Cardíaca: Série de Casos

Ana Luiza Alves Nicoletti[1], Amanda Cristina de Souza[1], Valter Kuymjian[1], Jaqueline Kuymjian[2,3], Daniel F. Palmieri[2], Fabio F. Giuseppin[2], Danilo G. Fernandes[2], Simone N. Santos[2,3]

Faculdade de Medicina da Universidade[1]; Setor de Ecocardiografia, Hospital Brasília[2]; Eccos Diagnóstico Cardiovascular Avançado[3], Brasília, DF – Brazil.

Abstract

Introduction: Cardiac involvement in patients with systemic amyloidosis indicates a worse prognosis. Moreover, the diagnosis is delayed, since the signs and symptoms of this disease are nonspecific. Global longitudinal strain has been shown to be an important predictor of cardiac events. We report four cases of patients with cardiac amyloidosis submitted to ECHO Strain and magnetic resonance for comparison and diagnostic confirmation.

Case reports: The medical records of four patients with cardiac amyloidosis admitted in 2017 at a tertiary hospital were evaluated. The preservation of the apical segments of the ventricle was the pattern found in all global longitudinal strain. Magnetic resonance image showed predominantly subendocardial, diffuse and circumferential mesocardial late enhancement in all patients reported.

Discussion: On the spectrum of clinical manifestations of cardiac amyloidosis, heart failure was the most prevalent among the patients reported. Magnetic resonance image showed patterns of myocardial thickening and late subendocardial enhancement. In global longitudinal strain, we observed the preservation of the deformity in the apical segments, associated with a significant reduction of the deformity in the basal and middle segments of the left ventricle. The global longitudinal strain also allows differential diagnosis with hypertrophic cardiomyopathy and its findings were consistent with those of the magnetic resonance image, which reinforces its value in the early detection of the condition.

Keywords: Echocardiography; Amyloidosis; Magnetic Resonance Imaging; Hypertrophic Cardiomyopathy.

Resumo

Introdução: *O acometimento cardíaco em pacientes com amiloidose sistêmica indica pior prognóstico. Além disso, o diagnóstico é tardio, pois seus sinais e sintomas são inespecíficos. O strain longitudinal bidimensional tem se mostrado importante preditor de eventos cardíacos. Relatamos quatro casos de pacientes com amiloidose cardíaca submetidos ao strain longitudinal bidimensional e à ressonância magnética cardíaca, para comparação e confirmação diagnóstica.*

Relatos dos casos: *Foram avaliados os prontuários de quatro pacientes com amiloidose cardíaca admitidos em 2017 em um hospital terciário. A preservação da deformidade miocárdica nos segmentos apicais (apical sparing) do ventrículo esquerdo no strain longitudinal bidimensional foi encontrada em todos os pacientes estudados. A ressonância magnética cardíaca evidenciou realce tardio predominantemente subendocárdico, mesocárdico difuso e circunferencial em todos pacientes relatados.*

Discussão: *Diante do espectro de manifestações clínicas da amiloidose cardíaca, a insuficiência cardíaca foi a mais prevalente dentre os pacientes relatados. A ressonância magnética cardíaca mostra padrões de espessamento miocárdico e realce tardio subendocárdico. Ao strain longitudinal bidimensional, é possível observar a preservação da deformidade nos segmentos apicais, associada à redução significativa da deformidade nos segmentos basais e médios do ventrículo esquerdo. O exame também possibilita o diagnóstico diferencial com a miocardiopatia hipertrófica. Os achados ao strain longitudinal bidimensional foram condizentes com os da ressonância magnética cardíaca, o que reforça seu valor na detecção precoce da condição.*

Descritores: *Ecocardiografia; Amiloidose; Ressonância Magnética Nuclear; Cardiomiopatia Hipertrófica.*

Mailing Address: Ana Luiza Alves Nicoletti •
SEPN 707/907, Campus Universitário, Asa Norte. CEP: 70790-075, Brasília, DF, Brazil.
E-mail: ana.a.nicoletti@gmail.com
Manuscript received 25/2/2019; revised: 11/3/2019; accepted 3/10/2019

DOI: 10.5935/2318-8219.20200009

Short Communication

Introduction

Amyloidosis is a disease characterized by extracellular deposition of amyloid substance, a process that can cause structural and functional disorders in the affected tissue. At the molecular level, deposits arise from inadequate protein folding processes, generating toxic, insoluble aggregates with the capacity to settle in tissue B protein chains.[1]

Patients with amyloidosis and cardiac involvement have a worse prognosis, and their diagnosis is delayed due to nonspecific signs and symptoms of the disease.[1] Although the gold standard is endomyocardial biopsy, this new technique — two-dimensional longitudinal Strain (Strain 2D) — is another helpful early detection tool and is also considered a strong prognostic marker.[2]

We report four cases of patients with cardiac amyloidosis who underwent strain 2D echocardiography and Cardiac Magnetic Resonance Imaging (CMRI) for comparison and diagnostic confirmation.

Case report

We reviewed the medical records of four patients with cardiac amyloidosis admitted to a tertiary hospital in the city of Brasilia, in 2017, with diagnostic suspicion by strain 2D and characteristic pattern by CMRI.

Case 1 involves an 84-year-old female patient, with mild controlled hypertension, clinical presentation of heart failure (HF), who had clinical improvement after treatment, maintaining dyspnea on exertion. On echocardiogram (ECHO) (Figure 1): EF = 64%, with LV mass index = 150 g/m², septum = 18 mm; PW = 22 mm, E/e' ratio = 26, LAV index = 54 ml/m², Strain 2D = -8.8%, less reduced in the LV apical portions (Figure 2a). Cardiac catheterization showed no significant aortic valve injury. CMRI showed predominantly subendocardial and diffuse mesocardial circumferential late enhancement without respecting vascular territories.

Case 2 involves a 79-year-old female patient with HF despite optimal treatment and borderline renal failure. On ECHO: Severe functional mitral regurgitation due to annular dilation — Carpentier type IIIb (Figure 3), EF = 48%, LV mass index = 140 mg/m², septum = 15 mm, PW = 13 mm, E/e' = 18.5, LAV index = 78 ml/m², Strain 2D = -14.4%, preserved in the apical portions of the LV (Figure 2b). CMRI revealed abnormal findings similar to case 1, besides late atrial enhancement (Figure 4).

Case 3 involves a 60-year-old female patient with multiple myeloma and HF. On ECHO: EF = 63%, LV mass index = 123 mg/m², GLS = -6.5% (Figure 2c), preserved in the apical portions of the LV. CMRI revealed abnormal findings that are similar to previous cases.

Case 4 involves a 70-year-old male patient with HF and prostate cancer with previous surgeries. On ECHO: EF = 27%, LV mass index = 135 mg/m², septum = 15 mm, PP = 14 mm, E/e' = 23.7, LAV index = 47 ml/m², Strain 2D = -12.4% (Figure 2d), preserved in the apical portions of the LV. CMRI revealed abnormal findings that are similar to previous cases.

Table 1 shows the electrocardiographic findings. Reported patients were not submitted to endomyocardial biopsy until data collection.

Discussion

Amyloid infiltration in the cardiac form is usually due to light chain (AL) immunoglobulin deposits. The second form of amyloidosis with the highest prevalence of cardiac involvement is associated with transthyretin mutations (ATTR).[3] The differentiation between the two types may be suggested by some findings, such as wall thickness greater than 18 mm and septal involvement, both more frequent in the ATTR form.[4]

Clinical manifestations of amyloidosis begin nonspecifically; however, as the disease progresses and the degree of infiltration of amyloid deposits increases, the condition becomes more characteristic.[1] HF was the main clinical manifestation in all reported patients, in whom the signs of increased ventricular filling pressures were detected on echocardiography by high E/e' ratio in all patients. Myocardial infiltration in cardiac

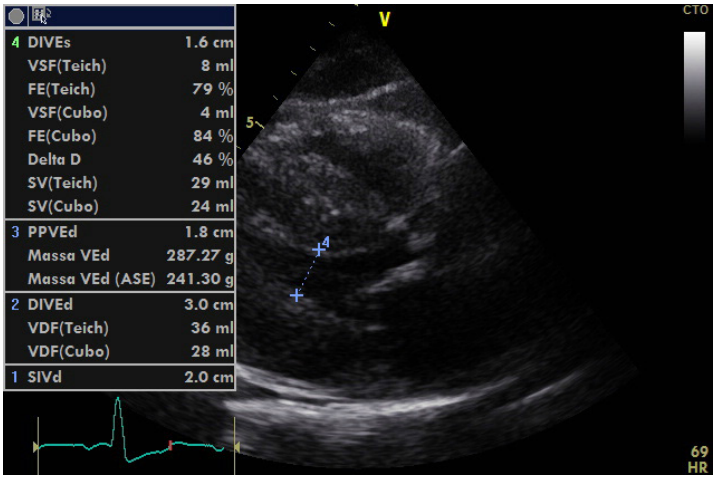


Figure 1 – *Parasternal longitudinal section on two-dimensional echocardiogram revealing significant increase in myocardial thickness in Case 1 patient.*

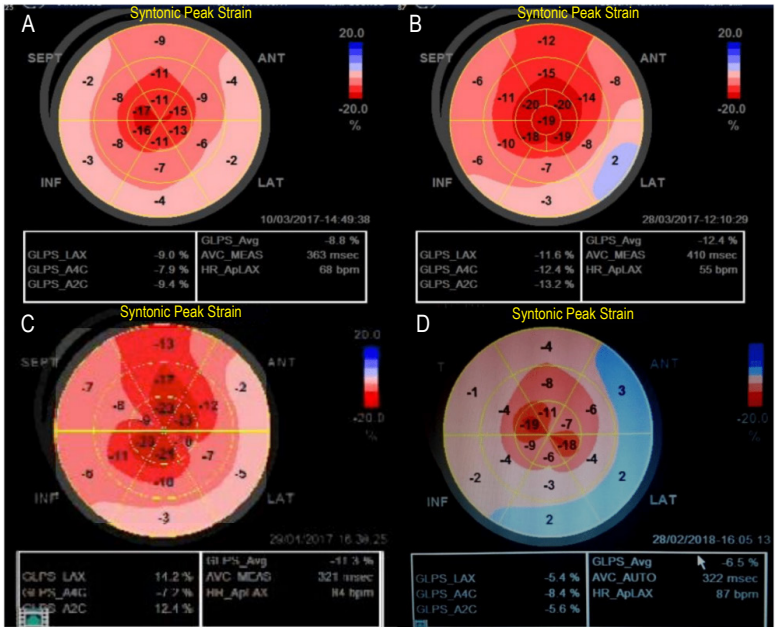


Figure 2 – *Bull's eye plot of two-dimensional longitudinal strain in cases 1 to 4 (fig 1A to 1D, respectively). Note that, in all cases, the longitudinal strain is more preserved in the apical region, unlike the middle and basal left ventricular segments.*

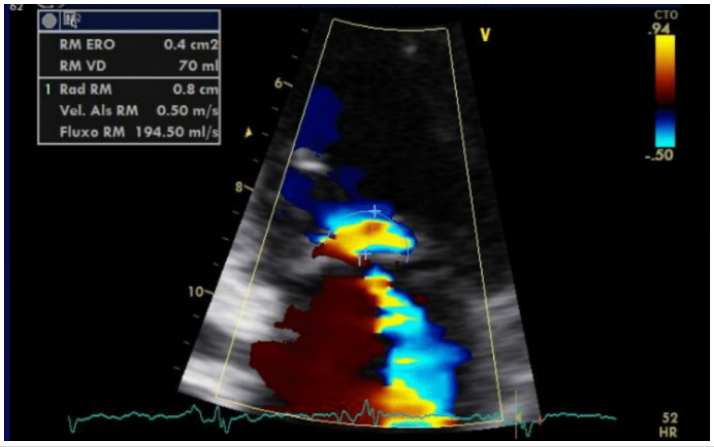


Figure 3 – *Calculation by the PISA (proximal isovelocity surface area) method demonstrating the quantification of the degree of mitral regurgitation in case 2 patient.*

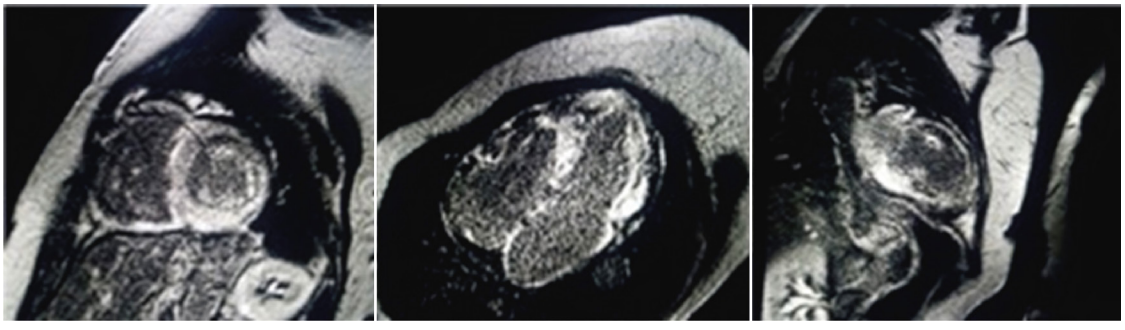


Figure 4 – *Cardiac magnetic resonance imaging showing mesocardial enhancement in the left ventricle, right atrium and left atrium, typical of amyloid infiltration.*

Table 1 - Ultrasound findings of reported cases.

