Role of T2 mapping in evaluation of Myocardial Edema in Acute Ischemic Injury

Sameh Abdullatif Aborezq, Amr Dorgham, Mohammad Ali Salem, Noha Behairy, Mohamed Talaat Ali,

Radiology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Email: Samehaborizk@gmail.com, sameh.abdellatif@kasralainy.edu.eg

Abstract

BACKGROUND: There is some limitations of the routine fluid sensitive sequences in evaluation of myocardial edema with some recent data emphasizing the role of T2 quantification in overcoming these problems. We aimed to assess these T2 quantified values in infarcted myocardium relative to remote regions as well as zones of microvascular obstruction in acute reperfused myocardial infarction patients to validate the reproducibility of T2 mapping in interpretation of such conditions compared to routine T2-weighted images.

METHODS: T2 values using a novel mapping technique were prospectively recorded in 16 myocardial segments in 30 patients admitted with acute myocardial infarction. Regional T2 values were averaged in the infarct zone and remote myocardium, both defined by a reviewer blinded to the results of T2 mapping.

RESULTS: T2 of the infarct zone was 71 ± 5 ms compared with 54 ± 3.4 ms in remote myocardium ($p < 0.0001$). T2 mapping helped at the detection of edematous myocardium in 29 of 30 patients. On the other hand, T2-weighted short tau inversion recovery images were negative in 6 and uninterpretable in another 3 due to breathing artifacts. Within the infarct zone, areas of microvascular obstruction were characterized by a lower T2 value 56.7 ± 5 ms within the area of MVO compared with 70.2 ± 8 ms for infarct tissue outside the area of MVO ($p < 0.0001$). T2 mapping provided good results in patients whom short tau inversion recovery imaging often submitted inadequate results.

CONCLUSIONS: T2 quantification using the novel mapping technique substantially could overcome the limitations encountered by T2-weighted short tau inversion recovery imaging in proper assessment of myocardial edema and thus adding more diagnostic accuracy in detection of acute myocardial injuries.

Keywords: acute myocardial infarction; cardiac magnetic resonance; edema; T2

Introduction

Detection of myocardial edema using a dark blood turbo spin-echo pulse sequence has previously been shown to allow early diagnosis of acute coronary syndromes and may identify both the area at risk and the amount of myocardial salvage post-reperfusion **(1)**.

T2 (spin-spin) relaxation time is the time constant governing the exponential decay of transverse magnetization. The fractional increase in T2 is substantially larger than the fractional increase in T1 when water content is increased, and this relationship was demonstrated in a canine model of acute myocardial infarction 30 years ago **(2)**. Various technical improvements since then have enabled the wide clinical use of T2W pulse sequence in CMRI for the qualitative or semi quantitative detection of myocardial edema and inflammation **(3).** One of these water sensitive sequences for detection of acute myocardial edema is Short Tau inversion recovery (T2 STIR) sequence which can be used for detection of myocardial edema either by measuring the signal ratios between the subjectively affected myocardium to the nearest skeletal muscles or relative to a signal behavioral change in a remote unaffected myocardium **(4)**. However, edema signal errors can be encountered in the known water sensitive sequences due to systemic affection of skeletal muscles or a frequent multi cardiac segment involvement. In addition, cardiac motion can alter the signal

from the lateral wall of the left ventricle. Moreover, the bright signal noted at the myocardium blood interface resulting from incomplete proton saturation can be also somewhat confusing in the T2 and TIRM sequences. Lastly, routine edema sequences can be misleading to define areas of intra myocardial hemorrhage. When hypo intense signals are noted in the core of an area of micro vascular obstruction (MVO), the intra myocardial hemorrhage (IMH) can be routinely diagnosed **(5)**. Cardiac MRI, despite that, is considered an excellent non-invasive method for assessment of acute myocardial edema whether being of an acute ischemic or inflammatory process **(6)**.

On the other hand, Quantification of T2 myocardial relaxation times promises to circumvent these limitations and is achieved by collecting multiple images with different T2-weighting, providing multiple points along the T2 decay curve for fitting of an exponential signal decay model **(7)**. When echoes of myocardial signals, per segment, are quantified below 60 msec, they are now considered normal. On the other hand, a myocardial signal above 60 msec represents area of myocardial edema being irrespective to the signals from the nearest skeletal muscle or the remote myocardium overcoming the aforementioned described limitations in routine fluid sensitive inversion recovery sequences **(8)**. As well, areas of reduced T2 mapping signals quantified in acute events in the core of an MVO segment are considered a marker of IMH.

