Review Article

Obstructive Cardiac Tumors

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Abstract

Cardiac tumors are considered rare clinical entities and can affect any cardiac tissue. Metastatic (secondary) cardiac tumors are more frequently diagnosed than primary tumors (malignant or benign). Both types can cause valve and/or inflow and outflow tract obstructions in any cardiac chamber, leading to symptoms of heart failure, as well as embolization and arrhythmia. Treatment of benign tumors is usually surgical, and that of metastatic and primary malignant tumors will depend on their origin and type, with poor prognosis. Recurrence of benign tumors is frequent. The aim of this article is to provide the clinician with tools to optimize diagnosis, differential diagnosis, and treatment of tumors with obstructive features causing heart failure.

Introduction

Cardiac masses are a frequent finding in clinical practice, encompassing a wide range of presentations, such as tumors, thrombi, vegetations, and anomalous structural changes.[1,2] Cardiac tumors, the type of mass to be discussed in this paper, can be divided into primary and secondary. Primary tumors are very rare, with a described incidence of 1.38/100 million individuals[3] and less than 1:2,000 autopsies.[1] It is estimated that 90% of these tumors are benign and originate from the myocardium or pericardium, consisting mainly of myxomas in adults and rhabdomyomas in children.[4] Malignant primary tumors, in turn, consist mainly of sarcomas, followed by lymphomas.[3] Secondary tumors (metastases) are malignant per se and have a higher incidence than primary tumors.[5]

Keywords

Heart Failure; Heart Neoplasms; Echocardiography; Magnetic Resonance Spectroscopy; Diagnostic Imaging.

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Cardiac tumors may be incidental findings, which has become increasingly more frequent in the last decade with advances in imaging methods.[6] They may be asymptomatic or lead to systemic manifestations, embolisms, and cardiac structural impairment. Depending on tumor location and size, the most frequent symptoms are dyspnea, chest pain, hypotension, cyanosis, syncope, and arrhythmias. These symptoms result from mass effect, which interferes with function of cardiac structural and with coronary or intracavitary blood flow.[7] The differentiation between benign and malignant tumors is important for prognosis, although it bears highlighting that even benign tumors may have important clinical repercussions, related to their location and size. The use of multimodality imaging is usually necessary to assess the etiology of cardiac tumors.[8] Mass location and aspect, image characteristics, and patient's age are some useful factors for diagnosis, which often rules out the need for biopsy. Obstructive cardiac tumors show a relatively predictable distribution in ventricles, atria, and valves, as presented in Figure 1.[9] It is worth emphasizing that the therapeutic approach should be individualized, considering factors such as possibility of tumor surgical resection, comorbidities, and prognosis of oncologic disease, in the case of secondary tumors. Therefore, treatment of cardiac tumors involves shared decision-making by the multidisciplinary team.[10]

This review focuses on the diagnosis and treatment of primary and secondary cardiac tumors whose clinical manifestation is associated with the hemodynamic obstruction caused by tumor, leading to heart failure, syncope, and shock. Pericardial and extracardiac tumors associated with cardiac compression and low cardiac output syndrome will not be approached.

Use of cardiovascular imaging for diagnosis of obstructive cardiac tumors

Intracardiac masses associated with shock, syncope, or low cardiac output require non-invasive investigation, avoiding invasive procedures such as tissue biopsy, if possible. Currently, multimodality imaging investigation allows for clarifying the etiology of most of these masses.

1) Transthoracic echocardiogram

a. Two-dimensional Doppler: widely available method, consisting of the front-line technique for diagnostic

