"You can leave your mask on": effects on cardiopulmonary parameters of different airway protective masks at rest and during maximal exercise

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Shareable abstract (@ERSpublications)
Protective mask use in healthy subjects is associated with modest respiratory discomfort and a slight reduction in exercise performance, mainly due to an increase in airflow resistance https://bit.ly/3aOCpwB

Cite this article as: Mapelli M, Salvioni E, De Martino F, *et al*. "You can leave your mask on": effects on cardiopulmonary parameters of different airway protective masks at rest and during maximal exercise. *Eur Respir J* 2021; 58: 2004473 [DOI: 10.1183/13993003.04473-2020].

Received: 10 Dec 2020
Accepted: 3 Feb 2021

Abstract

During the COVID-19 pandemic, the use of protective masks has been essential to reduce contagions. However, public opinion is that there is an associated subjective shortness of breath. We evaluated cardiorespiratory parameters at rest and during maximal exertion to highlight any differences with the use of protective masks.

12 healthy subjects performed three identical cardiopulmonary exercise tests, one without wearing a protective mask, one wearing a surgical mask and one with a filtering face piece particles class 2 (FFP2) mask. Dyspnoea was assessed using the Borg scale. Standard pulmonary function tests were also performed.

All the subjects (40.8±12.4 years; six male) completed the protocol with no adverse events. Spirometry showed a progressive reduction of forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) from no mask to surgical to FFP2 (FEV_1: 3.94±0.91 L, 3.23±0.81 L, 2.94±0.98 L; FVC: 4.70±1.21 L, 3.77±1.02 L, 3.52±1.21 L; p<0.001). Rest ventilation, O_2 uptake ($\dot{V}_{O_2}$) and CO_2 production ($\dot{V}_{CO_2}$) were progressively lower, with a reduction in respiratory rate. At peak exercise, subjects had a progressively higher Borg scale when wearing surgical and FFP2 masks. Accordingly, at peak exercise, $\dot{V}_{O_2}$ (31.0±23.4 $mL \cdot kg^{-1} \cdot min^{-1}$, 27.5±6.9 $mL \cdot kg^{-1} \cdot min^{-1}$, 28.2±8.8 $mL \cdot kg^{-1} \cdot min^{-1}$; p=0.001), ventilation (92±26 L, 76±22 L, 72±21 L; p=0.003), respiratory rate (42±8 $breaths \cdot min^{-1}$, 38±5 $breaths \cdot min^{-1}$, 37±4 $breaths \cdot min^{-1}$; p=0.04) and tidal volume (2.28±0.72 L, 2.05±0.60 L, 1.96±0.65 L; p=0.001) were gradually lower. There was no significant difference in oxygen saturation.

Protective masks are associated with significant but modest worsening of spirometry and cardiorespiratory parameters at rest and peak exercise. The effect is driven by a ventilation reduction due to increased airflow resistance. However, because exercise ventilatory limitation is far from being reached, their use is safe even during maximal exercise, with a slight reduction in performance.

Introduction

In March 2020, the World Health Organization declared a pandemic, coronavirus disease 2019 (COVID-19), caused by a new severe acute respiratory syndrome coronavirus 2, and this pandemic has heavily influenced social life and health organisation all over the world [1–5]. Among the different protective procedures introduced, the use of protective masks (both surgical masks and filtering face piece particles class 2 (FFP2)) has been indicated as essential to reduce viral transmission and contain the number of patients to avoid overloading healthcare systems [6–8].

However, despite the absence of definitive data on respiratory effects related to the use of protective masks, there is a general belief that their use is associated with shortness of breath during exercise and the need for greater respiratory effort even at rest, leading to the risk of reducing the application of an effective measure to contain infection.

In this study, we aimed to evaluate cardiorespiratory parameters, both at rest and during maximal exertion, through a cardiopulmonary exercise test (CPET) to highlight any differences with the use of surgical masks and FFP2 masks compared to normal conditions.

Methods

This study had an interventional, prospective, randomised, double-blind and crossover design.

In total, 12 healthy subjects, both male and female, were enrolled in July 2020. Inclusion criteria were age ⩾18 years and signed informed consent. Exclusion criteria were the presence of underlying cardiorespiratory diseases, history of COVID-19 infection, presence of any chronic drug treatment, and inability to perform or clinical contraindications against performing maximal exercise. Intense physical efforts were forbidden in the 24 h preceding each test. All subjects were non-smokers and none were professional athletes or involved in an intense exercise-training programme.

All subjects underwent three consecutive CPETs performed at least 24 h apart but within a 2-week timeframe. The CPETS were performed wearing a sham protective mask, a surgical mask (disposable medical mask, Aiminde, China) or an FFP2 mask (KN95 particulate respirator, BYD Care, China). In all conditions the masks were worn under the standard CPET silicone mask (Cosmed, Italy) prepared by medical personnel not associated with the study and they were externally indistinguishable from each other (figure 1). The absence of lateral air leakage was verified as a standard use procedure in CPET laboratories before each test. Specifically, after wearing the CPET mask, we performed maximal expiration and inspiration manoeuvres while closing the anterior mask valve with the palm of the hand, checking for any air leaks. The execution order of the CPETs was assigned in a randomised fashion to cover all possible combinations (figure 1). Symptom-limited incremental exercise tests were performed on an electronically braked cycle ergometer (Corival-Lode, The Netherlands) using a personalised ramp protocol (the same across the three CPETs in every subject) aimed at achieving peak exercise in ∼10 min [9]. All subjects had previously performed a CPET at our laboratory. During the execution of the tests, subjects were allowed to see their revolutions per minute (rpm), but all other variables, including time, workload, heart rate and gas exchange parameters, were obscured.