Patient	LA (mm)	LAV index (ml/m²)	LVEDD (mm)	S (mm)	PW (mm)	EF (%)	LV mass (g/m²)	GLS (%)	E/e'
1	45	54	36	18	22	64	150	-8.8%	26
2	46	78	41	15	13	48	140	-14.4	18.5
3	33	48	43	19	18	63	123	-6.5	20
4	84	47	45	15	14	27	135	-12.4	23.7

LA: left atrium; LVA: left atrial volume; LVEDD: left ventricular end diastolic diameter; PW: posterior wall; EF: ejection fraction; GLS: global longitudinal strain.

amyloidosis may cause HF with preserved EF or reduced EF in later stages.

The diagnosis of cardiac amyloidosis is usually made late, mainly due to nonspecific signs and symptoms. New diagnostic techniques are proving useful in early detection.[5] They include strain 2D echocardiography, which is based on the average of the values resulting from evaluation of longitudinal myocardial fiber shortening during systole at different ventricular sites,[6] providing information that is useful in diagnosis and prognosis.[2]

Hypertrophic cardiomyopathy is an important differential diagnosis to be considered in patients with suspected cardiac amyloidosis because it has similar morphological structures. Clinically, amyloidosis is a systemic disease and may present pleural effusion, which is commonly observed in hypertrophic cardiomyopathy in later stages of the disease.[7] Strain 2D helps distinguish amyloidosis from pathologies that include left ventricular hypertrophy;[6] however, specificity is 82%.[8] In cases of cardiac amyloidosis, the most observed pattern includes apical sparing, associated with significantly reduced strain in the basal and middle ventricular segments, as evidenced in all reported cases. In hypertrophic cardiomyopathy, on the other hand, a significant reduction in strain in the hypertrophic regions is observed, with no pattern of apical sparing.[9] Patients with hypertrophic cardiomyopathy typically demonstrate a pattern of fall in longitudinal strain from the ventricular apex to the base, although this tendency may be reversed in apical hypertrophy patterns and may lead to confusion with the apical sparing most commonly observed in amyloidosis.[10]

CMRI is an alternative to the diagnosis of cardiac amyloidosis, with good sensitivity (87%) and specificity (96%) for the form associated with ATTR. CMRI identifies myocardial thickening, and interatrial septal thickening may also occur,[5] as observed in the patient of case 2. Subendocardial late enhancement pattern in the left ventricle was observed in all reported cases. These findings are consistent with the results found in strain 2D, which underscores their value in the early detection of the condition and in the differentiation with pathologies that include similar clinical conditions and myocardial hypertrophy features.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Di Bella G, Pizzino F, Minutoli F, Zito C, Donato R, Dattilo G, et al. The mosaic of the cardiac amyloidosis diagnosis: role of imaging in subtypes and stages of the disease. Eur Heart J Cardiovasc Imaging. 2014;15(12):1307-15.
2. Senapati A, Sperry BW, Grodin JL, Kusunose K, Thavendiranathan P, Jaber W, et al. Prognostic implication of relative regional strain ratio in cardiac amyloidosis. Heart. 2016;102(10):748-54.
3. Mesquita ET, Jorge AJL, Souza Junior CV, Andrade TRd. Cardiac Amyloidosis and its New Clinical Phenotype: Heart Failure with Preserved Ejection Fraction. Arq Bras Cardiol. 2017;109:71-80.
4. Falk RH, Alexander KM, Liao R, Dorbala S. AL (Light-Chain) Cardiac Amyloidosis: A Review of Diagnosis and Therapy. J Am Coll Cardiol. 2016;68(12):1323-41.
5. Lee SP, Park JB, Kim HK, Kim YJ, Grogan M, Sohn DW.Contemporary Imaging Diagnosis of Cardiac Amyloidosis. J Cardiovasc Imaging. 2019;27(1):1-10.6. Abduch MCD, Alencar AM, Mathias Jr W, Vieira MLdC. Estudo da Mecânica Cardíaca pelo Speckle Tracking. Arq Bras Cardiol. 2014;102:403-12
7. Milani P, Basset M, Russo F, Foli A, Palladini G, Merlini G. The lung in amyloidosis. Eur Respir Rev. 2017;26(145):pii:170046.
8. Phelan D, Collier P, Thavendiranathan P, Popovic ZB, Hanna M, Plana JC, et al. Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. Heart. 2012;98(19):1442-8.
9. Liu D, Hu K, Nordbeck P, Ertl G, Störk S, Weidemann F. Longitudinal strain bull's eye plot patterns in patients with cardiomyopathy and concentric left ventricular hypertrophy. Eur J Med Res. 2016;21:21.
10. Haland TF, Almaas VM, Hasselberg NE, Saberniak J, Leren IS, Hopp E, et al. Strain echocardiography is related to fibrosis and ventricular arrhythmias in hypertrophic cardiomyopathy. Eur Heart J Cardiovasc Imaging. 2016;17(6):613-21.

A Three-Leaflets Mitral Valve Associated to Three Papillary Muscles in a Patient with Hypertrophic Cardiomyopathy

Válvula Mitral com Três Folhetos Associada a Três Músculos Papilares em Paciente Portador de Cardiomiopatia Hipertrófica

Antonio Tito Paladino[1,2], Luiz Antônio Vasconcelos[1], Leonardo Mello Guimarães de Toledo[1], Natalia Massoni[1], Mariana Oliveira Rezende[1], Natasha Soares Simões dos Santos[1], David Costa de Souza Le Bihan[1], Rodrigo Bellio de Mattos Barretto[1], Jorge Eduardo Assef[1]

[1]Departamento de Ecocardiografia, Instituto Dante Pazzanese de Cardiologia, São Paulo, SP, Brazil. [2]Departamento de Emergência Cardiovascular, Instituto Dante Pazzanese de Cardiologia, São Paulo, SP, Brazil.

Abstract

Mitral valve malformations are considered rare even in their association with other anomalies, except for mitral valve prolapse, which is found in approximately 10% of the population. Mitral valve abnormalities may affect any portion of the valve or subvalvular apparatus (annulus, cusp, tendinous cords or papillary muscles).[1,2] Mitral valve anatomy and function can be assessed by echocardiography, resonance or cardiac tomography, and is essential for potential therapeutic programming.[2]

Introduction

Malformations of the mitral valve are rare, even considering the association with other anomalies, exception made to mitral valve prolapse, that can be observed in almost 10% of the population.[1] Any part of the valvular or subvalvular apparatus can be affected (annulus, leaflets, tendinous cords and papillary muscles), causing stenosis or insufficiency.

Echocardiography, cardiac resonance and cardiac tomography can evaluate mitral anatomy and function precisely, being a cornerstone to diagnosis and treatment of such anomalies.[3]

Case Report

A 57-year-old woman with hypertrophic cardiomyopathy was referred for routine evaluation in our echo lab. Her transthoracic echocardiogram revealed asymmetric ventricular hypertrophy, with septal predominance and peak rest gradient in outflow tract of 152 mmHg. Interestingly, the mitral valve had an unexpected appearance of a Shamrock, with three leaflets and their corresponding papillary muscles (figure 1).

Keywords

Heart Defects, Congenital; Echocardiography; Magnetic Resonance Imaging; Tomography.

Mailing Address: Antonio Tito Paladino •
Instituto Dante Pazzanese de Cardiologia, Avenida Dr. Dante Pazzanese, 500, Vila Mariana. CEP 04012-909, São Paulo, SP, Brazil
E-mail: atpf40@gmail.com
Manuscript received 25/2/2019; revised 11/3/2019; accepted 3/10/2019

DOI: 10.5935/2318-8219.20200010

Doppler evaluation revealed moderate regurgitation without significant stenosis. There was also a systolic anterior movement of valve apparatus. Biventricular function was preserved and no other cardiac structural malformations were found. Mild pericardial effusion was seen, without any hemodynamic compromise.

For a better diagnostic evaluation, cardiac magnetic resonance imaging was performed. In cine images (2, 3, 4 chambers), three papillary muscles were well individualized, with tendinous cords attached to them. Two muscles were located in their usual position (mid part of inferolateral and anterolateral walls). Additionally, an accessory papillary muscle could be seen emerging from the basal segment of the inferolateral wall, which had been observed in two-dimensional transthoracic echocardiogram (Figure 2).

Three-dimensional transesophageal echocardiography confirmed the three papillary muscles, attached to three functional leaflets through tendinous cords.

Discussion

Tricuspid mitral valve has been described, associated or not with hypertrophic cardiomyopathy. Supernumerary papillary muscles and leaflets are conceivable, since both have the same embryology origin.[4,5]

In previous studies, three-leaflet mitral valves have been associated with left ventricle outflow obstruction, associated or not with hypertrophic cardiomyopathy.[3] This association, also described by other authors, is noteworthy and could suggest a relationship between the genetic disorders observed in hypertrophic cardiomyopathy and the embryology of papillary muscles and mitral leaflets.[3,6]

In this case, we need to emphasize that 3D transesophageal echocardiography was the imaging technique that allowed a better view of the mitral valve, with its “three-leaflet” morphology.

Authors’ contributions:

Research creation and design: Paladino Filho AT. Data acquisition: Paladino Filho AT, Rezende M, Soares N, Massoni N. Data analysis and interpretation:

Vasconcelos LA, Toledo L. Manuscript writing: LeBihan

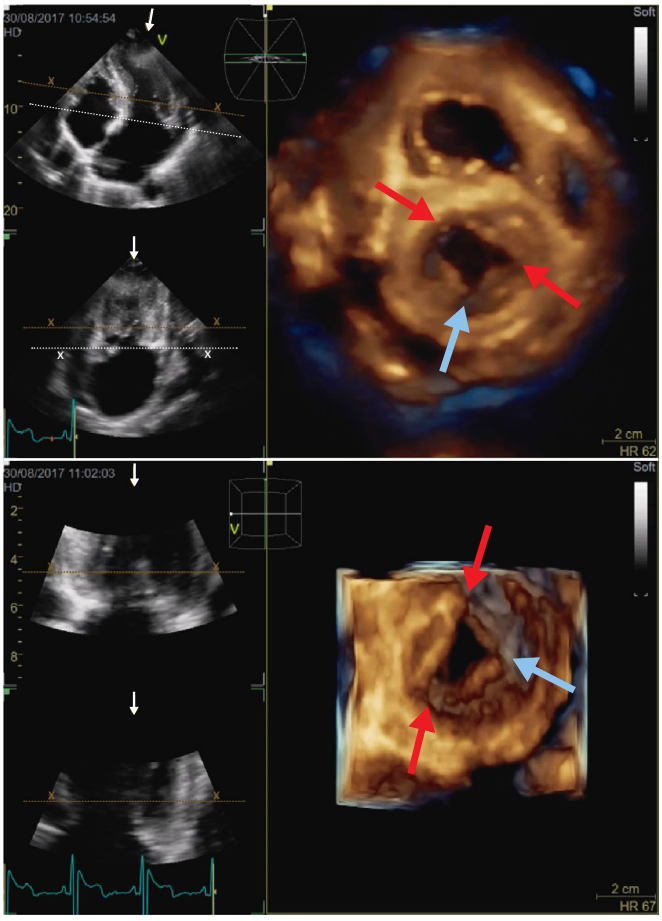


Figure 1 – *Red arrows: Anterolateral and posteromedial commissure. Blue arrow: "Extra commissure" dividing the posterior leaflet.*

