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A comparison of pulmonary function pre and post mild SARS-CoV-2 infection among healthy adults

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Abstract

Background SARS-CoV-2 infection frequently involves the respiratory system and may impact on pulmonary function tests (PFT) of recovered individuals. Studies which compare post-COVID-19 PFT to pre-illness measurements are scarce. The primary objective of this study was to assess the effect of COVID-19 on PFT soon after infection.

Methods In this prospective observational study, PFT were measured early following recovery from COVID-19 among healthy military aircrew. Spirometry values were compared to pre-COVID-19 measurements, and abnormality rates of lung volumes and diffusion capacity for carbon monoxide (DLCO) were assessed.

Results The study included 252 aviators, 97.6% males, mean age 34.9-years, following recovery from SARS-CoV-2 infection. Participants manifested mild symptoms (79.4%) or were asymptomatic (20.6%). Post-COVID-19 spirometry results 10.79 ± 5.67 days following infection were compared to measurements performed 41.3 ± 28.59 months earlier. Pre- and post-COVID-19 results were comparable, with similar minimal abnormalities rates (2% and 4.4%, respectively). In addition, there were no restrictive abnormalities following infection, and just 7.7% of individuals had a marginally low DLCO of 70–80% of predicted.

Conclusion Among vaccinated, healthy adults, mild COVID-19 had no significant impact on PFT early post-infection. The data suggest that systematic PFT testing might not be necessary for asymptomatic healthy individuals who recovered from mild COVID-19.

Keywords COVID-19, SARS-CoV-2, Pulmonary function test, Aviation medicine, Reduced oxygen breathing device, Coronavirus disease

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Background

COVID-19 illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can range from asymptomatic infection to critical disease and a fatal outcome [1, 2]. The disease mainly affects the lungs and the respiratory tract, sometimes leading to viral pneumonia and respiratory failure [2, 3]. Subjects who recover from COVID-19, especially from critical or severe disease, may remain symptomatic and suffer from abnormal lung functions for a prolonged time period [4–7].

Several studies have demonstrated that low pulmonary functions post-COVID-19, as well as radiographic abnormalities, tend to improve over time [5, 8, 9]. However, data comparing post-COVID-19 physiological measurements to pre-infection values is scarce. In particular, there is almost no data that assesses the changes in pulmonary function tests (PFT) resulting from SARS-CoV-2 infection among previously healthy individuals since PFT are usually not performed in such populations. While it has been recommended to measure PFT following severe COVID-19, it is unknown if such testing is required routinely in every case [10–12]. Moreover, in addition to sex and age, lung functions are impacted by lifestyle and comorbidities [13], all of which should be taken into account when trying to assess the sole effect of COVID-19.

Aeromedical standards require intact cardiopulmonary functions to cope with the physiological strains associated with aviation [14]. Many aeromedical authorities, including the Israeli Air Force (IAF), require PFT measurements as part of routine medical "fitness-to-fly" assessments. In addition, the IAF Aeromedical Center (AMC) mandated PFT as part of the medical evaluation to return to flying duties following COVID-19. This allowed us the unique opportunity to compare early post-COVID-19 PFT with pre-COVID-19 measurements among previously healthy military aircrew.

Methods

Study design and participants

This is a prospective observational study aimed to compare PFT in participants before, and after SARS-CoV-2 infection. Results are reported according to the STROBE statement.

Study participants included all active aircrew in the IAF who recovered from SARS-CoV-2 infection between December 1st, 2021, and February 28th, 2022. The diagnosis of SARS-CoV-2 infection was ascertained by either a positive real-time reverse-transcriptase polymerase chain reaction (RT-PCR) or a positive COVID-19 lateral flow assay from nasopharyngeal swabs. Testing for SARS-CoV-2 infection was performed in either symptomatic aircrew or post-exposure.

All IAF aircrew undergo annual routine health checkup in the AMC, which include examination by a flight surgeon, ophthalmology, ear, nose, throat (ENT), and cardiopulmonary assessment. Spirometry is performed at five years intervals, or earlier if clinically indicated. Aviators with missing pre-COVID-19 spirometry data were excluded.

National vaccination with the BNT162b2 (Pfizer/BioNTech) mRNA vaccine began in December 2020, and included a 2-dose schedule administered 21 days apart. A third vaccine dose (booster) was available and recommended from July 2021, for subjects who had received the previous vaccination dose at least 6-months earlier.

Back-to-flight protocol

COVID-19 recovered aviators underwent a systematic routine medical protocol which included a flight surgeon assessment and ancillary tests to determine their competence to return to operational flight duties. The protocol is categorized into two parts, a limited version required by all aircrew and an extended version required by aviators of high-performance aircrafts (jet fighters) who intend to return to flying duties less than 30-days after diagnosis, or according to the flight surgeon's discretion. In addition to a clinical assessment to validate resolution of significant symptoms, chest X-rays and spirometry were performed by all aviators ("limited protocol"). The "extended protocol" also included measurements of lung volumes and diffusion capacity and a reduced oxygen breathing device (ROBD) assessment.

