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Long-term effects of COVID-19 on endothelial function, arterial stiffness, and blood pressure in college students: a pre-post-controlled study

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Abstract

Background The COVID-19 has been shown to have negative effects on the cardiovascular system, but it is unclear how long these effects last in college students. This study aimed to assess the long-term impact of COVID-19 on arterial stiffness, endothelial function, and blood pressure in college students.

Methods We enrolled 37 college students who had been infected with COVID-19 for more than 2 months. Brachial artery flow-mediated dilation (FMD) was used to assess endothelial function, while arterial stiffness was evaluated using the ABI Systems 100, including variables such as ankle-brachial index (ABI), brachial-ankle pulse wave velocity (baPWV), carotid-femoral pulse wave velocity (cfPWV), heart rate (HR), and blood pressure (BP).

Results Our results showed that FMD was significantly impaired after COVID-19 infection ($p < 0.001$), while cfPWV and systolic blood pressure (SBP) were significantly increased ($p < 0.05$). Simple linear regression models revealed a significant negative correlation between post-COVID-19 measurement time and baPWV change ($p < 0.01$), indicating an improvement in arterial stiffness over time. However, there was a significant positive correlation between post-COVID-19 measurement time and diastolic blood pressure (DBP) change ($p < 0.05$), suggesting an increase in BP over time. There were no significant differences in ABI and HR between pre- and post-COVID-19 measurements, and no significant correlations were observed with other variables ($p > 0.05$). Conclusion: Our study demonstrated that COVID-19 has long-term detrimental effects on vascular function in college students. However, arterial stiffness tends to improve over time, while BP may exhibit the opposite trend.

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Introduction

In December 2019, the first case of infection and mortality caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in Wuhan, China [1]. Since then, the virus has spread globally, causing a pandemic. On December 7, 2022, China lifted all restrictions and many individuals who had not previously been infected with coronavirus disease 2019 (COVID-19) were subsequently infected. As of July 26, 2023, there have been 773,511,195 confirmed cases of COVID-19 worldwide, with 7,023,127 deaths reported [2]. In the past, the focus was primarily on the acute adverse effects of COVID-19 on the human body, but evidence suggests that it can have long-term detrimental impacts on individuals after infection [3]. In October 2021, the World Health Organization released a clinical case definition for the post-COVID-19 condition as symptoms that present 3 months after SARS-CoV-2 infection with a minimal duration of 2 months and cannot be explained by an alternative diagnosis [4]. Common symptoms include, but are not limited to, fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning [4].

The COVID-19 virus has been shown to have adverse effects on vascular function. Abbasi et al. demonstrated that patients experienced a range of increased cardiovascular risks one year after COVID-19 infection [5]. SARS-CoV-2 can invade the human body by binding to angiotensin-converting enzyme 2 (ACE2) receptors expressed in various tissues [6]. The binding of SARS-CoV-2 to ACE2 expressed in vascular endothelium can result in endothelial damage [7]. Previous studies have shown that the degree of arterial stiffness in elderly individuals with COVID-19 worsens during the acute phase and four months after infection, with impaired endothelial function [8, 9]. For the younger population, previous studies have indicated that COVID-19 has no impact on vascular and cardiac autonomic function in young adults [10]. However, there is also evidence suggesting that young individuals infected with COVID-19 experience increased arterial stiffness [11]. Arterial stiffness is closely related to vascular aging, and an increase in arterial stiffness is considered as an early marker for vascular aging [12]. The European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) recommend the use of pulse wave velocity (PWV) as a comprehensive and non-invasive measurement method for assessing arterial stiffness, as it is sufficiently simple and accurate [13]. PWV has been widely used as the gold standard for assessing arterial stiffness in clinical practice [14]. Vascular aging is also characterized by elevated systolic blood pressure (SBP), which is attributed to impaired generation and repair function of the vascular endothelium, leading to endothelial aging and associated vascular dysfunction, ultimately increasing the risk of cardiovascular diseases [15]. Brachial artery flow-mediated dilation (FMD), a non-invasive method for assessing endothelial function, has been widely used as an alternative marker for endothelial dysfunction in various clinical conditions such as asymptomatic atherosclerosis, coronary artery disease (CAD), congestive heart failure (CHF), and other cardiovascular diseases [16].

