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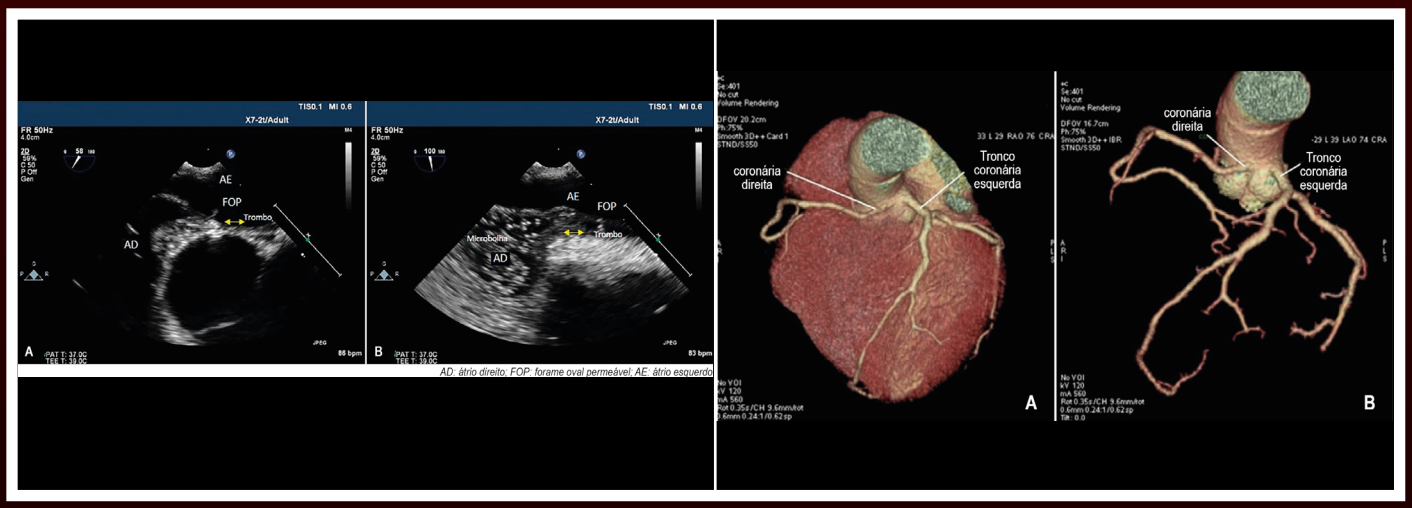

AD: átrio direito; FOP: forame oval permeável; AE: átrio esquerdo

Figura 1 – *Transesophageal echocardiogram showing the presence of a thrombus in the patent foramen ovale (PFO) without evidence of macrobubble passage. AD: right atrium; AE: left atrium.* **Figura 3 –** *Computed tomograpgy angiography. A e B: Improper RCA origin in the left Valsalva sinus, adjacente to the origin of the left main coronary artery.*

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Position Statement on Indications and the Safe Reintroduction of Cardiovascular Imaging Methods in the COVID-19 Scenario – 2021

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Content

Cover Letter

The objective of this position statement is to inform clinicians, cardiologists, and medical imaging specialists on the recommended procedures, flows, and protocols for the duration of the SARS-CoV-2 pandemic aiming at a more efficient protection of health care professionals and patients. Recommendations are based on the best available scientific evidence at the moment and on the consensus among experienced specialists. Since the first case of the new coronavirus disease (COVID-19) in Brazil, many changes in recommendations and a large scientific debate regarding some of them have occurred within various sources of scientific knowledge . This is due to our currently incomplete knowledge on COVID-19, including its pathophysiological processes and aspects of SARS-CoV-2 transmission. Another reason for a variability in recommendations is related to the epidemiological phase of the pandemic in each region of the country. Notably, in a country with continental dimensions such as Brazil, the pandemic can reach different transmission phases in a specific moment, thus requiring particular measures for each region and phase of the pandemic.

In the beginning of the pandemic, a phase of great attention and lack of knowledge on what the future held, the Cardiovascular Imaging Department (DIC) of the Brazilian Society of Cardiology (SBC) published a brief and essential version of a position statement. The document provided rapid and practical fundamental guidance regarding safety procedures during non-invasive cardiovascular imaging procedures. This document was absolutely essential at that moment for providing the best possible protection for health care professionals. After the publication of a summary document in the initial stage of the pandemic, DIC-SBC and its specialists have deemed timely to update that position statement (now published in the form of an official scientific publication); this should include not only a much wider view of the procedures in light of the data acquired since then, but also a customized orientation for each epidemiological phase of the pandemic that could be useful for professionals working in non-invasive cardiovascular imaging for the next months or possibly years of coexisting with COVID-19.

1. Introduction

In view of the new coronavirus disease (COVID-19) pandemic and its high transmissibility, an urgent reorganization of cardiovascular imaging services was necessary for minimizing exposure to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and ensure the protection of patients, physicians, and personnel without compromising patient assistance. It was recommended that elective outpatient examinations be deferred (when deemed non-essential) for reducing exposure and risk of cross-contamination, and that personal protective equipment (PPE)

be rationally used.[1-3] The use of PPE became mandatory for all personnel in the workplace, including reception workers, nursing technicians, nurses, technologists, biomedical scientists, and doctors. All patients were instructed to use masks. Specialists discussed, along with the requesting doctors, the actual need for test urgency and the most suitable cardiovascular imaging modality for each specific clinical situation. On the other hand, it is known that: (a) Cardiovascular imaging is frequently necessary for primary prevention, clinical management, and differential diagnosis in many situations, and chronically postponing it can be harmful; (b) COVID-19 can cause severe cardiovascular manifestations, especially in vulnerable individuals such as older people, immunosuppressed patients, or those with previous cardiovascular disease and/or cardiovascular risk factors (hypertension, diabetes, obesity); [4-6] (c) when the lungs are severely affected by COVID-19, the cardiac function can suffer greater impact, especially in the right ventricle. In a moment when the number of COVID-19 cases present a relative decrease, health care services will be able to progressively increase their working hours according to the pandemic tendency and guidance provided by local public authorities. Nevertheless, the reintroduction of cardiovascular imaging examinations should follow various safety protocols, as described in the next section.

2. Safety Protocols for the Reintroduction of Cardiovascular Imaging Examinations in the COVID-19 Era

Outpatient scheduling should be progressive and consider indications for appropriate use,[2,7] the indication priority, risk of COVID-19, and the phase of the pandemic. Areas going through the peak transmission phase should prioritize essential examinations (high-priority cases), that is, where the results are expected to bring clinical benefits or a change in management.[1,8] Medium-priority indications are those where examinations, although elective or in asymptomatic patients, can contribute to the implementation of primary or secondary prevention measures, in the adjustment of currently used medications, or in medium-term changes in management, potentially impacting the clinical outcome. Low-priority indications are those where tests could be deferred until after the peak of the pandemic and be gradually reintroduced once the number of cases is reduced.

Imaging examinations of patients with COVID-19, especially in outpatient settings, should be deferred (when possible) until the patient reaches the criteria for cure. At the moment of elaboration of this position statement, the Centers for Disease Control and Prevention (CDC) considers 2 criteria for releasing patients from isolation after COVID-19: The "symptom-based strategy" states that patients should be released from isolation 10 days after symptom onset; the "time-based strategy" considers that patients should be released 10 days after the first positive test (RT-PCR SARS-CoV-2).[9] These criteria can be adjusted according to orientations of the local infection committee. If the cardiovascular examination is considered essential, it should be directed to the clinical question (focused) but sufficiently complete to avoid repetition, and follow all recommendations regarding protective measures. In addition, redundant or rarely appropriate examinations can generate an additional financial impact to that caused by the pandemic. These recommendations on indications and prioritization are valid as long as the pandemic persists and are summarized in Table 1.

Defining "who," "when," and "how" cardiovascular imaging examinations should be used is fundamental for reducing contamination risks for the patients and health care professionals while ensuring high-quality assistance. These measures are described below.

2.1. Infrastructure and Safety Policies

• A triage questionnaire for defining COVID-19 risk should be applied when scheduling an appointment, at confirmation, and on the day of the examination (respiratory symptoms and contact with confirmed COVID-19 case). At admission, temperature checks should also be performed. The same triage protocol should be applied to the staff.

Table 1 – Indication prioritization for rescheduling cardiovascular imaging examinations according to the phase of the pandemic and COVID-19 risk

Level of priority	Prioritization rationale
High priority (Consider performing the examination in the next hours or the next 2 to 4 weeks)	• Acute cardiovascular symptoms or with recent worsening • Evaluation before urgent clinical therapy • Planning of urgent cardiovascular interventions • Safety monitoring of clinical therapy • Monitoring after recent invasive or surgical therapy **To be performed regardless of the pandemic phase**
Medium priority	• Progression monitoring of chronic myocardial disease or asymptomatic severe chronic valvular disease • Clinical therapies requiring monitoring • Monitoring of therapy results • Initial assessment of a new and unexplained heart murmur, even if asymptomatic **Defer until the deceleration phase of the pandemic, preferably for patients at low risk for COVID-19**
Low priority	• Routine evaluation of chronic disease in individuals not eligible for clinical, surgical, or invasive therapy **Defer until the control phase of the pandemic for patients at low risk for COVID-19**

Adapted from the recommendations of the American Society of Echocardiography.[10]

• Instructions regarding social distancing, mask use, and hand hygiene should be provided when scheduling an appointment and reinforced at admission.

• Telemedicine applications should be implemented.

• Visual displays containing information on protective measures should be placed on waiting rooms and strategic places (in more than one language).

• Hand sanitizer should be widely available.

• Patients should be instructed to arrive on time or to wait for their turn inside the car; the number of accompanying persons should be limited.

• The number of seats in the waiting room should be reduced so as to guarantee social distancing.

• Acrylic glass barriers or distancing cones should separate patients and the reception staff.

• The time between examinations should be extended for avoiding crowded rooms and allowing proper cleaning. Facilities should consider opening at non-business hours or weekends.

• Equipment and surface cleaning protocols should be performed after each examination according to the local infection control policies and the type of examination.

• Communication with patients or financial transactions should be preferably performed online.

• There should be 2 patient flows: One for patients with suspected or confirmed COVID-19 and another for patients without the disease. Rooms, equipment, and circulation areas should be separated for the 2 groups.

• Ideally, rooms should be well-ventilated and have negative pressure when performing procedures that generate aerosols (transesophageal echocardiography [TEE], exercise stress tests).

• PPE stocks should be continuously monitored and maintained.

• Contaminated material should be disposed of according to health surveillance agency guidelines.

2.2. Prioritizing Indications and Choosing the Cardiovascular Imaging Method

• Define the priority level of the examination (according to the local phase of the pandemic and the risk of COVID-19 [Table 1]).

• Select the best test for providing essential information on the patient's clinical condition.

• Consider replacing an examination for another with similar accuracy, but lower risk of COVID-19.

• Avoid performing multiple tests or inappropriately repeating the same examination.

2.3. Personnel Protection

• Practice frequent hand hygiene and constant mask use.

• Appropriately use PPE according to the required protection level (for droplets or aerosols). Table 2 summarizes the use of PPE according to the protection level required by each type of examination, the risk of COVID-19, and location.

• Participate in frequent institutional training on donning and doffing PPE, its duration of use and storage, as well as hand hygiene. Evidence shows that the highest chances of infection in professional settings occur at the moment of inadequate PPE removal. Steps and guidance for donning and doffing PPE are demonstrated in Figures 1 and 2.

• Limit the number of professionals in the examination and report rooms.

• In case of examinations that require close contact between the professional and the patient, such as echocardiography and vascular ultrasonography, consider the use of a plastic or acrylic glass barrier.

• Limit test duration by using more objective or focused protocols. In case of patients admitted with suspected or active COVID-19, ultrasound/echocardiography examinations should be performed at the bedside, without electrocardiographic monitoring. Images should be obtained first and measurements should be performed only after the professional leaves the room and the equipment is disinfected.

• If possible, concentrate appointments of patients with suspected or confirmed COVID-19 within a specific time frame for minimizing exposure and rationalizing the use of PPE.

2.4. Equipment Maintenance

• Restrict the PPE components to those minimally necessary for performing the examination in order to reduce the need for cleaning and disinfection after the procedure, as well as the risk of contamination and cross-transmission.

• Consider the use of a protective cover for the equipment and transducer (in case of ultrasound equipment), as long as it does not hinder equipment use or prolong test duration.

• All equipment and accessories should be cleaned and disinfected after each use according to equipment disinfection guidelines. Stress tests and TEE, or examinations performed on patients with aerosol emission (in the intensive care unit [ICU], on invasive or non-invasive ventilation) require longer appointments, since disinfection should be prolonged. Cleaning and disinfection protocols are detailed on Supplementary Material.

2.5. Special Precautions for Stress Tests

Stress tests are essential in the evaluation of patients with suspected or confirmed coronary heart disease. They include exercise or pharmacological stress tests with any of the nuclear cardiology imaging modalities (single-photon emission computed tomography/positron emission tomography [SPECT/PET]), echocardiography, or cardiovascular magnetic resonance imaging (CMR). However, stress tests can increase the risk of contamination by droplets and should be deferred (for patients at low risk for COVID-19) or cancelled (for patients with suspected or confirmed COVID-19). Pharmacological stress should have preference over exercise. Once the pandemic fades , when clinically appropriate, exercise stress tests should include additional precautions, such as:[1]

Statement

Table 2 – Use of personal protective equipment during cardiovascular imaging examinations in the COVID-19 era according to exposure risks

	TTE, CCT/CMR, pharmacological stress test (Echo/SPECT/PET/CMR)	TEE, exercise stress test (Echo/SPECT/scintigraphy)
Low risk for COVID-19	Standard safety level Mandatory hand hygiene Surgical mask	Protection against aerosols:** Mandatory hand hygiene N-95/PFF2 respirator* Isolation gown (preferably waterproof) Examination gloves Surgical cap Face shield; protection goggles when face shields not available Ideally, place patients with COVID-19 in negative pressure rooms Attempt to replace examination for an alternative method
Suspected or confirmed COVID-19 cases	Protection against droplets Mandatory hand hygiene N-95/PFF2 respirator* Isolation gown Head covering Examination gloves Safety goggles	

** In case of complete unavailability of N-95 respirators or equivalents, wear a single-use surgical mask in addition to a face shield. ** Also applicable to all examinations performed with patients admitted in intensive care units (ICUs), on invasive or non-invasive ventilation. These recommendations should be followed by all personnel directly involved in the procedure (physicians, nursing technicians, technologists, etc.). CCT: cardiovascular computed tomography; CMR: cardiovascular magnetic resonance imaging; Echo: echocardiography; PET: positron emission tomography ; SPECT: single-photon emission computed tomography; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.*

Figure 1 – *Sequence for donning personal protective equipment.*

Figure 2 – *Sequence for doffing personal protective equipment.*

• Assess the facility's air circulation patterns – consult with the engineering department on optimized equipment/staff. Given the uncertainty regarding the aerosol generating capacity of a stress test, an exclusive room should be used for exercise tests, if possible, with negative pressure.

• Avoid manual blood pressure measurement, if possible. Automatic blood pressure measurement is commonly used and reasonably precise both in stationary patients or those subjected to pharmacological stress.

• The supervising team should keep a distance (2 meters) from the patient, when possible.

• All staff involved in the test should wear a face shield (particularly during exercise stress echocardiography) and gloves, in addition to the PPE required for all examinations.

• When possible, the patient should be encouraged to wear a mask while exercising.

• If exercise is deemed necessary, consider testing for COVID-19 before the test.

•A careful choice of exercise protocol should be made since longer exercises increase the duration of patient-team interaction. The bicycle protocol is associated to lower levels of peak minute ventilation.

2.6. Special Precautions for TEE

Among all the echocardiography modalities, TEE is probably the one with the highest risk of health care team contamination due to the handling of the patient's airways, contact with fluids, close contact between the patient's mouth and the professional, and to the cough reflex that can happen during the probe passage towards the esophagus. Indications for this test should thus be carefully evaluated, and the highest precaution level is recommended (even for tests performed in the operating room or in patients that do not have suspected or confirmed COVID-19) [2,3,8,12,13] (see Table 2). Ideally, TEE should be performed in an exclusive room containing protective covers for the echocardiography equipment (isolation or waterproof covering) and for all the necessary equipment, in addition to a strict and lengthy disinfection protocol for environmental surfaces between each test (approximately 1 hour).

2.7. Special Precautions for Pediatric Echocardiography

Considering that children have a higher possibility of being infected with COVID-19 and be asymptomatic or show minimum symptoms, the triage measures that apply to adult patients can be insufficient, requiring adjustments in outpatient or inpatient echocardiography. In case of an active and cooperative patient, the echocardiography physician should preferably be the only person in contact with the child. Children under 2 years old have difficulties wearing masks, which leads to a higher risk of exposure to the virus. In addition to the main form of transmission of SARS-CoV-2 (through respiratory droplets), transmission through fomites has been assumed plausible.[14] Therefore, diaper changes should be avoided, if possible, during the examination and if necessary, performed with adequate hygiene. Due to the higher risk of an asymptomatic form of COVID-19 in children, some facilities located in endemic regions choose to test new pediatric hospital admissions for SARS-CoV-2.

2.8. Special Precautions for Fetal Echocardiography

In facilities where fetal echocardiography (FE) is performed within the cardiology sector, pregnant women should be separated from pediatric patients, both in waiting and procedure rooms. Differently from previous viral outbreaks (H1N1, SARS-CoV, MERS-CoV), which were associated to severe complications in pregnant women, current information (although limited) suggests that these patients are not more susceptible to SARS-CoV-2 infections or, if infected, are not more prone to developing severe complications.[15] However, given the uncertainty and possibility of an increase in risk as new data become available, the CDC alerts that pregnant women should protect themselves. Up to one accompanying person is allowed; for reducing exposure, the echocardiography room should ideally be occupied only by the pregnant patient and the examining physician.

3. Echocardiography in Adult Patients in the COVID-19 Era

Echocardiography is the first-line method in the diagnosis, prognostic evaluation, and therapeutic guidance of various cardiovascular diseases. During the new coronavirus outbreak, it remains a crucial imaging method, mainly due to its portability in comparison to other methods; this allows bedside examinations for isolated and/or critically ill patients.[13] However, since it entails a close contact between the physician and the patient, echocardiography poses a high risk of infection by COVID-19.[10]

3.1. Prioritization and Indications for Transthoracic Echocardiography in Adult Patients at Low Risk for COVID-19

Even in patients at low risk for COVID-19, the reintroduction of outpatient examinations should be progressive, considering priority criteria and the phase of the pandemic (see Table 1).[10,11,13] Next, we describe indications for each priority level.

3.1.1. High-priority Examinations (Essential Procedures)

• Individuals with acute cardiovascular symptoms or with recent worsening. Examples: New York Heart Association (NYHA) class III or IV heart failure, probable cardiac syncope, chest pain, arrhythmias, stroke, suspected acute valvular heart disease (mitral or aortic regurgitation), acute symptoms in patients with a prosthetic heart valve, or suspected symptomatic severe aortic stenosis with no previous diagnosis.[7]

• Evaluations before urgent clinical therapy, even in asymptomatic patients. Examples: baseline echocardiography prior to the initiation of chemotherapy or evaluation of left ventricle ejection fraction (LVEF) prior to implantation of a cardioverter defibrillator for primary prevention.

• Planning of urgent cardiovascular intervention: mitral valve repair, transcatheter aortic valve replacement (TAVR), left atrial appendage occlusion.

• Safety monitoring of clinical therapy. Example: chemotherapy follow-up in patients at high risk for cardiotoxicity, even if asymptomatic.

• Follow-up after recent invasive or surgical therapy. Example: suspected pericardial effusion after device implantation or heart surgery, even if asymptomatic.

• Suspected infective endocarditis with a high pre-test probability.

• Suspected pericardial disease or progression of pericardial effusion.

Indications for urgent (or high-priority) echocardiography in hospitalized patients are generally the same as before the pandemic (mechanical complications after acute myocardial infarction, tamponade, aortic dissection, and others).

3.1.2. Medium-priority Examinations

• Monitoring of the progression of chronic myocardial disease or asymptomatic severe chronic valvular disease. Examples: cardiomyopathy, aortic stenosis, primary mitral regurgitation, prosthetic valve dysfunction.

• New symptoms in patients with known heart or lung disease.

• Heart failure with reduced LVEF (HFrEF), when LVEF requires medical therapy or device implantation.

• Assessment before a routine procedure or therapy. Example: non-urgent surgery.

• Monitoring of therapy results. Example: treatment of regressing dilated cardiomyopathy or heart transplant rejection, Takotsubo syndrome (stress cardiomyopathy), Kawasaki disease, right ventricular (RV) dysfunction after pulmonary embolism (PE), pericardiocentesis, assessment of ventricular assistance device.

• Initial assessment of new unexplained heart murmur.

These examinations can be reintroduced in areas where the pandemic is waning .

3.1.3. Low-priority Examinations

These are elective examinations, requested annually or every two years for the follow-up of patients with asymptomatic chronic diseases or who have not shown changes in their health state, where the test result will not change treatment and/or short-term outcome. These examinations can be deferred to when virus transmission is reduced or restrictions are suspended or made flexible, especially if the patient has been subjected to echocardiography in the last 12 months.[16]

3.2. Prioritization and Indications for Transthoracic Echocardiography in Adult Patients with Suspected or Confirmed COVID-19

From a cardiovascular point of view, patients affected by SARS-CoV-2 can display evidence of myocardial dysfunction (both left and right), vascular alterations, arrhythmias, thromboembolic phenomena, and pericardial effusion.[4]

Therefore, echocardiography can also contribute to the clinical assessment of patients with COVID-19, in the following situations:[2,3,17-20]

• Incapacitating dyspnea. Dyspnea is very common in patients with pneumonia secondary to COVID-19 (a situation where troponine levels are also increased, possibly leading to a false hypothesis of myocarditis). In this case, normal levels of B natriuretic peptide (BNP), even with elevated troponine, can exclude the need for echocardiography. Lung ultrasonography, in experienced hands, can help in the differential diagnosis between heart failure and pneumonia.

• Patients with previous heart disease with changes in hemodynamic state or signs and symptoms of disproportionate involvement of the lungs.

• Cardiomegaly on chest X-ray.

• Clinically significant arrhythmias or those with abrupt beginnings.

• Chest pain with electrocardiographic alterations and/or elevated troponin levels. In case of strong myocarditis suspicion and if CMR is indicated as crucial for the treatment, echocardiography can be initially omitted.

• Hemodynamic instability, respiratory failure, and/or shock of uncertain etiology.

• Suspected pulmonary hypertension and/or right ventricular dysfunction.

In difficult acoustic windows, the use of an echocardiographic contrast agent can be employed to ensure test results, reduce test duration, and avoid inadequate diagnosis or other unnecessary tests.[21,22]

In patients with COVID-19, the examination should be focused on the clinical question. Serial echocardiography should be avoided unless there is clear change in the clinical state (hemodynamic instability). However, in the ICU, the echocardiogram is frequently used for monitoring the progression of critically ill patients, especially regarding fluid management. In this case, a focused ultrasound or focused echocardiography can be used. Protocols for these cases are described below.

3.3. Protocols for Transthoracic Echocardiography in Adult Patients in the COVID-19 Era

3.3.1. Focused Echocardiography

This examination is focused on the clinical question, but is sufficiently complete for including all clinical hypotheses. The protocol should be performed by echocardiographers in individuals with COVID-19 without electrocardiographic monitoring, and include the assessment of the following parameters: [2]

• Left ventricle: quantitative assessment of global systolic function (ejection fraction), signs of regional myocardial dysfunction, and cavity size.

• Right ventricle: assessment of global function, fractional area change (FAC) or tricuspid annular plane systolic excursion (TAPSE), cavity size, and tricuspid regurgitation velocity and pressure gradient, if possible.

Table 3 – Prioritization of CCT indications during the COVID-19 pandemic

	Low-priority indications	Medium-priority indications	High-priority indications (consider performing in the next hours or in up to 2 to 4 weeks)
CAD	Calcium score in asymptomatic patients		Acute chest pain with high enough suspicion of CAD
	Stable chest pain without high suspicion of CAD		Stable chest pain with high risk of cardiovascular events, or when high-risk anatomy is suspected
Structural cardiac disease	Patients with stable structural cardiac disease (TAVR, TMVR, LAA occlusion, together with the Heart Team)		Patients requiring urgent structural intervention (TAVI, TMVR, LAA occlusion)
Atrial fibrillation	Assessment of pulmonary veins for planning atrial fibrillation ablation	Evaluation of the left atrial appendage in **chronic** atrial arrhythmia before restoring sinus rhythm	Evaluation of the left atrial appendage in **acute** atrial arrhythmia before restoring sinus rhythm
Heart failure	Investigation of CAD as cause of heart failure in patients with stable cardiomyopathy		Hospitalized patient with acute cardiomyopathy and low or intermediate probability of CAD, where CCT can change management
			Evaluation of left ventricular assist device malfunction
Valvular	Assessment of aortic stenosis severity	Subacute or chronic prosthetic valve dysfunction	Acute and symptomatic prosthetic valve dysfunction, endocarditis, perivalvular extension of endocarditis or possible abscess
Masses/ congenital	Suspected benign cardiac masses or those unlikely to require biopsy or surgical planning		New suspected malignant cardiac masses or those requiring biopsy or surgical planning
	Elective assessment of congenital anomaly		Ruling out left ventricle thrombus after inconclusive echocardiography, when alternative methods (magnetic resonance) are not available

CAD: coronary artery disease; TAVR: transcatheter aortic valve replacement; TMVR: transcatheter mitral valve replacement; LAA: left atrial appendage; CCT: cardiovascular computed tomography.

• Valves: basic anatomical assessment and color Doppler; in case of signs of dysfunction, evaluate further.

• Pericardium: assessment of thickening or effusion.

3.3.2. Focused Ultrasound – Indications, Protocols, and Main Findings

The focused ultrasound, also known as point-of-care cardiac ultrasound, is widely used as a support tool in the diagnosis, management, and monitoring of patients with COVID-19.[23] The biggest advantages of this technique in patients with COVID-19 include its general availability in urgency/emergency settings and ICUs, its high diagnostic accuracy, and the wide range of clinical information that can be obtained through this examination. The focused ultrasound is also easily performed as a bedside examination – avoiding patient transportation to the radiology service and virus spread within the hospital. This test can be performed both with conventional ultrasound equipment or with portable or ultraportable (pocket-sized) devices; these are preferred due to easier disinfection and bedside use. All personal and equipment protective measures previously described should be performed. Among the applications of focused ultrasound in patients with COVID-19, we highlight lung and cardiac ultrasonography.

3.3.3. Focused Lung and Pleural Ultrasonography

Lung ultrasound (LUS) represents a fast alternative for evaluating the degree of pulmonary involvement and monitor the result of therapeutic interventions at the bedside. The diagnostic accuracy of LUS is similar to that of chest computed tomography (CT) in patients with respiratory complaints such as dyspnea and hypoxemia (85% sensitivity, 93% specificity for non-COVID-19 pneumonia).[24] Normal LUS findings have also presented an excellent correlation with chest CT results with no alterations of lung parenchyma such as ground-glass opacities. Therefore, LUS presents a high negative predictive value, allowing its use in patient risk stratification.[25] In addition to diagnosis and initial risk stratification, LUS is being widely used in the monitoring of critically ill patients COVID-19.[26] It contributes to decision-making on prone ventilation, extracorporeal membrane oxygenation (ECMO), and weaning from mechanical ventilation in acute respiratory failure.[27] LUS is also useful for ruling out other pathologies such as pneumothorax, which can occur in individuals on positive pressure ventilation.

Various LUS protocols are described in the literature. Regarding patients with COVID-19, at least 6 regions should be assessed in each hemithorax: anterior, anterior axillary

and posterior axillary regions above and below a line at the fourth intercostal space. Since COVID-19 lung affections are bilateral, multifocal, and not necessarily uniform, we highlight the importance of not focusing on specific areas of the thoracic wall and recommend a full chest assessment.[28,29] LUS findings in patients with COVID-19 are able to monitor the progression and extension of pulmonary affections identified by the chest CT and are described in Figure 3. Notably, pleural effusion is not a common finding of COVID-19, hence it indicates a low probability of SARS-CoV-2 infection. Throughout the recovery period, the lungs gradually return to normal; ultrasound assessment indicates that subpleural consolidations disappear, the pleural line normalizes, and A-lines reappear.[30]

3.3.4. Focused Cardiovascular Ultrasound

Focused cardiovascular ultrasound is being used by emergency physicians or intensivists for rapid assessment and screening for pre-existing cardiac and vascular diseases, as well as in the early detection of COVID-19-related myocardial alterations.[23] The objective of this ultrasound is to quantitatively assess left ventricular systolic function, right ventricular size and contractility, inferior vena cava size and collapsibility, in addition to severe vavular abnormalities and pericardial effusion.29 (Figure 4). A brief screening of patients with COVID-19 is indicated in the presence of high troponin and BNP in addition to electrocardiographic or hemodynamic changes, or in the case of suspected PE.31 In this case, one of the main advantages of focused ultrasound is that it reduces the need for conventional echocardiography, thus also decreasing the physicians' exposure and the need for equipment decontamination while also saving PPE. This examination is not equivalent to echocardiography, but it is capable of confirming or excluding a specific diagnosis during a quick bedside evaluation, thus contributing to therapeutic decisions. The focused ultrasound can also be used in the triage of patients that need echocardiography. On the other hand, without proper training, there is a risk of acquiring inadequate images that lead to false positive or false negative diagnoses. This could in turn result in unnecessary treatments that can be harmful, in inappropriate echocardiography indications, or in treatment delays. Therefore, the use of focused cardiac ultrasound should be based on institutional protocols, and we recommend an internal competence-

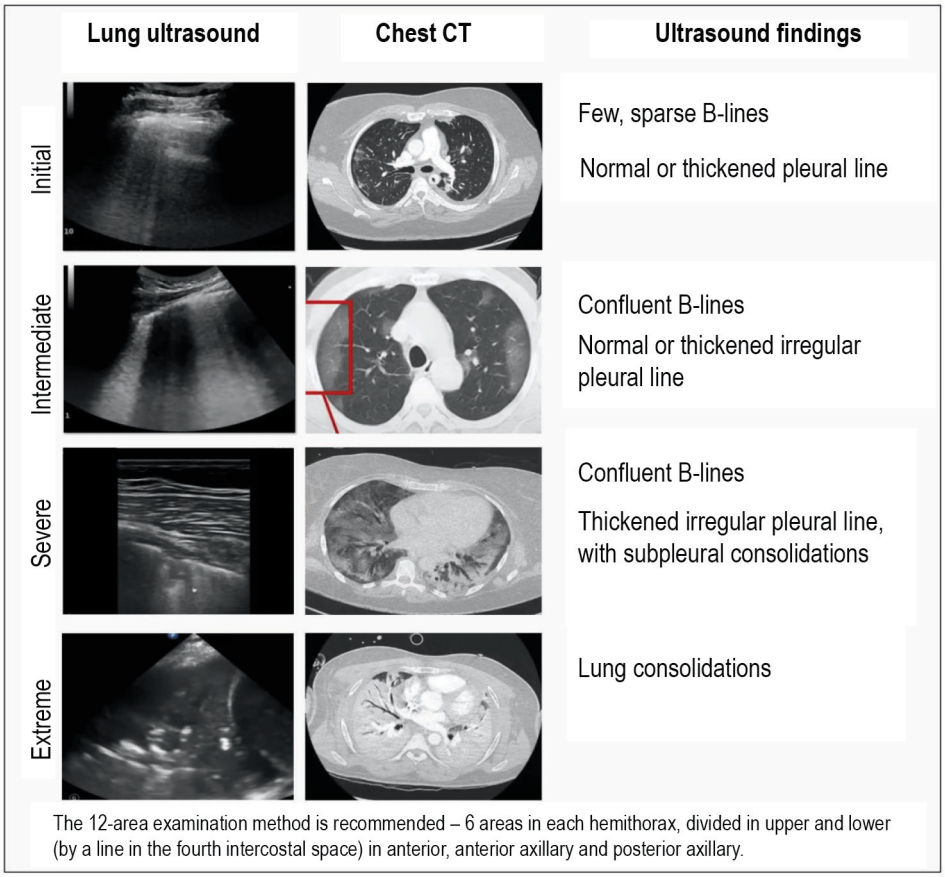

Figure 3 – *Lung ultrasound findings in patients with COVID-19 and their correlation with disease severity and tomography findings*

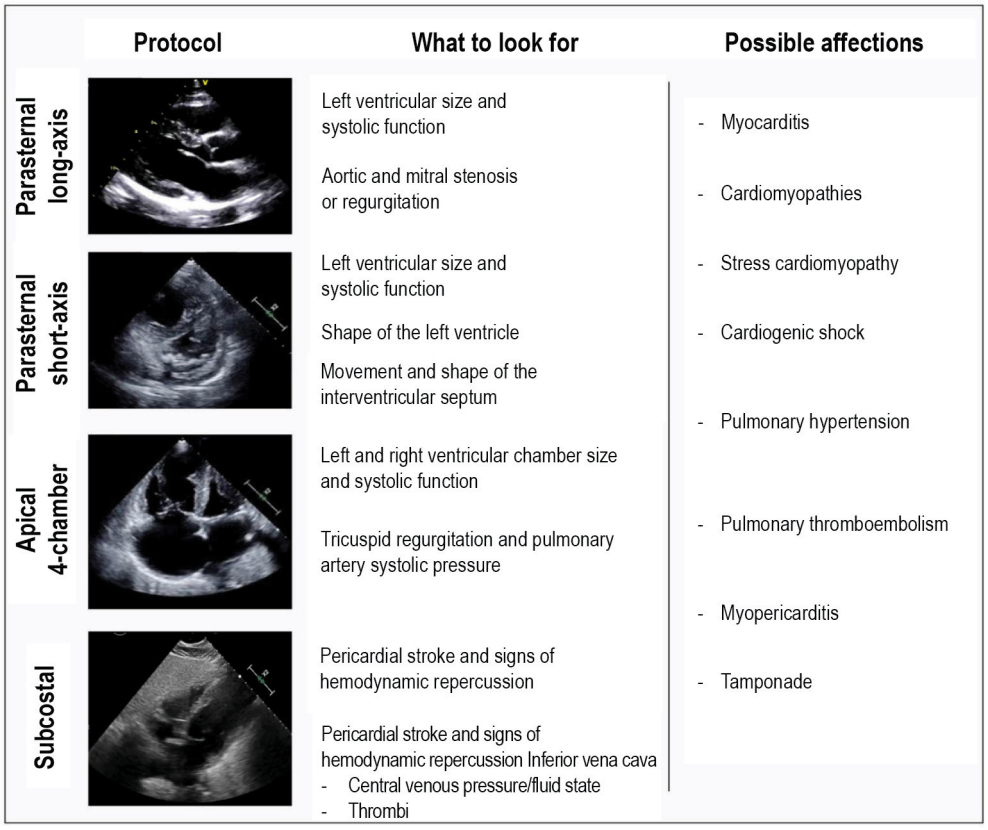

Figure 4 – *Protocols for the focused cardiovascular ultrasound. Windows, main findings, and possible diseases.*

based certification as well as constant quality assessments, considering that teaching and training methodologies for this method vary greatly.