All pulmonary function tests (PFT) were performed and interpreted according to ATS/ERS guidelines [13]. Spirometry tests were performed in the IAF AMC, both before COVID-19, as part of routine aeromedical assessments, and after recovery from COVID-19. Lung volume measurements by plethysmography and diffusion capacity for carbon monoxide were measured at the PFT laboratory of the Pulmonary Institute of "Chaim Sheba" Medical Center, a large tertiary medical center in Central Israel.

ROBD assessment

ROBD is routinely performed in the AMC as part of physiological training to familiarize aircrew with hypoxia symptoms [15]. This assessment was performed using Environics ROBD (Tolland, CT, USA). Subjects were exposed to gradually worsening hypoxic gas mixtures while continuously monitored by pulse oximetry (Palm-SAT 2500, Nonin, Plymouth, MN, USA). Subjects performed a simulated flight task while sequentially exposed to 2-min intervals of 11.5%, 10.5%, 9.5%, and 7.5% oxygen mixtures and then provided with 100% oxygen through an aircrew mask. The tests were terminated early if the

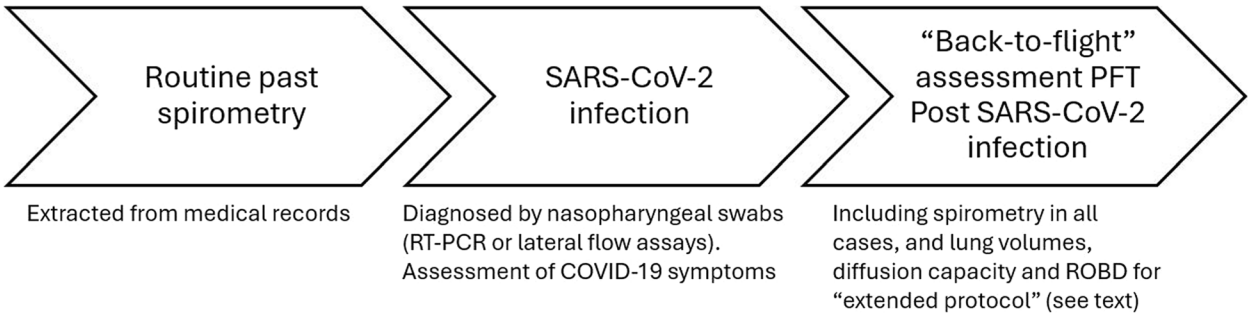

Fig. 1 Study design timeline. All subjects were assessed after SARS-CoV-2 infection using the "back-to-flight" protocols. Symptoms were recorded for the time of illness and re-assessed during the post-illness assessments. Results of spirometry performed as part of routine monitoring of military aviators were retrospectively retrieved from medical records

subjects reported intolerable symptoms or when oxygen saturation dropped to ≤ 50%. The tests were also considered positive ("abnormal result") if saturation dropped to ≤ 60% in less than 10 s following hypoxic exposure or if saturation failed to improve to ≥ 99% within 50 s after providing 100% oxygen.

Variables and outcomes

Past clinical and PFT data (before contracting SARS-CoV-2) were extracted from the participants' medical records. Post-infection data was collected prospectively as part of the AMC "back-to-flight" protocol. The day of the first positive swab for SARS-CoV-2 served as day 0 of illness for the study.

COVID-19-related variables included signs and symptoms, medications, diagnostic testing, and results of ancillary tests. COVID-19 severity was ranked according to National Institute of Health (NIH) guidelines as asymptomatic, mild, moderate (with clinical or radiographic evidence of lower respiratory tract disease and oxygen saturation ≥ 94% while breathing room air), severe (saturation < 94%, respiratory rate > 30/min, infiltrates over 50% of lungs volume, or PaO_2/FiO_2 ratio < 300), and critical (individuals who have respiratory failure requiring invasive or non-invasive ventilation, septic shock, or with multiorgan dysfunction) [16].

PFT variables included: forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), FEV1/FVC ratio, total lung capacity (TLC), residual volume (RV), diffusion capacity for carbon monoxide (DLCO). Measured values were compared to the Global Lung Function Initiative (GLI) reference equations to define the percent of predicted values (%pred) [17–19].

The primary outcome was a change in spirometry variables between pre- and post-COVID-19 measurements (FEV1, FVC, and FEV1/FVC ratio). Additional outcomes included post-COVID-19 lung volumes and DLCO measurements, and ROBD results (see Fig. 1 for study timeline flowchart).

We assessed PFT abnormalities rates by two methods, one based on %pred and second based on lower limits of normal (LLN). By %pred, PFT values below 80%pred were considered abnormal, an FEV1/FVC ratio < 0.7 was considered indicative of an obstructive pattern, while a TLC < 80%pred was used to diagnose a restrictive pattern. By LLN criteria, we considered values below the LLN as abnormal.

Sample size calculation

We calculated that to achieve a power of 80% with an alpha error rate of 5%, and assuming that 5% of cases have abnormal FVC%pred post-COVID-19 [5], a sample size of 152 subjects will be required [5].

