Impact of viral filters on accuracy of cardiopulmonary testing and spirometry

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To the Editor:

Airborne transmission commonly causes infectious diseases, including recent outbreaks of *Mycoplasma pneumoniae*, respiratory syncytial virus, influenza, and the coronavirus disease 2019 (COVID-19) global pandemic. Spirometry and cardiopulmonary exercise testing (CPET) are valuable diagnostic tools, but increased ventilation during exercise can heighten transmission risk, especially for highly infectious disease like COVID-19. Therefore, implementing preventive measures is crucial.

During the COVID-19 pandemic, viral filters were utilised in spirometry and CPET to prevent aerosol transmission. Manufacturers claimed these filters could eliminate 99.99% of viruses while maintaining accuracy. However, three articles reported different findings. With filters, Marques *et al.* [1] observed a significant increase in oxygen consumption ($\dot{V}_{O_2}$) (82.0% *versus* 90.5%, p=0.006); Stacey *et al.* [2] noted an increase in $\dot{V}_{O_2}$ (+5.6 mL·min^{-1}·kg^{-1}, p<0.001) and minute ventilation ($\dot{V}_E$) (+10.2 L·min^{-1}, p<0.001); and Bhat *et al.* [3] reported opposite changes in $\dot{V}_{O_2}$ in two subjects. These studies differed in terms of filter brands and placement. The first two studies positioned filters downstream of the testing circuit, while the third study placed them upstream. Accordingly, the impact of viral filters on CPET remained inconclusive.

Viral filters could affect CPET and spirometry results through various mechanisms. First, they introduced extra dead space. Secondly, filters induced resistance, attributed to the filter membrane and possibly from water vapour saturation within filters, as suggested in two previous consensuses [4, 5]. Lastly, retained exhaled carbon dioxide (CO_2) in filters increased CO_2 inhalation, stimulating respiratory drive. We hypothesised increasing resistance might decrease peak work rate (WR_{peak}), peak $\dot{V}_{O_2}$ ($\dot{V}_{O_2peak}$), forced expiratory volume in 1 s (FEV_1) and peak expiratory flow (PEF). CO_2 retention might elevate end-tidal CO_2 pressure (P_{ETCO_2}) and $\dot{V}_E$. Extra dead space could reduce forced vital capacity (FVC).

To prevent contamination of both the environment and equipment, we placed the filter at the proximal end (figure 1). 14 healthy participants without testing contraindications were recruited [6]. All the participants received oral and printed explanations and gave consent before undergoing spirometry and CPET twice within a 2-week interval, with spirometry preceding CPET on each visit. A virus filter (MicroGard II, Vyaire Medical GmbH) was placed between the face mask and the sample line during CPET (figure 1) or between the mouthpiece and the sample line during spirometry (figure 1). According to the manufacturers, the filter had a dead space volume of 55 mL±3% and a resistance of 36 Pa at a flow rate of 60 L·min^{-1}. The use of a filter or not was determined randomly by flipping a coin during the initial visit, and all tests were conducted by the same operator. The Institutional Review Board of Chang Gung Memorial Hospital approved the study protocol. Spirometry data was collected using digital spirometry *via* a mouthpiece, CPET was conducted with a face mask (figure 1) and the protocol was the same as in our previous study (Vyaire Cardiopulmonary Exercise Testing System, Vyaire Medical GmbH, Germany; SensorySuite Software, Germany) [7]. The participants, comprising five males and nine females, averaged (mean±SD) 31.5±6.1 years in age, 164.4±11.3 cm in height and 59.5±14.7 kg in weight. 13 participants underwent spirometry and 11 underwent CPET.

In CPET, $\dot{V}_{O_2}$peak remained unchanged (1542±365 *versus* 1561±363 mL·min^{-1}, p=0.563), while WR_{peak} demonstrated a borderline decrease with the filter (127±27 *versus* 132±27 Watts, p=0.058). P_{ETCO_2peak},

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The present study found that using viral filters at the proximal end of a spirometry and CPET test circuit did not significantly alter the test results, with the exception of a marginal decrease noted in peak work rate https://bit.ly/3Vkew95