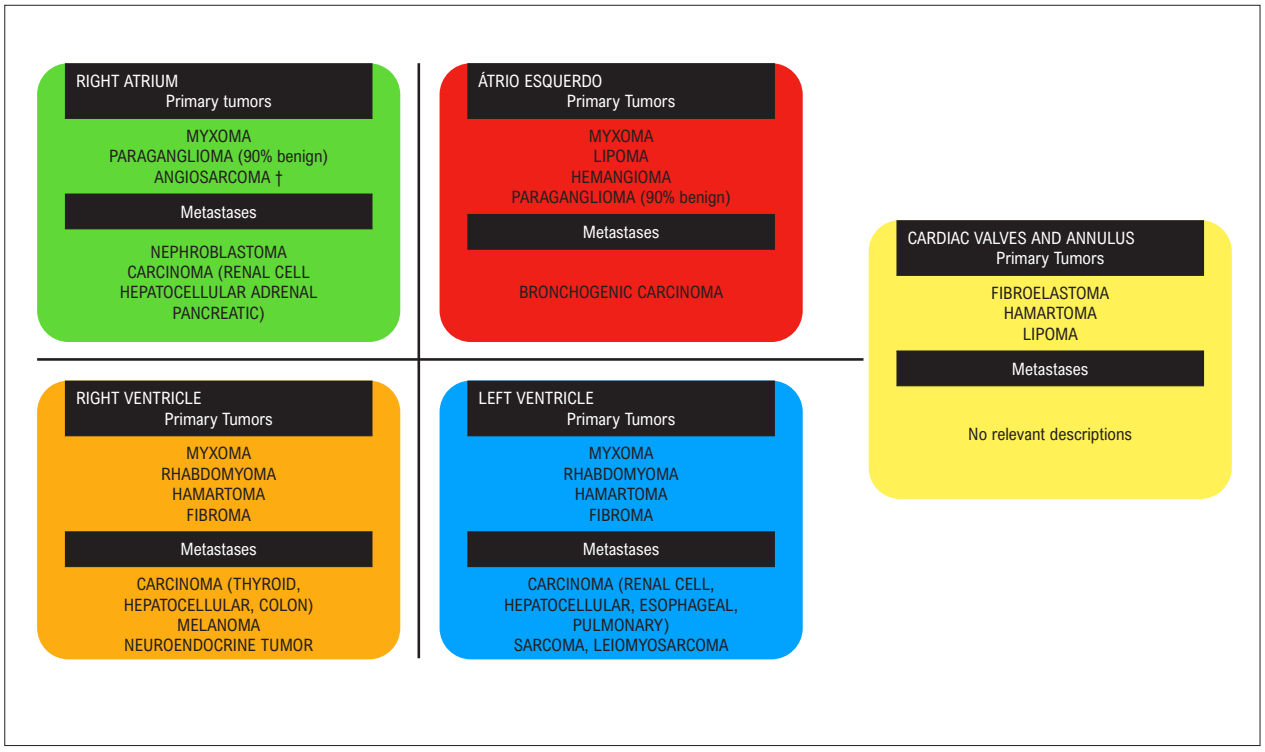

Figure 1 – *Specific location of the main obstructive cardiac tumors detected on transthoracic echocardiogram. Adapted from Griborio Guzman AG et al.* † *Malignant characteristic.*

investigation in suspected intracavitary mass. This test can determine tumor location, size, type of fixation, mobility, and hemodynamic consequences, in addition to assess the presence of pericardial effusion or other associated abnormalities. Furthermore, the use of Doppler allows for evaluating cardiac output and instant gradient between the chambers, important in cases of tumor obstruction (Figure 2). Its utility can be limited in patients with unfavorable acoustic window, such as obese patients, those with chronic obstructive pulmonary disease or subcutaneous emphysema, or in the investigation of masses coming from venae cavae or pulmonary branches.

b. Three-dimensional echocardiogram: it provides additional anatomical data for the spatial tumor characterization, which makes it possible to increase diagnostic accuracy of the method, help in surgical strategy, and monitor immediate and late outcomes of procedures.

c. Transesophageal echocardiogram: useful to supplement anatomical and functional assessment when the echocardiogram findings were not conclusive and for intraoperative assessment.

d. Contrast echocardiogram: malignant tumors, such as sarcomas, are highly vascularized, whereas benign ones, such as myxomas, are not. Thrombi, a very frequent and avascular condition, are the main differential diagnoses. Therefore, endocavitary contrast allows for characterizing the limits and the shape of masses, and also inform on the presence or absence of neovascularization surrounding the myocardium.[8]

2) Cardiac computed tomography

It has great accuracy for the anatomical definition of the tumor and its surrounding structures, enabling to assess the obstructive potential of these structures (Figure 3). Furthermore, it allows for complementary evaluation of coronary circulation, being useful in the assessment of concomitant obstructive coronary artery disease and possible surgical planning. Its use requires administering ionizing radiation and iodine contrast. Therefore, its use should be considered when other imaging tests were not conclusive.[8]

3) Cardiac magnetic resonance

This diagnostic method is essential in the etiologic definition of cardiac tumors and masses. It allows for tissue characterization, making it possible to define whether the content of the structure assessed is fat, fluid, fibrosis, or thrombus, for example. Assessment of cardiac tumor perfusion can define the magnitude of its vascularization, showing evidence of malignancy. It has excellent special/time resolution, allowing for an anatomical assessment of obstruction caused by tumor in the inflow and outflow tracts of cardiac chambers (Figure 4) and of intracavitary flows.[11,12]