T2 mapping signals can detect edematous myocardial territories in a variety of cardiac pathologies, including acute myocardial infarction, myocarditis, Tako-tsubo cardiomyopathy, and heart transplant rejection **(9)** overcoming the artifacts frequently encountered in conventional edema sequences such as the flow and motion artifacts which, as above described, can decrease the signal to noise ratio and increase the signal loss along the left lateral ventricular wall substantially prone to motion artifacts as those images' artifacts are much less to be encountered in T2 mapping per left ventricular segments when compared to the conventional edema sequences **(10)**. Being dependent upon three saturation sequences, the T2 mapping values are still under validation. Our purpose is to compare between both sequences (T2 mapping versus T2 STIR) in evaluation of myocardial edema in cases of acute ischemic injury.

Aim of the work

The study aims to assess these T2 quantified values in infarcted myocardium relative to remote regions as well as zones of microvascular obstruction in acute reperfused myocardial infarction patients to validate the reproducibility of T2 mapping in interpretation of such conditions compared to routine T2-weighted images.

PATIENTS & METHODS

Only STEMI Patients (30 patients) with AMI were retrospectively registered.

Full medical history and clinical and electrocardiographic findings were recorded. Pacemaker, critically ill patients or any CMR general contraindications represented the exclusion criteria.

CMR examination:

Examinations were performed using a 1.5-T CMR system and 48-element phased-array cardiac coil (Aera, Siemens, Germany). Initial localizers were taken then Balanced steady-state free precession (SSFP) cine imaging, in multiple planes, were obtained for assessment of wall motion abnormalities and volumetric analysis as well. T2-weighted short tau inversion recovery (T2-STIR) images obtained in basal, mid, and apical short-axis levels similar to the initial SAX cine slices.

T2 maps were acquired in the exact slice location as the T2-STIR images using a T2-prepared SSFP sequence with a single shot acquisition. Through acquiring three T2-weighted images, T2 maps were generated, in which, each image has a different T2 preparation time. Within the 3 images, the signal intensity of the corresponding pixels, after logarithmic transformation, were used to obtain the T2 value of each pixel.

Similarly, LGE imaging were obtained in the exact slice location in the prior short axis images using inversion-recovery sequence 15 min after 0.15 mmol/kg gadolinium-based contrast material administration.

The inversion time was adjusted to null the normal non affected myocardium. The study was performed in a breath-hold technique. Patients with poor breath-hold capacity was asked to have free breathing during single shot acquisition.

Image analysis:

Using Simpson's method with manual drawing of LV endo contour and automatic propagation through the 17 segments, the LV end-diastolic and systolic volumes were calculated and indexed per body surface area. Regional wall motion abnormalities were assessed using the standard 17-segment model and classified as normal, moderately hypokinetic, severely hypokinetic, akinetic or dyskinetic.

Myocardial necrosis was defined as hyper enhancement in the LGE images more than % standard deviations the normal remote myocardium and was classified per myocardial segment visually as no enhancement, sub endocardial (1% to 25%, 26% to 50% and 51% to 75%) and transmural (76% to 100%) enhancement. Microvascular obstruction (MVO) was identified as dark core areas surrounded by necrotic enhanced myocardium on LGE imaging.

T2 values were obtained from the quantitative T2 maps for each segment except for the cardiac apex (segment 17) to avoid the partial volume effects at this level with thin myocardium.

T2-STIR images were evaluated in the short axis slices and classified as positive for edema, negative for edema, or indeterminate. If the signals of the culprit artery segments exceeded these of the remote myocardium besides twice its standard deviation, we considered this as positive for edema **(11).**

As well, evaluation of myocardial necrosis and normal remote myocardium, blinded to T2 mapping results, was defined on the 16-segment model areas based upon LGE images together with the cine images for evaluation of wall motion abnormalities and the pertinent clinical data, ECG and the coronary angiogram results.

Segmental T2 values that previously had been obtained according to the 16-segment model were then averaged for the infarct zone and remote myocardium as defined by the blinded assessment.

