Magn Reson Med Sci 2021; 20; 139–151
doi:10.2463/mrms.rev.2020-0007
Published Online: May 11, 2020

REVIEW

Clinical Importance of Myocardial T_2 Mapping and Texture Analysis

Yasuo Amano[1*], Yuko Omori[1], Chisato Ando[2], Fumi Yanagisawa[1], Yasuyuki Suzuki[3], Xiaoyan Tang[4], Hiroko Kobayashi[4], Ryo Takagi[1], and Naoya Matsumoto[3]

Late gadolinium enhancement (LGE) magnetic resonance imaging (MRI) is valuable for diagnosis and assessment of the severity of various myocardial diseases owing to its potential to visualize myocardial scars. T_1 mapping is complementary to LGE because it can quantify the degree of myocardial fibrosis or edema. As such, T_1-weighted imaging techniques, including LGE using an inversion recovery sequence, contribute to cardiac MRI. T_2-weighted imaging is widely used to characterize the tissue of many organs. T_2-weighted imaging is used in cardiac MRI to identify myocardial edema related to chest pain, acute myocardial diseases, or severe myocardial injuries. However, it is difficult to determine the presence and extent of myocardial edema because of the low contrast between normal and diseased myocardium and image artifacts of T_2-weighted images and the lack of an established method to quantify the images. T_2 mapping quantifies myocardial T_2 values and help identify myocardial edema. The T_2 values are significantly related to the clinical symptoms or severity of nonischemic cardiomyopathy. Texture analysis is a postprocessing method to quantify tissue alterations that are reflected in the T_2-weighted images. Texture analysis provides a variety of parameters, such as skewness, entropy, and grey-scale non-uniformity, without the need for additional sequences. The abnormal signal intensity on T_2-weighted images or T_2 values may correspond to not only myocardial edema but also other tissue alterations. In this review, the techniques of cardiac T_2 mapping and texture analysis and their clinical relevance are described.

Keywords: *cardiac MRI, T_2-weighted imaging, myocardium, T_2 mapping, texture analysis*

Introduction

Late gadolinium enhancement (LGE) magnetic resonance imaging (MRI) is valuable for diagnosis and assessment of the severity of various myocardial diseases owing to its potential to visualize myocardial scar.[1–3] LGE MRI provides binary contrast between scarred and unscarred tissues, while T_1 mapping is complementary to LGE because it can quantify the degree of myocardial fibrosis or edema.[4–6] As such, T_1-weighted imaging techniques, including LGE using an inversion recovery sequence, contribute to cardiac MRI. Conversely, T_2-weighted imaging is widely used for identification of the pathological status in many organs, because T_2 values are correlated with edema, cellular proliferation, and vessel densities.[7,8] Because the scarring tissues or fibrosis are more prominent than neoplasms and inflammatory diseases in the myocardium, T_1-weighted imaging is more popular than T_2-weighted imaging in the field of cardiac MRI.

Recently, T_2-weighted imaging has been used to identify myocardial edema related to chest pain, acute myocardial diseases, or severe myocardial injuries.[9–13] However, it is difficult to evaluate the presence and extent of myocardial edema because of the low contrast between normal and diseased myocardium, image artifacts, and the lack of an established method to quantify the T_2-weighted images; therefore, some quantitative methods of myocardial T_2 are required to evaluate myocardial edema or injuries.

T_2 mapping quantifies myocardial T_2 values and help identify myocardial edema.[14,15] Texture analysis is a postprocessing method to quantify the tissue alterations that are reflected in any medical image. Texture analysis provides a lot of parameters, such as skewness, entropy, and grey-scale nonuniformity,

[1]Department of Radiology, Nihon University Hospital, Tokyo, Japan
[2]Division of Radiological Technology, Nihon University Hospital, Tokyo, Japan
[3]Department of Cardiology, Nihon University Hospital, Tokyo, Japan
[4]Department of Pathology, Nihon University Hospital, Tokyo, Japan

[*]Corresponding author: Department of Radiology, Nihon University Hospital, 1-6, Kandasurugadai, Chiyoda-ku, Tokyo 101-8309, Japan. Phone: +81-3-3293-1711, E-mail: yas-amano@nifty.com

Received: January 12, 2020 | Accepted: April 11, 2020

without the need for additional sequences.[16–18] The texture analysis has been applied to cardiac T_2-weighted images, which identifies diffuse myocardial tissue abnormalities associated with hypertrophic cardiomyopathy.[16] These MRI and post-processing tools may be valuable for evaluating myocardial diseases in clinical practice. In this review, the T_2-weighted cardiac MRI techniques, cardiac T_2 mapping, and texture analysis, and their clinical relevance for several myocardial diseases are described. We showed T_2-weighted images, T_2 mapping, or other imaging acquired by a 1.5T imager (Ingenia, Philips Healthcare, Best, The Netherlands).

Imaging Techniques Used in Cardiac T_2-weighted MRI

T_2-weighted imaging is widely used for tissue characterization and identification of pathologies in many organs, but cardiac and respiratory motion, high intensity of the pericardial fat and intraventricular blood, and blood flow artifacts prevent identification of myocardial injuries.[19] Therefore, electrocardiogram (ECG) gating and black-blood technique using double inversion recovery (IR), chemical shift suppression or short inversion time IR (STIR or triple IR) and breath-holding are required for cardiac T_2-weighted MR images with sufficient imaging quality.[19–22] Breath-holding is used to eliminate respiratory artifacts, and turbo spin-echo and parallel imaging techniques is used to reduce the breath-holding time.[19,22–24] Black-blood imaging technique combined with ECG gating reduce the blood signals, flow artifacts, and cardiac motion.[20] The stagnant blood flow adjacent to hypokinetic myocardium can show high intensity (Fig. 1a), and the changes in the RF thickness of IR pulse may reduce the signals in our experience. Spectrally selective fat suppression may provide a higher signal-to-noise ratio than triple IR in the T_2-weighted imaging, but it is more sensitive to magnetic inhomogeneity.[21] Therefore, either technique can be applied according to the magnetic field strength, MR images used, and shimming methods, to reduce fat signals from the pericardium and chest wall. Fat suppression improves the dynamic range identification of myocardial edema.

Quantitative Techniques of Myocardial T_2

Signal ratio measurement on T_2-weighted images

Measurement of the signal ratio between the myocardium and skeletal muscle is useful for the detection of myocardial edema associated with acute myocarditis.[10,25] This quantitative method is easy and fast in clinical practice. A gantry coil has been used to measure the signal intensities of the myocardium and skeletal muscle to avoid the geometrical factor or signal correction associated with the use of multichannel receiver coil and associated parallel imaging techniques. However, the multichannel coil is commonly used to improve image quality and throughput of the cardiac MRI examinations. The skeletal myositis can be associated with myocarditis.[26] As other quantitative methods, including T_2 mapping and texture analysis, emerge, the signal ratio measurement is becoming obsolete.

