European Heart Journal (2011) **32**, 1551–1560
doi:10.1093/eurheartj/ehr104

Cardiovascular magnetic resonance imaging for diagnosis and clinical management of suspected cardiac masses and tumours

Sandra Fussen[1†], Bart W.L. De Boeck[1,2*†], Michael J. Zellweger[1], Jens Bremerich[1], Kaatje Goetschalckx[1,3], Michel Zuber[2], and Peter T. Buser[1]

[1]University Hospital Basel, Basel, Switzerland; [2]Kantonsspital Luzern, Herzzentrum, 6000 Luzern 16, Switzerland; and [3]Gasthuisberg University Hospital, Leuven, Belgium

Received 10 October 2010; revised 22 January 2011; accepted 16 March 2011; online publish-ahead-of-print 15 April 2011

Aims To evaluate the diagnostic accuracy of cardiovascular magnetic resonance (CMR) imaging from a risk-stratification and therapeutic-management perspective in patients with suspected cardiac tumours.

Methods and results Cardiovascular magnetic resonance exams of 41 consecutive patients (aged 61 ± 14 years, 21 men) referred for evaluation of a suspected cardiac mass were reviewed for tumour morphology and signal characteristics in various unenhanced and contrast-enhanced sequences. Cardiovascular magnetic resonance-derived diagnosis and treatment were compared with clinical outcome and histology in patients undergoing surgery or autopsy ($n = 20$). In 18 of 41 patients, CMR excluded masses or reclassified them as normal variants; all were treated conservatively. In 23 of 41 patients, CMR diagnosed a neoplasm (14 'benign', 8 'malignant', and 1 'equivocal'); 18 of these patients were operated on, 2 managed conservatively, and 3 by palliation. During follow-up of 705 (inter-quartile range 303–1472) days, 13 patients died. No tumour-related deaths occurred in conservatively managed patients. Patients with a CMR-based diagnosis and treatment of benign tumour had a similar survival as patients without detectable tumour. Compared with histology, CMR correctly classified masses as 'benign or malignant' in 95% of the cases. Tumour perfusion, invasiveness, localization, and pericardial fluid were valuable to distinguish between malignant and benign tumours. Soft tissue contrast and signal intensity patterns in various sequences were valuable for excluding neoplastic lesions and helped to obtain tissue characterization at the histological level in selected tumour cases, respectively.

Conclusion Comprehensive CMR provides a confident risk-stratification and clinical-management tool in patients with suspected tumours. Patients where CMR excludes tumours can be managed conservatively.

Keywords Cardiac mass • Neoplasm • Prognosis • Management • CMR

Introduction

Cardiac tumours represent a rare but important cause of morbidity and mortality.[1–3] The therapeutic management of cardiac masses differs fundamentally according to the nature of the cardiac mass (neoplastic vs. non-neoplastic) and tumour type (benign or malignant, primary or secondary), and furthermore depends on clinical circumstances such as haemodynamic failure, invasive growth, and metastatic spreading, which either prompt for an intervention or rather make it irrational.[1,2] Cardiac magnetic resonance (CMR) imaging is considered the imaging modality of choice for the assessment of cardiac masses.[4] It permits high-quality, multiplanar imaging of tumour morphology, tissue composition, and perfusion. Additional assets of CMR are its ability to assess cardiac function, blood flow, and its large field of view that allows visualization of the paracardiac structures and the great vessels. Yet, studies demonstrating clinical advantages are sparse. We conducted a retrospective study to evaluate the diagnostic accuracy of CMR from a patient-management perspective in subjects with suspected cardiac or paracardiac tumours. For this

† These authors contributed equally to this work.

* Corresponding author. Tel: +41 41 2052250, Fax: +41 41 2052234, Email: bart.deboeck@ksl.ch

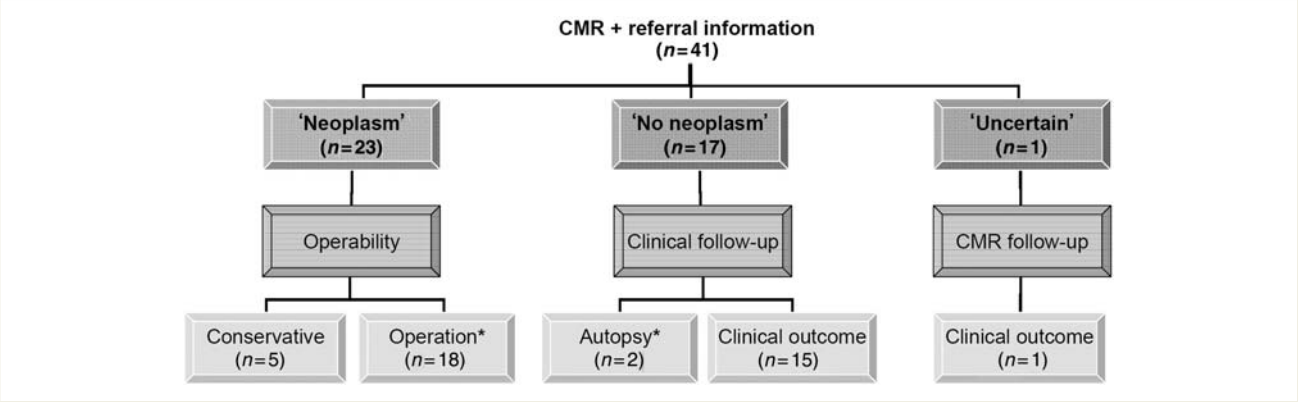

Figure 1 Cardiac magnetic resonance-based diagnosis, patient management, and available data. Of note, the blinded cardiac magnetic resonance assessment was not different from the initial reading on which the subsequent clinical considerations and the final patient management were based. 'Operability': cardiac magnetic resonance-based judgement of haemodynamic relevance, malignancy, dissemination, and operability of the mass as part of the clinical decision process. Bottom level displays data available for analysis as a result of this process. Asterisk denotes the histological specimens available.

purpose, CMR-derived tumour diagnosis was compared with the histological findings of biopsy specimens in patients undergoing surgery or autopsy. In patients declined from surgery based on the CMR diagnosis, the predicted benign character and presumed histology were compared with the clinical follow-up and outcome.

