Journal of Cardiothoracic Surgery

RESEARCH

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Repercussions of SARS-CoV-2 infection on intrapulmonary shunt in patients undergoing one-lung ventilation

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Abstract

Background Hypoxic pulmonary vasoconstriction is the most important regulatory mechanism by which right-to-left shunts decrease during one-lung ventilation (OLV), but the effects of pulmonary microarterial thrombosis and impaired HPV after SARS-CoV-2 infection on intrapulmonary shunt during OLV remain unknown. The aim of this study was to observe the changes of intrapulmonary shunt in patients undergoing thoracoscopic partial pneumonectomy at different periods after SARS-CoV-2 infection compared with patients without SARS-CoV-2 infection history.

Methods A total of 80 patients who underwent elective thoracoscopic partial lung resection and were classified as American Society of Anaesthesiologists (ASA) grades I-II were selected and divided into 4 groups ($n=20$ in each group): patients not infected with SARS-CoV-2 (Group A), patients infected with SARS-CoV-2 for 5–8 weeks (Group B), patients infected with SARS-CoV-2 for 9–12 weeks (Group C), and patients infected with SARS-CoV-2 for 13–16 weeks (Group D). For all patients, the same anaesthesia method was adopted, and anaesthesia was maintained with propofol, remifentanil, and cisatracurium. Radial artery and mixed venous blood gases were measured at 10 min of two-lung ventilation (TLV), 15 min of one-lung ventilation (OLV15), and 30 min of OLV (OLV30) in the lateral recumbent position to calculate the intrapulmonary shunt. Multiple linear regression analysis was employed to investigate the association between intrapulmonary shunt and SARS-CoV-2 infection.

Results Qs/Qt at TLV was significantly higher in Groups B and C than in Group A ($P<0.05$), and PaO_2 at TLV was significantly lower in Groups B and C than in Group A ($P<0.05$). Qs/Qt values at OLV15 and OLV30 were significantly higher in Group B, C or D than in Group A ($P<0.05$), and PaO_2 values at OLV15 and OLV30 were significantly lower in Groups B, C or D than in Group A ($P<0.05$). Multiple linear regression analysis revealed that SARS-CoV-2 infection (95%*CI* -4.245 to -0.679, $P=0.007$) was an independent risk factor for increased intrapulmonary shunt during TLV, while SARS-CoV-2 infection (95%*CI* 0.124 to 3.661, $P=0.036$), exacerbation of COVID-19 clinical classification (95%*CI* -5.203 to -1.139, $P=0.003$), and persistent symptoms (95%*CI* -12.122 to -5.522, $P<0.001$) were independent risk factors for increased intrapulmonary shunt during OLV after SARS-CoV-2 infection.

Conclusion SARS-CoV-2 infection increased intrapulmonary shunt and reduced oxygenation. Although oxygenation improved at TLV after 13–16 weeks of infection, intrapulmonary shunt and oxygenation under OLV took longer to recover.

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Trial registration Chinese Clinical Trial Registry, Retrospectively registered, Full date of first registration: 17/05/2023, Registration number: ChiCTR2300071539.

Keywords SARS-CoV-2, One-lung ventilation, Intrapulmonary shunt, Oxygenation

Introduction

Since the COVID-19 pandemic at the end of 2019, SARS-CoV-2 has infected hundreds of millions of people around the world. After three years of strict prevention and control, China adjusted its prevention and control strategy in December 2022, switching from Class A management of category B infectious diseases to Class B management of category B infectious diseases. There is a need to explore the perioperative effects of SARS-CoV-2 infection.The symptoms of SARS-CoV-2 infection are not limited to the acute phase but persist for a long time after the virus is cleared from the human body; that is, COVID-19 symptoms are long-term [1]. The respiratory system, the route of and the main system affected by SARS-CoV-2 infection, bears the brunt. The respiratory symptoms of COVID-19, whether severe respiratory distress syndrome in the acute phase or dyspnoea in the long COVID-19 phase [2], are manifestations of lung injury. The increase in intrapulmonary shunt secondary to lung injury is a key factor in the development of hypoxemia during the SARS-CoV-2 infection period [3], and the severity of intrapulmonary shunt is closely related to patient prognosis [4], though development of a shunt is likely multifactorial. The infection of SARS-CoV-2 impairs the mechanism of hypoxic pulmonary vasoconstriction (HPV) in the lung, leading to an increase in intrapulmonary shunt [5]. The shunt may be compounded by microemboli [3]. Autopsy of the lungs after severe disease showed fibrin deposition, diffuse alveolar damage, vascular wall thickening, and frequently occurring complement-rich microthrombi occluding lung capillaries and larger thrombi causing pulmonary artery thrombosis and embolism. Hypercoagulable state leads to further deterioration in ventilation/perfusion mismatch and lung tissue damage [6]. The severity of symptoms during the SARS-CoV-2 infection period varies, but all patients may have sequelae involving impaired pulmonary function [2]. HPV is the most important regulatory mechanism by which right-to-left shunts decrease during one-lung ventilation (OLV). This study investigated the changes in intrapulmonary shunt in patients undergoing thoracoscopic partial lung resection after SARS-CoV-2 infection to provide a reference for clinical anaesthesia.