Statistical analysis

Descriptive statistics are expressed as means with standard deviations or as absolute counts complemented by proportions. A comparative analysis of the variables, investigating the alterations before and after the onset of the SARS-CoV-2 infection, was conducted. For continuous variables, we utilized paired t-tests, whereas for categorical variables, we applied either the Fisher's exact test or the chi-square test. To assess the change between paired categorical variables, we used McNemar's test.

Data were analyzed with SPSS Version 25 (IBM Corporation, Armonk, NY, USA). A two-tailed p-value < 0.05 was considered statistically significant in all tests.

Ethical considerations

This study was approved by the Helsinki Committee and Institutional Review Board of the IDF Medical Corps (application no. 2155–2020). Informed consent was not required by the Board since all medical evaluations were performed as part of routine management and de-identified data were collected.

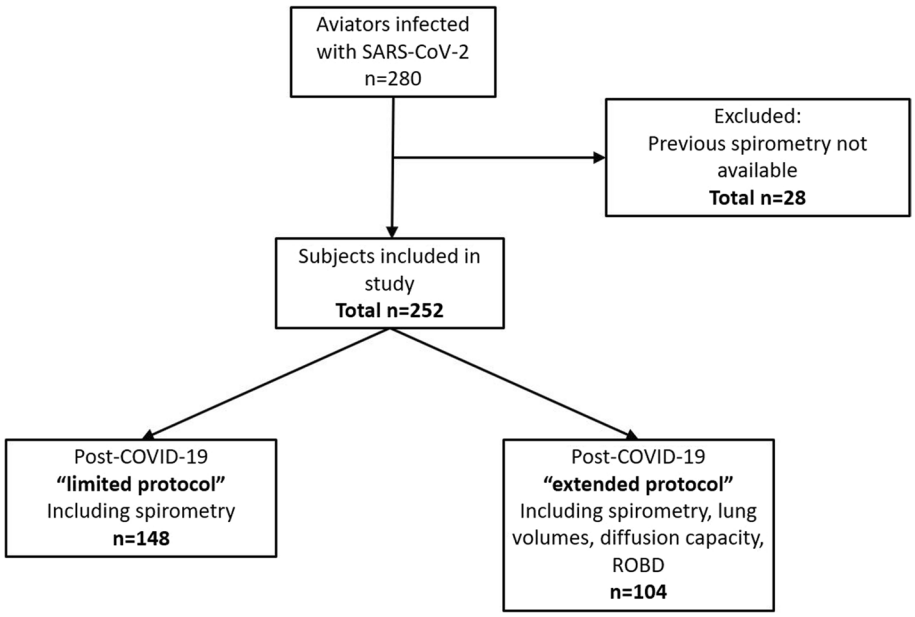

Fig. 2 Flowchart of study participants. A total of 280 military aviators contracted SARS-CoV-2 infection during the study period. Twenty-eight were excluded due to missing pre-infection spirometry results. All 252 participants underwent post-COVID-19 spirometry ("limited protocol"), while 104 underwent the "extended" back-to-flight protocol which also included lung volumes and DLCO measurements as well as ROBD testing

Results

A total of 280 aviators were diagnosed with SARS-CoV-2 infection during the study period. Twenty-eight aviators were excluded since pre-COVID-19 spirometry was not available (Fig. 2). From the remaining 252 aviators, the vast majority were males ($n=246$, 97.6%), mean age was 34.9 ± 9.89 years (range 20 to 63). Over half were high-performance aviators (136, 53.9%) (Table 1). Aircrew who underwent the "extended back-to-flight" protocol were on average younger than those who only required limited testing ($p=0.025$).

Two aviators (0.7%) were re-infected after a previous episode of SARS-CoV-2 infection. All participants have received three doses of the Pfizer-BioNTech mRNA vaccine (BNT162b2), except for the 2-reinfected subjects who received 2 doses.

Most subjects reported mild COVID-19 ($n=200$, 79.4%), and the rest were asymptomatic ($n=52$, 20.6%). Eighty subjects (31.7%) were able to state symptoms duration and reported an average duration of 2.21 ± 1.42 days. The complete profile of symptoms is presented in Fig. 3. The most frequent symptoms were runny nose

Table 1 Baseline Characteristics at the time of post-COVID-19 medical evaluation

	All cohort ($n=252$)	Extended protocol ($n=104$)	Limited Protocol ($n=148$)	*p*-value*
Age, years, mean ± SD	34.9 ± 9.7	33.6 ± 9.1	36.4 ± 10.2	0.025
Heart rate, bpm, mean ± SD	63.9 ± 11.1	63.6 ± 11.8	64.1 ± 10.3	0.728
Systolic BP, mmHg, mean ± SD	121.3 ± 12.3	119.9 ± 12.1	122.9 ± 12.4	0.063
Diastolic BP, mmHg, mean ± SD	74.4 ± 8	73.6 ± 7.9	75.2 ± 8.2	0.132
O_2 saturation, %, mean ± SD	98.4 ± 0.7	98.4 ± 0.7	98.5 ± 0.7	0.373
Male gender, n (%)	246 (97.6%)	133 (97.8%)	113 (97.4%)	1
History of prior SARS-CoV-2 infection, n (%)	2 (0.8%)	2 (1.5%)	0	0.5
Time from infection to evaluation, days, mean ± SD	11.30 ± 6.66	11.22 ± 5.36	11.35 ± 9.8	0.9403
Time since pre-infection spirometry, months, mean ± SD	44 ± 31.13	41.34 ± 32.03	41.81 ± 29.84	0.181

