Original Article

Correlation Between CMR T2 and Advanced Echocardiographic Right Ventricular Function Criteria in Patients With Major Thalassemia*

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ABSTRACT

Background: Tissue iron deposition is an important adverse effect in patients with major thalassemia, leading to right-sided heart failure. This study was performed to determine the association between cardiovascular magnetic resonance using T2-weighted sequences (CMR T2*) and advanced echocardiographic right ventricular (RV) function criteria in patients with major thalassemia at Rajaie Cardiovascular, Medical, and Research Center in 2014 and 2015.

Method: This comparative study assessed the association between CMR T2* and advanced echocardiographic RV function criteria in 38 patients with major thalassemia at Rajaie Cardiovascular, Medical, and Research Center in 2014 and 2015.

Results: CMR T2* was correlated with the RV E/E' (echo) (P = 0.0001, r = -0.681), TAPSE (echo) (P = 0.001, r = 0.504), RVEDV (CMR) (P = 0.008, r = 0.425), and RVEDV/BSA (CMR) (P = 0.005, r = 0.443) according to the Spearman test. Additionally, CMR T2* was associated with the basal RV Sm (echo) (P = 0.0001, r = 0.626), RV strain (echo) (P = 0.034, r = 0.382), RVEDV/H (CMR) (P = 0.002, r = 0.483), LVEDV (CMR) (P = 0.022, r = 0.372), and LVEDV/H (CMR) (P = 0.017, r = 0.385) according to the Pearson test.

Conclusions: Totally, according to the obtained results, it may be concluded that the RV E/E', TAPSE**,** basal RV Sm, and RV strain from echocardiography and the RVEDV, RVEDV/BSA, RVEDV/H, LVEDV, and LVEDV/H from CMR may be indicators of myocardial iron overload in patients with major thalassemia. ***(Iranian Heart Journal 2018; 19(1):15-20)***

KEYWORDS: CMR T2*, Advanced right ventricular function, Major thalassemia

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Beta thalassemia is a common hemoglobinopathy worldwide, especially in Iran. According to genetic inheritance, symptoms, and blood transfusion need, beta thalassemia may be divided into minima, minor, intermedia, and major subtypes. In the major type, regular blood transfusion may result in normal growth and activity and inhibit bone-marrow activation, osteoporosis, and cosmetic problems. However, iron overload and hemosiderosis is inevitable due to a prolonged blood transfusion. [1]

Iron deposition can be seen after the saturation of iron carrier proteins, leading to organ injury—especially cardiotoxicity, which is the main cause of the death in major thalassemia patients despite some chelators. [1] Since iron chelators are usually used with delay due to the late diagnosis of the symptoms and echocardiographic findings, the prognosis can be worse. [2, 3] It is usually presented as congestive heart failure, leading to death if not treated. [4]

Cardiovascular magnetic resonance using T2-weighted sequences (CMR T2*) is currently used to assess the iron load in the liver and heart. A noninvasive modality, the diagnostic power of CMR T2* is widely regarded as accurate in some organs. [5-9] In patients with a reduced ventricular function, a T2* value less than 20 ms is correlated with iron overload. Furthermore, patients with T2* values less than 10 ms are in higher risk for heart failure in the upcoming year. Tissue echocardiography is another noninvasive method for the assessment of diastolic and systolic dysfunction at early stages. The association between CMR T2* and a decreased left ventricular function has been demonstrated in some studies. There are a few studies in the existing literature on the relationship between CMR T2* and the right ventricular (RV) function in echocardiography. If such association is found, it may be used as a predictive tool for myocardial iron overload. This finding may in turn confer a faster and less expensive determination of chelators to prevent further left ventricular dysfunction. The present study was performed to determine the association between CMR T2* and advanced echocardiographic RV function criteria in patients with major thalassemia.

METHOD

This comparative study was performed among 38 patients with major thalassemia at Rajaie Cardiovascular, Medical, and Research Center in 2014 and 2015. The exclusion criteria were comprised of pulmonary artery systolic pressure of 35 mm Hg or more (by echocardiography), moderate-to-severe valvular heart disease, congenital heart diseases, and contraindication for CMR. The hemoglobin level of all the patients was within the therapeutic range. The association between CMR T2* and advanced echocardiographic RV function criteria was assessed in the study population.

Data analysis was performed among the 38 patients using SPSS, version 24.0 (Statistical Procedures for Social Sciences; Chicago, Illinois, USA). The χ^2, Fisher, Pearson, and Spearman tests were used and the results were considered statistically significant at *P* values less than 0.05.