T_2 mapping

T_2 mapping is a quantitative method for identifying and estimating myocardial injuries. T_2-prepared steady-state free

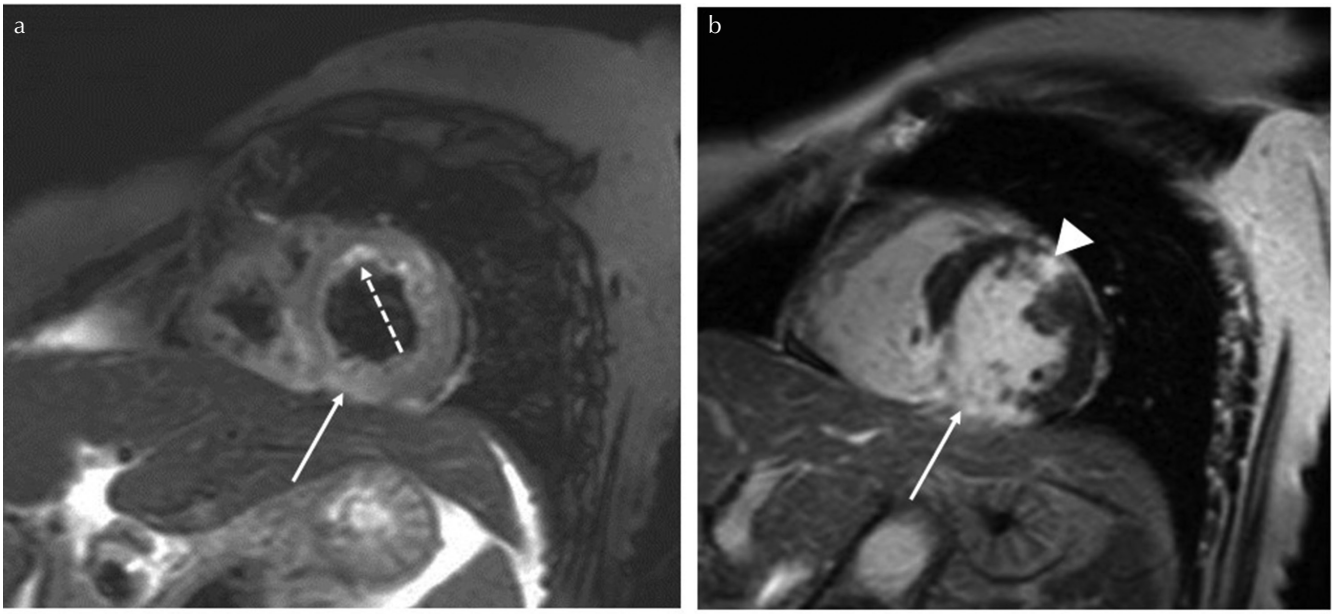

Fig. 1 Myocardial infraction. T_2-weighted imaging visualizes only acute myocardial infarction (**a**, arrow), while both acute (arrow) and chronic infarction (arrowhead) show late gadolinium enhancement (**b**). The dotted arrow shows the stagnant flow artifact adjacent to chronic myocardial infarction (**a**).

precession or multi-echo gradient- and spin-echo imaging sequences are used for T_2 mapping.[27–29] ECG gating, fat and blood signal suppression, and fast data acquisition techniques are commonly applied to T_2 mapping to measure myocardial T_2 values accurately during a single breath-holding.[16,27–29] Otherwise, navigator gating is used to minimize respiratory artifacts.[5] The advantages of T_2 mapping over T_1 mapping are the fewer selection of MRI sequences, the reduced variability of myocardial T_2 values (i.e., 45–55 ms) despite magnetic field strength, imaging sequences and MR machine vendors, its high sensitivity to myocardial edema, and the ability of visual comparison between T_2 mapping and T_2-weighted images.[29] These allow us to refer to previous reports about myocardial T_2 mapping, although the range of normal myocardial T_2 values should be determined in each institution.[30] We are also able to determine the imaging planes of T_2 mapping appropriately by referring to the T_2-weighted images. By contrast, myocardial T_1 values are greatly affected by magnetic field strength, and many T_1 mapping sequences have been reported.[4,30] No comparison has been made between T_1 mapping and non-contrast-enhanced T_1-weighted images. A limitation of T_2 mapping is its inability to quantify myocardial fibrosis, which is a common pathology associated with various myocardial diseases.

Texture analysis

Texture analysis is a quantitative postprocessing method based on statistical analyses.[17,18] The histogram is a well-known quantitative analysis which gives the grey-level value of each pixel. From the histogram, the mean value, variance, skewness, and 90% percentile of a certain area are derived, which can characterize the signal intensity pattern of the area reflecting the corresponding tissues in the body. The spatial variation and correlation between the grey-level value of the one pixel and that of its neighbor may reflect the texture of tissues.[17,18] The neighboring pixels can be defined in any direction in the medical images. If many pixels have the same grey-level on a certain direction, for example, the region of interest may consist of the uniform biological tissues. The degree of grey-level changes, randomness, or inhomogeneity of the pixel distribution can be calculated, and these texture features may reflect the degeneration, necrosis, and mixture of several tissues in the pathology. As such, texture analysis provides a variety of parameters, such as entropy and grey-scale nonuniformity, and can be applied to any imaging modality, sequence, and pathology (Fig. 2).[17,18,31,32] Texture analysis has been already used in the field of cardiac MRI, resulting in the identification of myocardial tissue alterations.[16,31,32] A combination of T_2 mapping and texture analysis has been also performed to evaluate myocarditis showing the acute-onset symptoms.[33] In this case, texture analysis is applied to grey-level reflecting myocardial T_2 values. The advantages of texture analysis are its abundant parameters, the lack of necessity for additional imaging sequences, which allows for retrospective analysis of the past image series, and the existence of open-access software.[17,18] There is a possible demerit to

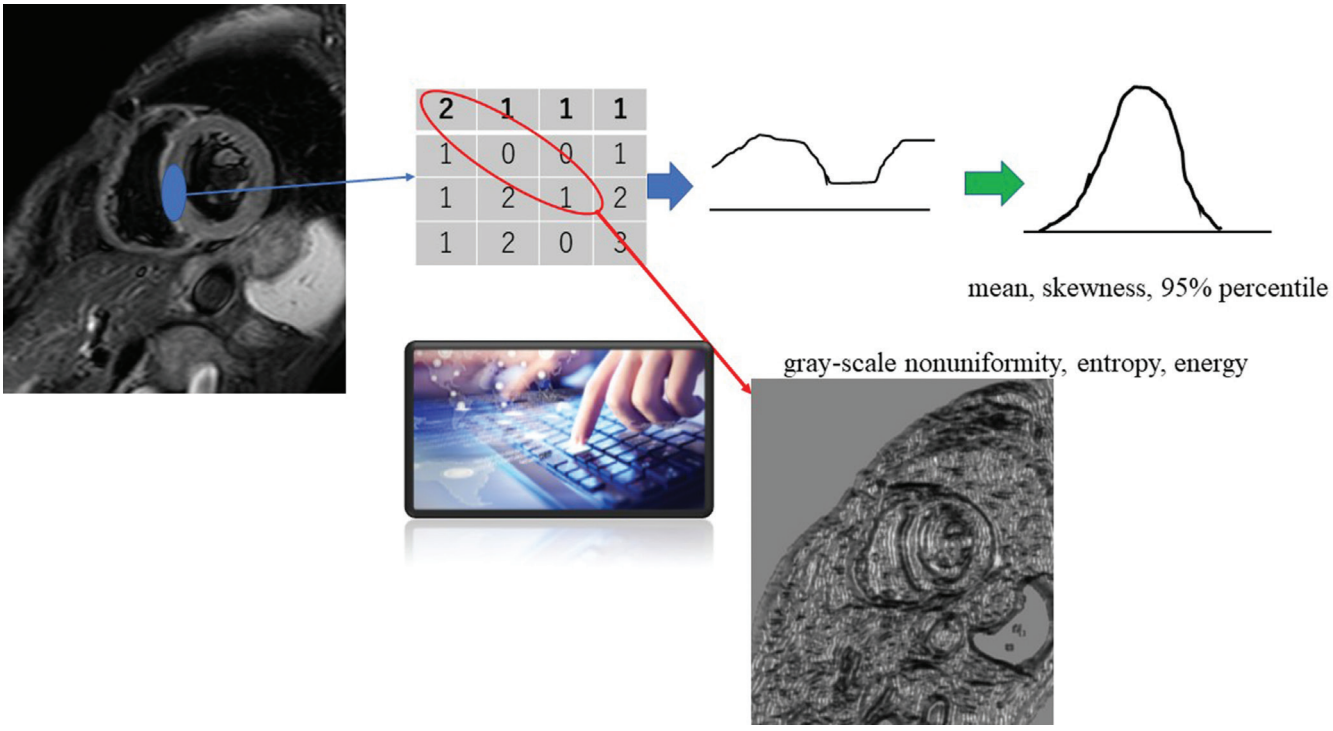

Fig. 2 Texture analysis provides numerous information about the structure and appearance of the tissues by descring nurmerical variables, their statistical features, and correlation and distribution of the variables.

texture analysis: too many parameters are difficult to use in clinical routines and may overfit the quantitative data. Thus, we should select several parameters from more than 200 provided by texture analysis with artificial intelligence or empirically.[32] It is also difficult to determine pathological alterations of the myocardium that are consistent with abnormal variables given by the texture analysis.

