



**HAL**  
open science

## Assessment of Myocardial Stiffness in Patients With Left Ventricular Hypertrophy

Emma Burnhope, Alessandro Polcaro, Jurgen Runge, Inka Granlund, Filippo Bosio, Marian Troelstra, Adriana D.M. Villa, Amedeo Chiribiri, Gerald Carr-White, Jessica Webb, et al.

► **To cite this version:**

Emma Burnhope, Alessandro Polcaro, Jurgen Runge, Inka Granlund, Filippo Bosio, et al.. Assessment of Myocardial Stiffness in Patients With Left Ventricular Hypertrophy. *JACC: Cardiovascular Imaging*, 2022, 15 (6), pp.1163-1165. 10.1016/j.jcmg.2022.01.009 . hal-04047356

**HAL Id: hal-04047356**

**<https://hal.science/hal-04047356v1>**

Submitted on 21 Nov 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Public Domain

membership on the steering committee of the CORE320 trial, which is supported in part by Canon Medical Corporation. Drs Linde and Kühl have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

## REFERENCES

1. Ichikawa Y, Kitagawa K, Chino S, et al. Adipose tissue detected by multislice computed tomography in patients after myocardial infarction. *J Am Coll Cardiol Img.* 2009;2(5):548-555.
2. Kühl JT, Linde JJ, Køber L, Kelbæk H, Køfoed KF. The Transmural extent and severity of myocardial hypoperfusion predicts long-term outcome in NSTEMI: an MDCT study. *J Am Coll Cardiol Img.* 2015;8(6):684-694.

## Assessment of Myocardial Stiffness in Patients With Left Ventricular Hypertrophy

CMR Elastography Using Intrinsic Actuation



Left ventricular (LV) hypertrophy or LV wall thickening typically leads to increased myocardial stiffness, which may play an important role in the pathogenesis of heart failure.<sup>1</sup> We previously developed and validated a cardiovascular magnetic resonance (CMR)-based approach to quantify cardiac biomechanics by measuring the speed of flexural shear waves in the septum generated intrinsically by aortic valve closure.<sup>2</sup> Given this approach has the benefits of simple clinical applicability and seamless integration into the standard workflow, we applied it to the routine clinical CMR evaluation of a group of patients with known or suspected LV hypertrophy or thickening. This group included patients with hypertrophic cardiomyopathy (HCM), hypertensive heart disease, and cardiac amyloidosis. Exclusion criteria included contraindications to CMR, atrial fibrillation, and aortic stenosis. Data from patients were compared with data from healthy volunteers. All work was approved by the U.K. National Research Ethics Service.

Myocardial stiffness was estimated by the speed of the flexural shear wave component arising from the mechanical wave that propagates through the septum due to aortic valve closure. Speed was quantified through the wave's time of flight between 2 adjacent navigator beams positioned orthogonally to the septum.<sup>2</sup> Given our temporal resolution of 0.3 ms and a spatial separation of the navigators of ~30 mm, speeds up to ~15 to 20 m/s can be quantified reliably, with values greater than this potentially liable to the effects of discretization error and noise. Values were corrected for wave guidance biases

originating from the relatively thin wall thickness compared with wavelength.<sup>2</sup>

Healthy volunteers were significantly younger and had a more even sex balance than the disease cohort (**Figure 1A**). All 3 disease groups had elevated precontrast  $T_1$ , signifying the presence of interstitial expansion secondary to fibrosis (HCM and hypertension groups) or amyloid fibril deposition. Two-thirds of the HCM group and 17% of the hypertensive cohort had patchy or diffuse midwall fibrosis on late gadolinium enhancement imaging.

Myocardial shear wave speed was significantly elevated in patients with HCM ( $15.2 \pm 10.6$  m/s;  $P < 0.001$ ), cardiac amyloidosis ( $14.0 \pm 4.8$  m/s;  $P < 0.001$ ), and hypertension ( $7.7 \pm 4.8$  m/s;  $P < 0.004$ ) compared with healthy control subjects ( $3.5 \pm 1.3$  m/s), as assessed using Student's *t*-tests. Receiver-operating characteristic analysis using the Youden index identified a shear wave speed of 6.3 m/s provided the optimal ability to discriminate diseased myocardium (C-statistic: 0.916) with a sensitivity of 83% (95% CI: 69.2%-92.4%) and specificity of 100% (95% CI: 83.2%-100%). In the whole cohort, there was a modest but statistically significant association between shear wave velocity and age (**Figure 1B**), driven by differences in the age of presentation of the underlying diseases. However, other investigators have found weak associations even among normal subjects.<sup>3,4</sup>

Although our control subjects were significantly younger, the differences between the disease and control groups were very large and outside the variation seen in the control subjects (**Figure 1B**). Interestingly, independent of age, hypertension did not always lead to elevated myocardial stiffness, a finding reflecting the heterogeneity of the myocardial response to this disease. However, for those patients whose wave speed was elevated, the difference with the control subjects was highly significant. This is in stark contrast to the HCM and amyloid groups, which always showed elevated stiffnesses with no overlap with the control group. Some patients had values beyond 20 m/s, thus representing unrealistically high stiffness values (>400 kPa) indicative of noise, which is more impactful at very high wave speeds (ie, short time delays).