Materials and methods

Clinical data and grouping

This study was approved by the Ethics Committee of the Affiliated Hospital of Yangzhou University [approval number: 2022-YKL12-(class 01)], and informed consent was provided by patients or principals. Our study has been registered with the Chinese Clinical Trial Registry under registration number ChiCTR2300071539. Patients who underwent thoracoscopic partial pneumonectomy for pulmonary nodules at our hospital between December 2022 and May 2023 were included in the study. The inclusion criteria were as follows. The control group comprised patients without SARS-CoV-2 infection, and the remaining groups comprised male and female patients only infected once with SARS-CoV-2.The Omicron variant was the predominant strain during the study period, and the diagnostic accuracy of the Polymerase Chain Reaction assay was not affected. Therefore, in this study, the Reverse Transcription-Polymerase Chain Reaction positive throat swabs collected from the patients were determined as SARS-CoV-2 infection, and the clinical classification included mild and common COVID-19 patients (Clinical classification of COVID-19: (1) Mild: clinical symptoms are mild, and no pneumonia is seen on CT scans. (2) Common: clinical symptoms related to COVID-19, such as fever and/or respiratory symptoms, and pneumonia is seen on imaging. (3) Severe: any one of the following: 1. respiratory rate≥30 breaths/min;2. finger pulse oxygen saturation≤93% when breathing air in a resting state;3. $PaO_2/FiO_2 \leq 300$mmHg;4. progressive aggravation of clinical symptoms, and lung imaging shows obvious progress of >50% within 24–48 h.), American Society of Anaesthesiologists (ASA) grades I and II, an age of 25–75 years old, a body mass index (BMI) of 18.5–24.9 kg/m^2, and no major organ dysfunction. The exclusion criteria were as follows: critically ill patients with SARS-CoV-2 infection (requiring oxygen therapy or a ventilator to maintain ventilation), patients with preoperative pulmonary infection, patients with moderate or more severe anaemia, hypoproteinaemia, or hypoxemia, patients with water-electrolyte and acid-base balance disorders, patients with haemorrhagic coagulation dysfunction, patients with a history of radiotherapy, chemotherapy or immunotherapy, patients with a history of chronic lung disease or asthma, and patients with a history of thoracic surgery. A total of 85 patients who underwent elective thoracoscopic partial lung resection were selected. Five patients were excluded from the study due to intraoperative conversion to thoracotomy. The patients were divided into 4 groups ($n=20$) based on whether they were infected with SARS-CoV-2or the time infected with SARS-CoV-2: patients not infected with SARS-CoV-2 (Group A), patients infected with SARS-CoV-2 for 5 to 8 weeks (Group B), patients infected with

SARS-CoV-2 for 9 to 12 weeks (Group C), and patients infected with SARS-CoV-2 for 13 to 16 weeks (Group D) (Fig 1).