Clinical Application and Relevance of Quantitative Myocardial T_2

Myocardial infarction

T_2-weighted cardiac MRI is useful for differentiating between acute and chronic myocardial infarction because of its potential to identify "acute" myocardial injury, myocardial edema (Fig. 1).[9] The discrepancy between T_2-weighted and LGE imaging indicate the area at risk that can be salvaged by intervention, although there are some controversies about the ability of cardiac MRI to identify the area at risk.[34] In addition, myocardial edema in acute myocardial infarction may suggest a poor prognosis for patients even without myocardial scarring.[35] T_2 mapping and texture analysis have been used to identify acute myocardial infarction and to differentiate between acute and chronic infarction (Fig. 3).[31,36] These techniques provide quantitative and precise identification of the myocardial edema associated with coronary artery diseases (Fig. 4).

Myocarditis

T_2-weighted imaging is useful for detecting myocardial edema associated with acute myocarditis (Fig. 5a).[10] The myocardial edema localizes in the subepicardial region dominantly and shows noncoronary distribution, as LGE does. (Figs. 5a and 5b)[19] Although the signal ratio between the myocardium and skeletal muscle was measured to identify myocarditis, T_1 or T_2 mapping should be used to quantify the edema accurately (Figs. 5c and 5d).[14,15,25,26] Pan et al.[26] have indicated that

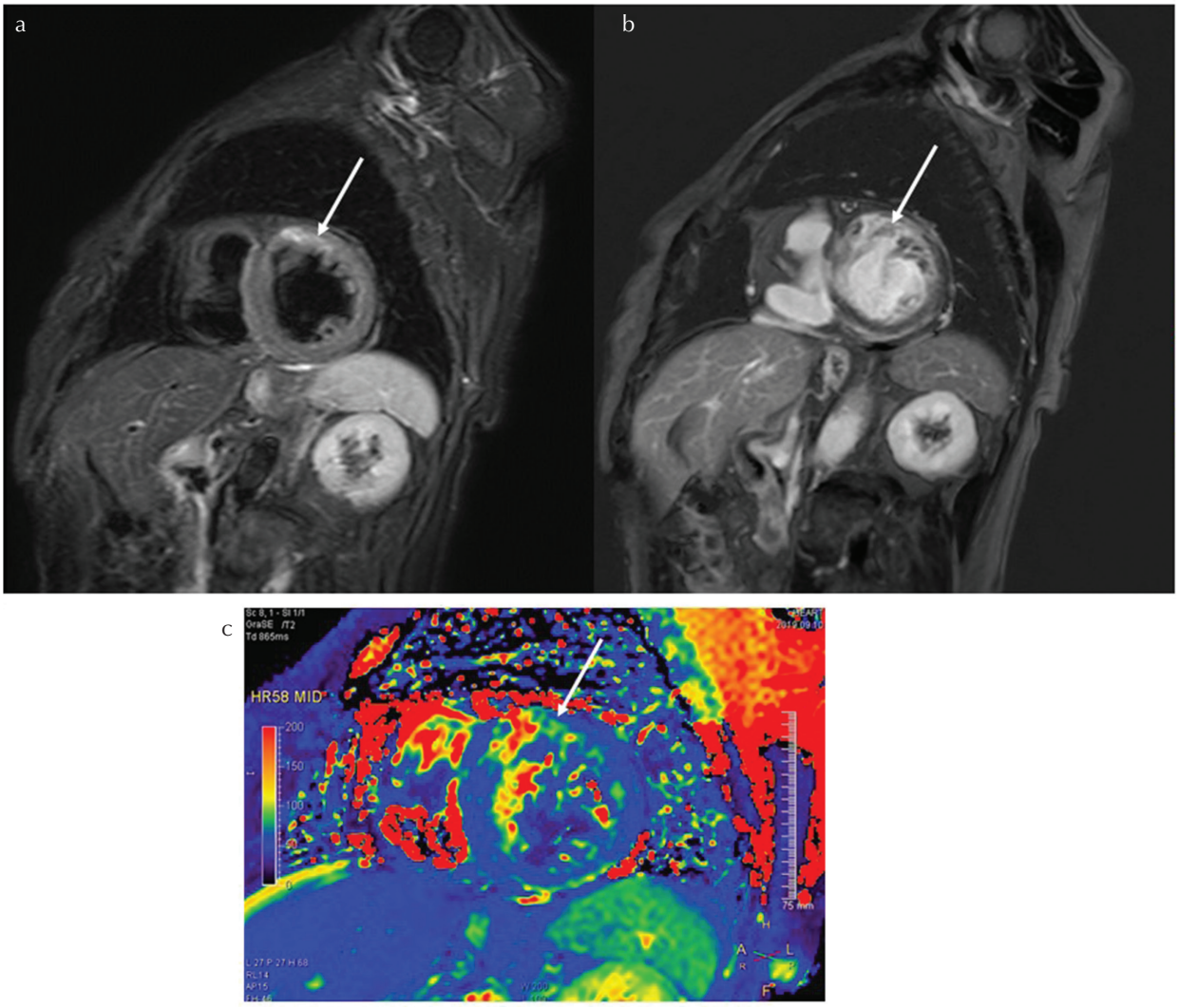

Fig. 3 Acute myocardia linfarction. T_2-weighted (**a**) and late gadolinium enhancement images (**b**) show acute myocardial infarction at the anterior region (arrow). T_2 mapping shows that the T_2 value of infarction is 61 ms and that of noninfarcted myocardium is 57 ms (**c**).

