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 criteria1 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.1 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.5 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 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.

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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.

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