

CARDIAC TUMORS AND PSEUDOANEURYSMS

Relevant Guidelines

ESC 2022 Guidelines on cardio-oncology

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CARDIAC TUMORS

Cardiac neoplasms can be categorized according to their histological characteristics (benign or malignant) and their site of origin (metastatic or primary). Metastatic lesions are exponentially (20- to 30-fold) more common than primary lesions and uniformly malignant.¹

Primary Cardiac Tumors

Primary cardiac tumors are a rare entity across all age groups with a reported prevalence of 0.001-0.03% in autopsy series.² Primary tumors consist 0.3% to 0.7% of all cardiac tumors, whereas metastasis to the heart from other primary cancers is 30 times more common.³ Approximately 75% of primary cardiac tumors are benign and of those the majority are myxomas.^{4,5} Cardiac lipomas and papillary fibroelastomas occur in adults and are usually asymptomatic. Of the malignant tumors, which often occur in the young, 75% are sarcomas.³ Malignant primary cardiac sarcomas are usually located in the right atrium and are most commonly angiosarcomas (Figure 1). In the left atrium, the most common malignant tumors are pleomorphic sarcoma (also known as malignant fibrous histiocytoma) and leiomyosarcoma.³ Rhabdomyomas are the most common tumors during foetal life and childhood, followed by fibromas. Ventricular fibromas have a high propensity to cause malignant arrhythmias, and if they are not managed appropriately, mortality is high. The outcomes of surgical resection are good.⁶

Aetiology

The genetics of primary cardiac tumors is poorly understood especially for those that occur sporadically. Myxomas are familial in 10% of cases. **Carney syndrome** (or complex) is an autosomal dominant syndrome characterized by familial recurrent cardiac and mucocutaneous myxomas arising from mesenchymal cells, pigmented lesions over the lips, conjunctiva, and genitalia, adenomas of the breast and thyroid, and endocrinal abnormalities including Cushing syndrome and acromegaly. Genetic studies have identified mutations in the gene coding protein kinase A, regulatory subunit 1- α (PRKAR1 α).⁷ There are no demonstrable associations with malignant sarcomas.

Presentation

Systemic or pulmonary embolization, congestive heart failure from intracardiac obstruction, and arrhythmias may occur. Cardiac myxoma is the most common primary cardiac tumor to produce emboli to virtually any organ or tissue.⁸ Cerebral aneurysm secondary to embolic tumor fragments is a life-threatening complication. Cardiac sarcomas may be left or right heart; pulmonary artery sarcomas are extremely rare. Left atrial sarcomas tend to be more solid and less infiltrative than right-sided sarcomas, and they tend to metastasize later. They

usually present with symptoms of blood-flow obstruction and severe congestive heart failure. Right-sided cardiac tumors are usually malignant and appear as bulky, infiltrative masses that grow in an outward pattern. These are usually fast-growing tumors that metastasize early and do not present with congestive heart failure until late in the disease.³

Investigations

Cardiac magnetic resonance (CMR) has high diagnostic accuracy among patients presenting with suspected cardiac tumours (Figure 2).⁹ A CT of the chest with contrast agent is needed to exclude lung metastasis of malignant tumors. Two-dimensional transthoracic and transesophageal echocardiography underestimate tumor mass by as much as 24%.³

Therapy

Myxomas are completely excised under cardiopulmonary bypass; this may not always be feasible.⁴ Recurrence occurs in 3% of the cases and may be local or in extracardiac locations such as the brain, lung and other tissues. Thus, follow-up for more than 10 years is advisable.² Malignant primary cardiac tumors have a dismal prognosis and without surgical resection, the survival rate at 9 to 12 months is only 10%.³ The greatest risk factors for mortality are advanced age, higher comorbidity index, hemangiosarcoma histology, and the presence of metastases.¹⁰

Cardiac Metastases

Cardiac metastases are much more common than primary tumors.¹ The frequency of secondary metastatic tumors to the pericardium, myocardium, great vessels, or coronary arteries is between 0.7% and 3.5% at autopsy in the general population and up to 9.1% in patients with known malignancies.^{11 12} In a postmortem survey of 7289 malignant neoplasms, the highest rate was reported in pleural mesothelioma (48.4%), melanoma (27.8%), lung adenocarcinoma (21%), undifferentiated carcinoma (19.5%), lung squamous cell carcinoma (18.2%), and breast carcinoma (15.5%). Approximately 14% of patients with multiple distant metastases also have cardiac involvement.¹¹

Pathophysiology

Tumors can reach the heart via hematogenous or lymphatic spread, and transvenous or direct extension. The pericardium is the most frequently involved site comprising 64 to 69 of all cardiac metastases.¹¹ Epicardial and myocardial involvement (25-30%) and endocardial and intracavitary metastases (3-5%) are more rare.¹²

Presentation

Potential clinical manifestations are presented in Table 1. The most common sign is pericardial effusion. The possibility of cardiac metastasis should be considered in any patient with a malignancy and new cardiac symptoms.

