18F-FDG PET/CT imaging in the workup of cardiac and pericardial masses

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Cardiac and pericardial masses represent a rare, but large spectrum of different entities with variable morbidity and mortality.[1] Beside intra-cardiac thrombi, calcifications, and vegetations, primary and secondary tumors are the most important differential diagnosis in the workup of cardiac and pericardial masses.[2] Neoplastic lesions of the heart are mostly of secondary etiology, arising from extra-cardiac malignant tumors with a prevalence of 2-18%.[2,3] Primary tumors of the heart are more often benign than malign and include, with descending prevalence, myxoma, fibroelastoma, lipoma, fibroma, rhabdomyoma and hemangioma[4] Primary malign tumors like angiosarcoma, undifferentiated- or other soft tissue sarcoma, and mesothelioma are extremely rare and account for about 10% of primary cardiac tumors,[5] whose prevalence ranges between 0.0017% and 0.028%.[3,6] Cardiac masses may unlike compared to other organs, have hemodynamic consequences with blood flow obstruction, embolism, valve affection, and electrical or mechanical myocardial dysfunction due to myocardial infiltration. Therefore, the clinical presentation of patients with cardiac masses shows wide variability and ranges from asymptomatic low-risk incidental findings to patients suffering from stroke, acute or chronic heart failure symptoms. Hence, beside the assessment of hemodynamic consequences, early differentiation of cardiac masses and distinction from benign and malign tumors has enormous implication on treatment strategies and prognosis. Although imaging of cardiac masses has improved with the use of 3-dimensional imaging modalities like 3D-echocardiography, cardiac computed tomography (CCT) and cardiac magnet resonance imaging (CMR), definitive diagnosis of cardiac masses using solely noninvasive imaging remains challenging.[7] Diagnosis is often complicated by poor acoustic window and high inter-observer variability in echocardiography, unavailability of metabolic assessments in CMR and the unknown significance of incidental smaller lesions. As there is a lack of guidelines or consensus statements about the noninvasive diagnostic workup of patients with cardiac masses, approaches vary between centers. The gold standard to discriminate benign and malign lesions is based on the histopathological classification, assessed by biopsy or surgery, which are both by its nature associated with higher complication rates compared to noninvasive strategies. Therefore, improvement of the diagnostic accuracy of noninvasive imaging is required to: (a) reduce the rate of patients with asymptomatic benign entities undergoing unnecessary biopsy or surgery and (b) to identify patients requiring treatment due to malignancy in an early stage.

^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography imaging (FDG PET/CT) is a well-established functional imaging technique, which is widely used in clinical oncology to identify cancer metastasis as well as primary tumors. It combines the excellent spatial resolution of CT imaging to provide structural information with the ability of PET to visualize and quantify metabolic processes by the use of ^{18}F-FDG radiotracer. Nevertheless, evidence about its use in cardiac tumors is low and was longtime limited to case reports, small single-center studies[8-11] and one study including exclusively patients with secondary malignant tumors.[12] Two recent trials, conducted by Qin et al[13] and

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Table 1. Overview of studies investigating SUV_{max} cutoff scores for delineation between benign- and malign cardiac masses by FDG PET/CT

Author	Year	n	SUV_{max} cutoff	Sensitivity	Specifity
Yin et al	2021	59	3.8	93.1	93.3
Qin et al[13]	2020	64	6.75	92.1	88.9
D'Angelo et al[14]	2020	60	4.9	86.8	94.4
Rahbar et al[9]	2012	24	3.5	100	86
Shao et al[8]	2011	23	3.5 - 4.0	76.9	100
Nensa et al[10]	2015	20	5.2	100	92

D'Angelo et al[14] included a relatively large number of patients with cardiac masses (n = 64 and n = 60, respectively). Results of Qin et al were promising and showed high accuracy for the diagnosis of malignancy by FDG PET/CT. A maximal standardized uptake value (SUV_{max}) of 6.75 was found as optimal cutoff to distinguish between benign and malign masses. Sensitivity and specificity could be increased if CT features like tissue infiltration, involvement of epicardium, irregular tumor margin, presence of necrosis and pericardial- or pleural effusion and involvement of more than one chamber or vessel were considered. Main limitations were that some patients with extra-cardiac tumors, without suspicion for cardiac involvement were included and the lack of proper low-carbohydrate/high-fat diet to suppress ^{18}F-FDG accumulation in healthy myocardium. The objective of the study of Qin et al. was to determine the usability of FDG PET/CT in the workup of cardiac masses and the limitations of the study could confound cutoff-values for SUV_{max}, and lead to sample-bias. Furthermore, it remained unclear whether FDG PET/CT imaging could provide information beyond the standard echocardiography assessment. The study of D'Angelo et al did not suffer from such limitations and reported comparable results with a sensitivity of 86.8% and a specificity of 94.4% for a SUV_{max}-cutoff of 4.9.[14] As remarked by the authors of both studies, confirmation of their results and additional validation of the proposed cutoff score is warranted.