Methods of anaesthesia

All patients fasted from food and drink before the operation. The radial artery and right internal jugular vein were accurately positioned under ultrasound guidance. The length of the catheter inserted into the right internal jugular vein was 18 cm, allowing it to reach the right atrium as confirmed by transthoracic echocardiography. Mean arterial pressure (MAP), heart rate (HR), nasopharyngeal temperature, peripheral capillary oxygen saturation (SpO_2), and central venous pressure (CVP) were monitored, and the Narcotrend Index (NI) was monitored using a Narcotrend monitor (MT MonitorTechnik GmbH, Germany). All patients underwent general anesthesia. Anesthesia was induced by administering an intravenous bolus injection of midazolam at a dose of 0.05 mg/kg, propofol at a dose range of 1.5-2.0 mg/kg, sufentanil at a dose of 0.5 μg/kg, and cisatracurium at a dose of 0.15 mg/kgAfter satisfactory muscle relaxation, a double-lumen bronchial catheter was inserted, and a fibreoptic bronchoscope was positioned. The ventilation mode was volume control+PEEP 5 cmH_2O (1 cmH_2O=0.098 kPa) ventilation. Tidal volume (V_T) was calculated based on adjusted body weight. Specifically, V_T was 8 ml/kg during two-lung ventilation (TLV) and 6 ml/kg during OLV. The fraction of inspired oxygen (FiO_2) was maintained at 100% during both TLV and OLV, the inspiratory-to-expiratory time ratio (I: E) ratio was 1:2, and the non-ventilated side of the double-lumen tube was open to the atmosphere during OLV. The ventilation frequency was adjusted to maintain $P_{ET}CO_2$ at 35–45 mmHg (1 mmHg=0.133 kPa). Propofol, remifentanil, and cisatracurium were intravenously infused at 4–8 $mg{\cdot}kg^{-1}{\cdot}h^{-1}$, 0.1–0.2 $\mu g{\cdot}kg^{-1}{\cdot}min^{-1}$, and 0.1 $mg{\cdot}kg^{-1}{\cdot}h^{-1}$, respectively, to maintain anaesthesia, and the doses of propofol and remifentanil were adjusted to maintain an NI value between 26 and 46 and MAP within the range of ±20% of