Integrated (lung and cardiac) focused ultrasound is ideal for adequate characterization of volume status, subjacent ventricular function, monitoring of fluid state, and titration of vasopressor drugs in case of inotropic support. In patients with RV dysfunction, focused vascular ultrasound for investigating deep vein thrombosis (DVT) can complete the assessment.

3.4. Prioritization and Indications for Stress Echocardiography in the COVID-19 Era

In patients at low risk for COVID-19, with proper indication and when deferring is not possible or recommended (such as in preoperative cancer patients or those with a high pre-test probability of obstructive coronary artery disease [CAD]), pharmacological stress tests are preferred because they are not considered aerosol-generating. Another alternative for investigating selected cases of chronic coronary arterial disease during the pandemic is to prioritize computed tomography (CT) coronary angiography.[10] Once a very low local prevalence of COVID-19 is reached, exercise echocardiography can return to being the first choice, but with additional safety procedures as previously described.

3.5. Prioritization and Indications for Transesophageal Echocardiography in Adult Patients in the COVID-19 Era

TEE causes additional concern, since the risk of equipment and professional contamination through droplets and aerosols is very high. Therefore, the incremental value of TEE in relation to transthoracic echocardiography (TTE) should be carefully evaluated on a case-by-case basis together with the assistant physician. For the duration of the pandemic, alternative methods should preferably be chosen, especially in patients with COVID-19.[2,12] One of the main indications for TEE — screening for intracavitary thrombi — can be performed through CT angiography, which presents a lower risk of staff contamination. This alternative is obviously only available for patients who can be transported and with preserved renal function. Whenever possible, complete diagnosis should be achieved through TTE, leaving TEE for critical situations with possible changes in management, especially in the ICU or operation

room where no other methods are available and the clinical question should be promptly answered. In areas where the pandemic is decreasing, the reintroduction of TEE for outpatients should follow strict criteria, and each case should require an individual evaluation. It is recommended that outpatient scheduling be restored based on patient priority, considering one's previous position on the waiting list, clinical indications and conditions (symptomatic or asymptomatic), and potential impact of the examination in the patient's clinical history (for example, tests required for further procedure scheduling).[2,12,13] Additional measures for TEE scheduling and test safety are described in Table 2. Among the various indications for TEE, high priority is given to the following:[32]

• Infective endocarditis with valvular or paravalvular involvement.

• Type A aortic dissection (Stanford) in unstable patients (if stable, prefer CT; if associated with suspected aortic insufficiency, perform TTE).

• Beginning of mechanical circulatory support.

• Acute myocardial infarction with suspected mechanical complications not detected by TTE (ventricular septal defect, left ventricular free wall rupture, or papillary muscle rupture).

• Prosthetic valve dysfunction poorly defined in TTE or CT.

• Monitoring of patients on venovenous ECMO for treating COVID-19 pneumonia.

• Intraoperative evaluation of the result of mitral valve repair, septal myectomy, or in the diagnostic and management of complications.

• Hemodynamic instability due to undifferentiated shock in individuals with inadequate acoustic windows for TTE (such as those in the perioperative period of cardiac surgery or on prone ventilation).

• Screening for thrombi in the left atrial appendage prior to electrical cardioversion for restoring sinus rhythm in an unstable patient or with unavailable cardiovascular computed tomography (CCT) (CCT with low contrast infusion is the first choice for patients with COVID-19).

TEE is not recommended in the following cases:

• Screening for infective endocarditis in patients with transient fever and no bacteremia or new heart murmur.

• Transient bacteremia with identified pathogen not typically associated to infective endocarditis or with documented non-endovascular source of infection.

• Re-evaluation of a previous echocardiogram in stable individuals when no changes in therapy are being considered.

4. Pediatric, Congenital, and Fetal Echocardiography in the COVID-19 Era

The echocardiographic examination in children can result in increased risk for the staff and community, considering that although these patients have a reduced occurrence of severe COVID-19, many infected children can be asymptomatic or minimally symptomatic. In addition, pediatric care requires the company of an adult, thus demanding adjustments in specialized care. Since the pediatric population with congenital heart defects is different from the corresponding adult one regarding the risk of COVID-19 transmission and indications for echocardiography, the aim of this topic is to update indications and protocols for TTE and FE in this population.

4.1. Prioritization and Indications for Transthoracic Echocardiography in Pediatric and Congenital Patients

Within the pediatric age group and considering patients with congenital heart defects, absolute indications include suspected congenital heart defect, postoperative and preoperative evaluation of congenital heart defects, children with acquired heart disease, heart transplant, increased risk of impaired cardiac function (chemotherapy treatment), and cardiac complications associated with respiratory infections.[33,34] These indications should be categorized as high, medium, or low priority, as demonstrated in Table 2, when reintroducing examinations at the outpatient level according to the hemodynamic repercussions and clinical reasoning.

4.2. Optimization of the Transthoracic Echocardiography Protocol in Pediatric and Congenital Patients

TTE should be performed in the usual manner due to the wide anatomical variability and challenges regarding the evaluation of systolic and diastolic function, thus leaving focused assessment for other applications such as the emergency sector, pediatric intensive care, and in suspected of confirmed COVID-19 patients. In case of a potentially complicated examination, the patient should be referred to a more experienced physician; this increases the probability of an adequately detailed, precise, and quick examination without the need for additional practical support. Recently, an alert regarding multisystem inflammatory syndrome in children and teenagers has been released; this disorder has been described as a generally late clinical presentation associated with COVID-19, characterized by similar manifestations to those of the typical or incomplete Kawasaki syndrome and/or septic shock syndrome.[35] The most affected age range includes school-age children (mean age 9 years), which differentiates this disorder from the Kawasaki syndrome; symptoms are predominantly gastrointestinal. Virtually 100% of cases have heart affections with LVEF impairment, which has been described by various groups. In addition, patients present cardiogenic shock and coronary artery involvement with variable degrees of dilation, and some groups have reported aneurysms. Respiratory symptoms are mild, and skin rash and mucosal involvement may also occur.[35,36] In case of clinical suspicion of multisystem inflammatory syndrome in children and teenagers, the main objectives of echocardiography are to identify possible left ventricular dilation, measure systolic function through LVEF, quantify the valvular regurgitation, evaluate the morphological aspect of coronary arteries (dilation and/or aneurysm), and pericardium.

4.3. Prioritization and Indications for Fetal Echocardiography

FE assessment faces challenges in the final stage of pregnancy where perinatal and neonatal planning and decision-making are required. At first, patients with low-risk pregnancies were instructed to not perform FE; those with moderate-risk pregnancies should defer FE for when the COVID-19 risk was reduced or until 28 weeks of pregnancy; finally, women with high-risk pregnancies should promptly schedule and perform the examination.[15] However, as the pandemic progressed, considering that pregnancies would continue and fetal cardiac diseases can be critical, we recommend that FE be performed according to the previously published guidelines.[37,38] The examination should be performed following PPE protocols for the pregnant patient and health care professional. Echocardiographic assessment should be as complete as possible, avoiding re-evaluations.

The possibility of prenatal or perinatal infection should be considered when newborns are transferred to the pediatric or cardiac neonatal intensive care unit after birth. Data on the vertical transmission of SARS-CoV-2 are still scarce;[39,40] however, if the new mother tests positive for the virus in the 14 days after birth, the newborn should also be tested and managed as a positive case until a negative result is confirmed.

Echocardiographic tests in the pediatric population and in patients with congenital heart defects remain crucial during the SARS-CoV-2 pandemic and their health care should be guaranteed, minimizing risks for the professional team, patients, and the general public.

4.4. Prioritization and Indications for Transesophageal Echocardiography in Pediatric Patients

In patients with congenital heart defects, TEE is considered a part of intraoperative care and hemodynamic interventions. In outpatient cases, considering the high risk of exposure to SARS-CoV-2, this examination should be deferred or substituted for an alternative modality such as TTE associated with agitated saline contrast, cardiovascular computed tomography (CCT) or CMR with contrast agents. As for children, the risks and benefits of aerosol-emitting procedures should be weighed along with those of patient transportation, disinfection of the CCT/CMR room, contrast administration or radiation in CCT, in addition to prolonged exposure in case of CMR.

4.5. Protocol for Transesophageal Echocardiography in Pediatric Patients

Due to the unreliability of using symptoms in the prediction of COVID-19 status in children, a specific recommendation has been proposed for TEE in these patients:[15]

1. All pediatric patients should be considered positive for COVID-19 in TEE, unless with negative tests in the last 48 to 72 hours. In case of a negative test, TEE can be performed using standard precautions (gloves, mask, and eye protection).

2. In pediatric patients without negative COVID-19 tests in the last 72 hours, who were intubated before arriving to the operation room, the risk of producing aerosols is considered low. The probe can be introduced by the anesthesiologist or examining physician, according to the institution's standard procedures and precautions.

3. In asymptomatic patients without negative COVID-19 tests in the last 72 hours who require intubation in the operation room, this procedure should be performed by the anesthesiologist using appropriate PPE and air purifying respirators. This process should be followed by a 20- to 30-minute waiting period, depending on local protocols and environmental factors, for allowing complete room air exchange. During this period, people should not be allowed in the room. The TEE probe should ideally be introduced by the anesthesiologist immediately after airway stabilization for minimizing the exposure of other professionals. After the waiting period, the examining physician can manipulate the probe according to standardized procedures and precautions.

4. Children with positive COVID-19 tests or with symptoms should be isolated. Probe introduction by the anesthesiologist is strongly advised for minimizing the exposure of other professionals. The team of health care professionals in the operation, recovery, or procedure rooms should use strict isolation equipment at all times and be trained in PPE donning and doffing. Only essential personnel are allowed in the operation room (only one echocardiography physician) for reducing exposure risk and saving PPE.

5. Vascular Ultrasonography in the COVID-19 Era

One of the situations requiring the biggest caution in patients infected by the SARS-CoV-2 virus is the development of coagulopathies, mostly characterized as a tendency for venous, arterial, and microvenous thrombosis. Klok et al.[31] evaluated the incidence of venous thromboembolism (VTE) and arterial thrombotic complications in 184 patients with COVID-19 admitted to an ICU. Despite the VTE prophylaxis performed in all patients, a 31% incidence of thrombotic complications was observed.[31] Accordingly, there was an increase in demand for vascular ultrasonography (VUS) during the pandemic, especially for the venous VUS in patients with COVID-19, most of which were hospitalized. For this reason, a deeper discussion on this examination is performed below.

5.1. Prioritization and Indications for Vascular Ultrasonography in Patients at Low Risk for COVID-19

Considering outpatients without COVID-19, the types of examinations should be categorized according to indication priority (see Table 1). High-priority (essential) examinations include venous VUS for DVT screening, as well as the carotid and vertebral artery VUS in patients with suspected stroke. Considering patients with peripheral obstructive disease, a priority for arterial VUS should depend on surgical treatment indications.

Other examinations should be categorized as medium or low priority by the assistant physician, as long as there are no indications for urgent invasive treatments. These include VUS of the aorta and its branches, VUS for varicose vein assessment, and carotid artery VUS in screening for carotid artery disease in the preoperative period of cardiac surgery.

5.2. Prioritization and Indications of Vascular Ultrasonography in Patients with COVID-19

• Suspected pulmonary thromboembolism (PTE): VUS has a low accuracy in diagnosing PTE, but can be indicated in case of high bleeding risk, when the result should change management, or when PTE suspicion is high and there is no available CT angiography.[41]

• Suspected DVT: In individuals with high clinical suspicion of DVT and bleeding risk, lower limb venous VUS is recommended.[41]

• Suspected acute arterial occlusion of upper or lower limb (arterial VUS).

• Stroke of unknown cause (carotid and vertebral artery VUS).

5.3. Situations Where Vascular Ultrasonography is Not Recommended for Patients with COVID-19

Venous VUS should not be used as a marker for altering a patient's anticoagulant therapy management.

Laboratory tests cannot indicate the need for this examination; hence, high D-dimer values do not justify VUS for DVT screening. In case of negative D-dimer results, there is no need for VUS in DVT screening.

Upper limb DVT has low morbidity in critically ill patients, thus there is no routine recommendation for venous VUS in this region.

In conclusion, VUS is not recommended in situations where its results will not determine changes in management or are not a prerequisite for urgent surgery.

5.4. Optimization of Vascular Ultrasonography Protocols

The complete venous VUS protocol is the recommended method for investigating DVT; however, point-of-care 3- or 2-point compression ultrasound in critically ill inpatients with COVID-19 seems to be a reasonable option, except if the pain reported by the patient is located in the infrapatellar segment (then, the complete protocol should be performed). The 3-point protocol assesses compressibility in all proximal veins of the evaluated lower limb. The 2-point protocol evaluates the compressibility of the common femoral vein 1 to 2 cm above and below the saphenofemoral junction (in the inguinal fold) and in the popliteal vein up to the confluence of the leg veins.[42] Total or partial absence of compressibility in the affected vein, as well as vascular swelling due to an intraluminal thrombus detected by 2-dimensional techniques , are ultrasonographic signs of DVT. The sensitivity of the 3-point compression method is considered greater than that of the 2-point method (90.57% vs 82.76%), with similar specificity (98.52%).[43]

In addition to a shorter exposure period for the professional, the point-of-care VUS protocol can be performed by the emergency physician, provided proper training is involved. After the pandemic, when possible, the complete protocol should be given preference.

Other VUS examinations, such as the carotid and vertebral artery VUS and limb arterial VUS, when necessary, should follow previously established protocols.[44] All protective and PPE measures should be followed as previously discussed.

6. Cardiac Magnetic Resonance in the COVID-19 Era

6.1. Prioritization and Indications

The COVID-19 pandemic caused an important reduction in the number of outpatient requests for CMR, leaving only high-priority examinations: Clinical suspicion of myocarditis, differential diagnosis of cardiac masses, as well as other exceptional situations such as the assessment of complex ventricular arrhythmias.

CMR is well-defined as the preferred method for the reliable assessment of ventricular function, cardiac volumes, ischemia, myocardial viability, as well as in the detection of areas of myocardial fibrosis, study of infiltrative and deposition diseases, structural evaluation of patients with cardiac arrhythmias, and in specific cases, for complementing the echocardiographic evaluation of valvular and congenital heart diseases. In patients with low risk for COVID-19, prioritization should follow the rationale presented in Table 1. CMR has the advantage of providing, with one test, a global assessment of the heart with multiple functional and structural data, thus avoiding multiple trips to the hospital or clinic; this reduces patient circulation and optimizes resources.[45] In patients with COVID-19, CMR allows the diagnostic of myocarditis, perimyocarditis, acute myocardial infarction with no evidence of obstructive coronary artery disease (MINOCA), Takotsubo syndrome, and the differentiation between ischemic and inflammatory presentations. Conversely, the patient's risk of transmission and instability in the acute phase should be carefully evaluated and the examination could be deferred, whenever possible, until the criteria for cure are attained. On the other hand, a recent study evaluated myocardial injury in patients who had recovered from COVID-19 and showed a high prevalence of nonischemic delayed myocardial enhancement and preserved systolic function, already with no evidence of edema, suggesting permanent myocardial damage.[46] CMR can thus be an important tool for better comprehending the mechanisms of myocardial injury and for assessing myocardial damage after recovery from COVID-19.

6.2. Optimizing Cardiac Magnetic Resonance Protocols

CMR protocols should be reduced (maximum 30 minutes) for all clinical indications; the focus should be on evaluating myocardial function through cine magnetic resonance imaging (MRI), while myocardial tissue characterization should be performed through late gadolinium enhancement. A T2 weighted anatomical sequence can be performed for detecting myocardial edema in case of suspected acute myocardial inflammation. When available, T1, T2, and/or T2* mapping associated with cine MRI sequences and late enhancement

constitute an optimized and efficient protocol.[11] When evaluating myocardial ischemia, the physician should focus on perfusion sequences under pharmacological stress, subsequently adding cine and late enhancement sequences after stress. CMR can also be employed in the diagnosis of intracavitary thrombi, with a fast and directed study using late gadolinium enhancement and avoiding the need for TEE, thus reducing the examining physician's exposure to potential contamination. The evaluation of cardiac masses is adequately performed with high sensibility using CMR and can identify benign or malignant characteristics; it is though quite limited in the diagnostic of vegetations due to their small dimensions and mobile characteristics. Mass characterization should follow the routine protocol, which uses cine MRI sequences, T1 weighted anatomical sequences with or without fat suppression, T2, rest perfusion, and late enhancement, always focused on mass localization. Congenital diseases can have optimized assessment with the use of 3D resonance angiography associated with cine MRI sequences, and in case valve assessment is needed for complementing the echocardiography, ventricular function assessment through cine MRI should be prioritized and protocols should be directed to the valvular apparatus with flow mapping sequences.[47]

7. Cardiovascular Computed Tomography in the COVID-19 Era

7.1. Prioritization and Indications

CCT can be used in the evaluation of multiple forms of heart diseases in all stages of the COVID-19 pandemic in a fast, efficient, and safe manner.[48] For this, depending on the local stage of the pandemic, the risk of exposure to the virus in the examination should be weighed with the benefit of its results for patient management and treatment.[11] Table 3 proposes the prioritization of indications during the COVID-19 pandemic.

As for indications, the main diagnostic and prognostic characteristics of CCT should be taken into consideration when making a decision:[49]

- The ability of CCT to precisely exclude high-risk CAD can prevent admissions and save resources, as well as recommend hospitalization for patients with detected disease (especially those reluctant to seeking emergency care).
- The fundamental role of CCT in the preoperative anatomical assessment of structural cardiac diseases reduces the risk of acute and chronic complications associated with interventions.
- CCT can be preferred over TEE for ruling out thrombi in the left atrial appendage and intracavitary thrombi before cardioversion, reducing chances of cough and aerosol generation related to TEE.
- In patients suspected or confirmed for COVID-19, the benefits of CCT in most clinical scenarios should not exceed the risks of exposure and infection of the personnel. Each case should be evaluated individually.

8. Nuclear Cardiology in the COVID-19 Era

Nuclear cardiology has a solid knowledge base on clinical experience, as well as diagnostic and prognostic values. All procedures in this area have the advantage of using widely automated protocols and equipment, which allows less contact between the health care professional and the patient. Moreover, except for exercise myocardial scintigraphy and ventilation/perfusion scintigraphy, no other nuclear medicine methods generate aerosols.[50] These aspects could reduce exposure to the virus and infection propagation while also saving precious resources.[51]

8.1. Prioritization and Indications

Nuclear cardiology has a superior role in the pandemic scenario considering patients without COVID-19. The rationale for prioritizing examinations should be as described in Table 2. The main indications include:[11]

- Evaluating ischemia in patients with known CAD.
- Evaluating patients with chest pain syndromes. It is particularly useful for patients who are poor candidates for non-invasive anatomical imaging (such as those with stents or coronary artery calcification, who are allergic to contrast agents, or have a risk of impaired renal function).
- Evaluation of myocardial viability.
- Screening for amyloidosis.
- Identification of the inflammatory stages of sarcoidosis.
- Identification of infections in implanted devices.

On the other hand, a nuclear cardiology assessment is generally not necessary in the treatment of acute heart disease in patients with COVID-19. Ventilation scans or exercise stress tests should be omitted in areas going through the peak phase of the pandemic and/or in any patient with a known or suspected COVID-19 infection due to the high risk of aerosol emission.[52] Specific considerations on the ventilation/perfusion scintigraphy protocol are described below.

8.2. Ventilation/Perfusion Scintigraphy

Currently, the gold standard for ruling out PE in patients with COVID-19 is the CT pulmonary angiography. However, this method cannot be used in patients with contraindications for iodinated contrast agents. A potential alternative relies in lung perfusion single-photon emission computed tomography (SPECT) using macroaggregated albumin tagged with ^{99m}Tc. Due to the high risk of aerosol production associated to ventilation scintigraphy (aerosols tagged with ^{99}mTc), the American Society of Nuclear Medicine and Molecular Imaging discouraged the classical combination of ventilation/perfusion images in patients with COVID-19.[53] Ventilation scans should be omitted in patients with known or suspected COVID-19; therefore, the use of perfusion lung scintigraphy associated with chest CT or X-ray has been proposed.[54]

For optimizing protocols amidst the pandemic, one should follow good imaging practices that allow for a safe and efficient examination, as already described; these include mainly:

• Performing protocols that minimize the procedure duration without affecting test precision, eg, only using imaging stress tests when indicated.

• Avoiding protocols that may generate aerosols – give preference to pharmaceutical stress over exercise stress whenever possible.

Figure 5 is a proposition that summarizes the general protocol for reintroducing cardiovascular imaging examinations. Firstly, it is necessary to define whether the test is essential at any given moment. If it is essential (urgent or high-priority), define whether the patient has a high risk for COVID-19 and which method would lead to the lowest risk of exposure, even with the use of PPE. In case the examination is not essential/urgent, evaluate the local stage of the pandemic: when the area is at the peak stage, defer lower priority examinations. If the pandemic is decelerating in the area in question, reintroduce test scheduling according to the patient's risk for COVID-19 and indication priority, within appropriate criteria; finally, define PPE and patient flow according to COVID-19 risk and type of test. Tables 1, 2, and 3 summarize the indication prioritization, safety protocols, and PPE to be used according to the type of test and COVID-19 status. Among cardiovascular imaging examinations, echocardiography is considered first-line. However, in view of the need for minimizing the examining physician's exposure to SARS-COV-2 and rationally using available resources, alternative methods can be used to answer the clinical question, especially in stable patients or those with uncertain symptoms or who were referred to other imaging examinations.[8]

9. Conclusion

The COVID-19 pandemic has forced the medical community to reconsider performing cardiovascular imaging examinations. Adaptations and changes were necessary due to the worldwide impact of this pandemic. The return to "normality" in cardiovascular imaging services should be progressive and adapted to regional differences within the country. Considering the impact of cardiovascular diseases in the population morbidity and mortality, cardiovascular signs and symptoms cannot be neglected. Therefore, even amid a pandemic situation where all attention is turned to fighting COVID-19, patients and physicians should be encouraged to perform cardiovascular investigations and be assured that these will happen in a safe environment. This position statement reflects the opinion of specialists based on national and international guidelines and the scientific evidence available at the moment, seeing that knowledge on COVID-19 is constantly evolving. In this environment, recommendations can guide the health care team and protect patients and professionals without compromising care. In addition, these recommendations, the constant dialog between medical imaging specialists, clinical staff, and patients constitutes the best and most efficient measure for facing the COVID-19 pandemic.

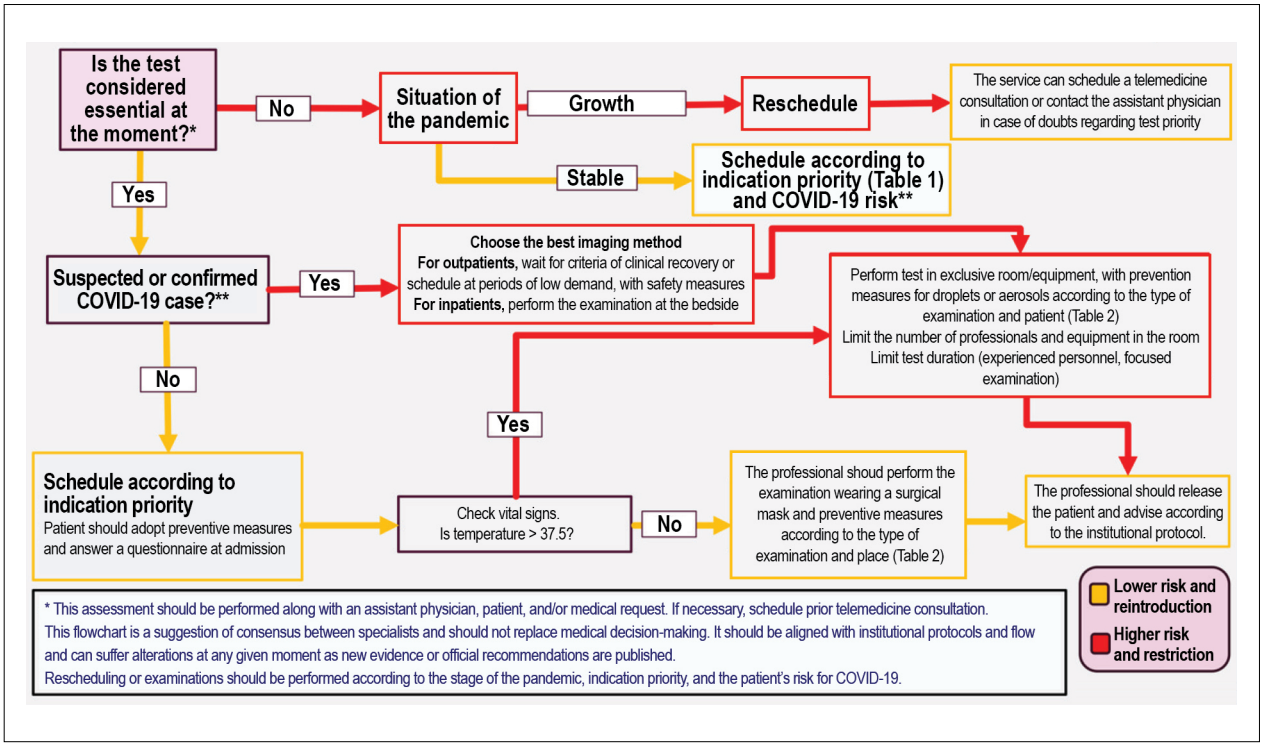

Figure 5 – *Flowchart for reintroducing cardiovascular imaging examinations in the COVID-19 era*

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Diagnostic yield of magnetic resonance imaging in heart failure with left ventricular dysfunction?

Devemos Realizar Ressonância Magnética Cardíaca em Pacientes com Insuficiência Cardíaca e Disfunção Ventricular sem Diagnóstico Etiológico Definido?

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Abstract

Background: Heart failure with reduced ejection fraction is responsible for half of heart failure cases worldwide and implicates in substantial morbidity and mortality. However, even with clinical history and physical examination associated with conventional complementary exams, many patients remain without etiological diagnosis. Cardiac magnetic resonance has offered the possibility to clarify a variable proportion of these cases.

Objective: To verify how much cardiac magnetic resonance contributes to etiologic diagnosis of heart failure with left ventricular ejection fraction <50% in a specialized service.

Methods: We included individuals referred to cardiac magnetic resonance with heart failure and left ventricular ejection fraction <50% by transthoracic echocardiogram, without defined etiology, from January, 2017 to June, 2018 in a tertiary hospital.

Results: The sample consisted of 87 patients, with average age of 45±16 years, 49% male and left ventricular ejection fraction 32%±13. Of the patients, 55,3% had etiological diagnosis through cardiac magnetic resonance: 33,4% myocarditis, 11.5% non-compaction cardiomyopathy, 6.8% Chagas disease, and for hypertensive heart disease, amyloidosis and arrhythmogenic right ventricle dysplasia, 1,2% each. Late gadolinium enhancement was positive in 61% and non-ischemic pattern predominated (50,5%). Reverse remodeling occurred with normalization of ventricular function in 13% of patients.

Conclusion: The performance of cardiac magnetic resonance in patients without etiologic diagnosis of HF with left ventricle dysfunction is clinically significant, since it contributed more than 50% of the time to the etiology and prognosis of patients. This positive impact occurred in a tertiary cardiology teaching service, so it is possible that in other circumstances the role of the cardiac magnetic resonance may be even greater than that here presented.

Keywords: Heart failure; Cardiomyopathy, dilated; Diagnostic imaging; Magnetic resonance.

Resumo

Fundamento: A insuficiência cardíaca com fração de ejeção reduzida é responsável por metade dos casos de insuficiência cardíaca no mundo e associada à morbidade e à mortalidade substanciais. Contudo, mesmo com história clínica e exame físico associados a exames complementares convencionais, muitos pacientes permanecem sem diagnóstico etiológico. A ressonância magnética cardíaca oferece a possibilidade de esclarecer esses casos.

Objetivo: Verificar em que medida a ressonância magnética cardíaca contribui com o diagnóstico etiológico da insuficiência cardíaca com fração de ejeção do ventrículo esquerdo <50% em um serviço especializado.

Métodos: Foram incluídos indivíduos encaminhados para ressonância magnética cardíaca com insuficiência cardíaca e fração de ejeção do ventrículo esquerdo <50% ao ecocardiograma transtorácico, sem etiologia definida, de janeiro de 2017 a junho de 2018, em hospital terciário.

Resultados: A amostra foi constituída de 87 pacientes, com idade média de 45±16 anos, sendo 49% do sexo masculino e fração de ejeção do ventrículo esquerdo 32%±13. Tiveram diagnóstico etiológico por meio da ressonância magnética cardíaca 55,3% dos pacientes: 33,4% miocardite, 11,5% cardiopatia não compactada, 6,8% cardiopatia chagásica e 1,2% para cardiopatia hipertensiva, amiloidose e displasia

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arritmogênica do ventrículo direito, cada. O realce tardio miocárdico foi positivo em 61%, e predominou o padrão de realce tardio não isquêmico (50,5%). Houve remodelamento reverso com normalização da função ventricular em 13% dos pacientes.

Conclusão: O rendimento da ressonância magnética cardíaca em pacientes sem diagnóstico etiológico da insuficiência cardíaca com disfunção ventricular é significativo do ponto de vista clínico, pois contribuiu, em mais de 50% das vezes, com a etiologia e o prognóstico dos pacientes. Esse impacto positivo ocorreu em serviço terciário e de ensino em cardiologia, sendo possível que, em outras circunstâncias, o papel da ressonância magnética cardíaca seja inclusive maior do que o aqui apresentado.

Palavras-chave: Insuficiência cardíaca; Cardiomiopatia dilatada; Diagnóstico por imagem; Ressonância magnética.

Introduction

Heart failure with reduced ejection fraction (HFREF) is responsible for half of the cases of hospitalization for heart failure (HF). Ischemic heart disease is the main cause of HFREF, but several other conditions can result in systolic ventricular dysfunction.[1-6] The initial evaluation (physical, laboratory, and echocardiography) elucidates the cause in most cases, but many patients remain undiagnosed and are often classified as having idiopathic dilated cardiomyopathy (IDC).[7]

IDC is defined as left ventricular (LV) dilation and systolic dysfunction with no coronary artery disease (CAD) or abnormal ventricular overload.[1] The social and economic impact of adverse events caused by this cardiomyopathy is amplified by more often affecting people in the first few decades of life.[2] In this context, the establishment of a defined etiology can not only drive different therapeutic management, it can also provide prognostic information for the patient, family, and society.

Cardiac magnetic resonance (CMR) imaging can determine the etiology of certain cardiomyopathies through morpho-functional evaluation and delayed gadolinium enhancement (DGE) presence and pattern.[8-11] The detection of a nonischemic DGE pattern can exclude coronary angiography, saving resources and avoiding complications inherent to an invasive procedure with significant potential for contrast nephropathy. This screening may be even more relevant in HFREF patients since more than half have no significant CAD.[3,4]

This study aimed to evaluate the potential contribution of CMR in the diagnosis of HF with systolic ventricular dysfunction without a defined etiology in a referral hospital for cardiovascular diseases.

Methods

This study involved the retrospective selection of all CMR examinations performed between January 2017 and June 2018 at Ana Nery Hospital, a tertiary reference center of the Unified Health System in Salvador, BA, Brazil. This service has a Medical Residency Program in Cardiology. The study population consisted of patients with HF and an ejection fraction < 50% (previously determined on transthoracic echocardiography [ECHO]), with no etiology defined at the initial evaluation who were referred to the CMR for diagnostic research (Figure 1).

The exclusion criteria were known history of CAD, myocardial infarction, or previous revascularization; primary valve disease; known history of hypertrophic cardiomyopathy or congenital heart disease; and previously defined cardiomyopathy diagnoses.

Magnetic resonance imaging

All patients underwent CMR using a 1.5 T device (Avanto, Siemens Medical Solutions, Germany). An eight-channel coil was used to receive the signals. Exploratory images were obtained to guide four-, three-, and two-chamber image acquisitions. Ventricular short-axis cine steady-state free precession magnetic resonance imaging (MRI) synchronized with electrocardiography was obtained in apnea, with 20 images per cardiac cycle. The acquisition parameters included 8-mm slice thickness, 300 of field of view, and 128 × 128 matrix. Image sets were acquired using 8–12 short-axis slices (8-mm slice thickness with 2 mm between cuts) to cover the entire cardiac volume. After the administration of a bolus of contrast (gadoteric acid 0.5 mmol/mL) at a dose of 0.2 mmol/kg, T1-weighted images were acquired using an inversion-recovery sequence and a rapid gradient-echo with small angle excitation (4.8-ms echo; 1.4 × 2.4 × 7 mm voxel size, 20º flip angle).

Morpho-functional and tissue findings

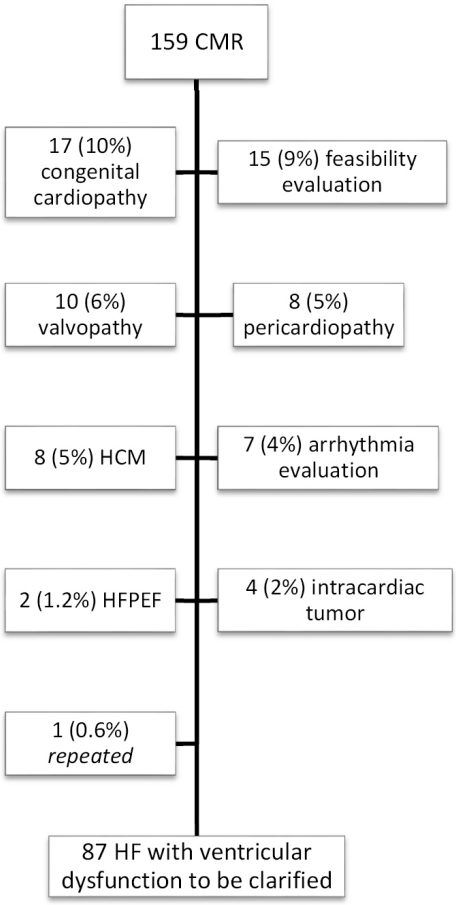
Dynamic images were acquired using the cine MRI technique with gradient-echo sequence to study the functional and morphological aspects of the heart. DGE was used to evaluate the regions affected by myocardial fibrosis, which were classified into two patterns, ischemic (subendocardial or transmural DGE in coronary territory) and nonischemic (other patterns).

Diagnostic criteria

Myocarditis and pericarditis: The presence of myocardial DGE of meso- or epicardial pattern associated or not with T2 hypersignal (edema) was considered the criterion for myocarditis, while the presence of DGE and T2 hypersignal in pericardial topography was the criterion for pericarditis, often associated with pericardial effusion.

Non-compaction cardiomyopathy (NCC): Suggested by the presence of trabeculation, with a non-compaction to compaction myocardium thickness ratio > 2.3 and a non-compaction myocardium mass > 15 g/m² or > 25% of the LV mass.

Hypertensive cardiomyopathy: The diagnosis was suggested by the clinical association of hypertension with concentric LV hypertrophy and minimal or no DGE.



CMR, cardiac magnetic resonance imaging; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFPEF, heart failure with preserved ejection fraction.

