Surgical Management of Cardiac Neoplasms

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Introduction

Primary cardiac tumors are rare forms of heart disease reported in both adult and children and first described by Realdo Colombo in 1559 [1, 2]. Several occasional reports are available on this topic in the past medical literature. In 1809, Burns described an atrial tumor determining valvular obstruction [3]. A series of six atrial tumors, probably myxoma, was published by King in 1845 [4]. Barnes et al in 1934 made the first antemortem diagnosis of a cardiac sarcoma using electrocardiography and biopsy of a metastatic lymph node [5]. In 1936, Beck successfully resected a teratoma external to the right ventricle [6], and Mauer removed a left ventricular lipoma in 1951 [7].

However, prior to the advent of modern cardiac surgery the correct *antemortem* diagnosis of an intracardiac tumor was largely academic, since effective therapy was not possible. A new approach in the management of cardiac tumors was made possible by the introduction of cardiopulmonary bypass by Gibbon in 1953, and by the advent of echocardiography, which provided a noninvasive method for accurately diagnosing intracardiac mass [8–14].

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Indeed in the last decades, major advances in noninvasive cardiovascular diagnostic techniques—especially echocardiography, computed tomography, and magnetic resonance imaging (MRI)—have greatly facilitated the approach to cardiac neoplasm.

Clinical signs and symptoms of a cardiac tumor are often nonspecific and a high index of suspicion remains the most important element for diagnosis. Indeed, cardiac neoplasms can produce a broad array of systemic findings, including fever, cachexia, malaise, and arthralgias. Relevant signs and symptoms are considered:

1. progressive heart failure without apparent cause, not responsive to medical therapy
2. pericardial effusion, often hemorrhagic
3. persistent arrhythmias, Wolff-Parkinson-White syndrome, A–V blocks
4. embolic phenomena and symptoms mimicking systemic vasculitis or infective endocarditis
5. severe dizziness or syncope
6. signs of valvular or sub-valvular obstruction

When suspecting a more conventional valvular and/or myocardial disease, the presence of atypical signs may raise the suspicion of cardiac tumors. For example, left atrial myxomas may produce auscultatory findings similar to mitral stenosis, whose characteristics may change with patient position, and mimic the symptoms of a mitral disease. Furthermore, the well-described "tumor plop" is an early diagnostic sound sometimes confused with a third heart sound. The diagnostic tumor plop occurs just after the opening snap of the mitral valve and is believed

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to be secondary to contact between the tumor and endocardial wall.

Cardiac tumors may display several findings on plain chest roentgenograms, usually nonspecific. These include alterations in cardiac contour, changes in overall cardiac size, specific chamber enlargement, alterations in pulmonary vascularity, pericardial effusions, and intracardiac calcification (rhabdomyomas, fibromas, hamartomas, teratomas, myxomas, angiomas). Visualization of intracardiac calcium in an infant or a child is unusual and should immediately raise the suspicion of an intracardiac tumor. Mediastinal widening, due to hilar and paramediastinal adenopathy, may indicate the spread of a malignant cardiac tumor.

Two-dimensional echocardiography, and more recently real-time three-dimensional echocardiography [15], provide adequate information regarding tumor size, attachment, and mobility, all important variables to plan operative resection of the cardiac mass. It may also facilitate the differentiation between left atrial thrombus and myxoma. Moreover, continuous-mode Doppler ultrasonography may be useful for evaluating the hemodynamic consequences of valvular obstruction and/or incompetence caused by cardiac tumors.

Transesophageal echocardiography provides an unimpeded view of the cardiac chambers and atrioventricular (AV) septa and appears to be superior to transthoracic echocardiography in many patients. Its potential advantages include improved resolution of the tumor and its attachment, and the ability to detect small masses not visualized by transthoracic echocardiography (<3 mm diameter). Transesophageal echocardiography has been routinely used to guide the percutaneous biopsy of right-sided cardiac masses, thus allowing successful sampling of the target tissue for preliminary histologic evaluation [16]. Transesophageal echocardiography should always be considered when the transthoracic study is suboptimal or confusing [17, 18].

Cardiac computed tomography (C-CT) can provide useful information in view of its high resolution and ability to accurately depict cardiac morphology without limitations because of acoustic windows. It can also provide some information regarding the nature of the tumor by measuring X-ray attenuation, and possible tumor expansion to adjacent tissues. Multidetector computed tomography (MDCT) is useful for the evaluation of calcification and fat content within a mass. Furthermore, the high spatial resolution of MDCT is beneficial to define small lesions, making this technique a useful tool for staging malignant tumors. CT appears also useful in the evaluation of the potential involvement of pericardial and extracardiac structures. C-CT however provides less information regarding characterization of tissues in comparison to cardiac MRI. Disadvantages of the method also include the use of radioactivity and of nephrotoxic contrast mediums [19–21].

Cardiac magnetic resonance imaging (C-MRI) allows for a more sophisticated assessment of the tumor relation to adjacent structures, thus improving the planning of a proper resection strategy. It also allows the detection of myocardial infiltration by the tumor and/or expansion of the mass to the pericardium or to adjacent structures [19–21]. C-MRI may also contribute to the characterization of the composition of the tumor by studying the signal in T1- and T2-weighted images, as well as the enhancement of the signal after gadolinium administration [22]. Recent technologic advances in cardiac MRI have resulted in the rapid acquisition of images of the heart with high spatial and temporal resolution and excellent myocardial tissue characterization [23]. Furthermore, administration of contrast medium may help to differentiate a cardiac tumor from a thrombus and/or from blood flow artifacts [19–23].

Cardiac catheterization and selective angiocardiography are usually not necessary since adequate preoperative information may be obtained by one or more of the above-mentioned less invasive imaging techniques. However, several circumstances exist in which the risk and expense of cardiac catheterization are outweighed by the supplemental information it may provide. These situations include cases in which (a) noninvasive evaluation has not been adequate; (b) a malignant cardiac tumor is considered likely (cardiac angiography may provide valuable

information regarding the degree of myocardial, vascular, and/or pericardial invasion, as well as visualization of the vascular supply of the tumor, the source of its blood supply, and its relation to the coronary arteries); and (c) other cardiac lesions may coexist with a cardiac tumor (i.e., coronary artery disease) and possibly dictate a different surgical approach [24, 25].

The major angiographic findings in patients with cardiac tumors include (a) compression or displacement of cardiac chambers or large vessels, (b) deformity of cardiac chambers, (c) intracavitary filling defects, (d) marked variations in myocardial thickness, (e) pericardial effusion, and (f) local alterations in wall motion [24, 26].

The major risk of angiography is peripheral embolization due to dislodgement of a fragment of tumor or of an associated thrombus.

The diagnosis of cardiac tumors and the estimation of their grade cannot be made with the sole use of imaging methods and histological confirmation is always necessary. This can be achieved with minimally invasive techniques, such as cytological examination of pericardial or pleural fluid, or by means of echocardiographically aided percutaneous or transvenous cardiac biopsy. In cases where diagnosis cannot be established, biopsy via thoracoscopy or even thoracotomy may be needed [16, 27, 28].

Primary Benign Cardiac Tumors

Surgical Technique

The surgical management of cardiac tumors began in 1936 when Beck successfully resected a teratoma external to the right ventricle [6]. In 1951 Mauer resected a left ventricular lipoma [7] and Bhanson and Newman in 1952 removed a large right atrial myxoma using inflow caval occlusion [29]. In 1954 Crafoord for the first time removed successfully a left atrial myxoma using cardiopulmonary bypass [30], whereas Kay et al. first removed a left ventricular myxoma in 1959 [31]. By the early sixties, owing to the progressive safety of cardiopulmonary bypass and to the increased use of echocardiography, atrial myxomas started to be removed successfully on a more routine-based approach [8, 32].