Currently, there is no research investigating the long-term effects of COVID-19 infection on vascular function in college students.

This study discovered significant alterations in endothelial function, arterial stiffness, and blood pressure levels among college students during the 2- to 5-month period following COVID-19 infection.

Patients and methods

Study design

This study utilized a pre-post design to assess the long-term effects of COVID-19 infection on vascular function in college students. Vascular endothelial function, arterial stiffness, and blood pressure were recorded before and after COVID-19 infection. All pre-COVID-19 measurements were conducted between September 20th and September 24th, 2022, and post-COVID-19 measurements were conducted between February 2023 and June 2023 at Guangdong Provincial Key Laboratory of Physical Activity and Health Promotion, Guangzhou Sport University. The same measurement protocol as before COVID-19 infection was employed after COVID-19 infection. In this study, we aimed to assess the enduring impacts of COVID-19 on the vascular function of college students by conducting follow-up measurements a minimum of two months post-infection. To gain a comprehensive understanding of the recovery status of all participants two months after infection, we conducted a comparative analysis of their conditions before and after COVID-19. Furthermore, to explore the disparities in vascular endothelial recovery during the early versus late convalescent phases, we employed the median time post-infection as the threshold for stratifying the participants into distinct groups. This categorization allowed for a more precise investigation of the changes in vascular function over time post-infection. By meticulously comparing hemodynamic indicators, including endothelial function, arterial stiffness, and blood pressure, between the early recovery group and the late recovery group, we

were able to delineate the temporal trajectory of vascular recovery following COVID-19.

Participants

All participants were college students. Inclusion criteria were as follows: (1) aged between 18 and 25 years, regardless of gender; (2) no prior history of COVID-19 infection before the COVID-19 restrictions were lifted in China, with a confirmed diagnosis of COVID-19 infection after December 2022 as well as a time interval of at least 2 months since infection; (3) no other physical or mental illnesses, and no significant history of surgical interventions; (4) no recent medication use within the past three months; (5) participants who had undergone cardiovascular testing in our laboratory before the COVID-19 infection.

Exclusion criteria were as follows: (1) smoking; (2) exercise regularly (3–5 times a week, about 30 min each time, for at least 6 weeks or more); (3) presence of heart disease or musculoskeletal disorders, and a history of major surgical interventions; (4) inability to comply with the trial protocol; (5) COVID-19 infection resulted in hospitalization.

A total of 37 participants were recruited for this study, which was approved by the Ethics Committee of Guangzhou Sport University (Protocol number: 2023LCLL-53). Before the beginning of the experiment, all participants were informed about the purpose of the study and signed written informed consent forms. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki.

Study measurements

Endothelial function

The vascular endothelial function can be assessed using the non-invasive FMD measurement, which is associated with coronary artery endothelial function and independently predicts cardiovascular disease (CVD) outcomes [17]. Before the test, participants were instructed to rest in a quiet and temperature-controlled environment for 15 min. The FMD test was performed using a non-invasive ultrasound system (UNEXEF38G, UNEX, Nagoya, Japan) equipped with a high-resolution linear array transducer and edge tracking function [18, 19]. The participant was placed in a supine position, and the H-type transducer was utilized to capture the longitudinal view of the right brachial artery. The average value of the arterial diameter was recorded over a 10-heartbeat period at the end of diastole, establishing the baseline diameter for the artery. The probe was then kept in place, and a 5-minute ischemic occlusion was performed with a cuff inflated to a pressure 50 mmHg above the systolic blood pressure. The maximum diameter of the artery post-ischemic reactive hyperemia was documented from 30 s to 2 min

following the release of the cuff. Taking into account the effects of shear stress, the probe was delicately positioned over the pulsatile site of the brachial artery, located 5–10 cm proximal to the right elbow joint of the participant (ensuring no heavy compression was applied to the brachial artery). Upon obtaining a complete and clear visualization of the intima-media complex, the probe was firmly fixed in place for the entire duration of the assessment. All testing was performed by an operator with substantial experience. The calculation formula is as follows: FMD (percentage) = ([peak diameter - baseline diameter]/baseline diameter) × 100 [20].