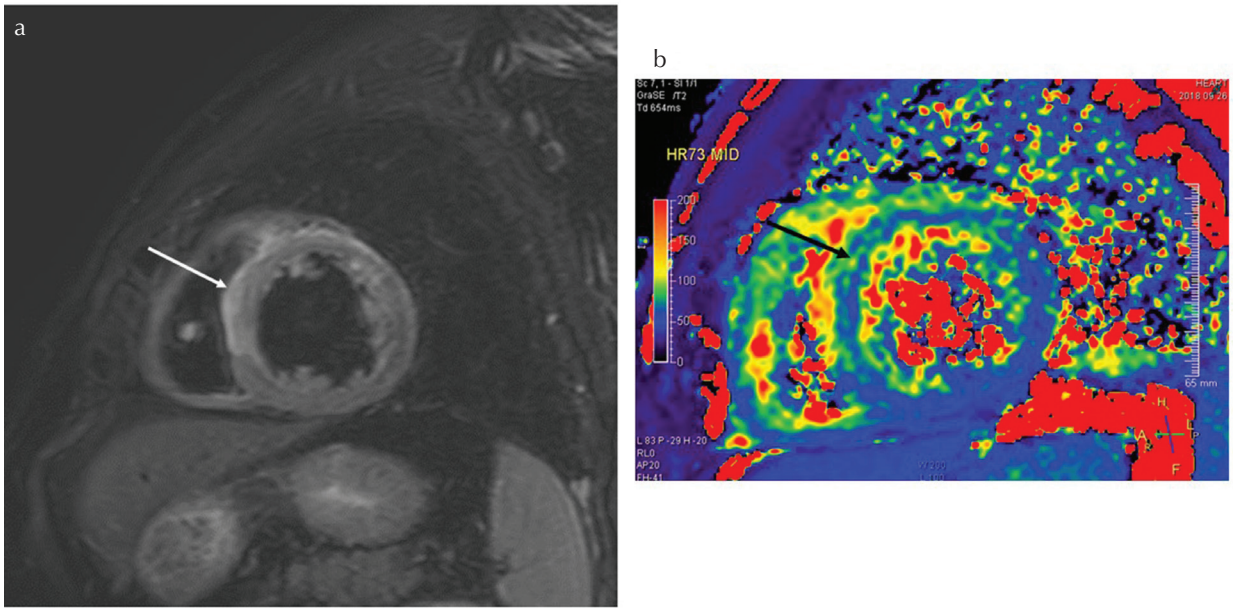

Fig. 4 Acute myocardia linfarction. T_2-weighted imaging indicates acute myocardial infarction at the septal region in a patient with renal impairment that is contraindicated for a gadolinium-based contrast agent (**a**, arrow). T_2 mapping shows that the T_2 value of infarction is 65 ms (arrow) and that of noninfarcted myocardium is 43 ms in this patient (**b**).

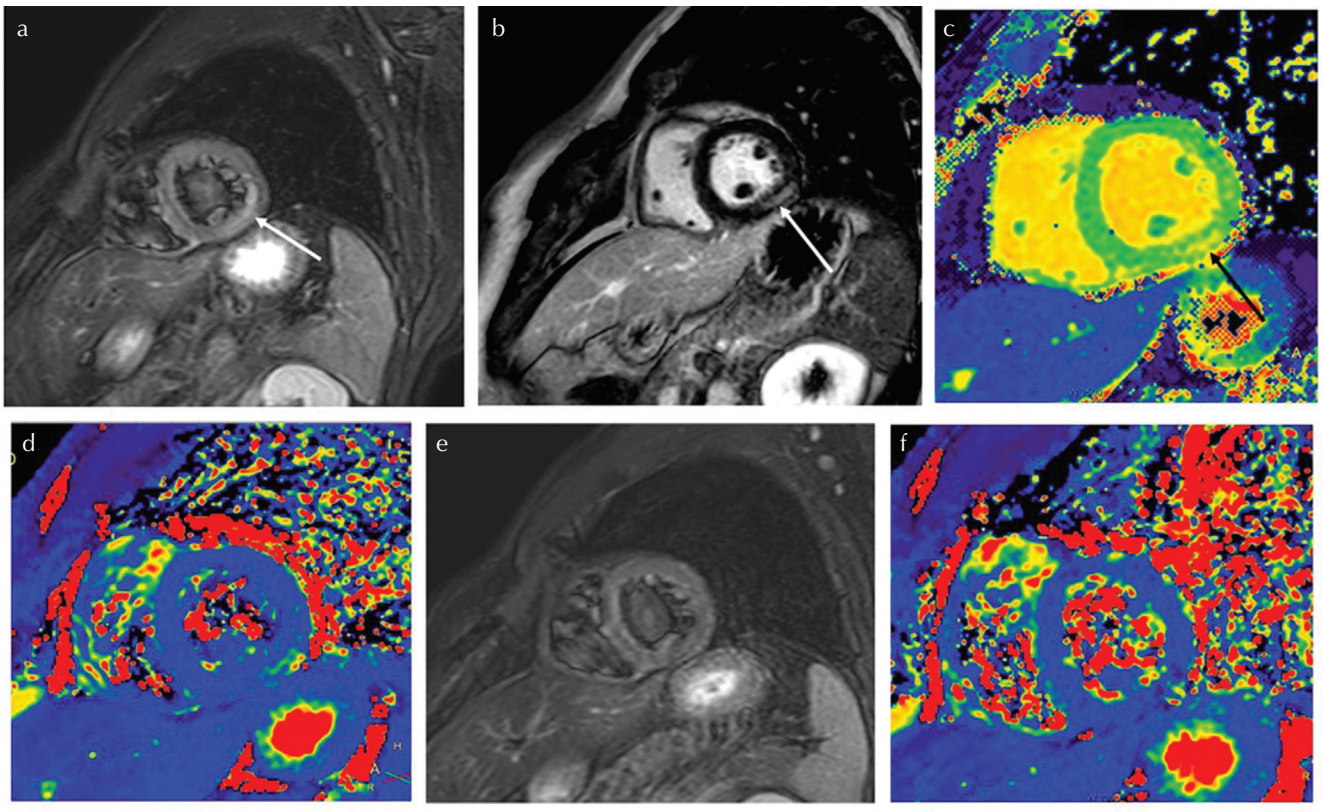

Fig. 5 Acute myocarditis. T_2-weighted imaging shows acute myocarditis as an abnormally high intensity at the inferior lateral region (**a**, arrow). The lesion shows late gadolinium enhancement (**b**, arrow). T_1 mapping shows that T_1 of the inflammation is 1251 ms (arrow) and T_1 of the normal myocardium is 1063 ms (**c**). T_2 mapping shows that T_2 of the myocarditis is 66.1 ms and that of the normal myocardium is 51.5 ms (**d**). After successful treatment, T_2-weighted imaging does not show high intensity (**e**). The myocardial T_2 value of the inferior lateral myocardium is normalized to 44 ms (**f**).

native T_1 mapping has a better sensitivity than traditional Lake Louise criteria using T_2 signal ratio and early and late gadolinium enhancement for identifying acute myocarditis. Lurz et al.[37] have shown that T_2 mapping identifies both acute and chronic myocarditis better than T_1 mapping. Therefore, T_2 mapping as well as T_2-weighted and LGE imaging should be used for detection, assessment of the severity, and follow up of myocarditis (Figs. 5a, d–f, 6). In a recent paper, the texture analysis applied to T_2 mapping can define infarct-like myocarditis with high sensitivity and specificity.[33]

Stress-induced (Takotsubo) cardiomyopathy

Stress-induced cardiomyopathy is characterized by its clinical history, severe chest pain, and peculiar apical morphology and hypokinesis as well as high signal intensity on the T_2-weighted images with no or little LGE (Fig. 7a).[19,38] T_2 mapping is available for detecting myocardial edema in this disease (Fig. 7b), because the high intensity induced by a stagnant flow can hinder the apical myocardial edema on the T_2-weighted images even using black-blood technique.[39]

Sarcoidosis

T_2-weighted imaging and T_2 mapping are useful for detecting "active" inflammatory or granulomatous lesions associated with cardiac sarcoidosis (Figs. 8a–8c).[13,40] The lesions can be consistent with the abnormal metabolism shown by ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET; Fig. 8d).[19] T_2 mapping is reported to be valuable for early recognition and assessment of activity of the cardiac sarcoidosis.[40] In addition, T_2-weighted imaging can be used to evaluate the response of myocardial edema associated with sarcoidosis to steroid therapy.[41] By contrast, the discrepancy between LGE and T_2-weighted image or T_2 mapping indicates the scarred tissues in cardiac sarcoidosis (Fig. 9).