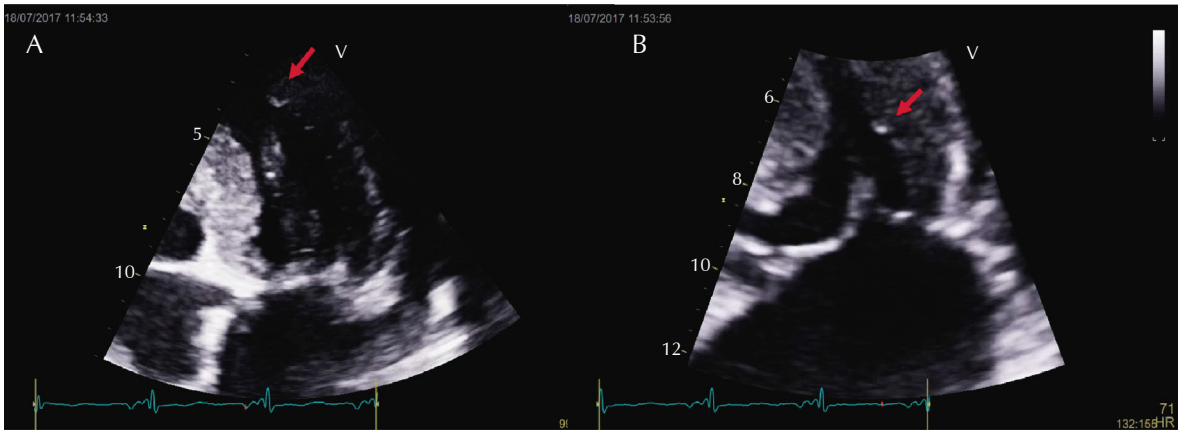


Figure 2 – *A) Apical implant of antero-lateral papillary muscle. B) Extra papillary muscle (basal position).*

DCS, Bellio R, Paladino AT. Critical revision of the manuscript for important intellectual content: Assef JE. Bibliographic research: Paladino AT, Massoni N.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Rosanio S, Simonsen CJ, Starwalt J, Keylani AM, Vitarelli A. Trileaflet Mitral Valve with Three Papillary Muscles Associated with Hypertrophic Cardiomyopathy: A Novel Case. Echocardiography. 2015;32(9):1435-7.
2. Kaple RK, Murphy RT, DiPaola LM, Houghtaling PL, Lever HM, Lytle BW, et al. Mitral valve abnormalities in hypertrophic cardiomyopathy: echocardiographic features and surgical outcomes. Ann Thorac Surg. 2008;85(5):1527-35, 1535.e1-2.
4. Klues HG, Maron BJ, Dollar AL, Roberts WC. sity of structural mitral valve alterations in hypertrophic cardiomyopathy. Circulation. 1992;85(5):1651-60.
5. Dal-Bianco JP, Levine RA. Anatomy of the mitral valve apparatus: role of 2D and 3D echocardiography. Cardiol Clin. 2013;31(2):151-64.
6. Chachoua A, Abboub B, Ghemri S, Hammoudi N. Trileaflet mitral valve associated with a bicuspid aortic valve. J Cardiol Cases. 2015;13(2):37-39.
3. Irwin RB, Macnab A, Schmitt M.Tri-itral valve in combination with hypertrophic cardiomyopathy. Eur Heart J. 2011 ;32(5):534..

Inferolateral post-myocardial infarction pseudoaneurysm. A rare case report

Pseudoaneurisma pós-infarto inferolateral. Um raro relato de caso

Gabriel De Castro Vaz Leal[1], Renato de de Aguiar Hortegal[1], Antonio Tito Paladino Filho[1], Diandro Marinho Mota[1], Rodrigo Barreto de Bellio Mattos[2], Louis Nakayama Ohe[1]

[1]Setor de Pronto-Socorro do Instituto Dante Pazzanese de Cardiologia, São Paulo, SP, Brazil. [2]Setor de Ecocardiografia do Instituto Dante Pazzanese de Cardiologia, São Paulo, SP, Brazil.

Abstract

We report the case of a 76-year-old male patient with a history of ST-segment elevation myocardial infarction (STEMI) for 3 years. He was admitted to the Emergency Room with a new chest pain episode that began 40 days before and was diagnosed with left ventricular (LV) pseudoaneurysm through 3D transthoracic echocardiography and cardiac magnetic resonance imaging scans. The patient underwent angiography of the coronary arteries, identifying lesions with a multiarterial pattern. Surgical treatment and LV aneurysmectomy were performed with good clinical evolution.

Introduction

The heart presents, by anatomical divisions, the endocardium, myocardium and pericardium (visceral and parietal). Rupture of endocardial and myocardial layers, mainly secondary to ischemic heart disease (55% of the cases),[1] with containment of rupture by the presence of pericardial adherences, gives rise to what we call pseudoaneurysm.[2]

Left ventricular (LV) pseudoaneurysm is a very rare complication with unclear prognosis and is associated with high mortality rates.[3] Therefore, rapid recognition of the condition with proper establishment of the therapy is related to better survival.[1,4]

Case Report

A 76-year-old male patient, hypertensive, diabetic and former smoker, admitted to our emergency room complaining of chest tightness for 40 days.

In August 2016, patient was diagnosed with ST-segment elevation myocardial infarction (STEMI) of the inferolateral wall and did not undergo primary angioplasty or fibrinolytic therapy at the time. Patient was discharged from the hospital, with outpatient cardiac follow-up, remaining asymptomatic throughout the following period. About 40 days prior, there was recurrence of chest pain tightening associated with exertion, with improvement at rest, of lower intensity compared to the AMI pain. The patient was then submitted to echocardiography and outpatient cardiac magnetic resonance imaging that suggested diagnosis of pseudoaneurysm in the LV inferolateral wall. Patient was using Losartan 100 mg/day; Furosemide 20 mg/day; Metoprolol 100 mg/day; AAS 100 mg/day; Simvastatin 40 mg/day; Metformin 850 mg 3 times/day; Glibenclamide 20 mg/day.

Physical examination showed hypertension, blood pressure (BP) 198 x 104 mmHg, heart rate (HR) 60 bpm and normal respiratory parameters — respiratory rate 20 irpm and saturation 97%. Regarding cardiac and pulmonary workup, there were no abnormal findings on auscultation — absence of adventitious noises or cardiac murmurs, and normophonetic heart sounds were observed, with two-stroke regular rhythm. Other aspects were normal on physical examination.

No significant abnormal findings were observed on admission laboratory tests (blood count, electrolytes, renal profile and myocardial necrosis markers).

Admission ECG showed sinus rhythm, inactive zone and abnormal repolarization in the inferolateral wall (Figure 1).

Vectorcardiogram reveals, in the frontal plane, the first vector directed to the top, with clockwise rotation of the vectorcardiographic loop. Such aspect is compatible with lower inactive zone. Moreover, there is a distortion of the path of end of ventricular activation (folding phenomenon), a finding that is usually related to marked distortion of the myocyte architecture in the basal segments. In the horizontal plane, activation forces are shifted to the left and back with T loop outside the QRS loop. The T loop has a discordant secondary T-type T-wave appearance. The QRS-T spatial angle is increased.

In summary, the vectorcardiographic aspect is compatible with lower inactive zone and suggestive of inferolateral basal fibrosis (Figure 2).

3D transthoracic echocardiography revealed moderate left atrial enlargement (indexed volume: 45 mL/m^2); septum: 10 mm; posterior wall: 5 mm; aortic root: 33 mm. LV ejection fraction (LVEF) = 48% (by the Simpson's method, excluding the pseudoaneurysm area). Akinesia of middle and basal segments of the inferior wall, hypokinesia of the distal segment of inferior and inferoseptal walls. Myocardial contractility preserved in the other LV segments. Pseudoaneurysm image

Keywords

Aneurysm,False; Diagnosis; Aneurysm, False/diagnostic imaging.

Mailing Address: Gabriel De Castro Vaz Leal •
Av. Dr. Dante Pazzanese, 500, Vila Mariana, CEP: 04012-909, São Paulo, SP, Brazil
E-mail: gabrielcsa@hotmail.com
Manuscript received 19/8/2019; revised 29/8/2019; accepted 31/10/2019

DOI: 10.5935/2318-8219.20200011

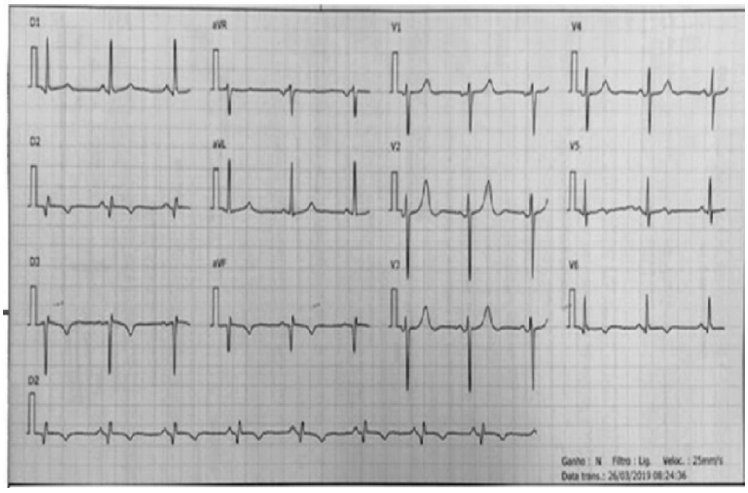


Figure 1 – *Electrocardiogram.*

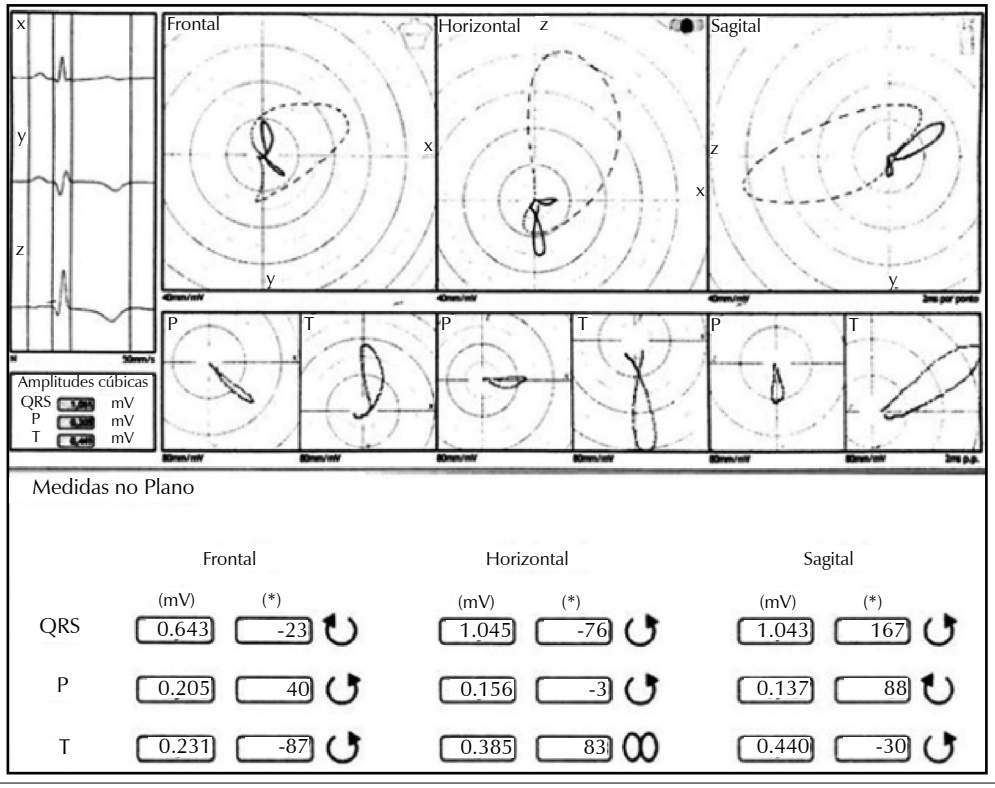


Figure 2 – *Vectorcardiogram.*

related to the inferolateral wall, below the mitral valve plane, measuring 25 mm in its neck and 45 mm in its longest length, with inner flow on Doppler and echogenic image located at its edges, suggesting thrombus. Heart valves with no significant morphofunctional abnormalities. No pericardial effusion. Three-dimensional echocardiogram enabled a better view of the pseudoaneurysm, providing high-definition images, making it easier to plan the surgical procedure and promoting greater patient safety. (Figure 3)

