JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2023

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER

Letters

RESEARCH LETTER

Shear-Wave Elastography Reflects Myocardial Stiffness Changes in Pediatric Inflammatory Syndrome Post COVID-19

Multisystem inflammatory syndrome in children (MIS-C) has been reported in children and adolescents who had previously shown positive test results for SARS-COV-2 infection.[1] Studies have linked MIS-C to myocardial inflammation but have reported varying effects on systolic and/or diastolic function when studied with conventional echocardiography. Strain imaging could detect subclinical systolic alterations in MIS-C patients even with preserved ejection fraction (EF).[2]

However, deeper assessment of diastolic function and long-term follow-up of those patients are lacking. Therefore, a tool for a better characterization of diastolic dysfunction in those patients, both in the acute phase and at follow-up, would be desirable.

Recently, shear wave elastography (SWE) using high frame rate (HFR) echocardiography has been proposed as a new tool for the noninvasive assessment of diastolic function. Shear waves (SW) are mechanical vibrations generated by eg, mitral valve closure (MVC). They propagate through the myocardium with a velocity depending directly on myocardial stiffness (MS), which is one of the determinants of diastolic function.[3]

To our knowledge, this is the first longitudinal study showing sequential changes in natural SW velocities during the course of a disease in a pediatric population. In this study, we aimed to test the clinical ability of SWE to detect changes in MS in patients with MIS-C during hospital admission and over 6 months follow-up. Being based on risk-free echocardiography, SWE could be of added value for the follow-up care of patients with myocarditis.

In our prospective cohort study, children with MIS-C according to the World Health Organization criteria[1] were prospectively followed up over 6 months. Age-matched healthy volunteers (HV) were sought through public announcement. Exclusion criteria were history of any previous documented underlying cardiac pathologic condition. This study was approved by the local ethical committee, and written informed consent was obtained from the parents of all participants.

Both HV and MIS-C patients underwent conventional echocardiography as well as HFR imaging for SWE using a fully programmable experimental scanner. Acquisition and analysis of HFR images has been previously described.[3] In the MIS-C patient group, the examination was performed at admission and repeated at 2 weeks, 6 weeks, and 6 months after discharge (Figure 1A).

Data from 37 participants, 7 MIS-C patients (age 7 ± 4 years; 71% male) and 30 age-matched HV (age 8 ± 3 years; 53% male) were analyzed. On admission, compared with the HV, MIS-C patients had lower left ventricular ejection fraction (LVEF) (50% ± 6% vs 63% ± 2%; $P = 0.002$), lower global longitudinal strain (GLS) (−16.82% ± 3.08% vs −21.88% ± 1.22%; $P = 0.005$) as well as higher E/E' (7.69 ± 1.39 vs 5.67 ± 0.39; $P = 0.008$).

