Computed Tomography of Cardiac Malignancies

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The earliest description of cardiac tumors was reported in France in 1562, but little was understood about the etiology of these malignancies before the contemporary era of advanced medical imaging. These tumors are rare, frequently asymptomatic, and associated with short survival times once they are advanced enough to become symptomatic. For centuries, it was a disease noted at autopsy, but the emergence of modern medical imaging has made it possible for clinicians to diagnose cardiac malignancies earlier.

Patients with cardiac malignancies usually die within 1 year of diagnosis because many have metastatic disease stemming from the multiple-organ spread of cancers arising in other tissues, or because primary heart tumors frequently are asymptomatic until they are advanced and life threatening. In addition, these rare malignancies are associated with nonspecific symptoms and seldom are the initial suspected diagnosis once symptoms appear, often resulting in delayed diagnosis. For example, cardiac sarcomas, which arise in mesenchymal and nonepithelial tissues, are the most common type of heart malignancy and are known as “great mimickers” because of their nonspecific symptomatology. As they grow, cardiac tumors frequently cause progressive heart failure and sudden cardiac death or spread to distant organs causing metastatic disease and organ failure. Most patients with primary cardiac malignancies die of progressive heart failure caused by the primary tumor.

Symptoms and the patient’s prognosis are related to the location and size of the primary cardiac tumor. The prognosis for these patients also hinges on early-stage diagnosis and rapid initiation of treatment. Effective treatment depends on accurate assessment of tumor size, contours, precise location, and resulting functional impairment. Diagnostic imaging—particularly echocardiography, computed tomography (CT), and magnetic resonance (MR) imaging—plays a central role in cardiac imaging.
Oncology, and there is an emerging role for positron emission tomography (PET).

Because distinct cancer etiologies and histologies are associated with different morphologies, degrees of vascularity, and primary tumor locations in the heart, diagnostic imaging can provide tentative insights into the probable type or subtype of a tumor. However, definitive diagnosis requires a pathologist's histological examination of a tumor biopsy sample obtained during tumor resection or an endomyocardial biopsy procedure, or cytological examination of aspirates from pericardial effusion.

**Anatomy**

The workhorse of the circulatory system is the heart, a fist-sized, 4-chambered muscular pump. Through its rhythmic contractions, the heart supplies blood to the body's network of arteries, capillaries, and veins, which deliver oxygen and nutrients to cells and carry away cellular-metabolic wastes.

Situated at the middle mediastinum, between the sternum and the fifth through eighth vertebrae, more than half of the heart lies to the left of the chest's midline. The apex, or lower contour, of the heart abuts the diaphragm. The heart's diameters and external contours provide radiographic landmarks used in the diagnosis of cardiac disorders.

The heart wall is composed of several tissue layers, the outermost of which is a lubricated lining, or sac, composed of fibrous pericardium, which encompasses the entire organ. Immediately beneath the pericardium are parietal and visceral (epicardial) tissue layers collectively referred to as the *serous pericardium*. The pericardial space is a thin pericardial fluid-containing gap between the fibrous pericardium and the heart; the epicardium adheres to the external surface of the heart and constitutes the heart's outer wall. Beneath the serous pericardium is a layer of fatty connective tissue containing coronary blood vessels, and beneath that, a deeper, thick layer of myocardium situated immediately atop the endocardium, which is composed of squamous epithelial cells and lines the interior of the heart muscle and the connecting blood vessels. The heart wall extends into the interior chambers of the heart to separate the atria and ventricles, the heart's functional units.

The largest component of the heart is the myocardium. It is composed of branching muscle cells joined by end-to-end junctions, called *intercalated disks*, to form a continuous mass. These electrically interconnecting subunits work together in a tightly coordinated manner to allow heart contractions that push blood through the heart's chambers with considerable force.

Heart cells receive their nutrients and oxygen from the right and left coronary arteries. After moving through the heart's capillary network, blood collects in the cardiac venous network of confluent vessels that drain into the right atrium through the coronary sinus.

Waves of myocardial contraction force blood through the heart's 4 chambers: the right and left upper atria and right and left lower ventricles. The septum separates these chambers. The interatrial septum is the portion of the septum separating the right and left atria, and the ventricular or interventricular septum separates the right and left ventricles.

Blood from the body's venous system is delivered into the right atrium, then through the right ventricle to the left pulmonary artery. Blood received from the left pulmonary veins enters the left atrium and then, via the left ventricle, supplies the aortic arch and the body's arterial network. Atrial walls are thinner than ventricular walls in part because they require less contractile force to move blood to the ventricles than the ventricles require to force blood further distances into the great arteries.

Valves that connect the heart's chambers ensure that blood flows in the proper direction, from atrium to ventricle and from ventricle to artery; when blood flows back against the flaps of the valve from the receiving chamber or vessel, the flaps close to prevent backflow. At the base of the heart valves is a ring of tissue called the *annulus*. The atrioventricular valves that connect the atria and ventricles are called *cusp valve* because their flaps are pointed at the tips. The right atrioventricular valve is called the *tricuspid valve* because it has 3 flaps, whereas the left atrioventricular valve has 2 flaps and is known as the *bicuspid or mitral valve*. Blood exiting the ventricles does so via the crescent-shaped flaps of the semilunar valves; the pulmonary semilunar valve supplies the left pulmonary artery, and the aortic semilunar valve supplies the aorta (see Figure 1).
mesothelioma of the heart, like pulmonary mesothelioma, is associated with asbestos exposure. In rare instances, cardiac lymphomas have been noted in children infected with HIV. One 2014 study in Serbia suggested that bacterial cytotoxins in drinking water might contribute to cardiac malignancy risk. Cases of cardiac sarcoma and lymphoma also have been reported anecdotally as possibly linked to medical prosthetic materials, such as the polymers used in mitral valve-replacement prosthetic rings or internal cardiac defibrillator implants, and laboratory studies have shown that some of these materials can provoke tumorigenesis in animals. Sarcomas in organs other than the heart have been linked to exposure to ionizing radiation and vinyl chloride as well as inherited cancer syndromes.