Ventilation rate ($\dot{V}_E$) and respiratory gases were measured breath by breath (Quark PFT Cosmed cart, Cosmed, Roma, Italy). Heart rate (HR), 12-lead ECG and haemoglobin saturation (S_{aO_2}) (measured using a finger oxymeter) were monitored continuously, while blood pressure (BP) was monitored with a cuff sphygmomanometer at rest and every 2 min during exercise. Anaerobic threshold was identified using a V-slope analysis of oxygen uptake ($\dot{V}_{O_2}$) and carbon dioxide production ($\dot{V}_{CO_2}$), and it was confirmed by specific trends of $\dot{V}_E$ *versus* $\dot{V}_{O_2}$ ($\dot{V}_E/\dot{V}_{O_2}$) and CO_2 ($\dot{V}_E/\dot{V}_{CO_2}$), and of end-tidal O_2 tension (P_{ETO_2}) and CO_2 tension (P_{ETCO_2}) [10, 11]. Peak exercise was the highest $\dot{V}_{O_2}$ value observed. Respiratory gas exchange ratio (RER) was calculated as $\dot{V}_{CO_2}/\dot{V}_{O_2}$. The $\dot{V}_{O_2}$/work relationship was calculated throughout the exercise test, while the $\dot{V}_E$ *versus* $\dot{V}_{CO_2}$ slope was calculated from the beginning of exercise up to the respiratory compensation point [12]. The y-intercept of the $\dot{V}_E$ *versus* $\dot{V}_{CO_2}$ slope relationship, a value related to dead space in $\dot{V}_E$, was calculated as previously reported [13]. All tests were analysed *a posteriori* by a CPET expert blinded to the steps of the study. Specifically, five steps of exercise were considered: rest, peak, 25%, 50% and 75% of maximal workload reached in the test with the sham mask. Consequently, for surgical and FFP2 mask tests, data for intermediate steps were reported at the workload (watts) corresponding to 25%, 50% and 75% of the maximal workload of the sham mask test. Accordingly, except at peak exercise, respiratory and gas exchange parameters were analysed in each patient at isowatts.

The Borg scale [14] was used to assess the subjects' degree of dyspnoea at rest, after 3 min, after 6 min and at peak exercise.

Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) were assessed immediately before and after the end of each exercise as a mean of three consecutive measures (MicroRPM respiratory muscle testing, Vyaire).