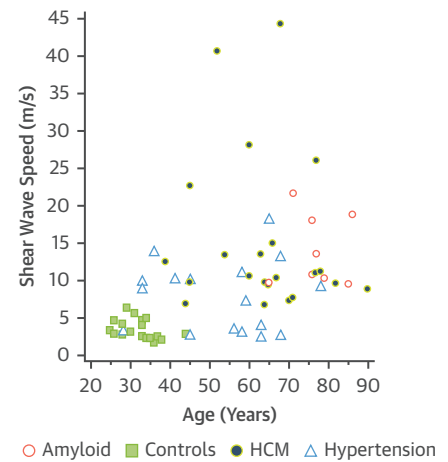
Petrescu et al<sup>5</sup> also used intrinsically generated shear waves but measured by ultrasound to resolve differences in myocardial stiffness between patients with cardiac amyloidosis and healthy control subjects. These investigators obtained a mean velocity of  $5.6 \pm 1.1$  m/s in their amyloid cohort, less

**FIGURE 1** Baseline Characteristics and Shear Wave Speed in Patients and Control Subjects

**A**

	Healthy Volunteers (n = 20)	Hypertensive Heart (n = 18)	Cardiac Amyloid (n = 8)	Hypertrophic Cardiomyopathy (n = 22)
Mean Age (years)	31 ± 5	53 ± 14	77 ± 7	64 ± 13
Gender (% Male)	50	83	88	59
Mean indexed LV-EDV (ml/m <sup>2</sup> )	72 ± 11	87 ± 13	83 ± 23	83 ± 19
Mean LVEF (%)	63 ± 2	59 ± 5	46 ± 11	64 ± 8
Mean LV maximal wall thickness (mm)	6 ± 2	13 ± 2	15 ± 2	16 ± 4
Mean indexed LV mass (g/m <sup>2</sup> )	47 ± 9	76 ± 19	78 ± 26	75 ± 22
LA size (cm <sup>2</sup> )	16 ± 3	24 ± 4	28 ± 7	26 ± 5
Mean native T1 (ms)	N/A	1,291 ± 66	1,548 ± 105	1,344 ± 64
LGE presence (%)	N/A	17	100	64
Mean corrected shear wave speed (m/s)	3.48 ± 1.28	7.74 ± 4.79	13.99 ± 4.78	15.22 ± 10.56

**B**



**(A)** Clinical and imaging characteristics. **(B)** Shear wave speed vs age. Among the control subjects, there was no significant association with age. For the whole cohort, there was a statistically significant but modest association (Spearman's rank  $\rho = 0.54$ ;  $P < 0.001$ ). Values  $> \sim 15$  to 20 m/s are susceptible to the effects of noise and discretization error. HCM = hypertrophic cardiomyopathy; LA = left atrial; LV = left ventricular; LV-EDV = left ventricular end-diastolic volume; LGE = late gadolinium enhancement; LVEF = left ventricular ejection fraction.

than one-half of our value (14 m/s). However, this finding may reflect differences in selecting other wave components and considering wave guidance effects, as well as differences in the underlying disease severity (the mean ejection fraction in their amyloid group was 56%, in contrast to 46% in the current study). In their 20- to 39-year-old cohort of control subjects, Petrescu et al<sup>5</sup> found shear wave velocities after aortic valve closure of  $3.5 \pm 0.7$  m/s, velocities that closely match our data ( $3.5 \pm 1.3$  m/s).

Using an acoustic radiation force-based ultrasonic approach, Villemain et al<sup>4</sup> similarly found elevated shear wave velocities in patients with HCM. However, in comparison, our shear wave velocities translated to significantly greater myocardial stiffness, which most likely reflected the different

cardiac time points at which the studies were performed (immediately after end-systole vs end-diastole) and the different center frequencies of the shear waves.

Collectively taken, CMR elastography using shear waves generated by aortic valve closure is clinically feasible, fits easily into the workflow, and hence can add myocardial stiffness to the armament of diagnostic parameters provided by CMR. This technique may play a valuable role in the evaluation of patients at risk of heart failure.

Emma Burnhope, BM, PhD  
 Alessandro Polcaro, MS  
 Jurgen H. Runge, PhD  
 Inka Granlund, BSc

Filippo Bosio, BSc  
 Marian A. Troelstra, MD  
 Adriana D.M. Villa, MD, PhD  
 Amedeo Chiribiri, MD, PhD  
 Gerald Carr-White, PhD  
 Jessica Webb, PhD  
 Reza Razavi, MD  
 Jordi Martorell, PhD  
 Ralph Sinkus, PhD  
 Tefvik F. Ismail, MBBS, PhD\*

\*School of Biomedical Engineering and Imaging Sciences  
 St Thomas' Hospital  
 Fourth Floor Lambeth Wing  
 Westminster Bridge Road  
 London SE1 7EH, United Kingdom  
 E-mail: [tevfik.ismail@kcl.ac.uk](mailto:tevfik.ismail@kcl.ac.uk)  
<https://doi.org/10.1016/j.jcmg.2022.01.009>

© 2022 by the American College of Cardiology Foundation. Published by Elsevier.