4) PET/CT

Positron emission tomography-computed tomography (PET/CT) is a method that combines CT from radiology and PET scan from nuclear medicine in a single test and helps in tumor staging and in the assessment of recurrence and

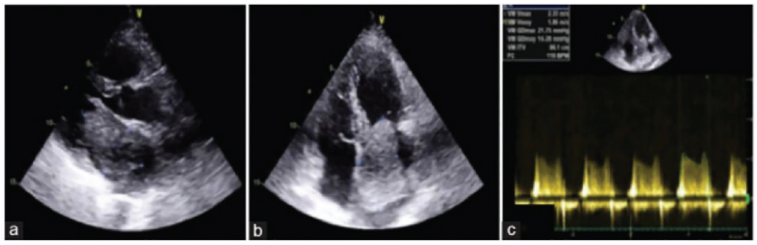

Figure 2 – *Giant left atrial myxoma in an adult at two-dimensional echocardiogram. A) Parasternal long axis view. B) four-chamber apical view. In both images, the tumor blocks the left ventricular inflow tract. C) Continuous Doppler showing increased mean gradient (14 mmHg) compatible with obstruction.*

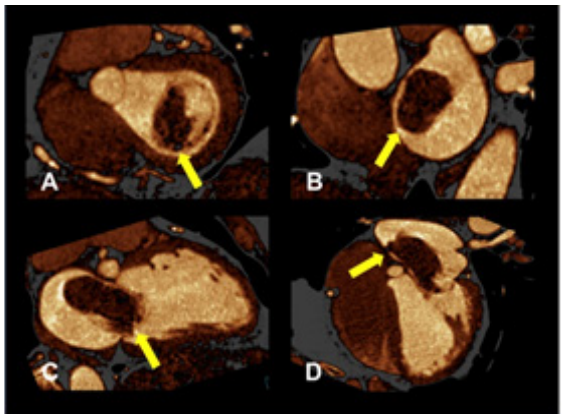

Figure 3 – *Cardiac computed tomography from a 58-year-old male patient evidencing myxoma on right and left atria (arrows). A,B) Short axis images of the left atrium revealing tumor protrusion into the mitral valve, partially blocking the left ventricular inflow tract. C) Two-chamber image showing the size of the mass in its larger axis. D) Four-chamber image of the heart in which is possible to observe a tumor pedicle adhered to the interatrial septum and the relationship between the mass and the mitral valve orifice. Image Courtesy of Dr. Tiago Augusto Magalhães.*

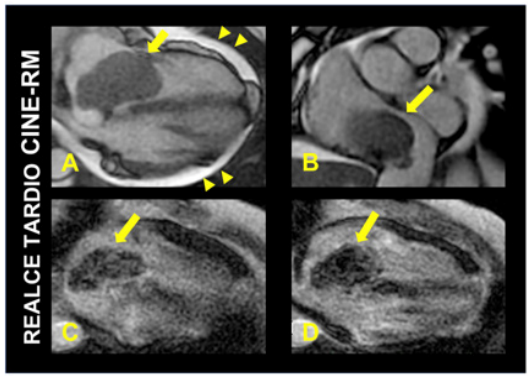

Figure 4 – *Cardiac magnetic resonance of 34-year-old female patient with a voluminous mass occupying the right atrium (arrows). A) Four-chamber cine magnetic resonance imaging scan showing a right atrial mass occupying part of the tricuspid valve plane during ventricular diastole and partially blocking the right ventricular inflow tract. This image also reveals discrete pericardial effusion (arrow heads). In B), short axis view of the right atrium depicts partial obstruction of inferior vena cava ostium by the atrial mass. C,D) Late enhancement images showing paramagnetic contrast uptake, which makes the diagnosis of intracavitary thrombus unlikely. Dynamic perfusion images of the mass (not shown) revealed signs of a highly vascularized structure, suggesting the diagnosis of malignant neoplasm. Image Courtesy of Dr. Tiago Augusto Magalhães.*

therapeutic response of several types of cancer. This test has no limitations with regard to acoustic window, metallic prostheses, and kidney failure.[8,13-16] PET/CT uses radiopharmaceuticals to define images, such as fluorine-18 fluorodeoxyglucose (^{18}F-FDG). The uptake of this substance by tumor cells reflects their metabolic activity and level of disease aggressiveness, helping to differentiate between malignant and benign tumors and thus avoiding cardiac biopsies and unnecessary invasive treatments.[12]