Figure 1 – *Patient selection flowchart.*

Amyloidosis: Presence of concentric ventricular hypertrophy, often associated with biatrial enlargement, with global circumferential subendocardial DGE or difficulty canceling the myocardial signal in this sequence.

Arrhythmogenic right ventricular cardiomyopathy: The imaging Task Force Criteria were followed.[12]

Chagas cardiomyopathy: The pattern of inflammatory cardiomyopathies (such as myocarditis) was followed, with the peculiarity of presenting apical and lateral aneurysms in addition to predominant fibrosis in basal and/or apical inferolateral segments, often extensive and large, associated with any DGE patterns (subendocardial, endocardial, subepicardial, and transmural), making the diagnosis highly suggestive of the disease.

Ethical aspects

The present study was observational and retrospective and in no way influenced any patient's clinical management. Despite this, it was approved by the Ethics Committee since it guaranteed privacy in the use of medical record data and respecting the best practices of use of medical information. Any information considered potentially important for clinical practice would be passed on to the attending physicians, who would decide the best course of action.

Statistical analysis

Categorical data are expressed as number and percentage, while continuous data are shown as mean ± standard deviation. The test version of the Statistical Package for Social Science software (IBM) was used for the analyses.

Results

A total of 159 patients underwent CMR in the referral period. Of them, 87 (54%) had an indication for diagnostic evaluation of cardiomyopathy (Figure 1).

The study population was predominantly young, with a mean age of 45 ± 16 years and equally distributed by sex. The presence of risk factors for CAD showed that 35% had hypertension, 9% had diabetes, 8% had dyslipidemia, 8% were smokers, and none had a history of stroke or acute myocardial infarction.

As for the functional evaluation by CMR, the mean LV ejection fraction was 32%. There was a high occurrence of regional motility dysfunction and moderate to severe mitral regurgitation. Desynchrony (inter- and intraventricular) was present in 10% of cases, with three patients in functional class (FC) III (with LVEF by CMR of 16–32% in resynchronizer preimplantation evaluation, with one of extensive fibrosis, one of septal fibrosis, and one of absent fibrosis). The others were asymptomatic or had an FC II at the time of the CMR (LVEF by CMR of 48–60% with little or no fibrosis).

Other variables such as mean left atrial diameter and indexed LV diastolic volume are described in Table 1.

Table 1 – Function, delayed enhancement research, and ventricular diameter determined on cardiac magnetic resonance (N = 87).

Variable	
Left ventricular ejection fraction	32±13
Indexed final diastolic volume, mL/m^2	156±84
Left atrium, mm	40±8.8
Moderate to severe mitral regurgitation	36.9
Abnormal cine magnetic resonance imaging (regional wall motility)	90.2
Desynchrony	10

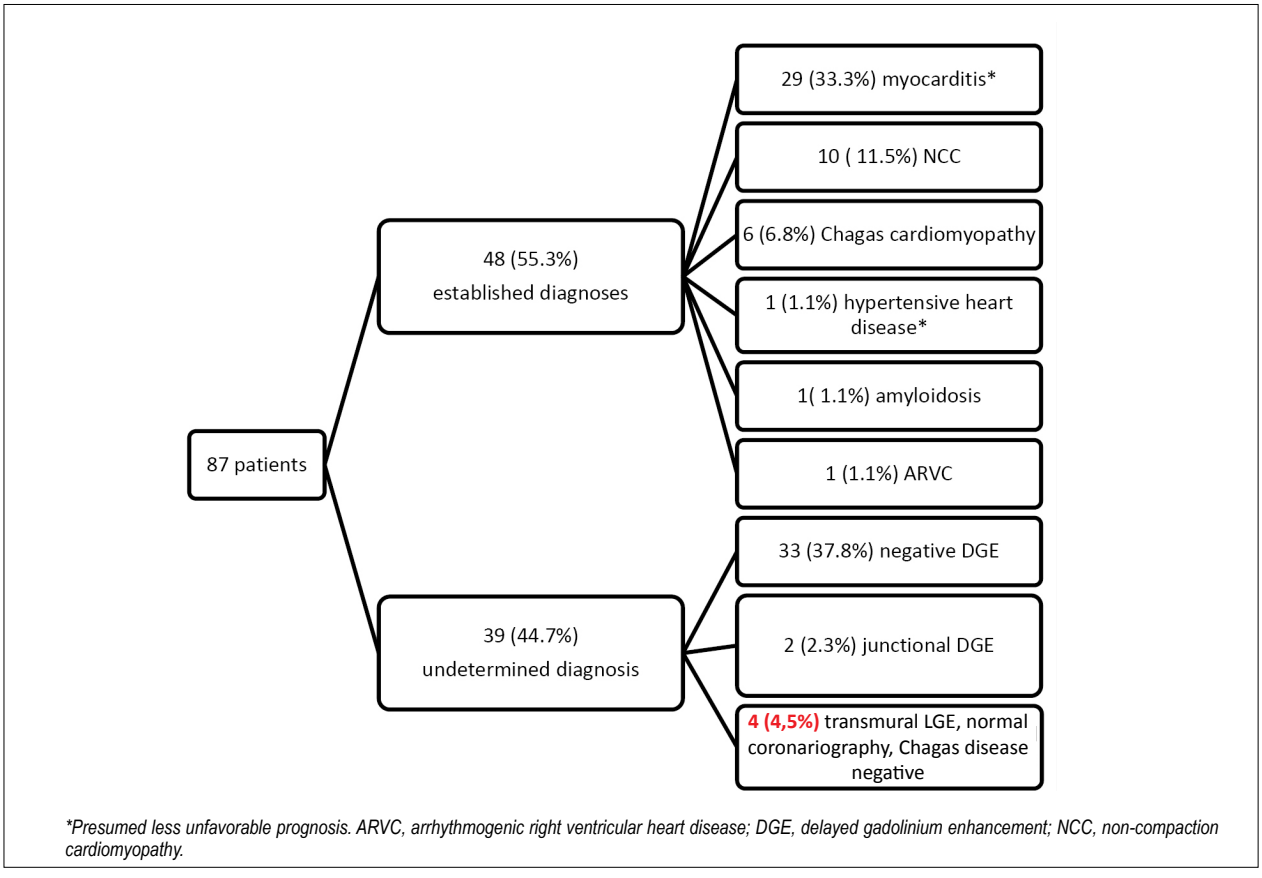
Results are expressed as mean ± standard deviation or %.

A total of 53 (61%) patients had a positive DGE. Of them, the DGE pattern was nonischemic in 44 (50.5%) and ischemic (subendocardial or transmural) in nine (10.3%), three of whom normal coronary arteries, five of whom had presumed Chagas heart disease, and one of whom had amyloidosis.

CMR identified a specific or very suggestive pattern of the HF etiology with ventricular dysfunction in 48 patients (55.3%) (Figure 2). Of the established diagnoses, 38.6% corresponded to diseases with a presumed less unfavorable prognosis (myocarditis, normal CMR, and hypertensive heart disease).

LVEF normalization by CMR (reverse remodeling) was seen in 12 (13.8%) patients who had a previous mean LVEF on ECHO of 40% (the mean interval between the ECHO and CMR exams was 5.5 months). CRM diagnoses in this group were represented by three myocarditis cases and nine undiagnosed cases (four progressed from a dysfunctional ECHO to a normal CMR, one had ischemic DGE with normal scintigraphy, and four had no fibrosis). All reverse remodeling cases were treated with optimized HF medical therapy.

In 39 (44.7%) patients, CMR information was insufficient for a significant diagnostic contribution, of which 33 (37.8%) had a negative DGE, two had junctional DGE, and four ischemic DGE, but with significant CAD excluded by complementary tests and negative Chagas



**Presumed less unfavorable prognosis. ARVC, arrhythmogenic right ventricular heart disease; DGE, delayed gadolinium enhancement; NCC, non-compaction cardiomyopathy.*

Figure 2 – *Diagnostics established by cardiac magnetic resonance in 87 patients with heart failure and ventricular dysfunction under etiological investigation.*

serology (Figure 2). In this group, 15 (46.8%) patients underwent previous coronary angiography, which revealed no coronary obstructions.

Discussion

This study highlights the importance of CMR in elucidating the etiopathogenesis of IDC without a defined etiological diagnosis. Despite the undetermined initial clinical and complementary tests, CMR helped identify the etiology in 55.3% of cases. In Brazil, there are no data that assertively address this issue. Maron et al.[8] and Parsai et al.[9] claim that approximately 50% of cardiomyopathy etiologies remain unknown, with 20–30% being possibly attributable to genetic causes. In such circumstances, CMR can be a useful diagnostic tool in the decision-making process as an intermediate or even definitive step.

The presence of DGE was consistent with the data on with HFREF patients.[3,11,13] It should be noted that the presence of DGE alone is associated with a threefold increase in mortality and hospitalization rates regardless of LVEF.[13] However, the predominance of the nonischemic DGE pattern did not corroborate the findings of other studies.[3,14,15,16] This may be partly related to the predominance of young patients without CAD as well as the large percentage of patients with myocarditis.

The considerable occurrence of diagnoses with a presumed less unfavorable prognosis highlights the relevance of CMR as an instrument to guide the progressive characteristics of diseases in HF. Defined or suggested diagnoses can assist doctors, patients, and family members with therapeutic/social planning and improve prognostic information.

The NCC diagnosis in 11.5% of patients may not necessarily constitute a specific etiological diagnosis. According to some authors, it can correspond to the common final pathway of several heart diseases[18] and indicate hypertrabeculation instead of genetic disease (which must be associated with other clinical data). Thus, even if it does not show other secondary causes of HF, distinguishing between adaptive hypertrabeculation and true NCC (familial or sporadic, primary or triggered by overlapping heart disease) is a challenge.

Patients without a defined diagnosis and negative DGE may have idiopathic IDC. This is partly because IDC shows no fibrosis on CMR (it classically presents as septal wall linear mesocardial DGE).[19] However, it is worth recalling other causes of ventricular dysfunction and dilation that usually present no DGE, such as alcoholic, peripartum, and Takotsubo cardiomyopathy.[1,8] The correlation with clinical history is greatly important to excluding such secondary cardiomyopathies. The absence of DGE, despite contributing little to the diagnosis, is an important piece of information in the clinical follow-up. These patients have a lower chance of adverse events and a better response to ventricular resynchronization therapy when necessary.[2]

As for other cases without defined etiology, the junctional DGE found in two patients can be justified by pressure overload secondary to IDC or, less likely, final-stage HCM with dilation.

In this study, CAD was previously excluded by the attending physicians as a cause of cardiomyopathy, but 11% of the tests presented ischemic DGE. Most of them suggested Chagas cardiomyopathy (six patients, later confirmed by new serology); however, four patients had negative serological tests despite positive epidemiology. These cases may correspond to serological false negatives or the lack of a second serology confirmation since there are no other classical causes of segmental fibrosis besides myocardial infarction and Chagas cardiomyopathy, especially in patients from endemic areas.

The absence (or little extension) of fibrosis is associated with a greater chance of reverse remodeling.[1,2] This premise was verified in the present study, with 13.8% of patients presenting normalized ventricular function and, of them, only two had small-sized positive DGE.

In addition to the more favorable prognosis inherent to this group of patients, the relevant role of optimized drug treatment in HF stands out in all patients.

The proportion of patients with normal CMR despite a previous ECHO revealing a reduced ejection fraction and a past history of HF symptoms corresponds to cases of myocarditis with good progression and ventricular function recovery. According to the risk classification of myocarditis, patients with low-risk syndromes (mild to moderate dysfunction without associated ventricular arrhythmias) usually present no symptoms and recover function in 1–4 weeks.[17] However, the great operator-dependency of ECHO was maximized in the present context since these tests were received from different services.

The patients in the present study were a decade younger and had fewer risk factors for CAD than what has been described in the literature for HF patients.[3-6] These data corroborate the probable definition of undetermined diagnoses as being idiopathic IDC, as it is established that this cardiomyopathy often affects people in the first few decades of life.[2]

In the context of IDC research, CMR may play a restrictive (gatekeeper) role in indicating coronary angiography in HFREF patients, since more than half have no significant CAD.[3,4] Thus, coronary angiography would not be necessary in patients without a defined etiology and nonischemic DGE. In HF, in addition to being susceptible to vascular complications and bleeding, the risk of nephrotoxicity and relevant morbidities should be considered, especially in patients with more severe disease.

The relevance of CMR in the proposed patient profile was researched in a specialized tertiary center. Its usefulness is likely to be even greater in clinical practice, in which non-specialists manage HF.

Limitations

The limitations of the present study include its small sample size and retrospective characteristics. In addition, patients with a borderline ejection fraction were included, as many showed an improved ejection fraction on CMR, a finding that requires highlighting. Other limiting factors are basal ECHO data being provided by several echocardiography laboratories, while CMR

was performed only at the studied reference center by a team of three cardiologists.

Due to call failure, it was not possible to conduct new serological studies for Chagas disease in the four patients with ischemic DGE and negative coronariography who had only one previous negative serology result.

It is noteworthy that, within the analyzed period, our bioimaging service faced two prolonged equipment breakdowns, with tests paused for 8 months, in addition to another 4 months due to medical team changes in the sector, which justified the reduced mean examination production. After these situations were normalized, a mean 30 CMR procedures were performed each month.

Conclusion

The performance of CMR in patients without etiologic diagnosis of HFREF is clinically significant since it contributed to the etiology and prognosis of more than 50% of cases. This positive impact was reported in a tertiary cardiology teaching service; thus, CMR may have an even greater role in circumstances other than those presented here since non-specialists often manage HF.

Authors' contributions

Research concept and design: ATF Barreto, MLBG Bezerra, and RMV Melo; data collection: ATF Barreto, BO Isabella, VA Reis, ATF Barreto, MLBG Bezerra, and VA Reis; data analysis and interpretation: ATF Barreto, MLBG Bezerra, BO Isabella, and VA Reis; statistical analysis: ATF Barreto and RMV Melo; manuscript writing: ATF Barreto, MLBG Bezerra, RMV Melo, BO Isabella, and LCS Passos; critical review of the manuscript for important intellectual content: MLBG Bezerra, RMV Melo, and LCS Passos.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Comparative Analysis of the Coronary Arteries Flow Pattern in Secondary Myocardial Hypertrophies and by Sarcomeric Mutation

Análise Comparativa do Padrão de Fluxo de Artérias Coronárias das Hipertrofias Miocárdicas Secundárias e por Mutação Sarcomérica

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Abstract

Background: Coronary flow with a diastolic predominance increases two to five times in hyperemia, mediated by vasodilation (coronary flow reserve, CFR) and, in hypertrophy, relative ischemia may occur. In secondary hypertrophy (LVH), the flow, normal at rest, becomes ischemic due to increased demand. In hypertrophic cardiomyopathy (HCM) with perivascular fibrosis, collateral vessels appear to increase the irrigation of hypertrophied segments.

Objective: To determine the coronary flow pattern in patients with secondary hypertrophy and hypertrophic cardiomyopathy, evaluating the coronary flow reserve.

Methods: Coronary flow was evaluated in 34 patients with secondary hypertrophy, 24 with hypertrophic cardiomyopathy and in 16 controls. The anterior descending artery was detected with transthoracic Doppler with adequate equipment calibration. In the hypertrophic cardiomyopathy group, the flow of collaterals from the hypertrophic region was evaluated. In the control and secondary hypertrophy groups and in six patients in the hypertrophic cardiomyopathy group, the intravenous dipyridamole (0.84 mg) coronary flow reserve was calculated. The data were compared by variance with a significance of 5%.

Results: In secondary hypertrophy there was an increase in mass index and blood pressure, and in hypertrophic cardiomyopathy an increase in relative thickness predominated. Ejection fraction and diastolic dysfunction were higher in the hypertrophic cardiomyopathy group. The coronary flow reserve was lower in the hypertrophic cardiomyopathy group, and flow of collaterals was also detected, with a reduction in the coronary flow reserve.

Conclusion: the analysis of coronary circulation with transthoracic Doppler is possible in normal and hypertrophic individuals. Patients with secondary hypertrophy and hypertrophic cardiomyopathy have a decrease in the coronary flow reserve, and patients with hypertrophic cardiomyopathy show a hyper flow of dilated collateral vessels observed in the hypertrophic region, with a decrease in the coronary flow reserve.

Keywords: Fractional flow reserve, myocardial; Echocardiography Doppler; Cardiomegaly.

Resumo

Fundamento: *O fluxo coronariano com predomínio diastólico aumenta duas a cinco vezes na hiperemia, mediada por vasodilatação (reserva de fluxo coronariano), podendo, na hipertrofia, ocorrer isquemia relativa. Na hipertrofia secundária, o fluxo em repouso torna-se isquêmico pelo aumento da demanda. Na cardiomiopatia hipertrófica com fibrose perivascular, há funcionalização de vasos colaterais, para aumentar a irrigação dos segmentos hipertrofiados.*

Objetivo: *Determinar o padrão do fluxo coronariano em pacientes com hipertrofia secundária e cardiomiopatia hipertrófica, avaliando a reserva de fluxo coronariano.*

Métodos: *Avaliamos o fluxo coronariano em 34 pacientes com hipertrofia secundária, em 24 com cardiomiopatia hipertrófica e em 16 controles. A artéria descendente anterior foi detectada com Doppler transtorácico com calibração adequada do equipamento. Nos grupos controle e com hipertrofia secundária, foi calculada a reserva de fluxo coronariano com dipiridamol (0,84 mg/kg) endovenoso. O mesmo procedimento foi realizado em seis pacientes do grupo com cardiomiopatia hipertrófica, nos quais também foi avaliado o fluxo das colaterais da região hipertrófica. Os dados foram comparados por variância com significância de 5%.*

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Resultados: *Na hipertrofia secundária, houve aumento do índice de massa e, na cardiomiopatia hipertrófica, predominou o aumento da espessura relativa. A fração de ejeção e a disfunção diastólica foram maiores no grupo com cardiomiopatia hipertrófica. A reserva de fluxo coronariano foi menor no grupo com cardiomiopatia hipertrófica, sendo detectado, também, fluxo de colaterais com redução da reserva de fluxo coronariano.*

Conclusão: *A análise da circulação coronariana com Doppler transtorácico é possível em indivíduos normais e hipertróficos. Pacientes com hipertrofia secundária e cardiomiopatia hipertrófica apresentam diminuição da reserva de fluxo coronariano, e aqueles com cardiomiopatia hipertrófica mostram fluxo de vasos colaterais dilatados observados na região hipertrófica, com diminuição da reserva de fluxo coronariano.*

Palavras-chave: *Reserva fracionada de fluxo coronário; Ecocardiografia Doppler; Cardiomegalia.*

Introduction

Normal myocardial irrigation is provided by epicardial conductance vessels and intramural resistance vessels connected to an extensive serial and parallel capillary network. Capillaries are connected to post-capillary veins, venules, and epicardial veins that flow into the right atrium through the coronary sinus. Also, the collateral circulation vessels form an extensive anastomotic network that connects the various vascular compartments, usually in a non-functional state.[1]

Coronary flow is determined by the relationship between systemic blood pressure and the resistance of epicardial vessels, resistance vessels, capillaries, and the venous system, with the greatest resistance at the intramural vessel level.[2] Capillaries, which individually offer great resistance due to their parallel arrangement, have lower total resistance.[3] Collateral vessels, although non-functional, can be functionalized in acute situations (ischemia, sudden demand increase, or increased myocardial mass) and are present in patients and normal subjects.[4]

The heart works in an almost exclusively aerobic regime, with high oxygen consumption and an exceptional capacity to extract this gas, but with limited anaerobic capacity; thus, a decreased oxygen supply (myocardial ischemia, for example) triggers a rapid cascade that can result in arrhythmia and cardiac arrest requiring constant self-regulation. The difference between basal flow and hyperemia is called coronary flow reserve (CFR), the vasodilation capacity of intramural vessels designed to increase myocardial flow and perfusion in cases of increased oxygen consumption, i.e., the quotient between flow velocity or volume at maximum hyperemia and at rest. Under normal conditions, CFR increases two- to five-fold compared to basal flow.[5] The coronary flow regime is biphasic and predominantly diastolic (Figure 1).[6]

Patients with ventricular hypertrophy due to increased myocardial mass have a greater need for oxygen. When the wall thickness is ≤15 mm as commonly happens in secondary hypertrophies (systemic arterial hypertension), the coronary flow at rest is normal but with a decreased CFR. In this condition, myocardial ischemia without coronary obstruction can occur when there is an increased cardiac output due to increased extravascular resistance caused by myocardial mass expansion, perivascular fibrosis, and a decreased number of capillaries per muscle area. In patients with significant ventricular hypertrophy and a wall thickness ≥17 mm, more common in forms caused by sarcomeric mutation (hypertrophic cardiomyopathy [HCM]), present a largely increased basal coronary flow. This phenomenon

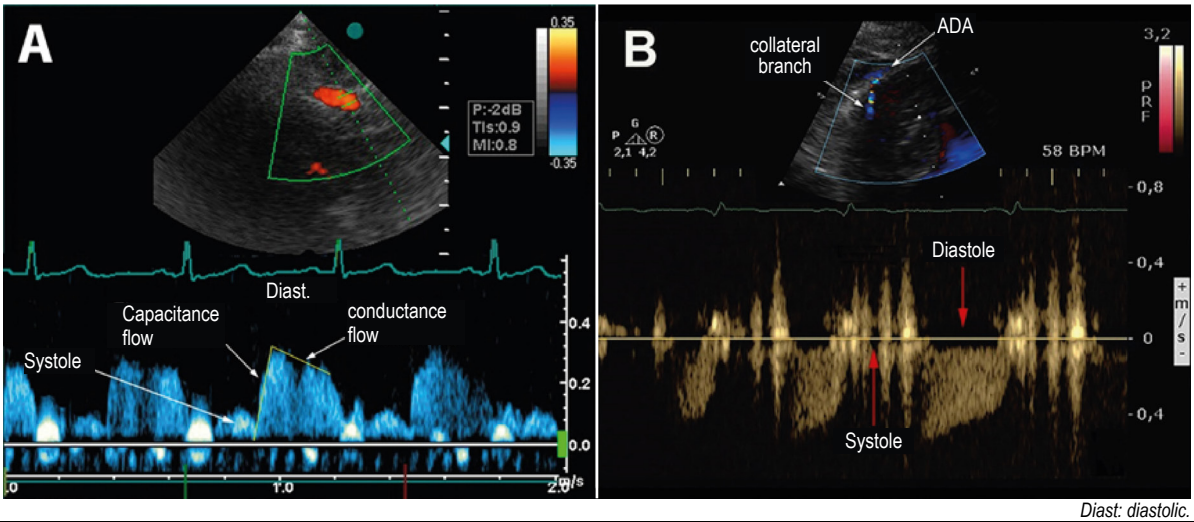


Figure 1 – *(A) Coronary flow in a conductance artery (middle third of the anterior descending branch) obtained using pulsed Doppler from the parasternal position. There is a predominance of diastolic flow with capacitance and conductance or resistance flows. The ramp slope in this phase represents vascular tone. (B) Coronary flow in a collateral vessel in an intramural direction from the anterior descending artery. Note the systolic reverse flow moving away from the transducer during diastole.*

occurs because intramural resistance vessels do not dilate to supply the increased myocardial mass resulting from middle layer hypertrophy and intima hyperplasia, which reduce their lumen[7] and functionalize the collateral circulation vessels, which start to present flow.[8] CFR is also reduced.[9]

Objective

To determine the velocimetric coronary flow pattern and CFR in patients with secondary left ventricular hypertrophy (LVH) and HCM versus normal subjects.

Methods

Coronary flow was evaluated in 58 patients with secondary LVH separated into two groups: 34 patients with arterial hypertension (LVH group) with a mean age of 53 ± 10 years, 26 of whom were male; and 24 patients with HCM (HCM group) with a mean age of 47 ± 14 years, 15 of whom were male. A total of 16 subjects with no evidence of heart disease (control group) with a mean age of 48 ± 9 years, 11 of whom were male, were also evaluated.

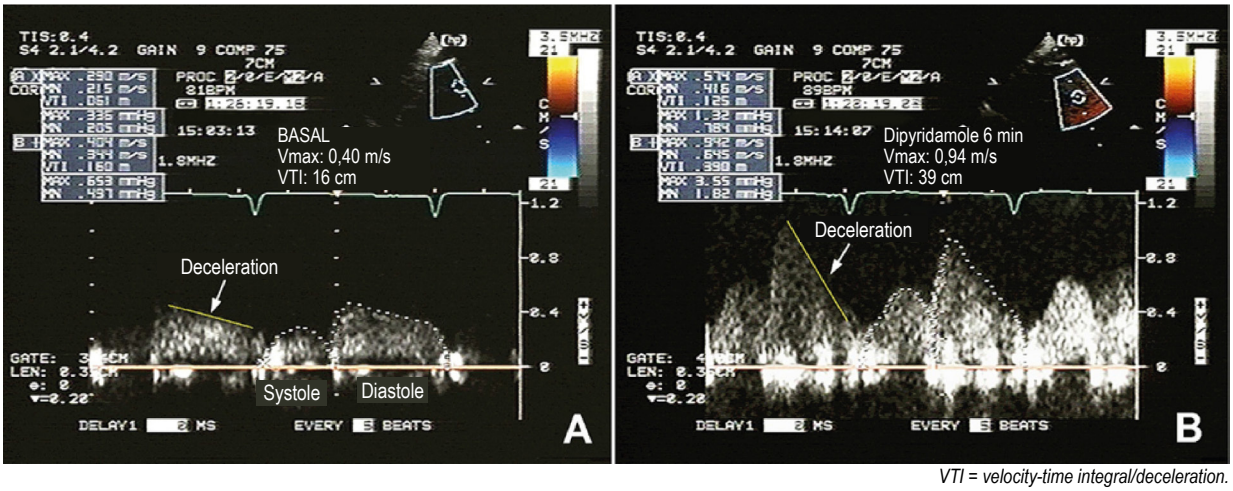
The LVH group consisted of patients with chronic systemic arterial hypertension and LVH. The HCM group was formed by patients with a disproportionately increased regional or global LV wall thickness with no apparent cause or increased afterload.

LV size and function were determined by measuring the diastolic septum and wall thickness and the diastolic and systolic LV diameters. Left atrial (LA) diameter and indexed volume were also determined according to current guidelines.[10] The LV Global Longitudinal Strain (GLS) was calculated in all participants in the control group, 27 in the LVH group, and 20 in the HCM group.

The flow of the anterior descending artery (ADA) was obtained by transthoracic color Doppler in the spectral pulsatile modality, with color flow velocity calibrated from 20 to 30 cm/s, a high persistence level, and low filtration. The spectral Doppler velocity was calibrated to obtain low flow velocities.[11] The transverse parasternal window modified at or below the papillary muscles was used to obtain the tracings. The maximum diastolic velocity (cm/s) and diastolic velocity integral (cm) were calculated in the spectral pulsed wave Doppler tracing (Figure 2) as well as in the dilated intramural vessels (probably collateral) found in the hypertrophic region in the HCM group (Figure 1B).

All participants in the control group, all patients in the LVH group, and six of the 24 patients in the HCM group had the CFR calculated with a slow intravenous bolus of dipyridamole 0.84 mg/kg administered over a 4-min interval.[5] As the test was not performed to analyze pharmacological stress, atropine was not infused, but in all cases aminophylline was administered at a dose of 120–240 mg at 8–10 min after the dipyridamole injection, to finish the examination. The intramural vessel flow present in the hypertrophic segments was also recorded in patients of the HCM group. The intramural vessel CFR was calculated in the six patients who received the dipyridamole infusion.

Since CFR may be influenced by microcirculation changes and epicardial vessel stenosis, there were some inclusion criteria for patients with hypertrophy to enter the control group. Control group participants were recruited among kidney donors undergoing coronary angiography without obstructive changes (seven subjects); patients undergoing cineangiography for diagnostic purposes without evidence of coronary stenosis, or valve and myocardial changes (five subjects); patients undergoing pharmacological stress echocardiography with no evidence of segmental contractility changes or clinical data suggestive of coronary stenosis (four subjects). All participants were normotensive with no kidney, valve or myocardial disease, and four had controlled type 2 diabetes mellitus. The LVH group included systemic arterial hypertension and myocardial hypertrophy patients undergoing



VTI = velocity-time integral/deceleration.

Figure 2 – *Coronary flow reserve in a subject with no evidence of heart disease. (A) Biphasic basal flow with diastolic predominance showing a slow deceleration ramp, indicating high flow progression resistance with a maximum diastolic velocity of 0.40 m/s and a velocity integral of 16 cm. (B) Flow obtained 6 min after the infusion of a bolus of dipyridamole 0.84 mg/kg showing increased deceleration velocity (decreased resistance) and increased diastolic (0.94 m/s) flow and integral (39 cm) velocity, estimating a CFR of 2.35 for velocity and 2.44 for the integral.*

hemodialysis without evidence of significant stenosis on coronary angiography. The patients in the HCM group had generalized ventricular (five patients), asymmetric septal (obstructive in six, non-obstructive in three), mid-ventricular (five patients; two with intraventricular gradient), apical (seven patients; one with intraventricular gradient), and lateral wall (one patient) hypertrophy. None of these patients had systemic arterial hypertension or segmental contractility changes related to the coronary territories. Twelve patients underwent coronary angiography without evidence of significant obstruction. Sixteen patients underwent clinical research with evidence of HCM or sudden death in the family. Eight patients had controlled type 2 diabetes mellitus. Other exclusion criteria were fascicular or atrioventricular blocks of any degree, aortic valve disease greater than mild severity, coronary artery disease clinically or hemodynamically recognized, dilated cardiomyopathies, and infiltrative myocardial diseases.

The data were compared between groups by the parametric analysis of variance test complemented by the Tukey analysis to determine sample mean differences at a 5% statistical significance.

Results

Increased mass index (mean 207.6 g/m² ± 49 g/m²) and relative thickness (mean 0.45 ± 0.09), characterizing LV concentric hypertrophy, was predominant in patients with systemic arterial hypertension (LVH group). The patients in the HCM group presented a lower mass index increase (mean 176.2 g/m² ± 78.5 g/m²) and a greater relative wall thickness increase (0.75 ± 0.32). The ejection fraction (59.6% ± 4.7% versus 56.5% ± 10.4%, $p < 0.0001$) and the E/e' ratio (11.7 ± 4.4 versus 6.5 ± 1.8, $p < 0.0001$) were higher in the HCM group. The increased LA size and indexed volume in patients with LVH were significantly greater in the HCM group. The LV GLS was slightly decreased in the LVH group (-17.5% ± 2.8%) and moderately decreased in the HCM group (-14.9% ± 3.63%). Table 1 shows the demographic data, LV and LA sizes, and LV function parameters. Table 2 shows the coronary flow results at baseline and after dipyridamole infusion, with a more reduced CFR in the six HCM patients than in the LVH patients (1.75 ± 0.58 versus 2.08 ± 0.61). Patients in the HCM group also presented intramural vessel flow, probably collateral, with a decreased CFR both in epicardial and intramural vessels in the six patients receiving dipyridamole.

Discussion

Conductance epicardial vessels travel across the surface of the heart, and a few perforate it. Intramural resistance vessels present a proximal pre-arteriolar compartment with an intramural pathway and a distal arteriolar compartment connected to an extensive capillary network at a ratio of one capillary to each myocardial fiber in a serial and parallel arrangement. There are about 4,000 capillaries/mm² of myocardium. In turn, the capillaries connect to the post-capillary veins, followed by venules and epicardial veins, which flow into the coronary sinus. There are also collateral circulation vessels with no muscle fibers forming an extensive anastomotic network that connect the various vascular compartments with intramural pathway, from the epicardial to the endocardial region, normally in a non-functional state.[12]

Coronary flow resistance is distributed in percentages as epicardial vessels with <5% of the total resistance, pre-arteriolar vessels with 30%, and distal (arteriolar) compartment with 40%. Capillaries provide great individual resistance, but due to their parallel arrangement, the capillary network offers the least resistance in the entire system.[13] The venous network offers approximately 7% of the total coronary resistance. Collateral circulation vessels can be functionalized in acute situations (ischemia, suddenly increased demand, or increased myocardial mass). As they have no muscle layer, these vessels do not contract, possibly playing an important role in the flow balance between different coronary territories. Their number decreases with age.[14] Of the blood volume contained by the myocardium (12 mL/100 g of muscle), 90% are contained in the capillary bed.

Table 1 – Patients' demographic data and cavity size and function.

	Controls	LVH	HCM	$p_{(1-2)}$	$p_{1-3)}$	$p_{(2-3)}$
Age, years	48.38 ± 9.52	53.32 ± 10.07	47.42 ± 14.04	< 0.0001	0.20	< 0.0001
Sex (M, F)	11 M. 5 F	26 M. 8 F	15 M. 9 F	-	-	-
LA volume, mL/m²	27.00 ± 9.6	33.1 ± 11.3	48.1 ± 22.9	< 0.0001	< 0.0001	< 0.0001
LA diameter, mm	31.0 ± 4.1	36.2 ± 5.8	40.0 ± 7.2	0.004	< 0.0001	< 0.0001
LVEF, %	56.44 ± 4.84	56.50 ± 10.43	59.62 ± 4.74	0.47	< 0.0001	< 0.0001
Mass index, g/m²	104.22±13.95	207.57 ± 49.22	176.19 ± 78.46	< 0.0001	< 0.0001	< 0.0001
Relative thickness	0.30 ± 0.04	0.45 ± 0.09	0.75 ± 0.32	0.04	0.0006	0.006
LV GLS, %	-19.1 ± 3.2	-17.5 ± 2.8	-14.9 ± 3.6	0.002	< 0.0001	< 0.0001
Mitral E wave, cm/s	77.14 ± 15.44	63.38 ± 11.89	82.24 ± 34.70	< 0.0001	0.0014	< 0.0001
E/A ratio	1.18 ± 0.35	0.90 ± 0.28	1.26 ± 0.60	0.05	0.36	0.02
Tissular e' wave, cm/s	13.60 ± 2.99	10.33 ± 2.30	7.36 ± 2.95	< 0.0001	< 0.0001	< 0.0001
E/e' ratio	5.79 ± 1.17	6.46 ± 1.81	11.75 ± 4.38	0.04	< 0.0001	< 0.0001
SBP, mmHg	128.75 ± 12.32	151.47 ± 12.88	138.33 ± 10.94	< 0.0001	< 0.0001	< 0.0001
DBP, mmHg	78.13 ± 9.64	92.79 ± 8.98	87.92 ± 6.20	< 0.0001	< 0.0001	< 0.0001

F, female; DBP, diastolic blood pressure; GLS, global longitudinal strain; HCM, hypertrophic cardiomyopathy; LA, left atrium; LVEF, left ventricular ejection fraction; LV, left ventricle; LVH, hypertensive hypertrophy; M, male; SBP, systolic blood pressure

Table 2 – Coronary flow and coronary flow reserve in normal subjects and in patients with acquired ventricular hypertrophy and hypertrophic cardiomyopathy.

