CEEOR

Compliance with inhaled corticosteroid therapy in asthma patients who have COVID-19 leads to better outcomes

Sedlák V [1], Tichopád A [2], Jeseňák M [3], Solovič I[4], Brecikováa K [5], Rybář M [2], Rožánek M [2]

[1] University Hospital, Hradec Králove, Czechia, [2] Charles University, Prague, Czech Republic, [3]University Hospital, Martin, Slovakia, [4]Catholic university Ružomberok, Slovakia, [5]CEEOR s.r.o., Prague, Czech Republic

OBJECTIVE

The extensive use of inhaled corticosteroids among asthma patients has frequently been reported as a preventive measure against developing severe forms of COVID-19 (1). The critical role of patients' correct use of inhalation aerosol delivery devices has been well acknowledged yet recently shown to pose a persisting challenge (2-4). It was shown that patient's adherence to medication delivered via an inhalation device can be as low as 10% - greatly due to various inhalation systems in use and frequent need for combination therapy (2). Vytřísalová et al. suggested a Five-Steps Assessment tool, which uses five simple steps to determine the adherence to an inhaled medication application technique (A-AppIT) (2). The main goal of the study was to verify or disprove the hypothesis that Adherence to an Inhaled Medication Application Technique (A-AppIT) is negatively correlated with COVID-19 severity, likely due to the incomplete or absent protective effect of inhaled corticosteroids (ICS).

METHODS

❖ A cross-sectional observational retrospective study involving 63 specialists (pulmonologist and immune-allergologists) treating asthma patients who were diagnosed with COVID-19 in Czech and Slovak Republic

❖ Anonymous patient data were collected from medical records of 833 adults between February to June 2022 including demographics, medical history, the asthma grade and asthma-specific medication, VC and FEV1 and their change (difference between before and after COVID-19), hospitalization, quality of life by EQ-5D, the A-AppIT score according to Vytřísalová et al. (2), (inclusion criteria: patient diagnozed with asthma not later than January 2019, who contracted COVID-19 from March 2020-March 2021; aged ≥ 50 years)

Results

Patient disposition, demographics and epidemiology

- In total 518 (62.16%) women and 315 (37.84%) men were included in the study. The mean age in years of all patients was 61.8 (SD 8.2), 60.8 (SD 7.7) for men and 62.4 (SD 8.4) for women.
- Of the total 833 patients, 428 (51.4%) had moderate persistent, 345 (29.9%) mild persistent, and 60 (7.2%) severe persistent asthma.
- The majority (92%) of all patients used chronic inhalation treatment prior COVID-19, the second most used therapy was asthma reliever inhalation therapy (78%). After diagnosis of COVID-19, 43% of patients had changed their pharmacotherapy. The biggest increase in the prescription was observed in the systemic oral corticoids (14% vs. 29%). The most frequently used inhalation systems before COVID-19 were pMDI (46%) and the remaining 43% of patients used both types.

Table 1 Characteristics of the cohort of patients who used ICS and the analysis cohort

