

Scientific letter

Impaired myocardial deformation assessed by cardiac magnetic resonance is associated with increased arrhythmic risk in hypertrophic cardiomyopathy



Deformación miocárdica basada en resonancia magnética cardíaca y riesgo arrítmico en la miocardiopatía hipertrófica

To the Editor,

Despite the advances in sudden cardiac death (SCD) prediction in hypertrophic cardiomyopathy (HCM), interest in new risk markers is growing.¹ Late gadolinium enhancement (LGE) quantified as a percentage of left ventricular (LV) mass in cardiac magnetic resonance (CMR) has been suggested as an independent predictor for SCD.² Areas of interstitial fibrosis or myocyte disarray also seem to be important to the genesis of ventricular arrhythmias.³

Tissue tracking imaging enables quantitative assessment of myocardial mechanics by evaluating myocardial deformation. Reduced strain was shown to correlate with interstitial fibrosis³ and strain values were described as being lower in areas of hypertrophied nonenhanced myocardium, suggesting that mechanisms such as myocyte disarray may also contribute.⁴ Given the

combination of image quality with the possibility of easy postprocessing analysis, feature tracking cardiac magnetic resonance (FT-CMR) is increasingly used in clinical practice. Global measurements are more reproducible than regional ones; although feasible, there is limited experience of the use of 3D strain measurements.

Our aim was to analyze the association between LV 2D global strain measurements using FT-CMR, morphologic features and prognostic markers in HCM.

We retrospectively reviewed consecutive HCM patients followed up clinically at 2 referral centers, who were older than 16 and had a diagnostic CMR assessment during follow-up. Those with HCM caused by metabolic or syndromic diseases or with evidence of coronary artery disease (coronary stenosis $\geq 50\%$ or subendocardial LGE on CMR) were excluded. We defined “ventricular arrhythmias” (VA) as nonsustained ventricular tachycardia on 24h-Holter monitoring (timing decided by the attending physician), sustained ventricular tachycardia, ventricular fibrillation or SCD. SCD risk was estimated using the score proposed in the European Society of Cardiology 2014 guidelines.

CMR imaging was acquired on 1.5 T scanners and imaging analysis was performed by 2 expert readers (one in each center).

Table 1

Clinical and CMR characteristics of total population and after stratification by presence of VA

	Total (n = 109)	Stratified		P
		HCM with VA (n = 26)	HCM without VA (n = 73)	
<i>Clinical characteristics</i>				
Age, y	59.2 ± 16.2	62.1 ± 15.2	57.3 ± 16.6	.174
Male, %	60.6	73.1	57.5	.162
Atrial fibrillation, %	9.2	15.4	8.2	.448
LA diameter, cm	44.0 ± 8.3	47.1 ± 11.2	42.9 ± 6.8	.061
Maximal wall thickness, mm	19.9 ± 4.8	20.6 ± 3.8	19.6 ± 5.3	.072
Obstructive HCM, %	25.8	30.4	24.3	.559
Syncope, %	6.2	12.0	4.2	.176
Family history HCM, %	24.5	22.7	25.0	.828
Family history SCD, %	20.4	16.0	21.9	.526
VA, %	26.3	-----	-----	
SCD risk score, %/5 y	3.12 ± 2.98	5.85 ± 4.42	2.13 ± 1.21	< .001
ICD implanted, %	11.5	25.0	6.9	.026
<i>CMR characteristics</i>				
LA area, cm ²	28.6 ± 7.2	32.2 ± 9.4	27.7 ± 6.1	.032
LV end-diastolic volume, mL	148.8 ± 35.5	156.5 ± 40.0	144.1 ± 33.6	.188
LV mass, g	170.6 ± 70.3	187.5 ± 76.0	159.2 ± 61.7	.116
LV ejection fraction, %	63.7 ± 10.0	59.9 ± 13.7	65.6 ± 8.1	.104
LGE presence, %	80.0	88.5	79.7	.385
LGE extension, % of LV mass	7.7 ± 6.7	10.2 ± 8.9	7.2 ± 5.7	.161
GLS, %	-14.8 ± 4.0	-13.2 ± 4.1	-15.5 ± 3.7	.011
GRS, %	34.4 ± 13.3	28.1 ± 11.2	36.5 ± 12.1	.020
GCS, %	-17.5 ± 4.8	-15.3 ± 4.6	-18.3 ± 4.3	.017

CMR, cardiac magnetic resonance; GCS, global circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LA, left atrium; LGE, late gadolinium enhancement; LV, left ventricle; SCD, sudden cardiac death; VA, ventricular arrhythmias. Unless otherwise indicated, values are mean ± standard deviation or percentage.