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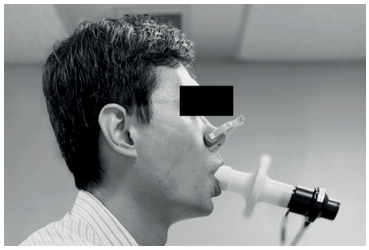
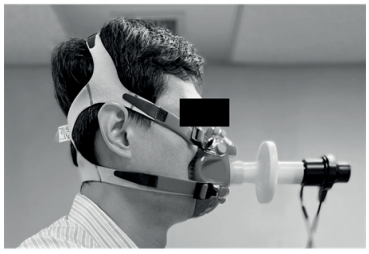
Variables	Unit	With filter	Without filter	p-value	Experimental equipment
Spirometry, n=13 (the filter was placed between the mouthpiece and the sample line)					
FVC	L	3.32±1.11	3.37±1.05	0.423	
FEV_1	L	2.77±0.89	2.79±0.88	0.937	
FEV_1/FVC	%	82.80±9.74	81.23±10.15	0.347	
PEF	$L{\cdot}s^{-1}$	5.41±1.95	5.42±1.74	0.754	
MEF_{75}	$L{\cdot}s^{-1}$	5.02±1.88	4.83±1.72	0.382	
MEF_{50}	$L{\cdot}s^{-1}$	3.49±1.52	3.24±1.25	0.382	
MEF_{25}	$L{\cdot}s^{-1}$	1.36±0.88	1.41±0.84	0.783	
CPET, n=11 (the filter was placed between the face mask and the sample line)					
WR_{peak}	Watt	127±27	132±27	0.058	
$\dot{V}_{O_2peak}$	$mL{\cdot}min^{-1}$	1542±365	1561±363	0.563	
$\dot{V}_{CO_2peak}$	$mL{\cdot}min^{-1}$	1978±501	1935±440	0.203	
$\dot{V}_{O_2peak}$/BW	$mL{\cdot}min^{-1}{\cdot}kg^{-1}$	26.1±3.9	26.3±3.2	0.790	
Peak breathing frequency	min^{-1}	39.4±5.4	40.4±7.0	0.477	
Peak tidal volume	L	1.564±0.397	1.459±0.423	0.114	
$\dot{V}_{Epeak}$	$L{\cdot}min^{-1}$	59±14	58±10	0.609	
P_{ETCO_2rest}	kPa	4.44±0.46	4.47±0.46	0.959	
P_{ETCO_2peak}	kPa	5.81±0.43	5.69±0.42	0.386	
Peak RER		1.21±0.10	1.24±0.08	0.332	
WR_{AT}	Watt	53±14	52±14	0.766	
$\dot{V}_{O_2AT}$	$mL{\cdot}min^{-1}$	877±259	859±162	0.959	
$\dot{V}_{O_2AT}$/BW	$mL{\cdot}min^{-1}{\cdot}kg^{-1}$	14.9±1.8	14.6±1.7	0.919	
EqO_{2VT1}		22.1±2.7	22.1±2.3	0.838	
EqO_{2nadir}		20.8±2.3	20.5±3.0	0.646	
$EqCO_{2nadir}$		25.0±1.9	24.4±2.2	0.169	
$\dot{V}_E$–$\dot{V}_{CO_2}$ slope		28.03±4.81	27.22±3.86	0.333	
$\Delta\dot{V}_{O_2}$/WR	$mL{\cdot}min^{-1}{\cdot}W^{-1}$	10.11±1.18	9.73±1.45	0.721	
OUES		1.72±0.38	1.81±0.62	0.594	

FIGURE 1 Spirometry and cardiopulmonary exercise testing (CPET) data with and without filters and experimental equipment. Data are presented as mean±SD, unless otherwise stated. AT: ventilatory anaerobic threshold; BW: body weight; $EqCO_{2nadir}$: the smallest value of ventilatory equivalent for CO_2; EqO_{2nadir}: the smallest value of ventilatory equivalent for O_2; EqO_{2VT1}: ventilatory equivalent for O_2 at ventilatory threshold 1; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; MEF_{75}: maximal expiratory flow at 75% of FVC; MEF_{50}: maximal expiratory flow at 50% of FVC; MEF_{25}: maximal expiratory flow at 25% of FVC; OUES: oxygen uptake efficiency slope; P_{ETCO_2}: end-tidal carbon dioxide pressure; PEF: peak expiratory flow; RER: respiratory exchange ratio; $\dot{V}_{CO_2}$: CO_2 production; $\dot{V}_E$: minute ventilation; $\dot{V}_{O_2}$: oxygen consumption; WR: work rate.

peak $\dot{V}_E$ ($\dot{V}_{Epeak}$) and other measured CPET parameters also showed no significant differences (figure 1). Spirometry showed no significant differences in FVC, FEV_1, FEV_1/FVC, PEF, maximal expiratory flow at 75% of FVC (MEF_{75}), maximal expiratory flow at 50% of FVC (MEF_{50}) and maximal expiratory flow at 25% of FVC (MEF25) between tests (figure 1).