Methods

We retrospectively reviewed the CMR exams of all patients ($n = 41$) referred between January 2002 and August 2009 for the first evaluation of a cardiac or paracardiac mass, detected or suspected at echocardiography ($n = 39$) or thoracic computed tomography (CT; $n = 2$). Patients with suspicion of thrombus were considered only if the referral question explicitly included tumour as differential diagnosis. Clinical charts were reviewed for patient characteristics, disease symptoms, medical history, and neoplastic disease established prior to initial echocardiography and CMR. Data on disease course and outcome were gathered from the time of CMR diagnosis until the date of study closure (February 2010). Follow-up status was ascertained in all patients by checking hospital records and by contacting the patients' general practitioners with a short questionnaire on vital status, type and date of major cardiovascular events, and last follow-up date. In patients undergoing surgery or autopsy, intra-operative macroscopic and histological findings were also recorded (*Figure 1*).

Cardiac magnetic resonance imaging protocol

Cardiac magnetic resonance studies were performed on a 1.5 T system equipped with a phased-array body coil (Sonata & Avanto, Siemens, Erlangen, Germany). As a standard CMR protocol for the evaluation of tumours and masses in our institution ('cardiac tumour protocol'), image sequences typically included axial T2-weighted turbo spin echo sequences (T2-TSE) covering the entire thorax and breath-hold segmented steady-state free precession cine imaging sequences in four-chamber and short-axis views. T1-weighted turbo spin echo sequences (T1-TSE) were targeted on the tumour mass. First-pass perfusion images through the lesion and myocardium were acquired by a contrast-enhanced saturation recovery gradient-recalled echo sequence after a bolus of 0.2 mL/kg (0.1 mmol/kg) gadobenate dimeglumine (Multihance, Bracco, Mendrisio, Switzerland) infused at 4 mL/s and followed 10–15 min later by late gadolinium enhancement (LGE) imaging using a breath-hold inversion-recovery gradient-echo sequence. In addition, early contrast-enhanced T1-TSE, fat-saturated T1-TSE, and/or black blood fat-saturated (triple inversion recovery) T2 spin sequences were added if deemed necessary for further tissue differentiation.[5] All images were acquired under supervision of an experienced (Level III) cardiologist and/or radiologist.

Evaluation and interpretation of cardiac magnetic resonance images

Cardiac magnetic resonance images were retrospectively evaluated during consensus reading sessions by at least one cardiologist and one radiologist, to whom only the referral question was available. Lesions were categorized as neoplastic or non-neoplastic lesions, with the former further differentiated into benign or malignant tumours and the latter into normal variants or non-neoplastic masses, respectively. For suspected neoplastic lesions, a histological diagnosis was postulated according to previously suggested criteria based on a qualitative assessment of tumour morphology and signal intensity in each of the available CMR sequences (*Table 1*).[5–9] Evaluation of tumour morphology included tumour location, shape and mobility, tumour border definition and/or tissue infiltration, and the presence of pericardial effusion. The tissue composition of a lesion was estimated based on the signal characteristics and qualitatively scored as homogenous or heterogeneous. In addition, in each sequence tumour signal intensity was assessed qualitatively as hypo-, iso-, or hyperintense with reference to the normal myocardium. Finally, tumour vascularization and the presence of interstitial fibrosis or extensive acellular areas within the mass were qualitatively scored as present or absent on first-pass perfusion imaging and delayed contrast-enhanced imaging, respectively.

Statistical analysis and reporting

Statistical analysis was performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Categorical data are summarized as frequencies and percentages; continuous variables are expressed as mean ± SD or as median

Table 1 Typical features of most common cardiac tumours and masses in their classical presentation

	Preferential location	Morphological characteristics	Pericardial effusion*	Signal composition	T2-weighted TSE	T1-weighted TSE	Contrast enhancement	Perfusion CE-SR-GRE
Benign tumours								
Myxoma	IAS intracavitary	Lobular or frond-like, pedunculated, mobile	No	Heterogeneous	↑	↔	+/−	? (−)
Lipoma	Any chamber, endo/myocard	Smooth, broad based intracavitary ± mobile	No	Homogenous	↑ FS	↑↑ FS	−	? (−)
Fibroelastoma	Valves	Small, round, ± mobile	No	Homogenous	↔ ↑	↔	+	? (−)
Haemangioma	Any chamber, endo/myocard	Lobular ± mobile	Infrequent	Heterogeneous	↑	↔	+	? (+)
Fibroma	Ventricular myocard	Smooth/encapsulated, immobile	No	Homogenous	↑	↔ ↓	− (outer rim +)	? (−)
Rhabdomyoma	Ventricular myocard	Smooth, sometimes multiple	No	Homogenous	↔↑	↔ ↓	As myocardium	?
Malignant tumours								
Rhabdomyosarcoma	Myocard	Lobular, invasive	Possible	Heterogeneous	↔	↔	+/(−)	? (+)
Liposarcoma	Atrium or myocard	Lobular, invasive	Possible	Heterogeneous	↔	↔ ↑ FS	+/(−)	? (+)
Sarcoma: angio/leio/osteo-	Atrium/veins	Sessile, lobular, invasive, obstructive	Common	Heterogeneous	↑	↔	+	? (+)
Lymphoma	Myo/pericard	Lobular, multiple lesions	Common	Heterogeneous	↔ ↑	↔	+	? (+)
Metastases	Any chamber variable	Often smooth, sometimes multiple	Common	Heterogeneous	↑	↔	+/(−)	+
Non-neoplastic								
Thrombus: fresh	Infarct area, left auricle	Adjacent scar	No	Homogenous	↔ ↑	↔ ↑	−	−
Thrombus: old	Infarct area, left auricle	Adjacent scar	No	Homogenous	↓ ↔	↓ ↔	−	−/(+)
Benign cysts	Para-/pericard	Smooth, circumscribed liquid (homogeneous)	No	Homogenous	↑	↓	−	−
Variants (muscular)	Wall contact	As normal variants	No	Homogenous	↔	↔	+	+

Based on refs,[5–9] asterisk indicates the absence of heart failure. FS indicates that the high signal can be suppressed by fat-specific saturation prepulses. ? indicates currently unknown; as expected from histology.