Secondary Obstructive Cardiac Tumors

Secondary cardiac tumors, such as cardiac metastases, are the most frequent cardiac tumors in clinical practice, being 22 to 132 times more common than primary cardiac neoplasms.[17,18] Cardiac metastases may occur by four routes: a) direct extension, b) bloodstream, c) lymphatic system (more frequent), d) intracavitary diffusion through the vena cava or pulmonary veins. Right cardiac chambers receive most of the lymph drained and are more affected by metastases. Secondary tumors are located on the myocardium, endocardium, or pericardium and can affect all ages.[19] Cardiac metastases may be found in up to 18% of individuals with stage IV cancer,[20] especially melanoma and lymphoma.[21] Thoracic neoplasms such as lung, breast, and esophagus cancer, are also among those more commonly associated with cardiac metastases.[18,22]

In most cases, cardiac metastases are clinically silent and diagnosed only on post-mortem examination.[10] When symptomatic, their main clinical manifestation is pericardial effusion, with varied degrees of severity. In tumors affecting the myocardium, infiltration and cardiac wall edema, causing arrhythmias, such as atrial fibrillation or flutter, and even atrioventricular block. Manifestations associated with systolic or diastolic ventricular dysfunction may occur, especially in patients with tumors with a diffuse ventricular involvement. Acute myocardial infarction is rare and may result from

thrombus or from perivascular or extrinsic compression. In tumors that disseminate through the vena cava, such as renal carcinoma and hepatocellular carcinoma, there may be complete right atrial obstruction and tricuspid valve block, resulting in a clinical pattern similar to that of pericardial constriction or myocardial restrictive disease.[20]

As previously highlighted, right cardiac chambers are the most involved in secondary tumors, with right chamber obstruction being one of the most severe presentations of metastatic tumors. These cases manifest with signs and symptoms of right heart failure, such as ascites, jugular swelling, lower limb edema, cyanosis, syncope, right bundle branch block, systolic ejection murmur along left sternal border, pulmonary hypertension, and even sudden death. Cases of pulmonary embolism secondary to tumor fragmentation and displacement[23-25] have already been described. Neuroendocrine tumors can be more associated with heart failure due to valve involvement, as occurs in carcinoid syndrome. A study reported the case of a metastatic nonfunctioning neuroendocrine tumor that caused outflow obstruction.[26]

There are numerous case reports of metastases causing ventricular outflow tract obstruction related to neoplasms of several primary sites, such as soft tissue sarcoma, lymphoma, leukemia, liposarcoma, ovary carcinoma, renal cell adenocarcinoma, hepatic tumors, pancreatic and colorectal adenocarcinoma, and even squamous cell carcinoma of the base of the mouth.[24,25,27-30]

Although less common, there are reports of left ventricular inflow (Figure 5) and outflow obstruction in individuals with synovial sarcoma of the foot and grade III pleomorphic leiomyosarcoma, both undergoing treatment with chemotherapy and radiation therapy and evolving to death after 3 and 6 months.[27] The main manifestation of left ventricular obstruction is progressive dyspnea. The masses can infiltrate ventricular wall and advance to the outflow tract, causing flow restriction. Similar presentations were also described in an individual with clear cell carcinoma; even after surgical removal of the mass, the patient died after 1 month.[31]

One of the most important invasive diagnostic methods is pericardioscopy, which allows inspection of the pericardium and epicardium and permits tissue acquisition. It is a powerful diagnostic tool, especially in diseases of unknown origin, particularly when combined with pathological and molecular methods.[10] In cases of right ventricular obstruction, the use of a Swan-Ganz catheter may be useful, and catheterization may allow for tumor biopsy, although the procedure carries a non-negligible risk.[25] The treatment of secondary cardiac tumors depends on the analysis of complications and clinical manifestations associated with the presence of cardiac metastasis, prognosis, and patient's functional status,[32] with no specific guidelines for each situation. Hemodynamically significant arrhythmias should be treated with cardioversion and radiofrequency ablation, when indicated. In cases of advanced blocks, implantation of a pacemaker may be necessary. Surgical treatment should be considered in the following cases: a) prognosis is favorable; b) no involvement of other metastatic sites; c) when the tumor can be completely removed; or d) in the presence of obstructive tumors. Adjuvant chemotherapy and/or radiation therapy should be performed together, according to tumor specificity.[10]