Cardiac magnetic resonance imaging, the most precise and accurate method, was performed because the patient remained stable and showed us very useful high-definition

images, which helped us plan the surgery procedure. CMRI revealed LV with increased dimensions and overall thickness (diastolic and systolic diameters of 80 mm and 72 mm, respectively); other cardiac cavities with preserved dimensions and overall thickness. LVEF 45%, moderate LV systolic dysfunction at the expense of large inferior and inferolateral pseudoaneurysm, with 37-mm neck, sitting 12mm away from the posterior mitral plane with thrombus lining and filling the inferior posterior portion of the pseudoaneurysm. Discreet (laminar) pericardial effusion. Presence of late coronary and transmural pattern enhancement areas (>50% of the segment area) in the inferior and inferolateral segments, suggesting myocardial fibrosis and without viability, consistent with the aneurysmal segments, compatible with previous AMI. Viability preserved in the other segments (Figures 4 and 5)

Cardiac catheterization revealed right dominance, multiarterial pattern with segmental lesion of up to 60% in the middle third of the right coronary artery, followed by occlusion in the distal middle third with recanalization aspect and 80% lesion in the distal third; anterior descending artery with 50% ostial lesion and 2nd marginal branch of moderate importance with 70% ostial lesion.

The patient underwent surgical repair of the ruptured LV portion, with double pericardial patch, without geometric LV reconstruction. Coronary arteries were not approached (unfavorable distal beds). Extubation and weaning of vasopressor drugs was performed on the 1st postoperative day (POD) with favorable hemodynamic evolution. Discharge from the intensive care unit on the 2nd POD, with hospital discharge on the 5th POD for outpatient follow-up.

Discussion

The most common pseudoaneurysm sites, evaluated by a series of case reports, are the posterolateral and inferior wall after acute myocardial infarction, which is compatible with inferior infarction (twice more common in pseudoaneurysm formation than previous infarction).[3,5] This condition is also described in the postoperative period of cardiac surgery, trauma and infections.[6]

The clinical picture presented by patients with this complication is variable. Chest pain and dyspnea are the most common conditions. Sudden death is less common (3% of the cases) and about 12% are asymptomatic. On physical examination, 2/3 of the patients present murmur, usually indistinguishable from the murmur of mitral regurgitation.[3,5]

About 95% of the cases present abnormal electrocardiographic findings, mostly non-specific. Only 20% have ST-segment elevation. [3]

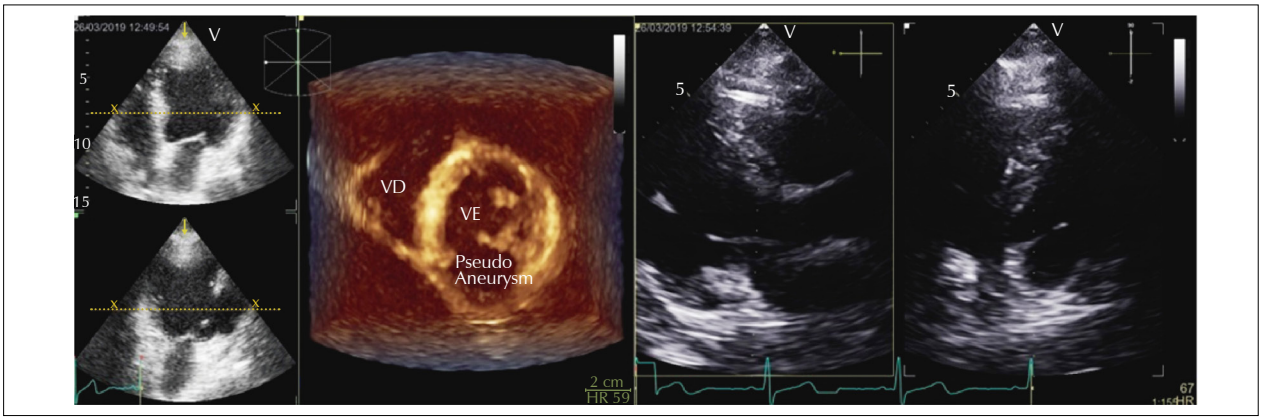


Figure 3 – *Transthoracic echocardiogram.*

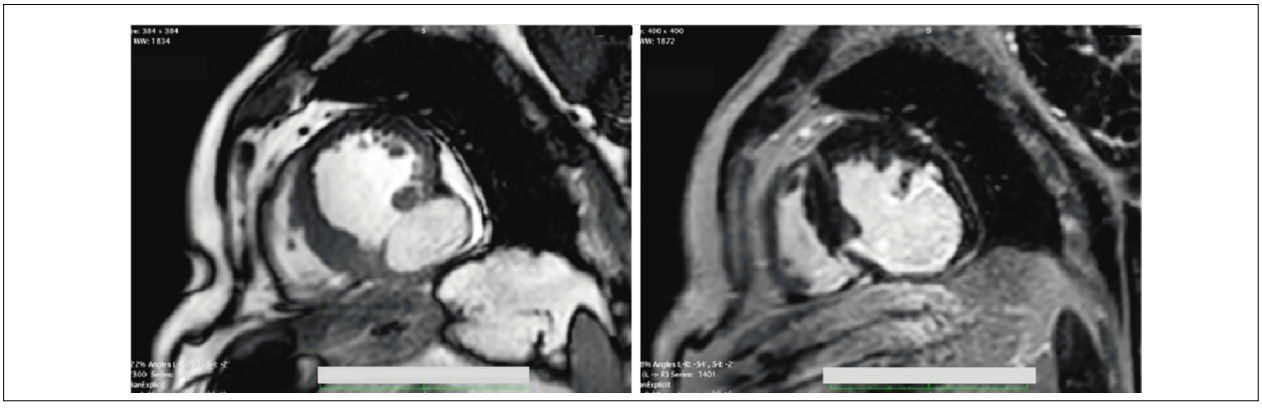


Figure 4 – *Cardiac magnetic resonance imaging – Short axis.*

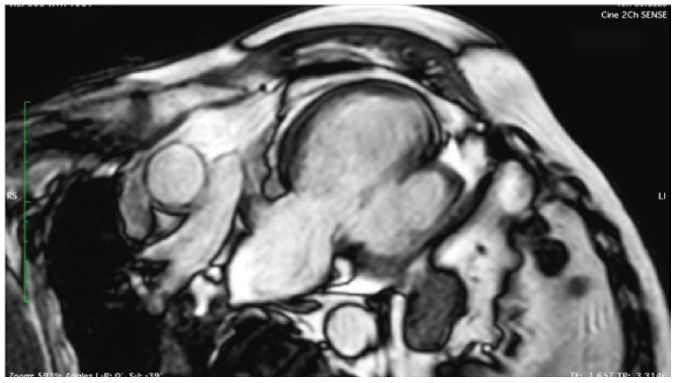


Figure 5 – *2-chamber cardiac magnetic resonance imaging.*

Noninvasive methods, such as echocardiography (especially transesophageal study, which presents greater accuracy) and magnetic resonance imaging are useful in the diagnosis of this complication and should be encouraged.[4,7–9] Angiography, however, is still the most reliable test for diagnosis.[2]

Untreated pseudoaneurysms have a risk of rupture ranging from 30–45%, with 100% mortality without specific therapy and 50% with the specific therapy established. In cases of specific therapy established before rupture, perioperative mortality is around 10%.[2]

Left cineangioventriculography is an accurate method, and when associated with coronary angiography, it allows for better surgical planning, as mitral valve dysfunction and the need for coronary artery bypass grafting are common conditions.[2]

Therefore, for diagnosis, we should be aware of a patient that had previous AMI and persists with dyspnea or chest pain or the one that had a new murmur on physical examination and should then be investigated with imaging methods that corroborate the diagnosis, so that any repair corrections can be quickly arranged.

Conclusion

Left ventricular pseudoaneurysm is a rare condition with high mortality rates when not properly treated. Rapid clinical suspicion and the support of complementary imaging methods (such as magnetic resonance imaging and 3D echocardiography) are fundamental for the diagnosis of this condition and support management. Surgical therapy is still the best method currently described for pseudoaneurysm repair and should be promptly established as soon as the diagnosis is confirmed.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

Authors' contributions:

Research creation and design: Leal GCV, Hortegal RA, Paladino Filho AT.

Data acquisition: Leal GCV. Data analysis and interpretation: Leal GCV, Hortegal RA, Paladino Filho AT. Manuscript writing: Leal GCV, Hortegal RA, Paladino Filho AT, Mora DM. Critical revision of the manuscript for important intellectual content: Ohe LN. Echocardiographic images: Barreto RBM.

References

1. Frances C, Romero A, Grady D. Pseudo-aneurisma ventricular esquerdo. J Am Coll Cardiol. 1998;32:557.
2. Gomes MC, Lima LC, Gonçalves LA, Motta GG, Reis FR, Rabelo RC, et al. Pseudo-aneurisma de ventrículo esquerdo por rotura cardíaca após infarto agudo do miocárdio: tratamento cirúrgico. Rev Bras Cir Cardiovasc. 1997;12(2):141-4.
3. Jacob JL, Buzellei G, Machado NC, Garzon PG, Garzon SA. Pseudo-aneurisma do ventrículo esquerdo. Arq Bras Cardiol. 2007;89(1):e1-e2.
4. Falcão JL, Falcão SN, Garcia MF, Arruda AL, Hueb AC, Jatene FB, et al. Left ventricular pseudoaneurysm associated to severe mitral insufficiency, complicating inferolaterodorsal acute myocardial infarction. Arq Bras Cardiol. 2005;84(6):488-91.
5. Yeo TC, Maluf JF, Oh JK, Seward JB. Perfil clínicos e resultado em 52 pacientes com pseudo-aneurisma cardíaco. Ann Intern Med. 1998;128:299.
6. Pacheco JB, Reis MB, Grangeiro LS, Monteiro RS, Tiossi R, Lopes DO, et al. [Diagnosis and following of post infarction left ventricular pseudoaneurysm]. Revista Brasileira de Ecocardiografia. 2005;18(1):63-8.
7. Moreno R, Gordillo E, Zamorano J, Almeira C, Garcia-Rubira JC, Fernandez-Ortiz A, et al. Long term outcome of patients with postinfaction left ventricular pseudoaneurysm. Heart. 2003;89(10):1144-6.
8. Prête R, Linka A, Jenni R, Turina MI. Surgical treatment of acquired left ventricular pseudoaneurysms. Ann Thorac Surg. 2000;70(2):553-7.
9. Ropers D, Achenbach S, Pfeiffer S. Left ventricular pseudoaneurysm following myocardial infarction. Heart. 2004;90(5):555.

Acute myocardial infarction after myocardial scintigraphy with dipyridamole

Infarto Agudo do Miocárdio após Cintilografia Miocárdica com Dipiridamol

Rafael Alessandro Ferreira Gomes[1,2,3], Isabelle Conceição Albuquerque Machado Moreira[2], Otávio Guilherme de Moraes Cardoso[2], Alexandre Gomes de Souza Melo[2], Aluísio Roberto Andrade Macêdo Junior[3]

[1]Universidade de Pernambuco, Recife, PE, Brazil. [2]Hospital de Aeronáutica de Recife, Jaboatão dos Guararapes, PE, Brazil. [3]Hospital Dom Hélder Câmara, Cabo de Santo Agostinho, PE, Brazil.