RESULTS

The echocardiographic RV function indices and the indices of the right and left ventricular functions and volumes in CMR are presented in Table 1. As is depicted in Table 2, an RV E/E' (echo) more than 6 was significantly accompanied by a CMR T2* value less than 20 ($P < 0.0001$) or myocardial iron overload.

Table 1. Echocardiographic right ventricular function indices and the indices of the right and left ventricular functions and volumes in CMR

	Minimum	Maximum	Mean	Std. Deviation
RV E/E’	3.50	9.10	5.0474	1.24656
TAPSE	16.00	28.00	23.2368	3.11435
Basal RV Sm	9.00	18.70	13.8342	2.30584
RV Size	26.00	40.00	31.7105	4.19077
RV Strain	19.00	30.00	24.5677	3.19441
CMR T2*	2.60	57.00	25.1000	13.31770
RVEDV	64.00	226.00	118.3684	33.46997
RVESV	29.00	122.00	57.1053	19.35276
RVEF	30.00	62.00	51.4211	6.84828
RVEDV/BSA	49.00	134.00	81.4474	17.70127
RVESV/BSA	22.00	70.00	39.0789	10.68563
RVEDV/H	43.00	122.00	74.5000	17.73034
RVESV/H	19.00	66.00	35.6053	10.54088
LVEDV	61.00	215.00	127.8947	34.04194
LVESV	24.00	110.00	58.3421	17.84055
LVEF	43.00	75.00	54.0526	6.31578
LVEDV/BSA	46.00	150.00	86.7368	19.11937
LVESV/BSA	17.00	76.00	39.6053	11.08332
LVEDV/H	40.00	127.00	80.3158	17.98964
LVESV/H	16.00	64.00	36.5263	9.88512

CMR, Cardiac magnetic resonance; RV, Right ventricular; TAPSE, Tricuspid annular plane systolic excursion; EDV, End-diastolic volume; ESV, End-systolic volume; EF, Ejection fraction; BSA, Body surface area; H, Height; LV, Left ventricular

Table 2. Comparison of the RV E/E’ (echo) and CMR T2*

			RV E/E’ 6		Total
			.00	1.00	
CMR T2* 20	.00	Count	1	12	13
		% within CMRT2* 20	7.7%	92.3%	100.0%
	1.00	Count	25	0	25
		% within CMRT2* 20	100.0%	0.0%	100.0%
Total		Count	26	12	38
		% within CMRT2* 20	68.4%	31.6%	100.0%

Table 3. Comparison of the RV strain (echo) and CMR T2*

			RV Strain 20		Total
			.00	1.00	
CMR T2* 20	.00	Count	2	8	10
		% within CMRT2* 20	20.0%	80.0%	100.0%
	1.00	Count	0	21	21
		% within CMRT2* 20	0.0%	100.0%	100.0%
Total		Count	2	29	31
		% within CMRT2* 20	6.5%	93.5%	100.0%

As is demonstrated in Table 3, a CMR T2* value less than 20 was not related to the RV strain (echo) (P = 0.097). In 7 cases, there was a poor echo window for the assessment of the RV strain. As is shown in Table 4, CMR T2* was correlated with the RV E/E’ (echo) (P = 0.0001, r = -0.681), TAPSE (echo) (P = 0.001, r = 0.504), RVEDV (CMR) (P = 0.008, r = 0.425), and RVEDV/BSA (CMR) (P = 0.005, r = 0.443) according to the Spearman test. Furthermore, as is illustrated in Table 5, CMR T2* was related to the basal RV Sm (echo) (P = 0.0001, r = 0.626), RV strain (echo) (P = 0.034, r = 0.382), RVEDV/H (CMR) (P = 0.002, r = 0.483), LVEDV (CMR) (P = 0.022, r = 0.372), and LVEDV/H (CMR) (P = 0.017, r = 0.385) according to the Pearson test.

