SCIENTIFIC RESEARCH

TEXTURE ANALYSIS OF MAGNETIC RESONANCE T1 MAPS AND EXTRACELLULAR VOLUME IN HEART FAILURE COMPARED WITH NORMAL CONTROLS

Chau Thi Ngoc Anh[1], Ming - Ting Wu[2]

SUMMARY

Objective: To assess the T1 and extracellular volume (ECV) maps of left ventricle (LV) of patients with non-ischemic heart failure (NIHF) by cardiac MRI

Materials & Methods: This retrospective study included 23 NIHF (mean age = 48.1 years, 12 M), 25 matched healthy control (HC) performed CMR on 3T scanner (Skyra, Siemens). NIHF was diagnosed by echocardiography, coronary artery angiogram and myocardial perfusion SPECT. Native T1 map was obtained by modified MOLLI 5-3 sequence and ECV was calculated 12 min. after GBCA 1.5 dose with 4-3-2 sequence on 4C view. Texture analysis was performed with LIFEx(www.lifexsoft.org). We also measured the wall thickness (WT) and outer diameter (OD) of LV.

Results: NIHF had larger OD of LV (78 +/- 16 mm) than the HC (57+/-6 mm) (P,0.001) while the WT had no difference (10.9 +/- 3.4 mm vs. 10.2 +/- 2.6 mm, p=0.41). Native T1 was significantly higher in NIHF patients (1310+/- 48 ms) compared to HC (1208+/- 72 ms) (p<0.001), while the ECV showed no difference (29+/- 4.8% vs. 27+/- 5%, p=0.30). The texture analysis of T1 and ECV map¬¬¬s showed no difference in the first-order textures and had significant difference in several second-order textures, such as GLRLM, GLZLM. There was inverse correlation of ECV and WT of LV in NIHF (r=-0.61, p=0.002).

Conclusions: In NIHF with preserved WT of LV, texture analysis of T1 and ECV maps showed difference in the mean value of native T1 and texture features, which is promising as a base for machine learning with future larger cohort.

Keywords: *Texture annalysis; T1 maps; extracellular volume; heart failure; cardiovascular magnetic resonance*

[1] *Thu Duc City Hospital, Viet Nam*

[2] *Kaohsiung Veterans General Hospital, Taiwan*

INTRODUCTION

Non-ischemic heart failure is a widely prevalent disease characterized by myocardial dysfunction resulting from a variety of causes, some of which have yet to be fully defined. In ambulatory and hospitalized patients with clinically manifest heart failure primary cardiomyopathy is diagnosed in 2-15%, while in recent large scale therapeutic trials the proportion of patients with nonischemic heart failure ranged from 18-53% (1). Lack of accurate and noninvasive characterization of diffuse myocardial disease limits recognition of early cardiomyopathy and effective clinical management in NIHF. Endomyocardial biopsy is the suggested gold standard for detection and classification of myocardial tissue abnormalities, yet its invasiveness, low diagnostic yield, and paucity of proven consequential management pathways limit its widespread use in guiding clinical management (2). Recent studies have shown that T1- mapping techniques provide new insight into the quantification of fibrosis, of infiltration or scar and post-contrast myocardial T1 has been shown to significantly correlate with histological areas of fibrosis (3,4,5).

Texture analysis is a technique used for the quantification of image texture. Quantification of the intrinsic heterogeneity of different tissues and lesions is necessary as they are usually imperceptible to the human eye (6). In addition, texture can be quantified using different algorithms. To date, the TA of cardiovascular magnetic resonance (CMR) T1 and ECV maps have not been reported in non-ischemic heart failure.

We hypothesized that the extraction of texture of cardiac MRI images using T1 and ECV maps could find the textures that differ between pathological and normal myocardium, and this will be the basis for the future developing of machine learning.