Currently, operative excision is the treatment of choice for most benign cardiac tumors, very often resulting in a complete cure. Although many cardiac tumors appear histologically benign, they all are potentially lethal as a result of intracavitary or valvular obstruction, peripheral embolization, and/or disturbances of rhythm or conduction. Therefore, it is mandatory to carry out the operation promptly after the diagnosis is established [13, 14, 33–35].

Through a median sternotomy, intramural and intracavitary tumors must be excised under direct vision using the heart–lung machine (Fig. 10.1) with bicaval or femoral cannulation (Fig. 10.2). The potential dislodgment of tumor fragments constitutes one of the major risk of the operation and may result in peripheral emboli and/or the dispersion of micrometastases, which may seed peripherally. To reduce this risk, manipulation of the heart prior to cardiopulmonary bypass and aortic cross-clamp positioning should be minimized ("*no-touch technique*"), as in other circumstances when dealing with any intracardiac friable mass (i.e., thrombus).

During the preliminary maneuvers to set the cardiopulmonary bypass, a transesophageal echocardiography may result extremely useful to define in detail the anatomy of the intracardiac mass, its relationship with any valvular apparatus, to guide in an uneventful cannulation of the cardiac chambers, and to monitor the integrity of the tumor during the initial surgical manipulations.

After establishing cardiopulmonary bypass, under mild hypothermia, the heart is separated from the systemic circulation by an aortic cross-clamp followed by the infusion of blood or crystalloid cardioplegia administered antegradely into the aortic root, and/or retrogradely into the coronary sinus. Although some epicardial tumors may be removed without the aid of extracorporeal circulation, intramural and intracavitary tumors must be excised under direct vision. The surgical approach will depend on the location of the cardiac mass (right-, left-, combined atriotomy, aortotomy, etc.). In view of the potential multifocal location of

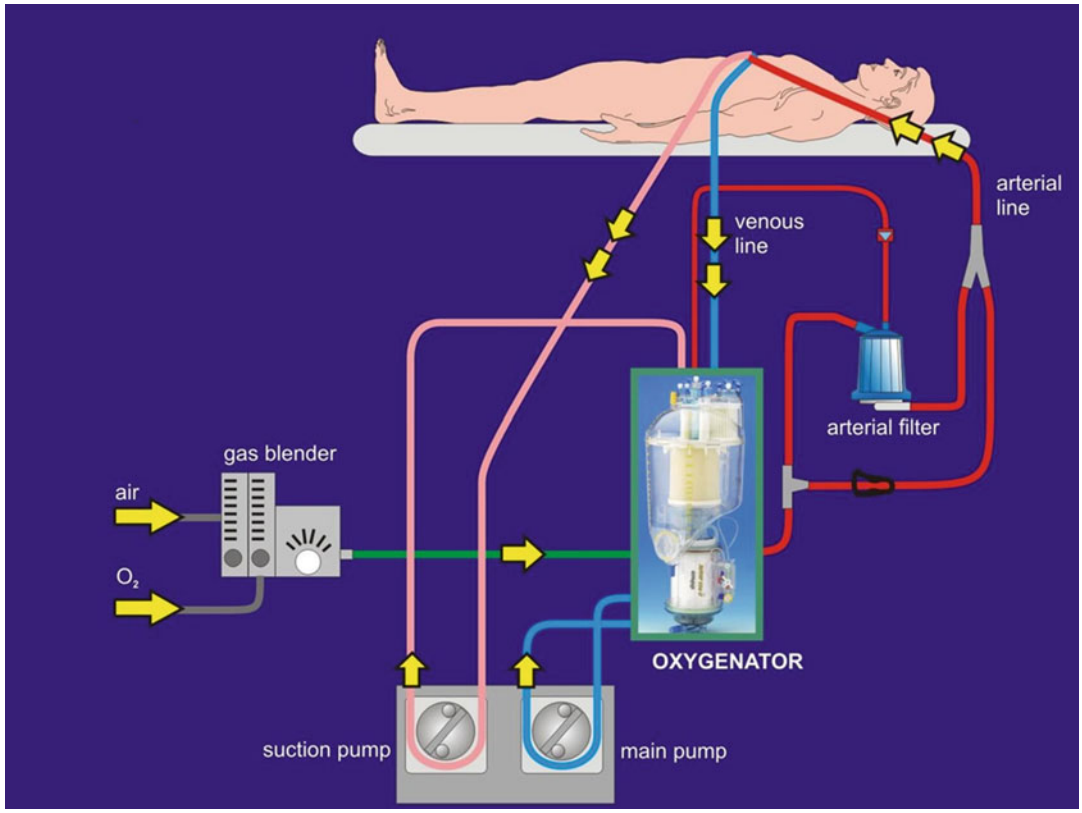

Fig. 10.1 Diagram of a cardiopulmonary bypass circuit. Venous blood is drained from the venae cavae/right atrium into the venous reservoir which is incorporated in the membrane oxygenator/heat exchanger unit. Arterialized blood exits the oxygenator and passes through a filter/bubble trap to the aortic cannula, which is usually placed in the ascending aorta. Suction systems and sources of gases are also represented

the cardiac tumors, all the cardiac chambers will need to be systematically explored. A good surgical exposure represents the fundamental principle to accomplish a complete, possibly *en bloc,* resection of the tumor. The ideal resection aims to include the tumor and a portion of the cardiac wall and/or interatrial septum, to which it is attached, spared by the disease. Variables with an impact on tumor resection are location, involvement of the myocardium and/or fibrous skeleton of the heart, and histology. To overcome the technical challenges of complete resection with accurate cardiac reconstruction, particularly of left-sided tumors with posterior extension, a technique of cardiac explantation, ex vivo tumor resection with cardiac reconstruction, and cardiac reimplantation—cardiac autotransplantation—has been successfully utilized [36–38].

Every care should be taken to remove the tumor without fragmentation. After tumor resection, the surgical field should be irrigated and carefully inspected for loose fragments. Whether blood removed from the surgical field during tumor manipulation should be discarded or returned to the pump circuit is controversial. Usually the cardiotomy suction is used during the operation, but the sole wall suction is utilized during the brief time that the tumor is actually excised in order to avoid tumor macroemboli entering the bloodstream via the perfusion circuit and the cardiotomy reservoir [8, 39, 40].

In the event of friable tumors located in the left (or right) cardiac chambers, the aorta (or the pulmonary artery) should be independently explored to exclude intraoperative migration of loose tumor fragments beyond the semilunar