Table 4. Association between CMR T2* and the echocardiographic right ventricular function indices and the indices of the right and left ventricular functions and volumes in CMR by the Spearman test

Spearman's rho		CMR T2*
RV E/E'	Correlation coefficient	-.681
	Sig. (2-tailed)	.000
TAPSE	Correlation coefficient	.504
	Sig. (2-tailed)	.001
RVEDV	Correlation coefficient	.425
	Sig. (2-tailed)	.008
RVESV	Correlation coefficient	.229
	Sig. (2-tailed)	.167
RVEF	Correlation coefficient	.180
	Sig. (2-tailed)	.279
RVEDV/BSA	Correlation coefficient	.443
	Sig. (2-tailed)	.005
RVESV/BSA	Correlation coefficient	.194
	Sig. (2-tailed)	.242
RVESV/H	Correlation coefficient	.217
	Sig. (2-tailed)	.192
LVEF	Correlation coefficient	.097
	Sig. (2-tailed)	.562
LVEDV/BSA	Correlation coefficient	.242
	Sig. (2-tailed)	.143

CMR, Cardiac magnetic resonance; RV, Right ventricular; TAPSE, Tricuspid annular plane systolic excursion; EDV, End-diastolic volume; ESV, End-systolic volume; EF, Ejection fraction; BSA, Body surface area; H, Height; LV, Left ventricular

Table 5. Association between CMR T2* and the echocardiographic right ventricular function indices and the indices of right and left ventricular functions and volumes in CMR by the Pearson test

Pearson Correlation		CMR T2*
Basal RV Sm	Pearson Correlation	.626
	Sig. (2-tailed)	.000
RV Size	Pearson Correlation	.108
	Sig. (2-tailed)	.519
RV Strain	Pearson Correlation	.382
	Sig. (2-tailed)	.034
RVEDV/H	Pearson Correlation	.483
	Sig. (2-tailed)	.002
LVEDV	Pearson Correlation	.372
	Sig. (2-tailed)	.022
LVESV	Pearson Correlation	.273
	Sig. (2-tailed)	.097
LVESV/BSA	Pearson Correlation	.206
	Sig. (2-tailed)	.214
LVEDV/H	Pearson Correlation	.385
	Sig. (2-tailed)	.017
LVESV/H	Pearson Correlation	.272
	Sig. (2-tailed)	.099

CMR, Cardiac magnetic resonance; RV, Right ventricular; TAPSE, Tricuspid annular plane systolic excursion; EDV, End-diastolic volume; ESV, End-systolic volume; EF, Ejection fraction; BSA, Body surface area; H, Height; LV, Left ventricular

DISCUSSION

The present study was performed to determine the association between CMR T2* and advanced echocardiographic RV function criteria in patients with major thalassemia. We found that CMR T2* was correlated with the RV E/E', TAPSE, basal RV Sm, and RV strain from echocardiography and the RVEDV, RVEDV/BSA, RVEDV/H, LVEDV, and LVEDV/H from CMR. Moreover, an RV E/E' more than 6 was significantly accompanied by a CMR T2* value less than 20 or myocardial iron overload. The major limitations of the current study were inability to conduct CMR for all the patients owing to economic constraints and the exclusion of some cases due to the presence of pulmonary hypertension and inaccurate measurement of the RV strain due to poor echo windows.

Alpendurada et al [10] found that myocardial iron deposition was allied to right ventricular dysfunction and was also predictive of left ventricular dysfunction, which chimes in with the findings of the current study. A meta-analysis by Rozelle Jade Javier et al [11] showed that increased iron overload was related to left ventricular dysfunction, increased Tei index, and shortened deceleration time; we had similar findings in our study vis-à-vis the left and right ventricular functions and volumes.

A study by Saravi et al [12] showed that tissue Doppler might predict myocardial iron overload and could be used for screening. Good applicability of this imaging modality was also seen in our study. In addition, Vogel et al [13] reported that wall motion disorders were the primary sign of heart disease despite a good cardiac function owing to iron overload, which might be easily found by tissue Doppler. We found similar results with respect to the relationship between CMR T2* and the RV diastolic function as measured by tissue Doppler imaging.

Seldrum et al [14] demonstrated that iron overload was correlated with left ventricular systolic and diastolic dysfunction. The authors showed that Twist in the left ventricle had an early involvement with the highest impact on T2* and recommended the use of Twist for the monitoring of the left ventricular systolic function in patients with iron overload. In our study, the RV E/E' had the highest relationship but with a reverse direction. Leonardi et al [15] reported a significant association between the EF and T2* as a good predictive factor for heart failure progression and modification of chelator therapeutics. The diastolic function parameters had a poor association with T2* and the EF. In our study, 9 factors had medium-level associations and the RV diastolic function (RV E/E') had a high level of association but in a reverse direction.

Totally, according to the obtained results, it may be concluded that the RV E/E', TAPSE, basal RV Sm, and RV strain from echocardiography and the RVEDV, RVEDV/BSA, RVEDV/H, LVEDV, and LVEDV/H from CMR may be the indicators of myocardial iron overload in patients with major thalassemia. Further studies with larger sample sizes and more power are required to attain more definite results.

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