	Mild COVID-19	Moderate COVID-19	Severe COVID-19	Unadjusted p-value
Gender	522 (80.06%)	104 (15.95%)	26 (3.99%)	0.051
Males	202 (82.11%)	34 (13.82%)	10 (4.07%)	
Females	320 (78.82%)	70 (17.24%)	16 (3.94%)	
Age (years) mean (SD)	59.93 (8.30)	61.86 (8.76)	60.65 (8.60)	0.096
Body mass index mean (SD)	28.63 (4.81)	30.42 (5.49)	32.68 (6.76)	<0.001
Anamnesis				
Diabetes mellitus I /II	107 (16.41%)	32 (4.91%)	8 (1.23%)	0.047
Ischemic heart disease	89 (13.65%)	25 (3.83%)	5 (0.77%)	0.255
Arterial hypertension	336 (51.53%)	72 (11.04%)	23 (3.53%)	0.030
Heart failure	19 (2.91%)	5 (0.77%)	1 (0.15%)	0.086
Chronic kidney disease	21 (3.22%)	9 (1.38%)	1 (0.15%)	0.131
Solid/Haematology Organ Transplantation	0 (0.00%)	0 (0.00%)	0 (0.00%)	-
Cancer in active therapy	4 (0.61%)	1 (0.15%)	0 (0.00%)	0.883
Active cigarette smoking	38 (5.83%)	9 (1.38%)	0 (0.00%)	0.316
Severity of asthma				0.004
Mild persistent	211 (32.36%)	26 (3.99%)	8 (1.23%)	
Moderate persistent	281 (43.10%)	63 (9.66%)	14 (2.15%)	
Severe persistent	30 (4.60%)	15 (2.30%)	4 (0.61%)	
Quality of life by EQ-5D[AS]	0.82 (0.17)	0.72 (0.19)	0.61 (0.25)	<0.001
Median (IQR) ICS daily dose equivalent before COVID-19[E]	700 (400-875)	800 (429-1280)	800 (400-1288)	11[K]