Statistics:

Categorical continuous data having normal distribution were expressed as mean ± SD while the other data with no normal distribution were expressed as median and inter-quartile range. Using a 2-sample t test or paired t test, the mean values of the continuous variables with normal distribution were compared. Correlation between continuous variables was computed with the Spearman rank correlation coefficient. Categorical variables were compared using the Fisher exact test. Statistical significance was correct at a 2-tailed probability level of less than 0.05.

RESULTS

Study population

30 patients were involved in the study divided into 21 male (70%) and 9 female (30%). None of the patients reported having previous major cardiac events. CMR was performed in all patients after they underwent coronary angiography. All patients did not develop arrythmias at the time of CMR examination.

LV structural and functional evaluation:

All studies were performed with a breath hold technique except for free breathing real-time cine imaging and single-shot LGE imaging were used in a total of 3 subjects with breathing difficulties during the examination.

The estimated global LV ejection fraction was an average of 48% and the median LV end diastolic volumes 127 ml +/- 27 ml. Myocardial infarction was confirmed and evidenced by variable subendocardial (30%) to transmural enhancement (70%) in LGE images concordant with prior catheter findings.

T2 mapping:
The mean T2 measured within the infarct zone was 71 ± 5 ms compared with 54 ± 3.4 ms in remote myocardium ($p < 0.0001$). For the entire study population, there was almost perfect discordance between the measures T2 values in the infarct region compared to remote myocardium.

T2 STIR imaging vs. T2 mapping:
T2 maps was obtained in all subjects and differentiated the injured myocardium relative to the remote one based upon the segmental T2 values. One case with extensive MVO was difficult to be interpreted by T2 maps for edema signal. On the contrary, it was possible to detect myocardial edema as areas of T2-STIR signal hyperintensity only in 21 patients (56.6%) at basal and mid ventricle levels (**figure 1 and 2**) while at apical levels, it was indeterminate in 40% of cases (12 cases). In 6 cases (20%) there was no edema in STIR images while in 3 cases (10%) it was indeterminate result. Three cases were not interpretable due to severe motion artifacts limiting the proper evaluation of STIR images (**Figure 3**).
Seriously, in all patients with negative, indeterminate or uninterpretable T2-STIR images, there was clear difference between the quantified T2 values between the infarct and remote myocardium using the T2 mapping sequence.

MVO and T2 signal intensity pattern
Overall, 15 patients had evidence of MVO on LGE imaging, 3 of them had features of hemorrhagic MVO. When comparing T2 maps with matching LGE images, T2 values in segments with extensive MO were lower compared with the T2 values measured in the infarct outside the MO area (**Figure 3**). In this subset of patients with evidence of MVO, the mean T2 was 56.7 ± 5 ms within the area of MO compared with 70.2 ± 8 ms for infarct tissue outside the area of MO ($p < 0.0001$). On the contrary, the T2 values were significantly low within the MVO in cases where a remarkable dark core area was noted in the STIR image likely hemorrhagic MVO (3 cases). The T2 values in the MVO of these 3 cases reached an average of 42.12 ± 4 ms compared to 56.7 ± 5 ms in the areas of MVO in the rest of the cases that did not show dark core within the STIR images (non-hemorrhagic MVO) ($p < 0.003$).