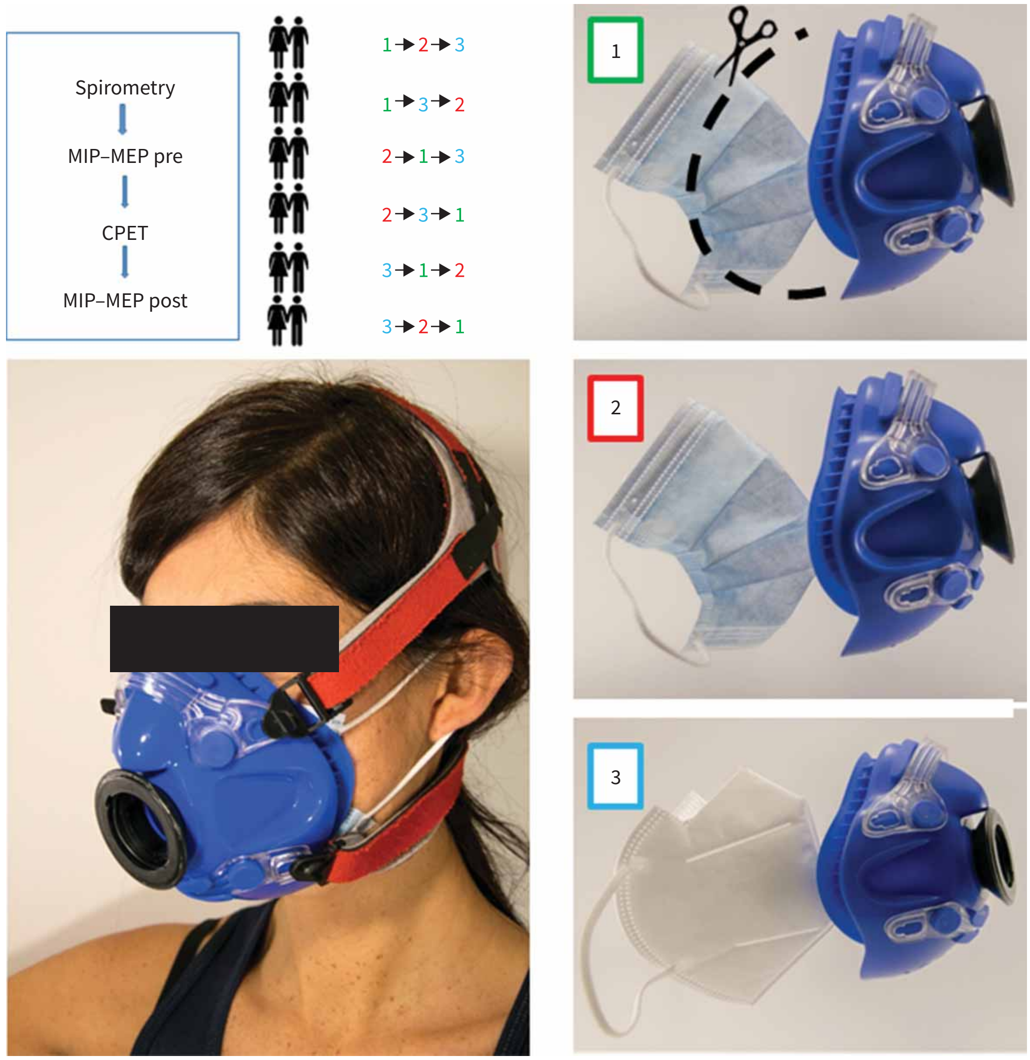

FIGURE 1 Schematic representation of the protocol procedures. The 12 subjects were randomised to perform the tests wearing the masks in a different sequence: 1) The mask was cut to mimic the "no mask" condition in a blinded manner; 2) surgical mask; 3) FFP2 mask. MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; CPET: cardiopulmonary exercise test.

Standard pulmonary function tests were also performed at rest with a standard mouthpiece and in all three study conditions through the CPET mask (Quark PFT Cosmed). Spirometry was performed according to current guidelines [15]. Predicted values are from Quanjer *et al*. [16].

All participants signed written informed consent and the protocol was approved by the local ethics committee (R1265/20-CCM 1344).

Statistical analysis

Data are reported as mean±SD or as n (%). CPET data were analysed breath by breath except for peak $\dot{V}_{O_2}$ analysis (averaged over 20 s).

Differences between the three protocol conditions were analysed by repeated measures ANOVA. Trends were assessed by ANCOVA.

For each subject, we calculated the workload corresponding to 25%, 50% and 75% of the maximal load reached during the test performed without wearing a mask, and we compared the corresponding $\dot{V}_E$, $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ values between the CPETs in the three conditions at the same workloads. Analyses were carried

TABLE 1 Rest values at cardiopulmonary exercise test in the three protocol conditions

	No mask	Surgical mask	FFP2	p-value for trend	p-value ANOVA	No mask *vs* surgical mask	No mask *vs* FFP2	FFP2 *vs* surgical mask
SBP mmHg	113±14	116±10	114±14	0.809	0.801	1.000	1.000	1.000
DBP mmHg	70±8	70±8	72±9	0.449	0.741	1.000	1.000	1.000
HR bpm	73±19	77±13	75±18	0.755	0.670	1.000	1.000	1.000
$\dot{V}_{O_2}$ mL·min^{-1}	355±56	321±78	276±90	0.014	0.023	0.223	0.023	0.373
$\dot{V}_{CO_2}$ mmHg	299±52	256±72	220±68	0.005	0.018	0.290	0.010	0.804
$\dot{V}_E$ L·min^{-1}	12.9±1.6	10.4±1.8	9.3±2.4	<0.001	0.001	0.001	0.002	0.452
RR breaths·min^{-1}	18.5±3.2	15.2±3.1	14.3±3.6	0.004	0.008	0.006	0.008	0.706
V_T L	0.71±0.13	0.71±0.18	0.69±0.24	0.756	0.918	1.000	1.000	1.000
P_{ETO_2} mmHg	109±6	107±6	107±8	0.069	0.000	0.002	0.003	1.000
P_{ETCO_2} mmHg	35.60±5.74	36.50±4.88	36.85±6.14	0.223	0.053	0.132	0.121	1.000
S_{aO_2} %	97.2±0.942	96.8±0.8	96.9±1.2	0.548	0.678	1.000	1.000	1.000
t_I s	1.14±0.38	1.30±0.43	1.41±0.59	0.002	0.000	0.003	0.000	0.029
t_E s	1.41±0.68	1.52±0.64	1.78±1.02	0.012	0.038	0.585	0.031	0.157
t_{Total} s	2.55±1.04	2.82±1.04	3.19±1.38	0.003	0.002	0.085	0.001	0.043
t_I/t_{Total}	0.45±0.04	0.47±0.05	0.46±0.08	0.688	0.082	0.080	1.000	0.959
MIP cmH_2O	81.83±18.20	83.28±16.63	85.17±16.18	0.630	0.223	1.000	0.281	1.000
MEP cmH_2O	82.56±26.26	83.00±23.83	80.75±24.17	0.857	0.915	1.000	1.000	1.000
FEV_1 L·s^{-1}	3.94±0.91	3.23±0.81	2.94±0.89	0.008	0.000	0.000	0.000	0.156
FVC L	4.70±1.21	3.77±1.02	3.52±1.21	0.017	0.000	0.000	0.000	0.286

Data are presented as mean±SD. SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; $\dot{V}_{O_2}$: oxygen uptake; $\dot{V}_{CO_2}$: carbon dioxide production; $\dot{V}_E$: minute ventilation; RR: respiratory rate; V_T: tidal volume; P_{ETO_2}: end-tidal oxygen tension; P_{ETCO_2}: end-tidal carbon dioxide tension; S_{aO_2}: arterial oxygen saturation; t_I: inspiratory time; t_E: expiratory time; t_{Total}: inspiratory+expiratory time; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity.