Median (IQR) ICS daily dose equivalent during COVID-19[E]	800 (523-1288)	875 (644-1625)	800 (640-1600)	0.136[K]

Statistically significant differences between groups are denoted in **bold**.
AS, analysis cohort, that is patients with COVID-19 severity assessed (N=652); E, calculated as an equivalent of dry budesonide powder; EQ-5D, EuroQol-5 Dimension; ICS, inhaled corticosteroids; K, Kruskal-Wallis test.

Effect of adherence on COVID-19 severity

- Among those 652 patients of the analysis cohort using inhaler containing ICS with known COVID-19 severity, 522 (80%) patients had mild, 104 (16%) moderate and 26 (4%) severe COVID-19.
- The A-AppIT (score from <=2 to 5) and the asthma grade were found to be predictors of COVID-19 severity (p=0.049 and <0.001; adjusted for age p=0.078 and <0.001), whereas age alone was not significant in the model (p=0.23). An increase in A-AppIT score, indicating means more correct inhalation technique, was associated with a lower COVID-19 severity score (mild < moderate < severe) by an odds ratio of 0.89 (95% CI 0.79- 1.01; Fig.1).
- An increase in the A-AppIT score was associated with a lower, however not significant (p=0.11), odd ratio 0.86 of hospitalization for COVID-19 (Fig. 2).
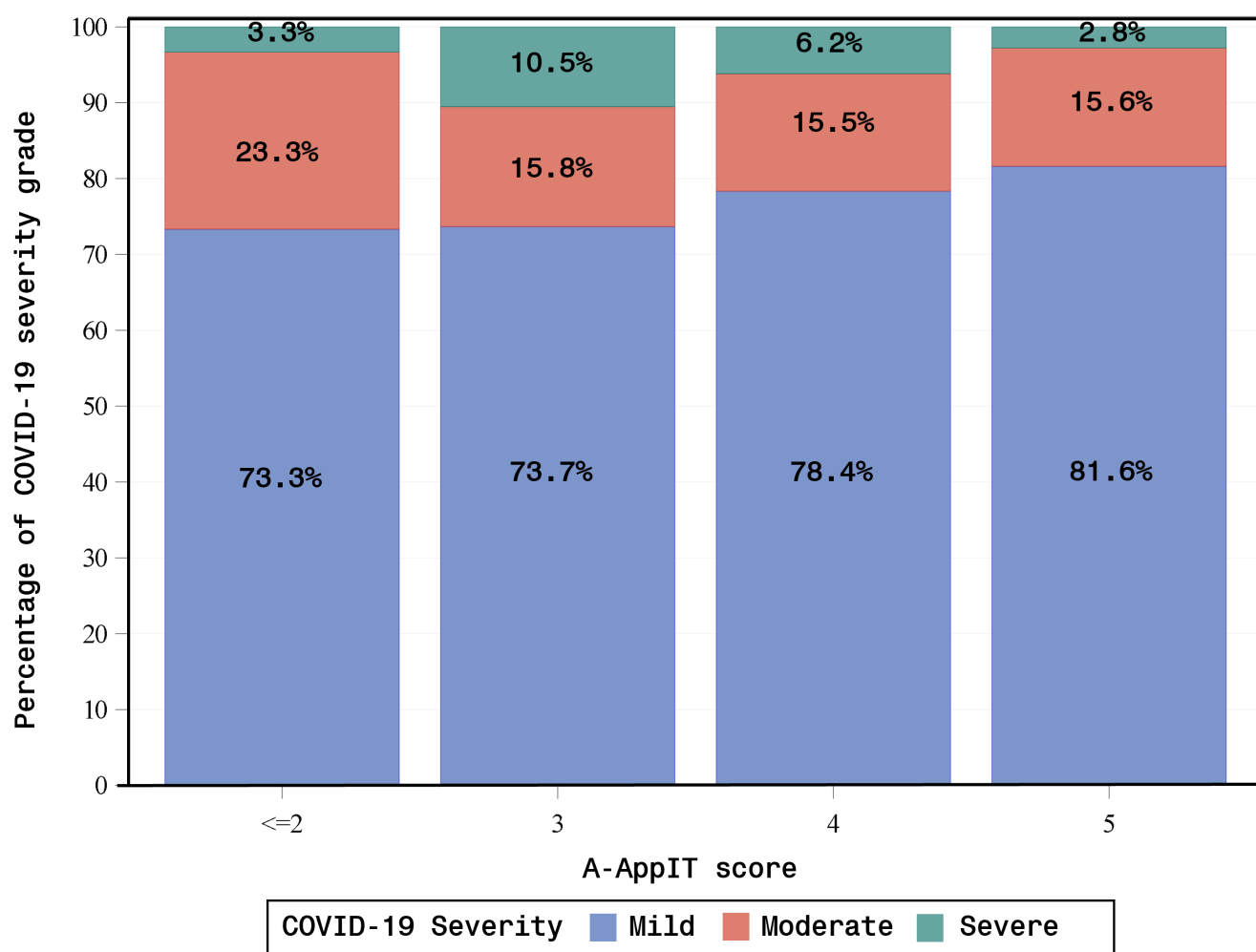