	Controls	LVH	HCM	$p_{(1-2)}$	$p_{(1-3)}$	$p_{(2-3)}$
Baseline HR, bpm	72.44 ± 11.19	71.53 ± 12.87	69.25 ± 18.17	0.20	0.008	0.02
Dipyridamole HR, bpm	78.94 ± 10.68	77.88 ± 12.84	69.00 ± 16.97	0.16	< 0.0001	< 0.0001
Baseline Vmax, cm/s	34.56 ± 12.29	31.32 ± 10.96	36.28 ± 18.66	0.001	0.01	< 0.0001
Dipyridamole Vmax, cm/s	133.37 ± 50.43	65.24 ± 18.06	67.30 ± 22.16	< 0.0001	< 0.0001	0.04
CFR Vmax	3.86±0.31	2.08±0.61	1.75± 0.58	< 0.0001	< 0.0001	0.06
Baseline VTI, cm	16.66 ± 6.85	13.14 ± 3.58	17.97 ± 4.86	< 0.0001	0.05	< 0.0001
Dipyridamole VI, cm	64.91 ± 25.87	29.42 ± 13.25	27.00 ± 7.34	< 0.0001	< 0.0001	0.004
CFR VTI	3.91 ± 0.18	1.99 ± 0.71	1.54 ± 0.17	< 0.0001	< 0.0001	0.005
Collateral Vmax, cm/s	-	-	60.22 ± 29.31	-	-	-
Collateral dipyridamole Vmax, cm/s		-	98.65 ± 43.86	-	-	-
Collateral CFR, Vmax	-	-	1.66 ± 0.44	-	-	-
Collateral baseline VTI, cm	-	-	24.11 ± 8.54	-	-	-
Collateral dipyridamole VTI, cm	-	-	33.92 ± 18.49	-	-	-
Collateral CFR VTI	-	-	1.56 ± 0.47	-	-	-

CFR, coronary flow reserve; Collateral, collateral artery; HCM, hypertrophic cardiomyopathy; HR, heart rate; LVH, hypertensive hypertrophy; Vmax, maximum coronary velocity; VTI, velocity-time integral

As the heart works in an almost exclusively aerobic regime, with exceptional oxygen extraction capacity, it has limited anaerobic capacity. For this reason, a decreased oxygen supply triggers a rapid ischemic cascade, which can culminate in arrhythmia and cardiac arrest. Due to these characteristics, a reduced myocardial reserve (<25%) demands constant self-regulation, which can increase coronary flow up to five times to supply the needs. As the myocardium responds immediately to an increased oxygen demand with a proportionally increased flow, this increase (hyperemia), or the CFR, is mediated by mechanical and metabolic factors. The mechanical factors include greater myocyte compression on the vessels during systole in the subendocardial region, where the intramural vessel diameter decreases about 20% during systole without changes in subepicardial vessel diameter.[15] This determines a biphasic flow regimen that is predominantly diastolic, with a smaller systolic component and an important diastolic component formed by a first phase of rapid increase (capacitance phase, intended to quickly fill the vessels emptied during the compression phase), followed by a slower descending ramp (perfusion), whose inclination depends on vascular tone (Figure 1).

Metabolic factors regulate the myogenic activity of vessels by releasing vasodilators (the main being adenosine and K^{+}_{ATP} and nitric oxide channels). This self-regulating mechanism keeps coronary perfusion constant in the different compartments despite pressure variations. Thus, the pressure is approximately 90 mmHg in epicardial arteries, 45 mmHg in the arteriolar network, 30 mmHg in the capillary network, and 5 mmHg in the venules. The autonomic nervous system also plays an important role in self-regulating coronary flow, especially with increased demand (exercise), when sympathetic stimulation causes vasodilation mediated by beta-adrenergic receptors and vasoconstriction mediated by alpha-adrenergic receptors. The endothelium also significantly contributes to coronary flow self-regulation.

Thus, CFR is the vasodilation ability of the intramural vessels to increase flow and myocardial perfusion in cases of increased oxygen consumption, i.e., the quotient between flow velocity or volume at maximum hyperemia versus at rest. Under normal conditions, CFR increases two- to five-fold compared to basal flow.

Some factors can change these mechanisms, whether due to epicardial vessel stenosis (coronary artery disease), microcirculation changes (diabetes), or even in ventricular hypertrophy.

In ventricular hypertrophy, the mechanism differs between forms. Patients with secondary ventricular hypertrophy (systemic arterial hypertension) with an overall wall thickness ≤ 15 mm have decreased coronary flow at rest with a decreased CFR and may present with myocardial ischemia without coronary obstruction in cases of increased cardiac output (relative ischemia). The mechanism of this decrease is due to the increased extravascular resistance caused by an increased myocardial mass, increased perivascular fibrosis, and decreased capillary density by muscle area, whose reduction is proportional to an increased myocyte volume. Some authors[16,17] suggest that microvascular and diastolic dysfunction increases baseline coronary flow reduction in hypertrophic ventricles. These patients predominantly present with an increased ventricular mass with normal-sized cavities (concentric hypertrophy).

Patients with more severe ventricular hypertrophy, usually caused by a sarcomeric mutation, with a wall thickness ≥ 17 mm have a predominantly increased relative wall thickness, with smaller LV cavities than the group with secondary hypertrophy, who also present with a higher ejection fraction but a lower GLS. In this group, diastolic function parameters show a significantly higher E/é ratio, which, associated with greater LA size and volume, indicates a greater increase in LV filling pressure. A higher baseline coronary flow velocity is observed, especially when compared to the LVH group, probably due to higher oxygen consumption under baseline conditions. As intramural resistance vessels are unable to expand to supply the increased myocardial mass due to

mid-layer hypertrophy and intimal hyperplasia, which reduce their lumen, the collateral circulation vessels apparently become functional and start to present a detectable flow on Doppler. These vessels, located in regions with greater hypertrophy, have no muscle layer; rather, they present a predominantly retrograde systolic flow due to muscle compression and increased anterograde diastolic flow velocity suggestive of hyperflow. It is important to highlight that the retrograde coronary flow found in epicardial vessel stenosis is associated with decreased diastolic flow only in the epicardial arteries, usually with no intramural vessel flow. Patients with HCM present with a normal or increased velocity intramural vessel flow (Figure 1). Despite the increase in velocity, however, a decreased CFR is observed in the epicardial and intramural vessels.

These coronary flow characteristics seem to corroborate the differences among the analyzed groups: hypertensive patients with LVH seem to have a more homogeneous hypertrophy distribution, with lower wall thickness, larger cavities, and a less decreased CFR than patients with HCM, which present segmental hypertrophy distribution with a myofibrillar disarray changing the physiology of intramural vessels, decreasing their vasodilation capacity and apparently functionalizing the collateral vessels, which show regional hyperflow and greater CFR decrease.

No patient or control showed signs of myocardial ischemia during the examination using dipyridamole, but 71% of them complained of respiratory distress (12 in the control group, 15 in the LVH group, and 14 in the HCM group), with tachypnea, shortness of breath, and expiratory wheezes, all of which improved after aminophylline administration.

Several studies[18-20] emphasized the prognostic value of CRF in patients with myocardial hypertrophy, and its decrease is considered a strong predictor of cardiovascular complications such as atrial fibrillation, sustained arrhythmias, heart failure progression, and death of cardiac cause.

Limitations

The main limitations of this study are technical problems with properly registering the ADA flow from the left coronary artery due to heart translation during the cardiac cycle and the patients' chest conditions as well as the small number of patients studied, mainly with HCM, which makes larger-scale studies necessary to validate the findings presented here.

Conclusion

When the appropriate technique is used, the study of coronary circulation using transthoracic Doppler is possible in normal subjects and patients with secondary or genetic hypertrophy. Patients with secondary hypertrophy due to systemic arterial hypertension or HCM due to a sarcomeric mutation present with a CFR below the normal range after dipyridamole infusion, which is more evident in HCM. Patients with HCM also show flow in dilated intramural vessels, probably in the collateral vessels, that can be visualized in most hypertrophic segments, with a CFR below the normal range and characteristically not showing systolic anterograde flow, maintaining an increased velocity anterograde diastolic flow in these vessels. This suggests collateral-mediated baseline hyperflow due to the inability to vasodilate intramural arterioles. This increased intramural circulation was not detected in the control group or in the secondary LVH group, being detected only in patients with HCM.

Authors' contributions

Research conception and design, data collection, analysis and interpretation, statistical analysis, manuscript writing, critical review of the manuscript for important intellectual content: CG Souza, JM Del Castillo; data analysis and interpretation, critical review of the manuscript for important intellectual content: M Mazzarollo; critical review of the manuscript for important intellectual content: S Alburqueque, ADM Sena, D Brindeiro Filho, CAM Silveira.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Anomalous Origin of the Right Coronary from the Left Coronary Sinus: How to approach?

Origem Anômala de Coronária Direita a partir do Seio Coronariano Esquerdo: como Conduzir?

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Introduction

Coronary artery anomalies (CAAs) are characterized by a changed vessel origin, path, or structure.[1] It is a rare condition, present in approximately 1% of the general population.[2] These anomalies include the anomalous aortic origin of a coronary artery (AAOCA), which can travel retroaortic, subpulmonic, prepulmonic, and inter-arterial courses.[3]

In general, these abnormalities remain asymptomatic until adulthood, being incidental findings on complementary tests or necropsy. However, they can also cause angina, syncope, ischemia, arrhythmias, or sudden death.[1,2] Sudden death can be the first presentation of this pathology in young athletes, representing the second leading cause of death in this group.[4]

This case report describes the case of a patient diagnosed with anomalous origin of the right coronary artery (RCA) after an episode of moderate-risk unstable angina and presents important details of the clinical management of this condition.

Case report

A 56-year-old man was hypertensive, pre-diabetic, sedentary, and obese and presented with dyslipidemia and a positive family history of coronary disease. The patient was admitted to the hospital to evaluate two episodes of prolonged moderate chest pain and tightness in the previous 24 hours without irradiation or associated factors that had already resolved on admission. There were no increased cardiac enzymes. An electrocardiogram showed sinus rhythm and signs of left ventricular overload with slight ventricular repolarization changes. The patient was stratified as having moderate-risk unstable angina and received a Thrombolysis in Myocardial Infarction score of 3 for non-ST coronary syndrome. Despite his initial clinical stability, the attending physician opted for coronary angiography when the patient was still in the hospital due to the typical characteristics of his pain and the presence of risk factors for coronary artery disease.

Keywords

Arteries; Coronary vessel anomalies; Coronary vessels; Diagnostic imaging.

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Cine coronary angiography showed the origin of the RCA in the left coronary sinus with a slit ostium, possible inter-arterial course (between the aorta and pulmonary arteries), and moderate ostial stenosis due to probable extrinsic compression (Figure 1A). Left coronary artery without stenosis (Figure 1B). Transthoracic echocardiography showed mild left atrium dilation, eccentric hypertrophy, grade I diastolic dysfunction, and preserved global and segmental systolic function of the left ventricle.

Computed tomography angiography of the coronary arteries confirmed the improper RCA origin in the left Valsalva sinus with an inter-arterial course and adjacent to the origin of the left main coronary artery (Figures 2 and 3). There was angulation at the origin (~23°), moderate proximal luminal reduction (slit-like orifice), and presence of calcified atherosclerotic plaque in the middle third of the RCA without reducing the lumen. The Agatston calcium score was 13, and coronary calcification was associated with a plaque in the middle segment of the RCA.

The patient was referred for myocardial scintigraphy, which showed normal myocardial perfusion and no signs of ischemia.

Maintenance clinical drug treatment without surgical intervention was chosen. The patient uses olmesartan medoxomil associated with amlodipine besylate (40/5 mg daily); indapamide (1.5 mg daily); spironolactone (25 mg daily); nebivolol hydrochloride (5 mg daily); MR trimetazidine dihydrochloride (70 mg daily); rosuvastatin (20 mg daily); XR metformin hydrochloride (1 g daily), and allopurinol (300 mg daily), and he remains asymptomatic with no new angina attacks at 1 year after the initial diagnosis. He has controlled systemic blood pressure, good glycemic and cholesterol levels, and no activity limitations.

Discussion

Although most CAAs are benign, not progressing with hemodynamic implications or influencing the patient's prognosis, their discussion is important due to their association with sudden death,[5] mainly in young athletes and usually triggered by rigorous physical exercise.[6] AAOCA comprises a portion of CAA cases, being subdivided into left and right CAAs, the latter originating from the left sinus of Valsalva.[7]

The coronary vessel originating from the contralateral sinus can trace different courses to reach the territory it irrigates.[3] Most patients with right CAA present with an inter-arterial course (between the aorta and the pulmonary trunk).[3,5,8] These anomalies may involve a changed ostium and coronary artery

Case Report

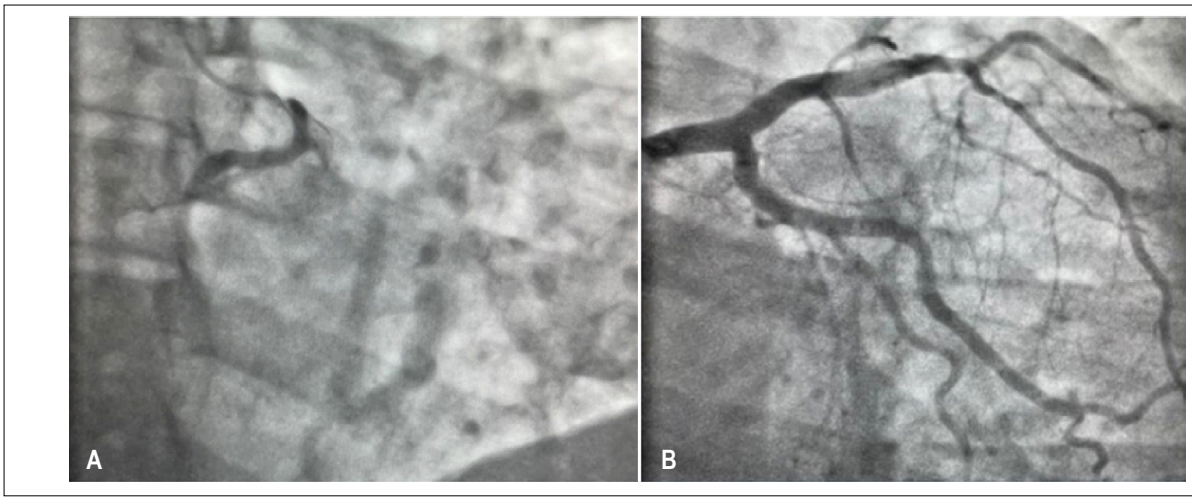

Figure 1 – *Cine coronary angiograpgy. A: Right, anomalus RCA and ostial/proximal stenosis (55%) B: Left coronary artery without stenosis.*

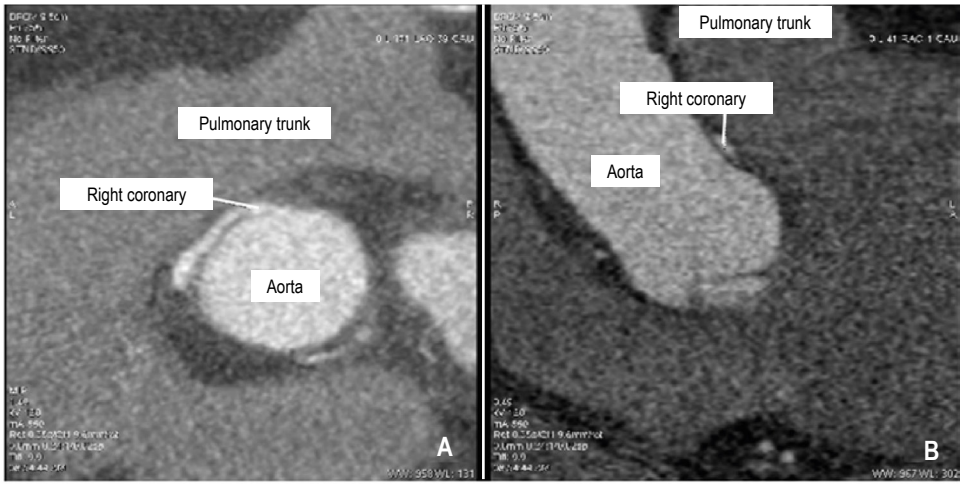

Figure 2 – *Computed tomograpgy angiography. A: Inter-arterial course between the aorta and pulmonar arteries. A e B: Improper right coronary artery origin.*

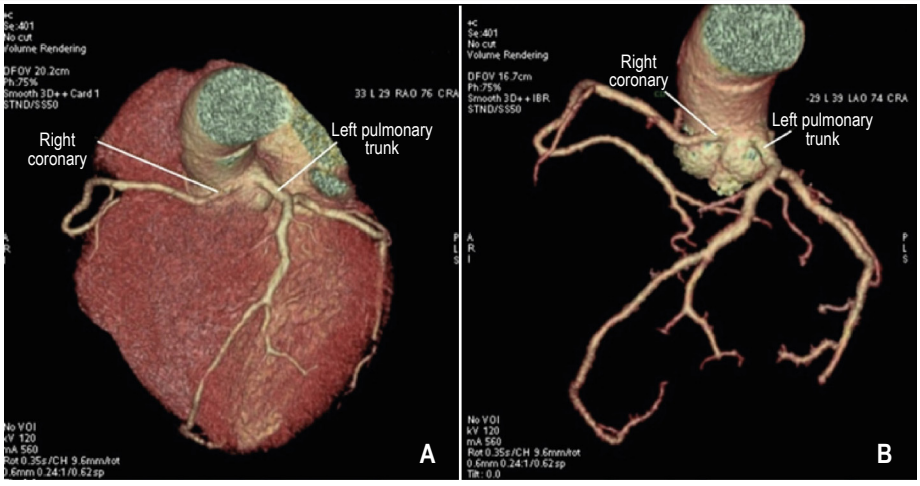

Figure 3 – *Computed tomograpgy angiography. A e B: Improper RCA origin in the left Valsalva sinus, adjacente to the origin of the left main coronary artery.*

angulation.[4,5] They result from an abnormal involution of the endothelial button-like junctions at the base of the common arterial trunk that join the coronary artery network to form the definitive arterial system or of the septation of the common arterial trunk.[5]

The inter-arterial course increases the degree of malignancy as well as the propensity for arrhythmias, myocardial infarction, and syncope.[3] The clinical presentation includes chest pain and dyspnea related to physical effort. However, there are asymptomatic cases in which sudden death is the first sign of the anomaly.[4]

The most accepted pathophysiological mechanism is that the proximal oblique course in the anomalous coronary artery shapes its ostium as a slit-like orifice instead of a circle, which can collapse with aortic expansion during systole, especially during exercise, decreasing blood flow supply to the myocardium.[7] During exercise, the systemic blood pressure and pulmonary territory increase, which can compress the inter-arterial coronary segment, causing dynamic obstructions and leading to ischemia and arrhythmias (including ventricular fibrillation). This can happen especially during more intense physical effort.[7] However, this explanation remains controversial.[3]

Abnormal changes can be classified into four classes by their functional repercussion and associated structural changes: I (benign and usually asymptomatic), II (relevant, associated with myocardial ischemia), III (severe ischemia, with potential risk of sudden death), and IV (severe, related to coronary atherosclerotic disease).[4]

There are no changes on physical examination, except in cases of structural cardiac injury. The diagnosis is usually made during an incidental finding during coronary angiography.[5]

Electrocardiography or stress test results may suggest ischemia, arrhythmia, or no evidence. Imaging tests allow better vessel visualization, anomaly classification, and risk stratification.[8]

Transthoracic echocardiography often identifies the origin and proximal segments of the coronary arteries. However, its sensitivity varies depending on the operator, patient age, echocardiographic window, and the analyzed anomaly.[9] Thus, coronary angiography is the best diagnostic method for identifying the anomaly. However, the definition of the coronary inter-arterial course is not accurate since it is a two-dimensional analysis method. Thus, the anatomical evaluation using three-dimensional methods has been increasingly used.[7] Computed tomography angiography, for example, more accurately defines the coronary location, shape, and angle of origin, as well as its course and relationship with the pulmonary artery and aorta.[5]

Surgical treatment is the standard of care in patients aged under 30 years with evidence of ischemia or ventricular arrhythmias and severe symptoms (such as previous infarction or sudden reversed death). However, the treatment of asymptomatic patients aged under 30 years and symptomatic patients without documented ischemia remains controversial, especially in older patients.[5]

The surgical risk outweighs the advantages of conservative treatment in many asymptomatic older patients.[5] Thus, the initial drug therapy (especially aiming at an effective beta-adrenergic block) can be implemented and periodically tested for its ability to lead to negative provocative ischemia tests.[3,5]

Percutaneous coronary intervention can be indicated, especially in patients at higher surgical risk, with good results in the short-term follow-up as previously described. In this case, a careful choice of therapeutic catheter and coronary guidewire is essential for greater support and an increased success rate. The use of drug-eluting stents should also be prioritized since the difficult selective catheterization of the anomalous coronary artery can hinder eventual reinterventions.[3]

To summarize, CAAs are rare and usually asymptomatic. However, the possibility of ischemia, myocardial arrhythmia, or even sudden death makes it mandatory for professionals to carefully screen patients for CAAs using more adequate imaging methods. An individual therapeutic plan should be implemented from the diagnosis depending on the patient's age and comorbidities, degree of habitual daily physical effort, and functional repercussion to reduce the morbidity and mortality related to CAAs, which can be treacherous, especially in young athletes.

In the case described here, the treatment of choice was the maintenance of clinical drug treatment since the patient showed normal myocardial perfusion without signs of ischemia. Although the inter-arterial course of this anomaly is associated with a higher occurrence of sudden death, especially after vigorous exercise, physical inactivity and, consequently, low daily physical effort made by the patient, associated with the absence of induced ischemia, reduce the risk of a fatal event and, thus, corroborate the therapeutic choice in this clinical case. Furthermore, the non-recurrence of anginal symptoms after drug treatment reinforces the initial noninterventional choice. The patient had a good clinical progression with the established therapy, remaining asymptomatic and without activity limitations in the subsequent evaluations.

Authors' contributions

Research concept and design: Almeida DC, Carrijo AMM, Souza MGS, O'Connell JL; data collection: Almeida DC, Carrijo AMM, Souza MG; data analysis and interpretation: Almeida DC, Carrijo MM, Souza MG, Martinelli FM, Fazzio FR, O'Connell JL; manuscript writing: Almeida DC, Carrijo AMM, Souza MG, Martinelli FM, Fazzio FR, O'Connell JL; critical review of the manuscript for important intellectual content: Martinelli FM, Fazzio FR, O'Connell JL.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Coronavirus Myocarditis: Case Report

Miocardite por Coronavírus: Relato de Caso

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Introduction

The first cases of coronavirus 2019 disease (COVID-19) were described in Wuhan, China, in the end of December 2019.[1] The identified pathogen was called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an RNA virus of the family Coronaviridae.[2] Due to its rapid spread, the World Health Organization declared COVID-19 a pandemic on March 11, 2020.[3] The main clinical presentation includes respiratory symptoms, such as fever, cough, myalgia, and dyspnea, that can progress to pneumonia or severe acute respiratory syndrome.[4] Among many other disorders, myocardial injury is widely described in the literature, especially associated with influenza and parvovirus B-19, but more clarifications are necessary with SARS-CoV-2 about the pathophysiology involved in the intense viral replication with systemic inflammatory involvement.[5,6]

SARS-CoV-2 is not only a cause of viral pneumonia, it also has important implications for the cardiovascular system, especially in men with risk factors, including older age, diabetes, hypertension, and obesity.[7] Cardiac injury was detected in 19.7% of cases; of the patients who died, 10.6% had coronary heart disease, 4.1% had heart failure, and 5.3% had cerebrovascular disease.[8] High cytokine concentrations are detected in the systemic inflammatory phase of COVID-19, such as interleukin 6 (IL-6), associated with an increase in troponin and other inflammatory biomarkers (D-dimer, ferritin, C-reactive protein, lactic dehydrogenase, procalcitonin, and leukocyte count), causing cardiovascular system injury.[8-10] Of these disorders, myocarditis comprises approximately 7.2% of the cardiovascular complications related to the novel coronavirus.[11] In this phase of disease progression, transthoracic echocardiography should be the method of choice to diagnose and monitor patients, improving the therapeutic management for providing hemodynamic data since patients with ventricular dysfunction are more likely to need mechanical ventilation, which consequently results in a worse prognosis.[3,12]

Keywords

Coronavirus; COVID-19; Echocardiography; Hospitalization; Myocarditis.

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This report presents the case of a patient with myocardial involvement induced by COVID-19 and its clinical and echocardiographic progression during hospitalization. The main objective is to demonstrate the degree of initial inflammatory myocardial impairment and its resolvability after clinical treatment demonstrated by echocardiography.

Case report

A 55-year-old hypertensive and diabetic woman was admitted to the emergency department of the authors' institution on April 10, 2020, reporting oppressive chest discomfort associated with nausea and vomiting that had started 4 hours earlier. The patient reported a 1-week history of a dry cough and runny nose and a fever peak of 38ºC during this period.

On physical examination, she was eupneic, conscious, and oriented, presenting a Glasgow Coma Scale score of 15, no fever and no changes on cardiac and pulmonary auscultation, blood pressure 150 mmHg/110 mmHg, heart rate of 84 beats per minute, wide and symmetrical peripheral pulses, respiratory rate of 18 breaths per minute, no abdominal abnormalities, no lower limb edema, and peripheral oxygen saturation of 98% on room air.

A 12-lead electrocardiogram showed anterolateral ST segment and J point elevation (Figure 1), and the patient was referred for cardiac catheterization, which evidenced the absence of coronary atheromatosis.

A sample for real-time polymerase chain reaction for respiratory virus research collected on April 11, 2020 tested positive for the novel coronavirus. However, despite a peripheral saturation greater than 94%, the patient progressed with dyspnea and required a nasal oxygen catheter at 3 L/min. A chest X-ray showed a slightly increased cardiac area, and the patient was referred for echocardiogram.

On April 14, 2020, the fourth day of hospitalization, she underwent transthoracic echocardiography (Figure 2) according to the updated recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging. The test showed a normal-sized left ventricle with slightly increased diastolic wall thickness (left ventricular diastolic diameter, 45 mm; left ventricular systolic diameter, 38 mm; mass index, 120.21 g/m^2; interventricular septum, 12 mm; and posterior wall, 12 mm) and diffuse hypocontractility, significant systolic dysfunction (ejection fraction, 32.98%), and diastolic dysfunction due to impaired relaxation. The right ventricle had a normal cavity and reduced systolic function (tricuspid annular plane systolic excursion [TAPSE], 16 mm). The right and left atria presented cavities with normal volume. The mitral, aortic, tricuspid,

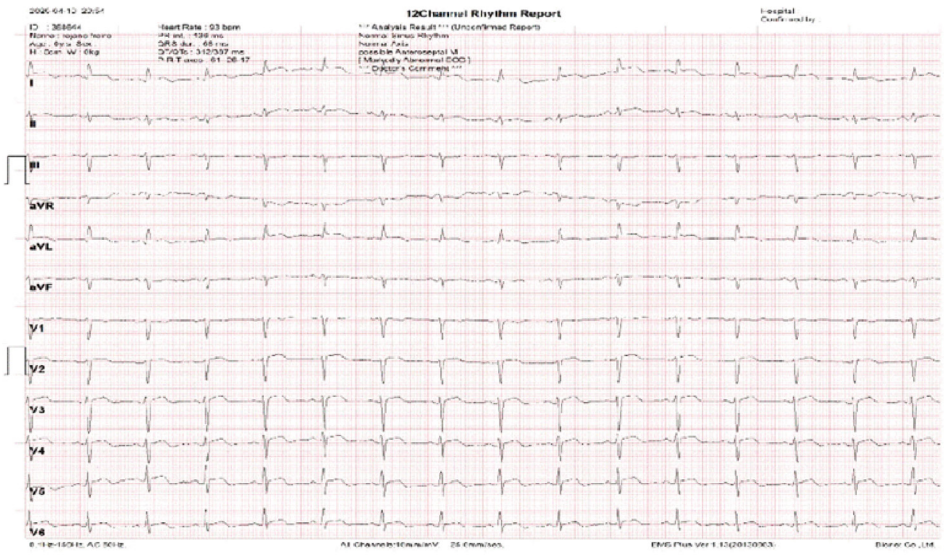

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Figure 1 – *Admission electrocardiogram.*

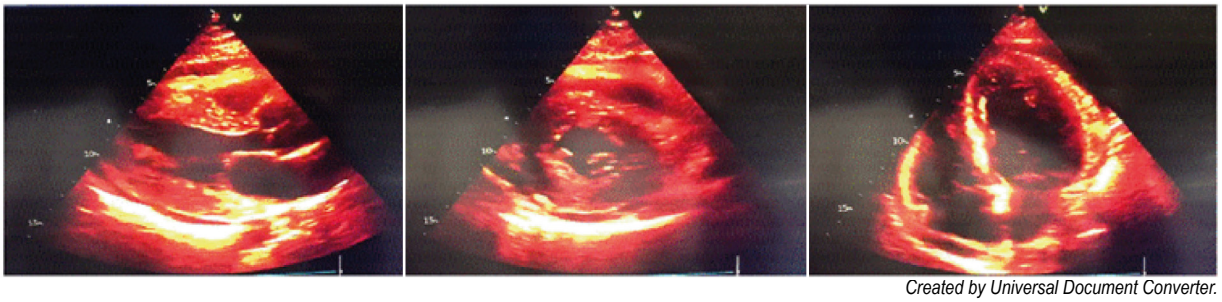

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Figure 2 – *Initial transthoracic echocardiogram.*

and pulmonary valves were functionally and morphologically normal. A mild pericardial effusion was also observed (without tamponade signs).

Considering the clinical and laboratory context, the patient underwent the following therapeutic regimen: chloroquine (400 mg twice a day on D1 and 400 mg daily from D2 to D5) associated with azithromycin (500 mg daily from D1 to D5) in addition to acetylsalicylic acid 500 mg four times a day. On April 15, 2020, the patient's condition worsened to include a cough and purulent sputum, and Tazocin® was started on April 16, 2020. Figure 3 shows the chest X-ray performed on April 17, 2020, with good clinical and laboratory response (Table 1). During the use of chloroquine and azithromycin, the corrected QT interval ranged from 387 ms (April 10) to 437 ms (April 17), returning to 367 ms (April 20).

Before hospital discharge, the patient underwent a repeat control echocardiogram on May 11, 2020, which showed a normal left ventricular cavity with normal wall thickness and contractility, normal systolic and diastolic function (left ventricular diastolic diameter, 47 mm; left ventricular systolic diameter, 28 mm; interventricular septum, 8 mm; posterior wall, 8 mm; and ejection fraction, 61%; global longitudinal strain, 20%; no pericardial effusion), right ventricle with normal thickness and normal systolic function recovery (TAPSE, 31 mm) (Figure 4). Table 2 shows the changed initial echocardiogram measurements compared to controls.

Discussion

Cardiovascular system injuries are probably multifactorial and may be caused by direct cardiac damage by the virus or by systemic inflammation and thrombosis, causing an imbalance between high metabolic demand and low reserves.[12] Myocarditis can be associated with acute heart failure in COVID-19 patients, such as fulminant myocarditis, with rapid progression and severe ventricular dysfunction associated with diffuse myocardial edema.[12] Therefore, some mechanisms have been proposed to explain the pathophysiology of

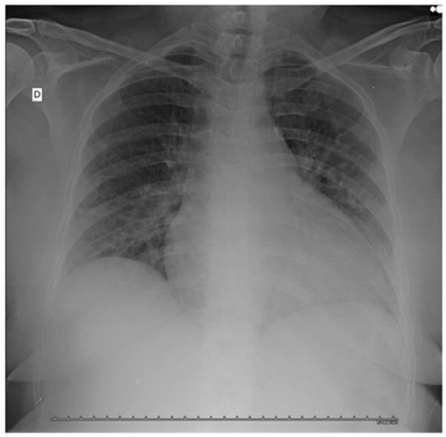

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Figure 3 – *Chest radiograph taken during hospitalization.*

Table 1 – Laboratory tests during hospitalization.

	RV	April 11, 2020	April 14, 2020	April 17, 2020	April 20, 2020
Troponin, ng/mL	< 0.014	0.975	1.080	0.982	0.141
Creatinine, mg/dL	0.5-0.9	0.94	0.66	0.91	0.86
Urea, mg/dL	< 50	60.9	46.2	38.6	34.8
Sodium, mmol/L	136-145	139.1	124.6	138.1	135.4
Potassium, mmol/L	3.5-5.1	4.32	4.57	4.19	5.59
Chlorine, mmol/L	98-107	103.2	93.0	102.7	101
Total calcium, mg/dL	8.6-10.2				9.88
Albumin, g/dL	3.4-4.8				4.18
Lactic dehydrogenase, U/L	135-225	-	513.98	338.13	-
Oxaloacetic transaminase, U/L	10-35	105.71	167.61	43.3	31.85
Pyruvic transaminase, U/L	10-35	125.0	325.0	200.82	110.95
C-reactive protein, mg/L	< 5	7.29	40.62	10.13	3.48
Hemoglobin, g/dL	14-17	11.5	10.5	10.7	12
Hematocrit, %	40-54	34	31	32.5	36.3
Leukocyte, UL	3.600-11.000	5.290	6.830	5.860	5.511
Lymphocyte, %	20-50	25.1	34.6	35.5	33.8
Platelets, UL	150.000-450.000	270.000	289.000	322.000	372.000

RV, reference value.

myocarditis caused by the novel coronavirus. One form of aggression would be direct cell damage when the virus enters the cell by binding to angiotensin II enzyme receptors found in myocytes. Another mechanism would be via infected antigen-presenting cells, which activate CD8 T cells that would migrate to myocytes due to a hepatocyte growth factor cardiac tropism, causing cytotoxic inflammation. This inflammation could also be amplified by the cytokine storm syndrome, with IL-6 being its main mediator.[13] Patients with myocardial injury had a higher rate of intensive care hospitalization than those without it (22.2% versus 2.0%), progressing with a higher incidence of heart failure (52% versus 12%) and, consequently, a higher mortality rate (59% versus 1%).[14,15]

In this case, echocardiographic acute myocardial impairment changes caused by the novel coronavirus are relevant. Older patients are the most vulnerable to complications, as are those with cardiovascular diseases, diabetes, and obesity. According to data from the Brazilian Society of Cardiology, arrhythmias (16%), myocardial ischemia (10%), myocarditis (7.2%), and shock (1–2%) are some of the cardiological complications related to COVID-19.[12] Patients with cardiovascular risk factors (older age, hypertension, and diabetes), coronary artery disease, cardiomyopathies, and cerebrovascular diseases are more susceptible to developing the severe form of the disease, being classified as a risk group for COVID-19 complications.[11]

Transthoracic echocardiography proved to be a useful tool for evaluating the cardiac function of these patients, identifying systolic and/or diastolic left ventricular dysfunction and, most importantly, presenting relevant hemodynamic data, which is important to its clinical management. The echocardiogram can be used daily, or when necessary, as a tool for monitoring

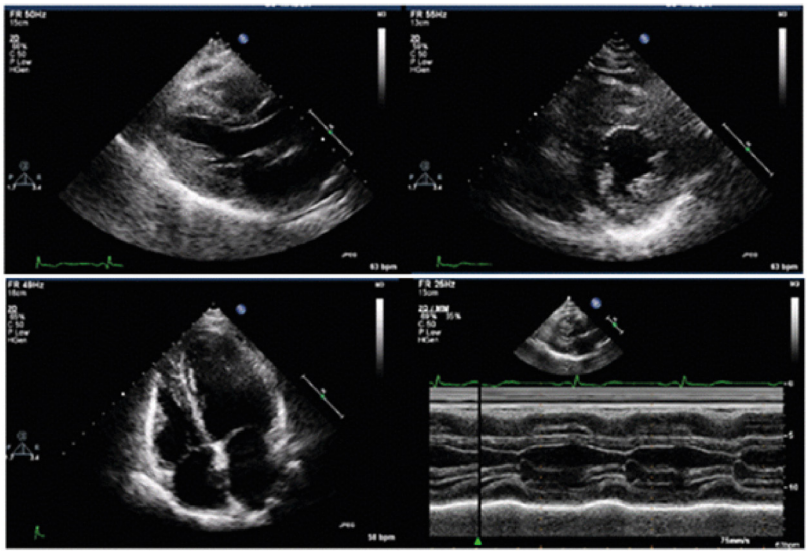

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Figure 4 – *Second transthoracic echocardiogram.*

Table 2 – Comparison of the changed echocardiogram measurements during myocarditis and after its resolution.