Arterial stiffness and blood pressure

Arterial stiffness was assessed using a PWV measurement device (BOSO ABI Systems 100, Bosch & Sohn, Germany) [21, 22]. Before the test, participants were instructed to lie flat and rest for 5 min with their hands and legs uncrossed. During the test, an experienced experimenter placed inflatable cuffs on the participant's limbs as instructed. The variables included ankle-brachial index (ABI), carotid-femoral pulse wave velocity (cfPWV), brachial-ankle pulse wave velocity (baPWV), blood pressure (BP), and heart rate (HR) were measured. The ABI is a marker for assessing lower extremity arterial stenosis and peripheral arterial occlusive disease (PAOD) caused by atherosclerosis [23]. The two most commonly used methods for measuring PWV are cfPWV and baPWV, both of which can assess aortic and systemic arterial stiffness, respectively [24]. These two markers are considered simple and reliable indicators of conditions of central and systemic arterial function [25, 26]. The device can measure baPWV on both sides of the body, referred to as LbaPWV (left brachial-ankle pulse wave velocity) and RbaPWV (right brachial-ankle pulse wave velocity).

Sample size considerations

In this study, G*Power software (version 3.1.9.7) was used to determine the required sample size for our research investigation. We assumed a medium effect size of 0.50, a significance level of 0.05, and a desired power of 0.80 for sample size estimation. G*Power recommended a total sample size of 34 participants to achieve the desired power level. By using G*Power for sample size calculation, we ensured that our study had sufficient statistical power to detect meaningful effects. This information guided our recruitment process and helped assess the feasibility of our research objectives.

Data analysis

Initially, the normality of the data was assessed using the Shapiro-Wilk normality test. For data that followed a normal distribution, a paired t-test was conducted. For data that did not follow a normal distribution, a

Table 1 Demographic and clinical characteristics of participants (*N*=37)

Characteristic	Statistics
Sex, N (%)	
Females	10 (27%)
Males	27 (73%)
Age - years	21.35±1.99
Height - cm	167.68±7.09
Weight - kg	61.8 (55.2 to 72.9)
BMI - kg/m²	21.5 (20.3 to 23.7)
The time of COVID-19 infection - days	114 (95 to 122)
Time interval before and after COVID-19 infection - days	188±22

Values are mean±standard deviation, or median (interquartile range). N (%)=10 Females and 27 Males and their respective percentages of the total number. BMI=body mass index

Table 2 Hemodynamic parameters at baseline and more than two months after COVID-19 infection (*N*=37)

Parameter	Pre-infection	Post-infection	*p*-value
FMD - %	11.2 (10.3 to 15.1)	10.8 (10.1 to 11.4)	0.001
cfPWV - m/s	5.86±0.70	6.30±1.00	0.022
LABI - m/s	1.07 (1.03 to 1.15)	1.05 (1.00 to 1.11)	0.22
RABI - m/s	1.07 (1.03 to 1.11)	1.06 (1.01 to 1.13)	0.81
LbaPWV - m/s	9.82±1.23	10.23±1.61	0.15
RbaPWV - m/s	9.88±1.36	10.23±1.36	0.20
HR - bpm	65 (58 to 74)	66 (60 to 77)	0.67
SBP - mmHg	107±12	110±13	0.047
DBP - mmHg	63±8	66±8	0.068

Values are mean±standard deviation, or median (interquartile range). FMD=flow-mediated dilation; cfPWV=carotid-femoral pulse wave velocity; LABI=left ankle-brachial index; RABI=right ankle-brachial index; LbaPWV=left brachial-ankle pulse wave velocity; RbaPWV=right brachial-ankle pulse wave velocity; HR=heart rate; SBP=systolic blood pressure; DBP=diastolic blood pressure

non-parametric test such as the Wilcoxon signed-rank test was employed. Descriptive statistics were computed for normally distributed data, including the mean and standard deviation, while for non-normally distributed data, the median and interquartile range were reported.

To evaluate the longitudinal changes in COVID-19 infected individuals during the complete timeline post-infection and to discern the differences in outcomes between the early and late stages of convalescence. The association between these changes (FMD, cfPWV, ABI, baPWV, HR, and BP) throughout the complete post-infection timeline and variables such as the time of COVID-19 infection, age, and body mass index (BMI) was analyzed using the Spearman correlation coefficient.