Certain gene mutations have been found in cardiac sarcomas including MDM2 proto-oncogene, E3 ubiquitin protein ligase (MDM2), epidermal growth factor receptor (EGFR), and platelet-derived growth factor (PDGFR) gene-copy-number duplications. The role of these genes in heart cancer risk or progression remains unclear. Two published reports described familial cardiac angiosarcoma as a presumably genetic syndrome associated with right-atrium angiosarcoma tumors exhibiting “excessively rapid” growth.

**Epidemiology**

Because cardiac malignancies are rare, less is understood about their causes and development than about the more common breast, lung, colorectal, or prostate cancers. Precise incidence rates and prevalence estimates for cardiac tumors are unknown. Much of the literature on cardiac malignancies reports case studies describing individual patients. Myxomas, or benign primary tumors, usually occur among women in middle adulthood, between 30 and 60 years of age. In an estimated 10% of cases, myxomas are hereditary and usually are multifocal, arising in 2 or more places.

Few epidemiological risk factors have been confirmed for primary cardiac malignancies, although malignant and benign tumors of the heart are more common in women than men.

Epidemiologic data suggest that malignant tumors of the heart occur with roughly equal frequency in men and women. Risk factors for primary cardiac malignancies have been linked to exposure to ionizing radiation and vinyl chloride as well as inherited cancer syndromes.

**Diagnosis**

Heart masses often are asymptomatic until they reach advanced stages and large sizes. However, CT and MR imaging have improved early-detection rates in recent years. When heart cancers are symptomatic, symptoms usually are nonspecific (eg, shortness of breath, particularly when lying down; cough or bloody cough) and they depend largely on tumor location and size.

A review of patients who received diagnoses over a 32-year period in Spain found that more than 90% of patients with primary cardiac malignancies...
were symptomatic. In addition, 70% had cardiac failure; these findings indicate advanced tumor stages at the time of diagnosis.17

Tumors likely to arise in a specific region of the heart are associated with a more consistent suite of symptoms, but they also are nonspecific and can overlap with those of other acute and chronic conditions. For example, advanced stage angiosarcomas can cause right heart failure, and advanced undifferentiated sarcomas can cause fluid accumulation in the lungs (pulmonary congestion).3

Systemic signs and symptoms depend on the location of a mass and can include1:

- Weight loss.
- Malaise.
- Fatigue.
- Anemia.
- Fever.
- Thrombocytosis (elevated blood platelet counts).
- Leukocytosis (elevated white blood cell counts).

Signs of embolization, such as stroke, myocardial infarction, retinal embolism, peripheral arterial embolism, or pulmonary embolism, also are possible.1 Other symptoms are indicative of cardiac chamber or valve obstructions, including pulmonary edema and chest pain, congestive heart failure, and syncope, and can result in sudden cardiac death.1 Cardiac tumors also can cause pericardial effusion, which sometimes leads to cardiac tamponade.1,3 In addition, tumors can disrupt the electrical and contracting function of the heart, resulting in arrhythmias such as atrial/ventricular tachyarrhythmias.1

Just as primary tumors elsewhere in the body can metastasize to the heart, advanced heart tumors can spread to other organs. Metastatic sarcomas in the lungs, brain, or bones can indicate the presence of a primary cardiac sarcoma.1 When a cardiac tumor is suspected, diagnostic imaging is performed to assess the tumors.

Medical Imaging

Medical imaging plays a central role in detecting and characterizing heart tumors and determining the functional involvement of the valves, atria, ventricles, coronary arteries, and other anatomic regions.1 Before surgery, cardiac catheterization coronary angiography sometimes is used to evaluate coronary artery disease in older adults or to assess a heart tumor’s vascularity, although multidetector CT (MDCT) with contrast-enhanced, cardiac-gated CT coronary angiography displays these vessels well and is less invasive than surgery.1,16 Endomyocardial biopsy during cardiac catheterization can be used to confirm a tentative diagnosis of a cardiac malignancy.1

Echocardiography was long the mainstay of heart cancer imaging.19-21 Transthoracic echocardiography can show heart morphology well in different planes and provides real-time functional information including tumor mobility.19 It is an excellent modality for seeing small tumors on the cardiac valves.20 Transesophageal echocardiography can overcome the limited acoustic window of transthoracic echocardiography and can display the pulmonary veins and descending aorta, but similar to transthoracic echocardiography, it cannot show the mediastinum well enough to detect tumors outside of the heart.19 Echocardiography shows functional bloodstream dynamics including valve obstruction caused by tumors and tumor-associated tamponade.20

Sarcomas sometimes can be differentiated from myxomas using echocardiography because of myxomas’ greater degree of tumor movement and distention in the intracardiac bloodstream.3,19 Doppler echocardiography provides bloodstream velocity data with which intrachamber blood pressure can be calculated.19 Three-dimensional transthoracic and transesophageal echocardiography can help locate and characterize heart cancers during preoperative planning and surgery.2,22

