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Letter to the Editor

SAECG parameters and left ventricular chamber sizes: Lesson from anemia conditions in thalassemia major patients

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β-Thalassemia is a genetic disease that leads to anemia with a prevalence in the world that varies from 3% to 30% and a particular preponderance among patients of Mediterranean origin [1]. Among transfusion dependent thalassemia patients (thalassemia major (TM)) [2], iron overload occurs secondary to transfusions and increased absorption of iron from the guts. The heart is one of the major organs affected with iron overload, and cardiac death remains the leading cause of death worldwide among TM patients. The effect of iron-overload on the heart in thalassemia is proposed to be secondary to a complex oxidative damage pathway leading to cellular apoptosis [3–6]. Initially abnormal diastolic function ensues leading eventually to systolic congestive heart failure (CHF) [7]. Sudden cardiac death (SCD) is thought to account for 5–7% of deaths among thalassemia patients [8,9]. Signal averaged electrocardiography (SAECG) identifies patients with ventricular late potentials (VLP) and earlier studies have shown that patients with impaired left ventricular ejection fraction with VLP are at increased risk of sudden cardiac death [10,11]. A recent study by Franzoni et al. showed the prevalence of VLP among Italian TM patients detected by SAECG was 31.5% (6/19) and with 67% of these patients (4/6) having non-sustained ventricular tachycardia (NSVT) [12]. In comparison 66 Lebanese TM patients – randomly selected from 400 patients regularly followed up at the Chronic Care Center – and 20 healthy controls underwent SAECG and Doppler echocardiography. In line with the literature several echo-Doppler parameters were significantly different in the TM group in comparison to the controls, however this was not observed in the SAECG criteria (Fig. 1). Moreover we found that despite no apparent differences between the Italian and the Lebanese TM patients the prevalence of VLP among the Lebanese TM was less (31.5% vs. 3% Italian and Lebanese cohorts, respectively) (Fig. 2). Ethnic variation in the prevalence of VLP based on the American College of Cardiology recommendations [11] remain a possible cause for this difference, especially that in a study performed in Southwestern France the prevalence of VLP in healthy individuals was 21% in comparison to 5% in a similar study performed in Germany [13,14]. Interestingly our study revealed that from the echo-Doppler parameters only the left ventricular chamber sizes were significantly correlated with SAECG criteria (Fig. 3). However with the absence of echocardiography data in the Italian study the possibility that different chamber sizes – probably because of different transfusion protocols followed in Lebanon and Italy – playing a role in the difference of VLP prevalence remains a speculative reason. Furthermore as anemia is a co-morbid illness in 50% of CHF patients [13,14], then probably anemia leading to secondary chamber enlargement should be taken into account as a possible confounding factor in future SAECG studies. This would be of importance specifically in

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studies utilizing SAECG for intracardiac defibrillator implantation decision making. In conclusion we find that investigating the contribution of SAECG in identifying patients at risk of SCD among TM patients is needed but no clinical recommendation could be currently made.

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	Mean ± SD		p-value
	TM Lebanon	Controls	
N	66	20	-
Males	33 (50%)	8 (40%)	0.02
Age	19.4±7.6	12.9±2.2	< 0.01
RMS μV	58.1±36.9	80.25±75.04	0.30
LAS ms	24.6±8.4	23.43±11.51	0.73
QRS ms	92±10.1	88.36±11.88	0.27
% VLP	3.0%	0%	-
Heart Rate	82.24±12.85	81.30±15.20	0.78
E cm/s	103.27±16.00	104.60±12.54	0.74
A cm/s	52.02±16.35	46.45±11.55	0.16
E/A	2.26±1.43	2.36±0.59	0.76
Dt ms	168.35±32.39	173.45±38.26	0.56
IVRT ms	63.61±11.36	54.55±6.86	< 0.01
Left Atrium (cm)	3.91±0.62	3.32±0.38	< 0.01
EDD (cm)	4.93±0.65	4.46±0.52	< 0.01
ESD (cm)	3.06±0.52	2.67±0.41	< 0.01
Septum (cm)	0.85±0.15	0.79±0.08	0.02
Free wall (cm)	0.78±0.14	0.70±0.09	< 0.01
EF%	61.12±7.53	63.86±6.64	0.13

Fig. 1. Comparison of echo-Doppler and SAECG parameters between TM patients and controls. FW = free wall, ESD = end systolic dimension, EDD = end diastolic dimension, E = early phase diastolic filling, A = atrial phase diastolic filling, IVRT = *iso*-volumic relaxation time, EF = ejection fraction, DT = declaration time , S and FW = septal and free wall thickness, respectively. RMS = root mean square of the terminal 40 ms (RMS40), LAS = duration of the terminal QRS of low amplitude signal <40 μV, QRS = filtered QRS complex duration.

	TM Lebanon	TM Italy*	p-value
N	66	19	
Males	33	12	
Age (years)	19.4±7.6	18.4±8.3	NS
RMS μ V	58.1±36.9	25.4±12.5	NS
LAS ms	24.6±8.4	36.4±11.3	NS
QRS ms	92±10.1	108.8±16.5	NS
% VLP ¥	3.0%	31.6%	
Ferritin	1997.2	2109.8	†

Fig. 2. SAECG results in the Lebanese and Italian TM groups NS not significant defined as *p* value > 0.05. [a]Franzoni et al. [12]. [b]As per criteria listed in Cain et al. [11]. [c]Standard deviation in Franzoni et al. [12] not available to allow comparison.

	QRS		LAS		RMS	
	r	p-value	r	p-value	r	p-value
EDD cm	0.42	**<0.01**	0.43	**<0.01**	-0.37	**<0.01**
ESD cm	0.35	**<0.01**	0.45	**<0.01**	-0.36	**<0.01**
E cm/s	0.06	0.61	-0.05	0.69	0.04	0.74
A cm/s	-0.05	0.68	-0.06	0.61	0.08	0.53
Dt ms	0.07	0.57	0.18	0.15	-0.13	0.30
IVRT ms	0.09	0.47	0.14	0.26	-0.18	0.15

Fig. 3. Correlation between individual SAECG parameters and echo-Doppler parameters of TM patients.

Disclosure

This study was not funded, and there is no potential conflict of interest for any of the participants.

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