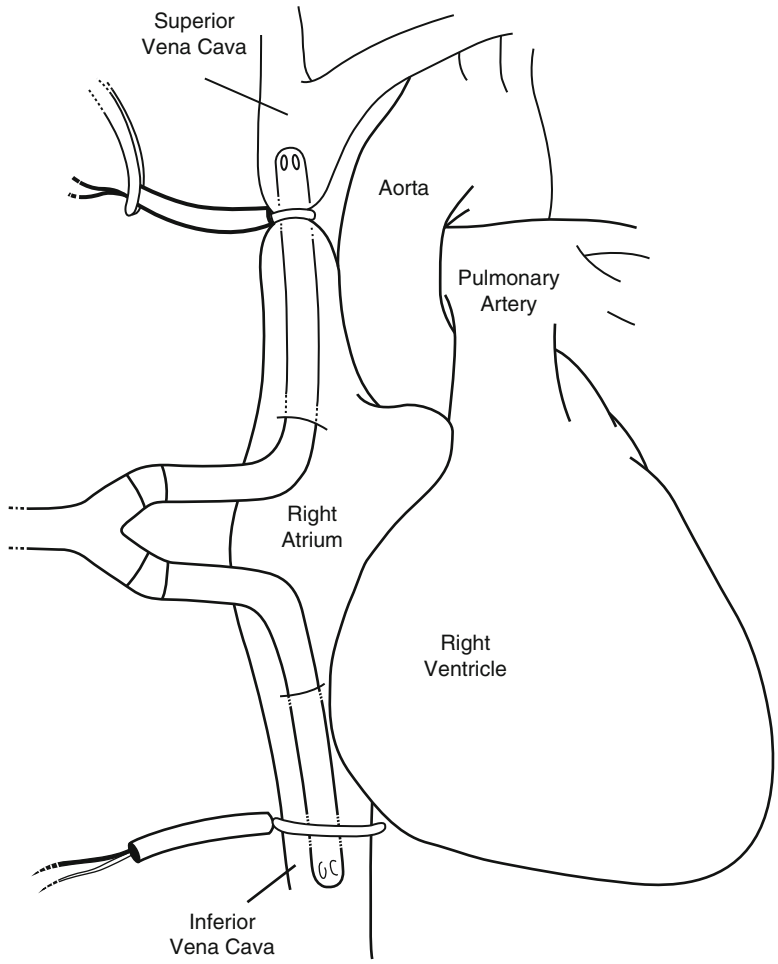

Fig. 10.2 Cannulation of the superior and inferior vena cava from incision in the right atrium. Caval snares are always used to allow safe opening of the right atrium

valves. The use of an intra-aortic filter (Edwards Embol-X System, Edwards Lifescience, Irvine CA) may help to reduce the event of systemic embolization in case of friable tumors located in the left cardiac chambers [41].

Ventricular tumors are usually approached through the AV valves if located in the ventricular inflow, or through the semilunar valves when located in the ventricular outflow tract.

In the event of tumors involving a cardiac valve, the surgical strategy should still aim to a complete resection of the mass, although trying to preserve the native valve by means of several well-described reparative techniques. When this is not possible, a valve prosthesis may be used.

The major surgical consideration in excision of ventricular tumors includes location, potential for a complete resection, preservation of adequate ventricular myocardium, maintenance of proper AV valve function, and preservation of the conduction system. It is not always possible to remove a ventricular tumor completely, and partial removal is only palliative. Children with extensive fibromas have been treated with cardiac transplantation. In selected cases of right ventricular tumors, a right heart bypass (cavopulmonary anastomosis) has also been utilized [11–14, 33, 42–48].

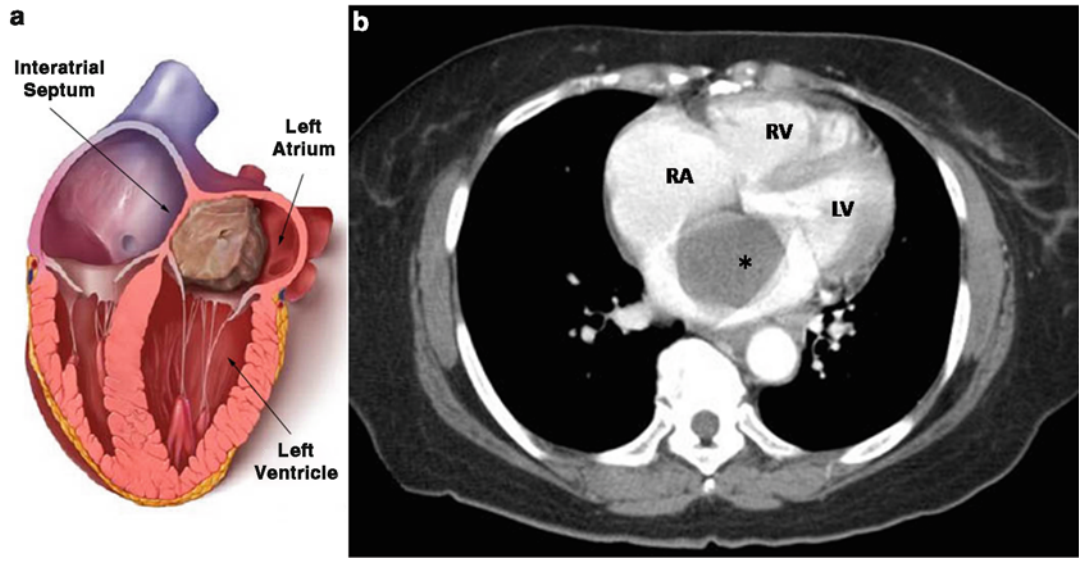

Fig. 10.3 (**a**) Diagram of a left atrial myxoma (75% of all cases) attached to the interatrial septum, above the mitral valve. (**b**) Cardiac-CT showing a left atrial mass (myxoma) (*asterisk*) attached to the interatrial septum. *RA* right atrium, *RV* right ventricle, *LV* left ventricle

Coming off cardiopulmonary bypass, transesophageal echocardiography may provide useful information on complete tumor excision, valve/prosthesis function in case of repair/replacement, absence of residual shunt in case of septal reconstruction, myocardial function, and de-airing.

Left Atrial Myxoma

Myxoma is the most common type of primary cardiac tumor, accounting for 1/3 to 1/2 of all cases. They may occur in any chamber of the heart but have a special predilection for the left atrium, from which approximately 75% originate. Left atrial myxomas generally arise from the interatrial septum at the border of the fossa ovalis (Fig. 10.3a, b), but can originate anywhere within the atrium, including the appendage. Surgical resection is the only effective therapeutic option for patients with cardiac myxoma and should not be delayed because death from obstruction to flow within the heart and/or embolization may occur in as many as 8% of patients awaiting operation [8]. Left atrial myxomas can be approached by an incision through the anterior wall of the left atrium, anterior to the right pulmonary veins, eventually extended behind both cavae to achieve greater exposure. Exposure and removal of large tumors attached to the interatrial septum however may be facilitated by a right atrial approach, which allows easy removal of tumor attached to the fossa ovalis with full-thickness and large excision at the site of attachment and easy patch closure of the atrial septum if necessary (Fig. 10.4a, b) [49]. As mentioned, the tumor should be removed without fragmentation. Nevertheless, after removal the surgical field should be irrigated and inspected for loose fragments. In case of atrial wall rather than septal attachment, large full-thickness excision of tumor insertion should be aimed whenever possible. A systematic inspection of the other cardiac chambers to exclude other tumor location potentially overlooked by the utilized imaging techniques is always recommended.

Histologic evaluation of the primary lesion is obviously mandatory to elaborate the most appropriate patient management and follow-up [11–14, 33, 35, 42, 49–51].

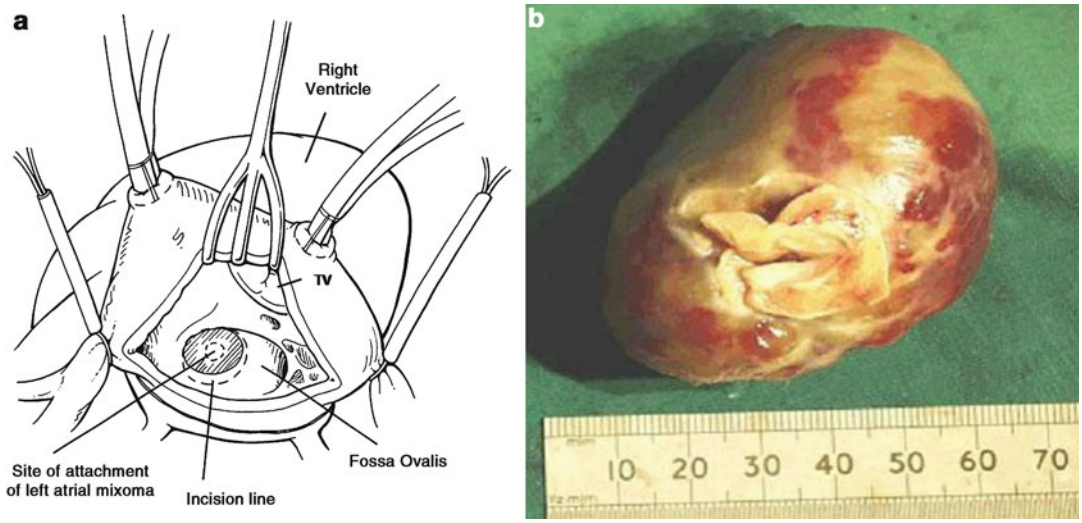

Fig. 10.4 (**a**) Right atriotomy and exposure of the left atrial myxoma through the fossa ovalis. Reprinted with permission of the Italian Society of Cardiology. *TV* tricuspid valve. (**b**) Left atrial myxoma with its base of attachment to the interatrial septum, excised with surrounding tissue