Fig. 1 Relative frequencies of patients with given COVID- 19 severity grades by the adherence score (A- AppIT). A- AppIT, adherence to an inhaled medication application technique.
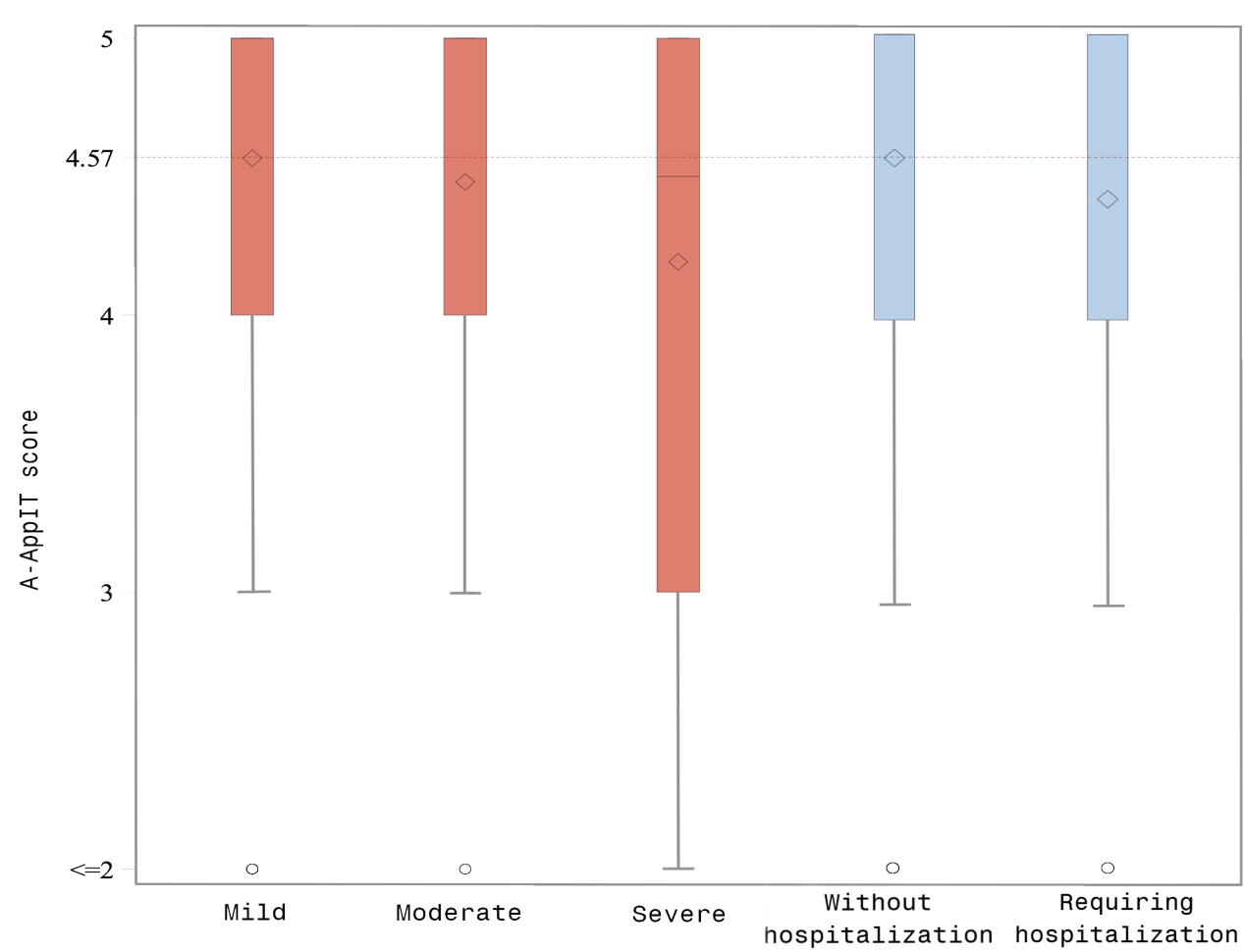
Fig. 2 Adherence score (A-AppIT) by COVID-19 severity and hospitalization status. The A-AppIT (score from <=2 to 5) and the asthma grade were found to be predictors of COVID-19 severity (p=0.049 and <0.001; adjusted for age p=0.078 and <0.001). A- AppIT, adherence to an inhaled medication application technique.