Furthermore, based on the results of the correlation analysis, a simple linear regression (SLR) analysis was conducted to explore the relationship between the time of COVID-19 infection and the changes of LbaPWV, RbaPWV, and diastolic blood pressure (DBP) before and after COVID-19 infection.

A significance level of $p < 0.05$ was considered to indicate statistical significance in the analysis. The statistical analysis was performed using Stata (version 12.0).

Results

A total of 37 participants were included in this pre-post-controlled study. Each participant visited the laboratory twice. The demographic and clinical characteristics of the participants are presented in Table 1. In our study, we meticulously analyzed the temporal aspects of health assessments related to COVID-19 infection. The median interval from infection onset to the second follow-up test was 114 days (IQR: 95 to 122 days). We also determined the mean time from the pre-COVID-19 assessment to the post-COVID-19 follow-up to be 188 days, with a relatively small standard deviation of 22 days, indicating

consistency among participants. The range extended from 144 to 219 days, acknowledging some variability. This detailed analysis ensures a robust understanding of the temporal context and accounts for variability in our study outcomes.

The hemodynamic measurements results are presented in Tables 2 and 3.

Endothelial function

By conducting a Wilcoxon signed-rank test, we found a significant difference in FMD between pre- and post-COVID-19 infection (Z=−3.20, $p < 0.001$). The median FMD after COVID-19 infection was 10.8%, with an IQR of 10.1–11.4%, while the median FMD before COVID-19 infection was 11.2%, with an IQR of 10.3–15.1%.

However, while stratified by the median time post-infection into early (*n*=20) and late recovery (*n*=17) groups, differences in FMD were noted. In the early recovery group, a significant difference in FMD was observed (*p*=0.044), whereas the late recovery group showed no significant change (*p*=0.290). Specifically, in the early recovery group, the median FMD prior to COVID-19 infection was 12.65%, with an IQR of 10.30–15.38%, which decreased to a median of 10.80% post-infection, with an IQR of 9.68–11.55%. In contrast, the late recovery group exhibited a median FMD of 11.00% before infection, with an IQR of 10.45–12.95%, and a median FMD of 11.10% after infection, with an IQR of 10.30–11.35%, indicating a trend towards stability in FMD values.

Arterial stiffness and blood pressure

The study's findings indicate that throughout the course of COVID-19 infection, there was a significant increase in cfPWV with a mean difference of 0.44 m/s (*p*=0.022) and SBP with a mean difference of 3.24 mmHg (*p*=0.047). DBP also exhibited an increase, though it was

Table 3 Hemodynamic measurements stratified by early and late recovery from COVID-19

Parameter	Early recovery			Late recovery		
	Pre-infection	Post-infection	*p*-value	Pre-infection	Post-infection	*p*-value
FMD - %	12.65 (10.30 to 15.83)	10.80 (9.68 to 11.55)	0.044	11.00 (10.45 to 12.95)	11.10 (10.30 to 11.35)	0.290
cfPWV - m/s	5.97 ± 0.66	6.33 ± 1.00	0.172	5.74 ± 0.74	6.27 ± 1.03	0.067
LABI - m/s	1.08 ± 0.07	1.05 ± 0.08	0.415	1.10 (1.03 to 1.15)	1.05 (1.00 to 1.13)	0.309
RABI - m/s	1.05 ± 0.06	1.08 ± 0.08	0.132	1.10 ± 0.05	1.05 ± 0.09	0.066
LbaPWV - m/s	9.55 (8.95 to 10.18)	10.15 (9.55 to 11.68)	0.035	9.88 ± 1.42	9.48 ± 0.84	0.257
RbaPWV - m/s	9.60 (9.22 to 9.98)	10.10 (9.83 to 11.75)	0.010	9.98 ± 1.50	9.63 ± 0.79	0.398
HR - bpm	68 ± 9	67 ± 9	0.348	63 ± 10	68 ± 14	0.122
SBP - mmHg	108 ± 10	110 ± 11	0.214	106 ± 14	110 ± 15	0.132
DBP - mmHg	66 ± 6	66 ± 7	0.979	60 ± 9	66 ± 9	0.008

Values are mean±standard deviation, or median (interquartile range). Participants were categorized into early (*n*=20) and late (*n*=17) recovery phases based on the median interval from the initial COVID-19 diagnosis to the follow-up assessment. The median interval defining early and late recovery phases was 114 days

not statistically significant, with a mean difference of 2.65 mmHg (*p*=0.068). No significant changes were observed in other arterial stiffness measures such as baPWV, ABI, and HR (*p*>0.05).