Investigations

Echocardiography is essential but CMR provides additional tissue characterization with a higher resolution than CT. Positron emission tomography/CT may assist differentiation of malignant tumors from benign ones and allows imaging of the entire body to detect distant extracardiac metastatic disease. Malignant cells can be identified in the majority of pericardial effusions. Exploratory thoracotomy and open or endomyocardial biopsy may also be needed.

Therapy

Cardiac tamponade requires immediate pericardiocentesis. Recurrent effusions may need subxiphoid or transthoracic pericardial windows and percutaneous tube pericardiostomy. Surgical resection is indicated for intracardiac obstruction or when it allows complete removal of the tumor in the context of good prognosis. Radiotherapy and chemotherapy may also be indicated.¹³

PSEUDOANEURYSMS OF THE HEART

A pseudoaneurysm is a rupture of a blood vessel or of the myocardial wall that is contained by pericardium, thrombus, or adhesions, and has typically a narrow neck.¹ A true aneurysm is contained by all layers of the myocardium or vessel and displays a paradoxical movement, bulging outward during systole. Although their natural history is not well defined, pseudoaneurysms usually have a greater risk of rupture (30-45%) and should thus be considered for immediate repair.²

Aetiology

Myocardial infarction is the most common cause of LV pseudoaneurysms. Aortic valvular surgery and endocarditis (pseudoaneurysms at the mitral-aortic intervalvular fibrosa), blunt or penetrating trauma, and radiofrequency ablation are less common causes.^{1,2} Pseudoaneurysms of the native coronary arteries may occur after stenting or after spontaneous coronary arterial dissection, whereas pseudoaneurysms of bypass grafts tend to occur at suture line sites or after stenting.^{1,2}

Diagnosis

Patients may be asymptomatic or present with a murmur and/or heart failure. Systemic embolism may also occur. Rupture results in tamponade, shock or sudden death. Transthoracic echocardiography has low sensitivity to detect pseudoaneurysms; transoesophageal echocardiography, cardiac CT, and MRI offer a higher diagnostic yield.³

Treatment

Ventricular pseudoaneurysms are more likely to rupture when they are relatively acute (<3 months), large, or located within the anterior or lateral ventricular wall.⁴ Saphenous vein graft pseudoaneurysm should be considered for repair if large (>1 cm) or if associated with symptoms.⁵ Surgical repair or percutaneous closure may be used.⁶ Conservative management may be considered in high-risk patients with chronic pseudoaneurysms. The use of anticoagulation is controversial since it may increase the risk of rupture.

References

1. Maleszewski JJ, et al. Neoplasia and the Heart: Pathological Review of Effects With Clinical and Radiological Correlation. *J Am Coll Cardiol*. 2018;72:202-227. doi: 10.1016/j.jacc.2018.05.026
2. McManus B, et al. Primary Tumors of the Heart. In LibbyP, Bonow RO, Mann DL, Zipes DP (Eds): *Heart Disease*. 1815-1828, Saunders 2008. 2008.
3. Leja MJ, et al. Primary cardiac tumors. *Tex Heart Inst J*. 2011;38:261-262.
4. Pacini D, et al. Primary benign cardiac tumours: long-term results. *Eur J Cardiothorac Surg*. 2012;41:812-819. doi: 10.1093/ejcts/ezr067
ezr067 [pii]
5. Hoey ET, et al. MRI and CT appearances of cardiac tumours in adults. *Clin Radiol*. 2009;64:1214-1230. doi: 10.1016/j.crad.2009.09.002
S0009-9260(09)00321-3 [pii]
6. Jones JP, et al. Ventricular fibromas in children, arrhythmia risk, and outcomes: A multicenter study. *Heart Rhythm*. 2018;15:1507-1512. doi: 10.1016/j.hrthm.2018.06.018
7. Shetty Roy AN, et al. Familial recurrent atrial myxoma: Carney's complex. *Clin Cardiol*. 2011;34:83-86. doi: 10.1002/clc.20845
8. Haroun MJ, et al. Now you see it, now you don't? *Circulation*. 2015;131:1872-1879. doi: 10.1161/CIRCULATIONAHA.115.015652
9. Shenoy C, et al. Cardiovascular magnetic resonance imaging in suspected cardiac tumour: a multicentre outcomes study. *Eur Heart J*. 2021. doi: 10.1093/eurheartj/ehab635
10. Sultan I, et al. Long-Term Outcomes of Primary Cardiac Malignancies Multi-Institutional Results From the National Cancer Database
JACC. 2020.
11. Bussani R, et al. Cardiac metastases. *J Clin Pathol*. 2007;60:27-34. doi: jcp.2005.035105 [pii]
10.1136/jcp.2005.035105
12. Goldberg AD, et al. Tumors metastatic to the heart. *Circulation*. 2013;128:1790-1794. doi: 10.1161/CIRCULATIONAHA.112.000790
13. Bruce CJ. Cardiac tumours: diagnosis and management. *Heart*. 2011;97:151-160. doi: 10.1136/hrt.2009.186320