BP Blood pressure

* *p*-value for comparison between subjects who underwent the extended protocol vs. those who underwent the limited protocol

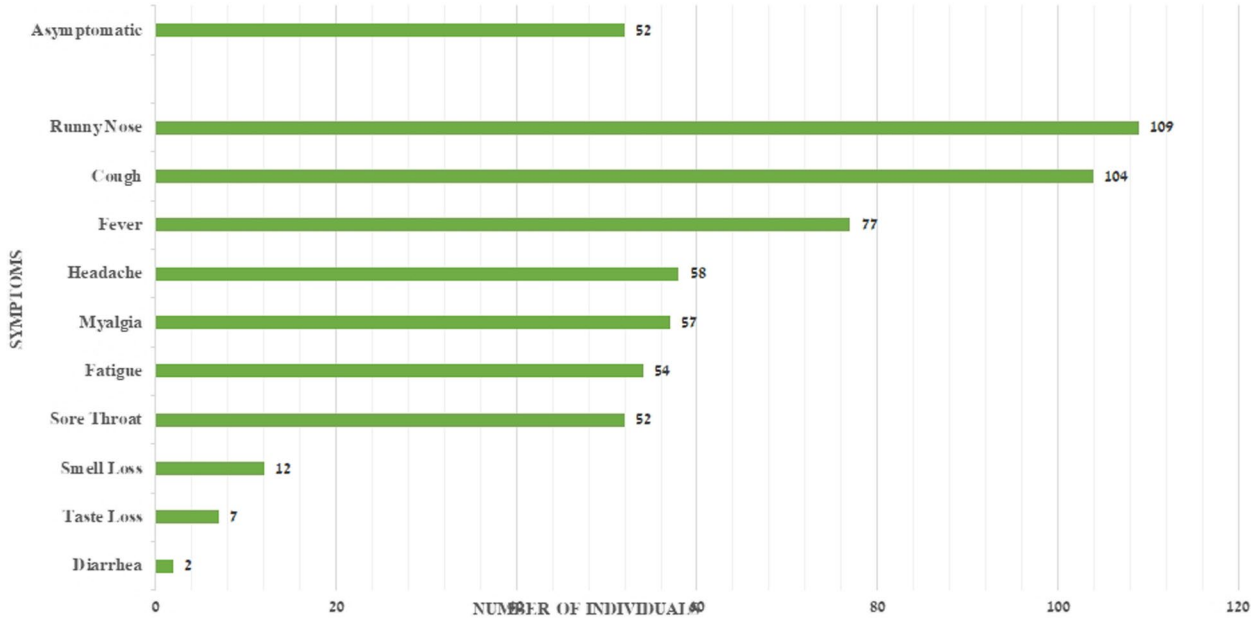

Fig. 3 COVID-19 Symptoms. Symptoms were recorded at the first assessment after an aviator was diagnosed with SARS-CoV-2 infection. Fifty-two of 252 were asymptomatic (20.6%), while the rest had mild disease

(109, 43.3%), cough (104, 41.2%), and fever (77, 30.6%). None of the participants required specific COVID-19 therapy, and none were hospitalized for COVID-19.

The post-COVID-19 medical evaluation and "back-to-fly" protocol were performed an average of 10.79 ± 5.67 days after diagnosis (range 5–42 days). During this examination, 32 aviators (11.4%) were still symptomatic and reported cough (3.8%), runny nose (2.9%), loss of smell or taste (1.4%), or sore throat (1.1%).

Pulmonary function tests results

Post-SARS-CoV-2 infection spirometry was performed for all participating aircrew, while lung volumes and diffusion capacity were measured for 104 ("extended protocol"). The average time between pre- and post-infection spirometry was 41.3 ± 28.59 months. Spirometry results, including absolute values and %pred of FEV1, FVC as well as FEV1/FVC ratios, were comparable for the pre- and post-SARS-CoV-2 infections measurements (Table 2).

The proportions of subjects with abnormal spirometry values according to the %pred criteria (< 80%pred) were low (2–4.4%) and also of similar magnitude between pre- and post-COVID-19 tests. According to those an FEV1/FVC ratio < 0.7, seven subjects displayed an obstructive, compared with six subjects before SARS-CoV-2 infection. Four of the aviators with post-COVID-19 obstructive patterns also had such results prior to infection. A lower proportion of subjects had abnormal FEV1 or FVC values according to LLN criteria (0.4–0.8%), with similar rates of low FEV1/FVC ratios (Table 2), which was mostly derived from high FVC values rather than abnormally low FEV1.