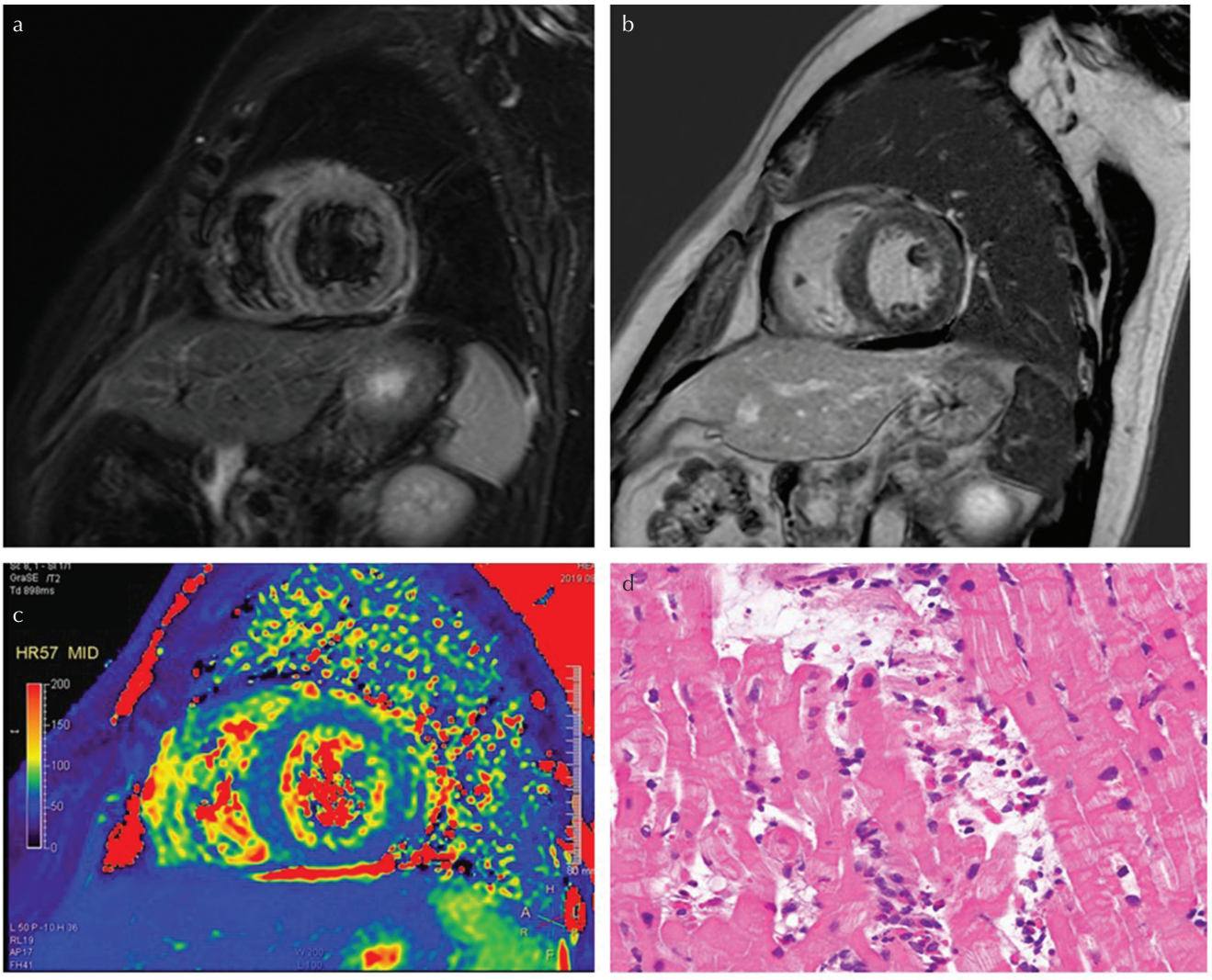

Fig. 6 Chronic myocarditis/T_2-weighted (**a**) and late gadolinium enhancement images (**b**) do not identify any myocardial injuries. T_2 mapping gives an increased T_2 of 60.0 ms (**c**). Endomyocardial biopsy reveals infiltration of inflammatory cells (**d**, hematoxilyn and eosin staining).

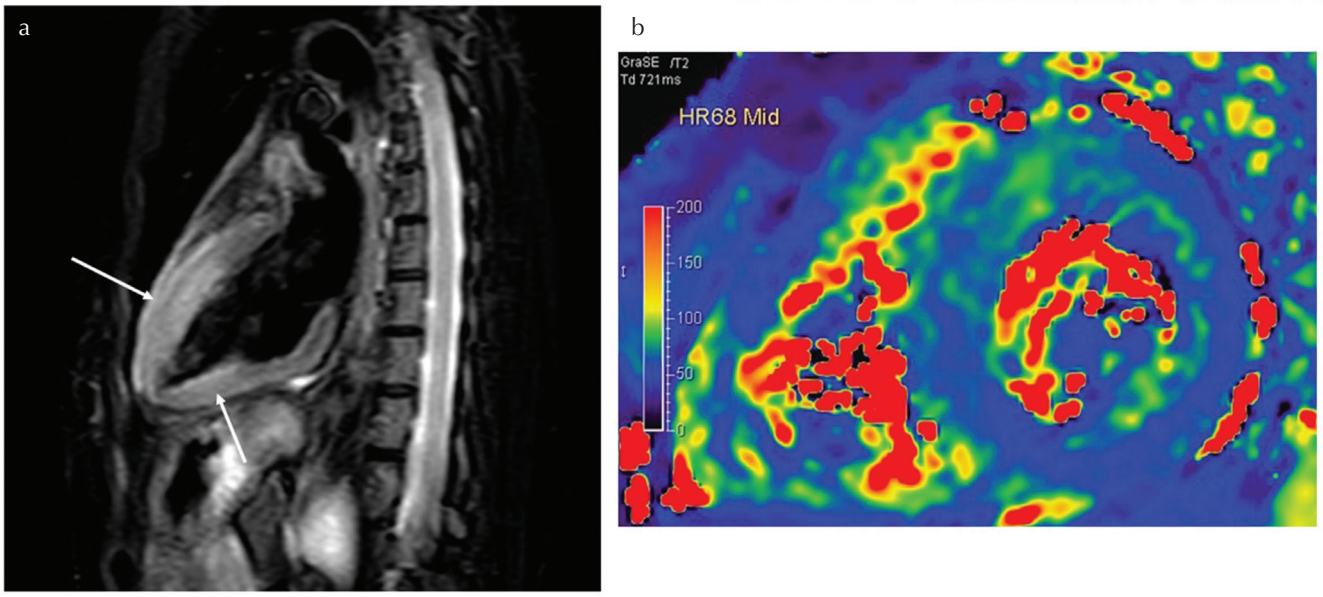

Fig. 7 Takotsubo cardiomyopathy. T_2-weighted imaging shows high intensity in the apical myocardium and middle anterior myocardium (**a**). T_2 mapping provides greater T_2 value of 72 ms in the apical septum (green colored, **b**).

