

## Mid- and long-term atrio-ventricular mechanics in children after recovery from asymptomatic or mildly symptomatic SARS-CoV-2 infection

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**Background:** Clinical manifestations of children's coronavirus disease-2019 (COVID-19) were initially considered less severe compared with adult patients. However, there is now increasing evidence of a "long-tail" of COVID-19 related symptoms lasting for several months after recovery from the acute infection. Long COVID-19-related symptoms and mechanisms are poorly characterized and understood, with several phenotypes reported, often driven by long-term tissue damage (such as lung, heart and brain) and pathological inflammation due to viral persistence and/or immune deregulation.

**Purpose:** The objective of this study was to evaluate atrio-ventricular mechanics, by means of two-dimensional speckle-tracking echocardiography, in previously healthy children recovered from asymptomatic or mildly symptomatic severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in a long-term follow-up.

**Methods:** We analysed a cohort of 157 paediatric patients, mean age  $7 \pm 4$  years, who had a confirmed diagnosis of SARS-CoV-2 infection and were asymptomatic or mildly symptomatic for COVID-19. Patients underwent standard transthoracic echocardiogram and speckle tracking echocardiographic study 148 $\pm$ 68 days after diagnosis. One hundred seven age, sex, and body surface area comparable healthy subjects were used as control group.

**Results:** Left ventricular ejection fraction was within normal limits in postCOVID-19 cases and CTRL with no significant differences between the two groups (postCOVID-19: 65.6 $\pm$ 4% vs CTRL: 65.0 $\pm$ 5%,  $p=0.182$ ).

Left ventricular (LV) global longitudinal strain (postCOVID-19:  $-20.5 \pm 2.9\%$ ; CTRL:  $-21.8 \pm 1.7\%$ ;  $p < 0.001$ ) was significantly reduced in cases compared with CTRLs. An amount of 11 (7%) postCOVID-19 cases showed impaired GLS values  $< -17\%$  and 95 subjects (60%) presented with a strain lower than  $-16\%$  in more than 2 segments. These subjects did not show any difference regarding symptoms or serological findings. Moreover, GLS was significantly reduced in children with disease's onset during the second wave of COVID-19 pandemic, compared with those during the first wave (second wave:  $-20.2 \pm 2.6\%$ ; first wave:  $-21.2 \pm 3.4\%$ ;  $p=0.048$ ). Finally, peak left atrial systolic strain was within the normal range in the postCOVID-19 group with no significant differences compared to CTRL (postCOVID-19:  $49.1 \pm 12\%$ ; CTRL:  $49.5 \pm 18\%$ ).

**Conclusions:** SARS-CoV-2 infection may affect left ventricular deformation in children despite an asymptomatic or only mildly symptomatic acute illness. Our data show an amount of 60% of children, recovering from asymptomatic or mildly symptomatic COVID-19, with still mild subclinical systolic cardiac impairment in the mid- and long-term follow-up after the infection. This subtle impairment was seen to be worse in children recovering from the second wave of COVID-19 compared to the first one.

A follow-up is needed to verify the reversibility of these alterations and their impact on long-term outcomes.