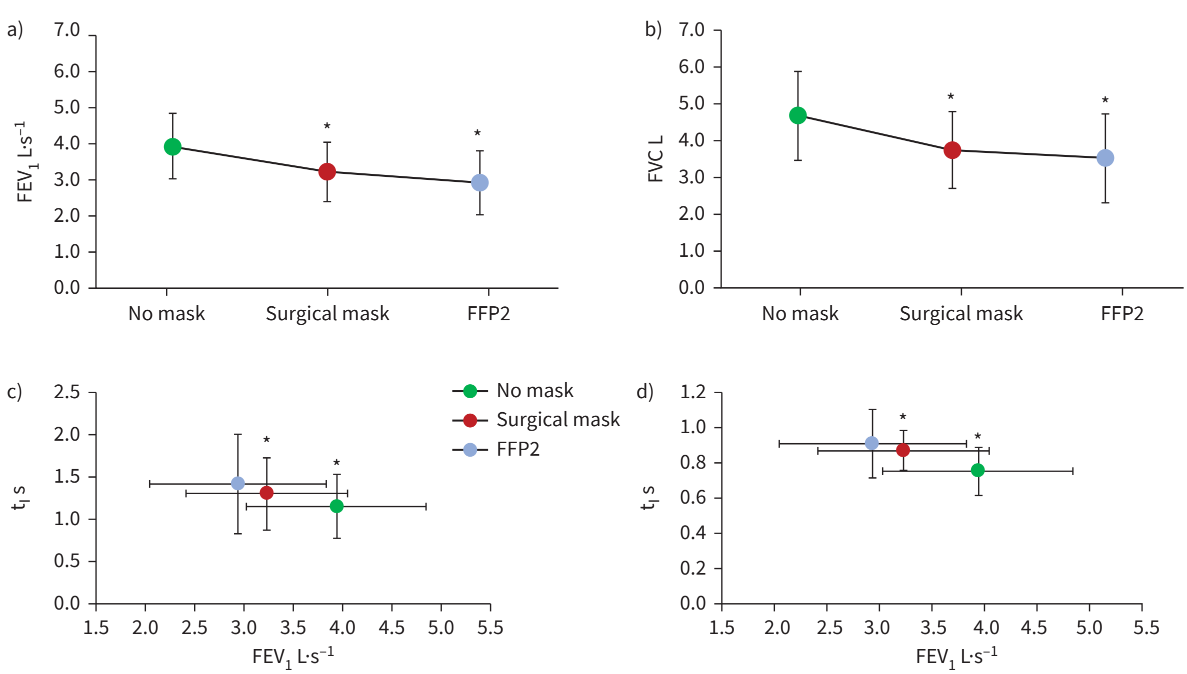

FIGURE 2 a) Forced expiratory volume in 1 s (FEV_1) and b) forced vital capacity (FVC) results obtained with no mask (green), with surgical mask (red) and with FFP2 (blue) at standard spirometry. c, d) Relationship between FEV_1 and inspiratory time (t_I) with sham mask (green), with surgical mask (red) and with FFP2 (blue) at rest (c) and at peak exercise (d). *: p<0.05 *vs* sham mask.

TABLE 2 Values at anaerobic threshold and at peak exercise, obtained at cardiopulmonary exercise test in the three protocol conditions

	No mask	Surgical mask	FFP2	p-value for trend	p-value ANOVA	No mask *vs* surgical mask	No mask *vs* FFP2	FFP2 *vs* surgical mask
Anaerobic threshold								
$\dot{V}_{O_2}$ mL·min^{-1}	1346±345	1163±329	1204±403	0.341	0.020	0.013	0.113	1.000
$\dot{V}_{O_2}$ AT mL·min^{-1}·kg^{-1}	19.18±4.77	16.41±4.00	17.02±5.34	0.273	0.028	0.019	0.110	1.000
HR beats·min^{-1}	125±22	120±16	119±12	0.402	0.531	0.805	0.803	1.000
$\dot{V}_E$ L·min^{-1}	39.5±8.5	31.4±7.0	31.1±9.0	0.016	0.007	0.006	0.007	1.000
$\dot{V}_{CO_2}$ L·min^{-1}	1288±361	1053±291	1086±382	0.164	0.007	0.009	0.014	1.000
Workload W	110±34	101±29	101±32	0.494	0.173	0.341	0.192	1.000
Peak exercise								
SBP mmHg	164±27	173±30	155±19	0.397	0.053	0.343	0.287	0.039
DBP mmHg	88±9	89±8	86±8	0.627	0.716	1.000	1.000	1.000
HR beats·min^{-1}	170±14	168±16	167±16.1	0.621	0.349	0.613	0.468	1.000
$\dot{V}_{O_2}$ mL·min^{-1}	2190±586	1928±498	1994±643	0.410	0.006	0.003	0.080	1.000
$\dot{V}_{O_2}$ peak mL·min^{-1}·kg^{-1}	30.96±6.71	27.50±6.92	28.24±8.79	0.380	0.001	0.001	0.093	1.000
$\dot{V}_{O_2}$ % pred	102±23	91±20	93±31	0.389	0.020	0.017	0.111	1.000
$\dot{V}_{CO_2}$ mL·min^{-1}	2578±763	2217±691	2268±794	0.317	0.017	0.012	0.028	1.000
$\dot{V}_E$ L·min^{-1}	92.3±26.0	76.2±21.6	71.6±21.2	0.034	0.003	0.002	0.007	0.946
RR breaths·min^{-1}	41.5±8.0	37.7±5.5	37.1±4.5	0.089	0.041	0.028	0.197	1.000
RER	1.16±0.07	1.15±0.08	1.15±0.08	0.668	0.665	1.000	1.000	1.000
V_T L·min^{-1}	2.28±0.72	2.05±0.60	1.96±0.65	0.235	0.001	0.044	0.001	0.660
S_{aO_2} %	97.3±1.2	96.5±1.2	95.1±3.1	0.017	0.132	0.362	0.252	0.520
P_{ETO_2} mmHg	118±3.0	115±3	114±3	0.021	0.013	0.053	0.020	1.000
P_{ETCO_2} mmHg	33.04±4.28	35.13±3.09	36.26±3.94	0.043	0.012	0.022	0.011	0.455
Workload watts	194±57	187±52	184±54	0.656	0.002	0.120	0.001	1.000
t_I s	0.75±0.14	0.87±0.11	0.91±0.20	0.010	0.004	0.009	0.017	0.369
t_E s	0.87±0.24	0.89±0.24	0.89±0.28	0.871	0.975	0.822	0.881	0.957
t_{Total} s	1.48±0.43	1.62±0.39	1.64±0.41	0.343	0.476	0.274	0.163	0.735
t_I/t_{Total}	0.46±0.05	0.50±0.08	0.53±0.09	0.170	0.315	0.329	0.267	0.899
MIP post cmH$_2$O	80.64±26.34	82.47±23.00	84.86±24.69	0.674	0.457	1.000	0.927	1.000
MEP post cmH$_2$O	75.94±18.19	80.97±29.07	77.97±24.34	0.837	0.614	0.958	1.000	1.000