Although transthoracic and transesophageal echocardiography offer good spatiotemporal resolution and are useful in assessing cardiac tumor size, contours, location, and movement, they offer relatively poor visualization of soft tissue and cardiac tumor infiltration compared with CT and MR imaging.19 Compared with echocardiography, imaging with MR—and to a lesser degree CT—offers excellent soft-tissue contrast and can show the full anatomic extent of disease, which is important in tumor staging.19,20 Both CT and MR imaging, with and without cardiac gating and the use of contrast agents, are increasingly important in diagnosing, characterizing, and planning treatment strategies for cardiac
malignancies initially detected with echocardiography as part of a multimodality imaging approach. Cardiac MR imaging requires slower image acquisition times than CT, but MR imaging is useful for showing tumor infiltration of myocardial tissues, chamber obstructions, and valve dysfunction. Because of its wide availability, rapid scan acquisition times, and better depiction of tumor calcifications and fat foci, CT will continue to play a central role in the anatomic imaging of suspected heart malignancies.

Single-photon emission CT has been investigated for the assessment of suspected carcinoid cardiac tumors, but it commonly is not used in the diagnostic imaging of heart cancers. In contrast, fludeoxyglucose F 18 PET (FDG-PET) is preferred for staging and assessing tumor responses to treatment for metastatic heart malignancies arising in distant tissues and shows potential as a diagnostic imaging modality for primary cardiac malignancy metastases. FDG-18 uptake quantification might improve differentiation of benign and malignant primary heart tumors because tumors usually have elevated glucose metabolic rates and, therefore, better FDG-18 uptake. However, evidence for the utility of PET and PET-CT in cardiac tumor imaging remains nascent.

**Computed Tomography**

Although relatively little empirical evidence is available on which to base imaging standards, expert consensus states that cardiac CT is:

- Inappropriate for initial evaluation of a suspected tumor or thrombus.
- An appropriate secondary imaging modality for characterizing cardiac masses.
- Appropriate for evaluating pericardial involvement and metastasis.

MDCT offers excellent spatial resolution for detection of mediastinal, pulmonary, or lymph node metastasis in primary cardiac malignancies. Access to MDCT is more widely available than MR imaging; however, the benefits and risks of MDCT and other examinations using ionizing radiation always should be weighed, particularly among young patients. For example, MDCT imaging generally is not recommended for evaluating suspected benign rhabdomyomas in children. Contrast-enhanced CT (CECT) involves iodinated contrast for which impaired renal function might be a contraindication. MDCT is efficient and can answer many questions about cardiac masses including:

- Their anatomical relationship to surrounding structures.
- Whether calcifications are present within the mass.
- The existence of hemorrhagic areas.

Advances in MDCT scan acquisition times have improved image quality, but with patients who have tachycardia, the image quality can be diminished. Heart rate sometimes can be managed with pharmacologic interventions. One advance in MDCT technology has been improved electrocardiographic (ECG) gating, which can increase intracardiac CT image quality by ensuring that scan acquisition occurs during a prespecified phase of cardiac motion.

The emergence of MDCT and development of ECG-gated MDCT scan acquisition have strengthened this modality’s advantages over echocardiography including “definitive” characterization of fatty and calcified foci within tumors and a wide field-of-view for superior detection of metastatic disease. In addition, volumetric CT image reconstructions are used to monitor cardiac tumors’ response to treatment and to detect tumor recurrence.

Respiratory motion has become less relevant as MDCT designs have surpassed 16 detector rows, but ECG-gated MDCT produces high-quality, precise images that improve the depiction of tumor margins. With CECT, retrospective cardiac gating in postscan image reconstruction also is possible. One protocol described in the literature for retrospective cardiac-gated multiphase CT calls for slice thicknesses of 1 mm to 1.5 mm to account for cardiac motion.

Intravenous iodinated contrast can be employed to improve image quality and avoid the risk of repeated CT scanning because of insufficient detail in noncontrast images. Iodinated contrast bolus tracking helps to time scan delays precisely, which ensures acquisition during the intended contrast phase. CECT scan acquisition parameters vary among facilities, specific imaging goals, and MDCT equipment designs and generations. Each imaging department should have written standard operating procedures available for
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Table 1

| Cancer Classification of Heart Tumors<sup>1,25</sup> |
|---------------------------------|---------------------------------|
| **Benign and pseudotumors**     | **Malignant**                   |
| adult cellular rhabdomyoma, cardiac fibroma, cardiac myxoma, cystic tumor of the atroventricular node, hamartoma of mature cardiac myocytes, hemangioma, histiocytoid cardiomypathy (Purkinje cell tumor), inflammatory myofibroblastic tumor, lipoma, papillary fibroelastoma, rhabdomyoma | angiosarcoma, cardiac lymphoma, epithelioid hemangioendothelioma, fibrosarcoma and myxoid fibrosarcoma, leiomyosarcoma, liposarcoma, malignant fibrous histiocytoma/undifferentiated pleomorphic, rhabdomyosarcoma, synovial sarcoma |
| **Metastatic**                  |                                 |
| from primary tumors of the lung, breast, skin, kidneys, ovaries, and/or esophagus |                                 |
| **Pericardial**                 |                                 |
| germ cell tumors, malignant mesothelioma, metastatic or secondary pericardial tumors, solitary fibrous tumor |                                 |
tumors arise from the endocardium of the left atrium in 75% to 90% of cases and the endocardium of the right atrium in 10% to 25% of cases.3,9,26 In most cases, myxomas develop on the interatrial septum.3