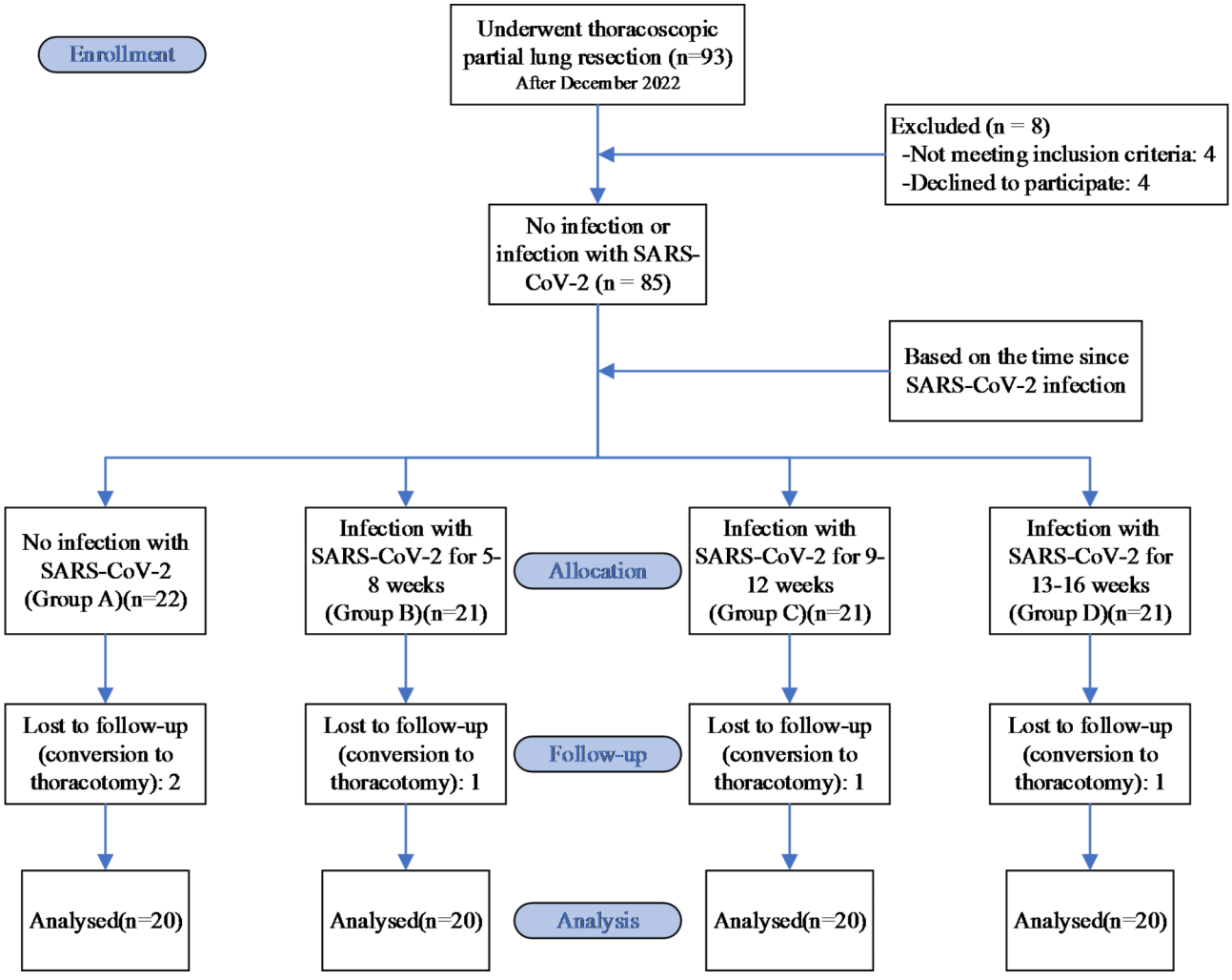

Fig. 1 Consolidated standards of reporting trials (CONSORT) flow diagram

the basal blood pressure. Intravenous fluids (crystalloid: colloid=2:1) were administered to maintain CVP at 5–12 cmH_2O.Phenylephrine was administered in cases where MAP decreased by more than 20%, while atropine was administered when the heart rate fell below 50 beats/min, and a warming blanket was used to prevent hypothermia.

Observation indicators

General patient data, surgical information, and persistent symptoms caused by COVID-19 were recorded. The persistent symptoms of COVID-19 encompass fatigue, dyspnea, musculoskeletal pain, smell/taste abnormalities, cognitive impairment, sleep disturbance, cough, and chest pain.

Primary outcome: The main outcome was intrapulmonary shunt after OLV. Arterial and venous blood gases, HR, and MAP were measured, always with the patient in the lateral position, in three phases: during two-lung ventilation (TLV), 15 min after beginning OLV (OLV15), and 30 min after beginning OLV (OLV30). An analyser (Model: GEM3500, Instrumentation Laboratory, USA) was used for blood gas analysis, and the intrapulmonary shunt rate was calculated using Qs/Qt=(CcO_2 -CaO_2)/(CcO_2 -CvO_2)×100% [7], where CcO_2 is the pulmonary capillary blood oxygen content, CaO_2 is the arterial oxygen content, and CvO_2 is the mixed venous oxygen content, the mixed venous oxygen content was replaced by venous blood oxygen content within the right atrium [8]:

$$CcO_2 = 1.36 \times Hb \times SAO_2 + PAO_2 \times 0.0031$$

$$CaO_2 = 1.36 \times Hb \times SaO_2 + PaO_2 \times 0.0031$$

$$CvO_2 = 1.36 \times Hb \times SvO_2 + PvO_2 \times 0.0031$$

where 1.36 is the oxygen-carrying capacity of haemoglobin (ml/g); SAO_2 is the alveolar capillary oxygen saturation, which is approximately equal to SaO_2; PAO_2 is the alveolar partial pressure of oxygen, which can be calculated using $PAO_2=FiO_2\times(Pb-PH_2O)-(PaCO_2/R)+[PaCO_2\times FiO_2\times(1-R)/R]$, where $PaCO_2$ is the arterial partial pressure of carbon dioxide, Pb is the atmospheric pressure (760 mmHg), PH_2O is the water vapour pressure at 37 °C (47 mmHg), R is the respiratory quotient (0.8), and when FiO_2=100%, PAO_2=713-$PaCO_2$; SaO_2 is arterial oxygen saturation; SvO_2 is mixed venous oxygen saturation, but assuming that the SvO_2 was equal to the saturation of the blood sample extracted from the right atrial ($SvcO_2$) [9]; and PvO_2 is mixed venous partial pressure of oxygen.

Secondary outcomes: Frequency of ventilation during mechanical ventilation.