For obstructive tumors, more aggressive measures are often necessary to ensure hemodynamic stability. Treatment strategies such as placement of prostheses (stents) on the right ventricular outflow tract in a patient with metastatic sarcomatoid carcinoma and emergency surgery with or without pulmonary and/or tricuspid valve repair followed by neoadjuvant chemotherapy have already been described.[23-25] In many cases, cardiac metastases are found in already disseminated tumors, in which palliative treatment with

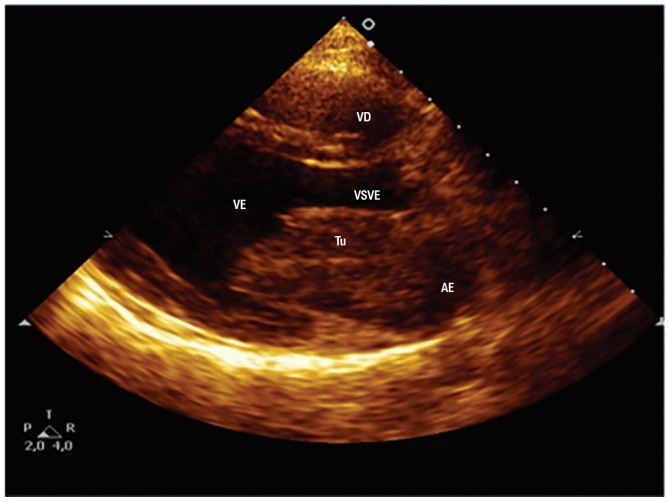

Figure 5 – *Transthoracic echocardiogram (parasternal longitudinal view). Tumor metastasis (osteosarcoma) originating from the right superior pulmonary vein and extending to the left atrium and protruding into the left ventricle. LA: left atrium; LV: left ventricle; Tu: tumor; LVOT: left ventricular outflow tract; RV: right ventricle. Image created by the authors.*

chemotherapy and/or radiation therapy is one of the only alternatives. The prognosis is usually poor, with death occurring in less than 6 months.[25,27-29,31,33]

Primary cardiac tumors

Cardiac tumors are rare (0.001% to 0.3%, according to pathological studies), and are classified as benign or malignant, and as primary or secondary (metastatic).

Secondary tumors occur more frequently. They have a variable location (myocardium, endocardium, and pericardium), different histopathological characteristics, can affect all ages. Furthermore, their clinical manifestations depend on location and hemodynamic involvement.[19]

In the pediatric population, most cases have a benign pattern and a satisfactory prognostic evolution. The primary benign tumors with greater prevalence and obstructive potential are, in an increasing order of frequency, rhabdomyomas, teratomas, fibromas, and myxomas.

Malignant tumors occur in nearly 10% of the cases and show an aggressive pattern, with limited prognosis and high mortality rates. Additionally, the most prevalent primary subtype is rhabdomyosarcoma.[34]

Benign primary tumors

Rhabdomyoma – The most common primary cardiac neoplasm in children, accounting for more than 60% of cardiac tumors in this population. Nearly 75% of the cases are diagnosed in the first year of life, mostly in the prenatal (through fetal echocardiography) or neonatal periods. It may be asymptomatic or manifest with signs of blood flow obstruction, as well as myocardial function involvement and arrhythmias. There is a strong correlation between cardiac rhabdomyoma and tuberous sclerosis, since this disease is present in 50% of children with the tumor, which may be ser unique or multiple.[19]

Rhabdomyoma has a biphasic growth pattern, with a progressive increase up to the beginning of the third trimester of pregnancy and total or partial regression up to the first year of life, which is why management tends to be conservative, unless the patient shows signs of cardiac decompensation. Rhabdomyoma is a non-infiltrative, non-metastasizing tumor usually located in the ventricles, especially in the septal region, and may cause fixed or dynamic obstruction of inflow or outflow tracts.[35]

Teratoma – Although rare, it accounts for 2/3 of pediatric cardiac tumors and is usually diagnosed in the fetal period. It is commonly located next to base vessels, and causes pericardial effusion and local myocardial impairment, which may lead to fetal or sudden death.