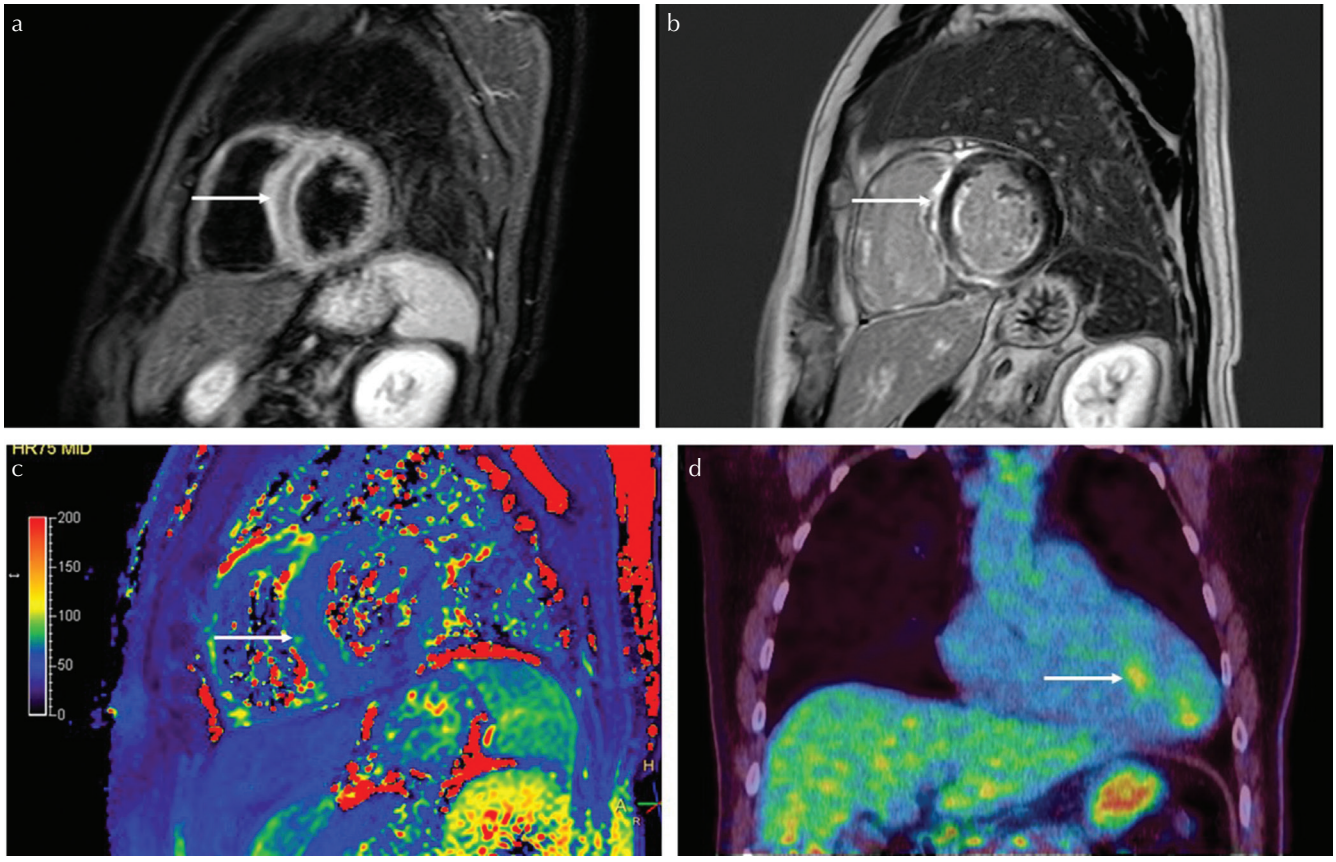

Fig. 8 Cardiac sarcoidosis. T_2-weighted (**a**) and late gadolinium enhancement images (**b**) show an "active" lesion at the septal region (arrow). T_2 mapping shows an increased T_2 of 59.5 ms (**c**, arrow). Positron emission tomography shows abnormal metabolism in the septal myocardium (**d**, arrow).

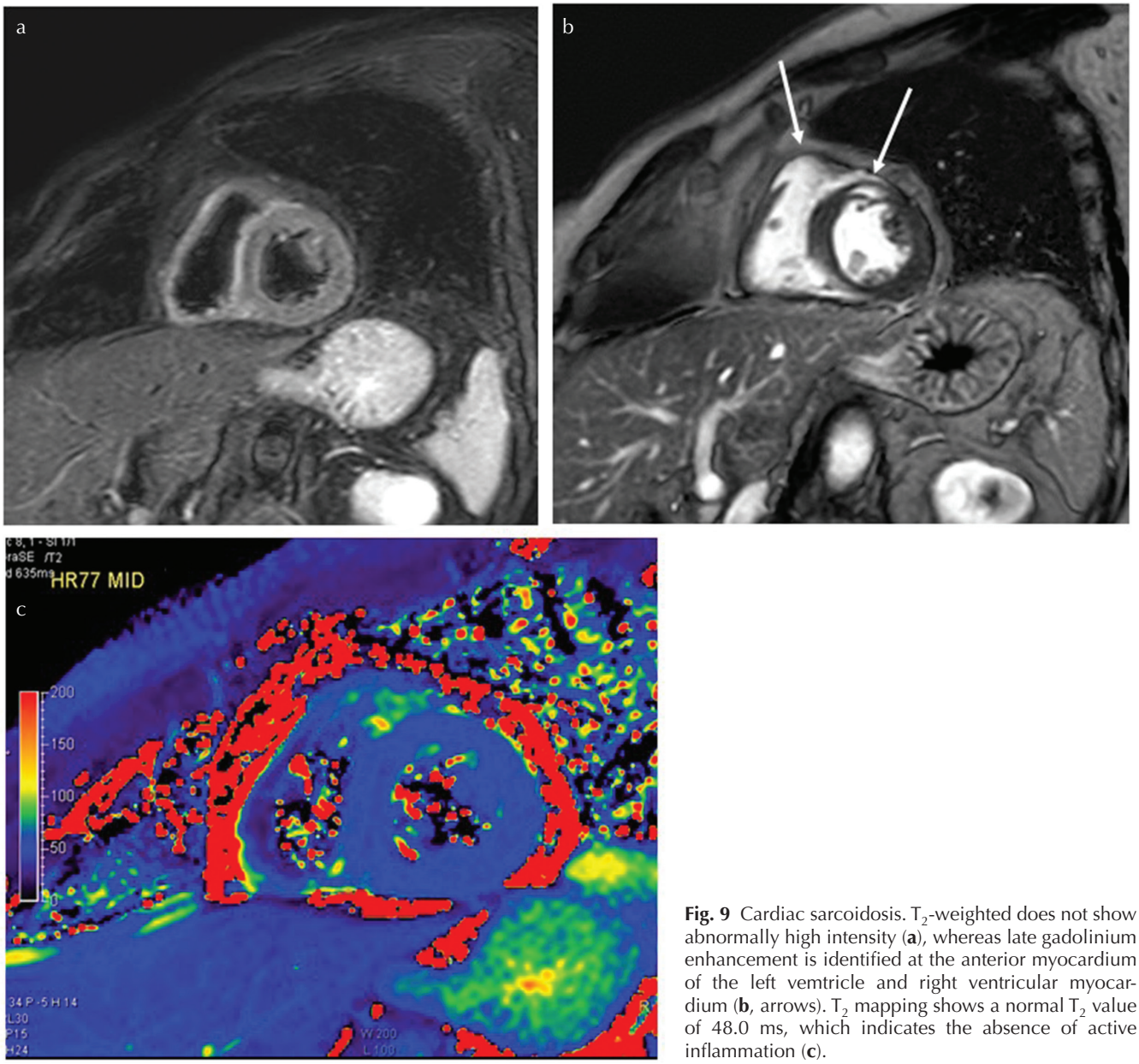

Fig. 9 Cardiac sarcoidosis. T_2-weighted does not show abnormally high intensity (**a**), whereas late gadolinium enhancement is identified at the anterior myocardium of the left vemtricle and right ventricular myocardium (**b**, arrows). T_2 mapping shows a normal T_2 value of 48.0 ms, which indicates the absence of active inflammation (**c**).