Right Atrial Myxoma

About 10 to 20% of all cardiac myxomas are found in the right atrium. Right atrial myxomas are more likely to have broad-based attachments; they also are more likely to be calcified and thus visible on chest radiographs. Right atrial myxomas can produce signs and symptoms of right-sided heart failure with venous hypertension, hepatomegaly, ascites, and dependent edema. The tumor may also simulate tricuspid valve stenosis by partially obstructing the valve orifice. If a patent foramen ovale is present, right-to-left atrial shunting may occur with central cyanosis, and possible paradoxical embolization [8].

When approaching right atrial myxomas, intraoperative echocardiography may be extremely helpful to promote safe venous cannulation, avoiding mass trauma and/or poor venous return related to an impinging tumor. Both venae cavae may be cannulated directly and caval snares are always used to allow opening of the right atrium. However, when low- or high-lying tumor pedicles preclude safe transatrial cannulation, cannulation of the jugular or femoral vein can provide venous drainage of the upper or lower body [52]. The right atrium may be opened widely for resection of the tumor and reconstruction of the atrium using pericardium or polytetrafluoroethylene, keeping in mind that resection of large or critically placed right atrial myxomas may require careful preoperative planning and special perfusion strategies. The tricuspid valve and the right atrium, as well as the left atrium and ventricle, should always be inspected carefully for multicentric tumors in patients with right atrial myxoma, with or without familial occurrence [49–51].

Ventricular Myxomas

Ventricular myxomas (6–8%) occur more often in women and children and may be multicentric [12–15, 53]. Right ventricular tumors typically arise from the free wall, and left ventricular tumors tend to originate in the vicinity of the posterior papillary muscle.

Ventricular myxomas may be approached directly through the AV valve or by detaching portion of the AV valve, for mass exposure and resection, and reattachment after excision. Small tumors in either outflow tract can be removed through the outflow valve [8]. If necessary, the tumor is excised through a direct incision into the ventricle, but this is unusual. It is not necessary to remove the full thickness of the ventricular wall

because no recurrences have been reported with partial-thickness excisions [49–51]. As mentioned for right atrial myxoma, in the presence of a ventricular myxoma inspection for other tumors is highly recommended because of the high incidence of multiple locations.

Overall 30-day mortality after removal of an atrial myxoma is below 5%, although excision of ventricular myxomas carries a higher risk (approximately 10%). Operative mortality may be increased by tumor unrelated variables such as advanced age, disability, and/or comorbidities. Long-term survival, freedom from complication, and quality of life are excellent in the nonfamilial form of myxoma [35, 48–51, 54, 55].

The recurrence of an intracardiac myxoma (described by 6 months and up to 11 years after the resection) may be related to an inadequate original resection, when at the same site of the original tumor, or to the presence of neoplastic fragments. Recurrence of nonfamilial sporadic myxoma is approximately 1–4% and possibly lower in patients with a normal DNA genotype [55, 56]. The rarer subgroup of patients with sporadic myxoma and abnormal DNA have a recurrence rate estimated at between 12 and 40%.

The recurrence rate is highest in patients with familial complex myxomas, all of whom exhibit DNA mutation [56]. Overall, recurrences are more common in younger patients. Most recurrent myxomas occur in the same or different cardiac chambers, and may be multiple particularly in familial complex myxomas. Extracardiac recurrence after myxoma excision, likely from embolization, local tumor growth, and invasion, has been observed in the brain, arteries, soft tissue, and bones [8].

In view of these considerations, patients who are treated initially for multicentric tumors, those whose tumors are removed from unusual locations in the heart or believed to have been incompletely resected and/or those with an abnormal DNA genotype, should be closely followed up [56, 57]. Furthermore, in those cases with delayed evidence of malignant characteristics within a resected mass mistakenly thought to be an *innocent* myxoma, complete patient rescreening is mandatory.

Lipoma

Lipomas are well encapsulated primary benign cardiac tumors, and consist of mature fat cells [9–12]. They are usually located in the subepicardium, in the left ventricle, in the right atrium, and in the interatrial septum (Fig. 10.5a, b). The nonencapsulated hypertrophy of the fat within the atrial septum, often in continuity with the epicardial fat, is known as *lipomatous hypertrophy*. Lipomatous hypertrophy is more common than cardiac lipoma, is more frequent in elderly, obese patients, and is usually an incidental finding during a variety of cardiac imaging or surgical procedures.

Often asymptomatic and incidentally discovered on routine chest roentgenogram, echocardiogram, or at surgery, lipomas may cause arrhythmias, conduction system disturbances, symptoms of heart failure, and sudden death, especially in cases where they reach a large size [58–60]. Large lipomas, particularly when associated with severe symptoms, should be resected. Smaller, asymptomatic tumors, incidentally discovered during cardiac operation undertaken for different indications, should be removed if excision is doable without adding risk to the primary procedure. In case of location in the atrial septum, patch reconstruction may be necessary. Cardiac lipomas are not known to recur.

Papillary Fibroelastoma

Papillary fibroelastomas are the most common tumors of the cardiac valves, accounting for 75% of all valvular tumors (Fig. 10.6a). They usually affect the elderly (age range 60 ± 16) [61], are generally small in size (<1 cm), and affect mainly the aortic or the mitral valve, even though tricuspid and pulmonary valves may also be affected. Occasionally, papillary fibroelastomas locate in the left ventricle, more often in the outflow tract, can be multifocal, and are associated with the hypertrophic obstructive cardiomyopathy [62–64]. Papillary fibroelastomas resemble a sea anemone with frond-like projections comprising dense elastin at the core of each frond, coated with collagen and lined by flat endocardial cells. Although frequently asymptomatic and often incidental findings at autopsy, papillary

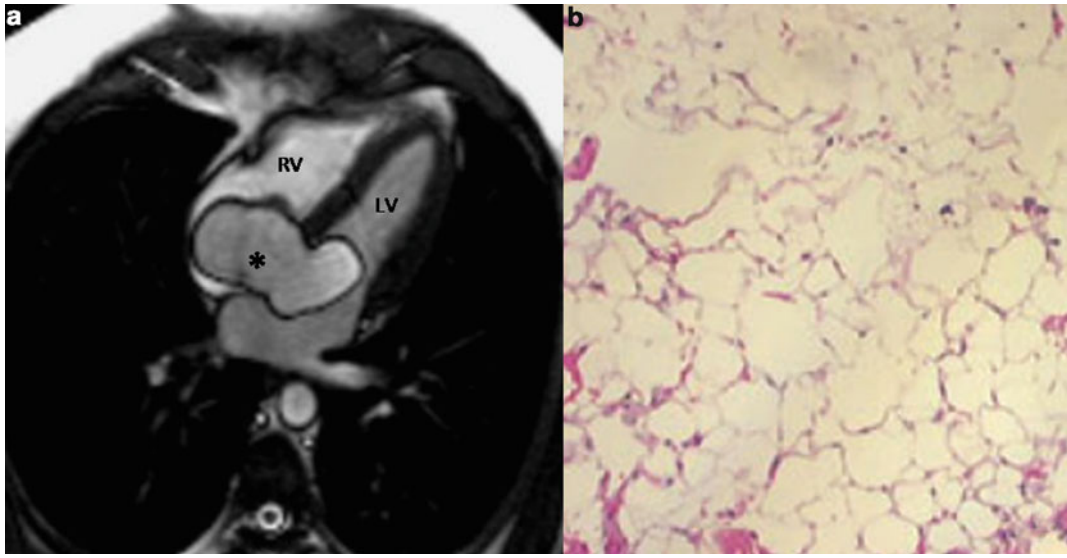

Fig. 10.5 (**a**) Cardiac-MRI of a huge lipomatous hypertrophy located in the interatrial septum (*asterisk*). *RV* right ventricle, *LV* left ventricle. (**b**) Microscopic views of the excised lipoma. Hematoxylin and eosin staining shows mature adipocytes (×100)