(inter-quartile range) as appropriate. A two-sided *P*-value of <0.05 was considered as statistically significant. Differences in CMR characteristics between malignant and benign masses were compared by Fisher's exact test. Survival for patients with tumours stratified by CMR as malignant, benign, or normal variants was compared by log-rank analysis on the Kaplan–Meier survival curves.

Results

The final study population comprised 41 patients (21 men, mean age 61 ± 14y), presenting with a mass alleged in echocardiography ($n = 39$) or incidentally found on a chest CT ($n = 2$). Presenting symptoms were heart failure ($n = 6$), stroke ($n = 4$), syncope ($n = 3$), acute coronary syndrome ($n = 2$), and pulmonary embolism ($n = 1$). In the remaining patients, the mass was revealed accidentally in the context of tumour staging ($n = 4$) or during elective work-up for weight loss, dyspnoea, hypertension, angina, or arrhythmias. The referral technique postulated the suspected mass to be neoplastic in 23 (56%) patients (malignant/benign: 7/15), non-neoplastic in four (10%), and remained uncertain about the nature of the lesion in the remaining 15 (36%) patients. Fourteen patients (34%) had a prior history of non-cardiac malignancy, (haematological malignancy $n = 4$, bronchus carcinoma $n = 3$, breast cancer $n = 2$, and oropharynx, ovarium, prostate, or seminoma each in $n = 1$), with documentation of non-cardiac metastatic spreading before CMR in four.

Cardiac magnetic resonance-based stratification and patient management

On the basis of the consensus reading of the CMR images, the suspected mass was identified and classified as neoplastic in 23 (56%) and as non-neoplastic or absent in 17 (42%) of the 41 patients. In one patient with a well-perfused and enhancing intramural left atrial mass, the initial CMR was equivocal on the presence of a malignancy or an inflammatory pseudotumour (*Figure 1*). After serial CMR and clinical assessments under immunosuppressive therapy, vasculitis involving the atrial wall was eventually established as diagnosis. *Table 2* lists the main findings in patients with a CMR diagnosis of cardiac neoplasm and/or histological data for comparison. Eight tumours were judged by the CMR experts to be malignant, 14 benign, and in one patient, consensus on the malignancy could not be reached. In the remaining patients, CMR either concluded on the presence of thrombus ($n = 2$), established the suspected masses as anatomical variants (atypically localized epicardial fat, lipomatous hypertrophy of the interatrial septum, prominent atrial cristae, and localized ventricular hypertrophy, each in 2), or could not detect any mass at all ($n = 7$). Cardiac magnetic resonance was the ultimate imaging technique used for tumour characterization in all patients.

A surgical procedure was proposed as final therapy and histological data were obtained in 18 of the 23 patients with neoplasm, whereas in five, surgery was declined because of evidence for disseminated cancer ($n = 3$) or for critically localized, benign tumours not justifying a high-risk intervention ($n = 2$). The latter five patients with and the remaining 18 patients without a neoplastic lesion diagnosed by CMR were managed conservatively with documentation of clinical events (*Figures 1* and *2*). Histological information on the nature of the suspected mass in this group thus failed, except for two patients who died and underwent autopsy within 40 days of the initial CMR.

Cardiac magnetic resonance findings compared with histology

In 16 out of 20 cases (80%) with available histopathological data, the CMR features in adjunct to the referral information permitted to classify the masses correctly as 'malignant neoplasm', 'benign neoplasm', or 'no neoplasm' (*Table 2*). Cardiac magnetic resonance experts misclassified two non-neoplastic masses as benign neoplasm and inversely failed to detect a small (8 × 8 mm) fibroelastoma, yielding an accuracy of 17 of 20 (85%) to classify masses correctly as neoplasm or not. One metastasis with extensive myxoid degeneration on gross pathological examination was misclassified as a benign myxoma. Thus, in dichotomizing masses as benign in nature or not, CMR was accurate in 19 of 20 (95%) of all cases. *Table 3* summarizes the most useful CMR criteria in the distinction between malignant and benign lesions.

Tissue and/or tumour characteristics on cardiac magnetic resonance

Individual signal characteristics of the alleged masses were highly variable. An integrative approach allowing for the interpretation of signal patterns (*Table 1*) enabled a certain level of virtual histological differentiation that proved helpful in selected clinical scenarios. Some typical patterns are described here.

Normal variants and non-neoplastic masses

In most (10/15, 67%) of the cases where CMR excluded masses ($n = 7$) or demonstrated anatomic variants that had been interpreted as a possible mass ($n = 8$), focal wall thickening or extensive epicardial tissue masses had evoked doubt about the presence of an intramural or epicardial tumour. Cardiac magnetic resonance diagnosis was based on the absence of soft tissue contrast in all driven sequences or on the demonstration of excessive fat deposition. Two small valvular lesions irrefutably demonstrated by echocardiography, of which one was histologically confirmed as fibroelastoma, were nevertheless missed. Thrombi ($n = 2$) were diagnosed based on the presence of an intracavitary mass without perfusion and late enhancement, but typically adjacent to the myocardium displaying delayed enhancement.[10] *Figure 3* provides an example in a patient referred with suspicion of apical tumour or hypertrophy.

Lipoma and lipomatous septal hypertrophy

Typical for these fatty masses was a homogeneous and hyperintense signal in cine and spin echo sequences, behaving similar to subcutaneous fat in all sequences and displaying signal loss after fat saturation prepulses (*Figure 4*). Whereas the lipoma ($n = 1$) was well defined and partially intramural, lipomatous hypertrophy rather presented as diffuse thickening of the interatrial septum and adjacent posterior right atrial wall, with sparing of the fossa ovalis. Echocardiography remained equivocal about the nature of the mass in all cases, erroneously suggesting metastatic infiltration in one patient (Case 24).