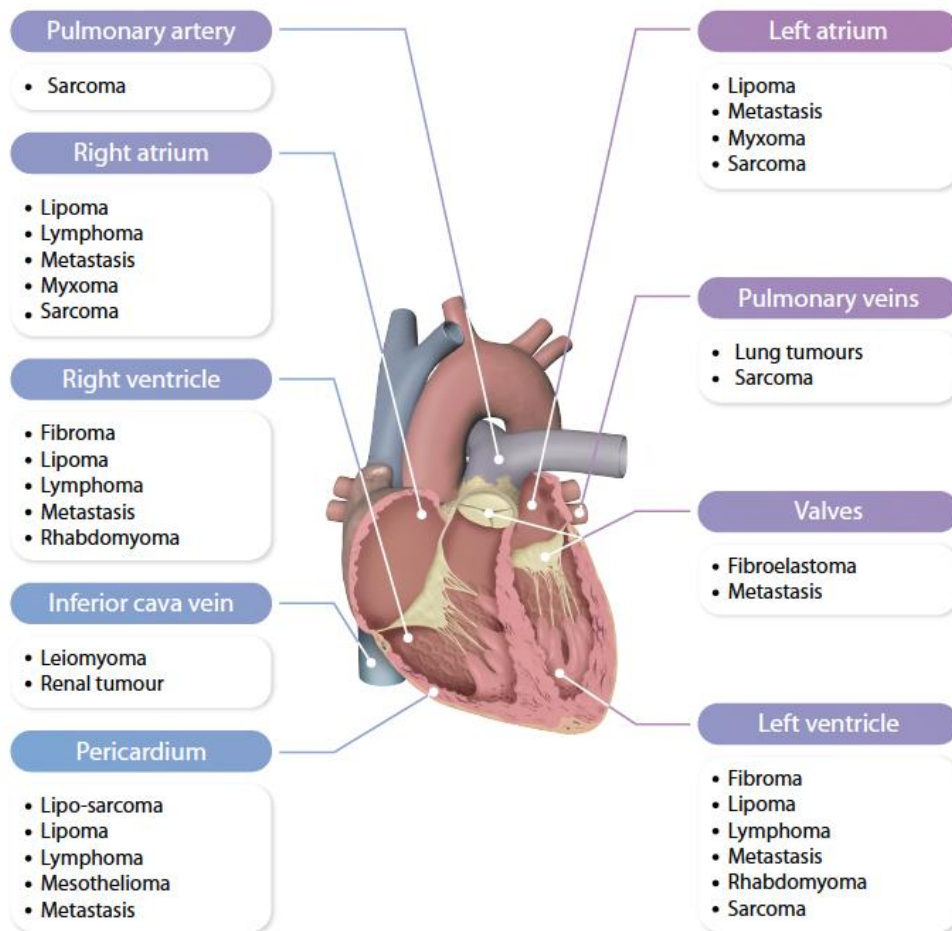


Figure 1. ESC 2022 GL on cardio-oncology. Location of primary and secondary cardiac tumours