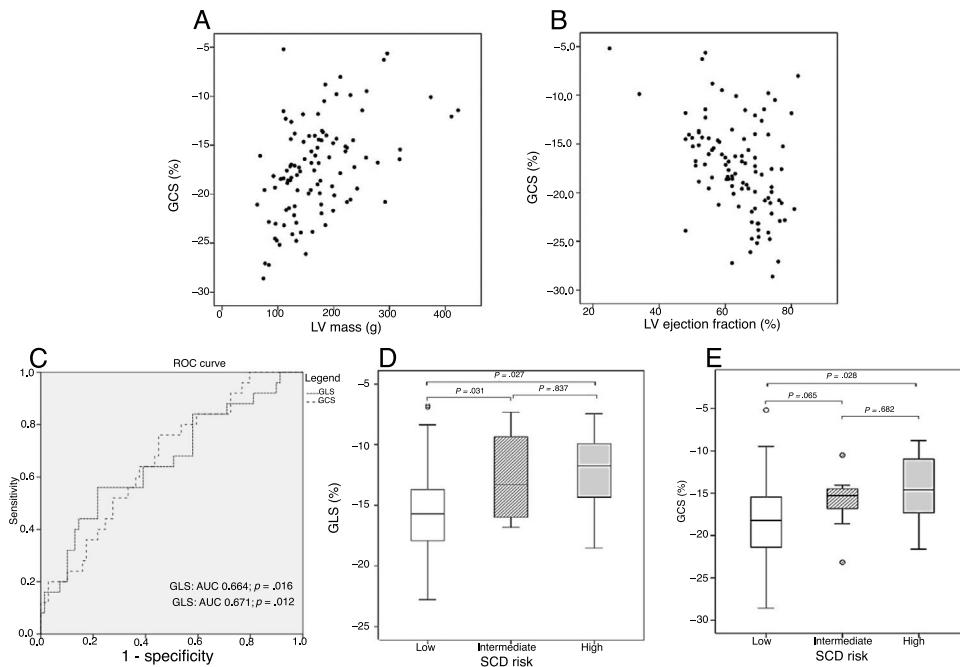


Figure 1. Scatter plots of GCS values relative to left ventricle mass (A) and ejection fraction (B) showing a correlation between the 2 variables. Receiver operating curve for the ability of GLS and GCS to predict ventricular arrhythmias (C). Boxplots of GLS (D) and GCS (E) stratified by sudden cardiac death risk category. AUC, area under the curve; GCS, global circumferential strain; GLS, global longitudinal strain; SCD, sudden cardiac death; LV, left ventricular.

LGE was assessed 10 to 15 minutes after intravenous administration of gadobutrol/gadoterate meglumine using a phase-sensitive inversion-recovery sequence. The LV short-axis stack of LGE images was first assessed visually for the presence of LGE. Quantification of LGE was then performed by 1 expert reader (N. Dias Ferreira) on all LGE-positive studies by measuring regions with signal intensity $> 5SD$ above remote myocardium and expressed as a percentage of LV mass. 2D peak global radial strain (GRS), global longitudinal strain (GLS) and global circumferential strain (GCS) were evaluated retrospectively on steady state free precession sequences using a commercially available software (cvi42, Circle Cardiovascular Imaging Inc, Calgary, Canada). Endocardial and epicardial borders were manually drawn in the end-diastolic and end-systolic frame in the long-axis slices and in all short-axis slices comprised between the base and the apex. GLS was averaged from the 3 standard longitudinal views while GRS and GCS were averaged from the basal, mid and apical LV short-axis planes.

Comparisons between groups were performed using the Student *t* test, Mann–Whitney *U*, Kruskal–Wallis, chi-square or Fisher exact tests as appropriate. Correlations were measured by the Spearman's coefficient. Statistical significance was defined as a *P* value $< .05$.