Table 2 Cases with cardiac magnetic resonance diagnosis of neoplasm and/or histological data

Case no.	Sex	Age	Prior malignancy	Echo or CT diagnosis	CMR diagnosis	Histology
Neoplasm diagnosed by CMR, operative treatment						
1[a]	F	61	Ovarium, M^+	M, cystic: meta	M, cystic: meta	M, meta
2[a]	M	65	Lung, M^+	E, meta/infectious	M, meta	M, meta
3[a]	M	55	inv.haemangiom	M, nonprim. card.	M, nonprim. card	M, haemangiosarcoma
4[a]	M	44	Synovia, M^+	M, meta	B, myxoma	M, meta (myxoid)
5	F	57	Breast	E, myxoma/meta	B, myxoma	B, myxoma
6[a]	F	75	Mult. Myel.	B, myxoma	B, myxoma	B, myxoma
7	F	78	Mult. Myel.	B, myxoma	B, myxoma	B, myxoma
8	M	63	Lung	E, myxoma/meta	B, myxoma	B, myxoma
9[a]	F	42	—	E, infectious/other	M, sarcoma	M, angiosarcoma
10	M	45	—	M, nonprim. card.	M, nonprim. card.	M, malignant thymoma
11[a]	M	68	—	M, nonprim. card.	M, nonprim. card.	M, undiff. sarcoma
12	F	58	—	B, myxoma	B, myxoma	B, myxoma
13	F	70	—	B, myxoma	B, myxoma	B, myxoma
14	M	70	—	E, myxoma/meta	B, myxoma	B, myxoma
15	M	61	—	B, myxoma	B, myxoma	B, myxoma
16	F	73	—	E, unclear mass	B, fibroma	NN, caseus calcification
17	F	50	—	B, myxoma	B, myxoma	NN, thrombus
18	M	62	—	B, myxoma	B, myxoma	B, myxoma
Neoplasm diagnosed by CMR, conservative management						
19[a]	F	63	Mult. Myel, M^+	M, meta	M, sarcoma	NA
20[a]	M	82	Lung	E, meta/myxoma	E, meta/myxoma	NA
21[a]	F	70	Breast	E, mass present?	M, meta	NA
22	F	86	—	B, myxoma	B, haemangioma	NA
23	M	44	—	E, unclear mass	B, lipoma	NA
Neoplasm excluded by CMR, conservative management, autopsy data available						
24[a]	F	61	Pharynx, M^+	M, meta	NN, IASH	NN, IASH
25[a]	F	78	—	NN, fibroelastoma	E, no mass seen[b]	NN, fibroelastoma[c]

Cases grouped according to the presence of a tumour diagnosed by CMR and/or availability of histological data, and by the presence or absence of prior malignancies. M^+, known extracardiac metastasis at time of referral; inv.haemangiom, invasive haemangioma; Mult. Myel., multiple myeloma; meta, metastasis; nonprim. card., non-primarily cardiac malignancy of mesenchymal or lymphoid origin; IASH, lipomatous hypertrophy of the interatrial septum; caseus calcification of the mitral annulus; E, equivocal; NN, non-neoplastic; B, benign; M, malignant; NA, not available.
[a]Died during follow-up.
[b]No mass seen considered as benign condition.
[c]Fibroelastoma is generally not regarded as a neoplasm.

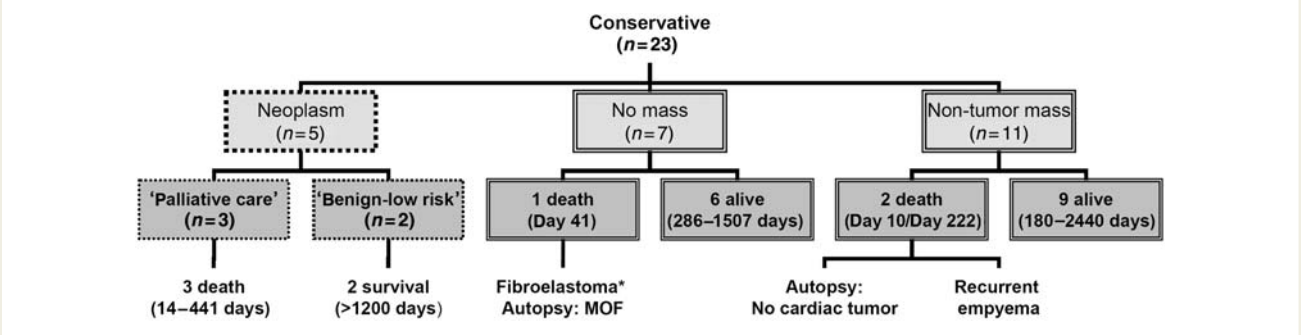

Figure 2 Diagnoses and outcome in conservatively managed patients. Asterisk indicates the fibroelastoma (8 × 8mm) resected on the occasion of combined coronary artery and valve surgery; patient died from post-operative multi-organ failure.

Table 3 Distinctive characteristics of benign and malignant masses

	Benign lesions ($n = 13$)	Malignant tumours ($n = 7$)	*P*-value
Previous cancer			
No/yes/metastatic	8/4/1	3/1/3	0.31
Localization			
RA	0	3	<0.01
LA	5	0	
IAS-left/right/mid	6/1/1	1[a]/0/0	
Pericard/paracardial	0/0	1/2	
Invasiveness			
No/invasive/compressive	11/2/0	1/3/3	<0.01
Pericardial effusion			
Yes/no	0/13	4/3	<0.01
Composition			
Homogenous/inhomogeneous	3/10	1/6	1.0
Signal intensity T1			
Hypo-/iso-/hyperintense	1/9/2	0/2/5	0.05
Signal intensity T2			
Hypo-/iso-/hyperintense	1/3/7	0/2/4	1.0
Perfusion			
Detected/none	1/8 ($n = 9$)	3/1 ($n = 4$)	0.05
Contrast enhancement			
None/weak/abundant	8/1/3[b] ($n = 12$)	1/2/3 ($n = 6$)	0.16

[a]As judged on CMR, intra-operatively, the tumour proved to be attached to the LA roof, not the IAS.
[b]9/1/2, P = 0.07 after accounting for fat as the reason for the high signal on LGE-imaging in lipomatous hypertrophy of the IAS.