Regarding additional PFT, all TLC measurements were within the anticipated range, thus excluding restrictive abnormalities. DLCO was lower than 80%pred in 8 aviators (7.7%) yet was above 70% in all cases. When considering LLN, only 2 subjects (1.9%) had abnormally low diffusion capacity, while TLC and RV results were all within normal range. Details of PFT results are summarized in Table 2.

There were no associations between age or COVID-19 symptoms and PFT results, nor were there associations between abnormal results of different tests (e.g. FEV1 and FVC).

ROBD testing

Two of the 104 subjects had abnormal ROBD testing (1.9%). One had a delayed recovery from hypoxia (over 50 s). He had no ongoing symptoms of illness, and all PFT were within normal range and unchanged from baseline. He resumed flight duties without further testing. The other aviator expressed significant symptoms under hypoxic conditions. He also had complete clinical recovery and normal PFT, yet he was temporarily restricted from flying.

Table 2 Lung function tests results

	Time	%pred	*p*-value	%pred abnormality rates n (%)	LLN Abnormality rates n (%)
FEV1%pred	**Pre**	99.7 ± 11.8	0.85	11 (4.4%)	-
	Post	99.5 ± 11.3		9 (3.6%)	-
FVC%pred	**Pre**	99.8 ± 13.1	0.72	6 (2.4%)	-
	Post	99.4 ± 11.5		5 (2%)	-
FEV1, L	**Pre**	4.22 ± 0.61	0.28	-	2 (0.8%)
	Post	4.16 ± 0.64		-	1 (0.4%)
FVC, L	**Pre**	5.03 ± 0.8	0.48	-	2 (0.8%)
	Post	4.98 ± 0.78		-	2 (0.8%)
FEV1/FVC	**Pre**	84.5 ± 7.33	0.93	6 (2.4%)	8 (3.2%)
	Post	84.44 ± 7.84		7 (2.8%)	6 (2.4%)
TLC%pred	**Post**	103.0 ± 10.45	NA	0 (0%)	
TLC z-score	**Post**	−0.03 ± 0.78		0 (0%)	
RV%pred	**Post**	112.08 ± 20.29	NA	6 (5.8%)	
RV z-score		0.13 ± 0.61		0 (0%)	
DLCO%pred	**Post**	96.36 ± 10.22	NA	8 (7.7%)	
DLCO z-score		−0.49 ± 0.72		2 (1.9%)	
ROBD	**Post**	NA	NA	2 (1.9%)	

DLCO Diffusion capacity for carbon monoxide, *FEV1* Forced expiratory volume in 1 s, *FVC* Forced vital capacity, *LLN* Lower limit of normal, *ROBD* Reduced oxygen breathing device, *RV* Residual volume, *TLC* Total lung capacity

* *p*-values for comparison between values pre-SARS-CoV-2 infection and post-SARS-CoV-2 infection

Discussion

In this study, we aimed to investigate the impact of SARS-CoV-2 infection on the pulmonary function of young, vaccinated, and healthy adults by comparing PFT performed before and shortly after the infection.

The results showed that the FEV1, FVC, and FEV1/FVC ratios were comparable to the pre-infection measurements, indicating that there was no significant decline in these parameters following SARS-CoV-2 infection. Furthermore, the total lung capacity (TLC) was within normal range for all subjects, suggesting that there were no restrictive pulmonary patterns observed after recovery.

It is worth noting that a small proportion of aviators had low-normal values for DLCO, indicating potential impairment in gas exchange. Although these values were below 80% of the predicted, none of them fell below the 70%pred threshold, and only two aviators had values slightly below the LLN (z-score of −1.76 and −1.8). Therefore, it can be inferred that the impact of SARS-CoV-2 infection on the diffusion capacity was mild, if any, in this population.

The majority of aviators who contracted COVID-19 were symptomatic, yet their symptoms were mild and transient. All the participants were previously healthy military aircrew, fully vaccinated (received 3 vaccine doses), and none required specific COVID-19 therapy or hospitalization, suggesting that the infection had a benign course in this population. Generally, normal PFT were measured shortly after contracting infection, as the post-COVID-19 medical evaluation and "back-to-fly" protocol were conducted approximately 9 days after diagnosis.

The vast majority of data regarding post-COVID-19 PFT is derived from publications that studied individuals who survived severe illness and is also biased towards subjects who remained symptomatic. Such studies reported significant rates of low DLCO, followed by lower rates of restrictive patterns (low TLC%pred or FVC%pred) [5–9, 20–22]. For example, DLCO were abnormally low in 30% of 146 subjects who recovered from mild COVID-19, while suspected restriction (FVC < LLN, TLC was not measured) was identified in 20%. However, those were individuals who had attended a hospital-based COVID-19 follow-up clinic, were older than our cohort, and have possibly had comorbidities, including prior respiratory illnesses. In addition, no pre-infection PFT were available for comparison [23]. A major limitation of most prior studies is that pre-illness PFT were not available. In fact, only a handful of studies compared pre- and post-COVID-19 PFT. Three studies report normal spirometry and no impact of mild COVID-19 among professional athletes [24–26]. Those studies, however, included very small cohorts (8 handball