Sample size calculating

The intrapulmonary shunt was treated as a continuous variable in this study, and its relationship with eight other variables was analyzed using multiple linear regression analysis. A coefficient of determination (R^2) of at least 0.2 was expected, while the obtained R^2 value was actually 0.45, surpassing the desired threshold. By employing $\alpha=0.05$, $\beta=0.2$, accounting for a dropout rate of 10%, and utilizing PASS software calculations, it was determined that a minimum sample size of 78 study subjects would be required for this research project; however, a total of 80 participants were ultimately included.

Statistical analysis

SPSS 23.0 software was used for the statistical analysis, and measurement data with a normal distribution are expressed as the mean±standard deviation. The comparison of measurement data between groups in general data was conducted using one-way analysis of variance. Repeated measurement design analysis of variance was employed for comparing repeated measurement data. Chi-square test, along with Fisher's exact probability method, was utilized for comparing count data when the theoretical frequency was less than 5. The variables with a significance level of $P<0.05$ in the univariate analysis, along with clinically significant variables, were included in the multiple linear regression analysis to identify risk factors associated with intrapulmonary shunt. A significance level of $P<0.05$ was considered to indicate statistical significance.

Results

There were no significant differences in age, sex, BMI, pulmonary function, percentage of lung collapse, OLV duration, blood loss or fluid replacement volume among the four groups ($P>0.05$) (Table 1).

Compared to TLV, PaO_2 significantly decreased at OLV15 and OLV30 ($P<0.05$), while ventilatory frequency and Qs/Qt significantly increased at OLV15 and OLV30 ($P<0.05$). In comparison with group A, PaO_2 was significantly reduced ($P<0.05$), and ventilatory ventilatory and Qs/Qt were significantly increased at TLV in groups B and C ($P<0.05$). Furthermore, compared to group A, PaO_2 was notably decreased at OLV15 and OLV30 in groups B, C, and D ($P<0.05$), whereas ventilatory ventilatory and Qs/Qt were considerably elevated at OLV15 and OLV30 in groups B, C, and D ($P<0.05$). There were no significant differences observed among the four groups regarding $PaCO_2$, Hb, MAP or HR values (Table 2).

There was no statistically significant difference in the type of infection observed among the subgroups infected with SARS-CoV-2 ($P=0.919$). In comparison to group B, group D exhibited a significant reduction in persistent symptoms ($P=0.010$) and dyspnea ($P=0.011$) (Table 3).

Table 1 Comparison of general patient data ($n=20$)

Item	Group A	Group B	Group C	Group D	F/χ^2	*P* value
Age (yr)	63.5 ± 9.1	61.6 ± 9.5	61.1 ± 12.2	59.2 ± 7.6	0.675	0.57
Male/Female	9/11	8/12	8/12	12/8	2.162	0.539
BMI (kg/m^2)	21.8 ± 2.0	21.3 ± 1.9	22.4 ± 2.2	22.2 ± 2.1	1.235	0.303
Smoking history	3 (15.0)	2 (10.0)	4 (20.0)	5 (25.0)	1.750	0.760
Hypertension	5 (25.0)	6 (30.0)	5 (25.0)	3 (15.0)	1.397	0.792
Diabetes	3 (15.0)	4 (20.0)	6 (30.0)	5 (25.0)	1.471	0.807
ASA grade I/II	5/15	7/13	6/14	6/14	0.476	0.924
FEV1 (% predicted)	95.0 ± 20.2	93.7 ± 16.1	92.7 ± 16.7	93.7 ± 11.7	0.06	0.98
FVC (% predicted)	95.5 ± 15.9	93.8 ± 14.1	96.3 ± 13.5	96.3 ± 10.8	0.144	0.933
FEV1/FVC (%)	81.3 ± 10.7	81.3 ± 7.9	78.6 ± 7.5	80.1 ± 7.5	0.447	0.72
Type of surgery					3.019	0.832
lobectomy	12 (60.0)	16 (80.0)	13 (65.0)	14 (70.0)		
segmentectomy	5 (25.0)	2 (10.0)	5 (25.0)	3 (15.0)		
wedge resection	3 (15.0)	2 (10.0)	2 (10.0)	3 (15.0)		
Right/Left side	12/8	9/11	13/7	8/12	3.409	0.333
OLV duration (min)	83.9 ± 37.4	93.5 ± 36.3	87.1 ± 35.0	79.3 ± 29.4	0.597	0.619
Blood loss (ml)	63.0 ± 22.0	75.0 ± 41.4	69.5 ± 22.1	63.5 ± 35.7	0.648	0.587
Fluid replacement volume (ml)	1197.5 ± 257.8	1272.5 ± 322.6	1187.5 ± 240.5	1215.0 ± 184.3	0.44	0.725