Introduction

Dipyridamole is a vasodilator that is widely used for detecting myocardial ischemia. Dipyridamole stress test is as sensitive and specific as those used with other agents, including dobutamine and exercise. Besides, dipyridamole stress testing is considered a safe and feasible alternative to other stress modalities. The most common abnormality found on electrocardiography during dipyridamole stress is ST-segment depression. ST-segment elevation is uncommon.[1] Acute myocardial infarction (AMI) after administration of dipyridamole is an extremely rare event.[2]

Objectives

To describe a case of myocardial infarction after induction of pharmacological stress with dipyridamole.

Case report

Female 62-year-old patient with metabolic syndrome and previous CAD with a history of coronary angioplasty with conventional stent to descending coronary artery in 2007. She was hospitalized with cholestatic jaundice and underwent endoscopic retrograde cholangiopancreatography three months before. The day after the endoscopic retrograde cholangiopancreatography test, she had episodes of burning epigastric discomfort irradiating to the precordial region, associated with nausea. On two occasions, she was taken to the emergency department, which interpreted the symptom as secondary to biliary disease, and was prescribed an antispasmodic drug, as her cardiological tests were normal (Electrocardiography — ECG and Troponin). As the patient would undergo cholecystectomy, a cardiological opinion was requested. Due to a history of CAD, exercise stress testing was requested. However, the test was ineffective due to chronotropic incompetence secondary to chronic beta-blocker use. Myocardial scintigraphy (MS) with pharmacological stress was then performed.

Keywords

Myocardial infarction; Radionuclide Imaging; Dipyridamole.

Mailing Address: Rafael Alessandro Ferreira Gomes •
Rodovia BR 101 Sul km 28, Centro, Cabo de Santo Agostinho-PE, Brazil.
E-mail: rgomesrecife@gmail.com
Manuscript received 20/06/2019; revised 28/6/2019; accepted 18/11/2019

DOI: 10.5935/2318-8219.20200012

After infusion of dipyridamole for 4 minutes, the patient presented severe and long-lasting epigastric pain with diffuse ST-segment elevation. Aminophylline and nitrate were infused, with improvement of ischemic symptoms and ST-segment elevation. However, the patient completed the test under atrial fibrillation and the scintigraphy images revealed an extensive area of transient hypoperfusion in the anterior, lateral and inferior walls (Figure 1). The patient was referred to the cardiac emergency department, where she presented, once again, epigastric pain and ventricular tachycardia with a pulse, and was immediately submitted to electrical cardioversion. ECG after cardioversion showed ST-segment elevation in the anterior wall (Figure 2). Then, she was transferred to hemodynamics, where cardiac catheterization showed total occlusion in the middle segment of the anterior descending artery. Drug-eluting coronary stent was uneventfully implanted at the occlusion site (Figure 2). She was discharged after 7 days of hospitalization.

Discussion

Dipyridamole acts indirectly by inhibiting adenosine reuptake, increasing its endogenous levels and promoting a potent vasodilating effect. Its adverse effects include hypotension, bradycardia, bronchospasm, chest pain, headache and dizziness.[2]

In the presence of dipyridamole, there is a "theft" or redirection of flow from the stenosed vessels, which has a high persistent resistance to coronary arteries with preserved vasodilation capacity. This "theft" phenomenon can be intracoronary (when it involves a single coronary segment) or intercoronary (when it involves multiple coronary segments). In addition, dipyridamole-induced vasodilation also decreases perfusion pressure through collateral vessels, so they may produce ischemia in myocardial segments dependent on these vessels.[3]

The incidence rate of ST-segment depression is reported in 6–25% of studies with dipyridamole. Transient ST-segment elevation is very uncommon and is more frequently observed in patients with severe ischemic heart disease, variant angina, and ventricular aneurysm.[1,4] AMI following dipyridamole infusion is extremely rare, with an estimated incidence of 1 case in 10,000 tests.[5]

In addition to ST-segment disorder, the patient also had atrial fibrillation and ventricular tachycardia (VT) with hemodynamic instability. VT following dipyridamole infusion is an even rarer event. In a study of 73,000 more patients

Case Report

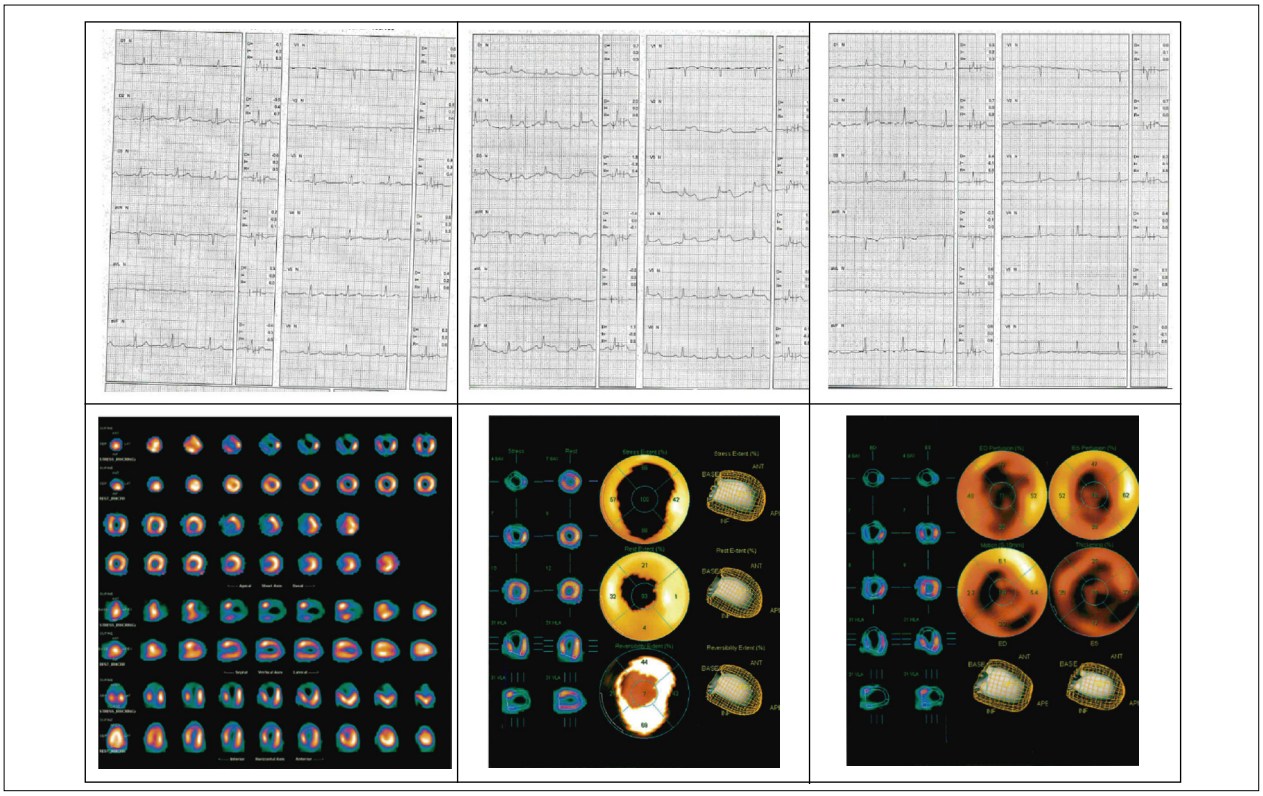


Figure 1 – *Myocardial scintigraphy.*

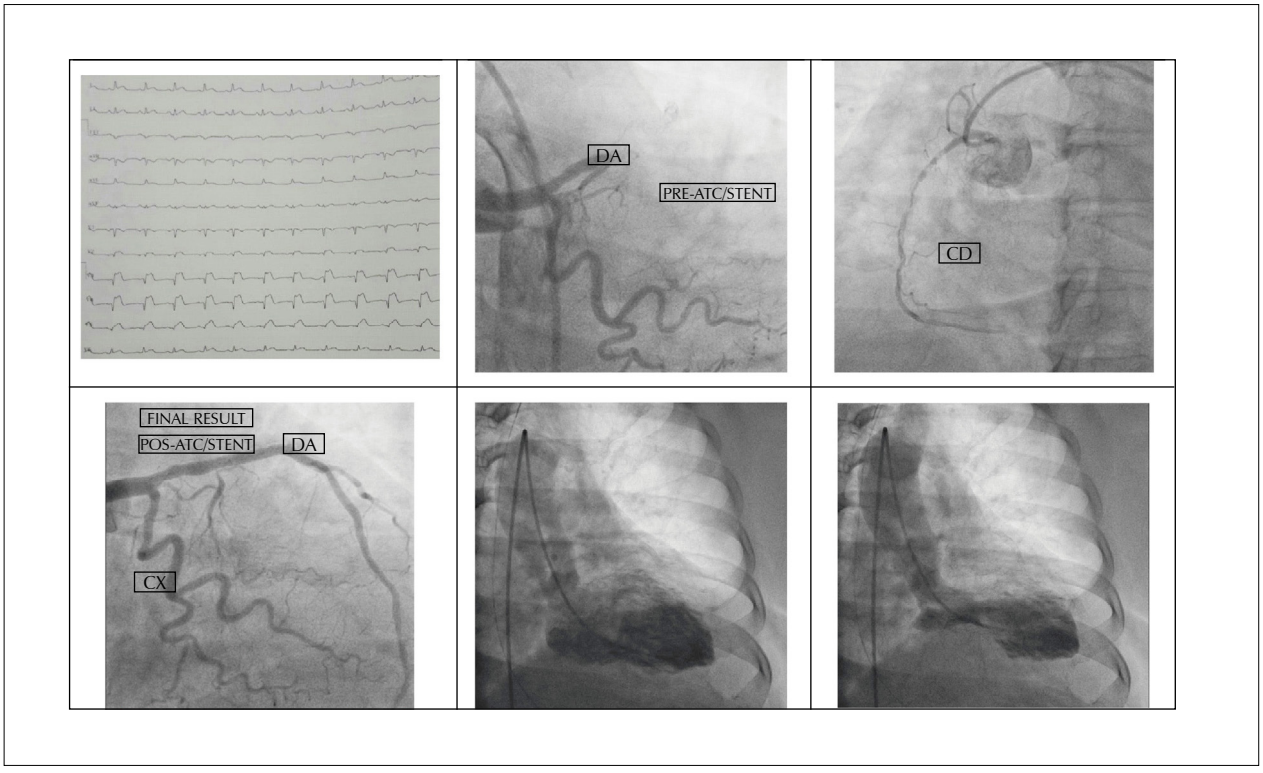


Figure 2 – *ECG on admission and coronary angiography.*

undergoing dipyridamole stress, the incidence of VT was 0.8 for every 10,000 tests.[5]

Some factors have been associated with ST-segment elevation, including coronary "theft," viable peri-infarct myocardium, collateral circulation-dependent occluded vessel, and transient changes in heart rate and blood pressure, as well as microvascular dysfunction and diabetes.[1] The use of dipyridamole may increase heart rate by 20–40% and usually causes a slight decrease in systolic and diastolic blood pressure. However, this myocardial demand does not generally lead to transmural infarction.[6]

Dipyridamole-induced ST-segment elevation has been reported in the literature in patients without coronary lesions at the end of the procedure following administration of aminophylline. In this scenario, sudden cessation of vasodilation stimulation leading to coronary vasospasm and the flow-theft phenomenon have been implicated.[3] Another possibility that could cause transmural ischemia during dipyridamole infusion would be severe hypotension caused by the drug.[2] In a study with 155 patients, of whom 67 underwent stress with dipyridamole alone, headache was identified in 40% of the patients, flushing in 30%, weakness in 22%, gastric discomfort in 10% and dizziness in 6%. A mean decrease in systolic blood pressure of 26 mmHg was observed in patients with no symptoms and 37 mmHg in those with dizziness.[7]

In this case, the mechanism leading to transmural ischemia could not be precisely determined. There were no reports of severe hypotension during the test or worsening of symptoms after aminophylline infusion. Besides, no vasospasm was found on coronary angiography, which does not rule out, but makes this hypothesis less likely. The event is likely to have occurred due to the phenomenon of intracoronary flow "theft" in a vessel with previous atheromatosis and impaired perfusion pressure. A fact that may corroborate this hypothesis would be occlusion in a single vessel in a non-proximal third, with no description of the presence of collateral vessels or significant atherosclerotic disease in other vessels.