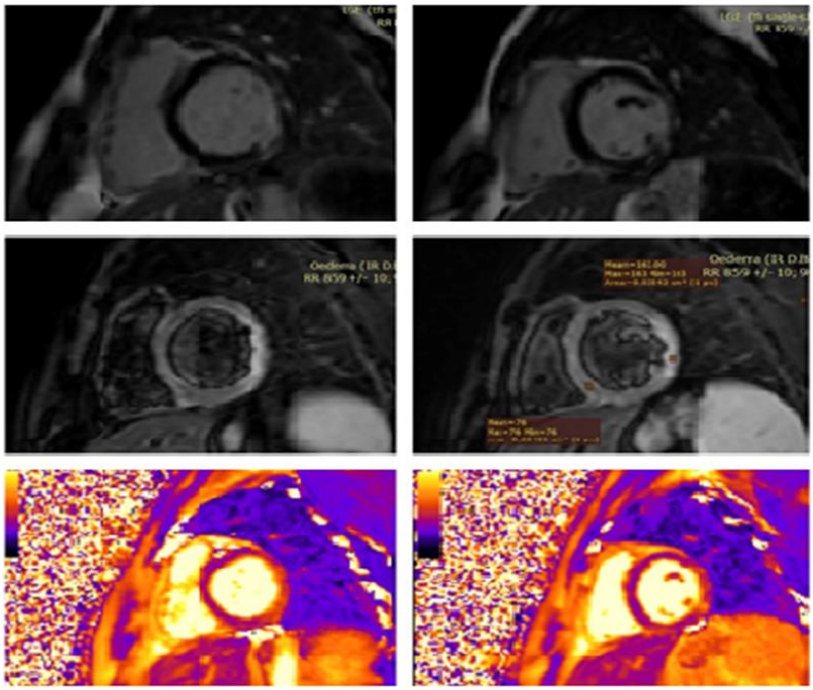

Figure 1: Short axis images at basal and mid ventricle levels from LGE, T2 STIR and T2 map images in two columns (right panel basal level, left panel mid ventricle) showing the delayed enhancement (more than 70% denoting transmural infarction) and the edema along lateral wall (LCX territory) with good segmental concordance between T2 STIR images and T2 maps even with visual inspection.

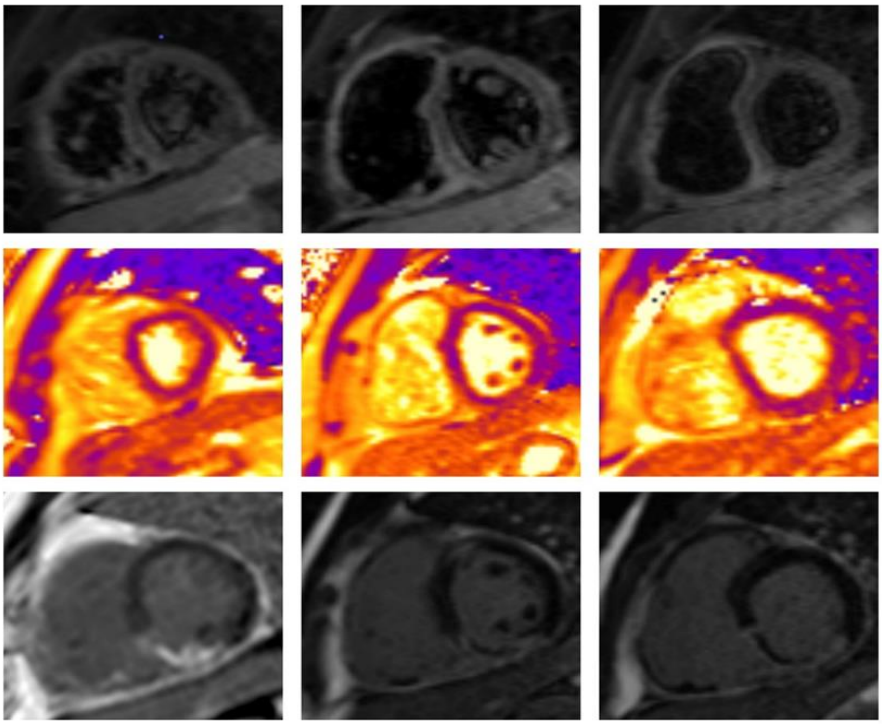

Figure 2: Sequential short axis images from apical to basal (left to right) at **T2 STIR**, T2 maps and LGE images (from up to bottom) showing the segmental concordance of edema pattern between both STIR images and the T2 maps at basal, mid and apical levels. There was edema of the RV free wall at basal and mid ventricle level in STIR images but not clear at T2 maps. Transmural enhancement and subendocardial dark core of MVO are noted at LGE images (last row) and the corresponding STIR and T2 map images with RV transmural enhancement at basal and mid ventricle levels.