All data are presented as the mean ± SD or N (%). ASA = American Society of Anesthesiologists, FEV1 = forced expiratory volume in 1 s, FVC = forced vital capacity, Right/Left side = The right or left side of the lung that is ventilated during one-lung ventilation

In this study, multiple linear regression was employed to investigate the impact of SARS-CoV-2 infection, age, gender, smoking history, FEV1, clinical classification, persistent symptoms, and dyspnea on Qs/Qt during TLV. The final multiple linear regression model exhibited statistical significance ($F=5.258$, $P<0.001$). The dependent variable, accounting for 37.2% of the variation in Qs/Qt during TLV, could be elucidated by SARS-CoV-2 infection ($R^2=0.372$). The table below presents the partial regression coefficient β and its corresponding 95% confidence interval for each independent variable (Table 4).

In this study, multiple linear regression was employed to investigate the impact of SARS-CoV-2 infection, age, gender, smoking history, FEV1, clinical classification, persistent symptoms, and dyspnea on Qs/Qt during 15 min after beginning OLV. The final multiple linear regression model exhibited statistical significance ($F=7.754$, $P<0.001$). The dependent variable, accounting for 46.6% of the variation in Qs/Qt during 15 min after beginning OLV, could be elucidated by SARS-CoV-2 infection, clinical classification, persistent symptoms ($R^2=0.466$). The table below presents the partial regression coefficient β and its corresponding 95% confidence interval for each independent variable (Table 5).

Discussion

Long-term lung injury may reduce the oxygenation of the body during lung surgery and increase the difficulty of anaesthesia management. In this study, intrapulmonary shunt and oxygenation under TLV began to return to pre-infection levels 13-16 weeks after infection with SARS-CoV-2. However, under OLV, intrapulmonary shunt and arterial oxygenation increased and decreased, respectively, within 16 weeks after infection, and there was no significant improvement. At the same time, with the increase of intrapulmonary shunt, the ventilation rate needs to be increased to maintain effective gas exchange under the premise of constant tidal volume.

In healthy lungs, HPV redistributes perfusion (Q) to areas with better ventilation (V) for optimal V/Q matching, and HPV is the fastest physiological response of pulmonary arteries to alveolar hypoxia [10]. When HPV is compromised, there is a V/Q mismatch, and intrapulmonary shunting increases. Caravita et al. [11], using dyspnoeic patients as controls, studied the HPV of SARS-CoV-2 infected patients under mechanical ventilation by monitoring haemodynamic changes through right heart catheterization, and their results confirmed that HPV was impaired in patients with SARS-CoV-2 infection. Pulmonary artery smooth muscle cells (PASMCs) and pulmonary artery endothelial cells (PAECs) are involved in the regulation of HPV, and their mitochondria regulate cellular oxygen sensing and induce apoptosis, respectively. SARS-CoV-2 disrupts oxygen sensing in PASMCs by targeting their mitochondria, in turn interfering with HPV rather than directly impairing the constriction of PASMCs [12]. PAEC apoptosis can be induced by SARS-CoV-2 infection. Endothelin is a high-efficiency vasoconstrictor released by PAECs during hypoxia, and both PAEC damage and the reduction in endothelin inhibit HPV [17]. In addition, there are microvascular changes in the lungs infected by SARS-CoV-2, including endothelial damage, alveolar capillary microthrombosis, and pulmonary vascular remodelling. These microvascular

Table 2 Comparison of blood gas analysis and haemodynamic results ($n=20$)