Myxomas might or might not produce symptoms.26 Right atrial myxomas usually are asymptomatic until they exceed a diameter of 5 cm and can be associated with narrowing of the tricuspid valve and atrial fibrillation.9 Similar to other types of benign tumors, cardiac myxomas can in some cases have serious and even life-threatening ramifications such as mitral valve obstructions.3,27,28 Other reported myxoma symptoms include dyspnea during physical activity or while lying down or sleeping, chest pain, dizziness, syncope, heart palpitations, clubbing of fingertips, Raynaud phenomenon (blueness of fingers), cough, fever, malaise, joint pain, or unintentional weight loss.9 When fragments of myxomas become dislodged in the turbulent atrial blood flow, they also can cause downstream emboli or thrombi that have been implicated in stroke or pulmonary hypertension in these patients.3,27,28

Calcifying amorphous tumors within the cardiac chambers sometimes are misdiagnosed as myxomas.26 These tumors are pseudotumors—calcified mural thrombi, usually found at the mitral valve or mitral valve annulus, the ring-shaped structure at the base of the valve.26,29 These tumors can cause antiphospholipid syndrome or kidney failure.26 Patients with calcifying amorphous tumors typically present with shortness of breath, syncope, and embolism.29

Other types of benign primary cardiac tumors are rhabdomyomas, fibroelastomas, and lipomas.3,26 Rhabdomyomas occur on the heart valves, and fibroelastomas occur on the aortic or mitral valve surfaces and usually are smaller than 1 cm in diameter, which can make them difficult to detect with CT or MR scans.3 Fibroelastomas represent 5% to 10% of benign primary heart tumors.3 Cardiac lipomas are benign fatty tumors that, comparable to myxomas, develop on the epicardium or the endocardial lining of the heart’s chambers and frequently invade the pericardial space.3,26 Cardiac lipomas typically are asymptomatic but can cause atrial fibrillation and other heart arrhythmias.3

Rarer benign primary cardiac tumors include neuroendocrine-cell paragangliomas and hemangiomas arising from capillary or other malformed vascular tissue.3 Benign cardiac fibromas composed of fibroblasts and collagen are extremely rare and usually found in children; only 100 cases have been reported.3,26 Although these benign tumors typically reach 5 cm in diameter, they can grow larger and destroy the left-ventricular chamber in which they are most often found, with life-threatening consequences for the patient.3

Cardiac masses that mimic malignancies include benign tumors and benign pericardial cysts. In addition, myocardial infarction–associated thrombi in adults, and to a lesser extent in children, can mimic malignancies.23,30 Benign congenital pericardial cysts typically are asymptomatic but can become infected or lead to compression of the heart by accumulating pericardial fluids, causing tamponade.30 The cysts do not connect to the pericardial space and appear on CT scans as thin-walled and homogenous masses.23 On CECT scans, they appear as nonenhancing lesions.25 Benign congenital pericardial cysts also exhibit water-value attenuation (see Figure 2).30 Among neonates and children, the most commonly diagnosed cardiac tumors are benign rhabdomyomas; benign fibromas; and benign teratomas, which also can occur as malignancies.30 Rhabdomyomas tend to regress through childhood and usually are not an indication for surgical resection.30 In contrast, pediatric cardiac fibromas usually are treated surgically.30

Primary Cardiac Malignancies

Most primary heart malignancies in adults and children are sarcomas.30 These are cancers that arise in nonepithelial soft tissues.1,30 Sarcomas usually are diagnosed as primary myocardial or pericardial tumors identified in the absence of primary tumors elsewhere in a patient’s body.1 Cardiac sarcomas occur in different histological subtypes (see Table 2).7 Angiosarcomas are the most frequent primary malignant tumor type found in the adult heart but are less common than rhabdomyosarcomas among children.3,30 Two morphologic types of cardiac angiosarcoma are known: the first type is a well-defined mass that extends into a cardiac chamber, and the second type is a diffuse infiltrating tumor along the pericardium.18
Cardiac angiosarcomas seem to be more common in men than in women, but precise estimates are not available. The tumors favor the right atrium and frequently involve the right atrial wall and pericardium. Cardiac angiosarcomas usually are more heavily vascularized than other heart tumors and typically are associated with focal hemorrhage and tumor necrosis. Angiosarcomas often are asymptomatic until they have already metastasized to the lungs or other distant organs. These tumors can become symptomatic after growing large enough to substantially obstruct the right atrium, causing right heart failure, pericardial effusion, and resulting tamponade.

Primary cardiac angiosarcomas appear on CT scans as large masses with multilobar contours. They arise from the right atrial wall in 80% of cases, and in others, from the right ventricle or the pericardium (see Figure 3). The tumors can be accompanied by pericardial or pulmonary effusions. Large angiosarcomas can obliterate and replace the right atrial wall and obstruct the atrium. In addition to a broad base of attachment, cardiac angiosarcomas tend to be well vascularized and hemorrhagic, with necrotic foci that cause a heterogeneous contrast appearance.