Data are presented as mean±SD. AT: anaerobic threshold; $\dot{V}_{O_2}$: oxygen uptake; HR: heart rate; $\dot{V}_E$: minute ventilation; $\dot{V}_{CO_2}$: carbon dioxide production; SBP: systolic blood pressure; DBP: diastolic blood pressure; RR: respiratory rate; RER: respiratory exchange ratio; V_T: tidal volume; S_{aO_2}: arterial oxygen saturation; P_{ETO_2}: end-tidal oxygen tension; P_{ETCO_2}: end-tidal carbon dioxide tension; t_I: inspiratory time; t_E: expiratory time; t_{Total}: inspiratory+expiratory time; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure.

out with the SAS statistical package v. 9.4 (SAS Institute Inc., Cary, NC, USA) and all tests were two-sided. $p<0.05$ was considered statistically significant.

Results

All subjects (40.8±12.4 years; six male, six female) completed the study protocol with no adverse events.

Data at rest

Spirometry performed with a mouthpiece showed a forced expiratory volume in 1 s (FEV_1) of 108±19% predicted and forced vital capacity (FVC) of 104±15% predicted. Spirometry, cardiorespiratory parameters and inspiratory/expiratory pressures measured at rest in the three experimental conditions are reported in table 1. Spirometry indicated a progressive reduction of FEV_1 and FVC from no mask to surgical mask to FFP2 (figure 2a, b). In parallel, inspiratory time (t_I) and expiratory time (t_E) increased both at rest and at peak exercise (figure 2c, d). Resting tidal volume (V_T) was unaffected by the type of mask; MIP and MEP were also unaffected (table 1). However, from no mask to surgical mask to FFP2, $\dot{V}_E$ was progressively lower owing to a reduction in respiratory rate (RR) and lower $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and P_{ETO_2}.

Exercise data

Exercise parameters are shown in table 2. In all conditions, a maximal or nearly maximal effort was reached, as confirmed by RER>1.05 in all cases. At peak exercise, all subjects had a progressively higher Borg scale value from no mask to surgical mask to FFP2 mask (figure 3), suggesting greater dyspnoea when wearing surgical and FFP2 masks. In parallel, a reduction of peak exercise workload (watts) was