Further analysis stratifying the recovery period by the median post-infection time revealed that in the early phase (*n*=20), there were significant increases in LbaPWV and RbaPWV (*p*=0.035 and *p*=0.010, respectively). In contrast, during the late recovery phase (*n*=17), DBP showed a significant increase (*p*=0.008), whereas no significant changes were noted in the early phase (*p*>0.05). Other indicators did not display significant differences across the recovery phases (*p*>0.05).

Correlation and regression analysis

To investigate the effects of BMI, age, and the change in time since COVID-19 infection on endothelial vascular function and arterial stiffness, we conducted further correlation and regression analyses using the change values from pre- to post-infection. The results of Spearman correlation analysis, which incorporated these change values, showed strong negative correlations between the change in time since COVID-19 infection and the change in baPWV (*p*<0.01), and a positive correlation with the change in DBP (*p*<0.01). Additionally, a significant positive correlation was observed between the change in RABI and the change in LABI (*p*<0.01). The change in LbaPWV and the change in RbaPWV exhibited a strong positive correlation (*p*<0.01), while the change in SBP and the change in DBP showed a moderate positive correlation (*p*<0.05). No significant correlations were found between BMI, age, and the changes in FMD, ABI, baPWV, cfPWV, HR, and BP (Table 4).To further investigate the impact of the time of COVID-19 infection on arterial stiffness, we conducted a linear regression analysis and illustrated the fitting effect using scatterplots. As shown in Figure 1, the time of COVID-19 infection had a significant negative effect on LbaPWV change (Fig. 1A), (regression coefficient: −0.045, *p*<0.001, R^2=0.38) and RbaPWV change (Fig. 1B), (regression coefficient: -0.042,

p<0.001, R^2=0.32), explaining 38% and 32% of the variation in changes, respectively. Additionally, there was a significant positive effect on DBP change (Fig. 1C), (regression coefficient: 0.140, *p*=0.024, R^2=0.14), accounting for 14% of the variation.

Discussion

The present study is the first pre-post-controlled study to examine the long-term effects of COVID-19 infection on vascular function in college students. The experimental results revealed that even mild COVID-19 infection in college students who did not require hospitalization resulted in significant changes in vascular function during 2 to 5 months post-infection. Our data indicated that endothelial dysfunction, increased arterial stiffness, and elevated blood pressure were the main manifestations of post-COVID-19 infection, which aligned with our hypothesis. Additionally, regression analysis demonstrated that as the time of COVID-19 infection increased, LbaPWV and RbaPWV decreased, suggesting a certain degree of improvement in arterial stiffness among young individuals over time. This is consistent with our stratification of the post-infection period into early and late recovery phases based on the median time of infection. During the early recovery phase, there was a significant increase in both LbaPWV and RbaPWV. In contrast, during the late recovery phase, these indicators showed no significant differences and tended to revert to levels prior to the COVID-19 infection. However, an unexpected outcome was observed for diastolic blood pressure (DBP), indicating a prolonged impact of COVID-19 on blood pressure levels. When we stratified the recovery period based on the median time since infection, we found no statistically significant difference in DBP during the early recovery phase. In contrast, the late recovery phase was characterized by a significant increase in DBP. This discrepancy may be attributed to the infection's effects becoming more pronounced over time, with the late recovery group showing more evident impacts compared to the early recovery group, where the effects might not

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Table 4 Correlations between participants' age, BMI, the time of COVID-19 infection, vascular endothelium, arterial stiffness, heart rate, and blood pressure parameters (N = 37)