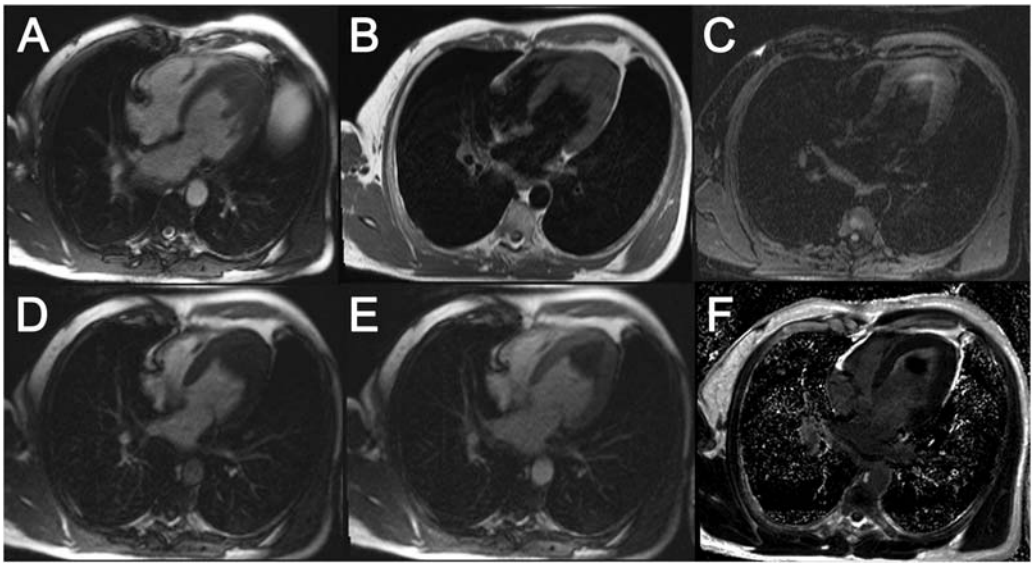

Figure 3 Apical thrombus adjacent to endocardial fibrosis in a patient with vasculitis. Being indistinguishable from the normal myocardium in cine imaging (*A*) and T1-weighted turbo spin echo sequences (*B*), the mass is hypointense in fat-saturated T2-weighted imaging and delineated by a hyperintense rim suggesting oedema (*C*). Contrary to the myocardium, signal intensity in the mass remains unchanged between the left ventricular phase (*D*) and the myocardial phase (*E*) of contrast passage, indicating poor or absent mass perfusion. Accordingly, there is no delayed uptake of contrast within the mass a rim of enhancement compatible with endocardial fibrosis is seen (*F*).

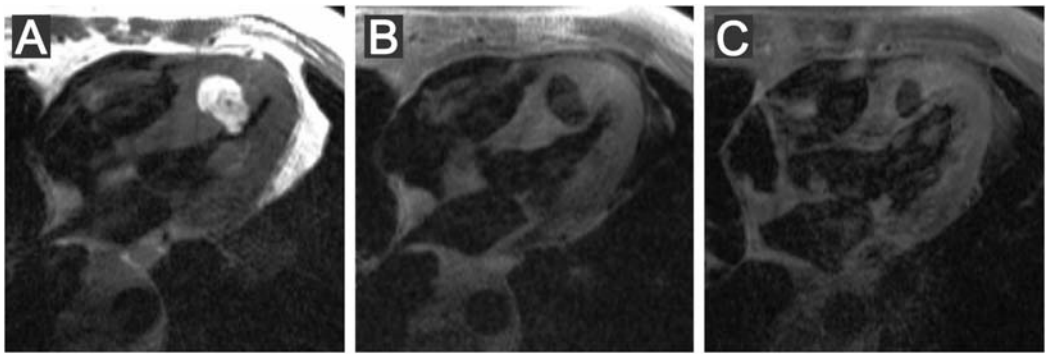

Figure 4 Septal lipoma. The signal intensity of the intramural tumour is homogeneous and behaves similar to subcutaneous fat in all sequences: the high signal in T1-weighted turbo spin echo sequences (*A*) is suppressed after a fat-specific saturation pulse (*B*). There is no detectable contrast uptake on fat-saturated T1-weighted turbo spin echo sequences repeated 10 min after gadolinium administration (*C*).

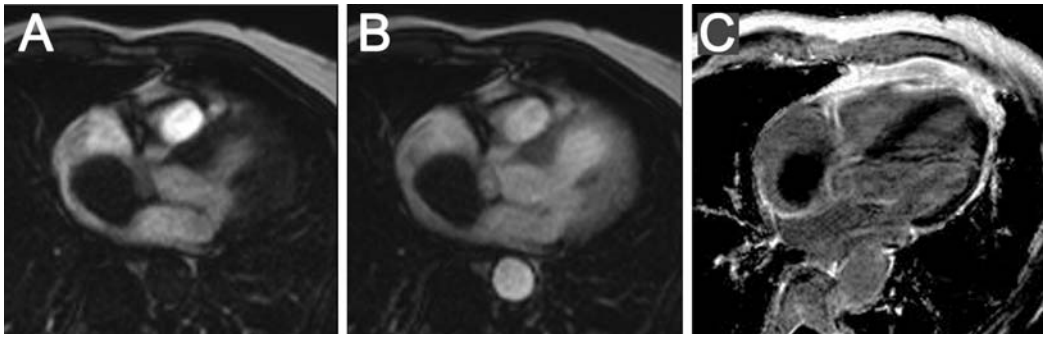

Figure 5 Perfusion and late enhancement study of a myxoma. A large mass with attachment to the right-sided interatrial septum is identified. On first-pass perfusion images taken during the ventricular (*A*) and myocardial perfusion phase (*B*), no noticeable perfusion is discerned. Delayed gadolinium enhancement of the tumour is also absent (*C*). The diagnosis of myxoma was confirmed at histology.

Myxoma

All histologically confirmed myxomas ($n = 9$) were heterogeneous in cine imaging, compatible with regional differences in cellularity and extensive myxoid stroma and with occasional focal necrosis and haemorrhage. Myxomas were typically hyperintense in T2-TSE and isointense in T1-TSE. Signal enhancement during first-pass perfusion and delayed enhancement was detected in 16 and 40% of the cases, respectively (*Figure 5*). Myxomas were pedunculated, mobile, and attached at the left (78%) or right (11%) interatrial septum. One myxoma (11%) grew in close contact with a pulmonary vein ostium. A thrombus mistaken for myxoma (Case 17) differed from the common pattern by a similar atypical localization (pulmonary vein ostium) and low signal in T2-TSE. A left atrial metastasis with extensive myxoid degeneration at histology had typical signal features of myxoma (Case 4). Nevertheless, clinical suspicion of metastasis was raised by concomitant visualization of pulmonary metastasis.