Conclusion

A rare case of AMI associated with significant arrhythmia after dipyridamole stress test has been reported. This finding further underscores the importance of proper monitoring of symptoms and ECG in patients undergoing pharmacological stress testing.

Authors' contribution

Research creation and design; data analysis and interpretation; manuscript writing: Gomes RAF. Data acquisition: Macêdo Junior ARA. Manuscript writing: Moreira ICAM, Macêdo Junior ARA. Critical revision of the manuscript for important intellectual content: Cardoso OGM, Melo AGS.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Mutlu H, Leppo J. Coronary steal and ST elevation during dipyridamole stress testing leading to coronary artery bypass grafting. J Nucl Cardiol. 2007;14(6):892-7.
2. Shah S, Parra D, Rosenstein RS. Acute myocardial infarction during regadenoson myocardial perfusion imaging. Pharmacotherapy. 2013;33(6):e90-5.
3. Safi AM, Pillai N, Rachko M, Chaudhry K, Stein RA. Dipiridamole-induced ST- segment indicative of transmural myocardial ischemia—a case report. Angiology. 2001;52(8):553-57.
4. Malouf D, Mugmon M. ST elevation occurring during stress testing. J Community Hosp Intern Med Perspect. 2016;6(2):30799.
5. Lette J, Tatum J, Fraser S, Miller D, Waters D, Heller G, et al. Multicenter Dipyridamole Safety Study Investigators: Safety of dipyridamole testing in 73.806 patients: The multicenter dipyridamole safety study. J Nucl Cardiol. 1995;2:3-17.
6. Lima RS, Vargas A, De Lorenzo A. Entendendo a resposta cronotrópica ao dipiridamol e seu valor prognóstico independente para mortalidade global e cardiovascular. Revista do DERC. 2010;52:e12-13.
7. Cortinas IV, Beretta M, Alonso O, Mut F. Novo teste combinado exercício-dipiridamol para cardiologia nuclear no esforço insuficiente: adequada sensibilidade diagnóstica mantendo prognóstico do exercício. Arq Bras Cardiol 2015;105(2):123-9.

Systemic-to-Pulmonary Collateral Impact in Premature Infant: Clinical Case Report

Impacto de Colateral Sistêmico-Pulmonar em Recém-Nascido Prematuro: Relato de Caso Clínico

Mirela Frederico de Almeida Andrade, Moisés Imbassahy Guimarães Moreira
Maternidade Federal Climério de Oliveira, Universidade Federal da Bahia, Salvador, BA, Brazil.

Introduction

Congenital heart disease with left-to-right (L-R) shunt is an additional challenge to premature newborn (PTNB) management. Prematurity is responsible for an increased risk of acute and/or chronic lung disease due to pulmonary immaturity. Cardiac disorders of pulmonary hyperflow may worsen this condition.

Patent ductus arteriosus (PDA) is a clinical condition that determines frequent pulmonary hyperflow, but it is not the only L-R shunt condition in this population. Besides PDA, aortopulmonary window (rare pathology) and systemic-to-pulmonary collaterals (SPCs) are differential diagnoses. The onset of SPCs can cause congestive heart failure (CHF) in PTNB and mimic PDA with hemodynamic repercussions.[1] On the other hand, SPCs can occur transiently without increased morbidity.[2]

SPCs are bronchopulmonary communications that increase or proliferate from some stimulus, such as hypoxia or hypercapnia, commonly found in this population.[3]

Echocardiography is a noninvasive exam of great importance in this context, since it is able to diagnose and evaluate the degree of hemodynamic repercussion caused by SPCs.

Given the scarcity of studies in the literature on SPC in PTNBs, a situation that may worsen morbidity in this population, we will present a case of this condition and discuss peculiarities of the theme.

Case Report

A 25-year-old mother, G3P3A0, uneventful prenatal on prenatal corticosteroids. Female newborn, second twin, extremely premature (GA = 28 5/7 weeks), suitable for gestational age (W = 932 g), donor fetus in feto-fetal transfusion, cesarean section due to first-twin fetal distress, APGAR 3/5/7. Did not cry at birth. She was intubated in the delivery room, presented clinical stability and was referred to a neonatal intensive care unit.

Keywords

Echocardiography; Infant, premature; Lung Diseases.

Mailing Address: Mirela Frederico de Almeida Andrade •
Rua do Limoeiro, 137 - Nazaré, Salvador - BA, CEP 40055-150
E-mail: mirelafalmaida@yahoo.com.br
Manuscript received 19/8/2019; revised 27/9/2019; accepted 18/11/2019

DOI: 10.5935/2318-8219.20200013

On the second day of life, echocardiography for prematurity protocol was performed. The test showed patent foramen ovale (PFO) and 1.2 mm CA without hemodynamic repercussion, still present with 1 mm on a control exam at 7 days of life, no longer detected at 14 days of life.

Received a surfactant dose due to grade 3 respiratory distress syndrome and mechanical ventilation ventilatory support for 17 days with maximum FiO_2 of up to 70%, followed by NIPPV (Nasal Intermittent Positive Pressure Ventilation) for 15 days, CPAP (Continuous Positive Airway Pressure) for 7 days and circulating O_2 for 5 days. Received antibiotics for 10 days for early neonatal infection. Remained stable with weight gain.

At 31 days of age, echocardiography was repeated due to difficulty weaning from oxygen therapy. It showed PFO, absence of flow in the ductus arteriosus topography, and presence of SPCs emerging from the descending aorta toward distal portions of the left pulmonary artery with continuous low-velocity flow from the aorta to the pulmonary tree (Figures 1 and 2). Left atrial/aortic ratio of 1.6 and left ventricular diastolic and systolic diameters were at the upper limit of normality. Volume restriction and diuretics were indicated, with good clinical outcome and successful weaning of oxygen therapy.

Discussion

In the early stages of fetal development, pulmonary blood is supplied by arteries from the dorsal aorta. By the 40th day of gestation, blood supply via cardiac anterograde flow through the pulmonary artery is associated with the first supply. Around the 50th day of gestation, the latter disappears.[1]

SPCs occur frequently in congenital heart disease with reduced pulmonary blood flow and pulmonary diseases such as Fallot's Tetralogy (most prevalent cyanogenic congenital heart disease), bronchiectasis and pulmonary bronchodysplasia.[4] Such conditions have chronic hypoxia in common. Thus, it is postulated that hypoxemia is a trigger for the development of SPCs in premature newborns, i.e., bronchopulmonary arterial communications that increase and/or proliferate (angiogenesis), generating an alternative pulmonary blood supply. In this situation, the lungs receive blood from pulmonary circulation as well as from systemic circulation, causing pulmonary hyperflow and its consequences.[5]

Shaugnessy et al., in a retrospective echocardiographic study, detected an incidence of 4% (20/500) of SPC in premature newborns. Median age at SPC detection was 21 days. Fourteen patients had previous exams that did not detect SPC, suggesting the evolutionary character of the condition. The average gestational age of the newborns was 28 +/- 3 weeks and the

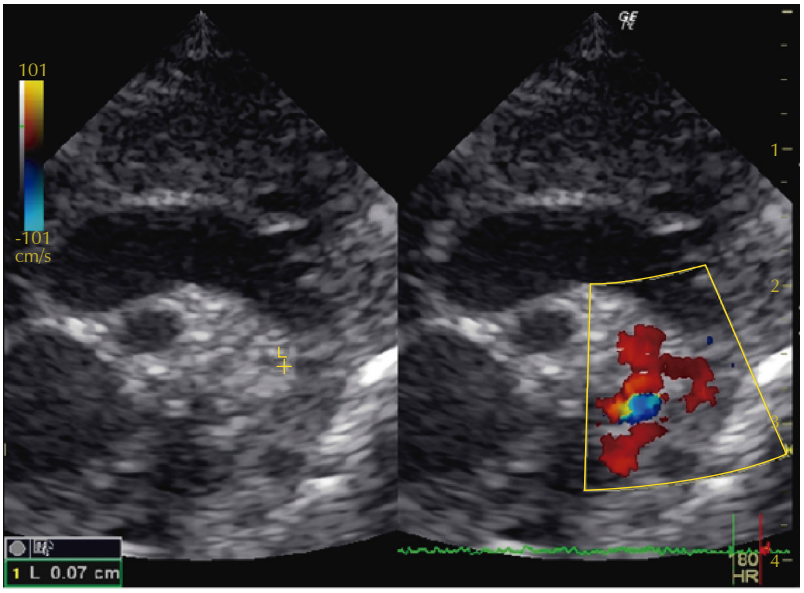


Figure 1 – *Systemic-to-pulmonary collateral emerging from the descending aorta toward the pulmonary tree.*

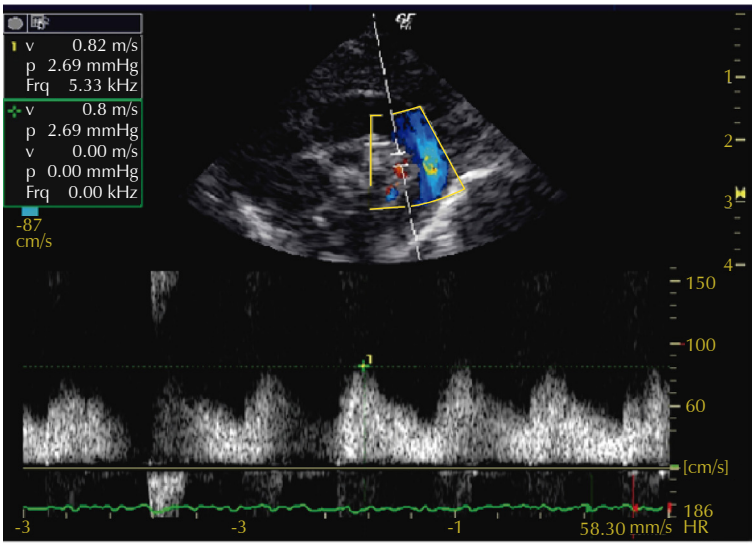


Figure 2 – *Continuous flow of systemic-to-pulmonary collateral.*

weight was 1,155 +/- 370 grams. Sixteen patients had hyaline membrane (80%) and 17 required orotracheal intubation (85%).[2] Such profile is similar to the one in this case.

Ancherman et al., in a prospective echocardiographic study, found an incidence of 66% (88 patients) of SPC in 136 newborns with very low birth weight (<1,500 grams). Patients with SPC stayed longer under positive pressure ventilation and in hospital. Of the 88 patients with SPC, 10 (11%) had CHF, mimicking hemodynamic repercussion due to PDA. Nine patients had improvement of symptoms with anti-congestive medications, which were discontinued after 3 months. One patient had CHF and needed catheterization for SPC embolization, progressing with improvement. At follow-up up to 1 year of age, most patients had regression of the SPCs.[1]

The discrepancy of incidence between the two studies may be justified by the methodological difference, as the first one is retrospective and the second one is prospective.