Parameter	Age	BMI	The time of COVID-19 infection	FMD	cfPWV	LABI	RABI	LbaPWV	RbaPWV	HR	SBP	DBP
Age	1											
BMI	-0.224	1										
The time of COVID-19 infection	0.052	0.192	1									
FMD	0.100	-0.131	-0.010	1								
cfPWV	0.319	0.130	-0.094	0.257	1							
LABI	0.072	0.026	0.047	-0.183	-0.167	1						
RABI	0.045	-0.237	-0.215	-0.159	-0.295	0.652[b]	1					
LbaPWV	0.128	-0.286	-0.505[b]	0.178	0.268	0.038	0.190	1				
RbaPWV	-0.228	-0.113	-0.507[b]	0.210	0.386[a]	-0.029	0.055	0.828[b]	1			
HR	-0.304	0.265	0.277	0.117	0.022	0.075	0.066	-0.234	-0.107	1		
SBP	0.147	-0.031	0.187	-0.104	-0.075	-0.128	-0.191	-0.042	0.031	-0.103	1	
DBP	0.163	-0.035	0.446[b]	0.067	0.124	-0.035	-0.083	-0.180	-0.009	0.093	0.351[a]	1

Values are Spearman coefficient r value. a: indicates $p < 0.05$; b: indicates $p < 0.01$. FMD = flow-mediated dilation; cfPWV = carotid-femoral pulse wave velocity; LABI = left ankle-brachial index; RABI = right ankle-brachial index; LbaPWV = left brachial-ankle pulse wave velocity; RbaPWV = right brachial-ankle pulse wave velocity; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure

have had adequate time to manifest. Currently, possible mechanisms for cardiovascular damage in the long-term effects of COVID-19 infection include the direct impact of the SARS-CoV-2 virus on the myocardium, microthrombotic injury to blood vessels and endothelium, and persistent systemic inflammation [27]. Libby et al. suggested that COVID-19 is a disease that ultimately affects the endothelium [28]. The impact of SARS-CoV-2 on the endothelial layer can be attributed to the binding of its spike (S) protein to ACE2 on the host cell surface, which facilitates viral entry into the host cell and subsequently leads to a condition known as endotheliitis [29]. SARS-CoV-2 infection can also elicit systemic inflammation and cytokine release, impairing the bioavailability of nitric oxide (NO) and leading to dysregulation of vascular tone, ultimately resulting in arterial stiffness [8]. Our study found that within 2 to 5 months following COVID-19 infection, there was a significant decrease in FMD and an increase in cfPWV, indicating long-term negative effects on endothelial function and arterial stiffness. A prospective study compared vascular function among healthy individuals, individuals with a history of COVID-19 infection 4 months prior, and individuals with hypertension and reported that both the COVID-19 patients and hypertensive patients exhibited similar FMD values, which were lower than those of healthy individuals [9]. Furthermore, another study found that in previously hospitalized COVID-19 patients, endothelial function improved at 6-month follow-up but remained lower than that in healthy individuals [30]. The study suggested that even in individuals without any pre-existing cardiovascular diseases before COVID-19 infection, the risk of cardiovascular diseases remained elevated within 12 months of COVID-19 infection [31]. However, contrary research findings indicated that COVID-19 (Omicron variant) did not have any impact on the vascular and cardiac autonomic function in young individuals [10]. A possible reason for this finding may be the limited sample size, with only 23 participants infected with COVID-19, which may not adequately reflect the impact of COVID-19 on the cardiovascular system.