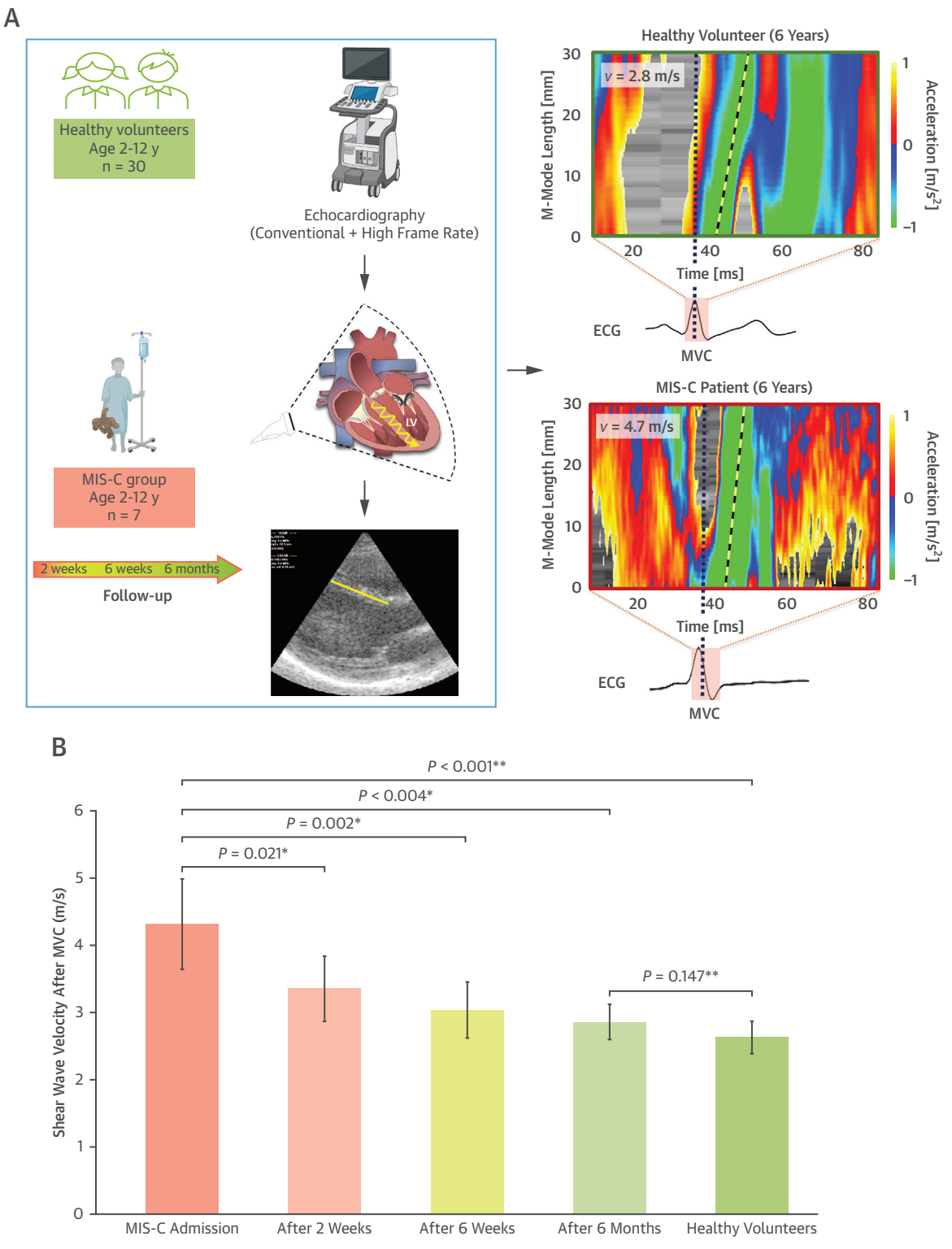
Septal SW velocities after MVC in MIS-C patients at admission were significantly higher compared to their values in age-matched HV (4.31 ± 0.67 m/s vs 2.62 ± 0.24 m/s, respectively; $P < 0.001$). The hallmark pathologic finding in MIS-C is myocarditis with myocardial edema as confirmed by CMR in many patients.[4] This makes the myocardial stiffer, with subsequent left ventricular diastolic dysfunction. This could explain why the measured SW velocities are significantly higher in MIS-C patients than in HV.

Moreover, during the follow-up of MIS-C patients, both LVEF and GLS improved significantly with recovery ($P = 0.004$ for both). LVEF normalized by 2 weeks, while GLS by 6 months, after discharge. This is in line with earlier reports of persisting abnormal strain patterns and myocardial edema beyond 2 weeks of illness even after clinical improvement.[4]

More interestingly, SW velocities in MIS-C patients changed significantly with recovery during follow-up and reached values corresponding to those in HV only after presumably full recovery by 6 months (SW after MVC 2.85 ± 0.26 m/s in MIS-C group vs 2.62 ± 0.24 m/s in HV group; $P = 0.147$) (Figure 1B). Our data indicate that the longitudinal follow-up observation of SW velocities could offer a sensitive parameter that reflects changes in myocardial stiffness as a result of myocardial inflammation. On the basis of our findings, SWE is a promising new noninvasive diagnostic and follow-up tool in children with cardiac diseases affecting MS.