Malignant tumours (primary and metastasis)

Malignant tumours typically (≥85%) presented on CMR as broad-based bulky masses with invasive or compressive growth and signal heterogeneity. Although not a universal finding, pericardial effusion was a common and highly specific feature (*Table 3*). Sarcomas ($n = 3$) were hyperintense in T2-TSE, had signal heterogeneity in multiple sequences, and heterogeneous uptake of contrast. All metastases ($n = 4$) were diagnosed in patients with previously demonstrated extracardiac metastatic spreading. Signal characteristics and contrast enhancement were variable and inconsistent. Compared with the referral technique, CMR diagnosed a primary cardiac sarcoma in a young woman with presumptive diagnosis of an inflammatory mass (*Figure 6*) and better documented infiltration and local spreading in all cases, aiding operative planning.

Cardiac magnetic resonance findings compared with clinical follow-up

Overall, and considered independently of therapeutic management, 13 deaths occurred over a median observation period of 705 (303–1472) days. All but one of the patients with a malignant tumour diagnosed on CMR died; on average within 377 (76–819) days. By the Kaplan–Meier analysis, mortality in patients diagnosed by CMR with a benign neoplasm [2/14, within 1160 (408–1650)

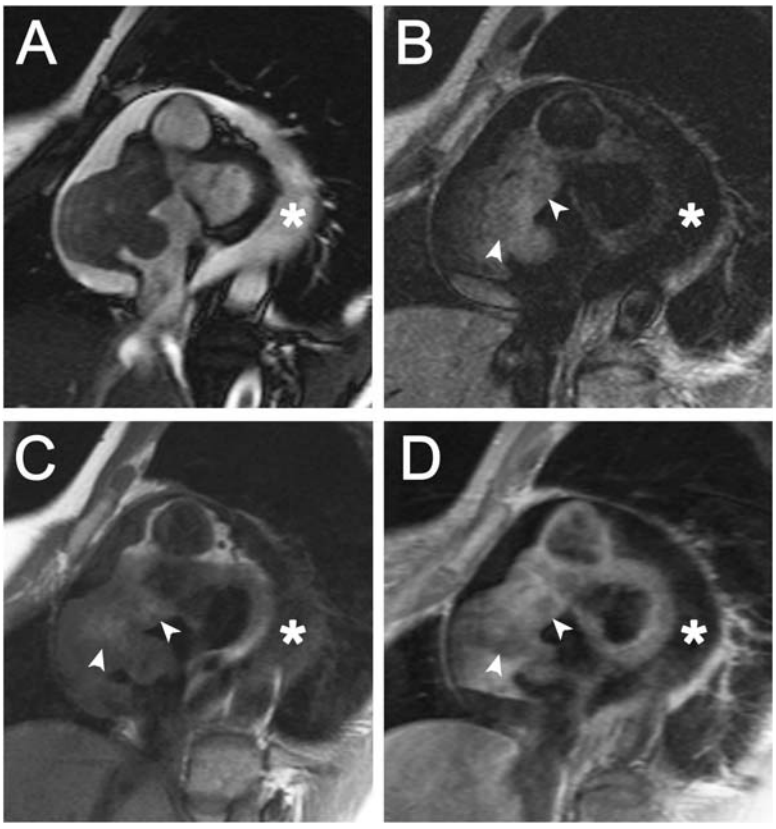

Figure 6 Primary cardiac sarcoma. Short-axis cine imaging (*A*), T2-weighted turbo spin echo sequences (*B*), and T1-weighted turbo spin echo sequences before (*C*) and after contrast (*D*), demonstrating an invasive right atrial tumour with inhomogeneous composition and extensive pericardial effusion (asterisks). The tumour displays areas where signal is lower in T2-weighted turbo spin echo sequences, higher in T1-weighted turbo spin echo sequences, and less enhancement after contrast is seen (arrowheads), compatible with intratumoral haemorrhage. The intermediate signal of the pericardial effusion in the T1-weighted turbo spin echo sequences suggests haemorrhagic effusion. An angiosarcoma was diagnosed.

days] was significantly lower than that in those diagnosed with a malignant tumour ($P < 0.01$) and did not differ from mortality in patients where CMR had concluded that a cardiac mass was either absent or non-neoplastic [3/18 within 745 (286–1492) days]. Of importance, of these five patients dying despite the diagnosis of a benign condition, only one patient (Case 4) was misclassified by CMR, whereas in four, the histological (Cases 6, 24, and 25) or clinical (relapsing empyema) data excluded the suspected mass as cause of death. As such, when considered from the perspective of CMR-guided therapy management ('intention to treat'), no tumour-related deaths occurred in conservatively managed patients other than in those receiving palliative care (*Figure 2*). Inversely, two patients without neoplasm were subjected to surgery after an erroneous CMR diagnosis of a benign neoplasm.

Discussion

The present study showed that a comprehensive CMR evaluation of tumour morphology, tissue composition, and perfusion in conjunction with information on tumour spread and operability can adequately direct patients to the appropriate therapeutic strategy. In particular, CMR excelled in its capacity to risk stratify patients by confidently excluding masses or reclassifying them as anatomical variants and by distinguishing benign from malignant processes. Although enhanced soft tissue contrast in various sequences increased depiction, delineation, and enhanced stratification of the masses compared with echocardiography, CMR faced limitations in depicting small valvular lesions and in tissue characterization at the histological level.