As well as other teratomas, cardiac teratoma is a solid mass with cystic and neuroepithelial components.[7,19]

Fibroma – This type of tumor may be associated with Gorlin syndrome, is mostly located in the septum or in the ventricular free wall, is usually nodular and solitary, can be well or poorly delimited, can present with calcifications or not, and has no tendency to regression. Treatment is surgical and involves complete resection, but it not always possible, due to tumor size and infiltrative aspect, which may lead to indication of heart transplantation.[7,34]

Myxoma – It is more common in adults, but may also occur in older children, and is often associated with genetic syndromes (LAMB, NAME and Carney) and endocrine diseases (adrenal hyperplasia, gigantism, and testicular Sertoli cell tumor).

It is mainly located in the left atrium, adhered to atrial septum or adjacent to the oval fossa, are typically pedunculated, and may also originate from the ventricular wall or from cardiac valves in variable proportions (Table 1).[9]

It may have an atrioventricular obstructive clinical pattern and cause embolic phenomena (paradoxical embolism) both for the pulmonary artery tree and for its periphery or the brain vascular territory, depending on the affected side (often the left one). It can also manifest with arrhythmias and signs and symptoms of decompensated acute heart failure, which brings potential risk of death.

Differential diagnosis is made with organized thrombus and with inflammatory diseases, due to the possibility of manifesting with constitutional symptoms resulting from cytokine release. It requires immediate diagnosis and surgical resection, due to the high risk of embolization (observed in up to 1/3 of patients).

Transthoracic echocardiogram is the initial diagnostic method, and transesophageal echocardiogram is the one with the highest sensitivity (95% vs. 100%). Cardiac magnetic resonance is a supplemental method that provides excellent tissue characterization and allows for identifying local invasion, in addition to permitting differentiation between myxoma and other types of tumors. PET /CT may be useful in differentiating malignancy and diagnosing neuroendocrine tumors. The prognosis of myxomas is excellent when they are treated with immediate surgical resection. Overall rates of survival are similar to those of the general population with the same age, although studies found a rate of postoperative recurrence from 1% to 6%.[7,9,34]

Primary malignant tumors

They are rare and show poor prognosis. Sarcomas are the most prevalent ones, although germ cell tumors, rhabdoid tumors, and lymphomas have also been described.[34]

Table 1 – Frequency of myxomas and their distribution according to cardiac chambers

Myxomas	Frequency (%)
Right atrium	12.7-28.0
Left atrium	60.0-90.0
Biatrial	1.3-8.5
Left ventricle	0.6-4.0
Right ventricle	1.7-8.0
Multifocal	0.8-1.6

Rhabdomyosarcoma - This is the most prevalent sarcoma subtype in the pediatric population, accounting for nearly 4 to 7% and often affecting cardiac valves. Clinical presentation is associated with the invasive or obstructive nature of the tumor, whose semiological characterization is difficult, due to its rapid growth. Nearly 46% of patients have metastatic disease at the time of diagnosis, which disseminated either via lymphatic system or by contiguity, and pulmonary artery tree obstruction is a manifestation to be considered. Treatment involves surgery, chemotherapy, and radiation therapy and is limited by tumor aggressiveness, thus resulting in low survival rates, which are below 1 year in most cases.[7,34]

Conclusion

This review about obstructive intracardiac tumors showed that their incidence is low, but they should be considered in patients diagnosed with intracardiac masses and showing hemodynamic impairment compatible with low cardiac output. In adults and children, myxoma stands out as the most common benign tumor, whereas tumor metastases (especially from melanomas and lung, kidney, and colon cancers) characterize the most frequent malignant cases and have limited prognosis.

Echocardiogram is still the most traditional diagnostic imaging method, providing the initial characteristics of the mass under investigation. Other methods, such as cardiac magnetic resonance, may be used in additional investigations. Special attention should be given to patients that have already been diagnosed with certain types of cancer and who evolve with progressive dyspnea.

In addition to frequent causes, such as anemia, differential diagnoses with obstructive intracardiac tumor should be considered as effects of chemotherapy, sarcopenia, ventricular diastolic or systolic dysfunction, pulmonary embolism, and restrictive syndromes. Treatment can be curative, such as in myxomas, or palliative, always considering the prognosis of the initial primary tumor.

Author Contributions

Conception and design of the research, Acquisition of data and Coordination: Cauduro SA, Dutra JPP; Writing of the manuscript: Cauduro SA, Dutra JPP, Fernandes F, Bonatto M, Santos MVC, Rocha LSO, Mialski TR, Nobrega APK, Brandão SCS, Barberato SH; Critical revision of the manuscript for important intellectual content: Cauduro SA, Dutra JPP, Fernandes F, Brandão SCS, Barberato SH.

Potential conflict of interest

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Ethics approval and consent to participate

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

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