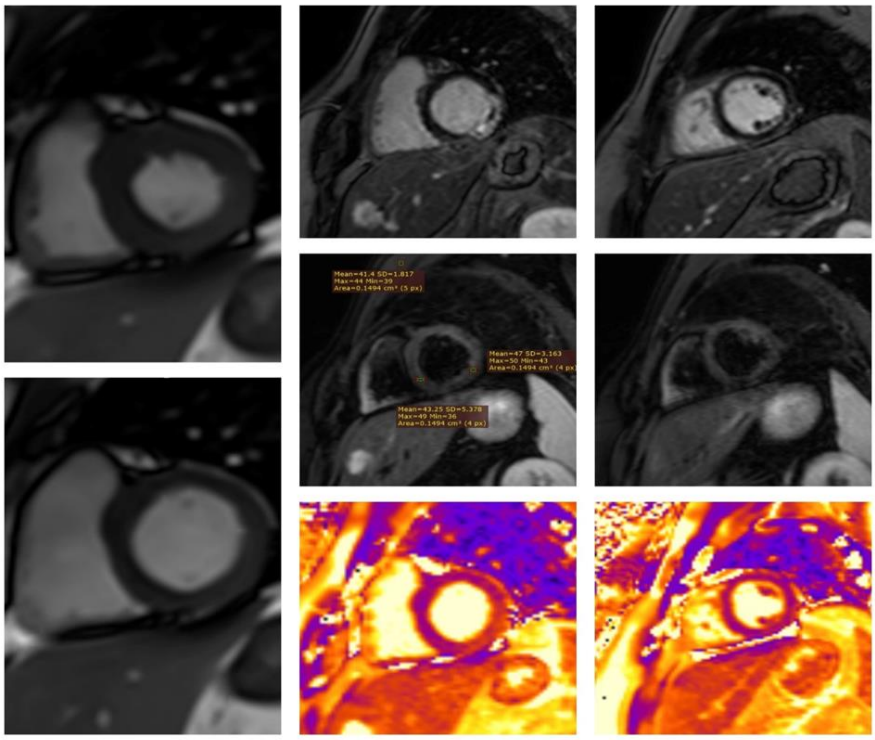

Figure 3: Left column two SSFP images at end systole (upper) and end diastole (lower) showing the relative hypokinesia along the infero lateral basal segment of the LV. The middle and right columns have basal and mid ventricle short axis images (from left to right) arranged as LGE (upper), TRIM images (middle) and T2 maps (lower) showing the clear obvious edema being color coded at the T2 maps while no edema signal changes at corresponding TIRM images. Also note the transmural enhancement in the LGE images with dark core thin rim of MVO appearing as a hypo intense core within the edematous segment at the color coded T2 map.

DISCUSSION

T2 mapping, being a quantitative method for myocardial edema imaging relying upon means of absolute values, has overcome the limitations of the dark blood T2 weighted TSE sequences such as the cardiac motion induced myocardial edema signal alterations and the bright rim artifacts noted at the endocardial border from stagnant blood as well as the limited contrast resolution between edematous and remote myocardium noted in the T2 weighted bright blood SSFP sequences (**12**). The T2 value of the infarcted segments is well known to be significantly higher compared to the normal T2 value of the remote myocardium with an excellent sensitivity for detecting ischemic edema than usual T2-weighted edema imaging sequences as it allowed better detection of the edema surrounding the necrotic core adding to the late enhancement sequence (**1**).

In agreement with that, our study outlined the efficacy of T2 mapping in evaluation of myocardial edema, based upon signal intensities relative to the routine fluid sensitive sequence with good sensitivity to myocardial edema when comparing the infarct zone with the remote myocardium using the LGE as the reference images. On the contrary, the fluid sensitive sequence shows some negative and indeterminate results for edema (30%) most of them was at apical levels and multi territorial affection highlighting the known limitations for this sequence such as the respiratory and cardiac motion artifacts and the subendocardial bright rim artifacts frequently encountered in usual T2 weighted edema imaging sequences.

Reperfusion hemorrhage is a well-known condition in such cases with AMI post reperfusion (**13**). Despite lack of intention to assess this pattern of reperfusion myocardial injury, in our study, we found 15 patients (50%) had MVO +/- intra myocardial hemorrhage, one of them was with extensive disease limiting the proper assessment of myocardial edema by T2 maps due to the known fact that edema will be higher only in the thin margins of the infarct zone and this could be affected by partial volume effects compared to the

large size of the MVO (**10**). Despite the higher sensitivity of T2* maps over the usual T2 maps or T2 weighted edema sequences in clear depiction of intra myocardial blood products depending on the fact that lack of a refocusing RF pulse (as usual in T2 weighting) in T2* maps can lead to substantial and maximal rapid loss of phase coherence in each echo time accentuating the para magnetic effects of blood products and thus giving much clear data about intra myocardial hemorrhage without comparative sensitivity to surrounding edema as in usual T2 weighting (**14**), we found signal reduction and consequently clear low signal intensity pattern in the T2 color coded maps in all cases of MVO/IMH reflecting the very high sensitivity of such images specially in cases of high thrombus burden as encountered in our study. Further studies should be done on a larger scale to determine the prevalence of reperfusion IMH in cases of AMI with different thrombus burden grades being a strong predictor of adverse outcomes (**15**) and to validate the T2 maps in accurate detection of reperfusion IMH in such different TB grades comparing it to T2* maps.