MATERIALS AND METHODS

Study populations

This retrospective study included 23 NIHF (mean age = 48.1 years, 12 males), 25 matched healthy control (HC) (mean age = 48.1 years, 12 males) were recruited between March 2017 and december 2019. The diagnosis of NIHF was base on the clinical examination, previous other investigation like echocardiography, coronary artery angiogram and myocardial perfusion SPECT, full the accepted criteria (7,8,9). Reduced LV ejection fraction compared with published refence ranges normalized for age and sex (10). Patients were excluded, if they had evidence of ischemic heart disease, defined as significant documented coronary artery disease, previous coronary revascularization, previous history of myocardial infarction, or evidence of ischemic type LGE, or inducible ischemia on stress testing.

Healthy controls without systemic illness or history of cardiovascular problems underwent 12 – lead electrocardiogram (ECG), echocardiography and CMR. All these examinations revealed no abnormalities. It was observed that the CMR had good image quality.

MRI acquisition

CMR was performed using 3T MRI machine (Skyra, Siemens, Germany) with 16 channel cardiac receiver coil. For all subjects, native and post -T1 mapping were performed with steady-state-free-precession single-breath-hold modified-Look-Locker inversion recovery (MOLLI) with (TR = 353.45 ms, TE = 1.08 ms, flip angle 35°, type 5-3)" and (TR = 444.72 ms, TE = 1.18 ms, flip angle 35°, type 4-3-2) on 4C view. ECV was calculated 12 minutes after gadolinium-based contrast agent 1.5 dose (0.15 mmol/kg of Gadovist, Bayer, Germany) with 20 ml saline flushing, and using the following formula: ECV = (1−hematocrit) × ($\mathbf{\Delta}R1_{myocardium}/\mathbf{\Delta}\ R1_{blood}$), where R1 is (1/T1 pre-contrast-1/T1 post-contrast).

Texture analysis

Texture analysis which was a process that consists of six steps: MRI acquisition, ROI (region of interest), ROI preprocessing, feature extraction, feature selection, and classification, was performed with LIFEx (www.lifexsoft.org). Digital Imaging and Communication in Mdecine (DICOM) file of native T1 and post-T1 mapping was imported into LIFEx for further analysis. The margins of the myocardium were drawn carefully using a freehand region of interest (ROI) tool, avoiding the papillary muscle and the epicardial fat (figure 1) Grey-level normalization was performed by rescaling the threshold to minimize the brightness and contrast variation on TA. Seven

subsets of features including image shape, histogram, conventional, GLCM, GLRM, NGLDM, GLZLM, and were extracted with a total of 47 texture features. The texture subsets and corresponding features are summarized in table 1. Histogram and GLCM are commonly used texture parameters. Histogram reflects the frequency of a voxels' gray level in the image. The gray level histogram is the result of the statistics of a pixel on the image with a gray level, and the GLCM is the statistics of 2 pixels with a certain distance to maintain a certain gray level. The grey-level run length matrix (GLRLM) gives the size of homogeneous runs for each grey level. This matrix is computed for the 13 different directions in 3D and for each of the 11 texture indices derived from this matrix, the 3D value is the average over the 13 directions in 3D. The element (i,j) of GLRLM corresponds to the number of homogeneous runs of j voxels with intensity i in an image and is called GLRLM thereafter. Similarly, The grey-level zone length matrix (GLZLM) [Thibault] provides information on the size of homogeneous zones for each grey-level in 3 dimensions (or 2D) (11)