Table 2

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiosarcoma</td>
<td>26-37 of all diagnosed primary cardiac sarcomas</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>20-35</td>
</tr>
<tr>
<td>Malignant fibrous histiocytoma/</td>
<td>11-24</td>
</tr>
<tr>
<td>undifferentiated pleomorphic</td>
<td></td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>8-9</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>3-9</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>5-6</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>4-7</td>
</tr>
<tr>
<td>Myxosarcoma</td>
<td>4</td>
</tr>
<tr>
<td>Fibromyxosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Malignant mesenchymoma</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Cardiac lymphoma</td>
<td>&lt; 1-2 of primary cardiac malignancies</td>
</tr>
</tbody>
</table>
When angiosarcomas involve the pericardium, the resulting pericardial thickening has been described as “sheet-like” on cardiac CT scans, compared with more nodular contours or hemorrhagic pericardial masses associated with rhabdomyosarcoma. On CT scans, angiosarcomas also can exhibit pericardial effusion with tumor infiltration of the myocardium, in contrast to synovial sarcomas that tend to exhibit pericardial infiltration. MDCT can help differentiate angiosarcomas from aggressive pericardial synovial sarcoma tumors, which have heterogeneous enhancement, multilobulated contours, and profound pericardial infiltration and tumor invasion of the tissue from which they arose.

Undifferentiated sarcomas represent between one-fourth and one-third of adult malignant primary cardiac sarcomas. In contrast to angiosarcomas, approximately 80% of undifferentiated sarcomas occur in the left atrium and tend to involve the mitral valve. Undifferentiated sarcomas also are seen in children. Frequently, an undifferentiated sarcoma involves the heart valves and appears on CT as a large, poorly attenuating or hemorrhagic mass, with myocardial infiltration that can result in an irregular or thickened appearance.

Rhabdomyosarcomas, composed of muscle cells, are the most common primary cardiac malignancy in children, representing up to 7% of primary cardiac sarcomas overall. Rhabdomyosarcomas usually occur at multiple cardiac sites, always involve myocardial tissues, and can grow to penetrate multiple heart chambers. They often have central tumor necrosis and involve heart valves more often than other heart cancers. They also frequently invade the pericardium or epicardial tissue and heart valves. On CT scans, rhabdomyosarcomas exhibit low attenuation and typically a central necrosis and infiltrative margins (see Figure 4).

Metastatic cardiac osteosarcomas usually are found in the right atrium. Primary cardiac osteosarcomas usually are found in the left atrium and less frequently in the left ventricle. Osteosarcomas are composed of bone-producing cells, and CT scans of these tumors frequently show dense calcifications. Cardiac osteosarcomas can
be misdiagnosed as myxomas, particularly in the left atrium, but can be differentiated by a broad base and tumor extension into the pulmonary veins. On CT images, dense calcifications within a low-attenuating tumor indicate a cardiac osteosarcoma (see Figure 5). Pericardial and atrial-septal infiltration also might be noted on CT images of osteosarcomas.

Primary cardiac lymphoma is less common than secondary cardiac lymphoma and typically is diagnosed in immunocompromised patients. Primary cardiac lymphomas usually involve aggressive B-cell accumulations appearing as nodules in the right—and sometimes left—cardiac chambers, without tumor necrosis. Heart valves rarely are involved.

In CT images, primary cardiac lymphoma lesions are varied and generally nonspecific, but they often include a hypodense or isodense appearance compared with the myocardial tissues, with heterogeneous enhancement and, frequently, pericardial effusion (see Figure 6). In one case, a “heart-shaped” sign was seen in PET-CT images of a 71-year-old woman with primary cardiac lymphoma. It was described as the “heart within the heart” sign, a bright signal at the right heart.

In children, among whom primary cardiac lymphomas are exceedingly rare, these malignancies appear on CT as low-attenuation masses with heterogeneous enhancement patterns. Most cardiac lymphomas in children are secondary, resulting from direct or hematogenous extension. Primary cardiac lymphomas in children usually involve the right cardiac chambers.

Another primary adult heart malignancy is leiomyosarcoma, a smooth-muscle tumor that can arise in the pulmonary vasculature and then extend into the left atrium via intracavitary extension, or vice-versa. These tumors frequently involve the left atrium, mitral valve, and pulmonary veins. Cardiac leiomyosarcomas also frequently invade the pulmonary veins, as well as the mitral valve; they appear on CT as left-atrial low-attenuation tumors with lobulated contours, usually attached to the posterior atrial wall, contrary to myxomas.

Figure 5. Left ventricular osteosarcoma in a 69-year-old man. A. Unenhanced CT scan of the chest reveals dense calcification (arrow), initially misinterpreted as a chronic calcification of the posterior medial papillary muscle. B. On an unenhanced CT scan obtained 6 years later, the left-ventricular calcifications have increased markedly (arrow). C. CECT scan reveals a large, low-attenuation mass occupying the left ventricle (arrow). D. Photograph of an autopsy specimen shows pericardial rind and extensive mural involvement from primary osteosarcoma. Calcified foci also are seen (arrows). Reprinted with permission from Araoz PA, Eklund HE, Welch TJ, Breen JF. CT and MR imaging of primary cardiac malignancies. Radiographics. 1999;19:1427.
Sarcoma Group system developed for soft-tissue cancers. The system includes scores for tumor differentiation, mitotic count, and extent of tumor necrosis. Heart cancers are classified as low-grade (G1), intermediate-grade (G2), or high-grade (G3) based on these 3 criteria. Tumor differentiation scores (1-3) reflect increasing dissimilarity to adult mesenchymal tissue; angiosarcomas receive a tumor differentiation score of 3.

Mitotic count scores (0-2) reflect ranges of tumor cell mitotic-division rates, measured as the number of mitotic divisions occurring under microscopic magnification of a set high-power field area. Tumor necrosis scores (0-2) are assigned for tumors without any evidence of necrosis (0), less than 50% tumor necrosis (1), or 50% or more tumor necrosis (2). The tumor differentiation score, mitotic count score, and tumor necrosis score are then summed to determine the tumor grade (G1 = total score < 4; G2 = total score of 4 or 5; and G3 = total score > 5).