The clinical picture may range from a transient benign condition (in most cases) to cardiac decompensation with interstitial edema and pulmonary alveolar edema, prolonging ventilatory support and oxygen supplementation time.[5] In 1995, Skinner described a PTNB with bronchodysplasia that presented clinical examination and echocardiogram suggestive of L-R shunt heart disease (PDA and SPCs). PDA ligation was performed, but there was no improvement. The SPCs maintained the CHF condition. The child died without clinical conditions for collateral closure.[6]

Color Doppler echocardiography is a noninvasive and affordable bedside imaging test that can diagnose SPC and its potential hemodynamic repercussion. Skinner et al. first published the use of color Doppler echocardiography for this diagnosis in 1995.[6] The suprasternal window is the best for SPC evaluation. Color Doppler can detect continuous flow mainly from the aortic arch, its branches and the proximal descending aorta toward distal portions of the pulmonary artery. This differentiates it from the SPC, whose terminal portion usually occurs at the distal part of the pulmonary trunk and is hourglass-shaped (SPCs are usually tortuous). The origin of the collateral is easily identified, but its distal portion in the pulmonary tree is not always visible. Signs of shunt repercussion such as enlargement of left chambers and reverse flow in the descending aorta should be investigated mainly in newborns whose respiratory evolution is not satisfactory.[1,2,5]

Goel et al. in 2018 suggested that the gold standard imaging tests for the evaluation of SPC in premature newborns with cardiac decompensation and refractory to anti-congestive medications were computed tomography, nuclear magnetic resonance or cardiac catheterization. Such tests would provide more accurate information on the number (several small vessels or few large vessels), pathway and diameter of the SPCs than the echocardiogram for interventional treatment (surgical ligation or coil occlusion).[5]

Conclusion

The presence of SPCs should be investigated as a cause of L-R shunt in PTNBs that do not have good respiratory pattern evolution. Color Doppler echocardiography is an affordable and sufficient imaging test to provide this diagnosis and to guide preliminary clinical management in this population, and the investigation may be complemented with other imaging methods when the outcome is delayed and unsatisfactory, requiring intervention.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Acherman RJ, Siassi B, Pratti-Madrid G, Luna C, Lewis AB, Ebrahimi M, et al. Systemic to Pulmonary Collaterals in Very Low Birth Weight Infants: Color Doppler Detection of Systemic to Pulmonary Connections During Neonatal and Early Infancy Period. Pediatrics. 2000;105(3):528-32.
2. Shaughnessy RD, Reller MD, Rice MJ, McDonald RW. Development of systemic to pulmonary collateral arteries in premature infants. J Pediatr. 1997;131:763-5.
3. Birnbacher R, Proll E, Kohlhauser C, Marx M, Schlemmer M, Dobner M, et al. Echocardiographic evidence of aortopulmonary collaterals in premature infants after closure of ductus arteriosus. Am J Perinatol. 1998;15(10):561-5.
4. Botenga AS. The significance of broncho-pulmonary anastomoses in pulmonary anomalies: a selective angiographic study. Radiol Clin Biol. 1969;38(5):309-28.
5. Goel D, Gupta P, Cooper S, Klimek J. A literature review of systemic to pulmonary collaterals in preterm infants to emphasise their existence and clinical importance. Acta Paediatr. 2018;107(11):1867-78.
6. Skinner JR, Silove ED. Aortopulmonary collateral arteries mimicking symptomatic ductal shunting in a preterm infant. Br HeartJ. 1995; 74:93-94.

Cardiac Arrest in Pacient with ALCAPA Syndrome. Case Report

Parada Cardiorrespiratória em Paciente com Síndrome de ALCAPA. Relato de Caso

Vivian Gamalho Pereira[1], Luis Alberto Batista Peres[1,2], Flávio Luis Pereira[3]

Centro Universitário da Fundação Assis Gurgacz, Cascavel, PR,[1] Universidade Estadual do Oeste do Paraná, Cascavel, PR,[2] Hospital Policlínica de Cascavel, Cascal, PR[3] – Brazil.

Introduction

Alcapa Syndrome, also known as Bland-Altman-Garland Syndrome, is a rare coronary anomaly in which the left coronary artery anomalously originates from the pulmonary artery. Two types of Alcapa syndrome are described: the infant type and the adult type. The infant type is the most symptomatic one and 90% of patients die in the first months of life, while the adult type is characterized by the formation of a collateral system between the right coronary artery (RCA) and the left coronary artery (LCA), with a shunt volume compensation mechanism at varying levels. The adult type tends to be asymptomatic, with collateral circulation decompensation leading to ischemia. The following is the report of a case of Alcapa syndrome in a 28-year-old female patient who presented an episode of cardiopulmonary arrest and remained at the intensive care unit for 33 days. [1-3]

Case report

Female patient, 28 years old, admitted to the emergency room after cardiopulmonary arrest (CPA), where she was resuscitated for 22 minutes and referred to the intensive care unit (ICU). The patient was sedated, on invasive mechanical ventilation, and presented severe hemodynamic instability dependent on vasoactive drugs (VAD). Pulmonary examination: vesicular murmur reduced at the bases, on mechanical ventilation with respiratory rate of 16 rpm, PEEP 5 cmH2O, FiO2 40%. Cardiovascular examination: heart rate of 76 bpm, VAD-dependent 85 mmHg MAP, sinus rhythm, systolic murmur in mitral focus (2+). Abdominal examination: distended tympanic abdomen with reduced hydroaereal noises. Lower limbs: no edema, bilaterally palpable pulses. History of mitral valve prolapse on metoprolol 25 mg daily. Laboratory tests revealed hematocrit 41.50%, hemoglobin 13.80 g/dL, leukocytes 11,000/mm^3, platelets 125,000/mm^3, creatinine 1.98 mg/dL, potassium 4.0 mEq/L, sodium 141 mEq/L, BNP 1080.3 pg/mL, troponin I 1,564 ng/mL, creatine phosphokinase MB fraction 109.01 U/L, normal and partial arterial blood gas with no particularities.

Keywords

Coronary Disease; Cardiology; Congenital Abnormalities.

Mailing Address: Vivian Gamalho Pereira •

E-mail: vivian.gamalho@hotmail.com

Manuscript received 29/8/2019; revised 18/10/2019; accepted 18/11/2019

DOI: 10.5935/2318-8219.20200014

On electrocardiogram, the patient presented sinus rhythm, signs suggestive of left ventricular hypertrophy and ventricular repolarization disorders in the upper lateral wall. As for imaging scans, chest radiography showed infiltration in the pulmonary bases; later, right perihilar opacification and bilateral pulmonary congestion. On transthoracic echocardiogram, the patient presented discrete left ventricular dysfunction (54% ejection fraction by the Teichholz method), no papillary muscle hyperrefringence, and presence of pericardial effusion in the inferior, posterior and lateral left ventricular walls, and mitral valve prolapse with moderate to severe regurgitation. Chest tomography showed a mixed pattern of acute respiratory distress syndrome (ARDS) and cardiac magnetic resonance imaging showed no abnormalities.

The patient remained at the ICU on mechanical ventilation with high PEEP and FiO2, and was subsequently tracheostomized. She presented repetitive episodes of nosocomial pneumonia, evolving to ARDS. The main events on evolution were acute lung edema and septic shock. She was prescribed various antibiotic regimens and used vasoactive drugs while in hospital.

After a few days, the patient presented hemodynamic and PO2/FiO2 ratio improvement and starting weaning of vasoactive drugs and mechanical ventilation. After four days on spontaneous ventilation, implantable cardiodesfibrillator was implanted as a primary prevention of sudden death. Thirty-three days after admission, she was discharged from the ICU. Coronary angiotomography was performed as an operative evaluation for the correction of mitral regurgitation, previously diagnosed on echocardiography. Incidental diagnosis of anomalous origin of coronary artery was delivered. Months later, she was referred for surgical procedure at another service, where she died during the surgery.

Discussion

We report the case of a patient with no previous diagnosis of Alcapa Syndrome, admitted to the Intensive Care Unit after cardiopulmonary arrest, presenting multiple complications in the evolution, being discharged after thirty-three days in hospital. The patient died during the surgery to correct coronary anomaly after a few months of diagnosis.

The Alcapa Syndrome is a rare coronary anomaly, with an incidence of 1 in every 300,000 live births. It is described as anomalous origin of the LCA from the pulmonary artery (PA), and is considered a pathway origin anomaly. In general, the Alcapa syndrome occurs in isolation, but there are rare cases of occurring in conjunction with other congenital pathologies. Two types of Alcapa syndrome are described: the infant type and the adult type. The infant type is more common and symptomatic, with the presence of chest pain (signaled by neonate irritation),

Case Report

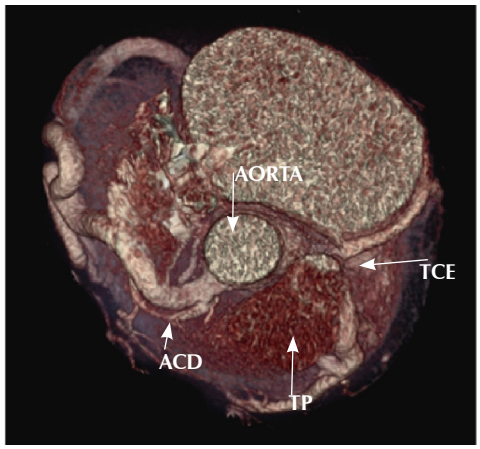


Figure 1 – *3D coronary computed tomography angiography reconstruction showing the pulmonary trunk (PT) originating the left main coronary artery (LMCA). On the side, the aorta originating the right coronary artery (RCA).*

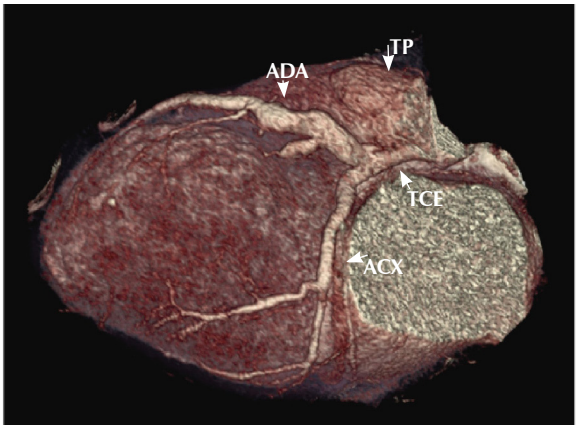


Figure 2 – *3D coronary computed tomography angiography reconstructions originating the LMCA, from which the anterior descending artery (ADA) and the circumflex artery (CxA) come out.*

pallor, sweating and dyspnea, with a high mortality rate. The adult type presents a clinical picture that may vary from asymptomatic (due to collateral compensation between RCA and LCA) and symptomatic (due to failure of collateral compensation). [1, 3-6]

Imaging tests of choice are multislice computed tomography (MSCT) and cardiac nuclear magnetic resonance imaging (MRI). MSCT shows direct morphology and anatomical variations, which could also be identified by MRI or angiography, but less accurately. MRI is used to make a more functional assessment and can identify the inverse flow in LCA. Another extremely important test, especially in the infant type, is the two-dimensional echocardiogram, which presents well-established criteria for diagnosing the Alcapa syndrome, namely: identification of dilated RCA, retrograde Doppler flow of the LCA to the pulmonary artery and collateral flow from the septal flow. Coronary angiography can also be used and requires three criteria to confirm the Alcapa syndrome: (1) LCA retrograde flow; (2) LCA originating from the pulmonary artery trunk; and (3) absence of LCA originating in the aorta. Functional tests, such as myocardial scintigraphy and Holter monitoring, should be performed annually on any adult with the ALCAPA syndrome, even in the absence of symptoms.[2, 4, 5, 7]

Therapeutic approach is divided into non-surgical and surgical. The non-surgical approach includes the use of beta-blockers to reduce ischemia and reduction of the patient's physical exertion to reduce myocardial work. However, this is not a consensual treatment. The most commonly used surgical approach is to repair the anatomy by redeploying the LCA in the ascending aorta. Heart transplantation is recommended for patients with severe cardiac dysfunction, contraindicating the commonly used surgical technique.[5,8]

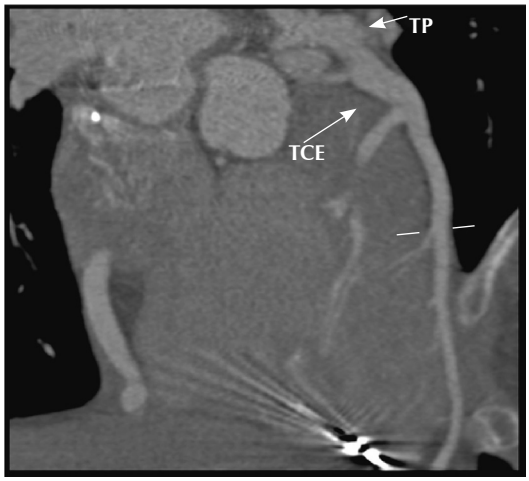


Figure 3 – *3D computed tomography angiography reconstructions showing the PT originating the LMCA.*

In the case described here, the clinical presentation was asymptomatic until adulthood, in which the patient presented a sudden CRA. Diagnosis was based on coronary angiography, performed as a preoperative examination to correct mitral regurgitation, previously seen on echocardiography. Initial treatment was with beta-blockers, prescribed due to mitral valve prolapse. Surgical treatment was proposed after diagnosis of Alcapa Syndrome.

