Electrogram-guided Endomyocardial Biopsy Yield in Patients with Suspected Cardiac Sarcoidosis

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Sarcoidosis is a multisystem disease that is characterized by T-cell mediated formation of noncaseating granulomas in affected organs. The disease commonly might involve hilar lymphadenopathy, lungs, liver, spleen, heart, and other organs. The natural course and prognosis of the disease generally depends on the extent of the disease and the organs affected where spontaneous remission occurs in around two-thirds of patient.[1] Involvement of the heart is recognized in around 30% of patients and is associated with poor prognosis.[2] The presentation of patients with cardiac sarcoidosis varies significantly; it can range from mild to severe disease such as heart failure and fatal arrhythmias. Patients with cardiomyopathies might require implantable cardiac defibrillators or cardiac resynchronization therapy for sudden death prevention.[3,4] Cardiac sarcoidosis can either present alongside extracardiac manifestations or isolated.[5]Diagnosis of cardiac

sarcoidosis presents a particular challenge since there is no gold standard diagnostic tool and the presentation is variable.[6] There are no disease-specific biomarkers that can reliably be used for diagnosis. Clinicians typically rely on current published guidelines for diagnostic criteria of cardiac sarcoidosis such as those of Heart Rhythm Society (HRS) and the Japanese Ministry of Health and Welfare (JMHW). The revised JMHW criteria provide a diagnosis either through histological evidence on biopsy or through the fulfillment of major and minor criteria that do not include cardiac PET whereas the HRS criteria provide either a definite pathway for diagnosis through histology or a clinical pathway for diagnosis of probable cardiac sarcoidosis that includes both cardiac PET and CMR as criteria.[7,8] A definitive diagnosis of cardiac sarcoidosis can be obtained if endomyocardial biopsy can show noncaseating granulomas in the context of suspected cardiac sarcoidosis and other granulomatous diseases are excluded. However, endomyocardial biopsy has a low sensitivity of 20-30% since it is limited by several factors such as technique, sampling, patchy distribution of granulomas, location of lesions, and stage of the disease at the time of biopsy.[5] Areas of inflammation and scarring typically show abnormal electrogram morphology, hence, it is thought that electrogram guidance may help in increasing the yield of endomyocardial biopsies. Electrogram guidance would potentially help avoiding normal myocardium during biopsy leading to increased yield and sensitivity.[9]

In their study, Ezzedine et al. assessed the diagnostic yield of electrogram-guided endomyocardial biopsy and investigated association between positive endomyocardial biopsy and prognosis in patients with suspected cardiac sarcoidosis.[10] This retrospective observational study included seventy-nine patients between 2011 and 2019 who had suspected cardiac sarcoidosis based on clinical presentation and findings on late gadolinium-enhancement cardiac magnetic resonance and/or cardiac positron emission tomography-computed tomography with N-13 NH3 perfusion imaging and F-18 fluorodeoxyglucose. Biopsy was done in patients suspicious of cardiac sarcoidosis in patients without extracardiac sarcoidosis or those with extracardiac disease but atypical/equivocal findings of cardiac sarcoidosis on imaging and meeting criteria in HRS guidelines as per the routine practice in Mayo Clinic. Mapping of the heart was performed prior to biopsy with partial guidance based on pre-procedural cardiac imaging. In patients with no identifiable abnormalities on electrogram, biopsies were taken from areas corresponding to those with abnormalities on pre-procedural imaging. Collected specimens were processed according to protocol and assessed by a blinded specialist. These specimens were considered positive if there was a combination of non-necrotizing granulomas, interstitial fibrosis, and scatted eosinophils. The study showed that electrogram-guided endomyocardial biopsy was associated with an adequate negative predictive value but low positive predictive value. A diagnosis of probable cardiac sarcoidosis can be made in patients with extracardiac manifestations according to established guidelines whereas in patients with suspected isolated cardiac sarcoidosis this is more difficult and as such biopsies play a more major role here. This study showed that, when guided by electrograms, endomyocardial biopsies had a higher diagnostic yield (41%) than that established in literature around 20-25%. Utilizing both abnormalities seen on both electrograms and on CMR or PET showed the highest diagnostic yield in endomyocardial biopsies. This acts as an important point of consideration for further research because accurate and timely diagnosis is paramount due to the diagnostics challenges and poor prognosis seen in cardiac sarcoidosis.[10]

Previous evidence had shown that a positive endomyocardial biopsy for sarcoidosis was associated with poor prognosis.[11]However, LVAD and transplantation-free survival was found to be similar regardless of status of endomyocardial biopsy in this study.[10] The authors explained that this could be explained by earlier detection of disease, differences in treatment, or more subtle detection of areas of involvement through electrograms. This study was well conducted but has been limited by its nature of being a retrospective observational study. Also, mapping was mostly limited to the right ventricle which may have underestimated the diagnostic yield of biopsies. This study represents the management done in a single tertiary care center which may not represent the same practice in other institutions with different facilities. Further multicenter and prospective studies are warranted to corroborate the data here and assess diagnostic and therapeutic modalities and long-term outcomes in patients.

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