Metastatic Cardiac Malignancies

Little is known about the incidence rates of metastatic or secondary heart tumors that spread to the heart from other organs such as the lung, esophagus, skin, or breast. However, metastatic cardiac tumors are more common than primary cardiac tumors, particularly in the pericardium. With advances in treatment and longer patient survival times for other cancer types that might spread to the heart, the incidence of cardiac metastases might be increasing.

Metastatic cardiac tumors are more common than primary cardiac tumors among adults but are rarer among children. Among adults, melanoma, renal cell carcinoma, and hepatocellular carcinoma can metastasize to right-chamber endocardial surfaces. Synovial sarcomas can arise in the pericardium and usually are aggressive tumors that appear radiographically similar to angiosarcomas.

Grading and Staging Primary Cardiac Malignancies

Because no grading system has been developed for heart cancers, cardiac malignancies are graded and staged using the French Federation of Cancer Centers.
other organs, possibly because of bloodstream velocities in the cardiac chambers.\textsuperscript{22} However, cancer arising in other organs can spread to the heart, and this occurs more frequently for some less common cancers.\textsuperscript{22} For example, melanoma, malignant germ cell cancers, and tumors in the mediastinum appear to be more likely to spread to the heart than other, more distant organs.\textsuperscript{22,34-38} Autopsy studies indicate that melanoma might spread to the heart in more than half of patients.\textsuperscript{22} Even so, more patients have metastatic heart tumors from mediastinal cancers, such as breast or lung cancer, than melanomas because those cancers are more common.\textsuperscript{22} Blood cell cancers, such as leukemias, and lymphomas also metastasize to the heart.\textsuperscript{1}

Although metastasis to the heart is rarer in children than in adults, it still is up to 20 times more frequent among children than are primary cardiac malignancies.\textsuperscript{30} When children have metastatic cardiac tumors, the cancer typically has spread from a distant sarcoma, lymphoma, Wilms tumor, or testicular cancer.\textsuperscript{30}

Metastasis or invasion by noncardiac primary tumors into the heart follows 4 potential pathways:\textsuperscript{1,3,26}

- Direct invasion – tumors in the mediastinal organs spread through organ walls into adjacent heart tissue as in advanced-stage esophageal tumors.
- Bloodstream seeding (hematogenous spread) – hematogenous extension, typically from melanomas, leukemias, or renal cell carcinomas; usually results in secondary tumors in the myocardium.
- Lymph system seeding – lymphatic extension, usually involving epithelial histologies.
- Intracavitary locoregional invasion from major blood vessels into the heart by tumors arising in the inferior vena cava.

Metastasis, pericardial effusion, and tissue invasion all are indications that a tumor is malignant.\textsuperscript{23} Calcifications sometimes are seen as small foci in myxomas, more commonly in the right atrium, and with fibromas and teratomas, but they appear on CT scans as large foci in osteosarcomas.\textsuperscript{23}

Metastatic cardiac tumors can grow aggressively and can disrupt heart function catastrophically.\textsuperscript{34} These tumors frequently are detected only after a patient dies.\textsuperscript{22} For this reason, metastatic heart tumors should be suspected when patients with cancer diagnoses exhibit new signs or symptoms of cardiac dysfunction—particularly patients with melanoma or a mediastinal primary-tumor diagnosis.\textsuperscript{34} Some authors recommend that heart metastasis be considered even when a patient without an existing cancer diagnosis exhibits signs or symptoms of cardiac dysfunction with no other clear cause.\textsuperscript{22,34} Depending on the exact location of metastases, signs can include lymphatic flow obstruction, potentially life-threatening pericardial effusion, or cardiac chamber filling defects.\textsuperscript{22,35,36}

Clinical symptoms associated with cardiac metastases are nonspecific and can include cough, dyspnea, tachycardia, cardiac arrhythmia, or heart failure.\textsuperscript{22,35} Symptom severity typically reflects the extent of metastatic invasion of the heart.\textsuperscript{22} Metastatic tumors in the myocardium are associated with atrial or ventricular arrhythmias, or both. Metastatic cardiac tumors also can cause electrical conduction defects in the heart and frequently result in abnormal electrocardiography findings. If metastatic tumors are compressing the heart, their location will determine whether surgical resection is attempted. However, because metastatic cardiac tumors usually are part of more widespread metastatic disease, most patients undergo palliative treatment rather than surgery or treatment with a curative intent.\textsuperscript{22}

Metastatic cardiac tumors can occur in any region of the heart but more frequently involve the pericardium; they usually are multifocal and often part of wider metastatic disease involving secondary tumors in other organ systems such as the liver or lungs.\textsuperscript{22,35-37} Metastatic melanoma appears to be more common in the right side of the heart than in the left.\textsuperscript{22} Metastatic tumors usually arrive in the heart as a result of direct extension or via bloodstream or lymphatic spread.\textsuperscript{36} Some believe that melanoma most frequently metastasizes to the heart via the bloodstream.\textsuperscript{22}

When metastatic cardiac tumors are suspected, patients typically are examined initially with echocardiography and subsequently with more detailed images using CT, gated CT, or MR imaging. FDG-PET, FDG PET-CT, or both might also be used. These modalities can help detect metastatic tumors of the heart and characterize their involvement with cardiac structures.\textsuperscript{22} Whole-chest imaging and whole-body nuclear imaging can detect metastases in other organ systems.\textsuperscript{22,39}