fibroelastomas are capable of producing obstruction of flow, particularly coronary ostial flow when located on the aortic valve (Fig. 10.6b). Most importantly, they may embolize to the coronary system or to the brain (or to the lung when right-sided), with potential life-threatening complications. Therefore, papillary fibroelastomas should be resected whenever diagnosed. In the event of a potential underlying coronary artery disease, invasive coronary angiography poses a significant risk of stroke in case of localization of the mass at the aortic valve level. In these patients, multislice-CT coronary angiography should be considered as a safer alternative [65]. Standard cardiopulmonary bypass with bicaval cannulation and conventional myocardial protection is utilized for tumor resection. Valve repair rather than replacement should follow the resection of these benign tumors whenever technically feasible, using conservative margins of resection with no observed recurrence after complete excision (Fig. 10.7a, b). In the rarer cases of a multifocal valve localization, valve replacement may be required. Worthy of note, the reported presence of dendritic cells and cytomegalovirus in the resected specimen suggests the possibility of a virus-induced tumor, therefore evoking the concept of a chronic form of viral endocarditis [66].

Fibroma

Fibromas are the second most common cardiac tumor of childhood, although they may also affect the adult population. These are solitary non-infiltrating intramural tumors, usually located in the left ventricle, mainly in the interventricular septum, and they are often mistaken for hypertrophic cardiomyopathy or apical thrombus (Fig. 10.8). Fibromas are non-encapsulated, firm, nodular, gray–white tumors potentially bulky, composed mainly of interlacing bundles of dense collagen and elastic fibers, and elongated fibroblasts. Deposits of calcium may be present. Symptoms may be related to chamber obstruction, impairment of contraction, and/or arrhythmias. Depending on size and location, fibromas may interfere with valve function, obstruct flow paths, or cause sudden death from conduction disturbances [8]. Surgical approach requires standard cardiopulmonary bypass with bicaval cannulation and conventional myocardial protection.

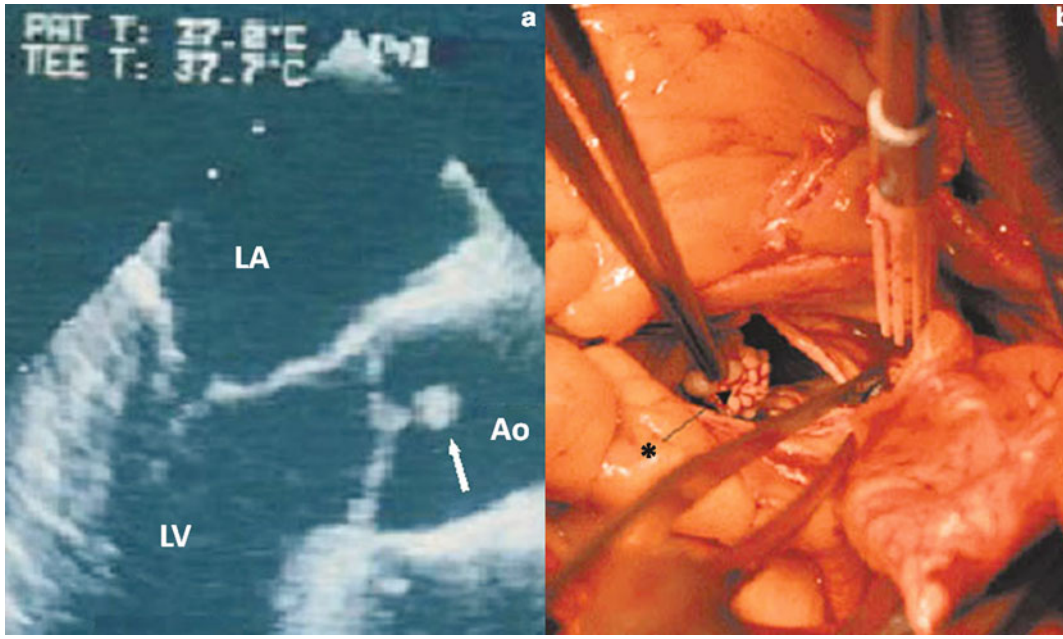

Fig. 10.6 (**a**) Transesophageal echocardiogram of a papillary fibroelastoma attached to the aortic valve (*arrow*). Reprinted with permission of the Italian Society of Cardiology. *LA* left atrium, *LV* left ventricle, Ao aorta. (**b**) Intraoperative view showing the papillary fibroelastoma attached to the right coronary aortic valve cusp (*asterisk*/*arrow*)

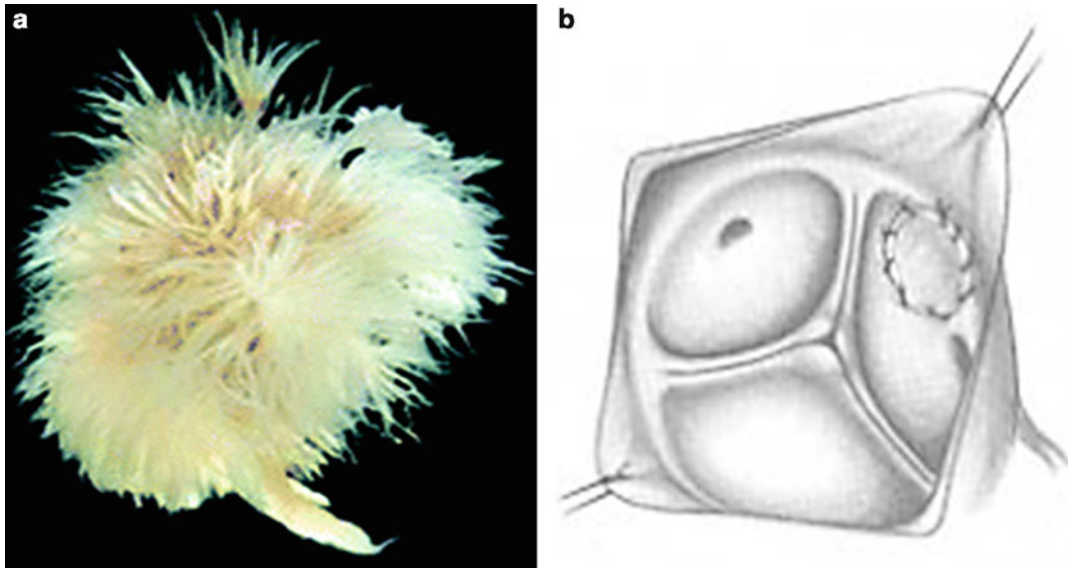

Fig. 10.7 (**a**) Papillary fibroelastoma after resection, with the typical sea anemone shape. (**b**) Diagram of an aortic valve patch reconstruction after repair. Reprinted with permission of the Italian Society of Cardiology.