This work was supported by the Wellcome/EPSRC Centre for Medical Engineering (WT 203148/Z/16/Z) and a KCL-University of Paris Joint Research Award (ANR-18-IDEX-0001). Dr Martorell has reported funding from Obra Social La Caixa. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. The authors are grateful to the administrative team and radiographers in the CMR Unit at King's College London for their help with and support of this work.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

## REFERENCES

- Hieda M, Sarma S, Hearon CM Jr, et al. Increased myocardial stiffness in patients with high-risk left ventricular hypertrophy: the hallmark of stage-B heart failure with preserved ejection fraction. *Circulation*. 2020;141:115-123.
- Troelstra MA, Runge JH, Burnhope E, et al. Shear wave cardiovascular MR elastography using intrinsic cardiac motion for transducer-free non-invasive evaluation of myocardial shear wave velocity. *Sci Rep*. 2021;11:1403.
- Wassenaar PA, Eleswarpu CN, Schroeder SA, et al. Measuring age-dependent myocardial stiffness across the cardiac cycle using MR elastography: a reproducibility study. *Magn Reson Med*. 2016;75:1586-1593.
- Villemain O, Correia M, Mousseaux E, et al. Myocardial stiffness evaluation using noninvasive shear wave imaging in healthy and hypertrophic cardiomyopathic adults. *J Am Coll Cardiol Img*. 2019;12:1135-1145.
- Petrescu A, Santos P, Orlowska M, et al. Velocities of naturally occurring myocardial shear waves increase with age and in cardiac amyloidosis. *J Am Coll Cardiol Img*. 2019;12:2389-2398.

## Myocardial Denervation and Left Ventricular Volume Predict Ventricular Arrhythmias in Patients With Ischemic Cardiomyopathy



The PAREPET (Prediction of ARrhythmic Events with Positron Emission Tomography) study (NCT01400334) identified burden of myocardial sympathetic denervation, and left ventricular end-diastolic volume index (LVEDVi), to provide enhanced risk prediction for sudden cardiac arrest

(SCA).<sup>1</sup> The surrogate of SCA in PAREPET was appropriate ICD discharge for VT/VF >240 beats/min. Previous studies have reported that regardless of the rate of the arrhythmia, appropriate ICD therapy portends a poor prognosis.<sup>2</sup> To determine whether the imaging predictors of SCA in the PAREPET study predict the risk for all ventricular arrhythmias (VAs), we performed a retrospective analysis of an expanded endpoint of all appropriate ICD therapies for VAs and adjudicated SCA from patients enrolled in the PAREPET study.

This study was approved by the University at Buffalo and Veterans Affairs Western New York Healthcare System Institutional Review Boards. Data from 204 patients with ischemic cardiomyopathy (LVEF <35%), not amenable to revascularization, enrolled in the PAREPET study, were evaluated. Myocardial denervation was assessed on <sup>13</sup>C-metahydroxyephedrine (HED) PET,<sup>3</sup> with HED defect calculated as an integrated sum of defect size and severity (% left ventricular [LV] myocardium) and used as a measure of denervated myocardium. LV volumes were determined from 2-dimensional echocardiography. Outcomes data were collected by either direct contact with the subjects, review of routine ICD interrogations, or review of electronic medical records. The outcome of VAs was defined as follows: 1) appropriate ICD shock; 2) appropriate antitachycardia pacing; 3) VAs in the monitored zone lasting >30 seconds; or 4) death occurring due to VAs that could not be terminated by ICD therapies. SCA was specifically defined as adjudicated sudden cardiac death or ICD shock for VT/VF >240 beats/min.

The mean age of the subjects was 67 ± 11 years (90% men). Over an average follow-up duration of 3.4 years (range to first event: 18 days to 7.2 years), VAs occurred in 61 subjects (SCA = 28). Subjects experiencing VAs had a significantly higher LVEDVi (101 ± 28 mL/m<sup>2</sup> vs 84 ± 29 mL/m<sup>2</sup>; *P* < 0.0001) and HED defect (31% ± 10% vs 26% ± 11%; *P* < 0.0001) compared with those who did not experience VAs. On multivariate regression analysis, with adjustment for demographic, clinical, and imaging variables, LVEDVi (HR: 1.18 per 10 mL/m<sup>2</sup>; 95% CI: 1.05-1.32; *P* < 0.005), HED defect (HR: 1.49 per 10% LV myocardium; 95% CI: 1.06-2.11; *P* < 0.02), and angiotensin inhibition therapy (HR: 0.35; 95% CI: 0.14-0.85; *P* < 0.02) were significant independent predictors of VAs. LVEF was not an independent predictor of VAs. The addition of HED defect and LVEDVi to a multivariate model incorporating LVEF, demographics, and routine clinical and laboratory variables improved the prediction of VAs in comparison with a model without HED defect and LVEDVi (net reclassification improvement for VAs = 0.46).