Gated cardiac CT imaging allows detailed visualization of metastatic tumor location, tissue involvement,
and effects on heart anatomy and function.\textsuperscript{22-23} CT is considered superior to MR for tissue characterization.\textsuperscript{39} For example, CT can sensitively detect calcifications or new tumor-recruited vasculature within a suspected cardiac mass.\textsuperscript{38,39} MR might be contraindicated for some patients (eg, those with obesity, claustrophobia, or cardiac pacemaker implants).\textsuperscript{39} Cardiac CT also allows detection of coronary artery disease, which can affect treatment options for cardiac tumors.\textsuperscript{39}

Each institution should have written cardiac imaging protocols that reflect the requirements of the specific imaging systems used. Brigham and Women’s Hospital in Boston published an MDCT angiography protocol for a 320-detector row MDCT scanner employing 80 kVp to 130 kVp, depending on patient body thickness, with up to 75 mL of nonionic contrast agent (depending on patient weight and kidney function) injected at a rate of 6 mL per second.\textsuperscript{39}

Pericardial malignancies usually are metastatic rather than primary tumors, but malignant mesothelioma, associated with asbestos exposure, is the most common primary malignancy of the pericardium.\textsuperscript{40} Malignant mesothelioma is accompanied by nodular “plaques” of tumors, and hemorrhagic effusions.\textsuperscript{40} Advanced lymphoma sometimes involves the heart and pericardium; between 16% and 18% of patients with lymphoma have cardiac involvement at autopsy.\textsuperscript{36} Axial CECT can identify pleural and pericardial involvement (see Figure 7).\textsuperscript{36} CT also might reveal obliteration of the superior pulmonary vein by metastatic lung tumors extending into the pericardium (see Figure 8).\textsuperscript{36}

Pericardial effusion and cardiac tamponade can be caused by metastatic tumors and many other conditions including trauma or aortic aneurysm; suspected pericardial metastases are evaluated initially with echocardiography, CT imaging, or both.\textsuperscript{38} CECT can help differentiate malignancies from pericardial “pseudo-masses” that can include cysts, hematomas, benign fibromas, teratomas, hemangiomas, or lipomas, all of which are benign.\textsuperscript{40} CECT can reveal pericardial fluid accumulations, metastatic tumors, compression of the cardiac chambers, and “angulation or bowing” of the interventricular septum.\textsuperscript{38} CECT of patients with cardiac tamponade also can reveal the presence of liver metastases (see Figure 9).\textsuperscript{38} Pleural fluid collections might be present in association with pericardial metastases.\textsuperscript{38} FDG-PET frequently is used to detect metastatic cardiac tumors.\textsuperscript{4,23} Melanoma metastases of the heart, in particular, are FDG avid, but still can be missed because of diffuse background uptake by healthy, metabolically-active myocardial tissue, which also is FDG avid.\textsuperscript{22,39} Other challenges encountered with this imaging modality include FDG uptake in benign lipomas and fatty deposits on the atrial septum, which can mimic malignancies in the heart.\textsuperscript{39} FDG-PET and FDG PET-CT allow whole-body staging—a particular advantage for staging metastatic disease in other organ systems in patients with suspected metastatic heart tumors; FDG PET-CT more sensitively detects extracardiac metastases than does CT or FDG-PET.\textsuperscript{22,37-39}

**Treatment of Cardiac Malignancies**

The clinical management of heart cancers is challenging.\textsuperscript{1,19} Because heart cancers are so rare, no investigators have undertaken randomized prospective clinical trials. Therefore, no evidence-based standard of care has been developed.\textsuperscript{1,2,19} Heart cancers demand rapid treatment—including surgery when possible.\textsuperscript{1,19} This can be challenging because treatment planning...
It is treated with a combination of systemic rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone (“R-CHOP”) chemotherapy, and sometimes with radiation therapy.\(^1,10\)

By definition, patients with metastatic heart tumors are not candidates for surgical resection. Palliative radiation therapy or chemotherapy might be recommended to alleviate symptoms in these patients.\(^1\)

Many patients who have primary heart cancers are not eligible for surgery because of late-tumor-stage diagnosis and the aggressively invasive nature of many heart cancers.\(^1\) Sometimes, patients with inoperable heart cancers might undergo palliative, incomplete tumor resections in an effort to slow tumor growth and alleviate symptoms.\(^1\)

Patients who have primary cardiac tumors that cannot be safely excised, or who already have developed metastatic disease, with heart tumors spreading to other organs, similarly are not considered candidates for surgery. They might receive palliative chemotherapy or radiation therapy.\(^1\) Primary cardiac angiosarcomas and lymphomas also have been treated in some cases with adjuvant or palliative radiation therapy including tumor-tracking PET-MR-guided adaptive radiation therapy for angiosarcoma.\(^41,42\)

When definitive surgical resection is attempted, neoadjuvant (presurgical) chemotherapy often is administered to shrink tumors and improve the probability of a complete tumor resection.\(^1\) Surgery is followed by adjuvant systemic chemotherapy to destroy residual tumor cells in the surgical margins, along with micrometastases in adjacent or distant tissues.\(^1\) However, tumor recurrence is common, even when surgery appears to leave no residual tumor tissue in place and the patient receives neoadjuvant or adjuvant chemotherapy.\(^1\)