With a incidence of ~0.03% (primary tumours) to ~2.0% (all tumours) in autopsy series[11–13] and 0.15% in echocardiographic series,[14] cardiac tumours are rare entities in clinical cardiology that pose particular challenges to diagnostic cardiac imaging. Cardiac tumours have a broad differential diagnosis and need to be distinguished from non-neoplastic masses. In addition, treatment is significantly directed by symptoms, haemodynamic, embolic, or arrhythmic implications, and by neoplastic nature, type, dissemination, or operability of the mass.[1–3,15] Optimal tumour characterization for clinical management therefore includes information on local tumour topology and invasiveness, and at best delivers some degree of tissue characterization. Being

non-invasive, cost-effective, quick, and widely available, echocardiography is usually employed as first-line imaging modality.[15,16] In fact, many masses—in the present study up to 50%—are coincidently detected during examinations for unrelated conditions. This technique was also found to have a primary diagnostic role in the detection of valvular lesions and to allow for a relatively confident diagnosis of typically localized myxomas. Incomplete or inadequate acoustic windows and rather poor tissue contrast restrict the capacity of echocardiography to properly evaluate and delineate peri- and paracardiac lesions[17] and to adequately differentiate among various tissue types.[18] The unrestricted field of view combined with superior soft tissue and blood pool contrast in various unenhanced CMR sequences renders distinct advantages under such circumstances.[4,5] Contrast agents further enhance detection and delineation of masses when distinction of intramural tumours from the normal myocardium still remains equivocal and are invaluable in the detection of intracavitary thrombi.[8,10,18,19] Thus, paracardiac, metastatic, and infiltrative processes may be assessed more readily or can inversely be excluded with more confidence by CMR. Indeed, referrals because of ambivalent echocardiographic findings comprised >30% of the CMR examinations and mostly related to intramural, retrocardial, or pericardial masses that could be confidently excluded by subsequent CMR.[20,21] In a study by Winkler and Higgins[21] including 34 patients followed for up to 2 years, CMR could exclude or reclassify cardiac masses to anatomic variants or other abnormalities in up to 58 and 20% of the masses suspected on echocardiography, respectively. The excellent outcome under long-term conservative treatment observed in our study provides evidence that refraining from surgical exploration or intervention in such patients is both justified and safe. In the case of suspicious small valvular lesions like fibroelastoma, CMR may however perform suboptimally[22] and rather an echocardiography-guided management, although often not surgical in nature, appears warranted.

Only a limited number of studies have systematically examined the value of various pulse sequences and/or contrast enhancement techniques in differentiating cardiac masses based on their tissue characteristics.[6–8] In the differentiation between malignant and benign lesions, the present data and a previous study by Hoffmann *et al.*[7] indicated an overall accuracy of 90–95% for an integrative CMR assessment of morphological features and signal characteristics. Yet, no single CMR feature was both highly specific and highly sensitive in the differentiation between benign or malignant cardiac and paracardiac masses. In particular, morphological features, such as right-sided or paracardiac location, invasive or compressive growth patterns and presence of pericardial effusion, emerged as single predictors for malignancy,[7,23] whereas individual signal characteristics had little predictive value *per se*. As illustrated in *Table 1*, this is partially explained by the high variability of single T1 and T2 signal characteristics among the various benign and malignant masses, which used in isolation consequently provide little information on the biological nature of the tumour. Nevertheless, confident CMR characterization is possible for some tumours and masses homogeneously composed of a tissue type with a more or less characteristic morphological and signal 'fingerprint', such as fat and lipomas, fibrosis and fibromas, and pericardial cysts.[5,7,8] Fat, for example, has very constant T1 and T2 signal properties that can be suppressed in a selective manner by fat-specific saturation prepulses. In the present population, these unique signal properties allowed for a confident risk stratification and conservative management of many patients with benign fatty masses. As opposed to homogeneous tissue characteristics in the above-mentioned conditions, a heterogeneous signal composition of the tissue indicative of focal haemorrhage, necrosis, calcification, or regional myxoid degeneration has been reported as a sensitive feature of malignancy.[7,8] It has, however, also been consistently reported in myxomas[7,24] and accordingly did not emerge as a distinctive feature in the present study. On the same grounds, post-contrast enhancement has been proposed as a feature of malignancy.[7,8,23] Late enhancement of myxoid stroma or necrotic areas within myxomas is, however, also rather common, amounting up to 40% in our study.[6–8] Intense, inhomogeneous enhancement early after contrast is also seen in benign cardiac haemangiomas.[25] Perfusion imaging aims at depicting tumour perfusion and capillary density by assessing the contrast wash-in dynamics at first passage. Fibroelastoma and thrombus are principally avascular masses and many benign tumours (e.g. fibroma, lipoma) are rather sparsely vascularized compared with the faster growing malignant tumours, with the noticeable exception of haemangioma.[1] The importance of first-pass perfusion imaging in tumour characterization has not been investigated before. In the subset of patients subjected to this technique, malignant lesions tended to display noticeable perfusion more frequently. Contrary to late enhancement, signal increase in first-pass contrast passage was rare in myxomas (16%). This potential benefit over late enhancement imaging requires confirmation in larger studies.

Finally, integration of imaging data with epidemiological probability and clinical data is an integral part of tumour stratification and clinical decision-making in daily practice. All patients with cardiac metastasis in our study had a history of extracardiac metastatic disease. On the other hand, CMR confidently differentiated lipomatous hypertrophy from metastatic infiltration and accurately diagnosed a few myxomas in cancer patients, while identifying cardiac infiltration in others. This highlights that CMR may convey independent information for differential diagnosis and operative planning in many patients.[7,20] Most importantly, in patients managed conservatively based on the CMR diagnosis, no tumour-related deaths occurred other than in those receiving palliative care because of documented metastatic disease. As such, from the perspective of CMR-guided therapy management ('intention to treat'), CMR was found accurate.

Limitations

It should be acknowledged that the eventual study outcome represents the result of a staged approach in which echocardiography was the gatekeeper to most of the CMR examinations. In the absence of a comparison free of potential referral bias, the additive value of CMR to echocardiography and clinical assessment remains difficult to establish. As either individual technique was found to yield specific limitations and to have some complementary assets, such combined approach may currently remain warranted. Another acknowledged limitation of the study is its retrospective design; despite all efforts to improve the consistency in CMR

interpretation by pre-specified scoring systems and review sessions blinded from other than the referral information, this inherently carries the risk of somewhat overestimating the favourable results for CMR. With technological advances, some typical CMR parameters (e.g. late enhancement and perfusion) have become readily feasible by echocardiography and/or CT and need to be explored in the future. More in general, also for most of the contemporary CMR sequences and for contrast applications in particular, tumour characteristics reported in previous studies remain scattered and scarce. Although our study adds more data to this field and is encouraging enough to endorse CMR as a decisive imaging modality in this orphan disease, prospective multicentre registries and/or studies[26] should follow to underscore the results.