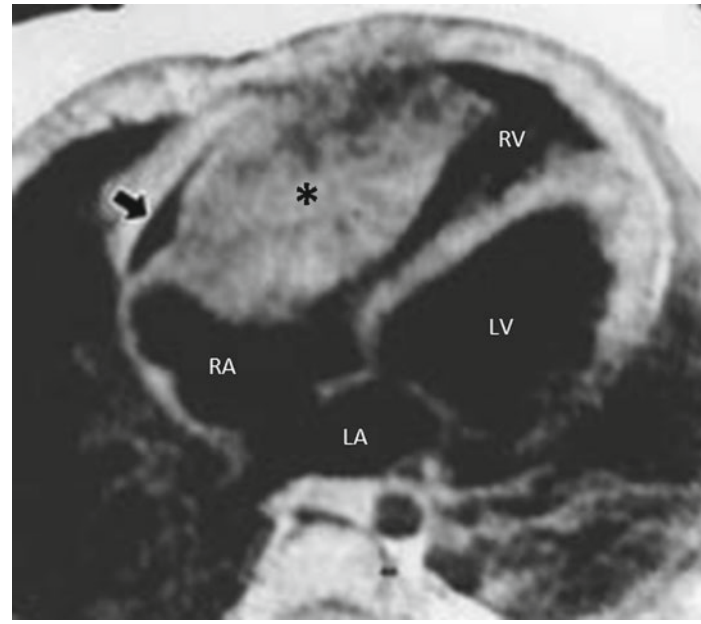

Fig. 10.8 Cardiac-MRI of a fibroma involving the right atrium and ventricle (*asterisk*), with associated pericardial effusion (*arrow*). Reprinted with permission of the Italian Society of Cardiology. *RA* right atrium, *RV* right ventricle, *LA* left atrium, *LV* left ventricle

Complete resection is usually successful when the tumor is localized, does not involve coronary arteries, AV valves, and/or the fibrous skeleton of the heart, and can be enucleated, usually through an epicardial approach, without entering the ventricle whenever possible. Video-assisted cardioscopy has been recently reported as a suitable and useful technique to assist removal of primary left ventricular fibroma with intracavitary extension [67]. Complete excision is usually curative. On the other hand, partial tumor removal is palliative although often followed by a prolonged survival [68]. Children with extensive fibromas, in good overall clinical conditions and with no specific contraindications, have been successfully treated with orthotopic cardiac transplantation [69]. In selected cases of extensive right ventricular tumors, a right heart bypass (cavo-pulmonary anastomosis) (Fig. 10.9a, b, c) has also been utilized [11–14, 33, 42–48] as a palliative solution or as a *bridge* to orthotopic cardiac transplantation [70].

Rhabdomyoma

Rhabdomyoma represents the most common cardiac tumor in children. Thought to be a myocardial hamartoma rather than a true neoplasm [71, 72], it usually presents during the first few days after birth. Occasionally sporadic, it is quite often associated with tuberous sclerosis (hereditary disorder characterized by hamartomas, seizures, developmental delay and behavioral problems, sebaceous adenomas) [53, 73, 74].

Rhabdomyomas are variable in size, usually multiple, and they affect the right and the left ventricle likewise. Firm, gray, nodular, and often intramural, they tend to project into the ventricular cavity, thus causing mechanical complications, such as obstruction of the ventricular outflow tract. On histology, they show large myocytes filled with glycogen and containing hyperchromatic nuclei. As for other intracardiac masses, clinical signs and symptoms depend on the size, location, and number of the tumors. Frequently enough, rhabdomyomas cause heart failure obstructing cardiac chambers and/or valvular orifice flow. Onset of symptoms may be represented by arrhythmias, particularly ventricular tachycardia, although sudden death may be the only effect of an undisclosed cardiac rhabdomyoma. Surgery may be advisable in symptomatic patients, without tuberous sclerosis, before 1 year of age. The tumor is removed easily in early infancy, and despite being non-encapsulated

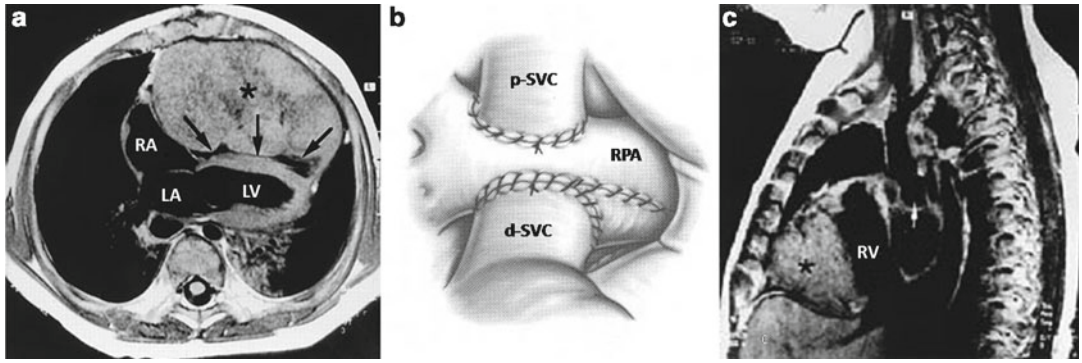

Fig. 10.9 Right heart bypass [cavo-pulmonary anastomosis (**b**, *diagram*)] in a case of extensive non-resectable right ventricular tumor (**a**, *asterisk*; *arrows* indicate residual right ventricular cavity). Reprinted with permission of the Italian Society of Cardiology. MRI control (**c**). *RA* right atrium, *RV* right ventricle, *LA* left atrium, *LV* left ventricle, p-*SVC* proximal superior vena cava, d-*SVC* distal superior vena cava, *RPA* right pulmonary artery

some can be completely resected. Partial resection may be conceivable to release the obstruction [75]. However, whenever planning a surgical strategy, it has to be considered that rhabdomyomas may regress spontaneously after birth, thus limiting indication to surgical resection to the actual symptomatic cases [73].

In case of multiple and extensive tumors, particularly in patients with tuberous sclerosis, surgery offers little benefit.

Other benign cardiac tumors (hemangioma, teratoma, paraganglioma, pheochromocytoma, cystic tumors of the AV node, etc.) are rarely observed. As mentioned, clinical signs and symptoms will be a result of intracavitary and/or valvular obstruction, peripheral embolization, and disturbances of rhythm or conduction, including sudden death. After the diagnosis, strict patient surveillance and multidisciplinary decision making relative to surgical indication are mandatory.

Primary Malignant Tumors

Malignant cardiac tumors continue to pose a therapeutic challenge to cardiac surgeons and oncologists because of the technical difficulty involved in extensive cardiac resections and the aggressive biological nature of the tumors.