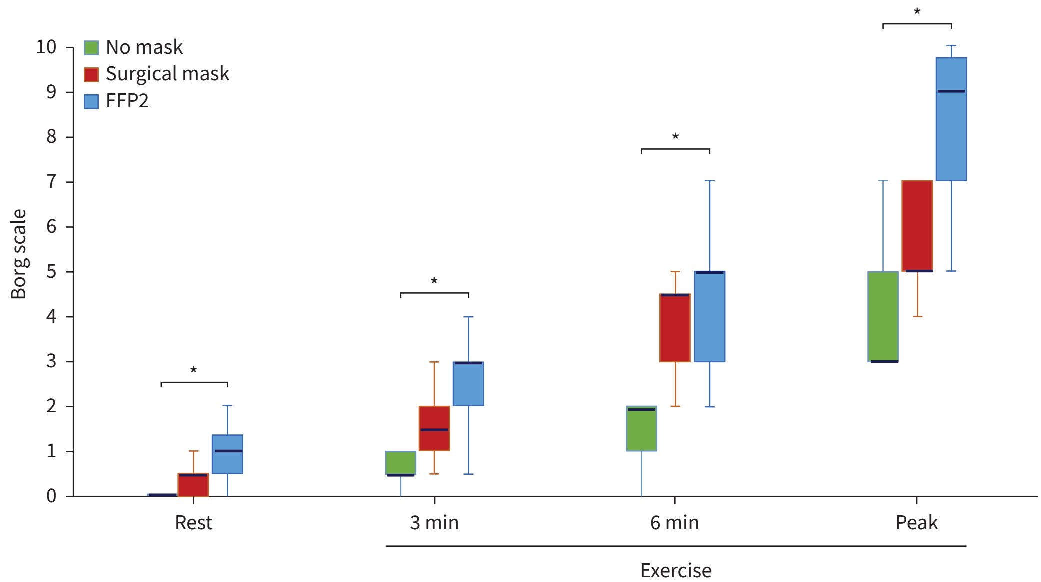

FIGURE 3 Box plot of Borg scale values declared by the subjects before the effort (rest), after 3 min of exercise, after 6 min and at peak exercise with sham mask (green), surgical mask (red) and FFP2 mask (blue). *: $p<0.05$ between groups.

observed when wearing an FFP2 mask, while HR and BP values did not differ. The anaerobic threshold was identified in all subjects and in all study conditions. At the anaerobic threshold (table 2), $\dot{V}_{O_2}$ was reduced when wearing a mask without a significant reduction of workload, and with unchanged HR and S_{aO_2} values. From no mask to surgical mask to FFP2 mask, the $\dot{V}_{O_2}$/work (9.7±1.0, 9.4±0.9, 9.7±1.3, respectively) and $\dot{V}_E/\dot{V}_{CO_2}$ slope relationship (27.5±3.7, 28.1±3.7, 26.6±5.0, respectively) did not show any significant change (p=NS). Similarly, the y-intercept [13] on the $\dot{V}_E/\dot{V}_{CO_2}$ relationship did not significantly change (4.9±2.1 L, 3.3±1.4 L, 3.5±1.4 L for no mask, surgical mask and FFP2 mask, respectively; p=NS). At peak exercise (table 2), $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, $\dot{V}_E$, RR and V_T were lower while wearing different types of mask. Figure 4 shows the behaviour of $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and $\dot{V}_E$ through exercise. In parallel to the $\dot{V}_E$ changes during exercise, S_{aO_2} (as a trend), P_{ETO_2} and P_{ETCO_2} varied. Specifically, despite a significant trend in oxygen saturation reduction, no significant inter-group difference was observed. This was paralleled by increased and reduced P_{ETCO_2} and P_{ETO_2}, respectively, from no mask to surgical mask to FFP2 mask. t_I was significantly longer during exercise wearing the two types of masks then in the standard condition. MIP and MEP, collected immediately after the end of exercise, did not differ across the groups.

Discussion

In this experimental study on healthy subjects, we demonstrated how the use of protective masks (both surgical and FFP2 masks) is associated with a significant worsening of FEV_1 and FVC and of cardiorespiratory parameters both at rest and at peak exercise. At rest, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and $\dot{V}_E$ decreased, the latter due to a RR reduction which was paralleled by an increase in t_I. At peak exercise, an increase in dyspnoea and a reduction in peak $\dot{V}_{O_2}$ measured during a standardised maximal effort at CPET were observed. The effect was predominantly driven by a reduction in $\dot{V}_E$. Our data suggest that $\dot{V}_E$ is reduced owing to a decrease in both RR and V_T along the three conditions, with a parallel increase in t_I.

During respiratory virus outbreaks, such as the current COVID-19 pandemic, protective masks, together with social distancing, have proven to be essential devices for the containing infection, both in everyday life and in hospitals, where health workers most often use FFP2 masks [8, 17, 18]. Breathing discomfort in members of the general population, who are not accustomed to daily mask use, has been frequently reported by word of mouth and social networks [19], even becoming a potentially dangerous political statement for some [20]. Several peer-reviewed publications have demonstrated the minimal clinical impact of wearing protective masks, both in healthy subjects and in patients with respiratory diseases (*e.g.* chronic obstructive pulmonary disease), although in the absence of accurate cardiorespiratory parameters [21–23]. Regardless, in the public opinion, the long-term practicability and tolerability of protective masks are still

