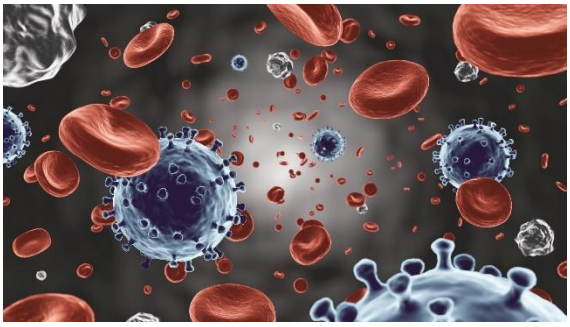
With Women most Affected COVID-19 Ages Arteries Prematurely

The authors examined how coronavirus disease 2019 (COVID-19) may accelerate vascular aging and its implications for long-term care.

The editorial suggests that the COVID-19 pandemic has left a measurable imprint on the vasculature that looks like accelerated aging and may be only partly reversible. It frames this legacy within post-acute COVID-19 syndrome (PACS), defined by the World Health Organization (WHO) as symptoms beginning three months after infection and lasting at least two months, which observational work suggests affects a substantial share of survivors.

The editorial notes that the CARTESIAN cohort included both asymptomatic and symptomatic survivors and did not explicitly apply the WHO criteria for PACS.

The most worrisome manifestations sit in the cardiovascular domain, ranging from dysautonomia and microvascular vasospasm to myocardial infarction and venous thromboembolism, and they are plausibly tied to endothelial injury, inflammation, and coagulation disturbances. The editorial asks whether these injuries can be captured by objective markers, how they relate to disease severity, which groups are most vulnerable, and how long they persist.



Results

Arterial stiffness assessed by carotid–femoral pulse wave velocity (PWV) is presented as a practical, non-invasive proxy for aortic stiffness and "vascular age," with known prognostic value beyond standard risk factors.

Prior reports that are limited by small sample sizes and heterogeneous methods suggested higher PWV during acute infection and in PACS, but they lacked stratification by clinical severity and sex, despite concerns that women may experience long COVID more often than men.

Against that backdrop, the authors highlight the multicenter COVID-19 effects on ARTErial StIffness and vascular AgeiNg (CARTESIAN) cohort for its scope and analytic rigor.

CARTESIAN enrolled 2390 participants across 34 centers and grouped them as COVID-19-negative controls (n = 391) and COVID-19-positive participants who were non-hospitalized (n = 828), admitted on general wards (n = 729), or admitted to the intensive care unit (ICU) (n = 146).

At a mean follow-up of six months after infection, adjusted PWV was significantly higher in all three COVID-19-positive groups relative to controls. Using an adjusted control PWV of 7.53 m/s as the reference, the absolute differences were +0.41 m/s (non-hospitalized), +0.37 m/s (hospitalized), and +0.40 m/s (ICU).

Contrary to an a priori expectation of a severity gradient, the overall cohort did not show a clear linear increase in stiffness from non-hospitalized to ICU levels. However, sex-stratified models revealed a strong pattern: Females across all COVID-19-positive strata had elevated PWV, peaking among those who required ICU care with an adjusted increase of +1.09 m/s, whereas males did not differ significantly from controls. A formal sex-by-group interaction was observed in the non-hospitalized and ICU strata.

Persistent symptoms at six months were reported by 42% of COVID-19-positive participants; among females, persistence aligned with higher PWV (adjusted difference +0.39 m/s), a relation not seen in males. The editorial notes that the study did not explicitly define PACS by WHO criteria but infers that PWV could act as a physiologic correlate of symptom persistence in females and perhaps a prognostic marker of vascular injury.

Sex Differences and Mechanistic Insights

Methodological strengths receive emphasis, as CARTESIAN used a validated surrogate for vascular aging in PWV; included a large, international sample with near-equal sex distribution; and applied hierarchical mixed models that accounted for clustering by device, recruitment setting, and country income level.

Importantly, 12-month data for 1024 participants permitted exploration of trajectories: controls showed the expected age-related PWV progression, whereas many COVID-19 survivors demonstrated declining PWV, hinting that part of the stiffness signal may abate as autonomic imbalance and inflammation recede. In a small within-person subset that changed from COVID-19-negative to COVID-19-positive between visits, PWV rose after infection, supporting temporal association and partial reversibility.

The editorial interprets these dynamics as consistent with a composite injury in which some components (for example, endothelial activation, inflammatory tone, autonomic dysregulation) are transient while others likely represent irreparable damage.

The sex-specific findings provoke key mechanistic and epidemiologic questions. How do they reconcile with the higher acute mortality risk in males with COVID-19? The editorial contemplates survivor bias (where severely affected males may not survive to be measured), hormonal influences, such as the known effects of estrogen on endothelial function, and social determinants, including differential exposure and access to care. It also raises the possibility that women could have a more maladaptive myocardial or neurohormonal response to COVID-19-induced aortic stiffness and wave reflections, thereby translating similar arterial changes into greater clinical impact.

From a measurement perspective, the absolute PWV differences were modest and near device detection thresholds, prompting a call for correlative studies that tie PWV changes to long-term symptoms and hard outcomes.

The inflammatory and thrombo-inflammatory milieu of COVID-19 provides plausible biology. Elevated interleukins (IL)-1 and IL-6, tumor necrosis factor (TNF), and chemokines such as monocyte chemoattractant protein-1 (MCP-1), together with neutrophil extracellular trap formation (NETosis), have all been implicated in endothelial dysfunction and vascular remodeling. Such processes could stiffen central arteries and elevate systolic load, with downstream effects on cardiac load and function.

The editorial suggests that this pathobiology may be more consequential in some subgroups, particularly females with symptom persistence, thus aligning the clinical signal with mechanistic plausibility.

Conclusion

Clinically, the message is practical and cautious. Routine cardiovascular risk assessment should be considered for patients with PACS, with special attention to females who report ongoing symptoms. Although CARTESIAN was not designed to test specific therapies, it underscores the importance of aggressive management of traditional risk factors, patient education about expected trajectories, and careful follow-up.

For researchers, the agenda includes dissecting sex differences in post-viral endothelial function and immune responses; validating PWV as a prognostic biomarker for PACS; and evaluating whether targeted strategies can reverse or mitigate the signal.

Policy makers are encouraged to recognize the vascular legacy of COVID-19 as measurable and potentially mitigable, warranting resource allocation for longitudinal surveillance and for trials to test modifiable targets.

To summarize, the editorial portrays COVID-19 as having aged the arteries of many survivors, with females bearing a disproportionate share of the burden and with signs that part of the injury may wane over time. The central challenge moving forward is to identify modifiable targets that prevent stiffness during future surges and to craft therapies that lessen long-term cardiovascular consequences for those already affected.

Source:

https://www.news-medical.net/news/20250819/COVID-19-ages-arteries-prematurely-with-women-most-affected.aspx