In our study, we obtained a segmental territorial edema in a case with a proven coronary artery disease only in T2 maps but with no relevant edema changes in the conventional T2 prepared inversion recovery images. This pattern added more diagnostic accuracy in such condition and this can be a hopeful choice as well, in non-ischemic non territorial acute myocardial edema conditions helping in better evaluation of the overall disease pattern and its reversibility with medical management. This came in agreement with Montant and his colleagues when they described the sensitivity of T2 mapping over the usual T2 prepared inversion recovery sequence being much higher for the T2 maps as they can easily visualize areas of increased water content in different myocardial segments in a color coded visual pattern with a territorial or non-territorial distribution overcoming the partially limiting adverse motion and subendocardial bright rim artifacts in usual TIRM sequence and thus helping in proper delineation of different edema patterns in other conditions of non-ischemic myocardial edema (**16**).

Similarly, we got one patient (3%) with a multi vessel coronary artery disease. We found a difficult assessment of myocardial edema using the conventional STIR images but it was more obvious in the T2 maps helping better delineation of segmental myocardial edema highlighting the more sensitive T2 maps over the conventional edema sequences with less imaging artifacts and easier color-coded visual assessment even with small alteration of myocardial edema pattern compared to the lower tissue contrast between the edematous and non-edematous remote myocardium by the routine dark blood inversion recovery imaging.

Inversely, in this study, we found one case with acute dominant RCA territory MI seen having biventricular involvement of nearly the whole RV free wall and the LV RCA territory through the marked hypokinesis/almost akinesia of the whole RV wall, enhancement in the late Gadolinium inversion recovery images, subtle edema in the routine TIRM images similar to RCA territory of the LV and dilatation of the RVEDV relative to this of the left ventricle reaching 1.3:1 (**Figure 2**). On the contrary, it was difficult in the T2 mapping images to visualize such edema pattern in the RV free wall. This came in agreement with Daniel Messroghli and his colleagues (**17)** stating the difficult application of such breath old parametric mapping techniques, owing to their limited spatial resolution, in evaluation of acute RV myocardial free wall injury being thin relative to the native LV.

T1 mapping is another recent quantitative method by which extra cellular volume can be estimated for differentiation between different cardiomyopathies as well as detection of fibrosis and edema using native and post contrast series however T2 mapping showed better edema sensitivity (**18).**

Limitation

Our study deserves some comments. Having a limited number of patients with limited inclusion criteria of acute myocardial injury has put some limitations about our knowledge regarding the feasibility and reproducibility of T2 mapping in other conditions of acute myocardial injury. Moreover, the disease etiology cannot be definitely identified only by T2 mapping or TIRM sequences as there are no specific patterns in ischemic heart diseases for which LGE images were a must in all our patients to define such disease condition.

Conclusion

In summary, this study outlined the diagnostic value of T2 mapping playing an additional role in clear and easy identification of multi territorial acute ischemic injuries. Further studies, on a large scale, are recommended to assess the reproducibility of T2 mapping in ischemic and non-ischemic acute myocardial injuries.

Abbreviations

AMI:
Acute myocardial infarction
MVO:
Microvascular obstruction
LGE:
Late gadolinium enhancement
STIR:
Short Tau inversion recovery
STEMI:
ST segment elevation myocardial infarction
CMR:
Cardiac magnetic resonance
SSFP
Steady state free precession
ECG:
Electrocardiography
TR:
Time to repeat
TE:
Time to Echo
LV:
Left ventricle
SAX:
Short axis
PSIR:
Phase sensitive inversion recovery images

TI:
Inversion time
IMH:
Intra myocardial hemorrhage
RV:
Right ventricle
LVEF:
Left ventricular ejection fraction
RVEF:
Right ventricular ejection fraction

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