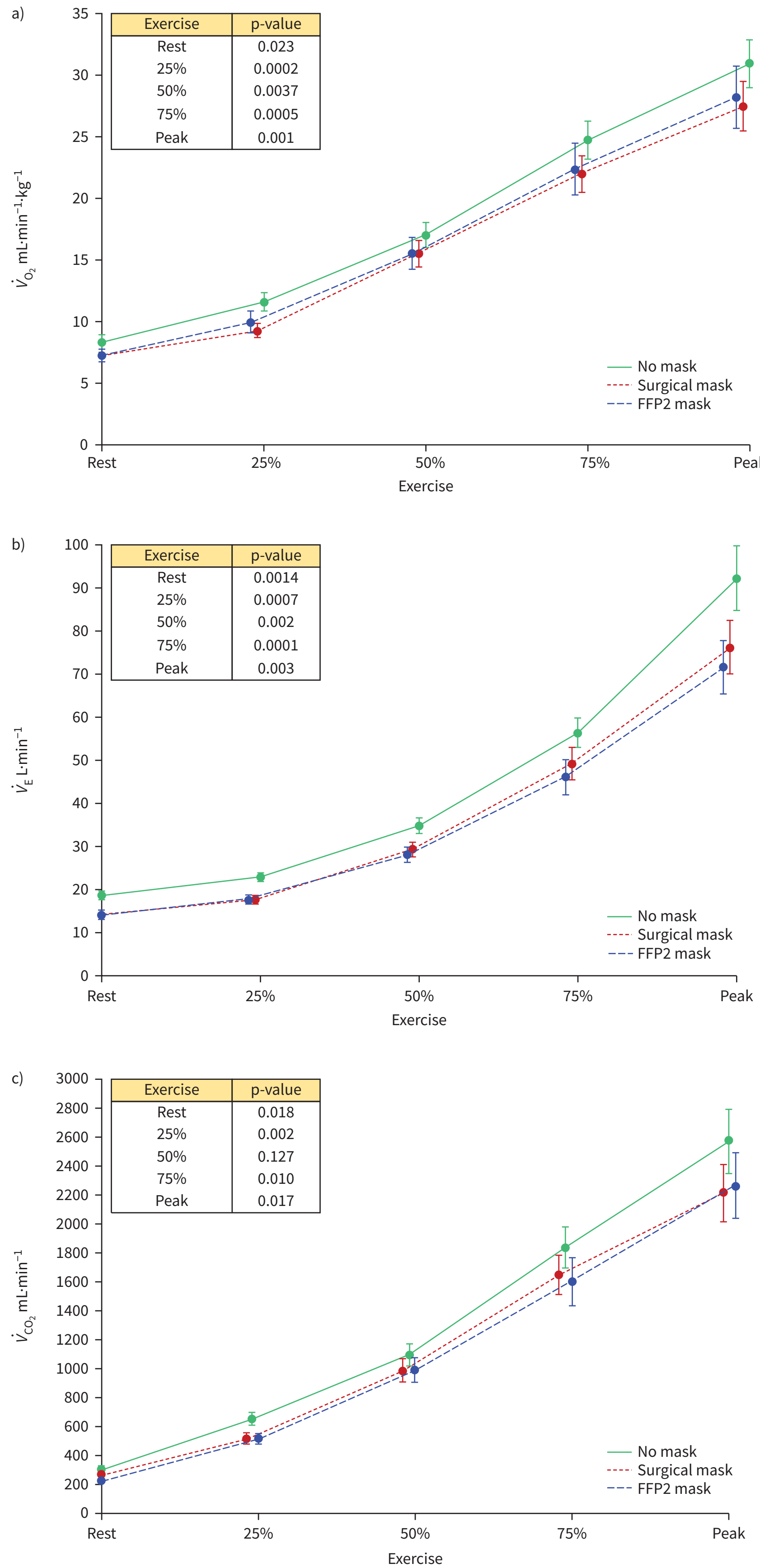
a)
Exercise | p-value
Rest | 0.023
25% | 0.0002
50% | 0.0037
75% | 0.0005
Peak | 0.001
$\dot{V}_{O_2}$ mL·min^{-1}·kg^{-1}
0 5 10 15 20 25 30 35
Rest 25% 50% 75% Peak
Exercise
No mask
Surgical mask
FFP2 mask
b)
Exercise | p-value
Rest | 0.0014
25% | 0.0007
50% | 0.002
75% | 0.0001
Peak | 0.003
$\dot{V}_E$ L·min^{-1}
0 10 20 30 40 50 60 70 80 90 100
Rest 25% 50% 75% Peak
Exercise
No mask
Surgical mask
FFP2 mask
c)
Exercise | p-value
Rest | 0.018
25% | 0.002
50% | 0.127
75% | 0.010
Peak | 0.017
$\dot{V}_{CO_2}$ mL·min^{-1}
0 200 400 600 800 1000 1200 1400 1600 1800 2000 2200 2400 2600 2800 3000
Rest 25% 50% 75% Peak
Exercise
No mask
Surgical mask
FFP2 mask

FIGURE 4 Trend of cardiopulmonary variables during ramp exercise compared to the percentage of exercise performed. The exercise percentage was calculated with respect to the peak workload reached by each subject during the basal test (with sham mask). 25% workload: 48±14 W; 50% workload: 98±28 W; 75% workload: 145±42 W. Peak workload for sham mask: 194±57 W; surgical mask: 187±52 W; FFP2 mask: 184±54 W ($p<0.05$ among the three conditions). a) Oxygen uptake ($\dot{V}_{O_2}$). b) Minute ventilation ($\dot{V}_E$). c) CO_2 production ($\dot{V}_{CO_2}$).

questioned, and, in spite of their mandatory use, they are frequently worn below the nose and mouth, rendering them useless.