Primary malignant tumors are relatively rare, accounting for upto 25% of all primary cardiac tumors in third level referral centers. They usually affect people aged 30–50 years, and are mainly represented by sarcomas (angiosarcoma, rhabdomyosarcoma, leiomyosarcoma, liposarcoma, osteosarcoma, fibrosarcoma, and malignant fibrous histiocytoma) and lymphomas [9–14]. Angiosarcomas are usually located in the right chambers of the heart (Fig. 10.10a, b), whereas other sarcomas affect the left atrium more frequently. Lymphomas with bi-atrial localization have also been reported (Fig. 10.11) [76]. Malignant tumors have usually a poor prognosis in view of the extensive infiltration of the myocardium, the frequent obstruction of intracardiac flow, and the occurrence of metastases [28]. Indeed, a metastatic spread has been demonstrated at autopsy in more than 75% of all patients who died of a primary cardiac sarcoma, mostly involving lungs, mediastinal lymph nodes, and spine. The nonspecific clinical signs and symptoms include congestive heart failure, dyspnea, atypical chest pain, malaise, anorexia, and weight loss. Arrhythmias, syncope, sudden death, pericardial effusion, and tamponade have also been reported [77]. Chest X-ray can offer indirect findings from the enlargement of cardiac chambers, the occurrence of calcification, or pericardial effusion. Two-dimensional echocar-

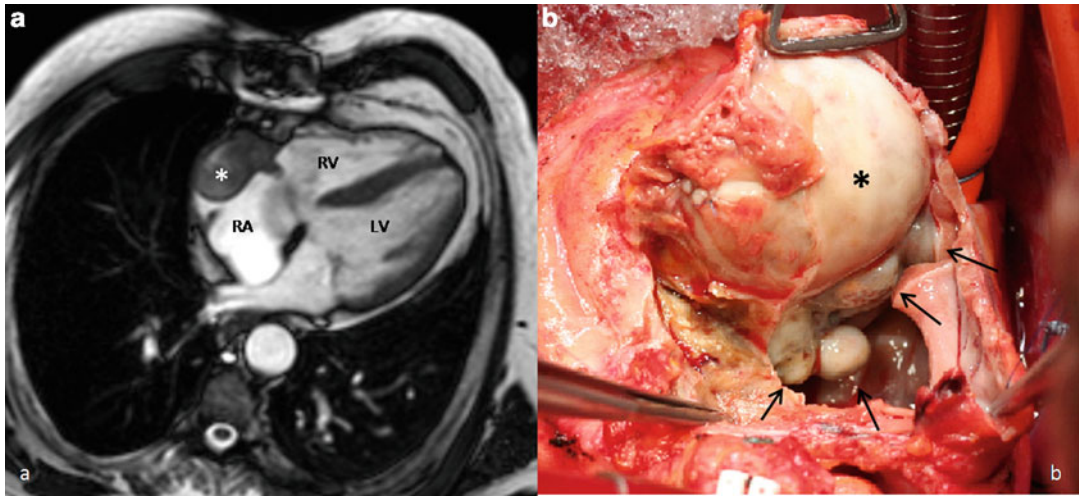

Fig. 10.10 (**a**) Cardiac-MRI of an angiosarcoma involving the right atrium and the right atrio-ventricular junction (*asterisk*). *RA* right atrium, *RV* right ventricle, *LV* left ventricle. (**b**) Intraoperative view of the tumor (*asterisk*), with multilobulated extensions (*arrows*)

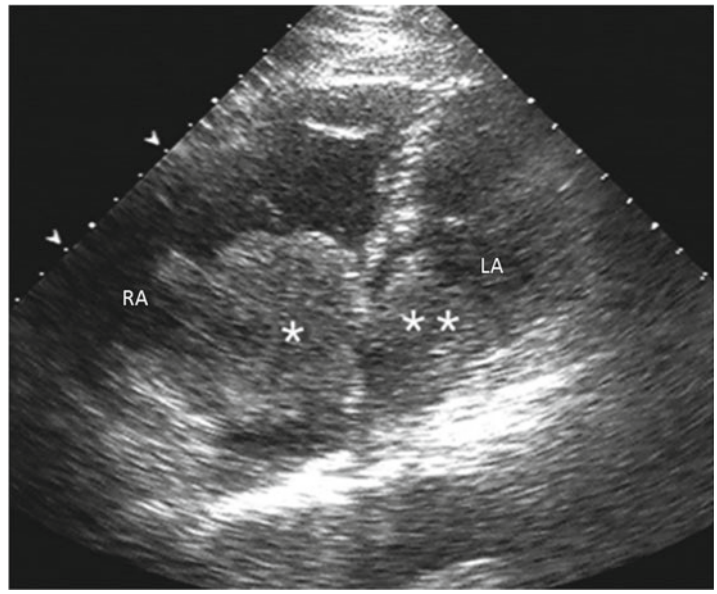

Fig. 10.11 Modified four-chamber echocardiographic view. Bi-atrial lymphoma filling almost entirely the right atrium (*asterisk*) and less extensively the left atrial chamber (*double asterisk*). *RA* right atrium, *LA* left atrium

diography provides adequate information regarding tumor location, size, attachment, and mobility all important variables to plan operative resection of the cardiac mass. If malignancy is suspected, chest CT and/or MRI may grossly guide on the histologic nature of the mass and provide detailed anatomy of the tumor, thus helping in staging and assessing its resectability. Cardiac catheterization may offer useful information about myocardial, vascular, and/or pericardial infiltration, and on the presence of tumor feeding vessels. Malignancy may be suggested and coronary involvement suspected by the evidence of a *tumor blush* (Fig. 10.12a, b), although this finding is not

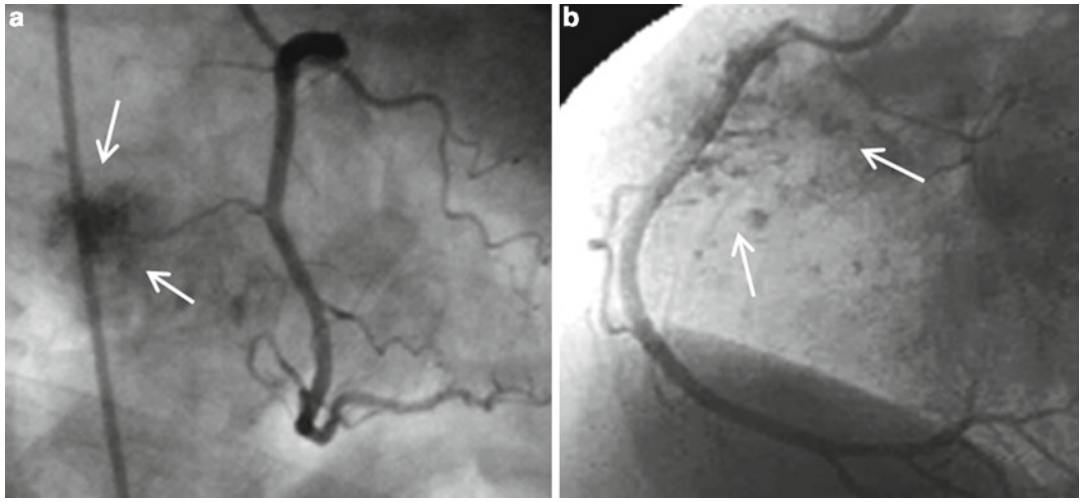

Fig. 10.12 Typical *tumor blush* (*arrows*) at coronary angiography in right atrial sarcomas

pathognomonic having been found also in myxomas [8]. Finally, transesophageal echocardiography guided transvenous endomyocardial biopsy is a very important tool to define tumor histology and to interpret metastatic lesions, thus helping to plan the most efficacious therapeutic strategy which usually involves a combination of surgery, chemotherapy, and radiation therapy [77–80].

The decision to resect a primary malignant tumor is based on several variables, including tumor location and size, histology, grade of myocardial infiltration, relationship with the cardiac valves and the fibrous skeleton of the heart, absence of metastatic spread, and potential for a radical excision of the mass. Other more general variables, such as age, overall clinical conditions, frailty, and comorbidities, will also need to be considered to finalize the surgical strategy [34, 36, 76–82].

Currently, chemotherapy, radiation therapy, or a combination of both are used as an adjuvant to decrease tumor size and facilitate surgical resection. In this perspective, a multidisciplinary decision-making approach relative to the overall therapeutic management is mandatory.

Based on the surgical approach and clinical behavior, cardiac sarcomas can be classified as right heart sarcomas, left heart sarcomas, and pulmonary artery sarcomas.

If complete resection is possible, respecting the anatomical and functional integrity of the heart, surgery provides better palliation and can improve survival vs. medical therapy alone [76–82].

