Endomyocardial biopsy for histological analysis is an important diagnostic tool in non-ischaemic cardiomyopathy. However, endomyocardial biopsy is invasive and associated with some risk, albeit low. The diagnostic yield is also low, because (1) pathology is often heterogeneous, (2) current interventional techniques do not permit targeted biopsy, and (3) histological analysis can be difficult. For these reasons, endomyocardial biopsy has lost favour among adult cardiologists, except in cardiac transplant, where patients usually undergo serial biopsies to monitor graft health. Understandably, a non-invasive alternative to endomyocardial biopsy would be attractive to clinicians and patients alike.

The great advantage of cardiovascular magnetic resonance (CMR) compared with other non-invasive imaging modalities is tissue characterization. Patterns of late gadolinium enhancement (LGE) can differentiate between viable and infarcted myocardium, and between ischaemic and non-ischaemic cardiomyopathy.1 Even though LGE informs diagnosis and prognosis in ischaemic cardiomyopathy,2 there is less concrete evidence that LGE is as useful in non-ischaemic cardiomyopathy, which is characterized by diffuse myocardial fibrosis. This is because LGE interpretation relies on relative difference in signal intensity between ‘normal’ and ‘abnormal’ myocardium, although quantification using thresholds based on multiples of signal intensity standard deviation (SD) is possible.

\(T_1\) mapping has emerged as the most promising CMR technique for the identification and quantification of diffuse fibrosis. There is a growing body of observational data showing that differences exist in myocardial \(T_1\) values between normal subjects and patients with a wide range of disease processes, including dilated or hypertrophic cardiomyopathy,3 ischaemia,4 amyloid,5 iron overload,6 Takotsubo cardiomyopathy,7 and myocarditis.8 \(T_1\) values also identify subclinical myocardial involvement in systemic disease6,9 and provide prognostic information.10 An important histological commonality of diffuse myocardial disease is expansion of the extracellular space. Pre- and post-contrast \(T_1\) or extracellular volume pixel-by-pixel maps can reveal abnormalities not apparent with traditional LGE imaging.11

The pioneering study by Illes et al.12 demonstrated for the first time a correlation between post-contrast \(T_1\) values and the degree of histological fibrosis in patients with heart failure. Others have corroborated this finding in non-ischaemic cardiomyopathies including hypertrophic cardiomyopathy and aortic stenosis.13 In this issue of the European Heart Journal – Cardiovascular Imaging, Illes et al.14 provide further corroborative evidence in patients undergoing cardiac transplant or surgical myectomy. Although the transplant patient sample size was small (\(n = 11\)), the authors should be commended for obtaining whole heart specimens for histological analysis. In these 11 patients, a statistically significant correlation was observed between extent of LGE (signal intensity threshold of 6 × SD) and histological fibrosis determined by Masson’s trichrome and Picrosirius red stains (\(R = 0.91, P < 0.001\)). The authors were conscious of the methodological limitations of the study, in particular the delay between CMR and transplantation (592 days) due to the fact that most patients had devices implanted, precluding further MRI studies. Notwithstanding the primary focus on association with LGE, the authors strove to measure post-contrast \(T_1\) values, but these were only available in four patients and no pre-contrast (or ‘native’) \(T_1\) values were obtained. Nevertheless, a statistically significant correlation was observed between post-contrast \(T_1\) values and histological fibrosis (\(R = -0.64, P = 0.002\)), although larger sample sizes are needed to confirm this finding.

In the future, CMR could also improve diagnosis by improving the yield from endomyocardial biopsy. Pre-procedural LGE imaging or \(T_1\) mapping could inform on the presence or absence of overt disease and could advise the interventionist where to target the biopsy. On the other hand, if LGE imaging or \(T_1\) mapping showed only epicardial enhancement in a patient with suspected myocarditis, then the yield from endomyocardial biopsy is likely to be very low and maybe not worth attempting. Without a doubt, the preferred strategy would be biopsy performed under real-time MR guidance with a MR-visible biopsyome, which would enable precise targeting of abnormal tissue (e.g. highlighted by LGE) and reduce risk by avoiding iatrogenic injury to important structures.

An indisputable challenge to widespread adoption of \(T_1\) mapping remains ongoing technological sequence development preventing standardization of imaging and post-processing methodologies,15 and determination of reference normal values, which in turn prevents efficient translation into clinical practice. The Australian group is...
visionary in emphasizing the need for histological cross-referencing of novel non-invasive imaging measurements. Such evidence is crucial to cement the future role of CMR in the diagnosis and treatment of cardiomyopathies. An international registry of combined histology findings and non-invasive imaging measurements would help build the necessary evidence. Such a registry would require collaboration between non-invasive imaging, histopathology, and interventional disciplines.

Finally, the chronicity of non-ischaemic cardiomyopathy necessitates monitoring of disease progression and response to therapy. The risk associated with repeated endomyocardial biopsy is difficult to justify in most patients. $T_1$ mapping could offer a non-invasive alternative, but further outcome studies are required to evaluate whether $T_1$ values change over time, and if so, to determine the clinical significance of this change.

References

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