Funding

This study was supported by a grant from the Stiftung für kardiovaskuläre Forschung Basel, Switzerland.

Conflict of interest: none declared.

References

1. Roberts WC. Neoplasms involving the heart, their simulators, and adverse consequences of their therapy. *Proc (Bayl Univ Med Cent)* 2001;**14**:358–376.
2. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumours: diagnosis and management. *Lancet Oncol* 2005;**6**:219–228.
3. Elbardissi AW, Dearani JA, Daly RC, Mullany CJ, Orszulak TA, Puga FJ, Schaff HV. Survival after resection of primary cardiac tumors: a 48-year experience. *Circulation* 2008;**118**(Suppl. 14):S7–S15.
4. Hundley WG, Bluemke DA, Finn JP, Flamm SD, Fogel MA, Friedrich MG, Ho VB, Jerosch-Herold M, Kramer CM, Manning WJ, Patel M, Pohost GM, Stillman AE, White RD, Woodard PK. ACCF/ACR/AHA/NASCI/SCMR 2010 expert consensus document on cardiovascular magnetic resonance: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. *J Am Coll Cardiol* 2010;**55**:2614–2662.
5. O'Donnell DH, Abbara S, Chaithiraphan V, Yared K, Killeen RP, Cury RC, Dodd JD. Cardiac tumors: optimal cardiac MR sequences and spectrum of imaging appearances. *Am J Roentgenol* 2009;**193**:377–387.
6. Semelka RC, Shoenut JP, Wilson ME, Pellech AE, Patton JN. Cardiac masses: signal intensity features on spin-echo, gradient-echo, gadolinium-enhanced spin-echo, and TurboFLASH images. *J Magn Reson Imaging* 1992;**2**:415–420.
7. Hoffmann U, Globits S, Schima W, Loewe C, Puig S, Oberhuber G, Frank H. Usefulness of magnetic resonance imaging of cardiac and paracardiac masses. *Am J Cardiol* 2003;**92**:890–895.
8. Kaminaga T, Takeshita T, Kimura I. Role of magnetic resonance imaging for evaluation of tumors in the cardiac region. *Eur Radiol* 2003;**13**(Suppl. 4):L1–L10.
9. Buser PT, Buck T, Plicht B. Cardiac masses and tumours. In: Zamorano JL, Bax JJ, Rademakers FE, Knuuti JM, eds. *The ESC Textbook of Cardiovascular Imaging*. London: Springer-Verlag; 2010.
10. Mollet NR, Dymarkowski S, Volders W, Wathiong J, Herbots L, Rademakers FE, Bogaert J. Visualization of ventricular thrombi with contrast-enhanced magnetic resonance imaging in patients with ischemic heart disease. *Circulation* 2002;**106**:2873–2876.
11. Butany J, Leong SW, Carmichael K, Komeda M. A 30-year analysis of cardiac neoplasms at autopsy. *Can J Cardiol* 2005;**21**:675–680.
12. Reynen K. Frequency of primary tumors of the heart. *Am J Cardiol* 1996;**77**:107.
13. Lam KY, Dickens P, Chan AC. Tumors of the heart. A 20-year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med* 1993;**117**:1027–1031.
14. Sutsch G, Jenni R, von Segesser L, Schneider J. Heart tumors: incidence, distribution, diagnosis. Exemplified by 20,305 echocardiographies. *Schweiz Med Wochenschr* 1991;**121**:621–629.
15. Blondeau P. Primary cardiac tumors–French studies of 533 cases. *Thorac Cardiovasc Surg* 1990;**38**(Suppl. 2):192–195.
16. Pinede L, Duhaut P, Loire R. Clinical presentation of left atrial cardiac myxoma. A series of 112 consecutive cases. *Medicine (Baltimore)* 2001;**80**:159–172.
17. Freedberg RS, Kronzon I, Rumancik WM, Liebeskind D. The contribution of magnetic resonance imaging to the evaluation of intracardiac tumors diagnosed by echocardiography. *Circulation* 1988;**77**:96–103.
18. Gulati G, Sharma S, Kothari SS, Juneja R, Saxena A, Talwar KK. Comparison of echo and MRI in the imaging evaluation of intracardiac masses. *Cardiovasc Intervent Radiol* 2004;**27**:459–469.
19. Funari M, Fujita N, Peck WW, Higgins CB. Cardiac tumors: assessment with Gd-DTPA enhanced MR imaging. *J Comput Assist Tomogr* 1991;**15**:953–958.
20. Gomes AS, Lois JF, Child JS, Brown K, Batra P. Cardiac tumors and thrombus: evaluation with MR imaging. *Am J Roentgenol* 1987;**149**:895–899.
21. Winkler M, Higgins CB. Suspected intracardiac masses: evaluation with MR imaging. *Radiology* 1987;**165**:117–122.
22. Wintersperger BJ, Becker CR, Gulbins H, Knez A, Bruening R, Heuck A, Reiser MF. Tumors of the cardiac valves: imaging findings in magnetic resonance imaging, electron beam computed tomography, and echocardiography. *Eur Radiol* 2000;**10**:443–449.
23. Siripornpitak S, Higgins CB. MRI of primary malignant cardiovascular tumors. *J Comput Assist Tomogr* 1997;**21**:462–466.
24. Grebenc ML, Rosado-de-Christenson ML, Green CE, Burke AP, Galvin JR. Cardiac myxoma: imaging features in 83 patients. *Radiographics* 2002;**22**:673–689.
25. Luna A, Ribes R, Caro P, Vida J, Erasmus JJ. Evaluation of cardiac tumors with magnetic resonance imaging. *Eur Radiol* 2005;**15**:1446–1455.
26. Bruder O, Schneider S, Nothnagel D, Dill T, Hombach V, Schulz-Menger J, Nagel E, Lombardi M, van Rossum AC, Wagner A, Schwitter J, Senges J, Sabin GV, Sechtem U, Mahrholdt H. EuroCMR (European Cardiovascular Magnetic Resonance) registry: results of the German pilot phase. *J Am Coll Cardiol* 2009;**54**:1457–1466.