FDG PET for cardiac sarcoidosis requires a long-term fasting and cannot detect the myocardial scar, while cardiac MRI including T_2 mapping provides comprehensive information about cardiac sarcoidosis.[13,19]

Hypertrophic cardiomyopathy

LGE MRI is a powerful imaging tool for the diagnosis and prognosis of hypertrophic cardiomyopathy (Fig. 10a).[42] T_2-weighted imaging may provide additional information about myocardial injuries that are related to syncope and ventricular tachycardia (Fig. 10b).[11,12] T_2 mapping is available for confirming the presence of an abnormally high intensity on the T_2-weighted images in hypertrophic cardiomyopathy, "nonacute" cardiomyopathy (Figs. 10b and 10c).[29] However, T_2 mapping fails to evaluate diffuse myocardial damage associated with hypertrophic cardiomyopathy, which is identified by native T_1 mapping.[16,29,43] Texture analysis can be used to assess both regional and diffuse myocardial damages on the T_2-weighted images (Fig. 10d).[16] The higher value of grey-level nonuniformity on texture analysis might reflect structural heterogeneity such as myocardial disarray and fibrosis, while the lower value of abnormally high intensity on T_2-weighted images might be consistent with dilated lymph channels and increased water content leading to more homogeneous tissue contents.[16]

Dilated cardiomyopathy

Late gadolinium enhancement is valuable for diagnosis and risk stratification of dilated cardiomyopathy.[3] Recently, Yanagisawa et al.[6] have shown that native T_1 mapping is able

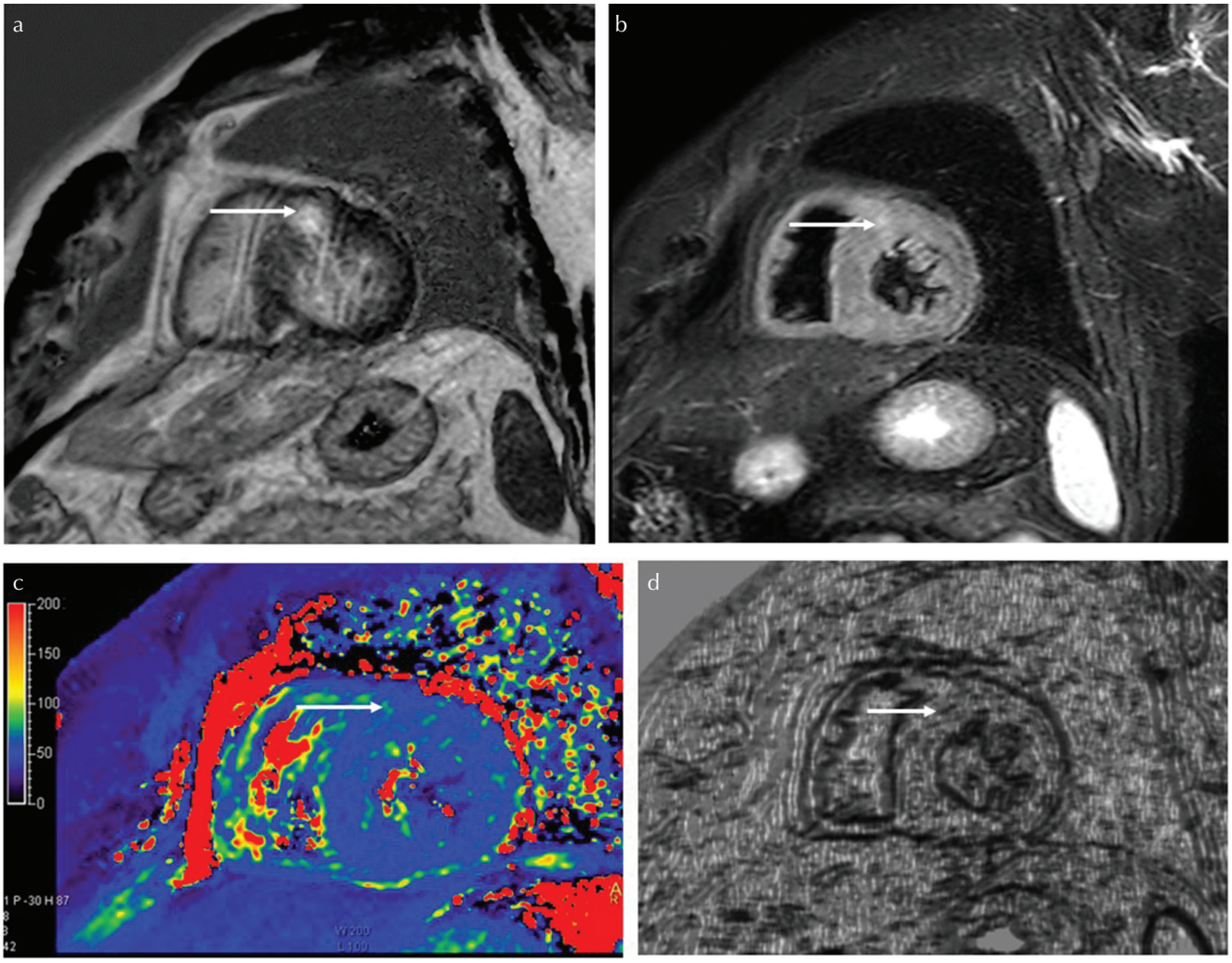

Fig. 10 Hypertrophic cardiomyopathy. Late gadolinium enhancement is identified at the right ventricular insertion point (**a**, arrow). T_2-weighted imaging shows high intensity in hypertrophic cardiomyopathy associated with syncope (**b**, arrow). T_2 mapping shows an increased T_2 of 62.0 ms at the insertion point (arrow), but the hypertrophied midseptal myocardium shows a normal T_2 of 50.0 ms (**c**). T_2 mapping fails to detect myocardial injuries of the hypertrophied region. Texture analysis provides a map of grey-level nonuniformity (GLNU; **d**). Compared with the GLNU of normal volunteers (53.7 ± 20.9), the insertion point has a lower GSNU of 38.3 (arrow) and the mid-septal region has a higher GLNU of 74.2.

to depict the myocardial scarring without gadolinium injection. T_1 mapping is also useful for detecting diffuse myocardial fibrosis associated with dilated cardiomyopathy (Fig. 11a).[43] T_2 mapping has not been widely applied to dilated cardiomyopathy[28,44], whereas we have encountered several patients who present with prolonged T_2 values of the myocardium (Fig. 11b). Prolonged T_2 values of the myocardium in dilated cardiomyopathy may not reflect myocardial edema but some qualitative changes in the water contents (Figs. 11b and 11c).[28,44,45]

Drug-induced cardiomyopathy

There are some drugs, especially anti-cancer agents, which induce cardiomyopathy. In one case report, cine MRI shows cardiac dysfunction with elevated myocardial T_2 values but no LGE.[46] T_2 mapping may be useful for detecting allergic reaction, inflammation, and edema associated with drug-induced cardiomyopathy (Fig. 12).[47,48] Thus, cardiac MRI including T_2 mapping is valuable for deciding to continue or cease anticancer treatment.

Chronic kidney disease

Chronic kidney disease is induced by several pathologies, including diabetes mellitus, hypertension, and glomerulonephritis. Chronic kidney disease and its causes may lead to coronary artery disease, myocardial hypertrophy, and fibrosis that are related to ischemic cardiomyopathy, ventricular arrhythmia, and sudden cardiac death (Fig. 13a).[49] Because of the risk for nephrogenic systemic fibrosis, LGE imaging cannot be performed in the patients with chronic kidney disease. Therefore, T_1 and T_2 mapping may be valuable for

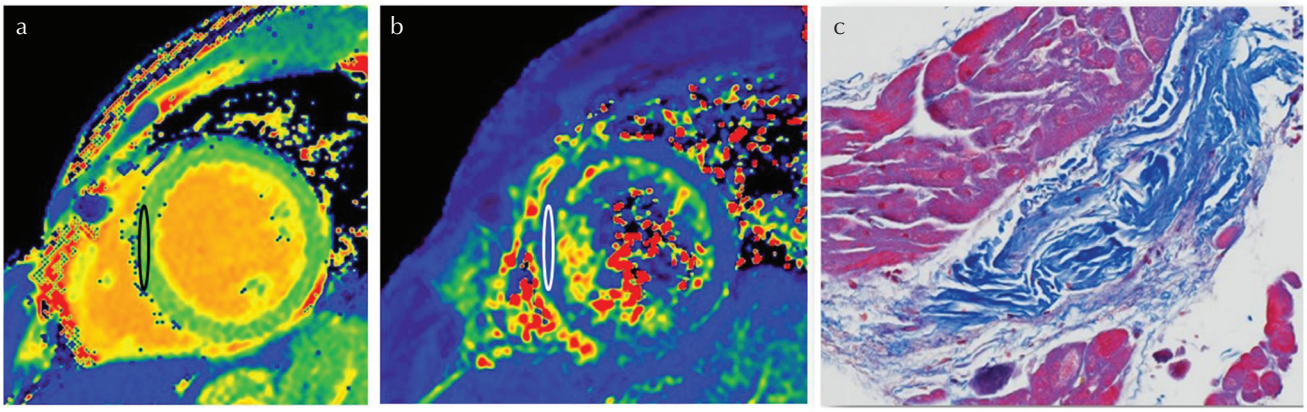

Fig. 11 Dilated cardiomyopathy after hypereosinophilia. A region of interest is placed on T_1 (**a**) and T_2 mapping (**b**); higher T_1 and T_2 values are shown (1160 and 62.0 ms, respectively). Endomyocardial biopsy reveals collagenous fibrosis but does not detect edema and eosinophils (**c**, Masson-Goldner staining).