	Echocardiogram April 14, 2020	Echocardiogram May 11, 2020
Interventricular septum, mm	12	8
Posterior wall, mm	12	8
Left ventricular diastolic diameter, mm	45	47
Left ventricular systolic diameter, mm	38	28
Fractional shortening, %	15.55	40.42
Ejection fraction, %	32.98	61
Left ventricular mass, g	197.5	121.66
Tricuspid annular plane systolic excursion, mm	16	31

hemodynamic parameters in critical patients, guiding their treatment with inotropic and/or circulatory support. In addition to the diagnosis, patients with ventricular dysfunction have a worse prognosis.[14]

Conclusion

This case report presented a form of myocarditis with diffuse myocardial involvement, transient left ventricular wall thickening, important initial impairment of the systolic function, and normalization of the left ventricular wall thickening and systolic function after approximately 1 month of treatment.

Authors' contributions

Research concept and design: Rocha AFB, Barros JLA, Canejo Sá M, Longo ACMS, Monteiro Júnior JGM, Silveira CAM; data collection: Rocha AFB, Barros JLA, Canejo Sá M, Longo ACMS, Monteiro Júnior JGM, Silveira CAM; manuscript writing: Rocha AFB, Monteiro Junior JGM, Silveira CAM, Del Castillo JM.; critical review of the manuscript for important intellectual content: Rocha AFB, Barros JLA, Canejo Sá M, Longo ACMS, Monteiro Júnior JGM, Silveira CAM; data analysis and interpretation: Rocha AFB, Barros JLA, Canejo Sá M, Monteiro Júnior JGM, Silveira CAM.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Lipoma in the Interventricular Septum – Case Report

Lipoma no Septo Interventricular – Relato De Caso

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Abstract

Primary cardiac tumors are a rare but mostly benign pathology found in up to 0.03% of autopsies. Among these benign tumors, with an incidence of 8.5%, lipomas are often located in the interatrial septum. When located in the interventricular septum, they are considered an even more unusual pathology with an unknown real prevalence. In most cases, the diagnosis is made incidentally on cardiovascular imaging and confirmed by histopathological examination. They are more commonly asymptomatic or feature nonspecific symptoms, but these lipomas can progress with arrhythmias, valve dysfunction, heart failure, and death, which highlights the importance of cardiovascular imaging methods in the differential diagnosis and to guide appropriate therapy. This report describes the case of a patient with an incidental echocardiographic finding of a cardiac mass located in the interventricular septum, followed by cardiac magnetic resonance imaging to better characterize the lesion and demonstrate its characteristics compatible with lipoma.

Introduction

Primary cardiac tumors are rare pathologies found in 0.001–0.03% of all autopsies performed.[1] About 75% of cases are classified as benign,[1] with myxomas being the most common, and lipomas being the second most prevalent with an incidence of approximately 8.5%, followed by papillary fibroids and rhabdomyoma.[2]

Cardiac lipomas are encapsulated tumors composed of mature fat cells. They are most commonly located in the interatrial septum, with a rare occurrence of unknown prevalence in the interventricular septum.[3,4] Due to the absence of symptoms in most patients, the diagnosis of cardiac lipomas is usually made incidentally on complementary imaging tests such as echocardiography[5] with a subsequent anatomopathological study for diagnostic confirmation.

Keywords

Diagnostic cardiovascular techniques; Echocardiography; Heart neoplasms; Lipoma.

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Case report

A 68-year-old woman attended an outpatient clinic complaining of dyspnea on moderate long-term exertion associated with dry cough. She had a previous medical history of systemic arterial hypertension treated with captopril 50 mg twice a day and chronic obstructive pulmonary disease under no maintenance treatment. A physical examination revealed a good general condition, blood pressure of 150 × 100 mmHg, heart rate of 86 bpm; cardiac auscultation revealed a regular rhythm twice with normophonetic sounds and no audible murmurs; pulmonary auscultation revealed an evenly distributed vesicular murmur, no adventitious breath sounds, and wide and symmetrical peripheral pulses with no postural hypotension, jugular turgency, lower-limb edema, or other semiological changes.

The investigation started with electrocardiography showing sinus rhythm, heart rate of 80 bpm, and nonspecific ventricular repolarization changes. Simple chest radiography showed signs of chronic obstructive pulmonary disease and a normal cardiothoracic index. Transthoracic echocardiography showed a normal-sized left ventricle and concentric remodeling, 56% ejection fraction estimated by the Simpson method, mild mitral valve regurgitation, mild tricuspid valve regurgitation, mild pulmonary hypertension, and a hyperreflective nodular image in the middle portion of the interventricular septum facing the right ventricle (Figure 1).

Cardiac magnetic resonance imaging was performed to better characterize the mass in the interventricular septum and clarify the diagnosis. The image showed a mass located in mid- and apical inferoseptal topography, more precisely in the inferior interventricular junction, with the same characteristics of the epicardial fat found in the right coronary artery measuring 3.5 × 1.5 cm, with hypersignaling in T1- and T2-weighted spin-echo black-blood sequences and fat saturation in the same weighted sequences compatible with lipoma (Figures 2–4). The mass surrounded the upper border of the right coronary artery, causing a slight degree of extrinsic diastolic compression in the lower interventricular septum wall in the apical portion.

The clinical history and complementary tests showed that the patient's symptoms were not related to the interventricular lipoma; rather, they were attributed to chronic obstructive pulmonary disease. Therefore, it was initially decided against an invasive biopsy procedure, which would normally be the method for diagnostic confirmation of the tumor, and instead maintain regular clinical follow-up with imaging and electrocardiography tests.

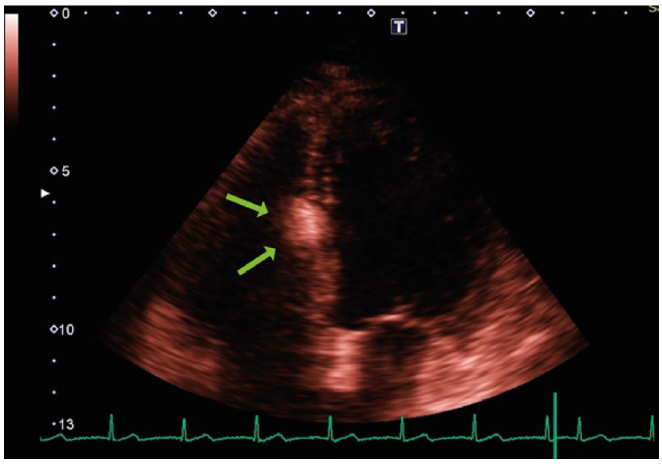
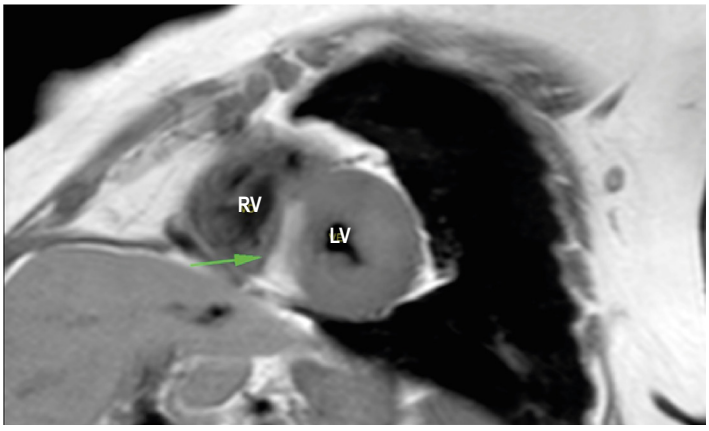
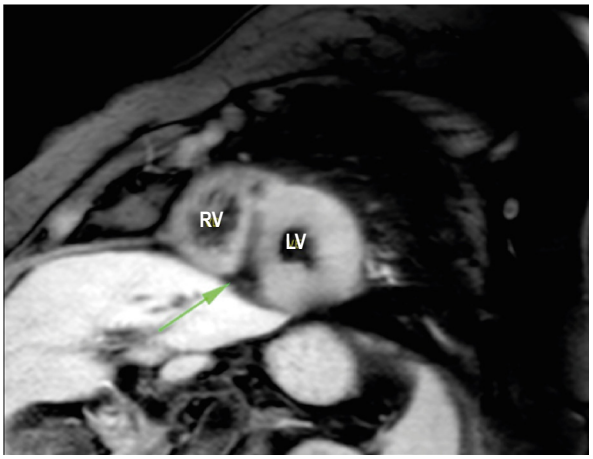


Figure 1 – *Apical four-chamber view showing a hyperreflective nodular image in the middle portion of the interventricular septum facing the right ventricle (arrows).*



RV, right ventricle; LV, left ventricle

Figure 2 – *T1-weighted black-blood sequence in short-axis view showing the focal area with hypersignaling in the mid-inferoseptal segment (arrow).*



RV, right ventricle; LV, left ventricle

Figure 3 – *T2-weighted black-blood sequence with fat saturation (short tau inversion recovery) showing focal hyposignaling in the mid-inferoseptal segment (arrow).*

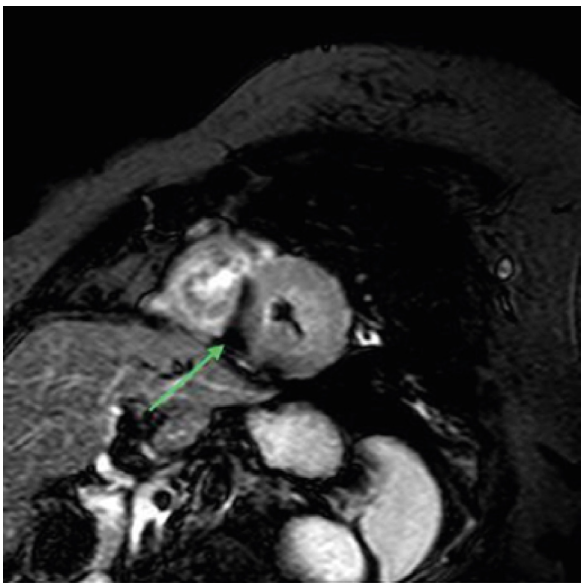


Figure 4 – *T2-weighted black-blood sequence with fat saturation (short tau inversion recovery) showing focal hyposignaling in the mid-inferoseptal segment (arrow).*

Discussion

Heart lipomas are rare tumors, an even more infrequent pathology when located in the interventricular septum.[1] Lipomas occur in all age groups and at the same frequency in both sexes.[5] Certain cardiac tumors are usually asymptomatic or have nonspecific symptoms. However, depending on their size, growth progression, and location, they can trigger variable presentations, such as valve dysfunction symptoms, heart failure, cardiac arrhythmias, extrinsic coronary vessel compression, and syncope.

Since most cases are asymptomatic, the diagnosis is usually made incidentally on echocardiography, computed tomography, or cardiac magnetic resonance, with the gold standard being the histopathological study of the lesion.[3] It is essential to emphasize that improved echocardiographic tests improve the diagnosis of cardiac tumors. Transthoracic echocardiograms are used to determine tumor location, size, shape, and mobility, while transesophageal echocardiograms are particularly useful to evaluate the insertion site and morphological characteristics of atrial and ventricular tumors.[1] In addition, the echocardiographic contrast can be greatly useful in the differential diagnosis of the mass since hypervascularization is more closely associated with malignancy.[6] Cardiac magnetic resonance imaging can characterize the tumor tissue though a sequence of specific electromagnetic pulses in addition to analyzing the degree of intramyocardial extension, tumor delimitation borders, and the relationship with adjacent higher-definition cardiac structures.[7] It is as acute as histopathology in the differential diagnosis of primary cardiac tumors since the masses often have a characteristic tissue composition[7] as in the case of lipomas (fat saturation).

The treatment of cardiac lipoma remains controversial,[8] with surgery being the method of choice for symptomatic patients, whereas conservative management is recommended for other patients[9] since it is associated with clinical monitoring and imaging tests to evaluate possible progression and adjacent structure invasion.

Modern cardiovascular imaging techniques allow for an earlier diagnosis of cardiac neoplasms, which are measured in the early stages, thus reducing the risk of complications. However, the treatment of cardiac lipomas located in the interventricular septum remains unclear, highlighting the importance of imaging tests in monitoring and decision-making. Thus, the present case contributes to the literature by reporting the clinical characteristics of a rare tumor in an unusual location.

Authors' contributions

Research concept and design: Thomé BB and Pazzini LV; data collection: Thomé BB and Pavan NR; manuscript writing: Thomé BB, Pazzini LV, and Almeida TS; critical review of the manuscript for important intellectual content: Almeida TS and Cabeda EV.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Cardiac Sarcoidosis as a Cause of Total Atrioventricular Block: Importance of Differential Diagnosis

Sarcoidose Cardíaca como Causa de Bloqueio Atrioventricular Total: Importância do Diagnóstico Diferencial

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Introduction

Sarcoidosis is a systemic granulomatous disorder of unknown cause that can affect virtually any organ. The extracardiac forms are usually benign and subjected to spontaneous remission. However, the prognosis may be unfavorable in case of cardiac involvement.

Symptomatic cardiac sarcoidosis (CS) is diagnosed in approximately 5% of patients with sarcoidosis.[1] However, based on some autopsy series, the prevalence of subclinical CS can reach 25–30%.[1]

Cardiac involvement is mainly characterized by compact non-caseous epithelioid cell granulomas that, depending on their extent and location, can lead to heart failure (HF) or cause potentially lethal arrhythmias, particularly ventricular, such as ventricular tachycardia (VT) and ventricular fibrillation (VF), and atrioventricular (AV) conduction disorders. The etiological diagnosis of CS can be of extreme clinical importance, especially in cases of advanced AV block (AVB), changing therapeutic measures and presenting significant prognostic implications.[1,2]

Case report

A 39-year-old man with a 3-month history of progressive tiredness and dizziness was referred for permanent cardiac pacemaker (PM) implantation due to a complete atrioventricular block (CAVB) on electrocardiography (Figure 1A) and New York Heart Association functional class III HF. Echocardiography showed dilation of the four cardiac chambers and significant left ventricular dysfunction with a left ventricular ejection fraction (LVEF) of 34%. Cardiac magnetic resonance confirmed the echocardiographic findings and showed a myocardial infiltrative aspect with delayed enhancement diffusely affecting the right ventricle (RV) and several left ventricular (LV) segments, such as the mesocardium and sub-epicardium, in addition to significant septal involvement.

To confirm the CS criteria, the patient underwent chest computed tomography, which showed which multiple lymph nodes, peri-lymphatic and mediastinal nodules, and peri-bronchial interstitial thickening compatible with the diagnostic hypothesis (Figure 2).

As recommended in the Heart Rhythm Society (HRS) guidelines for CS,[1] the patient received an implantable cardioverter-defibrillator (ICD), and immunosuppressive treatment with corticosteroids was promptly started. His condition progressed with a significant improvement in ventricular function, functional class, and pulmonary changes; subsequently, the conduction disorder regressed to a first-degree AVB.

After approximately 8 months, the patient presented with new disease activity, an episode of appropriate ICD therapy in the VF zone (Figure 1B). Considering the presence of methotrexate-induced hepatotoxicity, azathioprine was added to the corticosteroid treatment to stabilize the disease. Months later, he presented with symptomatic atrial fibrillation (AF) and was treated with rivaroxaban anticoagulation and subsequent electric cardioversion (ECV).

Since then, the patient has been clinically stable in functional class II (NYHA) with an LVEF of 40% and is receiving bisoprolol, amiodarone, spironolactone, furosemide, and rivaroxaban. As for the arrhythmic condition, he started to present significant sinus dysfunction (sinus frequency < 30 bpm), a new CAVB dependent on artificial cardiac stimulation, and recurrent AF (new ECV).

Discussion

The case described emphasizes the importance of the etiological diagnosis of an advanced AV conduction disorder (CAVB) associated with HF in a young patient who was previously asymptomatic and had no comorbidities. In this case, the CS diagnosis impacted his early treatment, with immunosuppressive therapies and the choice of the implanted device. In this case, the implantation of an ICD instead of a conventional PM as the primary method of preventing sudden cardiac death according to the recommendations of the Japanese Circulation Society and the HRS guidelines.[1,3] It is noteworthy that the patient had an episode of ventricular arrhythmia (VF range) in the follow-up period that was treated by the device.

The occurrence of CAVB in young patients is a warning

Keywords

Arrhythmogenic right ventricular cardiomyopathy/dysplasia; Atrioventricular block; Diagnosis; Sarcoidosis; Sudden death; Ventricular tachycardia.

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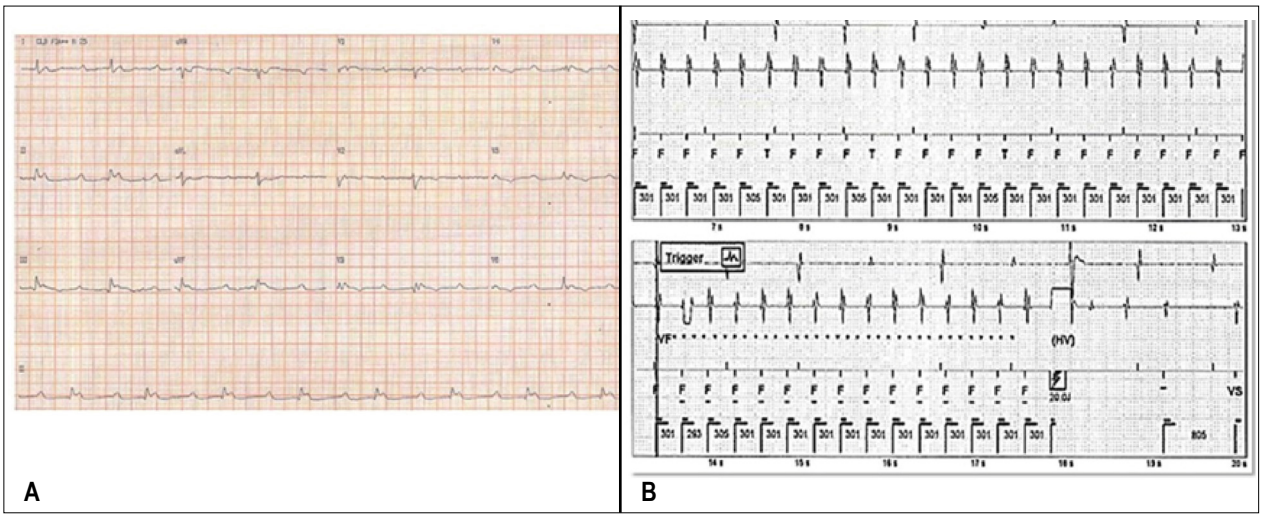

Figure 1 – *(A) Complete atrioventricular block. (B) Telemetry record of the device showing an episode of ventricular tachycardia (approximately 300 ms/200 bpm cycle) with effective therapy.*

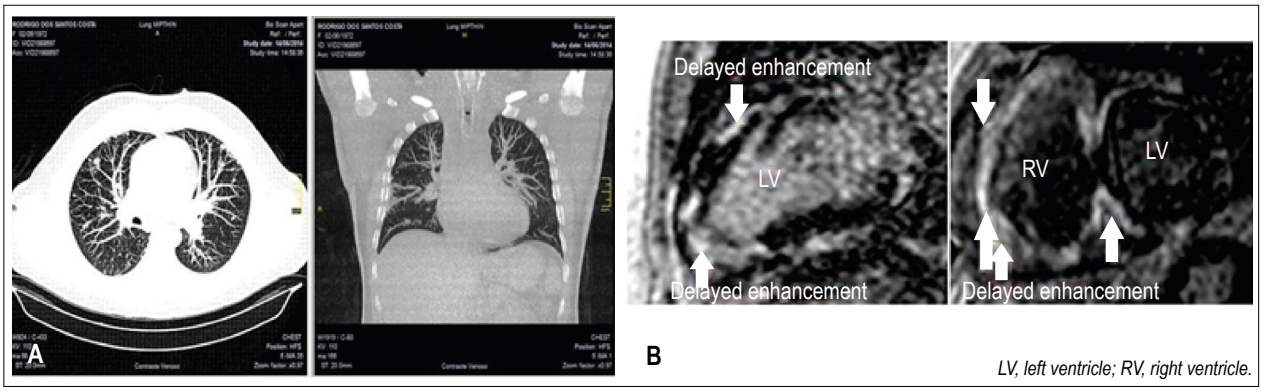

Figure 2 – *(A) Chest computed tomography image showing multiple lymph nodes, peri-lymphatic and mediastinal nodules, and peri-bronchial interstitial thickening. (B) Delayed enhancement diffusely affecting the right ventricle and several segments of the left ventricle in addition to significant septal involvement.*

factor for severe forms of heart disease requiring more detailed screening, particularly CS.[1,3,4] Kandolin et al. used endomyocardial biopsy to investigate 72 patients (aged < 55 years) with AVB of unknown etiology and reported findings compatible with CS in 14 of them (19%) and "probable" CS in four (6%) cases. In 44% of cases, symptomatic AVB was the first clinical sign of CS. Sarcoidosis patients had a significantly worse prognosis than those with idiopathic AVB.[5] The same was observed in a prospective Canadian study that diagnosed CS in 34% of patients (18–60 years old) presenting with advanced AVB.[6] These findings are extremely important considering that about half of the young patients without a definitive diagnosis can receive a PM implant.[1]

As a result, the HRS expert consensus recommends that patients < 60 years of age with high-grade idiopathic AVB should be routinely evaluated for CS.[1]

One of the fundamental aspects in making the differential diagnosis, with relevant clinical impact, is the possible clinical presentation overlap between CS and arrhythmogenic RV cardiomyopathy (ARVC/D),[2] which leads to the need to be familiarized with certain progressive characteristics, possibly distinct, between the two pathologies.

Unlike CS, high-grade AVB is rare in patients with ARVC/D dysplasia (ARVC/D).[2] A series of 113 patients with ARVC/D followed up for 10 years showed that none of them had a conduction disorder greater than first-degree AVB.[7] A good proportion of reported cases of severe AV conduction disorder attributed to ARVC/D were diagnosed before the advent of advanced imaging methods other than echocardiography and ventriculography, which may have influenced the diagnosis of CS.

Thus, although CS can have a clinical presentation that mimics the ARVC/D criteria, the simple presence of advanced AVB should support its diagnosis.[2]

In this regard, magnetic resonance imaging (MRI) can show greater basal septal impairment (presence of delayed enhancement) in patients with CS (unusual finding in ARVC/D) in addition to extracardiac abnormalities such as mediastinal lymphadenopathy and pulmonary changes.[1-2]

It is essential to establish the differential diagnosis between these two pathologies because the general features (i.e., CS immunosuppression and family screening for ARVC/D) and the specific conduction (conduction disorder) of the two clinical conditions are distinct.[1,2]

Another issue is the appropriate response to corticosteroid therapy in the acute phase of CS. Early treatment can lead to significant improvement or even prevent cardiomyopathy, suppress ventricular arrhythmia and, perhaps, decrease mortality.[1,3,8] Unfortunately, its use at a later stage and in the presence of advanced ventricular dysfunction does not seem to decrease morbidity or mortality, and it may even expose patients to unwanted side effects such as infection and complications related to implantable devices.[1]

The role of steroids in AVB is questionable. Although an initial meta-analysis showed that about half of AVB cases improved with steroids, device implantation is recommended because reversibility is unpredictable.[1] Even after an acute AV conduction recovery, myocardial inflammation can result in fibrosis and subacute/chronic healing of the exciting-conductor system.[1,3,8] The question is not whether it is possible to reverse CAVB with corticosteroid therapy, but whether the AV conduction disorder occurs more frequently in cases of greater myocardial impairment and an increased risk of ventricular tachyarrhythmia, as seen in the present case.

The most common CS presentation is symptomatic high-grade AVB, which is usually associated with ventricular dysfunction and arrhythmia.[1,9] The consensus of HRS specialists on arrhythmias in CS recommends ICD implantation in all CS patients with indications for permanent cardiac stimulation (class IIa).[1]

The recent registry study on Myocardial Inflammatory Diseases in Finland showed that high-grade AVB in CS is not a benign condition, even when it is the only sign of cardiac involvement. This was demonstrated by a 34% risk of sudden death within 5 years with the association of AVB and ventricular and/or VT dysfunction, and from 9% to 14% in cases of isolated AVB or mild LV dysfunction.[9]

The present case shows that the wide cardiac involvement caused by the disease can result in the coexistence of atrial and ventricular arrhythmias in the same person.[1,3] Compared to ARVC/D patients, the incidence of AF/atrial flutter and sinus dysfunction with the need for atrial stimulation is much higher in CS.[2] Thus, the implantation of a bicameral ICD would have several advantages, such as the maintenance of AV synchronism, AF detection, atrial stimulation, and electrogram interpretation of tachyarrhythmia events.[1]

Finally, the establishment of the differential diagnosis before device implantation is essential due to an MRI contraindication in most cases. Fortunately, this situation has improved with the availability of conditioned devices to perform MRI using 1.5-Tesla systems.[1-2] Otherwise, the use of positron emission tomography is recommended to diagnose and monitor patients with unconditioned devices.[1]

Authors' contributions

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Conflict of interest

The authors have declared that they have no conflict of interest.

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ALCAPA Syndrome in a Young Woman

Síndrome de ALCAPA em uma Mulher Jovem

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Abstract

An 18-year-old woman presented with a one-year history of syncope, angina, and palpitations. The critical clue was a dilated right coronary artery on transthoracic echocardiography. Computed tomography findings resulted in the diagnosis of anomalous origin of the left coronary artery from the pulmonary artery syndrome.

Introduction

Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) syndrome, also known as Bland-Altman-Garland Syndrome, was first clinically described by these authors.[1] As a rare congenital heart condition, ALCAPA is rarely found in adults since few affected individuals survive childhood without surgical repair. Here, we report a case of this rare congenital anomaly that presented as a one-year history of syncope, angina, and palpitations. The critical clue to the final diagnosis was a dilated right coronary artery on transthoracic echocardiography (TTE).

Case description

An 18-year-old woman had a one-year history of syncope at rest accompanied by angina and palpitations on exertion. Worsening dyspnea on exertion was evident. She had no coronary risk factors or family history of premature coronary artery disease or congenital heart condition. Physical examination results were unremarkable. Electrocardiography (ECG) findings included sinus rhythm, 67 bpm, embryonic r wave in V1–V3, and a biphasic T wave in the lateral wall. Holter monitoring showed no arrhythmia, and no episodes of cardiac arrhythmia on cardiac monitoring were detected during her hospital stay. Chest radiography findings were normal. Tests for serial cardiac enzymes were negative. TTE demonstrated mildly dilated left cardiac chambers with wall motion abnormalities (WMAs) of the proximal two-thirds of the anterior wall and anterior septum and a normal left ventricular ejection fraction. An unusual dilation of the right coronary artery (RCA) was observed (Figure 1). Cardiac magnetic resonance (CMR) documented hypokinesia of the basal and mid segments of the anterior wall and the anterior septum with subendocardial late gadolinium enhancement. No other associated cardiac anomalies were noted. These findings strongly suggested an anomalous origin of the left coronary artery (LCA). Multidetector computed tomography (MDCT) coronary angiography subsequently established the diagnostic hallmark of ALCAPA syndrome (Video 1). MDCT coronary angiography images revealed an LCA branching off from the main pulmonary artery (Figure 2, arrowhead). The RCA arose from the aorta (Figure 2, arrow) with collateral circulation to the LCA. A coronary angiogram performed before surgery revealed that all coronary arteries and their branches were ectatic with tortuous courses. An extremely large and tortuous right RCA arising from the right coronary cusp and extending collaterals to the left coronary system was evident (Figure 3). Steal phenomenon was evident, with retrograde flow from the LCA into the main pulmonary artery. The patient underwent surgical correction with aortic reimplantation of her left main coronary artery. Her postoperative course was uneventful. The patient is now followed regularly.

Discussion

The estimated incidence of ALCAPA is 1/300 000 live births (0.24–0.46% of all congenital cardiac anomalies).[2] Since its late presentation is usually described,[3,4] this may be a significant underestimation of its true incidence. ALCAPA syndrome is associated with early infant mortality and sudden adult death. Its clinical expression results from evolving morphological–functional alterations in the pulmonary circulation that occur after birth. After birth, pulmonary artery saturation and pressure gradually decrease, and flow from the pulmonary artery to the LCA stops. Retrograde flow occurs from the RCA collaterals to the pulmonary artery. By this time, left ventricular perfusion fully depends upon collaterals to the LCA developing from the RCA. Coronary steal syndrome develops, leading to hypoxic damage to the left ventricular myocardium. If left untreated, up to 90% of affected children die within the first year of life.[2] An estimated 10–15% of affected children reach adulthood.[5] Their survival depends on the extent of acquired collateral circulation. Those with a well-established collateral circulation between the right and left coronary vessels have the adult type of disease, while those without collateral vessels have the infant type. The manifestations and outcomes differ between the two types.[2] The adult type is characterized by collateral circulation between the RCA and the LCA via a shunt

Keywords

Adult, ALCAPA Syndrome, Bland-White-Garland Syndrome, Echocardiography.

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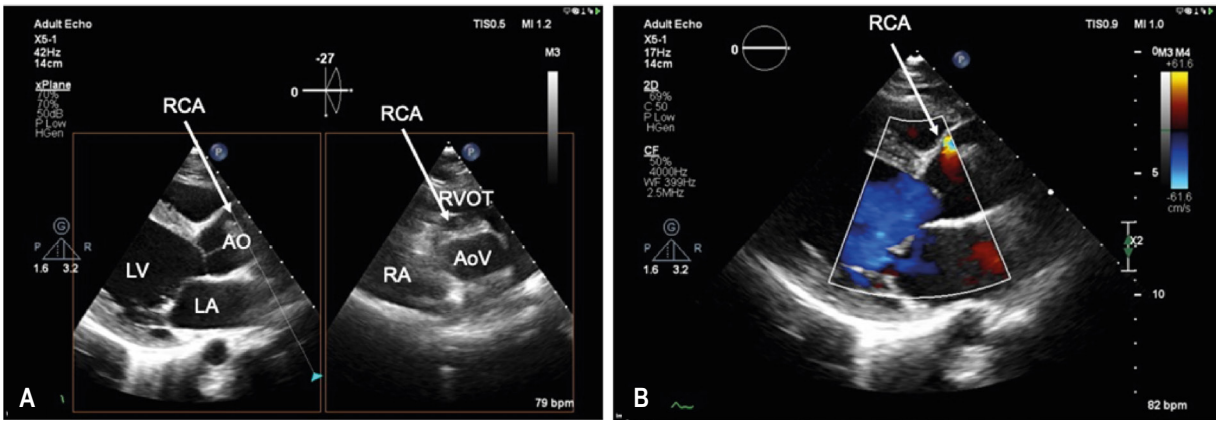
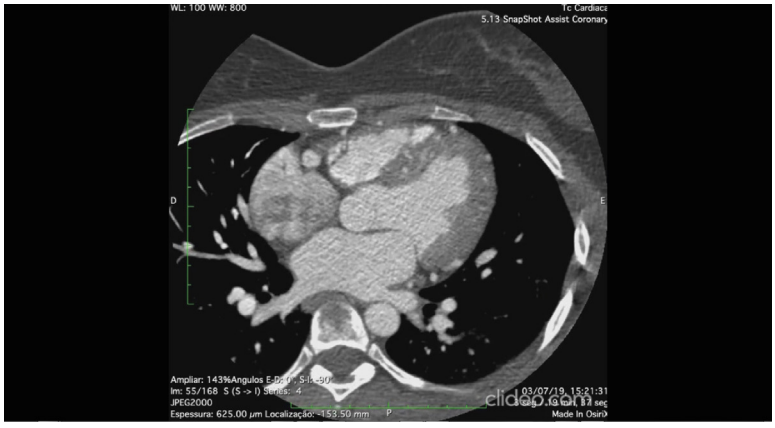


Figure 1 – *Transthoracic echocardiography examination. Panel A: (Right) parasternal long-axis view with dilated RCA. (Left) perpendicular cut along the RCA on PLAX. Parasternal short-axis view at the level of the ascending aorta with the right coronary artery on top. Panel B: Parasternal long-axis view of diastolic flow of visibly dilated RCA. AO, ascending aorta; AoV, aortic valve; LA, left atrium; LV, left ventricle; RA, right atrium; RCA, right coronary artery; RVOT, right ventricular outflow tract.*



Video 1 – *Multidetector computed tomography coronary angiography video demonstrating the abnormalities described in Figure 1.*

compensation mechanism. Symptoms and ischemia ensue whenever collateral circulation decompensation occurs. Most cases in adulthood demonstrate evidence of some degree of irreversible impairment of cardiac function.[6]

The one-year history of the syncope, angina, and palpitations triad was the initial red flag. This waiting period could be dangerous because cardiac arrest due to ventricular fibrillation can be the major clinical presentation of ALCAPA in adults.[7] The ECG findings may provide the first clue to the diagnosis. The ECG of a baby with ALCAPA syndrome usually shows typical signs of an anterolateral myocardial infarction with abnormal Q waves and transient ST changes in leads I, aVL, V5, and V6.[8] Our patient had an embryonic r wave in leads V1–V3 and biphasic T waves in the lateral wall. The critical clue to the final diagnosis was the TTE examination finding of unusual dilation of the RCA in conjunction with mildly dilated left cardiac chambers and WMAs on the LCA territory. The strong clinical- and echocardiography-based suspicions led to MDCT coronary angiography and CMR examinations. MDCT coronary angiography can reveal anomalous coronary arteries, as direct visualization of the LCA arising from the main pulmonary artery is the diagnostic hallmark of the syndrome. CMR elucidates the consequences of chronic myocardial ischemia, with hypokinesia of the LCA territory and subendocardial infarction. Indeed, imaging is pivotal to the ALCAPA diagnosis. CT coronary angiography provides an accurate and detailed description of the origin and course of the coronary arteries. CMR is used to make a more functional assessment and establish subendocardial ischemic changes or infarction (replacement-type fibrosis).[9]

Surgical treatment is suggested in patients with ALCAPA syndrome, even if asymptomatic. The objective of surgical repair is to restore normal coronary circulation and improve left ventricular myocardial perfusion.[2] Restoration of the coronary system prevents further ischemia and arrhythmias of acute ischemic origin. However, the anatomical substrate for ventricular arrhythmias in patients with old myocardial infarction will not be altered by the repair. Since our patient had myocardial scars from

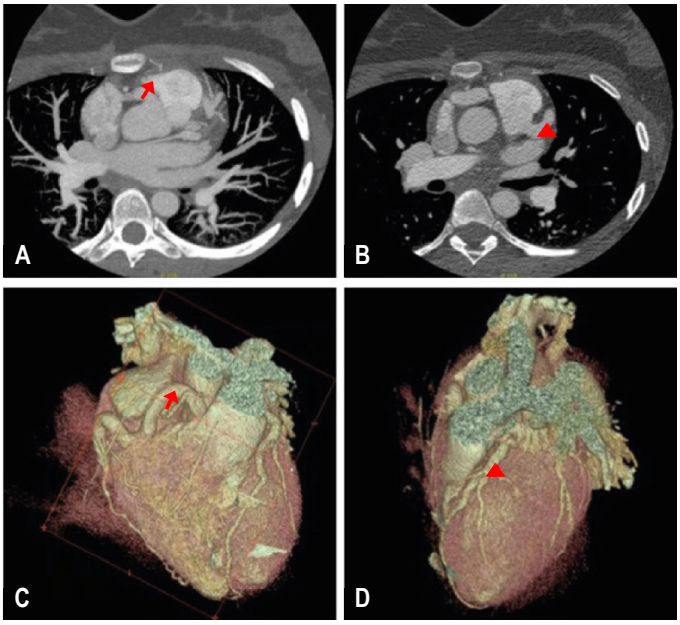


Figure 2 – *Multidetector computed tomography coronary angiography. Panels A and C: The RCA arose from the aorta (arrow) with collateral circulation to the LCA. Panels B and D: The LCA is branching off from the main pulmonary artery (arrowhead). AO, ascending aorta; ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery; PA, pulmonary artery; RCT, right coronary artery.*

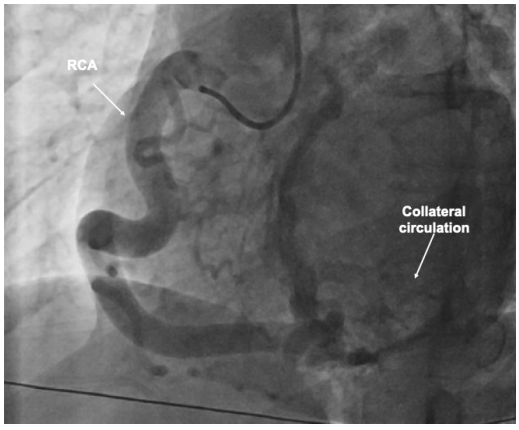


Figure 3 – *Invasive coronary angiography. The right coronary artery (RCA) with visible collateral circulation to the left coronary artery (LCA).*

chronic ischemia, long-term clinical and electrocardiographic (ECG and Holter ECG) monitoring continues.[7]

Conclusion

In this case report, the critical clue was the pathologic ECG findings of the ischemic heart and mildly dilated left cardiac chambers with unusual RCA dilation. CMR further demonstrated myocardial scarring, while MDCT established the diagnostic hallmark. It is critical to remember that the patient's complaints may be validated by the ECG findings and careful TEE.