Multiple studies have demonstrated that BP levels increased following COVID-19 infection [32–36]. SARS-CoV-2 enters the human body by binding to ACE2, which typically converts Angiotensin I in the renin-angiotensin-aldosterone system (RAAS) to Angiotensin II, thus influencing BP [37]. During hospitalization, critically ill patients infected with SARS-CoV-2 exhibited a significant increase in BP [38]. A retrospective study involving 153 patients revealed an increase in SBP and DBP following SARS-CoV-2 infection. Furthermore, 18 cases developed new-onset hypertension within 30 days [33]. Wrona et al. suggested that the sequelae of COVID-19 include newly developed diabetes, hypertension, and
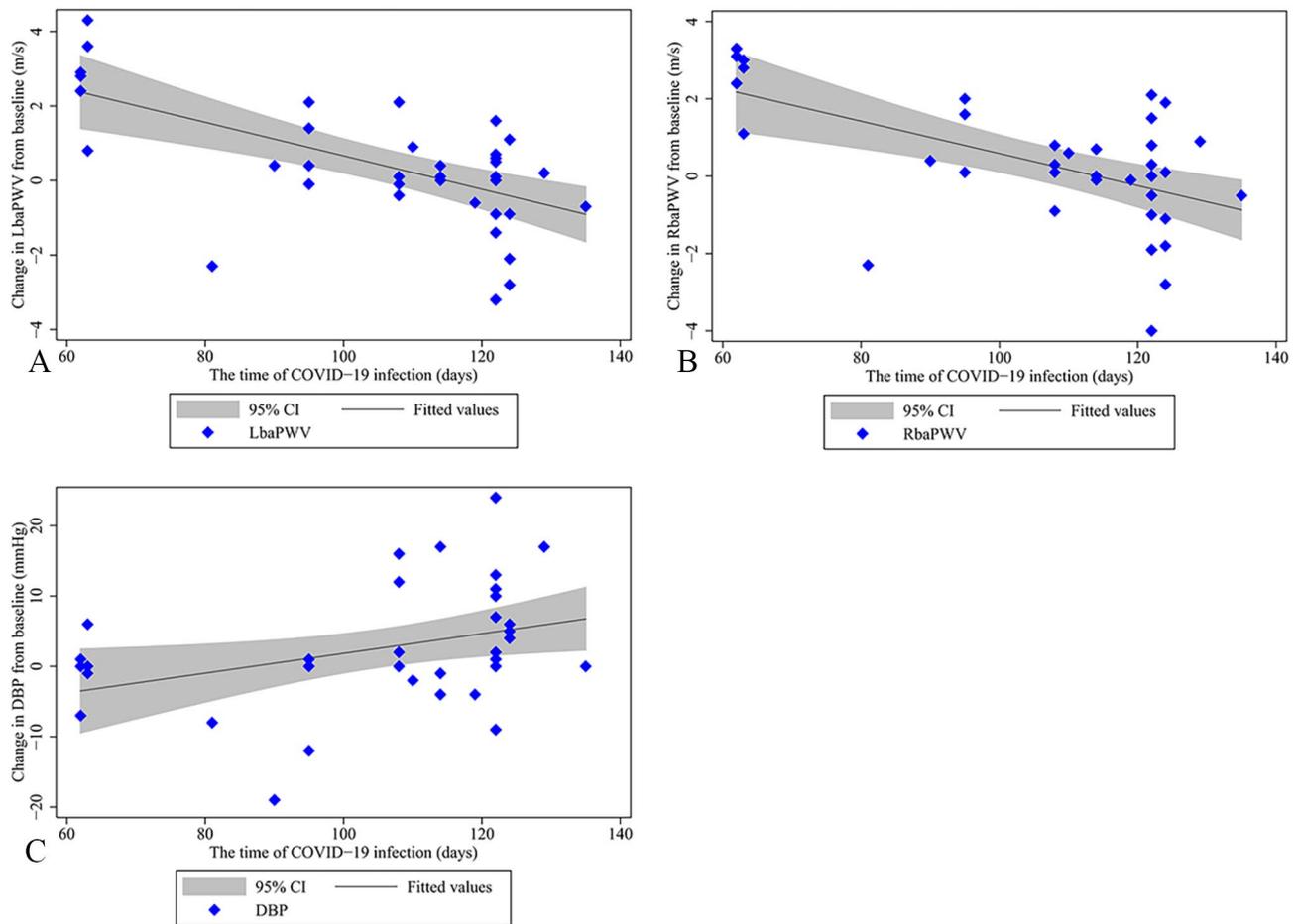
Fig. 1 The impact of the time of COVID-19 infection on LbaPWV, RbaPWV, and DBP. **A**: A reduction in LbaPWV with increasing time of COVID-19 infection was shown, as indicated by the SLR model with 95% confidence interval (CI) and fitting curve ($R^2 = 38\%$, $p < 0.001$). **B**: A reduction in RbaPWV with increasing time of COVID-19 infection was shown, as supported by the SLR model with 95% confidence interval (CI) and fitting curve ($R^2 = 32\%$, $p < 0.001$). **C**: An increase in DBP with increasing time of COVID-19 infection was shown, as depicted by the SLR model with 95% confidence interval (CI) and fitting curve ($R^2 = 14\%$, $p = 0.024$)

dyslipidemia [39]. Our study found that SBP significantly increased after COVID-19 infection, with a borderline significant elevation in DBP. The possible reason is that COVID-19 infection leads to an inflammatory response, and during the inflammatory process, inflammatory mediators (such as cytokines) produced in the body may cause vasoconstriction and increase blood pressure.