A total of 109 HCM patients (60.6% males), with a mean age of 59.2 ± 16.2 years, were included in the study. Mean follow-up was 39 ± 25 months and VA were documented in 26 patients (26.3%): 24 patients with nonsustained ventricular tachycardia and 2 with SCD. Mean estimated baseline SCD risk at 5 years was $3.12 \pm 2.98\%$ (79.1% low-risk, 11.6% intermediate-risk and 9.3% high-risk). LGE was observed in 80% of patients and involved $7.7 \pm 6.7\%$ of LV mass. Mean GLS, GRS and GCS were $-14.8 \pm 4.0\%$, $34.4 \pm 13.3\%$ and $-17.5 \pm 4.8\%$, respectively. Table 1 summarizes clinical and CMR characteristics of the total population and after stratification for the presence of VA.

Impaired strain values correlated with higher LV mass (GLS: $r = 0.46$; GRS: $r = -0.46$; GCS: $r = 0.47$ – figure 1A; $P < .001$ for all), reduced LV ejection fraction (GLS: $r = -0.33$; GRS: $r = 0.44$; GCS: $r = -0.41$ – figure 1B; $P < .003$ for all) and LGE extension (GLS: $r = 0.24$, $P = .027$; GRS: $r = -0.34$, $P = .001$; GCS: $r = 0.37$; $P < .001$).

Patients with VA had worse strain values (GLS $-13.2 \pm 4.1\%$ vs $-15.5 \pm 3.7\%$, $P = .011$; GRS $28.1 \pm 11.2\%$ vs $36.5 \pm 12.1\%$, $P = .02$; GCS $-15.3 \pm 4.6\%$ vs $-18.3 \pm 4.3\%$, $P = .017$), table 1. Receiver operating curve for the ability of GLS and GCS to predict VA showed an area under the curve of 0.664 (95%CI, 0.535–0.793) and 0.671 (95%CI, 0.552–0.789) respectively – figure 1C.

Patients with low estimated risk of SCD had better GLS values than those at intermediate (-15.5 ± 3.8 vs -12.6 ± 3.5 ; $P = .031$; figure 1D) and high-risk (-12.2 ± 3.6 , $P = .027$; figure 1D). They also had better GCS values compared with those at high-risk (-18.0 ± 4.5 vs -14.5 ± 4.3 , $P = .028$; figure 1E) and a tendency toward better values compared with patients at intermediate SCD risk (-15.9 ± 3.3 , $P = .065$; figure 1E).

The correlations found between strain and LV mass, ejection fraction and LGE extension are consistent with previous studies using FT-CMR.^{5,6} However, LGE extension was not significantly different in patients with or without VA. This might be explained in part by the relatively small population. Another study limitation was the residual number of sudden cardiac deaths; mirroring the methodology in other small studies, we have included nonsustained ventricular tachycardia in the arrhythmic composite outcome. Additionally, as we recruited only patients who underwent CMR, it is possible that a selection bias existed.

In our cohort, mean strain values were within the normal range. However, they were significantly better in patients with lower arrhythmic risk.

In conclusion, worse strain measurements were associated with a more severe HCM phenotype, the presence of VA and a higher estimated risk of SCD. Larger prospective studies are needed to

assess its incremental value relative to the existing markers of SCD risk in HCM.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at <http://dx.doi:10.1016/j.rec.2020.02.008>

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REFERENCES

- van der Bijl P, Podlesnikar T, Bax JJ, Delgado V. Sudden cardiac death risk prediction: the role of cardiac magnetic resonance imaging. *Rev Esp Cardiol.* 2018;71:961–970.
- Weng Z, Yao J, Chan RH, et al. Prognostic Value of LGE-CMR in HCM: A Meta-Analysis. *JACC Cardiovasc Imaging.* 2016;9:1392–1402.
- Almaas VM, Haugaa KH, Strøm EH, et al. Noninvasive assessment of myocardial fibrosis in patients with obstructive hypertrophic cardiomyopathy. *Heart.* 2014;100:631–638.
- Aletras AH, Tilak GS, Hsu LY, et al. Heterogeneity of intramural function in hypertrophic cardiomyopathy: mechanistic insights from MRI late gadolinium enhancement and high-resolution displacement encoding with stimulated echoes strain maps. *Circ Cardiovasc Imaging.* 2011;4:425–434.
- Hinojar R, Fernández-Golfín C, González-Gómez A, et al. Prognostic implications of global myocardial mechanics in hypertrophic cardiomyopathy by cardiovascular magnetic resonance feature tracking. *Relations to left ventricular hypertrophy and fibrosis Int J Cardiol.* 2017;249:467–472.
- Nucifora G, Muser D, Gianfagna P, et al. Systolic and diastolic myocardial mechanics in hypertrophic cardiomyopathy and their link to the extent of hypertrophy, replacement fibrosis and interstitial fibrosis. *Int J Cardiovasc Imaging.* 2015;31: 1603–1610.