Author contributions

Research creation and design: Campos D, Puga L, Guardado J, Saleiro C, Lopes J, Teixeira R, Gonçalves L. Análise e interpretação dos dados: Campos D, Puga L, Guardado J, Saleiro C, Lopes J, Teixeira R, Gonçalves L. Manuscript writing: Campos D, Puga L, Guardado J, Saleiro C, Lopes J. Critical revision of the manuscript for important intellectual content: Teixeira R, Gonçalves L.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Isolated Fungal Pulmonary Endocarditis: Role of Transthoracic Echocardiography from the Diagnosis to Follow-up

Endocardite Fúngica Isolada da Válvula Pulmonar: o Papel do Ecocardiograma Transtorácico do Diagnóstico ao Acompanhamento

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Introduction

Pulmonary valve endocarditis, an uncommon entity, is associated with important complications such as pulmonary emboli, severe valvular regurgitation, and right-sided chamber dilatation and is usually concomitant with tricuspid valve endocarditis. Intravenous (IV) drug and cardiovascular implantable electronic device use are known risk factors for this condition. *Staphylococcus aureus* is the most prevalent causative bacteria, whereas fungi are rarely involved. Here, we present a case of *Candida albicans*–induced pulmonary valve endocarditis.

Case presentation

A 29-year-old woman with a medical history including a diagnosis of acute myeloid leukemia diagnosis in 2017, cardiotoxicity due to chemotherapy with high doses of anthracycline in 2017, and hematopoietic stem cell transplantation in 2018 was admitted for elective oncological treatment due to acute lymphocytic leukemia relapse. On admission, she was hemodynamically stable and her physical examination was unremarkable. She developed febrile neutropenia and a catheter-related bloodstream candidemia infection during the hospitalization. Despite antifungal treatment, she had persistent fever, while signs of embolization in the lungs, liver, and spleen were detected by computed tomography.

Transthoracic echocardiography (TTE) (Figure 1) demonstrated multiple filamentous mobile echodensities attached to the pulmonary valve, the largest being 1.2 cm in length. Transesophageal echocardiography (TEE) confirmed isolated right-sided infective endocarditis (IE). The cardiac surgery team recommended continued medical therapy with antifungal treatment. A follow-up TTE performed one week later (Figure 2) showed progression of the vegetations, now extending into the right ventricle outflow tract (RVOT), without functional pulmonary valve impairment. The patient underwent surgical treatment with pulmonary valvuloplasty two weeks after the endocarditis diagnosis. Intraoperative echocardiography (Figure 3) showed extension of vegetation in the RVOT. Vegetation debridement was performed through a longitudinal pulmonary artery incision made above the valvular plane. During the procedure, two pulmonary leaflets were perforated and then promptly repaired. Culturing of the surgical material confirmed *C. albicans* infection.

The patient's recovery was uneventful, and she was discharged from the cardiac intensive care unit on the third day of antifungal treatment. TTE performed on the 14th postoperative day showed a residual small filamentary mobile image on the pulmonary valve with mild pulmonary regurgitation. Due to the poor prognosis of the hematologic disease, the patient was discharged on oral antifungal treatment and continued the chemotherapy cycles after one month.

Discussion

An estimated 5–10% of all IE cases are right-sided.[1] Nonetheless, an increase in the incidence of right-sided IE has been reported due to the global increase in intravenous drug use, greater use of central venous catheters in clinical care, and increased number of cardiovascular implantable electronic devices.[2] IE is more common in human immunodeficiency virus (HIV)–infected IV drug users than in HIV-uninfected IV drug users as reported by a case-control study in Baltimore (13.8 versus 3.3 cases per 1000 person-years).[3] The majority of cases involve the tricuspid valve, with the pulmonary valve accounting for less than 10% of all right-sided cases.[4]

The sensitivity of TTE may be comparable to that of TEE for diagnosing right-sided IE, with a reported sensitivity above 80% among IV drug users.[5] These results are due to right-sided vegetations being larger anterior structures that are closer to the transthoracic probe than to the transesophageal probe. Furthermore, the drug users are usually younger and have smaller body mass indexes, resulting in good acoustic transthoracic windows. TEE of the pulmonary valve can be challenging, even for experienced echocardiographers, and may have limited optimal visualization. Indications for TEE include a poor acoustic transthoracic window, suspected left-sided endocarditis, suspected pulmonary valve endocarditis, negative TTE and central catheterization results, a poor clinical course with no alternate diagnosis, or relevant or high

Keywords

Endocarditis; Echocardiography, Diagnosis.

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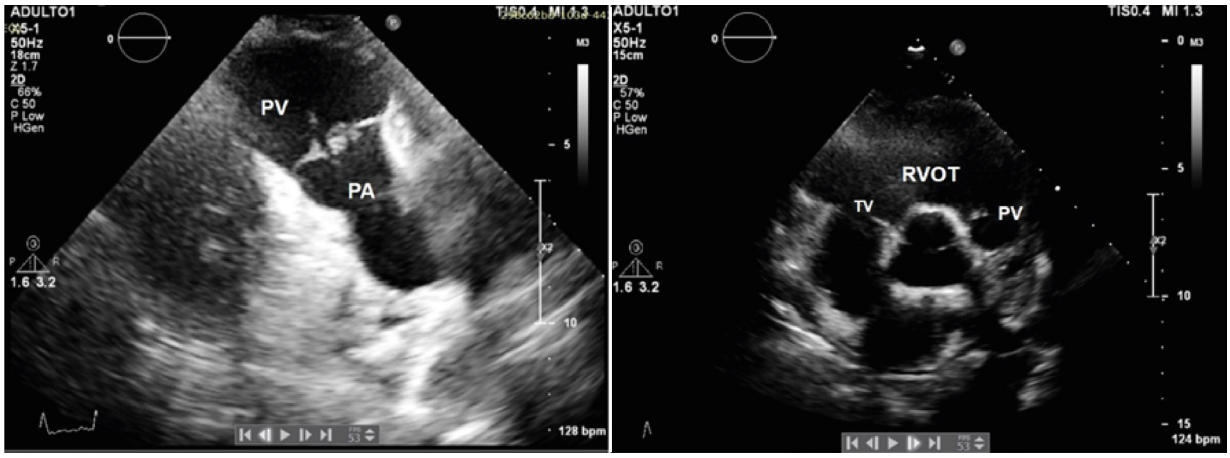
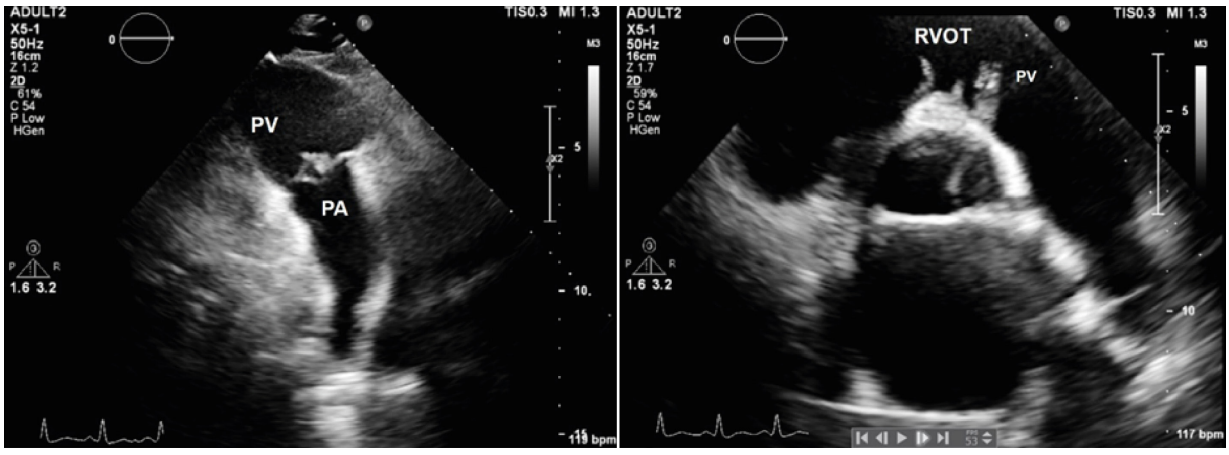


PA: pulmonary artery; PV: pulmonary valve; RVOT: right ventricular outflow tract; TTE: transthoracic echocardiography; TV: tricuspid valve

Figure 1 – *Left panel: TTE parasternal long-axis view of the RVOT showing a vegetation on the pulmonary valve. Right panel: TTE parasternal short-axis view of the RVOT.*



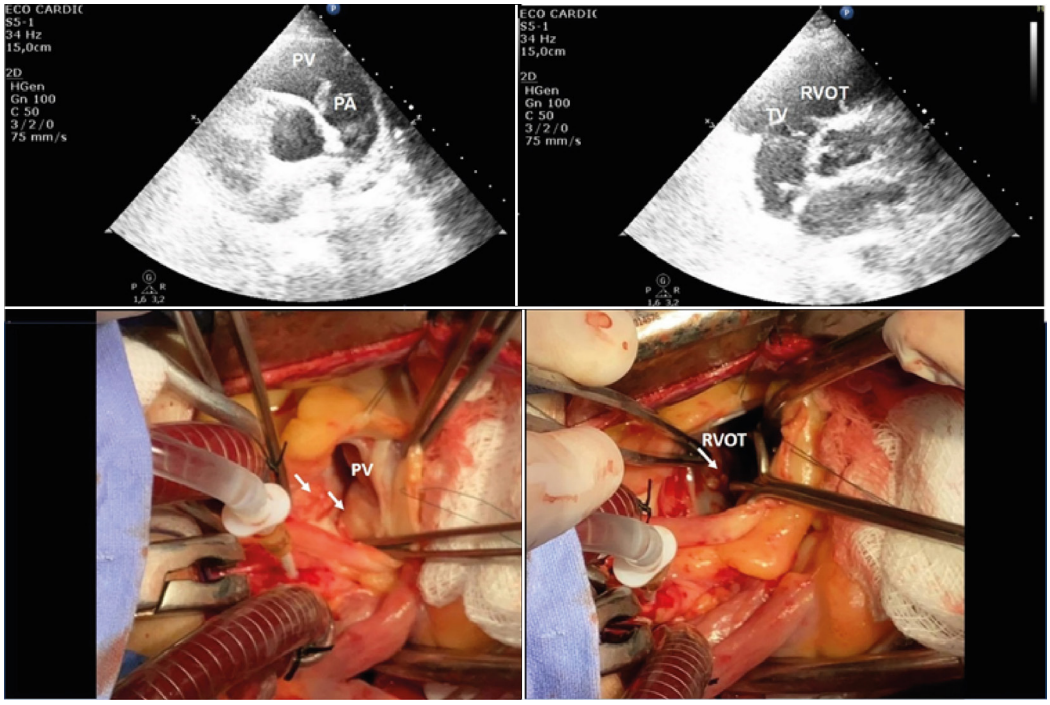
PA: pulmonary artery; PV: pulmonary valve; RVOT: right ventricular outflow tract; TTE: transthoracic echocardiography

Figure 2 – *Left panel: TTE parasternal long-axis view of the RVOT. Right panel: TTE parasternal short-axis view of the right ventricular outflow tract showing a vegetation on the RVOT.*

clinical suspicion.[5] TTE usually provides good visualization of the pulmonary valve cusps as well as the optimal angle for Doppler interrogation. In a published case series, the diagnosis of pulmonary valve IE was made by TTE in all cases.[6]

Surgical intervention is required in 15–30% of patients with right-sided IE,[7] with a reported operative mortality rate around 7% for patients with isolated tricuspid valve IE.[8] Surgical indications in right-sided IE were based on an aortic and mitral valve IE population, which had worse prognostic factors including very large vegetations (≥2 cm long),[9] a highly resistant organism and/or persistent bacteremia, recurrent septic pulmonary emboli, and a fungal etiology.[10] The case described here had a clear surgical indication since it was a *C. albicans*–induced IE with persistent bacteremia-like and septic pulmonary emboli despite antifungal treatment. Adequate surgical techniques include radical debridement of infected tissue and vegetation to preserve the valve,[6] which is preferred at the early stage of infection; valve repair using autologous pericardium or conserved xeno-pericardium; patching or restoring the valvular cusps[11]; valve replacement with a conduit; and biological or mechanical prothesis.[6]

Staphylococcus aureus, *Streptococcus* spp., and *Enterococcus* spp. are the most frequent bacteria leading right-sided IE patients to surgical treatment. Fungi were detected in approximately 3% of cases.[12] Factors associated with a poor prognosis included fungal etiology, vegetation size larger than 2 cm, presence of acute respiratory distress syndrome,[2] and a CD4 count below 200 cells/mm^3 in HIV-infected patients.[13]



PA: pulmonary artery; PV: pulmonary valve; RVOT: right ventricular outflow tract; TTE: transthoracic echocardiography; TV: tricuspid valve.

Figura 3 – *Upper left panel: TTE parasternal long-axis view of the RVOT. Upper right panel: TTE parasternal short-axis view of the RVOT showing extension of vegetations in the RVOT toward the tricuspid valve. Bottom left panel: surgical view of the pulmonary valve. Bottom right panel: surgical view of the RVOT.*

The case presented a difficult and complex therapeutic decision. Although pulmonary valve IE with candidemia and pulmonary septic embolization was a clear surgical indication in this young patient, relapse of acute leukemia *per se* indicated a poor prognosis. Despite the satisfactory surgical outcome in this case, we cannot extrapolate this result to other patients with malignant neoplasia and management decisions should be made on a case-by-case basis.

Conclusion

This was a rare case of pulmonary valve fungal endocarditis in the setting of acute leukemia relapse in a young adult that was managed with surgical resection. This case illustrates the usefulness of TTE in diagnosis, follow-up, and decision-making in right-sided IE. Although we performed TEE, the diagnosis and clinical management could have been made using TTE alone. Although surgical treatment had a satisfactory outcome in this case, management decisions should be made on a case-by-case basis with multidisciplinary coordination.

Authors contribution

Critical revision for intellectual content and conceptualization: Pianca EG, Branchi MN, Santos ABS; Image acquisition: Pianca EG, Santos ABS; Albrecht AS; Mastella B; Wender OCB. Supervision: Foppa M, Santos ABS; Writing – original draft: Pianca EG; Writing – review & editing: Branchi MN, Albrecht AS, Mastella B, Wender OCB, Foppa M, Santos ABS.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Cerebrovascular Disease as the Initial Manifestation of Apical Hypertrophic Cardiomyopathy

Doença Cerebrovascular como Manifestação Inicial de Cardiomiopatia Hipertrófica Apical

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Introduction

Apical hypertrophic cardiomyopathy (AHCM) is a condition that primarily involves the apex of the left ventricle. Two of its main characteristics are a non-obstructive physiology and apical hypertrophy of the left ventricle with giant negative T waves. AHCM is uncommon, and its prevalence is notably affected by ethnicity. The diagnosis is challenging to make and requires multimodal imaging techniques.[1,6] Here we describe two cases of AHCM with cerebrovascular disease as the presenting condition: Patient 1 had atrial fibrillation (AF), while Patient 2 showed evidence of aortic plaques as the possible embolic source. Nonetheless, Patient 2 also presented an akinetic apex. Hence, it was impossible to rule out the previous migration of an apical thrombus as the cause of the ischemic stroke. The main clinical lesson learned from our cases is that stroke in patients with AHCM is a multifactorial complication potentially caused by AF, aortic plaques, and intracavitary thrombus. Therefore, although AHCM is uncommon, it should be considered when determining the cause of cerebrovascular embolic events.

Case presentation

Patient 1

A 51-year-old woman with suspected multiple sclerosis presented with numerous sudden-onset and -cessation tachycardic events. During these events, she suffered from low cardiac output symptoms and occasional transient cerebral ischemia signs. She had a history of hyperthyroidism, uncontrolled arterial hypertension, and small vessel cerebrovascular disease. Computed tomography (CT) revealed multiple embolic cerebral infarcts. Electrocardiography (ECG) showed sinus rhythm with left-ventricular hypertrophy criteria and giant negative T waves (Figure 1). Transthoracic echocardiography (TTE) revealed a normal-sized left ventricle (LV) with a 24-mm apical hypertrophy (Figure 2). Other findings included conserved global and segmental mobility at rest, an LV ejection fraction (LVEF) of 67%, E/A ratio of 0.73 (impaired relaxation), and normal systolic pulmonary artery pressure (SPAP; 33 mmHg). In contrast, a 7-day Holter monitoring study revealed evidence of AF. Thus, anticoagulation with apixaban was initiated. The patient also received metoprolol, amlodipine/valsartan, atorvastatin, and amitriptyline.

Patient 2

A 75-year-old woman presented to the emergency room with somnolence, dysarthria, and ataxic movements. She had a history of essential arterial hypertension, which was diagnosed 3 years ago, in medical control. On CT, a hypodense zone in the left cerebellum was found, which was associated with an embolic origin. The ECG showed sinus rhythm with criteria for left-ventricular hypertrophy and giant negative T waves in the precordial leads. Transthoracic and transesophageal echocardiography (TEE) revealed a normal-sized LV with a 16-mm apical hypertrophy and an akinetic apex. Additional findings were an E/A ratio of 0.6 (impaired relaxation), LVEF of 65%, normal SPAP (32 mmHg), dilated left atrium, and mitral and aortic valve sclerosis paired with mild mitral and tricuspid insufficiency. Additionally, a grade 5 complex atheromatous plaque was noted in the ascending aorta at the sinotubular junction (Figure 3A). Moreover, there was evidence of diffuse atheromatosis in the aortic arch and the descending segment with diffuse intimal thickening and both simple and complex plaques (Figure 3B). Hence, the patient was treated with apixaban along with irbesartan/hydrochlorothiazide, atorvastatin, and fluoxetine. Table 1 compares the clinical and therapeutic parameters of the two cases.

Discussion

AHCM, also known as Yamaguchi syndrome, is an uncommon disease that was first described by Sakamoto *et al*. in 1976.[2] It accounts for 3% and 13–25% of hypertrophic cardiomyopathy cases in the United States and Japan, respectively.[3]

Clinically, AHCM has a nonspecific manifestation with no pathognomonic complaints. Accordingly, its diagnosis is often delayed by around 4.7 years.[4] However, some common clinical findings at presentation include atypical chest pain, dyspnea, exercise intolerance, palpitations, AF, and syncope or presyncope.[1] Patients may also have hypertension (30%) and family members with hypertrophic cardiomyopathy

Keywords

Cerebrovascular Disease; Echocardiography; Embolism; Hypertrophic Cardiomyopathy.

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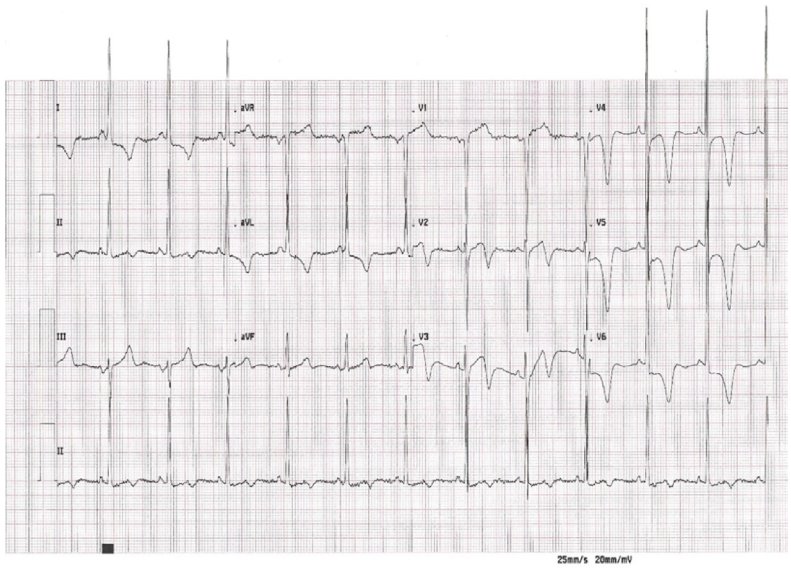

Figure 1 – *Electrocardiogram of Patient 1 showing evidence of left ventricle hypertrophy and giant negative T waves.*

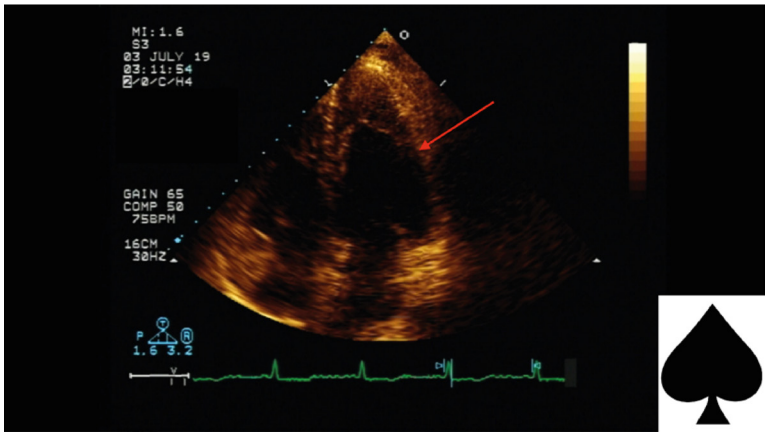

Figure 2 – *Transthoracic echocardiogram (apical 4-chamber view) of Patient 1 showing left-ventricular apical hypertrophy with the characteristic "ace of spades" shape.*

or a history of sudden cardiac death (26%).[1,8] Additionally, around 30% of patients with AHCM will present one or more morbid events such as AF, myocardial infarction, congestive heart failure, transient ischemic attack, stroke, ventricular tachycardia, and ventricular fibrillation.[4]

The reported prevalence of AF in AHCM is 12–31%.[4,5] Furthermore, cerebral embolic events were found to affect 6.7–18.8% of the patients, with left atrium size (hazard ratio, 1.2) and AF (hazard ratio, 5.5) as the main risk factors.[4,5] Both of our patients presented a cerebrovascular condition as a complication of AHCM, but only Patient 1 had evidence of AF, whereas Patient 2 presented with aortic plaques. However, Patient 2 also had an akinetic apex on TEE evaluation, which could represent a potential embolic source. This leads us to remark that, in patients with a history of stroke, hypertrophic cardiomyopathy (as well as other structural pathologies), along with AF and arterial plaques, should be considered potential sources of embolic events.

For the diagnosis of AHCM, a multimodality imaging approach is often used. This commonly starts with an ECG and includes echocardiography and cardiovascular magnetic resonance (CMR). In our case, the key signs that led us to the diagnosis of AHCM were the giant negative T waves and the left-ventricular apical hypertrophy with the classical "ace of

Table 1. Key patient characteristics.

Parameter / Study	Case 1	Case 2
	General	
Age [years]	51	75
Gender	Female	Female
Pre-existing medical conditions/comorbidities	- Paroxysmal tachycardia events with low cardiac output symptoms and transient cerebral ischemia signs - Uncontrolled essential systemic hypertension - Hyperthyroidism - Small vessel cerebrovascular disease - No evidence of diabetes mellitus or dyslipidemia	- Controlled essential systemic hypertension - Hip replacement surgery - Patient showed no evidence of diabetes mellitus or dyslipidemia
Atrial fibrillation evidence	Yes	No
	Studies/Laboratory tests	
ECG	- Sinus rhythm - Negative giant T waves in precordial leads - 7-day Holter monitoring revealed atrial fibrillation	- Sinus rhythm - Negative giant T waves in precordial leads
Computed Tomography	- Multiple cerebral infarctions with high suspicion of embolic origin	- Hypodense zone in left cerebellum with suspicion of embolic origin
Echocardiogram	- TTE 1. Normal sized left ventricle with apical hypertrophy of 24 mm 2. LVEF = 67% 3. E/A = 0.73 4. SPAP = 33 mmHg	- TEE 1. Normal sized left ventricle with apical hypertrophy of 16 mm 2. Akinetic LV apex 3. LVEF = 65% 4. E/A = 0.6 5. SPAP = 32 mmHg 6. Complex atheromatous plaque in the ascending aorta (Grade 5) 7. Diffuse atheromatosis in the horizontal portion and descending aorta 8. Dilated left atrium 9. Mitral and aortic valve sclerosis 10. Mild mitral and tricuspid insufficiency
	Treatment	
Anticoagulation	- Apixaban	- Apixaban
Antiplatelet therapy	No	No
Antihypertensive	- Amlodipine/Valsartan - Metoprolol	- Irbesartan/Hydrochlorothiazide
Statins	- Atorvastatin	- Atorvastatin
Other treatments	- Amitriptyline	- Fluoxetine

BNP: B-type natriuretic peptide; ECG: electrocardiogram; LV: Left Ventricle; SPAP: Systolic Pulmonary Artery Pressure; TEE: Transesophageal Echocardiography; TTE: Transthoracic Echocardiography.

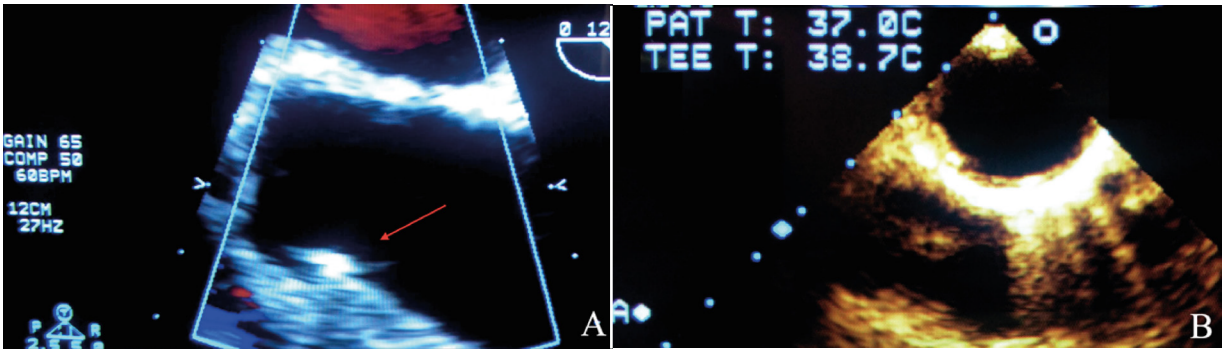

Figure 3 – *A) Transesophageal Doppler echocardiogram of Patient 2 showing a grade 5 complex atheromatous plaque in the ascending aorta at the sinotubular junction. The plaque has a heterogeneous appearance with a predominant calcific component, irregular borders, and debris. B) Transesophageal echocardiogram of Patient 2 showing diffuse atheromatosis in the descending aorta. There is evidence of diffuse intimal thickening and plaques that are simple (less than 5-mm protrusion) and complex (more than 5-mm protrusion).*

spades" shape observed on the echocardiogram (Figure 2). However, it is important to remember that giant negative T waves are not specific to AHCM since a considerable number of conditions such as Wellens' syndrome, cocaine ischemia, non-Q wave myocardial infarction, myocarditis, Takotsubo cardiomyopathy, massive pulmonary embolism, and subarachnoid hemorrhage could also cause them.[6]

In the diagnosis of AHCM made via echocardiography, the apex should be measured below the insertion of the papillary muscle, and it must be thicker than 15 mm (with a basal-to-apex wall thickness ratio of 1.3 or greater).[1,6] It is also important to measure the gradient between the apex and the left ventricular cavity since it increases the risk for thromboembolism, ventricular arrhythmias, and perfusion abnormalities.[1] Moreover, the global ejection fraction is commonly preserved, but signs of diastolic dysfunction are often observed, as seen in both of our cases.

TEE is helpful for detecting intracavitary thrombus and guiding cardiac surgery.[1] Unfortunately, false-negative results are possible in an echocardiography examination. Hence, CMR may be used. Relevant clinical findings of AHCM with CMR include the left-ventricular "ace of spades" silhouette and apical wall width greater than 15 mm, with a basal-to-apex wall thickness ratio exceeding 1.5.[1]

Valuable treatment options are available for patients with AHCM. In cases with a preserved ejection fraction, β-blockers or calcium channel blockers are recommended in maximal tolerated doses.[1,6] Patients with AHCM often present diastolic dysfunction and thus benefit from diastole prolongation.[1] Furthermore, surgical treatments such as apical myectomy are available.[1] Finally, there is no strong consensus about the prognosis of AHCM since it is considered a relatively benign disease, but a few cases are complicated by atypical angina, heart failure with a preserved ejection fraction, AF, apical aneurysm, thrombus, and cardioembolic stroke.[6] Table 2 presents the most important guidelines released by the American and European Cardiology Societies.

Conclusions

As previously discussed, AHCM is a relatively uncommon disease that is occasionally complicated by stroke. Both cases presented here demonstrated cerebrovascular embolic events as the leading manifestation of AHCM. It is interesting to note that one patient presented with AF, while the other had aortic plaques and an akinetic LV apex. We believe that these conditions are associated with AHCM with the cause of stroke. In contrast, Patient 1 had both AF and hyperthyroidism, a known cause of AF.[10] Thus, it is uncertain whether AF resulted from the hyperthyroidism or from the relationship between AHCM and diastolic dysfunction, leading to increased LV filling pressure, dilation of the left atrium, and an increased risk of AF.[2] Finally, as stated in the guidelines, since the echocardiography findings were conclusive of AHCM, we decided not to order a CMR scan. Figure 4 illustrates the mechanism of cerebrovascular embolic events as well as the diagnostic methods we used.

Author contributions

Research design: González-Rayas JM, Rayas-Gómez AL, Rico-Rosas A, Landa-Alvarado PD, León-Vargas IMP, González-Yáñez JM; Data collection: González-Rayas JM, Rayas-Gómez AL, Rico-Rosas A, Landa-Alvarado PD; Data analysis and interpretation: Rayas-Gómez AL, Landa-Alvarado PD, León-Vargas IMP, Ramos-Verdugo JM, González-Yáñez JM; Writing the manuscript: Rayas-Gómez AL, Rayas-Gómez AL, Rico-Rosas A, González-Yáñez JM; Critical review of the manuscript for important intellectual content: Rayas-Gómez AL, Landa-Alvarado PD, León-Vargas IMP, Ramos-Verdugo JM, González-Yáñez JM.

Conflict of interest

The authors have declared that they have no conflict of interest.

Table 2 - Current guideline recommendations regarding apical hypertrophic cardiomyopathy.

ACC/AHA (2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy)[7]		
Recommendation	**COR**	**LOE**
"CMR imaging is reasonable in patients with HCM to define apical hypertrophy and/or aneurysm if echocardiography is inconclusive."	IIa	B
"TTE combined with the injection of an intravenous contrast agent is reasonable if the diagnosis of apical HCM or apical infarction or severity of hypertrophy is in doubt, particularly when other imaging modalities such as CMR are not readily available, not diagnostic, or are contraindicated."	IIa	C
ESC (2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy)[9]		
Recommendation	**COR**	**LOE**
"CMR with LGE imaging should be considered in patients with suspected apical hypertrophy or aneurysm."	IIa	C
"In patients with sub-optimal images or with suspected LV apical hypertrophy or aneurysm, TTE with LV cavity opacification—using intravenous contrast agents—should be considered as an alternative to CMR imaging."	IIa	C

ACC: American College of Cardiology; AHA: American Heart Association; CMR: Cardiovascular Magnetic Resonance; COR: Class of Recommendation; ESC: European Society of Cardiology; HCM: Hypertrophic Cardiomyopathy; LGE: Late Gadolinium Enhancement; LOE: Level of Evidence; TTE: Transthoracic Echocardiogram.