In this context, we would like to congratulate on the important study presented by Yin et al. in this issue, which provided further information on the use of FDG PET/CT in patients with cardiac masses. They included 59 patients with newly diagnosed cardiac masses by echocardiography who underwent additional FDG PET/CT to differentiate cardiac masses in benign and malignant lesions. In contrast to Qin et al.[13] patients with incidental finding of cardiac masses in FDG PET/CT were not included. Diagnosis was subsequently confirmed by histopathologic characterization as the reference standard. The authors were able to demonstrate a high diagnostic accuracy for delineation between benign and malign lesions by FDG PET/CT when applying a SUV_{max}-cutoff of 3.8 (sensitivity of 93.1% and a specificity of 93.3%). Consequently, FDG PET/CT was superior to the use of echocardiography alone, which showed a sensitivity of 72.4% and a specificity of 76.7%. FDG PET/CT has demonstrated incremental diagnostic value over echocardiography by identifying seven malignant extra cardiac lesions and two malignant cardiac tumors that were initially considered as benign, based on echocardiography alone. Strengths of the study are, with respect to the low prevalence of cardiac masses, the relatively large sample size, the inclusion of different modalities (FDG PET/CT, echocardiography, histopathology) and the technique and evaluation of image acquisition meeting current standards. Limitations are the following: due to the need for a reliable reference standard to assure the diagnosis of malignancy, only patients with subsequent surgery (n = 57) or biopsy (n = 2) were included. Patients with low pretest-probability for malignancy who did not undergo surgery or biopsy were not included. Additionally, patients with secondary cardiac tumors that previously received tumor-specific treatment or in which surgery was contraindicated due to metastatic disease were not included either. Hence, the results to do not represent the full spectrum of patients with cardiac masses, since patients with benign entities and secondary cardiac metastases in known malignant disease maybe underrepresented in this cohort. Although different baseline characteristics exist, the results are in line with previous studies on the use of FDG PET/CT in patients with cardiac masses. Table 1 provides an overview of studies using FDG PET/CT in patients with cardiac masses and their proposed cutoff values for differentiation between malignant and benign lesions. The homogeneity between studies underlines the value of FDG PET/CT in the detection and differentiation of cardiac masses, also with regard to the diagnostic accuracy of different SUV_{max}.[13]

From a clinical point of view and based on the findings of Yin et al, patients with unknown dignity of cardiac

masses or patients with high pretest probability for malignancy and suspected extra cardiac metastasis may undergo additional FDG PET/CT imaging. In disseminated neoplastic disease or in patients with asymptomatic benign tumors, FDG PET/CT may not have an impact on the treatment strategy nor on the prognosis. Further, one has to be aware, that cardiac uptake of FDG is not a specific marker for cardiac neoplasms and may need further evaluation in some cases.[15] Although this study has proven a value for FDG PET/CT, transthoracic or transoesophageal echocardiography will remain the cornerstone in the diagnostic workup of cardiac masses, due to their ability to assess hemodynamic consequences, its availability and cost-effectiveness. Especially myxoma, papillary fibroelastoma, and angiosarcoma have characteristic structural patterns, allowing high diagnostic accuracy by the use of echocardiography, CMR and CCT without need for metabolic FDG PET/CT assessments.[1,7] If size, growth dynamic, invasiveness, and vascularization are highly suspicious for malignancy, and in cases of left-sided located benign tumors or right-sided symptomatic benign tumors, it has to be questioned if another imaging modality is necessary or prompt surgical excision should be preferred.[16] Nevertheless, comparison of other imaging modalities to FDG PET/CT is needed. Particularly the use of CMR is promising[10] with its ability to assess perfusion and to characterize the tissue including depiction of fibrosis, edema and fat. There is some evidence that combining FDG PET/CT with CMR leads to a higher accuracy compared to the use of these modalities alone.[10] Hence, the use of multimodality imaging, combining the advantages of the different methods should be evaluated in future studies.

To summarize, the management and workup of cardiac and pericardial masses remains challenging and a comprehensive multimodality imaging approach is crucial to delineate malignancy and hemodynamic consequences of cardiac and pericardial masses.[1] Awareness for the strengths and the weaknesses of different imaging modalities is required to choose the most appropriate approach on a case-by-case basis. Taken into account the results of the present study by Yin et al, FDG-PET/CT is useful in patients with cardiac masses of unknown dignity but also in cases with a high pre-test probability for malignancy and extracardiac involvement. FDG-PET cannot replace echocardiography and should be used as a secondary and complementary modality in selected cases.

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