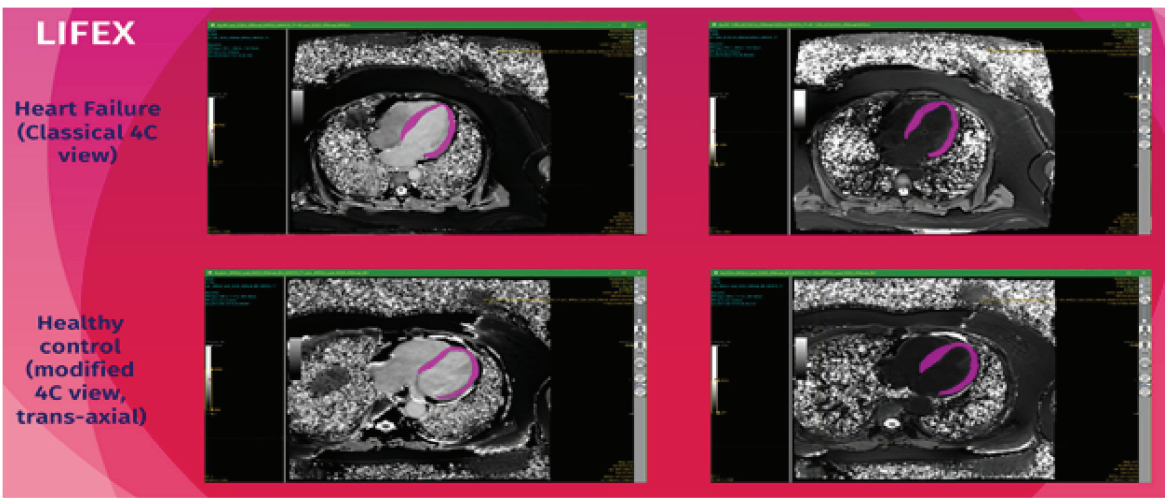

Figure 1. *Texture feature analysis*

Table 1. Texture subsets and corresponding features

4C plane with auto-contouring of the endocardial and epicardial borders for automatic quantification of wall thickness (WT) and outer diameter (OD) of LV were calculated using Oxiris software. The borders and the contours were manually edited as needed. LV myocardial thickness was measured as the perpendicular distance between the endocardial and epicardial borders of LV end-diastolic. Measurements of LV internal end-diastolic diameter (LVIDD) and septal and free end-diastolic wall diastolic thicknesses (IVSd and FWd). LV external end-diastolic diameter (LVEDD) was calculated per patient as LVEDD=LVIDD+IVSd+FWd.

Statical analysis

Continuous variables are presented as means ± standard deviations. The texture features derived from the T1 mapping of the heart in patient with NIHF and HC were compared. Comparisons between two groups were analyzed using the independent t-test. Correlation between ECV and WT was assessed using Pearson's test. A *p*-value of <0.05 was considered statistically significant. All the statistical analyses were performed using SPSS (V22, SPSS, Chicago, IL)

RESULTS

LV thickness and outer wall diameter

No significantly differences were found in thickness of IVS and FW between patients with INHF and control patients (p =0.424, p= 0.438). However, In the INHF group, LV outer wall diameter was significantly higher than that of HC (p<0.001); The values are summarized in table 2.

Table 2. LV thickness and outer wall diameter

		N	MEAN	SD	SIG
IVS thickness_ D_ cm	HC	25	1.023	0.256	0.418
	HF	23	1.094	0,343	0.424
FW thickness_ D_ cm	HC	25	0.732	0.365	0.437
	HF	23	0.866	0,374	0.438
LV ow_ D_ cm	HC	25	5.709	0.569	0.000
	HF	23	7.869	1,616	0.000

Native T1 map value and ECV

NIHF patients had greater T1 values than normal (1310 ± 48 vs. 1208 ± 72 ms, p<0.001) while the mean values of ECV of IVS and FW were not significantly different between both groups

Table 3. native T1 map value and ECV

		N	MEAN	SD	SIG
Native T1 map_IVS	HC	25	1208.440	72.285	0.000
	HF	23	1310.360	48.112	0.000
ECV_IVS	HC	25	0.270	0.050	0.304
	HF	23	0.290	0.048	0.303
ECV_FW	HC	25	0.260	0.040	0.587
	HF	23	0.270	0.047	0.589

TA of native T1 map - First-order textures

The results of the T test in table 4 showed that most of the histogram features had no significant variation between non-ischemic heart failure patients and healthy controls (p>0.05)