and 13 and 18 soccer players, respectively], and may be underpowered to detect differences. Four additional studies included larger cohorts. In one study, 33 of 67 subjects had spirometry results pre-COVID-19. A statistically significant decrease of 130ml in FEV1 was identified, while FVC and FEV1/FVC were unchanged [27]. Almost half of the subjects required hospitalization and oxygen support for COVID-19. In another study, pre- and post-COVID-19 PFT were retrospectively compared in 80 participants. The majority of subjects had underlying lung diseases, mostly asthma and chronic obstructive pulmonary disease, with abnormal baseline PFT. Most also had other non-pulmonary comorbidities. In this cohort, 75% had mild-moderate COVID-19, and post-COVID-19 PFTs were performed 77 days after illness on average. There was no difference in PFT values between pre- and post-COVID-19 measurements [28]. The largest study included 853 subjects from a Swedish birth cohort with asthma who had spirometry performed before and after the COVID-19 epidemic. SARS-CoV-2 infection was identified retrospectively based on positive viral serology. Thus, 243 subjects were seropositive (29%), with only one requiring hospitalization. Overall, there was a statistically significant yet numerically minimal increase in FEV1%pred and FVC%pred in the COVID-19 measurements, which is clinically irrelevant. A similar increase was noted among SARS-CoV-2 seropositive and seronegative participants [29]. There were no measurements of total lung capacity or DLCO. Last, in a prospective study that included 107 COVID-19 patients, there were faster declines of FEV1 and FVC over time compared with 499 non-infected controls. While those differences were small, they were still robust among individuals who did not require hospitalization for COVID-19. Mean TLC and DLCO (measured only post-COVID-19) were within normal ranges (90.15% ± 10.9 and 88.1% ± 17.1, respectively) [30]. Thus, available data regarding the impact of COVID-19 on the PFT of individual subjects is sparse and conflicting.

It is important to note that our study has limitations. The study population consists of healthy, mostly young, predominantly male aviators, from a single center, with no control group, which may bias the results and limit the generalizability of the findings. Indeed, several studies reported worse PFT outcomes among female survivors of severe or critical COVID-19, compared with males [8, 21, 22], which may also be relevant to recovery from mild or asymptomatic disease. The study was conducted when Omicron variants of SARS-CoV-2 (BA.1 and BA.2) became predominant in Israel, responsible for 98–100% of cases nationwide [31]. While genomic sequencing was not performed, it is safe to assume that the vast majority, if not all, of cases in our study, were indeed infected with Omicron subvariants. Reduced disease severity of COVID-19 resulting from Omicron variants, compared with other SARS-CoV-2 variants, has been reported, including lower risks for severe disease, hospitalizations, and mortality [32–34]. This could also explain the benign nature of the disease and post-COVID-19 measurements in our study. Full vaccination with an effective mRNA vaccine was universal in our studied population. Those factors may limit the generalization of our data. Another limitation is the absence of pre-COVID-19 plethysmography and DLCO data. Additionally, the study does not provide long-term follow-up data, and the impact of SARS-CoV-2 infection on pulmonary function beyond the immediate recovery period was not assessed. Despite those limitations, this is the largest study comparing pre- and post-COVID-19 PFT to date. We believe that our findings add support to the notion that mild COVID-19 has no or minimal effects on lung function.

Conclusions

We did not find any effect of mild or asymptomatic COVID-19 on spirometry values among the studied population and identified only uncommon minimal abnormalities in DLCO. This implies that routine surveillance with PFT may not be necessary among asymptomatic subjects who recovered from mild COVID-19. We suggest further validation of the results, which might also determine which subjects may require such testing.

Abbreviations

COVID-19	Coronavirus disease 2019
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
PFT	Pulmonary function test
ROBD	Reduced oxygen breathing device
IAF	Israeli Air Force
AMC	Aeromedical Center

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Authors' contributions

All authors significantly contributed to the study concept and design. Conceptualization were made by OBA, RRT and OW, data collection and analysis were performed by all the authors. OBA, BG and OW supervised the work. The first draft was written by RRT and YK, and all the authors commented on previous versions of the manuscript. All authors have read and approved the final manuscript

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Data availability

Additional data will be available upon reasonable request from the corresponding author, Dr. Ori Wand.

Declarations

Ethics approval and consent to participate

This study was approved by the Helsinki Committee and Institutional Review Board of the IDF Medical Corps (application no. 2155–2020). Informed consent