Recently, there has been an improvement in the prognosis of patients with ALCAPA due to the early diagnosis provided by imaging tests and improvement of surgical techniques. The success of surgical procedures varies depending on the myocardial condition at the time of diagnosis and patient's clinical repercussion. The later the diagnosis, the greater the chances of myocardial damage caused by ischemia and the greater the chances of ventricular dysfunction and mitral regurgitation. These findings may have a significant impact on the prognosis of these patients.[7]

We report the case of an adult female patient with Alcapa syndrome, diagnosed late after CRA, with recovery and later death during corrective surgery.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

References

1. Thebit ME. Anomalia Congênita de Coronária: Revelância Clínica, Exercício e Morte Súbita. Rev DERC. 2013;19(4):114-8.
2. Nau AL, Strapasson AF, Martins GF, Binotto CN. Origem anômala da artéria coronária esquerda a partir da artéria pulmonar - Relato de Caso. Resid Pediatr. 2019;9(1):12-5.
3. Angelini P. Revisando a síndrome de ALCAPA dos tipos infantil e adulto: as diferenças estão nos detalhes!. Rev Bras Cardiol Invasiva. 2007;15(4):334-6.
4. Ugalde PH, Rozas AS, Sanhueza FM, Yubini LM, García BS. [Anomalous left coronary artery origin from the pulmonary artery causing angina: Report of one case]. Rev Méd Chile. 2017;145(1):121-5. Spanish.
5. França JC, Godoy MF, Spotti MR, Santos MA, Pivatelli FC, Guimarães Neto WP. Larga supervivencia en paciente con síndrome de ALCAPA no corregido: Presentación de un caso clínico y revisión de la literatura. Insuf Card. 2018;13(1):45-9.
6. Koenig PR, Hizaji ZM. Congenital and pediatric coronary artery abnormalities. Up To Date [Internet]. 2018 [cited 2019 Dec 10]. Available from: https://www.uptodate.com/contents/congenital-and-pediatric-coronary-artery-abnormalities
7. Nacif MS, Luz JH, Moreira DM, Rochitte CE, Oliveira Júnior AC. Origem Anômala da Coronária (ALCAPA) em tomógrafo de 64 canais. Arq Bras Cardiol. 2010;94(6):143-6.
8. Almira MC, Gonzálex AE, Ricardo GS. Bland-White-Garland syndrome. Rev Cubana Pediatr. 2016;88(2).

Mixed Variety of Total Anomalous Pulmonary Venous Return in an Asymptomatic Newborn

Variedade Mista de Retorno Venoso Pulmonar Anômalo Total em Recém-Nascido Assintomático

Cláudio Henriques[1]; Andreia Palma[1]; Patrícia Silva[1]; Helena Andrade[1]; António Pires[1]

[1]Pediatric Cardiology Department, Pediatric Hospital, Coimbra, Portugal

Case Report

Total anomalous pulmonary venous return has an incidence of 7–9 per 100,000 live births, accounting for 0.7–1.5% of all congenital heart diseases. The most common type is the supracardiac, with the mixed form being the rarest. Moreover, it is one of the very few venous malformations known to cause cyanosis.[1]

The authors describe the case of a term newborn girl, whose first fetal scan was carried out only after the 20th gestational week. Fetal scans and laboratory work-up were normal and she was delivered vaginally at 38 weeks gestation. She was asymptomatic and remained at her mother's side. At 48 hours post-delivery, routine pulse oximetry was carried out, which showed peripheral oxygen saturation of 87%, with no signs of respiratory distress.

Transthoracic echocardiogram showed dilated right chambers, right-to-left shunt across a medium sized atrial septal defect, absence of normally draining pulmonary veins and posterior venous conduit draining to the right atrium (Figure 1). To better define the malformation, a coronary computed tomography angiography scan was carried out, which showed a

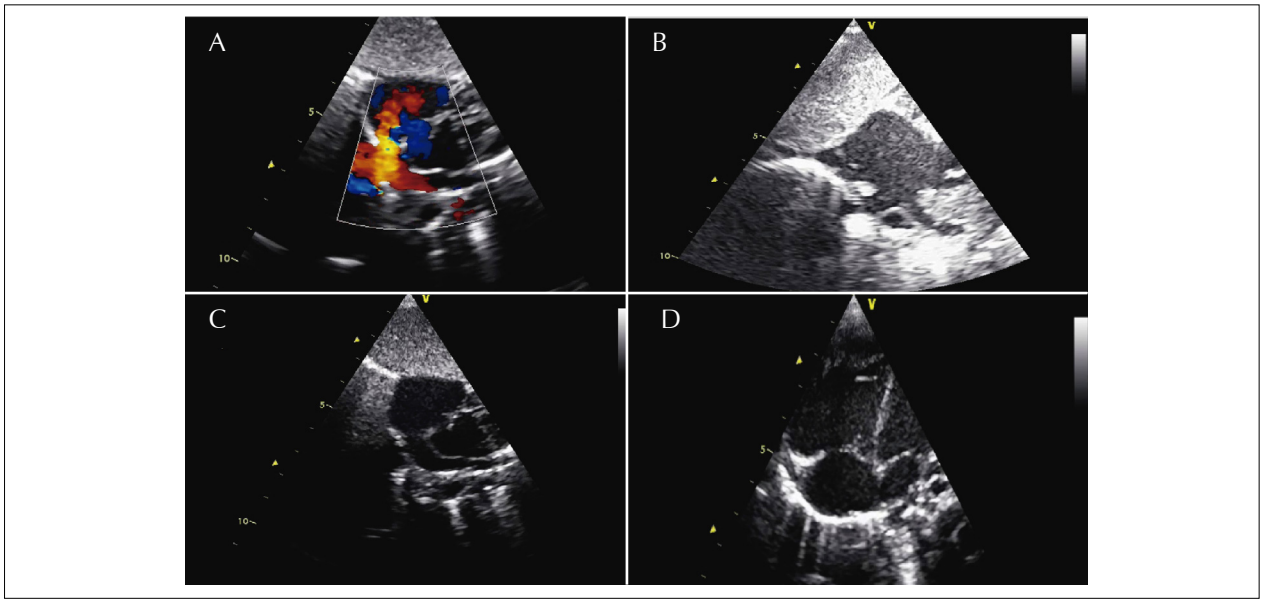


Figure 1 – *A) Subcostal view of transthoracic echocardiography with color Doppler revealing right-to-left shunt in the atrial septal defect (blue) and an anomalous pathway from a retro-atrial conduit emerging into the right atrium (red); B) Subcostal "bicaval" view with a right merging vase in the superior vena cava just before entering the right atrium; C) Anomalous retro-atrial conduit emerging into the right atrium; D) Apical four chamber view with dilated right sided chambers.*

Keywords

Congenital Heart Disease, Cyanotic Heart Disease; Paediatric Cardiology; Total Anomalous Pulmonary Venous Return; Newborn.

Mailing Address: Cláudio Henriques •
Hospital Pediátrico de Coimbra - Avenida Afonso Romão - 3000-602 Coimbra - Portugal.
E-mail: claudiojhenriques@gmail.com
Artigo recebido em 5/9/2019; revisado em 11/11/2019; aceito em 27/11/2019

DOI: 10.5935/2318-8219.20200015

mixed type of total anomalous pulmonary venous return, where the left pulmonary veins and the right inferior vein drained into the right atrium via a common trunk and right superior and middle pulmonary veins drained to the superior vena cava (Figure 2). Surgical correction was carried out at the age of 3 months, confirming the coronary computed tomography scan findings and with an excellent corrective result.

Discussion

The mixed variant or type IV of Darling's Classification of total anomalous pulmonary venous return is the rarest form of this entity. The surgical mortality rate is higher in this form, as are other related factors such as younger age at presentation and the presence of obstructive pulmonary veins.[2] Other than the early clinical presentation, our patient had no other associated anomalies, with an overall good outcome.

Prenatal fetal echocardiography is challenging, whereas postnatal echocardiography has a 97% sensitivity and specificity.[3] In our case, the diagnosis was postnatally, later confirmed by computed tomography angiogram and surgical findings.

Pulse oximetry prior to maternity discharge is an helpful tool to screen for asymptomatic congenital cardiac conditions.[4]

Authors' contributions

Research creation and design: Cláudio Henriques, Patrícia Silva, Andreia Palma. Data acquisition: Cláudio Henriques, Patrícia Silva. Manuscript writing: Cláudio Henriques, Andreia Palma. Intellectual support and revision: António Pires, Helena Andrade.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

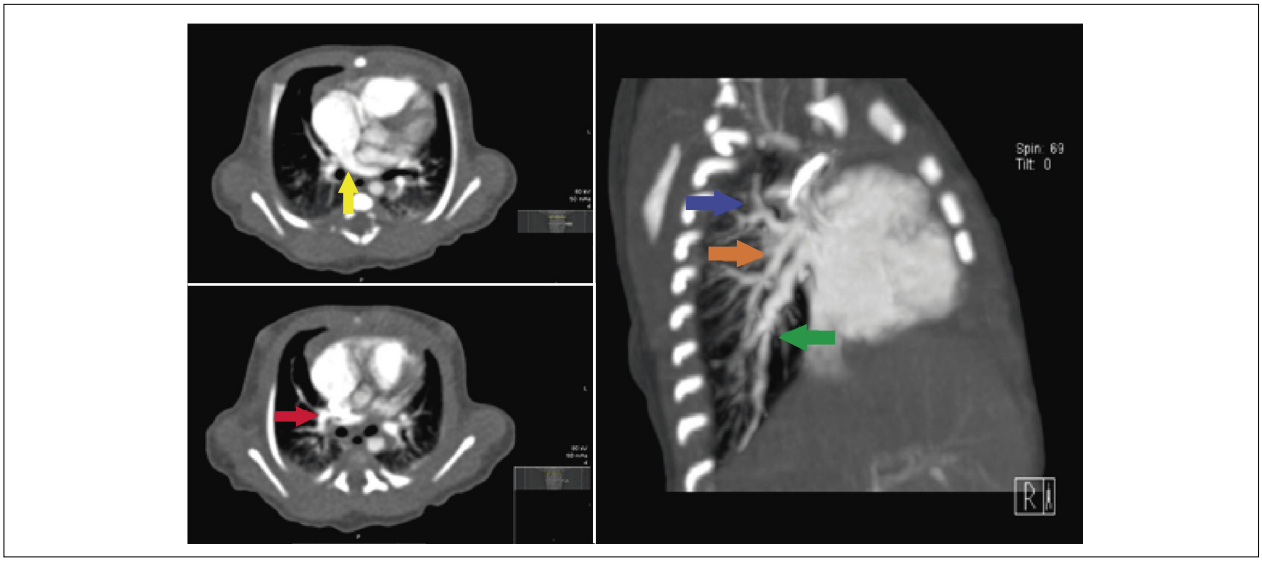


Figure 2 – *Axial view of the chest Computed Tomography Angiogram (left sided images) showing a common trunk coming from the left pulmonary veins and draining into the right atrium (yellow arrow) and the right inferior pulmonary vein merging into the aforementioned common trunk (red arrow). Right anterior longitudinal view of the chest Computed Tomography Angiogram (right image) revealing the right superior (blue arrow) and right middle (orange arrow) pulmonary veins flowing into the superior vena cava and the right inferior pulmonary vein merging into the common trunk, which in turn drains into the right atrium. The green arrow is highlighting the right inferior pulmonary vein.*

References

1. Kao CC, Hsieh CC, Cheng PJ, Chiang CH, Huang SY. Total Anomalous Pulmonary Venous Connection: From Embryology to a Prenatal Ultrasound Diagnostic Update. J Med Ultrasound. 2017;25(3):130-7.
2. Singh J, Mohite PN, Rana SS. Rare variant of mixed total anomalous pulmonary venous connection. J Cardiovasc Dis Res. 2012;3(3):248–50.
3. Zhang Z, Zhang L, Xie F, Wang B, Sun Z, Kong S, et al. Echocardiographic diagnosis of anomalous pulmonary venous connections: experience of 84 cases from 1 medical center. Medicine (Baltimore). 2016; 95(44):e5389.
4. Plana MN, Zamora J, Suresh G, Fernandez-Pineda L, Thangaratinam S, Ewer AK. Pulse oximetry screening for critical congenital heart defects. Cochrane Database Syst Rev. 2018;3(3):CD011912.