It is noteworthy that our regression model, when analyzing the 2- to 5-month post-infection period, showed that as the time of COVID-19 infection increased, baPWV decreased, while DBP increased. This suggests that arterial stiffness improved with time after COVID-19 infection but the virus had long-term effects on BP. Although previous studies had indicated that patients with COVID-19 showed gradual improvement in endothelial function during the 6-month follow-up period after discharge, their endothelial function still lagged behind that of healthy individuals [40]. Another study demonstrated that at least 6 months after infection,

COVID-19 survivors without other comorbidities associated with endothelial damage only showed mild evidence of endothelial dysfunction [41]. However, there were also studies indicating that the vascular damage became more severe with the progression of infection time [42]. Further investigation is warranted to explore the long-term effects of cardiovascular damage following COVID-19 infection.

In the present study, we did not observe a significant difference in the ABI index and HR between pre-post COVID-19 pandemic. Abnormal ABI values, defined as <0.9 or >1.3 m/s, are indicative of increased risk for overall mortality and cardiovascular mortality [43]. In our study, we observed no significant difference in the ankle-brachial index (ABI) values between the pre-infection and post-infection periods, regardless of whether the post-infection period was within the initial 2 to 5 months or stratified into early and late recovery phases based on the median time since infection. In all cases, the

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ABI values of all participants remained within the normal range. This may be attributed to the fact that our subjects consisted of young college students, and none of them were hospitalized due to COVID-19 infection. A recent study had indicated that SARS-CoV-2 induced vagal neuropathy, leading to autonomic dysfunction and potential long-term impairment of autonomic function [44]. Additionally, a study found that SARS-CoV-2 infection increased sympathetic nerve activation in young individuals, but had no significant effect on resting hemodynamics and speculated that the impact of COVID-19 on endothelial function and arterial stiffness may be more pronounced in older individuals [45]. Therefore, further investigation is warranted to identify the impact of COVID-19 on the autonomic nervous system, particularly its long-term effects.

Our study also has some limitations. Due to the retrospective nature of the pre-COVID-19 data, our sample size was limited, and further expansion was not possible. Additionally, the selection of young college students as the study population may affect the generalizability of the results. Furthermore, the duration between the pre- and post-measurements varied among participants.

In summary, our study indicates that even young college students with mild COVID-19 infections sustain significant adverse effects on endothelial function, arterial stiffness, and blood pressure within 2 to 5 months post-infection. Additionally, comparative data between early and late recovery phases, coupled with regression analyses across the entire timeframe, suggest that while vascular damage may diminish over time following COVID-19 infection, the elevation in blood pressure may endure for an extended period.

List of abbreviations

FMD	Flow-mediated dilation
ABI	Ankle-brachial index
PWV	Pulse wave velocity
BaPWV	Brachial-ankle pulse wave velocity
LbaPWV	Left brachial-ankle pulse wave velocity
RbaPWV	Right brachial-ankle pulse wave velocity
cfPWV	Carotid-femoral pulse wave velocity
HR	Heart rate
BP	Blood pressure
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
SARS-CoV-2	Syndrome coronavirus 2
COVID-19	Coronavirus disease 2019
ACE2	Angiotensin-converting enzyme 2
ESH	European society of hypertension
ESC	European Society of cardiology
CAD	Coronary artery disease
CHF	Congestive heart failure
CVD	Cardiovascular disease
PAOD	Peripheral arterial occlusive disease
NO	Nitric oxide
RAAS	Renin-angiotensin-aldosterone system

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was conducted with the approval of the Ethics Committee of Guangzhou Sport University (Protocol number: 2023LCLL-53) and adhered to the ethical guidelines outlined in the 1975 Declaration of Helsinki. Prior to the commencement of the experiment, all participants received detailed information about the study's objectives and provided their written informed consent.

Consent for publication
All participants involved in the study have provided their informed consent for the publication of the research results. This consent is in line with the ethical guidelines and ensures that any personal data or identifiable information will be appropriately anonymized to protect individual privacy. The participants understand that their contributions may be included in various forms within the publication, and they have the right to retract their consent at any time prior to the actual publication.

Competing interests
The authors declare no competing interests.

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