was not required by the Board since all medical evaluations were performed as part of routine management and de-identified data were collected.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Gandhi RT, Lynch JB, Del Rio C. Mild or moderate Covid-19. N Engl J Med. 2020;383(18):1757–66. https://doi.org/10.1056/NEJMcp2009249. Epub 2020 Apr 24 PMID: 32329974.
2. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med. 2020;383(25):2451–60. https://doi.org/10.1056/NEJMcp2009575. Epub 2020 May 15 PMID: 32412710.
3. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA. 2020;324(8):782–93. https://doi.org/10.1001/jama.2020.12839. PMID: 32648899.
4. Singh SJ, Baldwin MM, Daynes E, Evans RA, Greening NJ, Jenkins RG, et al. Respiratory sequelae of COVID-19: pulmonary and extrapulmonary origins, and approaches to clinical care and rehabilitation. Lancet Respir Med. 2023;S2213–2600(23):00159–5. https://doi.org/10.1016/S2213-2600(23)00159-5. Epub ahead of print. PMID: 37216955; PMCID: PMC10198676.
5. Lee JH, Yim JJ, Park J. Pulmonary function and chest computed tomography abnormalities 6–12 months after recovery from COVID-19: a systematic review and meta-analysis. Respir Res. 2022;23(1):233. https://doi.org/10.1186/s12931-022-02163-x. PMID:36068582;PMCID:PMC9446643.
6. Björsell T, Sundh J, Lange A, Ahlm C, Forsell MNE, Tevell S, et al. Risk factors for impaired respiratory function post COVID-19: a prospective cohort study of nonhospitalized and hospitalized patients. J Intern Med. 2023;293(5):600–14. https://doi.org/10.1111/joim.13614. Epub 2023 Feb 23 PMID: 36815689.
7. Guler SA, Ebner L, Aubry-Beigelman C, Bridevaux PO, Brutsche M, Clarenbach C, et al. Pulmonary function and radiological features 4 months after COVID-19: first results from the national prospective observational Swiss COVID-19 lung study. Eur Respir J. 2021;57(4):2003690. https://doi.org/10.1183/13993003.03690-2020. PMID:33419891;PMCID:PMC8082329.
8. Schlemmer F, Valentin S, Boyer L, Guillaumot A, Chabot F, Dupin C, et al. Respiratory recovery trajectories after severe-to-critical COVID-19: a 1-year prospective multicentre study. Eur Respir J. 2023;61(4):2201532. https://doi.org/10.1183/13993003.01532-2022. PMID:36669777;PMCID: PMC10066566.
9. Lenoir A, Christe A, Ebner L, Beigelman-Aubry C, Bridevaux PO, Brutsche M, et al. Pulmonary recovery 12 months after non-severe and severe COVID-19: the prospective Swiss COVID-19 lung study. Respiration. 2023;102(2):120–33. https://doi.org/10.1159/000528611. Epub 2022 Dec 23. PMID: 36566741; PMCID: PMC9932828.
10. George PM, Barratt SL, Condliffe R, Desai SR, Devaraj A, Forrest I, Gibbons MA, Hart N, Jenkins RG, McAuley DF, Patel BV, Thwaite E, Spencer LG. Respiratory follow-up of patients with COVID-19 pneumonia. Thorax. 2020;75(11):1009–16. https://doi.org/10.1136/thoraxjnl-2020-215314. Epub 2020 Aug 24 PMID: 32839287.
11. Antoniou KM, Vasarmidi E, Russell AM, Andrejak C, Crestani B, Delcroix M, Dinh-Xuan AT, Poletti V, Sverzellati N, Vitacca M, Witzenrath M, Tonia T, Spanevello A. European respiratory society statement on long COVID follow-up. Eur Respir J. 2022;60(2):2102174. https://doi.org/10.1183/13993003.02174-2021. PMID:35144991;PMCID:PMC9349784.
12. British Thoracic Society Guidance on Respiratory Follow Up of Patients with a Clinico-Radiological Diagnosis of COVID-19 Pneumonia. Available at: https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/resp-follow-up-guidance-post-covid-pneumonia/.
13. Stanojevic S, Kaminsky DA, Miller MR, Thompson B, Aliverti A, Barjaktarevic I, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. Eur Respir J. 2022;60(1):2101499. https://doi.org/10.1183/13993003.01499-2021. PMID: 34949706.
14. Dillard TA, Khosla S, Ewald FW Jr, Kaleem MA. Pulmonary function testing and extreme environments. Clin Chest Med. 2005;26(3):485–507, vii. https://doi.org/10.1016/j.ccm.2005.05.006. PMID: 16140140.
15. Artino AR Jr, Folga RV, Swan BD. Mask-on hypoxia training for tactical jet aviators: evaluation of an alternate instructional paradigm. Aviat Space Environ Med. 2006;77(8):857–63.
16. National Institutes of Health. COVID-19 treatment guidelines. Clinical spectrum of SARS-CoV-2 Infection. Available at: https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum. Accessed 27 Sept 2022.
17. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40(6):1324–43. https://doi.org/10.1183/09031936.00080312. Epub 2012 Jun 27. PMID: 22743675; PMCID: PMC3786581.
18. Hall GL, Filipow N, Ruppel G, Okitika T, Thompson B, Kirkby J, et al. Official ERS technical standard: Global Lung Function Initiative reference values for static lung volumes in individuals of European ancestry. Eur Respir J. 2021;57(3):2000289. https://doi.org/10.1183/13993003.00289-2020. PMID: 33707167.
19. Stanojevic S, Graham BL, Cooper BG, Thompson BR, Carter KW, Francis RW, et al. Official ERS technical standards: Global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians. Eur Respir J. 2017;50(3):1700010. https://doi.org/10.1183/13993003.00010-2017. Erratum. In: Eur Respir J. 2020 Oct 15;56(4) PMID: 28893868.
20. Menéndez R, Méndez R, Latorre A, González-Jiménez P, Peces-Barba G, Molina M, et al. Residual pulmonary infiltrates, symptoms and diffusion impairment at 1-year after severe COVID-19 infection have different associated factors. J Intern Med. 2023. https://doi.org/10.1111/joim.13642. Epub ahead of print. PMID: 37038609.
21. Wu X, Liu X, Zhou Y, Yu H, Li R, Zhan Q, et al. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study. Lancet Respir Med. 2021;9(7):747–54. https://doi.org/10.1016/S2213-2600(21)00174-0. Epub 2021 May 5. PMID: 33964245; PMCID: PMC8099316.
22. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology. 2021;27(4):328–37. https://doi.org/10.1016/j.pulmoe.2020.10.013. Epub 2020 Nov 25. PMID: 33262076; PMCID: PMC7687368.
23. Cortes-Telles A, Figueroa-Hurtado E, Ortiz-Farias DL, Zavorsky GS. Clinical predictors of lung function in patients recovering from mild COVID-19. BMC Pulm Med. 2022;22(1):294. https://doi.org/10.1186/s12890-022-02086-9. PMID:35909118;PMCID:PMC9339191.
24. Fikenzer S, Kogel A, Pietsch C, Lavall D, Stöbe S, Rudolph U, et al. SARS-CoV2 infection: functional and morphological cardiopulmonary changes in elite handball players. Sci Rep. 2021;11(1):17798. https://doi.org/10.1038/s41598-021-97120-x. PMID:34493765;PMCID:PMC8423785.
25. Gattoni C, Conti E, Casolo A, Nuccio S, Baglieri C, Capelli C, et al. COVID-19 disease in professional football players: symptoms and impact on pulmonary function and metabolic power during matches. Physiol Rep. 2022;10(11):e15337. https://doi.org/10.14814/phy2.15337. PMID: 35699134; PMCID: PMC9194973.
26. Gervasi SF, Pengue L, Damato L, Monti R, Pradella S, Pirronti T, et al. Is extensive cardiopulmonary screening useful in athletes with previous asymptomatic or mild SARS-CoV-2 infection? Br J Sports Med. 2021;55(1):54–61. https://doi.org/10.1136/bjsports-2020-102789. Epub 2020 Oct 5. PMID: 33020140; PMCID: PMC7536638.
27. Afsin E, Demirkol ME. Post-COVID pulmonary function test evaluation. Turk Thorac J. 2022;23(6):387–94. https://doi.org/10.5152/TurkThoracJ.2022.21230. PMID:36101980;PMCID:PMC9682963.
28. Lewis KL, Helgeson SA, Tatari MM, Mallea JM, Baig HZ, Patel NM. COVID-19 and the effects on pulmonary function following infection: A retrospective analysis. EClinicalMedicine. 2021;39:101079. https://doi.org/10.1016/j.eclinm.2021.101079. Epub 2021 Aug 13. PMID: 34405138; PMCID: PMC8360709.

