



Editorial

Chronic kidney disease with elevated myocardial native T1 – Is this only due to myocardial fibrosis?

The relationship and interaction between cardiac and renal disease is complex. An improvement in the cardiovascular system can have an improvement in the renal system [1] whilst a detrimental effect on the renal system can have a similarly negative effect on the cardiac system.

Patients with chronic kidney disease (CKD) have an increased risk of cardiovascular death and complications [2]. Cardiac remodeling in the presence of chronic kidney disease frequently involves left ventricular hypertrophy which is a marker of adverse prognosis and a hallmark of ureamic cardiomyopathy [3,4]. Other features include left ventricular dilatation and myocardial fibrosis [3].

T1 mapping is a well-established tool in cardiovascular magnetic resonance (CMR) in which multiple T1 weighted images are acquired and compiled creating a final image with the T1 values of the tissue [5]. When this is performed without contrast, the values provided are called native T1. Utilising native T1 to assess the presence of myocardial fibrosis is well established, histologically validated and carries prognostic significance [6,7]. Several studies have previously established that native T1 is elevated in CKD patients ranging from early CKD to end-stage renal failure [3,4,8]. However, there are many variables which can affect the native T1 values such as scanner type, tesla strength, gender and type of T1 mapping sequence [6,9].

In this study by Chen et al. [10], they demonstrated elevated native T1 values in patients with CKD compared to age and gender matched controls with both cohorts having more than 200 patients each. This is one of the largest studies looking into myocardial fibrosis in CKD patients. Furthermore, the native T1 values were correlated with aortic stiffness. The presence of increased arterial and aortic stiffness in CKD patients is consistent with the published literature [11]. However, it is the correlation of native T1 values and aortic stiffness which is the novel finding of this paper. Nonetheless, there are two important issues raised by this study's inference that raised native T1 is due to myocardial fibrosis.

Firstly, one unmentioned confounder of native T1 values is the influence of the T2 properties of the tissue [6]. A rise in T2 is normally seen in tissue with increased water or fat content. Native T1 and T2 are directly related. A rise in T2 results in a rise in native T1 values. This is particularly important as myocardial oedema which can result in a raised T2 could be present due to the tendency of CKD patients to have soft tissue oedema. T2 data has actually not been included in other T1 mapping papers looking into CKD patients [3,4,8]. T2 was not included in this study either so the influence of myocardial oedema is yet undetermined. Indeed, the data from which this study was performed does include T2 mapping data so we wait in expectation to see the subsequent results in this patient cohort (NCT03749551).

Further studies looking directly at the issue of myocardial oedema in CKD patients are also required.

The second issue is choice of CMR T1 mapping parameter for identifying myocardial fibrosis. For CMR, extracellular volume (ECV) is the second parameter which can be used to identify myocardial fibrosis. This can be done by performing post-contrast T1 mapping sequences allowing subsequent calculations of ECV. Whether ECV or native T1 has been shown to have the best correlation with histology has differences of opinion and further studies validating both parameters with histology will be most welcome. Previously, the Society of Cardiovascular Magnetic Resonance T1 mapping guidelines in 2017 indicated that ECV had better histological correlation [6] and there are more studies correlating ECV with histology [7].

Nonetheless, Chen et al.'s study provides additional data confirming previous studies findings that myocardial fibrosis as inferred by native T1 is present in CKD patients. Gaps in our knowledge include the lack of histological confirmation of the T1 mapping findings of myocardial fibrosis in CKD patients and the prognostic significance of T1 mapping in CKD patients.

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Declaration of Competing Interest

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References

- [1] T. Hama, K. Oikawa, A. Ushijima, N. Morita, T. Matsukage, Y.J. Ikari, et al., Effect of cardiac rehabilitation on the renal function in chronic kidney disease - analysis using serum cystatin-C based glomerular filtration rate, *Int. J. Cardiol. Heart Vasc.* 19 (2018) 27–33.
- [2] United States Renal Data System, *Epidemiology of Kidney Disease in the United States*, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2017.
- [3] M.P. Graham-Brown, D.S. March, D.R. Churchward, D.J. Stensel, A. Singh, R. Arnold, et al., Novel cardiac nuclear magnetic resonance method for noninvasive assessment of myocardial fibrosis in hemodialysis patients, *Kidney Int.* 90 (4) (2016) 835–844.
- [4] E. Rutherford, M.A. Talle, K. Mangion, E. Bell, S.M. Rauhalampi, G. Roditi, et al., Defining myocardial tissue abnormalities in end-stage renal failure with cardiac magnetic resonance imaging using native T1 mapping, *Kidney Int.* 90 (4) (2016) 845–852.
- [5] P. Kellman, M. Hansen, T1-mapping in the heart: accuracy and precision, *J. Cardiovasc. Magn. Reson.* 16 (1) (2014) 2.
- [6] D.R. Messroghli, J.C. Moon, V.M. Ferreira, L. Grosse-Wortmann, T. He, P. Kellman, et al., Clinical recommendations for cardiovascular magnetic resonance mapping

- of T1, T2, T2* and extracellular volume: a consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI), *J. Cardiovasc. Magn. Reson.* 19 (1) (2017) 75.
- [7] V.O. Puntmann, S. Valbuena, R. Hinojar, S.E. Petersen, J.P. Greenwood, C.M. Kramer, et al., Society for Cardiovascular Magnetic Resonance (SCMR) expert consensus for CMR imaging endpoints in clinical research: part I - analytical validation and clinical qualification, *J. Cardiovasc. Magn. Reson.* 20 (1) (2018) 67.
- [8] N.C. Edwards, W.E. Moody, M. Yuan, M.K. Hayer, C.J. Ferro, J.N. Townend, et al., Diffuse interstitial fibrosis and myocardial dysfunction in early chronic kidney disease, *Am. J. Cardiol.* 115 (9) (2015) 1311–1317.
- [9] X. Tong, V. Li, A. Liu, E. So, Q. Chan, K. Ho, et al., Cardiac magnetic resonance T1 mapping in adolescent and young adult survivors of childhood cancers: a case-control study, *Circulation Cardiovascular imaging* 12 (4) (2019) 1–3.
- [10] M. Chen, L. Arcari, J. Engel, T. Freiwald, S. Platschek, H. Zhou, et al., Aortic stiffness is independently associated with interstitial myocardial fibrosis by native T1 and accelerated in the presence of chronic kidney disease, *Int. J. Cardiol. Heart Vasc.* 24 (2019) 1–8.
- [11] N.C. Edwards, W.E. Moody, C.D. Chue, C.J. Ferro, J.N. Townend, R.P. Steeds, Defining the natural history of uremic cardiomyopathy in chronic kidney disease: the role of cardiovascular magnetic resonance, *JACC Cardiovasc. Imaging* 7 (7) (2014) 703–714.

Ming-Yen Ng

Department of Diagnostic Radiology, The University of Hong Kong,

Hong Kong

Corresponding author.

E-mail address: myng2@hku.hk.

Pui Min Yap

Department of Diagnostic Radiology, The University of Hong Kong,

Hong Kong

Kai Hang Yiu

Department of Medicine, The University of Hong Kong, Hong Kong

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