While $\dot{V}_{O_2peak}$ remained consistent, a slight decrease in WR_{peak} suggested some filter resistance. Unchanged P_{ETCO_2peak} and $\dot{V}_{Epeak}$ indicated minimal interference with CO_2 retention. However, previous studies demonstrated unchanged WR_{peak} but a significant increase in $\dot{V}_{O_2peak}$, contrary to our findings. There could be several reasons for this. First, the filter placement differed. Marques *et al.* [1] and Stacey *et al.* [2] positioned the filter downstream of the CPET circuit. This positioning likely affected the test results due to differences in airflow resistance between lower downstream and higher upstream airflow. However, placing the filter only upstream effectively prevents contamination of both the environment and equipment. Secondly, the filter brands varied. Marques *et al.* [1] and our study used Vyaire filters, while Stacey *et al.* [2] and Bhat *et al.* [3] used filters from MGC Diagnostics Corporation. Variation in dead space volume and resistance among filters might affect test results. However, none of these studies detailed these values. Finally, the study by Bhat *et al.* [3] included only two subjects. Overall, using filters (MicroGard II, Vyaire Medical GmbH) at the proximal end of the CPET circuit had no significant impact. However, in severe pulmonary disease patients, additional flow resistance may underestimate WR_{peak}.

The filters we used had a manufacturer-reported dead space of 0.055 L, matching closely with our findings of a 0.05 L mean difference in FVC with and without filters (3.32±1.11 *versus* 3.37±1.05 L, p=0.423). Although the spirometry did not allow dead space adjustment, the 0.055 L dead space represented only a 1.6% decrease in mean FVC with filters. Nevertheless, in patients with compromised lung function, minor dead space change could slightly underestimate FVC. Hence, we suggest incorporating dead space adjustment functionality into the spirometry system.

Our spirometry findings differ from the published literature. Prior studies noted significantly decreased FEV_1, with other parameters varying. Two studies demonstrated reduced FVC [8, 9], one reported an increase in FEV_1/FVC [10], two indicated a decrease in PEF [9, 10], and one showed MEF_{50} reduction [9]. Notably, manufacturer-provided data indicated variations in the dead space volume and resistance among these filters (Fuso *et al*. [8] used SpiroBac from DAR, Italy; Kamps *et al*. [9] used Microgard from SensorMedics, the Netherlands, and VitalGard from Vital Signs, UK; and Johns *et al*. [10] used PF30S from Pall Biomedical, UK). The dead space ranged from 35 to 92 mL, and the resistance ranged from 24.5 to 343 $Pa{\cdot}s{\cdot}L^{-1}$. However, details about the filter's position, dead space volume adjustment and resistance value were not clear in these articles, complicating direct comparison.

The sample size determination was based on previous literature [1–3], which enrolled 10, 12 and two participants to assess for the impact of a filter on CPET. The sample size of 11 in our study may appear small. However, the p-values from the Wilcoxon signed-rank test are: 0.058 for WR_{peak}, 0.563 for $\dot{V}_{O_2peak}$, 0.609 for $\dot{V}_{Epeak}$, 0.959 for $\dot{V}_{O_2}AT$, 0.423 for FVC, 0.937 for FEV_1, and 0.754 for PEF (figure 1). Power analysis, with alpha at 0.05 and power at 0.8, indicates the required sample sizes for achieving significance: 17 for WR_{peak}, 224 for $\dot{V}_{O_2peak}$, 626 for $\dot{V}_{Epeak}$, 740 for $\dot{V}_{O_2}AT$, 538 for FVC, 1343 for FEV_1 and 26 821 for PEF. These large sample sizes indicate the difficulty in detecting subtle differences to achieve a p-value <0.05, suggesting that the differences are not substantial, with the exception of WR_{peak}. Overall, using viral filters (MicroGard II, Vyaire Medical GmbH) at the proximal end of the testing circuit during spirometry and CPET did not significantly change outcomes in healthy individuals. In future clinical CPET filter use, provided that the filters are placed upstream and do not exceed the resistance of our study's filter (36 Pa at a flow rate of 60 $L{\cdot}min^{-1}$), their impact should be minimal. However, in patients with compromised lung function, additional resistance and dead space may affect the results. Thus far, there is no published literature investigating this issue and further research is warranted.

Sing-Ya Chang[1], Yi-Ting Chiu[2], Kuo-Cheng Liu[2], Meng-Ting Wei[2] and Shu-Chun Huang[2,3,4]

[1]School of Traditional Chinese Medicine, College of Medicine, Chang Gung University, Taoyuan, Taiwan. [2]Department of Physical Medicine and Rehabilitation, New Taipei City Municipal Tucheng Hospital, Chang Gung Memorial Hospital, New Taipei City, Taiwan. [3]Department of Physical Medicine and Rehabilitation, Chang Gung Memorial Hospital, Linkou, Taiwan. [4]College of Medicine, Chang Gung University, Kwei-Shan, Taiwan.

Corresponding author: Shu-Chun Huang (h0711@ms13.hinet.net)

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