Table 4. The first-order texture from histogram

		N	ME AN	SD	SIG
Pre Dĩast_HISTO_Skewness	HC	25	0.602	0.750	0.580
	HF	23	0.479	0.782	0.581
Pre Diast_HISTO_Kurtosis	HC	25	5.122	2.299	0.846
	HF	23	4.995	2.214	0.846
Pre Diast_HISTO_ExcessKurtosis	HC	25	2.122	2.299	0.846
	HF	23	1.995	2.214	0.846
Pre Diast_HISTO_Entropy_log10	HC	25	1.468	0.111	0.289
	HF	23	1.437	0.084	0.284
Pre Diast_HISTO_Entropy_log2	HC	25	4.876	0.370	0.289
	HF	23	4.774	0.280	0.284
Pre Diast_HISTO_Energy	HC	25	0.044	0.013	0.540
	HF	23	0.047	0.011	0.537

TA of native T1 map – Second-order textures

The several second-order textures like the grey-level run length matrix, the grey level zone length matrix showed significant differences ($p<0.05$)

Table 5. some texture features from second-order textures

		N	MEAN	SD	SIG
Pre Diast_GLRLM_LGRE	HC	25	0.006	0.012	0.030
	HF	23	0.001	0.001	0.028
Pre Diast_GLRLM_HGRE	HC	25	1 175.960	410.590	0.000
	HF	23	1616.442	396.286	0.000
Pre Diast_GLRLM_SRIGE	HC	25	0.004	0.006	0.016
	HF	23	0,001	0.001	0.015
Pre Diast_<GLRLM_SRHGE	HC	25	1114.234	396.508	0.001
	HF	23	1523,583	395.429	0.001
Pre Diast_GLRLM_LRHGE	HC	25	1480,519	477.646	0.000
	HF	23	2134,851	482.152	0.000
Pre Diast_GLRLM_RLNU	HC	25	733.563	247.254	0.021
	HF	23	585.954	168.7 1S	0.019

		N	MEAN	SD	SIG
Pre Diast_GLZLM_LGZE	HC	25	0.003	0.005	0.013
	HF	23	0.001	0.001	0.017
Pre Diast_GLZLM_I-IGZE	HC	25	1222.093	414.055	0.001
	H F	23	1 64 1 .G81	384.752	0.001
Prc Diast_GLZLM_SZLGE	HC	25	0.002	0.003	0.023
	HF	23	0.001	0.001	0.022
Pre Diast_GLZLM_SZHGE	HC	25	1O22.867	364.833	0.002
	HF	23	1376.036	373.932	0.002
Pre Diast_GLZLM_LZHGE	HC	25	3 152.461	861.726	0.000
	HF	23	5943.264	3098.747	0.000
Pre Diast_GLZLM_ZLNU	HO	25	394.972	126.505	0.022
	HF	23	323.820	72.025	0.020

Non-ischemic heart failure - LV thickness and ECV

When analyzed in the heart failure group, we found that LV thickness inverse to ECV of IVS (r=-0.61, p=0.002).