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Awake VA-ECMO in cardiogenic shock: an experience with future potential



Awake ECMO-VA en shock cardiogénico: una experiencia prometedora

To the Editor,

The current guidelines from the European Society of Cardiology for the treatment of cardiogenic shock (CS) put circulatory support with venoarterial extracorporeal membrane oxygenation (VA-ECMO) as the last therapeutic step after inotropes and invasive mechanical ventilation; in emergency situations, it is a suitable option.¹ In respiratory disease, there is increasing use of support with venovenous ECMO implanted in conscious patients who therefore have spontaneous breathing (awake ECMO). This modality aims to avoid intubation, invasive mechanical ventilation, and the associated sedation and immobility, and there is evidence of better postoperative outcomes in terms of complications and mortality.^{2,3} In the current literature, there is very limited evidence on VA-ECMO in CS. So far, only isolated cases and 3 small series (2 in adults and 1 in children) have shown that it is viable and has good outcomes as a rescue for acute CS (23 patients; 6-month survival, 70.8%)⁴ and in patients with advanced heart failure and INTERMACS profile 1 who require support as a bridge to device implantation (19 patients; 1-year survival, 84.2%).⁵

We present the positive experience from our hospital with a group of patients with CS treated with awake VA-ECMO. Of the 73 VA-ECMO implantations for CS between 2010 and 2018, 10 (13.7%) were implanted in patients with spontaneous breathing; 70% of these were in men, with a median [interquartile range] age of 50 [47–57] years. The median APACHE-II score was 16 [9–19], and the SAPS-II score, 30 [25–32]. The most common cause of CS was decompensation of advanced heart failure in patients awaiting transplant (7 patients; 71% in INTERMACS 1 and 29% in INTERMACS 2) and the rest were: 1 acute myocardial infarction

in Killip class IV, 1 septic cardiomyopathy, and 1 acute myocarditis (all 3 were in INTERMACS 1). The aim of circulatory support in the first 8 patients was as a bridge to transplant (7) or to decision on definitive treatment (1); 6 (75%) of these patients finally received a transplant and 2 died while on circulatory support (1 due to malignant cerebral infarction and 1 due to refractory multiorgan failure). In the patients with septic myocardopathy and acute myocarditis, the aim was as a bridge to recovery. Eight patients had implantation of an intra-aortic balloon pump: 5 had already had this implanted prior to ECMO support (those in INTERMACS 1), and 3 required it while on support to offload the left ventricle (table 1).

All ECMO implantations were performed in the intensive care unit with a femorofemoral configuration, except 1 which was implanted in the operating room with a femoroaxillary configuration. The median duration of support was 8 [6.5–11.9] days. Weaning was possible in 80% of the patients (all except the 2 who died), and the overall survival in the intensive care unit was 60%, while survival to discharge from hospital was 50%, similar to that of our general VA-ECMO series.⁶ While on ECMO, 3 patients required intubation and invasive mechanical ventilation due to acute pulmonary edema (2) or stroke (1) (table 2), with a median duration of invasive mechanical ventilation of 84 [57–96] hours; in our general series, this was 312 [126–564] hours. Prior to their intubation, these patients had been on awake ECMO for 6, 60, and 64 hours. The median stay in ICU was 16 [14–18] days and the median hospital stay was 37 [28–59] days.

Regarding complications, 9 patients (90%) had at least 1 complication associated with their circulatory support or clinical condition, with a distribution similar to that published in the literature. The most common complication was pericannular bleeding (5), followed by lower limb ischemia (4), other nonintracranial hemorrhage (n), stroke (1), and oxygenator failure (1). Other complications included acute kidney injury in 60% (5 before starting support and 1 after, who required renal replacement therapy, with complete recovery in 100%), infections