However, myocardial stiffness shows dynamic changes throughout the cardiac cycle, whereas velocities of natural SWs after MVC reflect the

FIGURE 1 **Average SW Velocities in MIS-C Patients and Healthy Volunteers**



(A, Left) All participants underwent conventional echocardiography and high frame rate imaging. This was repeated 3 times for MIS-C patients during follow-up. **(A, Right)** Tissue acceleration maps derived from M-mode drawn across the septum **(left, yellow line)** show shear waves (SW) after mitral valve closure (MVC) **(dashed line)** propagating as a tilted green-colored band. Its slope **(black/yellow dotted line)** represents SW velocity. **(B)** SW velocities in MIS-C patients are significantly higher than in healthy-volunteers (***P* value by use of independent *t*-test). They declined significantly with recovery (**P* values show the analysis of variance post-hoc test) and attained values comparable with those of healthy volunteers at 6 months.

myocardial state at the beginning of the isovolumetric interval. Observed SWs may therefore be in part influenced by contractility or afterload. Nevertheless, previous studies by our group[5] could show that SW velocities after MVC are mainly and closely linked to passive end-diastolic myocardial stiffness. Yet, it is necessary to validate the proposed method against a gold standard tool for assessing myocarditis in a larger cohort of patients.

Ahmed S. Youssef, MD
Thomas Salaets, MD
Stéphanie Bézy, MSc
Laurine Wouters, MSc
Marta Orlowska, MSc, PhD
Annette Caenen, MSc, PhD
Jürgen Duchenne, MSc, PhD
Alexis Puvrez, MD
Lien De Somer, MD
Bjorn Cools, MD, PhD
Jan D'hooge, MSc, PhD
Marc Gewillig, MD, PhD
Jens-Uwe Voigt, MD, PhD*

*Department of Cardiovascular Diseases
University Hospitals Leuven
Herestraat 49
3000 Leuven, Belgium

E-mail: jens-uwe.voigt@uzleuven.be

https://doi.org/10.1016/j.jcmg.2023.08.003

Dr Youssef is supported by a scholarship from the Egyptian ministry of research and higher education (2021 recipient) and by the fund for Cardiac Surgery (ref. 489708). Dr Salaets is supported by the Frans Van de Werf Fund for Clinical Cardiovascular Research (2022 recipient), by "De Kleine Hartjes VZW," and by the Research Foundation Flanders (FWO) (V401622N). Drs Caenen, Duchenne, and Voigt hold a personal research mandate of the FWO (12ZZN22N, 1211620N, and 1832922N, respectively). All other authors 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. Stephen F, Shana GC, Richard G, et al. Multisystem inflammatory syndrome in children and adolescents with COVID-19. *WHO Scientific Brief*; 2020. May 15.

2. Matsubara D, Kauffman HL, Wang Y, et al. Echocardiographic findings in pediatric multisystem inflammatory syndrome associated with COVID-19 in the United States. *J Am Coll Cardiol*. 2020;76(17):1947–1961.

3. Petrescu A, Santos P, Pedrosa JP, et al. Velocities of naturally occurring myocardial shear waves increase with age and in cardiac amyloidosis. *J Am Coll Cardiol Img*. 2019;12(12):2389–2398.

4. Theocharis P, Wong J, Pushparajah K, et al. Multimodality cardiac evaluation in children and young adults with multisystem inflammation associated with COVID-19. *Eur Heart J Cardiovasc Imaging*. 2021;22(8):896–903.

5. Bézy S, Duchenne J, Orlowska M, et al. Impact of loading and myocardial mechanical properties on natural shear waves. *J Am Coll Cardiol Img*. 2022;15(12):2023–2034.