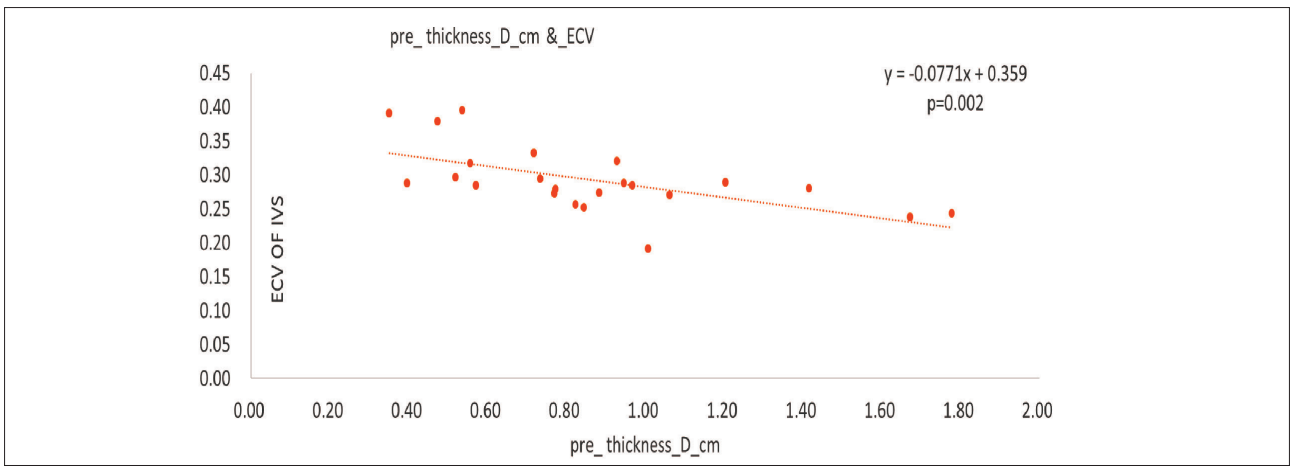

Figure 2. Relationship between LV thickness and ECV

DISCUSSION

In non ischaemic cardiomyopathy, ventricular dysfunction is a consequence of myocardial related to including haemodynamic pathology, infection, immunologic abnormalities, toxic injury, or genetic factors. Any of the cardiac pathology causing myocardial dysfunction results in abnormal myocyte growth, with a resultant cascade of gen activation stimulating cardiac remodeling. The hallmarks of cardiac remodeling are myocardial cell hypertrophy and cardiac dilation with increased interstitial matrix formation. In late stage, the pathologic progress is characterized by myocytolysis, a disruption of sarcomeres. In the chronic phase, some components increase and cause myocyte death, creating perivascular fibrosis within intramuscular vessels. This process causes fibrillary collagen to fill the place of dead myocytes. Ultimately, the disruption of mechanical power by the damaged myocytes becomes

detrimental, and the left ventricular wall becomes thinner and dilated (12) In the present study, LV thickness of NIHF was similar to that of HC. This result suggest that our patient group had not yet reached the stage of dilated cardiomyopathy. However, our study found a larger outer diameter of heart failure patients. This susggets that this parameter is more valuable in NIHF.

Native T1 map measures a composite signal from myocytes and interstitium. Also, it provides new insight into the quantification of fibrosis, infiltration or scar. Our study demonstrated that the mean T1 values were significantly differences between patients and normal groups while, ECV values were similarities in both groups. Moreover, it found that TA of native T1 images, especially the sencond-features is feasible for finding the difference of pathological and normal myocardium in NIHF. This study also has similar results with some studies on native T1 mapping application to distinguish some cardiomyopathies such as dilated cardiomyopathy, hypertensive disease, hypertrophic cardiomyopathy (author Ulf Neisius et al (13), author Shao et al (14)). The histogram and GLCM are two of the most commonly used texture parameters like the two studies above while in the present study showed that TA of T1 mapping had significant difference in several second-order textures, such as GLRLM, GLZLM, composite GLRM_LGRE, GLRLM_HGRE, GLRLM_SRLGE, GLRLM_SRHGE, GLRLM_SRHGE, GLRLM_LRHGE, GLRLM_RLNU, GLZLM_LGZE, GLZLM_HGZE, GLZLM_SZLGE, GLZLM_SZHGE, GLZLM_LZHGE, GLZLM_ZLNU. In comparison to first order features, where a lot of the spatial information was lost through the transformation of gray levels into counts in the histogram, GLRLM, and GLZLM features contain more information about the distribution of gray values since they account for the location of each voxel with regard to the neighboring voxels (15,16).

The present study had several limitations. First, the small sample size restricted the subgroup analysis of NIHF. Second, for the software property, we analyzed only one 4C view image. Two-dimensional texture features may produce a selection bias.

CONCLUSION

In NIHF with preserved WT of LV, texture analysis of T1 and ECV maps showed difference in the mean value of native T1 and texture features, which is promising as a base for machine learning with future larger cohort

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Correspondent: Chau Thi Ngoc Anh. Email: dr.chauthingocanh@gmail.com
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