Indicator	Group	TLV	OLV15	OLV30
PaO_2 (mmHg)	Group A	508.7 ± 59.7	266.9 ± 79.4[a]	262.1 ± 99.1[a]
	Group B	440.1 ± 62.3[b]	187.6 ± 70.5[ab]	170.4 ± 58.8[ab]
	Group C	444.0 ± 71.4[b]	189.0 ± 81.8[ab]	177.4 ± 96.4[ab]
	Group D	500.7 ± 47.7	195.1 ± 86.2[ab]	187.6 ± 77.1[ab]
$PaCO_2$ (mmHg)	Group A	38.6 ± 1.9	37.4 ± 3.2	38.2 ± 2.9
	Group B	38.7 ± 2.8	38.6 ± 4.3	37.7 ± 4.1
	Group C	39.0 ± 2.8	38.3 ± 3.9	37.9 ± 3.6
	Group D	39.0 ± 2.0	37.5 ± 3.8	38.1 ± 3.5
ventilation frequency (breaths/min)	Group A	11.1 ± 0.7	14.4 ± 0.7 [a]	14.4 ± 0.7 [a]
	Group B	12.2 ± 0.9 [b]	15.5 ± 1.2 [ab]	15.7 ± 1.2 [ab]
	Group C	12.1 ± 0.8 [b]	15.6 ± 0.9 [ab]	15.7 ± 1.0 [ab]
	Group D	11.2 ± 0.7	15.4 ± 0.9 [ab]	15.5 ± 0.7 [ab]
Qs/Qt (%)	Group A	14.0 ± 3.3	24.0 ± 3.8[a]	23.8 ± 3.5[a]
	Group B	20.3 ± 6.8[b]	30.1 ± 5.1[ab]	31.1 ± 3.9[ab]
	Group C	20.6 ± 6.6[b]	31.8 ± 7.7[ab]	29.9 ± 8.1[ab]
	Group D	15.5 ± 4.0	30.3 ± 6.2[ab]	29.4 ± 6.2[ab]
Hb (g/dL)	Group A	12.3 ± 1.9	12.3 ± 2.0	12.2 ± 1.9
	Group B	12.5 ± 1.5	12.5 ± 1.5	12.6 ± 1.4
	Group C	12.2 ± 2.0	12.1 ± 2.0	12.1 ± 2.0
	Group D	12.0 ± 2.1	11.9 ± 2.2	12.0 ± 2.1
MAP (mmHg)	Group A	82.2 ± 8.2	80.9 ± 6.9	82.0 ± 6.1
	Group B	81.5 ± 7.4	82.0 ± 6.7	81.6 ± 6.8
	Group C	83.6 ± 6.4	83.2 ± 4.9	82.6 ± 5.4
	Group D	81.8 ± 8.2	80.5 ± 6.9	81.8 ± 6.8
HR (times/min)	Group A	76.3 ± 6.3	76.0 ± 6.0	76.5 ± 5.6
	Group B	75.1 ± 6.5	74.5 ± 6.2	74.7 ± 6.1
	Group C	75.7 ± 6.5	74.8 ± 6.1	74.4 ± 6.4
	Group D	76.5 ± 6.6	75.4 ± 6.1	76.0 ± 5.2

All data are presented as the mean ± SD. Hb = haemoglobin concentration, MAP = mean arterial pressure, HR = heart rate. Compared with TLV, [a]$P < 0.05$; compared with Group A, [b]$P < 0.05$

complications may present only in the acute phase or may persist to the long COVID-19 phase, and intrapulmonary shunt is closely related to microvascular complications [13]. Therefore, the impact of SARS-CoV-2 infection on intrapulmonary shunt is multifaceted, including the direct inhibition of HPV by SARS-CoV-2 and changes in lung structure.

A study of 143 hospitalized patients with COVID-19 reported that 43.4% of patients still had dyspnoea 60 days after infection [14], and a study of 55 hospitalized patients found that during a 3-month follow-up period, the results of pulmonary function test results were abnormal for 25% of the patients, and pulmonary diffusion function decreased in 16% [15]. In this study, there was no significant difference in the results of pulmonary function tests before and after infection, a finding that may be related to the fact that the included patients were all asymptomatic or mildly symptomatic. A retrospective study of patients with long-term COVID-19 found that long-term pulmonary function damage was closely related to the severity of COVID-19 in the acute phase (that is, patients with tracheal intubation > non-intubated hospitalized patients > non-hospitalized patients), and the pulmonary function test results for non-hospitalized patients did not differ from those for patients without COVID-19 [16], which is consistent with the results of this study. The patients included in this study were all infected with SARS-CoV-2 for the first time; this decision was made because repeated infections cause repeated damage to the lungs, and the accumulated lung damage could have affected the study results.