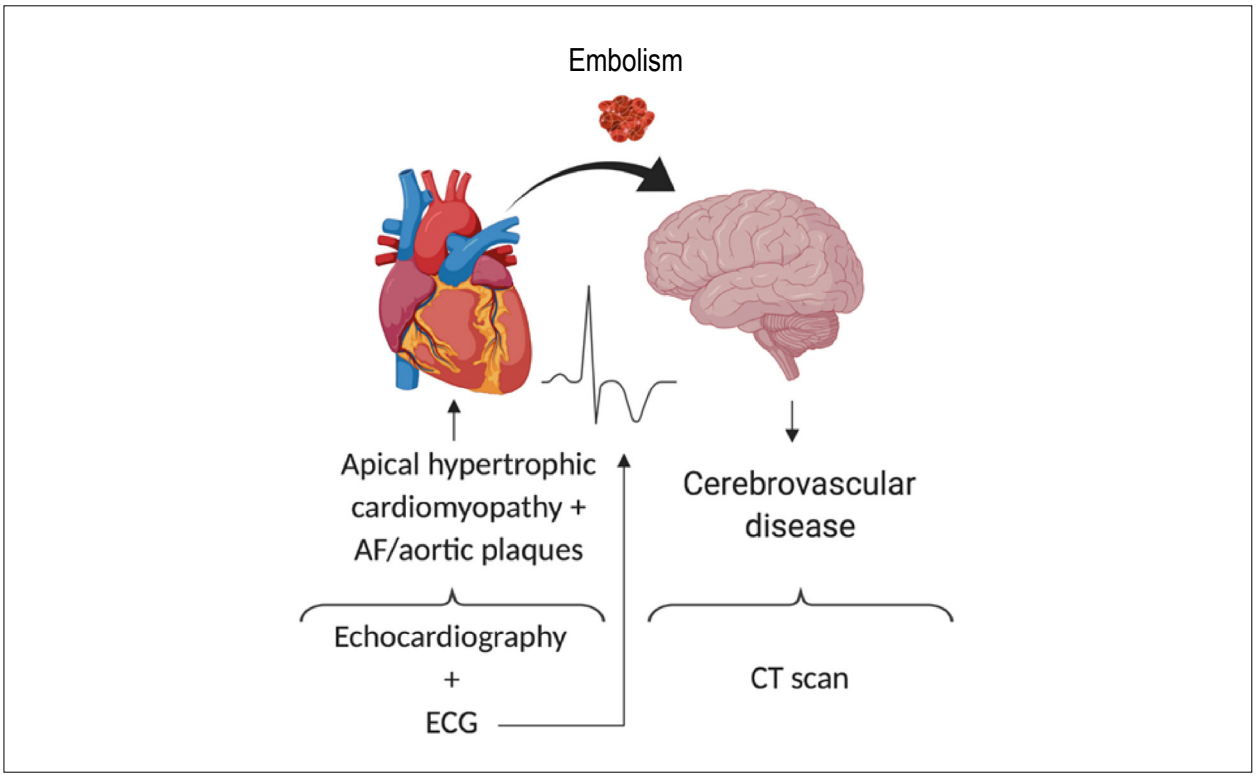

Figure 4 – *Central figure depicting the relationship between apical hypertrophic cardiomyopathy and cerebrovascular disease in our cases. The diagnostic modalities we used as well as the characteristic appearance of apical hypertrophic cardiomyopathy on the electrocardiogram are described. Created with Biorender.com. AF, atrial fibrillation; CT, computed tomography; ECG, electrocardiography.*

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Left Ventricular Free-Wall Rupture (Pseudoaneurysm) after Acute Myocardial Infarction in an Asymptomatic Patient

Ruptura de Parede Livre do Ventrículo Esquerdo (Pseudoaneurisma) pós-Infarto Agudo do Miocárdio em Paciente Assintomático

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Introduction

Left ventricular (LV) pseudoaneurysm after acute myocardial infarction may show nonspecific symptoms and be asymptomatic in up to 10% of cases. It demands investigation and a suspected diagnosis, with imaging methods playing a fundamental role in its diagnosis. This case report describes a pseudoaneurysm detected on a routine examination.

Case report

Our patient was a 64-year-old man with a previous history of insulin-dependent type 2 diabetes, chronic kidney disease undergoing dialysis, and previous acute myocardial infarction during myocardial revascularization. The patient was asymptomatic from a cardiovascular point of view and was using optimized medications when he underwent routine transthoracic echocardiography to monitor ventricular function. Moderate ventricular dysfunction was observed on the transthoracic echocardiogram, with an image suggestive of LV wall rupture in the apical region, an opening of approximately 8 mm, and a pericardial collection contained by a probable thrombus (Figure 1). Cardiac magnetic resonance (CMR) used for diagnostic complementation revealed significant LV dilation with a LV ejection fraction of 38% with the loss of basal, septal, and apical lateral akinesia in the anteroseptal and inferolateral segments, and mid-basal hypokinesia of the anterolateral and inferolateral segments. Transmural delayed enhancement areas were observed in the anterior, anteroseptal, inferoseptal, inferolateral, and anterolateral mid-basal segments in addition to circumferential in the apical segments. CMR also confirmed an LV wall rupture with no delayed enhancement areas after gadolinium infusion and the presence of a thrombus measuring 4.4 × 2.6 × 2.4 mm, a finding compatible with a pseudoaneurysm (Figure 2, Video 1).

The patient underwent new catheterization, which showed severe coronary disease, vein graft occlusion, and previous left internal mammary artery graft to the anterior descending artery (ADA) with good flow, no stenosis, but a distal ADA native bed occluded in the anastomosis.

The treatment of choice was invasive pseudoaneurysm correction and percutaneous occlusion with endoprosthesis (Amplatzer™).

Post-correction control computed tomography (CT) showed the Amplatzer™ prosthesis in the apical region with contrast extravasation through the lower apical region, delayed enhancement of the extracardiac collection (pseudoaneurysm measuring 71 × 60 × 30 mm), and delayed enhanced bleaching from the ventricular pseudoaneurysm (Figure 3).

The patient presented good clinical progression, remaining asymptomatic over the follow-up period.

Discussion

LV pseudoaneurysm is a rupture of the myocardium that remains contained in the pericardium by a pericardial adhesion or scar tissue without the presence of myocardium in its composition.[1,2] It has varied and nonspecific clinical presentations, being asymptomatic in up to 10% of patients as in the case presented here, which can delay early diagnosis. Most pseudoaneurysms are diagnosed in the chronic phase months or years after rupture of the ventricular wall, remaining without diagnostic confirmation in the acute phase due to its rapid progression and unfavorable prognosis.[3,4] Pseudoaneurysms tend to grow rapidly and with a high risk of rupture, which can lead to pericardial tamponade and sudden death. The main cause of pseudoaneurysm is acute myocardial infarction; however, it may be less frequently a consequence of chest surgery, trauma, or infection.[1,5]

Echocardiography, CT, and CMR are effective noninvasive methods of diagnosing and guiding possible treatment. The imaging diagnosis depends on visualizing the discontinuity between the ventricular cavity and the myocardium. The presence of a narrow aneurysmal neck, smaller than the cavity, is also highly suggestive of pseudoaneurysm. CMR has higher spatial resolution, sensitivity, and specificity to confirm pseudoaneurysm. The absence of aneurysmatic sacculation enhancement and the presence of delayed pericardial enhancement using the delayed enhancement technique also corroborate this diagnosis.[1,2,6,7]

Due to a high risk of rupture, pseudoaneurysm correction is the treatment of choice in most cases.[1,3] More advanced surgical techniques reduce the risk of complications to less than 10%.[3] The conservative treatment may reach pseudoaneurysm rupture rates of 43%, but it can be considered in asymptomatic patients and with aneurysms smaller than 3 cm.[1] More recently, the use of percutaneous treatment using occlusive prostheses

Keywords

Cardiac imaging techniques; Diagnostic imaging; False aneurysm.

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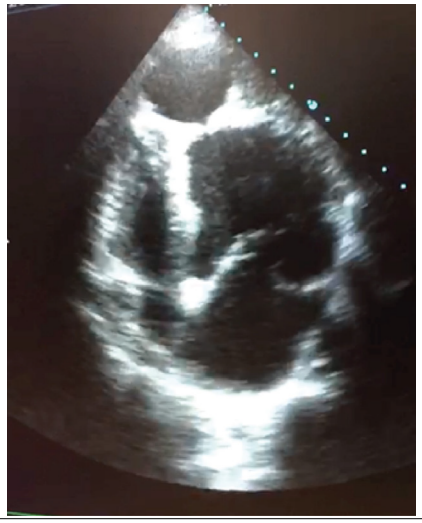


Figure 1 – *Echocardiography image in apical four-chamber view showing an apical pseudoaneurysm.*

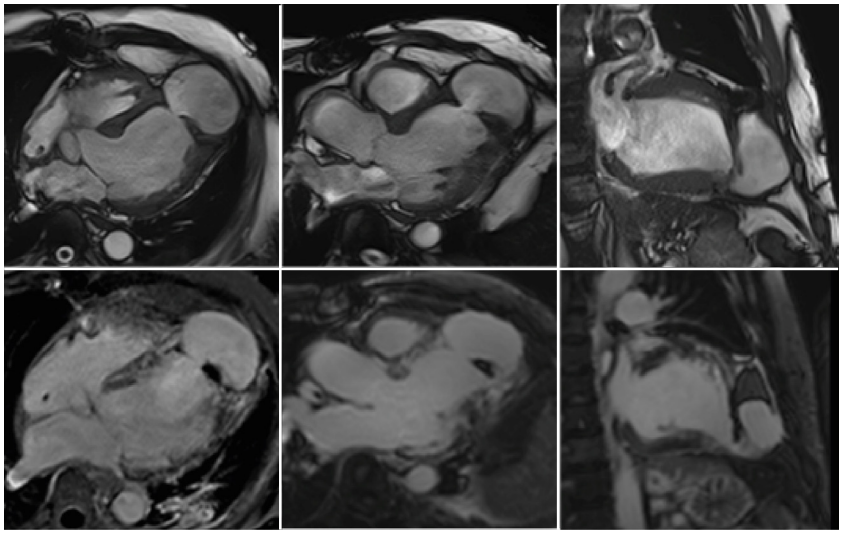


Figure 2 – *Cardiac magnetic resonance imaging in long-axis sections showing an apical pseudoaneurysm. Delayed myocardial enhancement in the same sections showed areas of fibrosis without enhancement of the aneurysmal region (absence of myocardium).*

as in the case described here, became an important option to treat this serious complication, showing good results, especially in narrow-neck aneurysms.[1,8]

Final comments

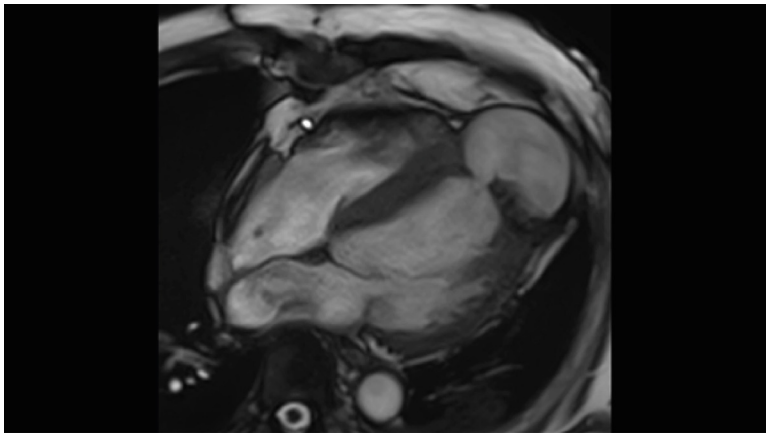
The development of a LV free-wall pseudoaneurysm is a rare and severe condition occurring after myocardial infarction, with a nonspecific clinical presentation. It has a reasonable risk of rupture and may progress to cardiac tamponade and sudden death. The treatment of choice is generally invasive, with progressively decreased complication rates related to the procedure. In this case, an asymptomatic patient was diagnosed on a routine examination finding, and treatment with an Amplatzer™ prosthesis showed a satisfactory result.

Authors' contributions

Research concept and design:Valerio, RS; Oshiro, FS; Rodrigues, AAE; Siqueira, MEM; Uellendahl, MM. ; manuscript writing: Valerio, RS; Oshiro, FS. critical review of the manuscript for important intellectual content: Rodrigues, AAE; Siqueira, MEM; Uellendahl, MM.

Conflict of interest

The authors have declared that they have no conflict of interest.



Video 1 – *Pseudoaneurysm in cine magnetic resonance imaging in longitudinal four-chamber section.*

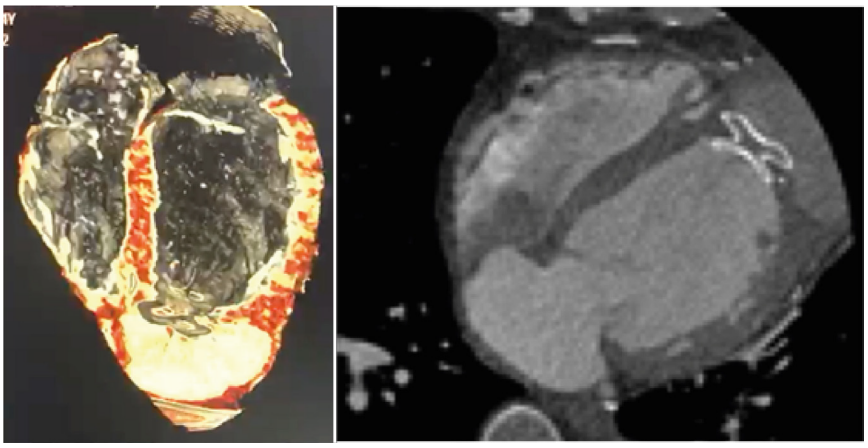


Figure 3 – *Computed tomograph showing pseudoaneurysm correction with an Amplatzer™ prosthesis.*

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Left Ventricular-to-right Atrial Shunt (Gerbode Defect) Associated with Interventricular Communication in a 42-year-old Patient

Shunt Ventrículo Esquerdo-Átrio Direito (Defeito de Gerbode) Associado à Comunicação Interventricular em Adulto

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Introduction

The Gerbode defect, a rare ventricular septal anomaly characterized by communication between the left ventricle (LV) and the right atrium (RA), represents approximately 0.08% of intracardiac shunts and less than 1% of congenital heart defects.[1] Although it classically has a congenital etiology, secondary causes of infective endocarditis, myocardial infarction (MI), and iatrogenesis have been reported.[2] The Gerbode defect was first described in 1857, and its first successful surgical treatment was reported by Kirby at the Hospital of the University of Pennsylvania.[3]

Here, we report an unusual case of congenital Gerbode defect in a 42-year-old patient whose diagnosis was challenging due to the presence of an additional shunt at the ventricular level.

Case report

A 42-year-old man from Jaraguá do Sul – Santa Catarina with a 3-month history of dyspnea on moderate effort was referred for a cardiological evaluation. A physical examination revealed jugular venous distension, a grade 4/6 systolic murmur at the left sternal border, and ascites. Electrocardiography demonstrated sinus rhythm and an inverted T-wave in the right precordial leads (V1–V4).

Transesophageal echocardiography and cardiac resonance imaging revealed slight perimembranous interventricular communication (IVC) with a high mean gradient but no clear signs of right chamber overload.

During follow-up, the patient developed right-sided heart failure that was refractory to conventional treatment with massive ascites that required two hospitalizations for paracentesis. Because of the clinical–imaging finding discrepancy, he underwent right heart catheterization, which revealed a significant oxygen saturation step-up in the right ventricle suggestive of a ventricular left-to-right shunt, estimated Qp/Qs of 2.1, moderate pulmonary hypertension, and signs of right ventricular dysfunction. Transthoracic echocardiography demonstrated a 7-mm turbulent jet from the LV outflow tract to the RA compatible with the Gerbode defect (Figure 1).

The defect was repaired via a median sternotomy using cardiopulmonary bypass, and the right chamber was accessed via right atriotomy. A 10-mm LV to RA communication was visualized and characterized as a Gerbode defect (Figure 2) as well as a 3-mm IVC next to the RV outflow tract. A suture was placed to correct both communications. The patient was discharged from the hospital on the seventh postoperative day, and significant symptom improvement was noted during follow-up.

Discussion

Gerbode defects can be defined as abnormal communications between the LV and the RA. This is anatomically possible because the normal tricuspid valve is more apically displaced than the mitral valve. Congenital LV-RA shunt is rare, representing 0.08% of all congenital cardiac anomalies.[1] In contrast, acquired LV-RA communication can be caused by iatrogenic mechanisms such as cardiac surgeries or percutaneous interventions performed close to the membranous RV septum and non-iatrogenic mechanisms such as endocarditis and acute MI.[2,5] In a review by Yuan et al., congenital etiologies represented 26.4% of cases, whereas the acquired form accounted for 72.7%.[2] Nevertheless, it is assumed that acquired forms are more often reported in scientific journals than congenital forms.[6] In our case, the defect was presumably congenital since the patient had no previous history of surgery, MI, or endocarditis. In addition, the presence of an associated interventricular shunt supported the congenital etiology.

Gerbode first categorized this pathology as type I (indirect form) and type II (direct form). In the indirect form, the shunt occurs from the LV to the right ventricle and then flows through a defect in the tricuspid valve into the RA. Thus, the communication occurs below the tricuspid valve. In contrast, in the direct form, the shunt occurs above the tricuspid valve and directly connects the LV to the RA.[1,7] This terminology was later modified to infravalvular and supravalvular to describe shunt location based on its relationship to the tricuspid valve.[8] Finally, Sakakibara and Konno included a third type (intermediate), which has infra- and supravalvular components.[8]

Keywords

Congenital heart defects; Ventricular septal defects; Heart Septal Defects, Ventricular.

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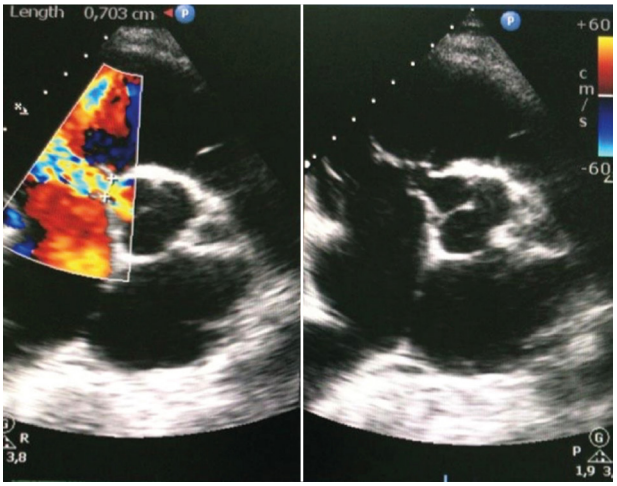

Figure 1 – *Color flow Doppler image from the parasternal transverse heart base view showing flow from the left ventricle to right atrium (left image).*

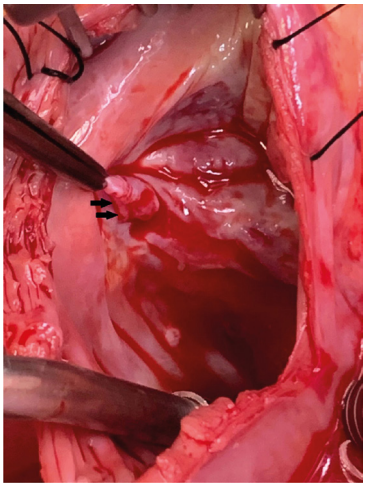

Figure 2 – *Right atrial view during the surgical procedure. The black arrows indicate the Gerbode defect.*

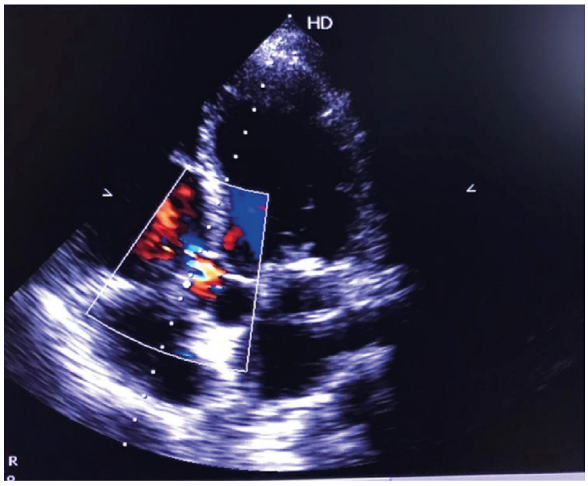

Figure 3 – *Color flow Doppler from 5 chamber apical view showing a perimembranous interventricular communication.*

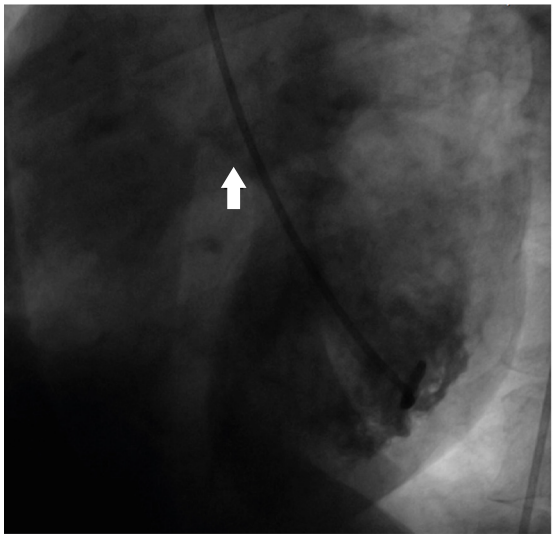

Figure 4 – *Cardiac ventriculography showing a communication at the level of the interventricular septum.*

In our patient, we found two defects that caused a left-to-right shunt: an LV-RA true communication (type II or supravalvular) and an IVC. There were no tricuspid valve abnormalities that could cause LV-RA indirect communication or characterize an infravalvular component. According to the literature, cardiac anomalies related to the Gerbode defect occur in approximately 1/3 of cases; among them, atrial septal defects are the most common.[9] Congenital abnormalities are more often associated with additional cardiac abnormalities than are acquired forms.[2]

Making the LV-RA communication diagnosis is always challenging due to its rarity and the limited diagnostic accuracy of tests such as transthoracic echocardiography.[2,6] However, some echocardiographic findings, such as a normal pulmonary arterial end-diastolic pressure, RA enlargement, leftward bowing of the interatrial septum, an atypical jet direction, and a high Doppler gradient, could suggest the defect.[9,10] The correlation of echocardiographic results among them can also be useful since they can present discrepant findings that are suggestive of Gerbode defect.[10]

The most accurate tests for making the Gerbode defect diagnosis are cardiac catheterization and transesophageal echocardiography.[1,2] In our case, the diagnosis of LV-RA communication was possibly hindered by the coexistence of a concomitant intracardiac shunt. In right heart catheterization, the associated IVC produced an oxygen saturation step-up in the right ventricle that did not help identify the shunt location, although the flow and pressure assessments were useful for confirming the hemodynamic repercussions.

Cardiac magnetic resonance can reveal further anatomical details of the defect and provide information such as accurate left and right heart volume and intracavitary flow measurements.[1] In our case, it failed to discriminate between IVC and LV-RA direct communication.

The need for treatment of Gerbode defect depends on several factors, including symptom severity, shunt magnitude, development time, concomitant anatomical abnormalities, and comorbidities. Small, chronic, and asymptomatic defects, with no signs of circulatory overload, can be managed conservatively, although some authors suggest that all LV-RA defects be repaired to prevent infective endocarditis since surgical treatment demonstrates excellent results.

Conclusion

Gerbode defect is a rare ventricular septal anomaly that results in LV-RA communication. Making this diagnosis is always challenging, and diagnostic delays may lead to worsening of the patient's clinical status. To prevent mistakes, it is important to raise the suspicion of this cardiac defect when faced with echocardiographic findings such as atypical jet direction and normal diastolic pulmonary arterial pressure. In our case, the coexistence of a shunt at the ventricular level and the non-elucidating complementary test results made the diagnosis more difficult, but the defect was repaired successfully and the clinical outcome was favorable.

Authors' contributions

Study concept and design: Takagui ASM; Baggio TC; Obtaining data: Savariz MB; Theilacker G; Baggio TE; data analysis and interpretation: Takagui ASM; Baggio TC; manuscript drafting: Savariz MB; Theilacker G; Baggio TE; and critical review of the manuscript for important intellectual content: Takagui ASM, Baggio TC.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Cardiac Intimal Sarcoma: A Rare Cardiac Tumor Entity

Sarcoma Cardíaco Intimal: uma Entidade Rara Dentre os Tumores Cardíacos

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Introduction

Malignant cardiac neoplasia is a rare entity with an extremely low incidence that has a nonspecific clinical presentation that may mimic other conditions. It can present arrhythmias and complications such as ischemia due to coronary flow obstruction.[1]

More than 75% of primary cardiac tumors are benign. Of the 25% of malignant tumors, 75% are sarcomas.[1-3] Primary cardiac tumors can have a primary or metastatic origin and are diagnosed by imaging methods. Primary tumors occur more frequently in the left chamber, especially in the atrial myxoma, while metastatic tumors originate from malignant melanomas, which occur more frequently in the right chambers.[1]

Cardiac muscle tumors are quite rare entities. Of malignant tumors, cardiac muscle sarcoma is the most frequent histological type and presents aggressively, with dissemination and local invasion potential as well as a high recurrence rate.[1,2] It used to be diagnosed by macroscopic findings at necropsy; however, with advanced imaging methods, today it can be diagnosed and treated earlier to optimize patient outcomes. Treatment consists of lesion excision associated with radiotherapy and chemotherapy.[1,3]

This report describes the case of a patient with cardiac sarcoma to illustrate its echocardiographic presentation pattern to determine whether the association of images and symptoms can lead to an earlier diagnosis, positively impacting the clinical outcome.

Case report

A 44-year-old man suddenly developed a nocturnal cough and palpitations that progressed over 3 days with orthopnea and dyspnea at rest, which made him seek medical assistance in the emergency department of a referral hospital. Upon admission, he was tachycardic and dyspneic and presented clinical signs of hypervolemia and venous capillary congestion on a chest X-ray. An electrocardiogram showed 2:1 atrial flutter (Figure 1). Drug treatment was started with antiarrhythmics and beta-blockers due to suspected tachycardiomyopathy, but the pace was not successfully controlled. Transesophageal echocardiography was performed to evaluate the possibility of electrical cardioversion, which showed an atrial mass of heterogeneous echotexture and lobulated contour, a pedicle located in the interatrial septum measuring 7.7 × 1.5 cm in its largest diameter. The mass had broad movement and entered the left ventricular cavity and the left atrial appendage, obstructing the mitral valve flow, suggesting an atrial myxoma (Figures 2 and 3). The patient underwent urgent excision of the cardiac tumor (Figure 4). The surgical procedure was technically difficult, with possible tumor residue *in loco*. Postoperatively, the patient presented a bradycardic junctional rhythm and episodes of atrial fibrillation with low ventricular response requiring a permanent pacemaker. The histopathological findings of the surgical specimen was compatible with an intimal sarcoma (Figure 5). Cranial and chest tomography were performed for staging; both showed secondary tumor implants. The patient is being followed up at an oncology center with proposed palliative chemotherapy.

Discussion

Primary cardiac muscle neoplasia is a rare pathology with an incidence in the literature of 0.0017–0.28% that has increased in recent decades.[1,2]

Cardiac sarcomas affect more men than women at a 2.5:1 ratio, usually presenting in the third and fourth decades of life.[3]

Intimal sarcoma tend to develop in the right atrium but is sometimes seen in the left atrium. In most cases, it can be confused with benign conditions such as myxoma or thrombus.[3]

Most sarcomas spread very quickly and cause death of myocardium invasion, blood flow obstruction, and/or distant metastases. Therefore, an early diagnosis is essential to successful treatment.[2] Metastatic disease can be present in up to 50% of patients at diagnosis.[4]

This type of tumor presents arrhythmias and conduction system changes more often than myxoma and secondary tumors due to the edema that can occur around the tumor, which is more common in pedicled than sessile tumors.[1]

Its clinical presentation can start with the onset of heart failure and nonspecific symptoms such as chest pain, syncope, and seizure.[1]

The Doppler echocardiogram has relevant sensitivity and specificity to diagnose intracardiac masses and is more often used due to its greater availability and noninvasive nature. This test assesses the size, location, valve leaflet involvement, presence of intracavitary blood flow obstruction, and signs of cardiac muscle invasion. The presence of pedicled or sessile vegetative lesion in one of the valve leaflets or in the valve apparatus can contribute to the diagnosis of cardiac tumor.[1]

Keywords

Sarcoma; Heart; Heart Diseases; Atrial flutter.

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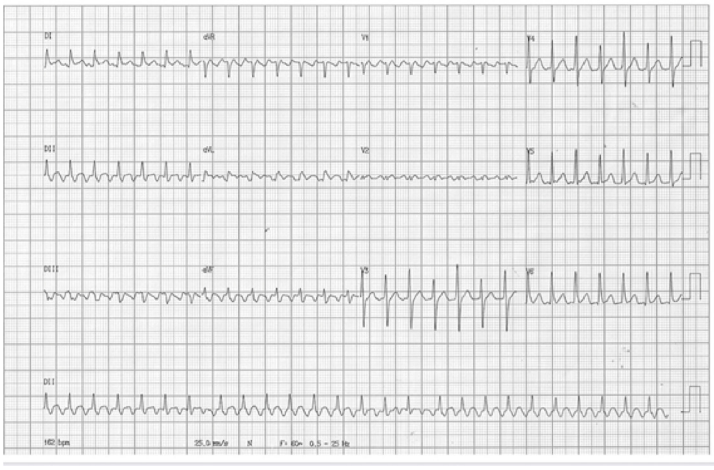

Figure 1 – *Electrocardiogram showing 2:1 atrial flutter.*

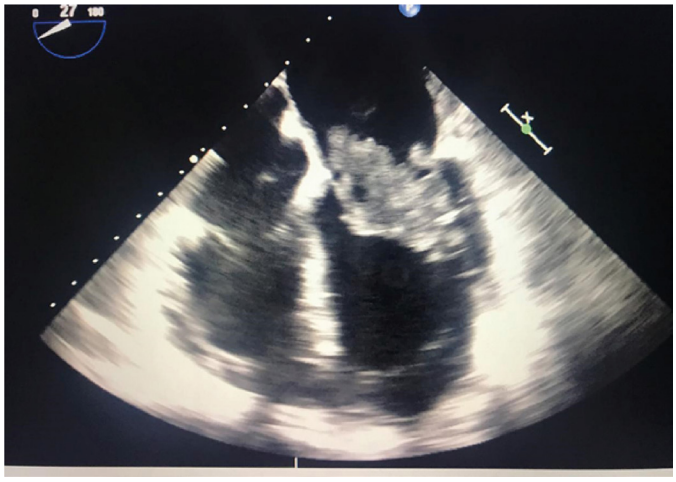

Figure 2 – *Transesophageal echocardiogram in apical four-chamber window view showing a left atrial mass entering the left ventricular cavity.*

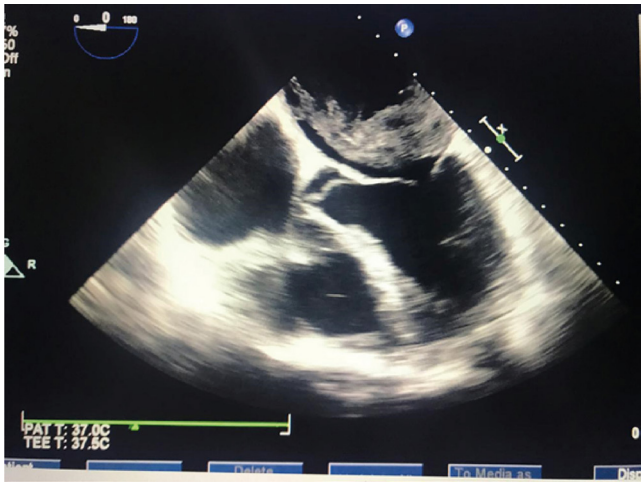

Figure 3 – *Transesophageal echocardiogram in apical four-chamber window view showing a left atrial mass.*

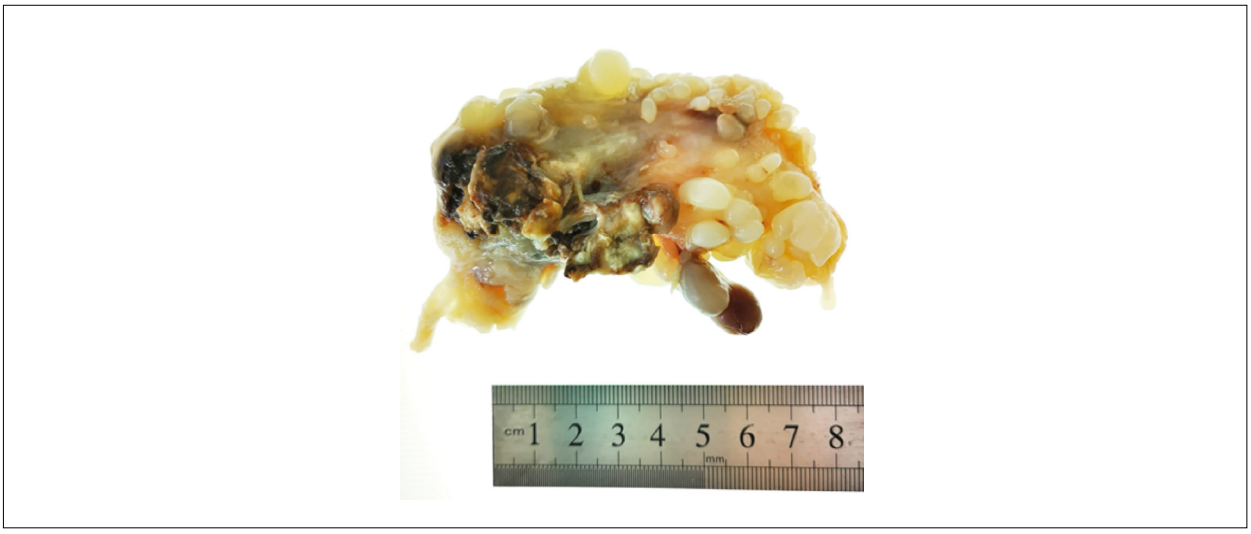

Figure 4 – *Surgical specimen.*

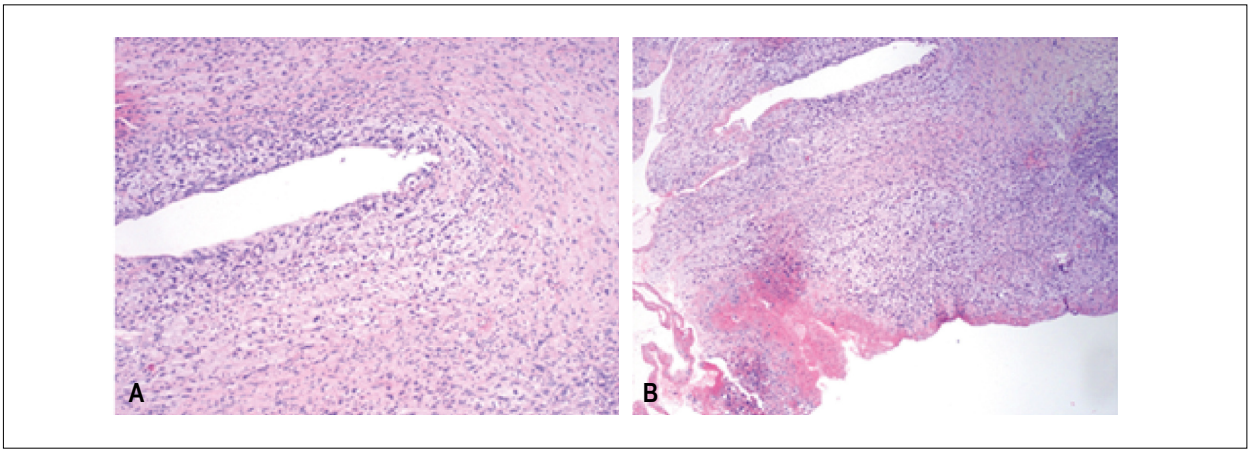

Figure 5 – *A) Low-magnification photomicrograph showing malignant neoplasm with an overlying fibrin layer (below), hypercellular zones, and focal tumor necrosis. Presence of cell densification around the vessel (above), hematoxylin and eosin, 40×. (B) Intermediate-magnification photomicrograph showing round and spindle cell neoplasia with atypia, hyperchromasia, and high mitotic activity in hyaline and myxoid backgrounds, hematoxylin and eosin, 200×.*

Computed tomography of the chest and magnetic resonance angiography provide more accurate information about tumor location, degree of local invasion, and distance and degree of resectability.[1]

Determination of the histological tumor type is important to guiding treatment. In this context, a biopsy is extremely important, which can be incisional, guided by computed tomography; or excisional, by surgical specimen analysis.[1]

Treatment consists of tumor resection, chemotherapy, and radiotherapy, with surgical resection possible in about 30% of cases.[3,5] Even despite complete resection, the disease has a high recurrence rate with a mean survival time of 6–12 months.[2,3,5]

Conclusion

Malignant cardiac tumors are rare entities, but they must be diagnosed early due to their high potential for dissemination and associated complications. In these cases, early clinical suspicion and the use of cardiologic imaging methods is important for timely diagnosis and adequate therapeutic planning.