As previously mentioned, a good surgical exposure represents the fundamental principle to accomplish a complete, possibly en bloc, resection of the tumor, encompassing the mass and about 1 cm portion of the surrounding cardiac tissue. Besides the routine use of cardiopulmonary bypass, deep hypothermia with circulatory arrest (<18 °C rectal temperature), providing a bloodless field unencumbered by cardiopulmonary bypass cannulas, can greatly improve exposure. Surgery may be technically demanding and the necessity of securing negative margins may entail further interventions such as coronary artery bypass, valve replacement, reconstructive procedures, pacemaker implantation, and pericardial repairs, thus resulting in an increased risk of postoperative complications.

To overcome the technical challenges of complete resection with accurate cardiac reconstruction, particularly of left-sided tumors with posterior extension, a technique of cardiac explantation, ex vivo tumor resection with cardiac reconstruction, and cardiac reimplantation—cardiac

autotransplantation—has been utilized [36–38, 77, 78, 83]. Surgical outcomes with cardiac autotransplantation are excellent in patients who do not require concurrent pneumonectomy [77].

In selected cases of right ventricular tumors, a right heart bypass (cavo-pulmonary anastomosis) has also been utilized as a palliation to prolong survival [11–14, 33, 42–48].

The role of orthotopic cardiac transplantation in the management of locally advanced non-metastatic cardiac tumors appears to be limited. Indeed, it has been shown that about two-thirds of the so treated patients die of local recurrence or distant metastases within a year. Nevertheless, about 25% of the patients managed by orthotopic cardiac transplantation have a mean survival of more than 2 years without recurrent disease [44–46, 48, 78, 84]. The overall poor availability of donors however represent another important limitation to the role of orthotopic cardiac transplantation in this cohort of patients.

Despite a good local control often achievable with surgery, postoperative adjuvant therapy is recommended to all patients. Indeed, long-term survival is frequently poor due to metastatic tumor recurrence. This is particularly true in case of incomplete tumor resection [77, 78, 82, 85, 86].

Secondary Metastatic Cardiac Tumors

Metastatic cardiac tumors are far more frequent (approximately from 30- to 40-fold) than primary tumors of the heart. Although almost every type of malignant tumor has the potential to reach the heart, they usually arise from melanomas, lung, breast, and renal cancer, as well as lymphomas. Metastases may originate from blood dissemination via coronary arteries (melanoma, sarcoma, bronchogenic carcinoma) or lymphatic channels of cancer cells, direct extension via adjacent tissues (lung, breast, esophageal, and thymic tumors), or propagation via the superior or the subdiaphragmatic vena cava to the right atrium (liver, kidney tumors) (Fig. 10.13a, b). The pericardium is most often affected by direct extension of thoracic cancer, resulting in pericardial effusion which may contain masses comprising either cancer cells or blood clots and fibrin. The myocardium is the target of hematologous and/or retrograde lymphatic metastasis.

Cardiac metastases rarely are solitary and nearly always produce multiple microscopic nests and discrete nodules of tumor cells [8]. Clinical symptoms are quite rare and mainly related to pericardial effusion or cardiac tamponade. Arrhythmias, conduction block, and congestive heart failure have been occasionally reported [87–89].

Priority is given to the management of the primary focus of the disease and the cardiovascular complications that are manifested [28]. Surgical therapy is limited to relieve the recurrent pericardial effusions or, occasionally, cardiac tamponade (subxiphoid pericardiotomy, pericardial window) [90]. In most instances, these patients have widespread disease with limited life expectancies.

Abdominal and pelvic tumors (renal, hepatic, adrenal, uterine) on occasion may involve the inferior vena cava, with an intraluminal thrombotic extension to the right atrium. Renal cell cancer represents 1–3% of all visceral cancers and 85–90% of malignant kidney tumors and is most frequently responsible for this phenomenon (4–10% of all patients) (Fig. 10.13a, b) [91, 92]. Clinical symptoms are often few and nonspecific and related to the progressive obstruction of the inferior vena cava (ascites, peripheral edema) and/or to the presence of an abdominal mass.

CT-scan and/or MRI are used to study the primary focus of the disease, while two-dimensional echocardiography and in some instances perfusion lung scintigraphy are utilized to evaluate cardiopulmonary involvement. Radiation and chemotherapy are not effective in relieving the obstruction of blood flow. However, if the kidney can be fully removed, as well as the tail of tumor thrombus, survival can approach 75% at 5 years [91, 92]. Surgical intervention, in the absence of metastatic spread, besides to remove the primary focus of the disease, including the thrombus in the inferior vena cava, the adjacent lymphatic structures, and, eventually, the involved caval wall, aims to prevent potentially massive pulmonary

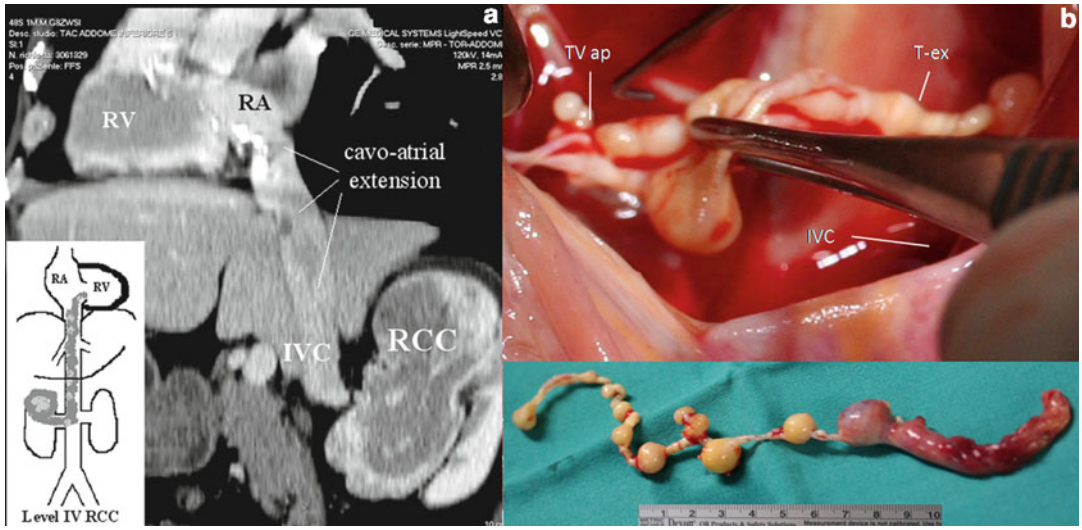

Fig. 10.13 (**a**) CT evidence of a right renal cell cancer (RCC) with neoplastic extension into the inferior vena cava (IVC) and right atrium (RA) [level IV cavoatrial tumor thrombus (*insert diagram*)]; *RV* right ventricle. (**b**) Intraoperative view. Tumor extension (T-ex) into the right atrium through the inferior vena cava (IVC), attached to the tricuspid valve apparatus (TV ap). Specimen after excision (*insert*)

embolism related to the fragmentation of the neoplastic tissue and/or thrombus. Renal cell tumors with atrial extension typically are approached with abdominal dissection to ensure full resectability of the renal tumor. Depending on the proximal extension of the tumor thrombus different surgical approaches have been recommended. In type III and IV disease, the exposure and isolation of the inferior vena cava are more extensive, requiring liver mobilization and sometimes an associated median sternotomy with or without the use of cardiopulmonary bypass and, in some circumstances, deep hypothermic circulatory arrest (DHCA) to improve exposure.

It is now accepted that neoplastic extension into the inferior vena cava is not a prognostically determining factor [92]. With no perinephric fat or lymph nodal involvement, it has been observed that the patients who undergo tumor excision with a radical nephrectomy and inferior vena cava thrombectomy have an overall and cancer-specific 5-year survival of 30–72%, with an operative mortality of 2.7–13% and an immediate palliation of symptoms of obstructive tumors [93–95].

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