Heart transplantation sometimes is an option for younger patients who have no metastatic disease.\(^1\) More complex autotransplantation treatments also have been tried in patients with left-heart sarcomas, involving the removal of the heart for tumor resection outside the patient’s body, surgical heart reconstruction, and reimplantation.\(^41,43\) Heart transplantation is associated with subsequent risks of noncardiac cancers, possibly because of the immunosuppression therapy undertaken with transplantation to avoid rejection of the new heart.\(^44,45\)

must involve coordination among cardiologists, surgeons, oncologists, and other specialists.\(^1\)

Unlike many heart cancers, primary cardiac lymphoma frequently responds favorably to chemotherapy.\(^19\)
However, heart surgery is dangerous and postoperative complications are a frequent cause of death among patients diagnosed with heart cancer. Overall, patient prognosis appears to depend more on the size and location of a tumor than its histological subtype. For example, cardiac sarcomas occurring in the right heart usually are bulky and infiltrative. Symptoms from the sarcomas do not appear until advanced stages, but the cancers metastasize early. As a result, a patient with cardiac sarcoma has an extremely poor prognosis. Prognosis is better for patients with cardiac lymphoma to about 1 year. However, heart surgery is dangerous and postoperative complications are a frequent cause of death among patients diagnosed with heart cancer.
left-atrial tumors, an absence of necrotic tumor regions, and no metastatic disease at the time of diagnosis.¹

Conclusion
The understanding of heart tumors has improved, but because they are relatively rare, an evidence base has yet to be accumulated to help determine optimal imaging, diagnostic, and treatment strategies.² Cardiac CT and MR imaging with and without contrast enhancement play important roles in differentiating tumor types and in the diagnostic characterization and staging of cardiac malignancies, as well as in treatment planning.¹⁸⁻²⁵ CT can provide anatomic and functional insight into cardiac tumors and their effects. Used as part of a multimodality imaging approach that also includes echocardiography and PET, MDCT will continue to improve early detection of these malignancies and patients’ survival times. Several authors recommended multimodality imaging approaches using echocardiography, MDCT, and MR imaging to leverage each modality’s strengths in achieving imaging goals and minimizing each modality’s limitations for various presentations of cardiac malignancies.⁸

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References


Directed Reading Quiz

Computed Tomography of Cardiac Malignancies

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Read the preceding Directed Reading and choose the answer that is most correct based on the article.

1. According to the article, ______ and ______ are increasingly important for diagnosing, characterizing, and planning treatment strategies for cardiac malignancies.
   a. transthoracic echocardiography; transesophageal echocardiography
   b. transthoracic echocardiography; computed tomography (CT)
   c. transesophageal echocardiography; magnetic resonance (MR)
   d. CT; MR

2. CT has been deemed appropriate for initial evaluation of a suspected cardiac tumor or thrombus and as a secondary imaging modality.
   a. true
   b. false

3. Multidetector CT is efficient and can answer many questions about cardiac masses including:
   1. anatomical relationship to surrounding structures.
   2. bloodstream velocity data.
   3. the existence of hemorrhagic areas.
   
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

4. One protocol described in the literature for retrospective cardiac-gated multiphase CT calls for slice thickness of up to ______ mm to account for cardiac motion.
   a. 0.5
   b. 1.5
   c. 2.5
   d. 3.5

continued on next page
5. When assessing cardiac tumors, CT enhancement is ______ for benign tumors.
   a. absent
   b. intense
   c. minimal
   d. modest

6. Cardiac malignancies usually are attached to the affected anatomy with a ______ base of attachment.
   a. broad
   b. narrow
   c. pedunculated
   d. poorly defined

7. Thrombi appear on contrast-enhanced CT as ______, low-attenuation filling defects and might contain spotty ______.
   a. isodense; opacities
   b. hypodense; calcifications
   c. hyperdense; atelectasis
   d. isodesmic; infiltrations

8. Approximately ______ % of all diagnosed heart tumors are benign.
   a. 30
   b. 55
   c. 60
   d. 75

9. Right atrial myxomas usually are asymptomatic until they exceed a diameter of ______ cm.
   a. 1
   b. 3
   c. 5
   d. 7

10. Calcifying amorphous tumors within the cardiac chambers sometimes are misdiagnosed as:
    a. myxomas.
    b. lipomas.
    c. rhabdomyomas.
    d. fibromas.

11. Which of the following mimic cardiac malignancies?
    1. benign tumors
    2. benign pericardial cysts
    3. thrombi associated with myocardial infarction
    a. 1 and 2
    b. 1 and 3
    c. 2 and 3
    d. 1, 2, and 3

12. ______ usually are more heavily vascularized than other heart tumors.
    a. Cardiac angiosarcomas
    b. Fibrosarcomas
    c. Rhabdomyosarcomas
    d. Undifferentiated sarcomas

13. When angiosarcomas involve the pericardium, the resulting pericardial thickening has been described as ______ on cardiac CT scans.
    a. an air crescent
    b. the tree-in-bud pattern
    c. sheet-like
    d. plate-like

14. ______ appear on CT imaging as large, poorly attenuating or hemorrhagic masses with myocardial infiltration.
    a. Angiosarcomas
    b. Fibrosarcomas
    c. Rhabdomyosarcomas
    d. Undifferentiated sarcomas

continued on next page
15. Metastatic cardiac tumors occur **least** often in the:
   a. endocardium.
   b. epicardium.
   c. pericardium.
   d. syncytium.

16. Prognosis is better for patients with _______ tumors, an absence of necrotic tumor regions, and no metastatic disease at the time of diagnosis.
   a. left-atrial
   b. left-ventricular
   c. right-atrial
   d. right-ventricular

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