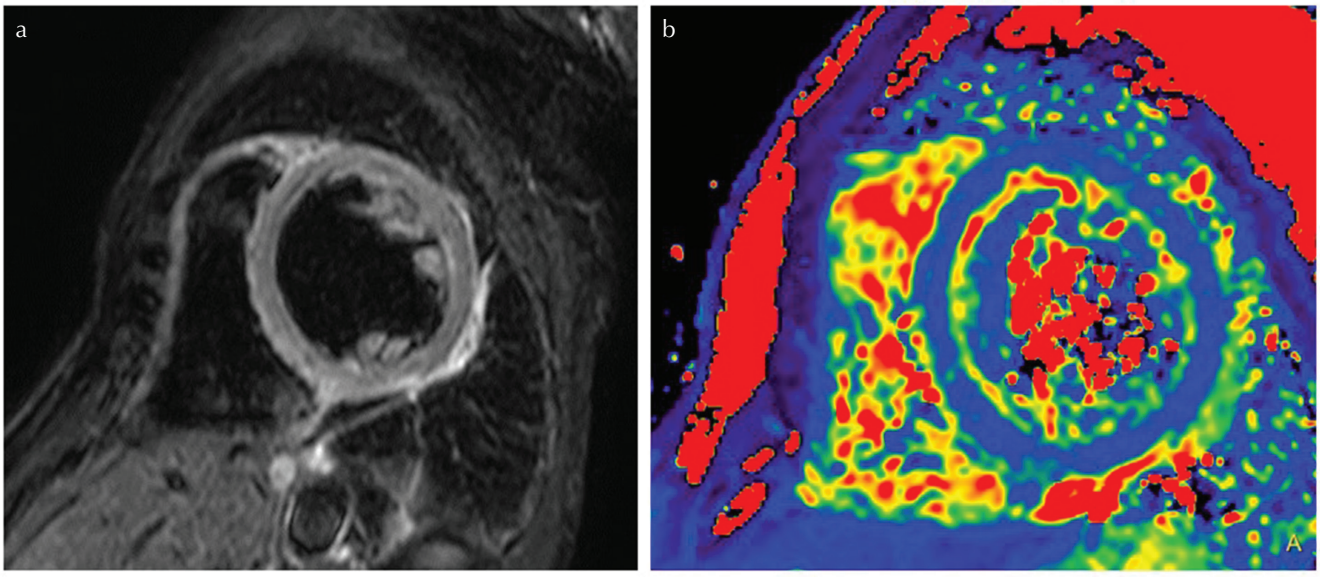

Fig. 12 Drug-induced cardiomyopathy. T_2-weighted imaging shows no abnormal intensity in cardiac dysfunction following the use of trastuzumab for breast cancer (**a**). T_2 mapping provide a higher T_2 value of 60.0 ms (**b**).

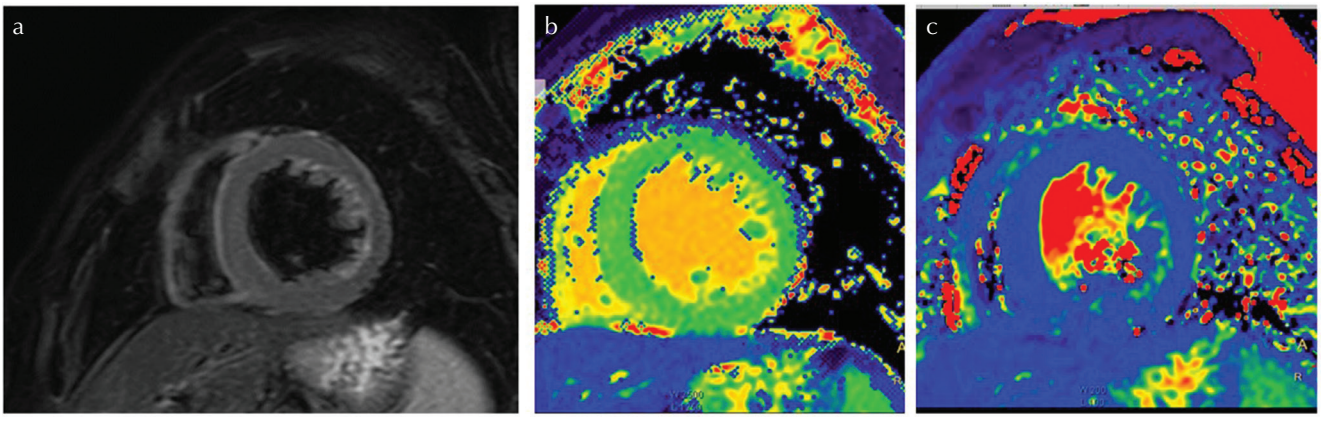

Fig. 13 Chronic kidney disease under dialysis. T_2-weighted imaging shows moderate myocardial hypertrophy without abnormal intensity (**a**). T_1 (**b**) and T2 mapping (**c**) provide slightly higher T_1 and T_2 values (1120 and 55.0 ms), respectively.

identifying the myocardial injuries associated with chronic kidney disease (Figs. 13b and 13c). Rutherford et al.[50] have shown the usefulness of T_1 mapping for this purpose, while Hayer et al.[51] have indicated that T_2 mapping is useful for evaluating myocardial injuries associated with chronic kidney disease. Further studies are warranted to determine the usefulness of T_2 mapping for quantifying myocardial injuries and their relationship with cardiac function and prognosis in patients with chronic kidney disease.

Conclusion

T_2-weighted MRI is useful for visualizing myocardial edema related to chest pain, acute phase, or severe myocardial injuries in myocardial infarction and nonischemic cardiomyopathy. Nevertheless, a quantitative analysis of myocardial T_2 is required to determine the myocardial injuries accurately. T_2 mapping quantifies myocardial T_2 values that are significantly related to the clinical symptoms or severity of cardiomyopathies. Texture analysis is a postprocessing method to quantify the tissue alterations that are reflected on the T_2-wighted images. Cardiac T_2 mapping and texture analysis complements T_2-weighted imaging owing to the quantitative analysis and fewer imaging artifacts.

Acknowledgments

This study was supported in part by the Grants-in-Aid for Scientific Research [KAKENHI] from the Japan Society for the Promotion of Science: Kiban (C) 17K10419. The authors appreciate the technical support of Naoki Shinoda, RT, and Hiroshi Yamamoto, RT (Nihon University Hospital). The contents of this review were partly presented at the 47th annual meeting of the Japanese Society of Magnetic Resonance in Medicine at the recommendation of Noriko Manabe, MD (Hokkaido University), and Professor Hajime Sakuma, MD (Mie University).

Conflicts of Interest

Yasuo Amano has received research funding from Guerbet Japan Co. Naoya Matsumoto has received lecture fee from Nihon Medi-Physics and Fujifilm Toyama Chemical Co, and research funding from Fujifilm Toyama Chemical Co. These fee and funding are not related to the topic of this study. The other authors declare no conflict of interest related to this study.

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