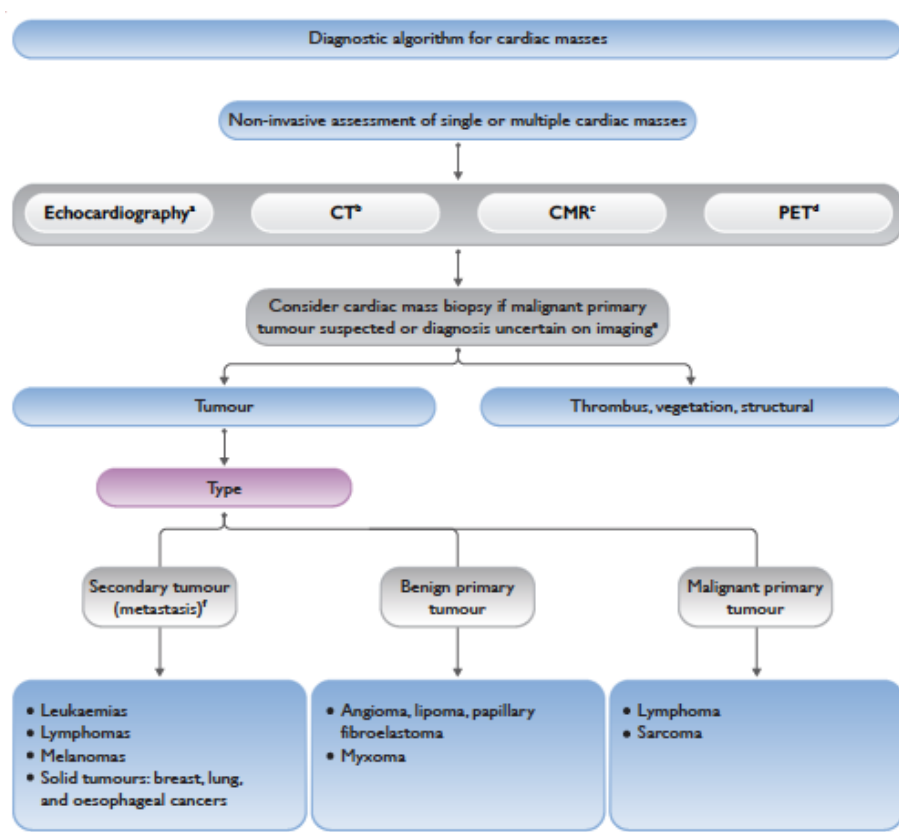


Figure 2. ESC 2022 GL on cardio-oncology. Diagnostic algorithm for cardiac masses.

CMR, cardiac magnetic resonance; CT, computed tomography; PET, positron emission tomography; TTE, transthoracic echocardiography.

a TTE/transoesophageal echocardiography: location, size, and haemodynamic disturbances. Contrast echocardiography to assess vascularization.

b Identify primary extra-cardiac malignancy. Reveal extra-cardiac changes. Staging of malignant lesions.

c Tissue characterization (fat infiltration, necrosis, haemorrhage, calcification, and vascularization). Exclude thrombus.

d Distinguish malignant vs. benign lesions. Staging of malignant lesions.

e Mass biopsy of suspected primary malignant cardiac tumours and/or biopsy of extracardiac masses if detected and safer to biopsy.

f 20–30 times more likely than primary tumours.

Table 1. ESC 2022 GL on cardio-oncology. Management strategies and surgery indications for symptomatic and asymptomatic patients with benign and malignant cardiac tumours

Classification		Management strategies	Surgery indications
Benign tumours	Asymptomatic	MDT discussion is required considering: tumour type, location, size, growth rate, and likelihood of embolism. Anticoagulation should be considered for left-sided tumours or right-sided tumours associated with an intracardiac shunt, according to the individual's embolic and bleeding risk	If left-sided and endocardial: even if small and incidental, a MDT is needed to consider the indication for surgical removal due to the embolic risk
	Symptomatic	Non-surgical management for: • Rhabdomyomas (possible spontaneous regression) • Intramural haemangioma (possible response to corticosteroids) • Unresectable cases: if antiarrhythmic therapy is sufficient	Surgical resection is indicated in all other cases. For large, benign, unresectable, symptomatic cardiac tumours (obstruction, severe HF, or malignant arrhythmias), heart transplantation may be indicated in some cases
Malignant tumours	Asymptomatic	Histopathological diagnosis is required	If primary cardiac sarcoma, a complete surgical resection may increase survival
	Symptomatic	Chemotherapy and/or RT are the only therapeutic options for secondary cardiac tumours. If primary cardiac lymphoma: chemotherapy	Secondary cardiac tumours may also be treated with palliative cardiac surgery

HF, heart failure; MDT, multidisciplinary team; RT, radiotherapy.

Table 2. Potential clinical manifestations of cardiac metastases

Pericardial metastasis
Pericarditis, pericardial effusions, and cardiac tamponade
Pericardial adhesions and constrictive pericarditis
Epicardial and myocardial metastasis
Atrial and ventricular arrhythmias and conduction disturbances, including atrial fibrillation with RVR, atrial flutter, complete AV block, PVCs, and ventricular fibrillation
CHF with systolic or diastolic dysfunction
Myocardial ischaemia or infarction from perivascular coronary artery compression, tumour embolism, or coronary invasion
Cardiac rupture
Endocardial and intracavitary metastasis
Intracavitary obstruction, left and right heart failure, cardiogenic shock
Pulmonary tumour emboli from right-sided metastasis
Stroke from tumour emboli from left-sided metastasis
Superior or inferior vena cava metastasis
Superior vena cava syndrome
Inferior vena cava syndrome
Right heart metastasis

AV Indicates atrioventricular; CHF, congestive heart failure; PVC, premature ventricular contraction; and RVR, rapid ventricular response. Goldberg AD, et al. Tumors metastatic to the heart. *Circulation*. 2013;**127**:1790–4 with permission from Wolters Kluwer.