In the present study, we selected 12 healthy subjects who were already familiar with CPET in our laboratory. The subjects were representative of the general population; indeed, their observed peak exercise $\dot{V}_{O_2}$ with no mask was 101% of the predicted value. Masks slightly affected the breathing pattern even at rest, as indicated by the light breathing discomfort experienced by some subjects (figure 2). A similar observation was made in two previous reports [24, 25]. We performed spirometry with a commercial CPET mask that had been demonstrated as adequate in previous studies [26, 27]. In the present study, spirometry with different masks showed a reduction in FEV_1 and FVC that was paralleled by a longer t_I [25]. This datum is consistent with an increased resistance to airflow during inspiration [25, 28]. Of note, some voluntary hyperventilation at rest was present in all conditions as shown by the relatively high RR and P_{ETO_2} values. However, a progressive reduction of $\dot{V}_E$, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and P_{ETO_2} was observed from no mask to surgical mask to FFP2 mask, revealing an involuntary adjustment of $\dot{V}_E$ to the variable flow resistance. Given the rapidity of this ventilatory adaptation (the masks were worn just before starting the CPET), these changes could be explained by a rapid adaptation of the chemoreceptor to tolerate higher arterial CO_2 and lower O_2 values. To summarise the data at rest: 1) subjects spontaneously adapted to the increased airflow resistance by reducing $\dot{V}_E$, P_{ETO_2}, $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ with an unchanged RER, suggesting rapid chemoreceptor response; 2) although RER was in the normal range for resting condition and sufficient resting time was allowed, some voluntary hyperventilation was present in all conditions as shown by RR and P_{ETO_2}; 3) the involuntarily altered breathing pattern was hampered by increased airflow resistance. Indeed, subjects responded to this resistance by self-adjusting t_I and t_E, likely to minimise their respiratory effort. In other words, given the increased cost of breathing while wearing protective masks, healthy subjects trigger an innate mechanism by maintaining their $\dot{V}_E$ to a lower set point.

Protective masks did not affect gas exchange kinetics pattern, given that the $\dot{V}_E/\dot{V}_{CO_2}$ slope and $\dot{V}_{O_2}$/work relationships were unchanged. However, a slight anticipation of the threshold metabolism was observed with protective masks. It must be underlined that we, as well as others [24, 25, 28], studied the effects on respiration of various types of surgical masks when worn under the standard CPET silicon mask both during spirometry and CPET. This was necessary to allow respiratory gas measurements. It is possible, but unknown, that the silicone mask *per se* influenced the respiratory function, albeit minimally.

The reported index of dyspnoea at peak exercise showed a clear worsening with mask wearing (figure 2). At peak exercise, with the different types of masks $\dot{V}_E$ showed a greater decrease than $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$, a datum accompanied by an increased t_I and again suggestive of increased resistance to airflow. Of note, true ventilatory limitation, as assessed by applying the standards for exercise limitation during CPET, was not observed [29]. Indeed, peak exercise breathing reserve, as measured by ($FEV_1 \times 35$)–observed $\dot{V}_E$ [30] was always >20 $L \cdot min^{-1}$, being 45.5±25.9 $L \cdot min^{-1}$ with no mask, 61.6±19.5 $L \cdot min^{-1}$ with a surgical mask and 66.1±22.9 $L \cdot min^{-1}$ with an FFP2 mask. Increased resistance of the masks was also shown by the spirometry data. The reduced $\dot{V}_E$ at peak exercise could be due to an increased airway opening resistance reducing ventilatory capacity, which would then lead to dyspnoea and reduced performance. The reduction of S_{aO_2}, $\dot{V}_E$ and V_T and the increase in t_I altogether support a $\dot{V}_E$-mediated effect of masks on exercise performance, which was clearly reduced as shown by the lower peak $\dot{V}_{O_2}$ and workload achieved. We did not observe signs of respiratory fatigue, as shown by an unchanged peak exercise MIP and MEP, or ventilatory limitation to exercise. Unfortunately, flow/volume curves during exercise were not performed to avoid any possible interference of these respiratory manoeuvres with peak exercise performance. Because our results were obtained in a population of middle-aged healthy subjects, more studies are needed to assess the cardiorespiratory effects of various protective masks on exercise performance in older subjects or in patients with proven exercise limitation. Finally, we analysed the effects of masks using a maximal workload incremental protocol aimed at achieving peak exercise in ~10 min performed in a temperature and humidity controlled laboratory located at sea level. This is the gold standard for maximal exercise performance evaluation [12, 31]. However, efforts performed with different exercise protocols (*e.g.* as for during daily life activities [32]), or in different ambient conditions (*i.e.* temperature, humidity or at altitude) may produce different results. Indeed, in these conditions the effects of protective masks are unknown.

In conclusion, the use of protective masks in healthy middle-aged subjects 1) slightly influences cardiorespiratory variables at rest and during exercise, and 2) reduces peak $\dot{V}_{O_2}$ by ∼10% due to an increase in airflow resistance, although $\dot{V}_E$ limitation was far from being reached. Accordingly, the general population should be aware that the use of protective masks in healthy subjects is associated with modest respiratory discomfort but their use is safe even during maximal exercise, albeit with a slight reduction in performance.

All raw data collected for the study will be made available to others after request. Data will be stored in anonymised form at www.zenodo.org when the paper is published.

Conflict of interest: M. Mapelli has nothing to disclose. E. Salvioni has nothing to disclose. F. De Martino has nothing to disclose. I. Mattavelli has nothing to disclose. P. Gugliandolo has nothing to disclose. C. Vignati has nothing to disclose. S. Farina has nothing to disclose. P. Palermo has nothing to disclose. J. Campodonico has nothing to disclose. R. Maragna has nothing to disclose. G. Lo Russo has nothing to disclose. A. Bonomi has nothing to disclose. S. Sciomer has nothing to disclose. P. Agostoni reports non-financial support from Menarini, Novartis and Boehringer, grants from Daiichi Sankyo and Bayer, and grants and non-financial support from Actelion, outside the submitted work.

Support statement: This work was supported by the Italian Ministry of Health. Funding information for this article has been deposited with the Crossref Funder Registry.

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