Authors' contributions

Research concept and design: Andrade RB; data collection: Corrêa LC; data analysis and interpretation: Freitas IA; manuscript writing: Alcantâra ACB; critical review of the manuscript for important intellectual content: Lino DOC, Lima CJM.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Echocardiographic Evaluation of Patients with Patent Foramen Ovale and Cryptogenic Stroke

Avaliação Ecocardiográfica de Pacientes com Forame Oval Patente e Acidente Vascular Cerebral Criptogênico

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Abstract

Recent studies have indicated that patent foramen ovale (PFO) may cause cryptogenic stroke in young patients presenting anatomical conditions that can favor it and that transcatheter occlusion reduces the incidence of stroke versus clinical treatment. A transesophageal echocardiographic study with agitated saline injection associated with the Valsalva maneuver can evidence right-to-left shunt with high sensitivity (89%) and specificity (92%). The Risk of Paradoxical Embolism trial evaluated the clinical characteristics of stroke patients with PFO; established a risk score for cryptogenic stroke; and used a multivariate regression model to identify six variables including age, presence of cortical ischemia, diabetes, hypertension, stroke, and previous transient ischemic attack. The highest scores were observed in young stroke patients without vascular risk factors, and the lowest scores were identified in older patients with vascular risk factors in which the PFO appeared to be incidental. Anatomical PFO conditions predispose patients to systemic embolism (PFO separation > 2 mm, PFO tunnel > 10 mm, angle between the inferior vena cava and the PFO flap < 10°, shunt intensity with Valsalva maneuver, and presence of interatrial septal aneurysm and Chiari network or prominent Eustachian valve). PFO closure can prevent paradoxical embolism by decreasing the incidence of stroke in high-risk patients.

Recent studies demonstrating that transcatheter occlusion of the patent foramen ovale (PFO) reduces the incidence of cryptogenic stroke versus drug treatment[1] have increased interest in the relationship between cryptogenic stroke and the presence of PFO.

Echocardiographic examinations and autopsies identified thrombi crossing the foramen ovale, confirming this mechanism as a cause of paradoxical embolism, i.e., a venous thrombus passing into the arterial circulation through a right-left shunt. However, this echocardiographic visualization is rare, with few studies published[2,3] (Figure 1).

Some clinical studies demonstrated a PFO predisposition to cause paradoxical embolism. Patients with diabetes, systemic arterial hypertension, and coronary artery disease present a low PFO predisposition to cause paradoxical embolism. On the other hand, a history of deep venous thrombosis, pulmonary embolism, pulmonary hypertension, prolonged travels, the Valsalva maneuver preceding the onset of stroke symptoms, migraine, and sleep apnea has been described as an independent risk factor for the association between PFO and cerebrovascular events.[4]

Although visualization of thrombi in the foramen ovale is uncommon, epidemiological observation leads to the belief that PFO is responsible for a considerable number of strokes.[5]

An autopsy study of 965 normal hearts showed a PFO prevalence of 27%, with similar distributions in men and women. This prevalence decreases with age, being 34% in people aged under 30 years, 25% between 30 and 80 years, and 20% over 80 years.[6] However, cryptogenic stroke patients show a particularly high prevalence of up to 40% in patients aged under 55 years.[7]

It is important to note that the presence of PFO in cryptogenic stroke patients is not the only etiology for paradoxical embolism. Other mechanisms can cause it, such as undetected atrial fibrillation, cardiac tumors (myxoma and fibroelastoma), presence of spontaneous echocardiographic contrast in the left atrium, rheumatic mitral valve disease, mitral valve ring calcification, biological and mechanical heart prostheses, hypercoagulability states, and ascending aorta atheroma.[8]

An echocardiographic study is part of the routine PFO evaluation, mainly transesophageal echocardiography (TEE) with agitated saline solution (bubble). A small shunt is considered when three to 10 bubbles pass, a medium shunt when 10–30 bubbles pass, and a large shunt if more than 30 bubbles are counted in the first beats after the injection.[9]

In addition to shunt detection, TEE evaluates the anatomical characteristics of PFO and the differential diagnosis with atrial septal defect and pulmonary shunt.[10,11]

Studies comparing TEE with bubbles and autopsy findings reported a sensitivity of 89% and a specificity of 92%, with autopsy being considered the gold standard.[12]

The performance of an efficient Valsalva maneuver associated with the use of bubble solution is extremely important. This aspect is often overlooked, especially when the test is performed under deep sedation, which can result in a false-negative result. The use of superficial sedation or local oropharyngeal anesthesia is recommended with bubble solution injection to diagnose PFO.[13]

Transcranial Doppler showed more sensitivity but less specificity than TEE in PFO diagnosis. This lower specificity

Keywords

Echocardiography; Foramen Ovale, Patent; Stroke.

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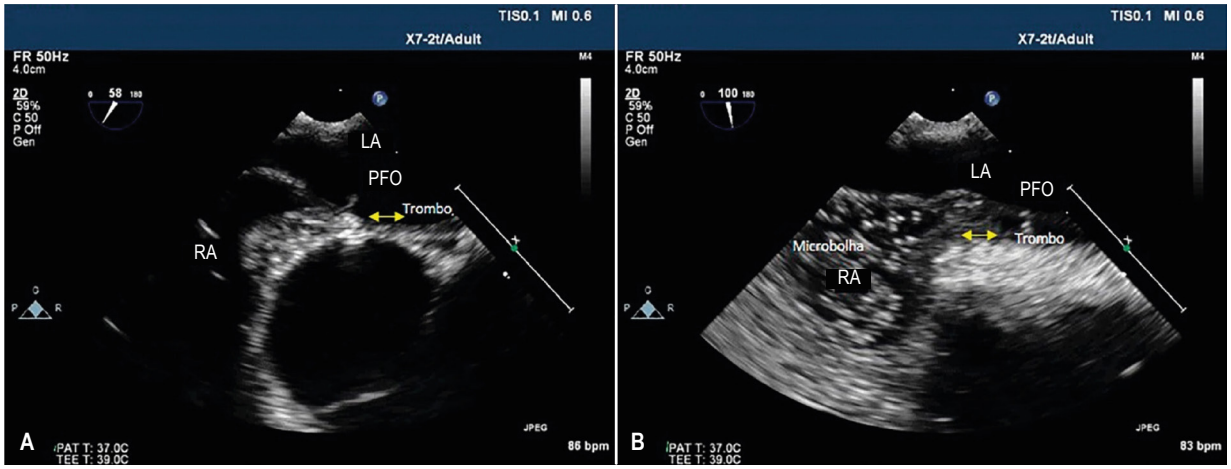


RA: right atrium ; PFO: patent foramen ovale; LA: left atrium.

Figure 1 – *Transesophageal echocardiogram showing the presence of a thrombus in the patent foramen ovale (PFO) without evidence of macrobubble passage. AD: right atrium; AE: left atrium.*

is justified by insensitivity to a differential diagnosis between cardiac and pulmonary shunt in addition to the limited diagnosis of anatomical changes that favor the presence of PFO, such as the presence of an interatrial septum aneurysm and septal mobility.[14]

As for the best therapeutic option for cryptogenic stroke patients (drug therapy or percutaneous closure), the CLOSURE trial in 2012[15] and the RESPECT[16] and PC trials[17] in 2013 showed no benefits of percutaneous therapy for PFO closure compared to drug therapy. However, the randomized CLOSE,[18] REDUCE,[19] and RESPECT[20] trials determined a therapeutic conduct change in 2017, as they demonstrated that percutaneous PFO closure is superior to drug treatment in preventing cryptogenic stroke in a specific population. After this conduct change, several studies have aimed to improve and more precisely determine which patients are most likely to benefit from interventional treatment.

The Risk of Paradoxical Embolism[21] study evaluated the clinical characteristics of cryptogenic stroke patients with PFO and proposed a risk score to stratify patients by age and the presence or absence of vascular risk factors. Using clinical and radiological data from 3,000 patients, a multivariate regression model identified six variables associated with cryptogenic stroke, establishing a score with 10 points to stratify the probability of PFO being associated with stroke or being an incidental event. The variables analyzed included age, presence of cortical stroke on an imaging study, and presence or absence of diabetes, systemic arterial hypertension, stroke, or previous transient ischemic attack. The risk score was calculated using these 10 variables for a period of 2 years in each group (Table 1).

Young patients with superficial stroke and no vascular risk factors have a high score. The prevalence of PFO increases from 23% in patients with 0–3 points to 73% in patients with 9–10 points. High scores are seen in young patients with few or no traditional risk factors experiencing superficial cerebral infarctions. The presence of PFO in patients with low scores, whoa re older, and who have vascular risk factors suggests an incidental onset. The risk of stroke or transient ischemic attack is estimated for a period of 2 years in each group[22] (Table 2).

A recent study showed that some anatomical characteristics of PFO predispose patients to the formation and passage of

Table 1 – Risk of Paradoxical Embolism (RoPE) score.

Characteristics	Points
No history of hypertension	1
No history of diabetes	1
No history of stroke or TIA	1
Non-smoker	1
Cortical ischemic stroke on imaging test (CT or MRI)	1
Age in years	
18-29	5
30-39	4
40-49	3
50-59	2
60-69	1
≥70	0

Source: Thaler et al.[21] CT, computed tomography; MRI, magnetic resonance imaging; TIA, transient ischemic attack.

Table 2 – Risk of stroke.

Total points	Risk of stroke being related to PFO (%)
0-3	0
4	38
5	34
6	62
7	62
8	84
9-10	88

Source: Kent et al.[22] PFO, patent foramen ovale.

thrombi from the right to the left atrium, causingsystemic embolisms.[23] These characteristics are:

• PFO width: a maximum separation between the septum primum and the septum secundum > 2 mm is considered large. A study comparing 58 patients undergoing PFO occlusion after cryptogenic stroke with 58 patients with asymptomatic PFO evaluated by TEE reported a wider PFO in the stroke group ($p < 0.001$).[24]

• Long tunnels > 10 mm occur more frequently in cryptogenic stroke patients (46% versus 17%, $p < 0.01$).

• The degree of right-left shunt is evaluated at rest and after the Valsalva maneuver using agitated saline contrast. The number of bubbles is counted in a single frame, indicating an important shunt with greater risk of stroke when greater than 20 (16% *versus* 5%, $p < 0.06$).

• The angle between the inferior vena cava (IVC) and the oval foramen flap must also be measured. An angle < 10° indicates a greater risk for stroke.

• Interatrial septal aneurysm is defined by the presence of redundant mobile tissue in the oval fossa region with a 10–15 mm phasic excursion during breathing.[25] Its prevalence on TEE is 2.2% in the general population.[26] Stroke patients present a high prevalence of septal aneurysm, 7.9–15% in patients with possible embolic stroke and 28% in patients with ischemic brain events and normal carotid arteries.[27] Two mechanisms have been proposed as responsible for paradoxical embolism caused by aneurysm or hypermobility of the interatrial septum:

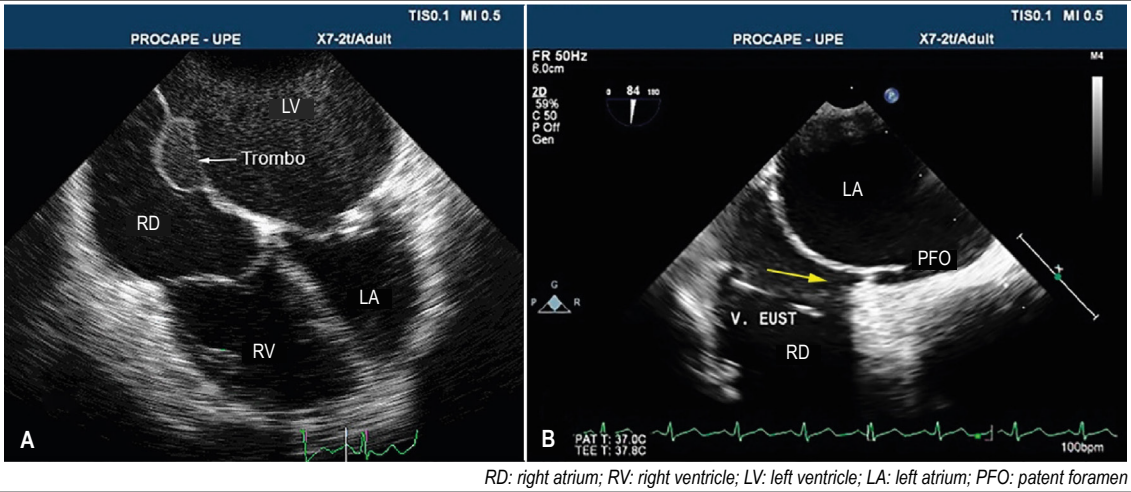
- As this aneurysm is frequently associated with PFO, paradoxical embolism would occur through the passage of the thrombus from the right to the left atrium, through the PFO (Figure 1). Intracardiac shunt has been identified in 78% of patients with aneurysms. There is also an interatrial shunt due to PFO in 54–84% of stroke patients with a septal aneurysm.

- Patients with atrial septal aneurysm without an intracardiac shunt can present small fibrin and platelet thrombi formed on the left side of the septum that break loose with aneurysm oscillation and cause a systemic embolism (Figure 2A).

• Eustachian valve and Chiari network: The Eustachian valve is located at the junction between the IVC and the right atrium, being redundant in some people (Figure 2B). The Chiari network consists of a mesh of filamentous and fibrous structures in the right atrium that originates in the region of the Eustachian and Thebes valves, is close to the IVC opening and inserted in the right atrium wall or in the interatrial septum. A review study of 1,436 TEEs detected the presence of the Chiari network in 2% of the tests, of which 83% had PFO and 27% had interatrial septal aneurysm. The Chiari network occurs more frequently in patients undergoing TEE due to cryptogenic stroke than in studies conducted for other indications (4.6% versus 0.5%).[28] These structures can direct the flow, which arrives through the IVC directly to the interatrial septum, favoring foramen ovale persistence, interatrial septum aneurysm, and, indirectly, facilitating a paradoxical embolism. PFO with a large right-to-left shunt was more frequently identified in patients with a Chiari network (55% versus 12%).[29]

The multivariate analysis of these observations showed that cryptogenic stroke patients with PFO had wider (>2 mm) and more extensive (>10 mm) PFO (Figures 3A and 3B), more mobile interatrial septa, prominent Eustachian valves and Chiari network, and a PFO-IVC angle < 10° (Figure 3C). These factors are independent predictors of ischemic brain events[23] (Table 3). A risk score for PFO being responsible for paradoxical embolism in patients with stroke was developed based on the echocardiographic analysis of these anatomical data (Table 4).

High scores are seen in young patients undergoing superficial cerebral infarctions with few or no traditional risk factors. Since affected patients are more likely to have low scores, be older, and have vascular risk factors, PFO may have an incidental PFO onset not causally related to an ischemic event. The risk of stroke or transient ischemic attack is calculated for a period of 2 years.



RD: right atrium; RV: right ventricle; LV: left ventricle; LA: left atrium; PFO: patent foramen ovale.

Figure 2 – *A: Transesophageal echocardiogram showing an interatrial septal aneurysm without evidence of PFO with the presence of a thrombus on the left side. B: Transesophageal echocardiogram showing the position of the Eustachian valve directing the flow towards the PFO (arrow). LA: left atrium; AD: right atrium; LV: left ventricle; RV: right ventricle; FOP: patent foramen ovale; V. Eust: Eustachian valve.*

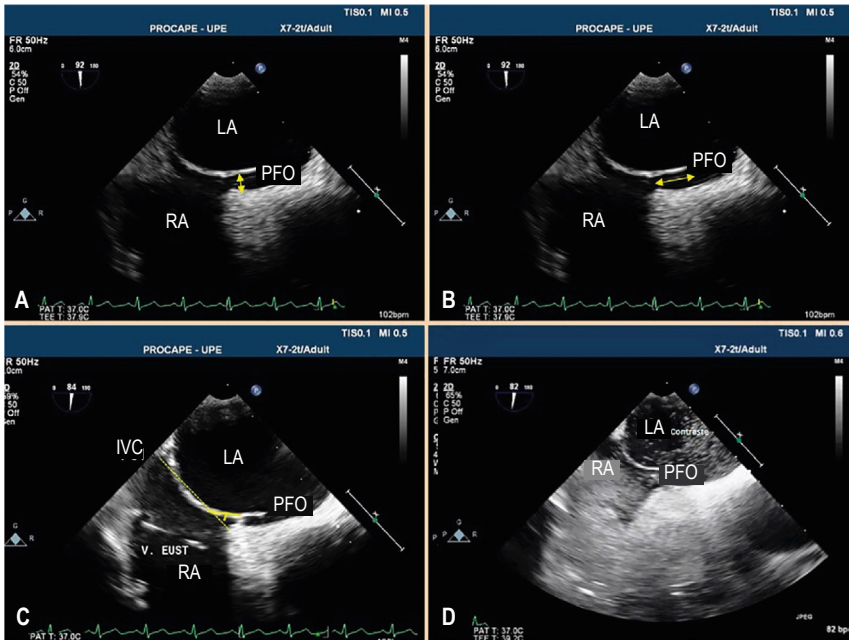


Figure 3 – *Characteristics of the patent foramen ovale (PFO). (A) PFO width, (B) PFO extension, (C) Angle between PFO and the inferior vena cava (IVC), (D) PFO with macrobubble injection showing shunt between the right atrium (AD) and the left atrium (AE). FOP: patent foramen ovale.*

Table 3 – Risk of stroke caused by patent foramen ovale.

Variable	Points
Long PFO tunnels (>10 mm)	1
Interatrial septum hypermobility	1
Extensive Eustachian valve or Chiari network	1
Large shunt during the Valsalva maneuver	1
PFO-IVC angle < 10°	1

Source: Nakayama et al.[23] IVC, inferior vena cava; PFO, patent foramen ovale.

Table 4 – Risk of stroke.

Score	Risk of stroke (%)
0	5
1	17
2	80
3	87
4	89

AVC: acidente vascular cerebral.

Conclusion

Percutaneous PFO closure can prevent paradoxical embolism and reduce the risk of recurrent cryptogenic stroke in high-risk patient groups. As a result, risk scores were developed to determine which patients will benefit from interventional therapy. The first observational study evaluating anatomical data by TEE allowed the development of a risk score that defines which patients with PFO may have cryptogenic stroke, for whom percutaneous closure would be indicated.[23]

New echocardiographic parameters for the evaluation of PFO open new diagnostic, prognostic, and therapeutic perspectives for young patients at risk of cryptogenic stroke as well as for patients aged over 60 years.

Authors' contributions

Research concept and design, data collection, analysis and interpretation, manuscript writing, critical review of the manuscript for important intellectual content: CAM Silveira; data analysis and interpretation, manuscript writing, critical review of the manuscript for important intellectual content: JM Del Castillo.

Conflict of interest

The authors have declared that they have no conflict of interest.

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Echocardiographic Image of Primary Mediastinal Sarcoma with Pericardial Invasion

Imagem Ecocardiográfica de Sarcoma Primário de Mediastino com Invasão de Pericárdio

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Primary mediastinal sarcoma is rare, corresponding to less than 1% of all soft tissue sarcomas and less than 10% of all primary mediastinal tumors.

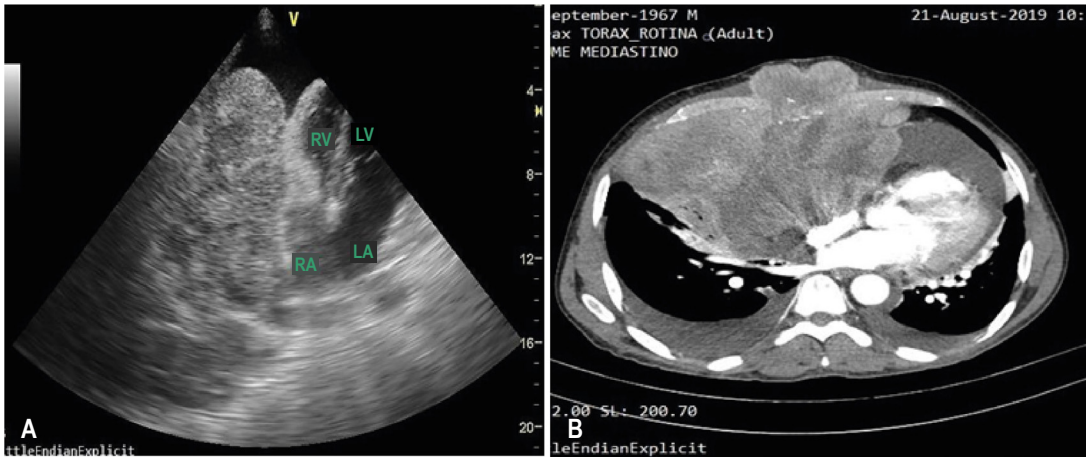
A 52-year-old man with signs and symptoms of cardiac tamponade underwent echocardiography of the right ventricle, which revealed significant pericardial effusion and an extensive heterogeneous mediastinal mass measuring approximately 15 × 8 cm in the pericardial space in close contact with the right chambers and causing diastolic collapse. The diagnostic hypothesis was a pericardial or mediastinal neoplastic process invading the pericardium. Subsequently, an immunohistochemical study confirmed a high-grade fusiform/pleomorphic cell sarcoma.

Authors' contributions

Research concept and design: Melo KPB and Maia RJC; data acquisition: Melo KPB, Maia RJC; data analysis and interpretation: Melo KPB and Maia RJC; statistical analysis: Melo KPB, Maia RJC; manuscript writing: Melo KPB, Maia RJC; critical review of the manuscript for intellectual content: Melo KPB, Maia RJC, Siqueira BJ, Araújo MLSC, Souza ACBM.

Conflict of interest

The authors have declared that they have no conflict of interest.



RV, right ventricle; LV, left ventricle; RA, right atrium; AE: LA, left atrium

Figure 1 – *(A) Transthoracic echocardiogram image showing a large pericardial effusion in an expansive process with close contact with the right cardiac chambers, mainly the right atrium. (B) Chest computed tomography image showing a large heterogeneous mass in the lower mediastinum with diffuse contrast medium uptake invading the sternum and the pericardium. The lesion deflects the heart to the left and is compressing the right heart chambers.*

Keywords

Echocardiography; Mediastinal neoplasms; Pericardium; Sarcoma.

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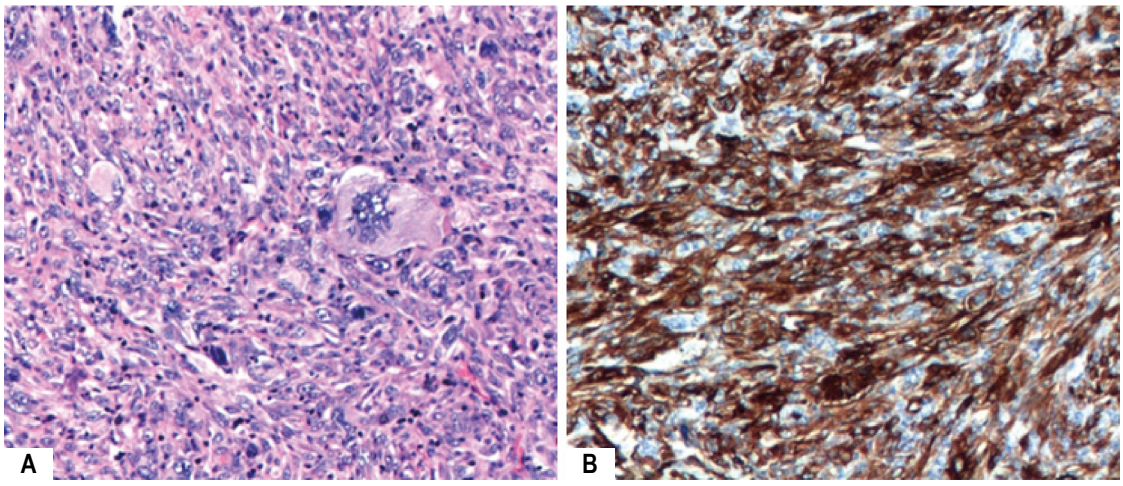

Figure 2 – *(A) Histopathological analysis showing malignant neoplasm composed of fusiform and pleomorphic cells with eosinophilic cytoplasm showing frequent atypical mitosis figures. Findings compatible with the diagnosis of high-grade fusiform/pleomorphic cell sarcoma. (B) Immunohistochemical study showing smooth muscle actin expression, indicating smooth muscle or myofibroblastic differentiation. High-grade leiomyosarcoma is one considered possibility.*

Eustachian Valve Endocarditis Associated with Complicated Cardiac Resynchronization Therapy Defibrillator Generator Pocket Infection

Endocardite da Válvula de Eustáquio Associada à Infecção Complicada do Gerador de Terapêutica de Ressincronização Cardíaca com Desfibrilador

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A 76-year-old male with ischemic cardiopathy was admitted with fever and purulent drainage from cardiac resynchronization therapy defibrillator generator pocket, two months after its implantation. Prompt device removal was performed. Cultures identified methicillin-sensitive *Staphylococcus aureus*. Transthoracic echocardiography revealed a highly mobile filamentous right atrial mass with 30mm in length, apparently attached to interatrial septum (Figure1 and Video 1). Transesophageal echocardiography (TEE) showed that the echogenic mass was attached to the Eustachian valve (EV) (Figure 2 and Video 2) and the diagnosis of EV endocarditis was made. There was no involvement of tricuspid valve. The patient completed a 4-week course of flucloxacillin, with good clinical response and without embolic complications. Repeat TEE revealed a significant decrease in vegetation size (Figure 3 and Video 3).

Authors' contributions

Research conception and design: MIFB Pires, I Almeida, ML Gonçalves, JM Santos, M Correia; data collection: MIFB Pires, I Almeida, ML Gonçalves, JM Santos, M Correia; manuscript writing: MIFB Pires, I Almeida, ML Gonçalves, JM Santos, M Correia.

Conflict of interest

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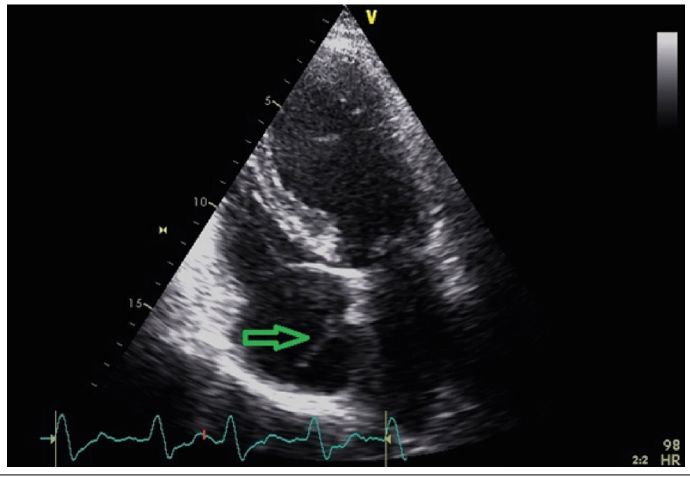

Figure 1 – *Transthoracic apical 4-chamber view showing a right atrial mass with 30mm, apparently attached to interatrial septum.*

Keywords

Cardiac resynchronization-therapy devices; Endocarditis; Heart valves.

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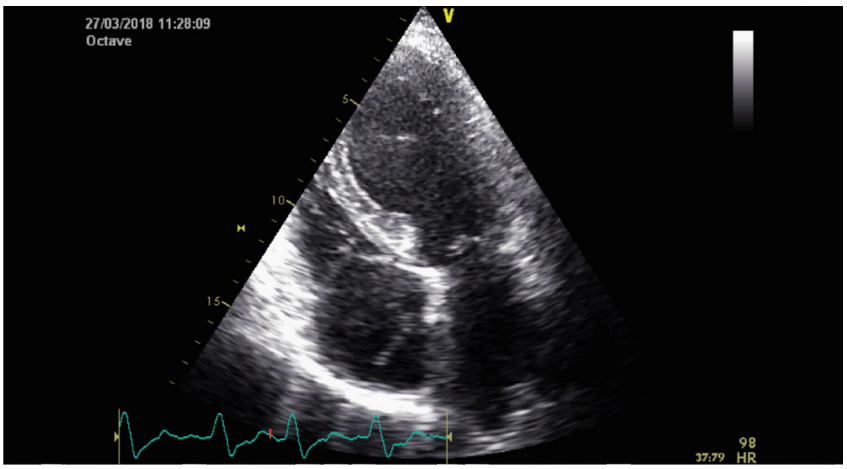


Video 1 – *Transthoracic apical 4-chamber view showing a right atrial mass with 30mm, apparently attached to interatrial septum.*

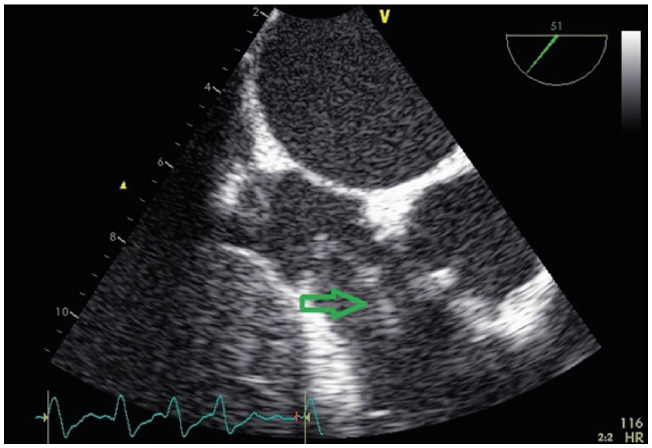
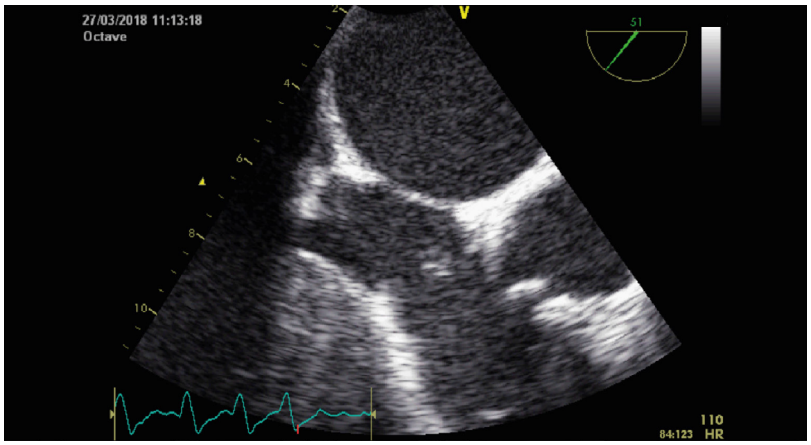


Figure 2 – *Midesophageal modified bicaval view showing a mobile filamentous mass attached to the Eustachian valve.*



Video 2 – *Midesophageal modified bicaval view showing a mobile filamentous mass attached to the Eustachian valve.*

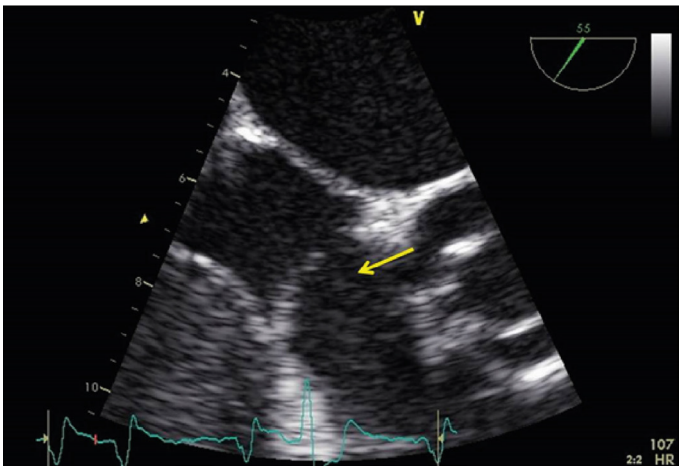
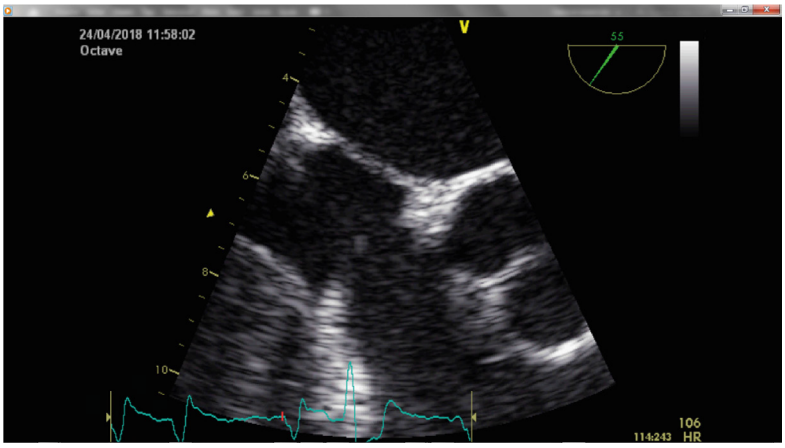


Figure 3 – *Modified bicaval view revealing the decrement of vegetation size during antimicrobial therapy.*



Video 3 – *Modified bicaval view revealing the decrement of vegetation size during antimicrobial therapy.*