29. Mogensen I, Hallberg J, Björkander S, Du L, Zuo F, Hammarström L, et al. Lung function before and after COVID-19 in young adults: a population-based study. J Allergy Clin Immunol Glob. 2022;1(2):37–42. https://doi.org/10.1016/j.jacig.2022.03.001. Epub 2022 Mar 30. PMID: 36647376; PMCID: PMC8966371.
30. Iversen KK, Afzal S, Ahlström MG, Nordestgaard BG, Schneider UV, Nielsen L, et al. Lung Function Decline in Relation to COVID-19 in the General Population: A Matched Cohort Study With Prepandemic Assessment of Lung Function. J Infect Dis. 2022;225(8):1308–16. https://doi.org/10.1093/infdis/jiab636. PMID:34979029;PMCID:PMC8755346.
31. Our World in Data. SARS-CoV-2 variants in analyzed sequences, Israel. Available at https://ourworldindata.org/grapher/covid-variants-area?country=~ISR. Accessed 15 Sep 2022.
32. Menni C, Valdes AM, Polidori L, Antonelli M, Penamakuri S, Nogal A, et al. Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study. Lancet. 2022;399(10335):1618–24. https://doi.org/10.1016/S0140-6736(22)00327-0. Epub 2022 Apr 7. PMID: 35397851; PMCID: PMC8989396.
33. Nyberg T, Ferguson NM, Nash SG, Webster HH, Flaxman S, Andrews N, et al. Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study. Lancet. 2022;399(10332):1303–12. https://doi.org/10.1016/S0140-6736(22)00462-7. Epub 2022 Mar 16. PMID: 35305296; PMCID: PMC8926413.
34. Lauring AS, Tenforde MW, Chappell JD, Gaglani M, Ginde AA, McNeal T, et al. Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study. BMJ. 2022;9(376):e069761. https://doi.org/10.1136/bmj-2021-069761. PMID:35264324;PMCID: PMC8905308.

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