Multiple linear regression analysis revealed that SARS-CoV-2 infection was an independent risk factor for increased intrapulmonary shunt during TLV, while SARS-CoV-2 infection, exacerbation of COVID-19 clinical classification, and persistent symptoms were independent risk factors for increased intrapulmonary shunt during OLV after SARS-CoV-2 infection. In our study, persistent symptoms were found to be significantly lower at 13–16 weeks post-infection compared to 5–8 weeks post-infection, which is consistent with the findings of

Table 3 Comparative analysis of pertinent data among subgroups with preoperative SARS-CoV-2 infection ($n=20$)

	Group B	Group C	Group D	χ^2	*P* value
Clinical classification				0.684	0.919
Mild	15(75.0)	17(85.0)	16(80.0)		
Common	5(25.0)	3(15.0)	4(20.0)		
Persistent symptoms	12 (60.0)	6 (30.0)	3 (15.0)[c]	9.231	0.010
Dyspnea	7 (35.0)	3 (15.0)	0 (0)[c]	8.877	0.011

All data are presented as the N (%).Compared with Group B, [c]$P < 0.05$

Table 4 Multiple linear regression analysis of Qs/Qt at TLV

Variables	β	95%CI	*P* value
SARS-CoV-2 infection	-0.459	(-4.245, -0.679)	0.007
Age	-0.034	(-0.142, 0.100)	0.727
Gender	0	(-2.335, 2.325)	0.997
Smoking history	0.018	(-3.492, 4.059)	0.881
FEV1	0.145	(-0.035, 0.143)	0.229
Clinical classification	0.264	(-0.193, 3.904)	0.075
Persistent symptoms	-0.214	(-6.249, 0.405)	0.084
Dyspnea	-0.156	(-7.293, 1.633)	0.210

Table 5 Multiple linear regression analysis of Qs/Qt at 15 min after beginning OLV

Variables	β	95%CI	*P* value
SARS-CoV-2 infection	0.328	(0.124, 3.661)	0.036
Age	0.046	(-0.089, 0.151)	0.611
Gender	0.083	(-1.232, 3.391)	0.355
Smoking history	0.052	(-2.856, 4.634)	0.637
FEV1	-0.028	(-0.100, 0.077)	0.799
Clinical classification	-0.419	(-5.203, -1.139)	0.003
Persistent symptoms	-0.601	(-12.122, -5.522)	< 0.001
Dyspnea	-0.177	(-7.890, 0.964)	0.123

Whitaker et al. [1]. Although persistent symptoms after SARS-CoV-2 infection were identified as an independent risk factor for increased intrapulmonary shunt OLV, no improvement in intrapulmonary shunting was observed in our study. However, we hypothesize that a longer recovery period may lead to resolution of persistent symptoms and potential improvement in intrapulmonary shunting during OLV.

This study has limitations. First, this was a single-centre study with a small sample size. Second, the patients with SARS-CoV-2 infection included in this study were all asymptomatic or mildly symptomatic; therefore, the changes in intrapulmonary shunt and oxygenation in these patients cannot represent the changes in intrapulmonary shunt and oxygenation in severely symptomatic patients. Finally, only patients with a single SARS-CoV-2 infection were included in this study; therefore, further research is needed to investigate intrapulmonary shunt during OLV in people with multiple infections. Third, we failed to measure mixed arterial oxygen saturation with the use of a pulmonary floating catheter; instead, we used central venous oxygen saturation in the right atrium.

In summary, SARS-CoV-2 infection increased intrapulmonary shunt and reduced oxygenation in patients. Although oxygenation improved under TLV 13–16 weeks after infection, intrapulmonary shunt and oxygenation under OLV took longer to recover.

Author contributions

M.L. acquired and analyzed data and prepared the manuscript; X.D. acquired data; J.Z. and D.Y. designed the study and revised it critically. All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

Funding

This work was supported by the New Technology Project of the Affiliated Hospital of Yangzhou University (Project Number: 2020-2022-059). The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Affiliated Hospital of Yangzhou University [approval number: 2022-YKL12- (Lesson 01)]. All study participants provided written informed consent without any deviation from the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 16 December 2023 / Accepted: 30 August 2024
Published online: 10 September 2024

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