Effect of adherence on lung parameters and quality of life

- Overall, unadjusted mean VC and the associated confidence intervals (88.2; 95%CI 86.8-89.5) and FEV1 (82.8; 95%CI 81.3-84.3) were lower after COVID-19 compared with unadjusted mean VC (91.3; 95%CI 89.8-92.5) and FEV1 (86.0; 95%CI 84.6-87.5) before COVID-19.
- Higher A-AppIT scores had a significant positive effect on reversal of reduced VC and FEV1 (p=0.027 and p<0.0001, respectively) calculated as the value after COVID-19 minus the value before COVID-19 in a model adjusted for age (p=0.54 and p=0.02, respectively), the baseline value (p<0.0001 and p<0.0001, respectively), and the asthma grade (p=0.02 and p<0.08, respectively)(Fig.3).
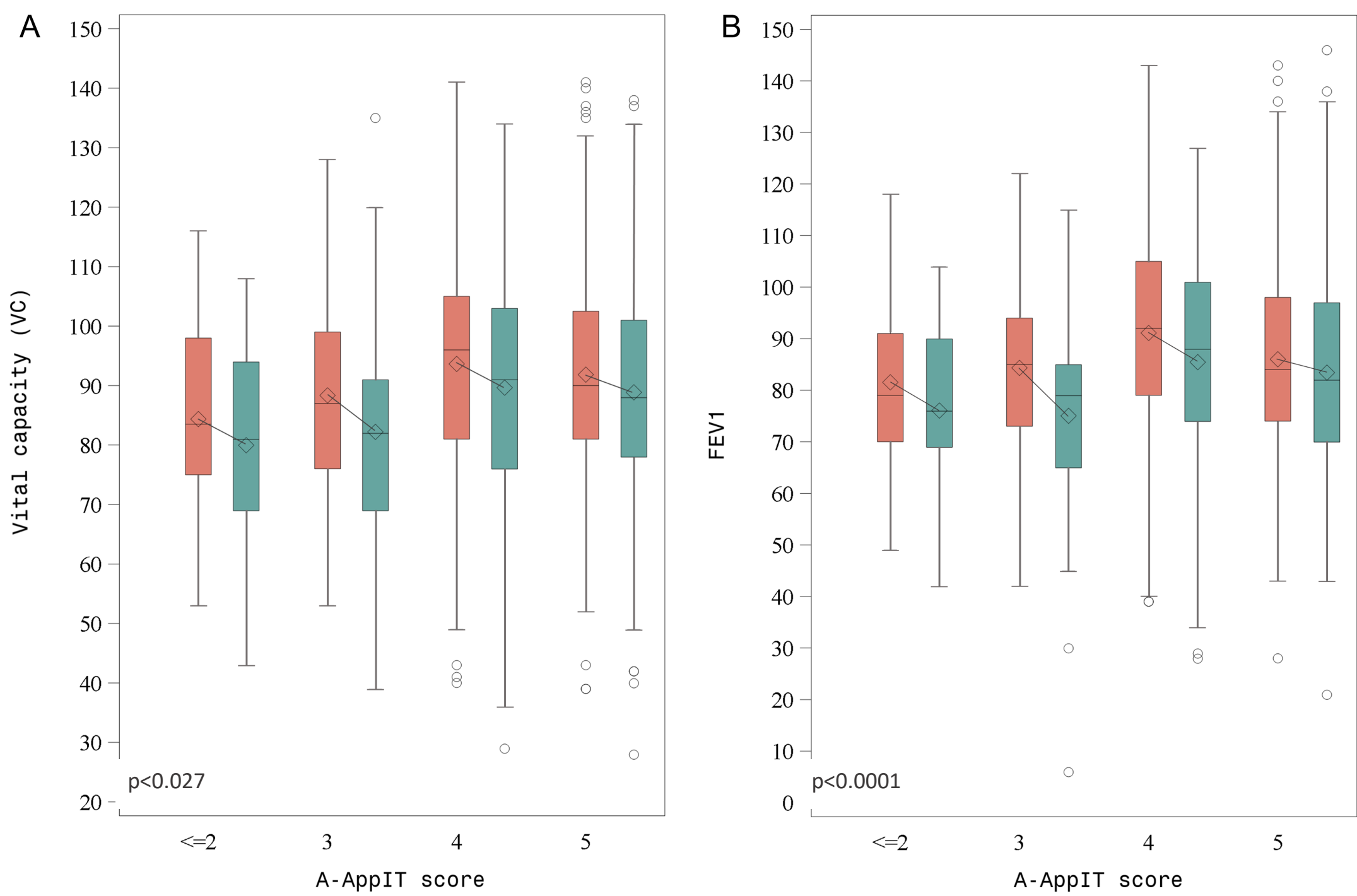

Fig. 3 (A) Unadjusted vital capacity (VC, %) prior (red) and after (green) COVID- 19 by the A- AppIT score. (B) Unadjusted forced expiratory volume in 1 s (FEV1, %) prior (red) and after (green) COVID- 19 by the A- AppIT score. Higher A- AppIT scores had a significant reversal effect on both VC (up to 1.7- fold; p=0.027) and FEV1 (up to 3.4- fold; p<0.0001) deterioration. A- AppIT, adherence to an inhaled medication application technique.

- Scoring higher in the A-AppIT was also associated with significantly improved EQ-5D utility and the VAS score (both p<0.0001) in a model adjusted for age (p=0.004 and p<0.10, respectively) and the asthma grade (both p<0.0001). Fig. 4 show the unadjusted EQ-5D utility by the A-AppIT.
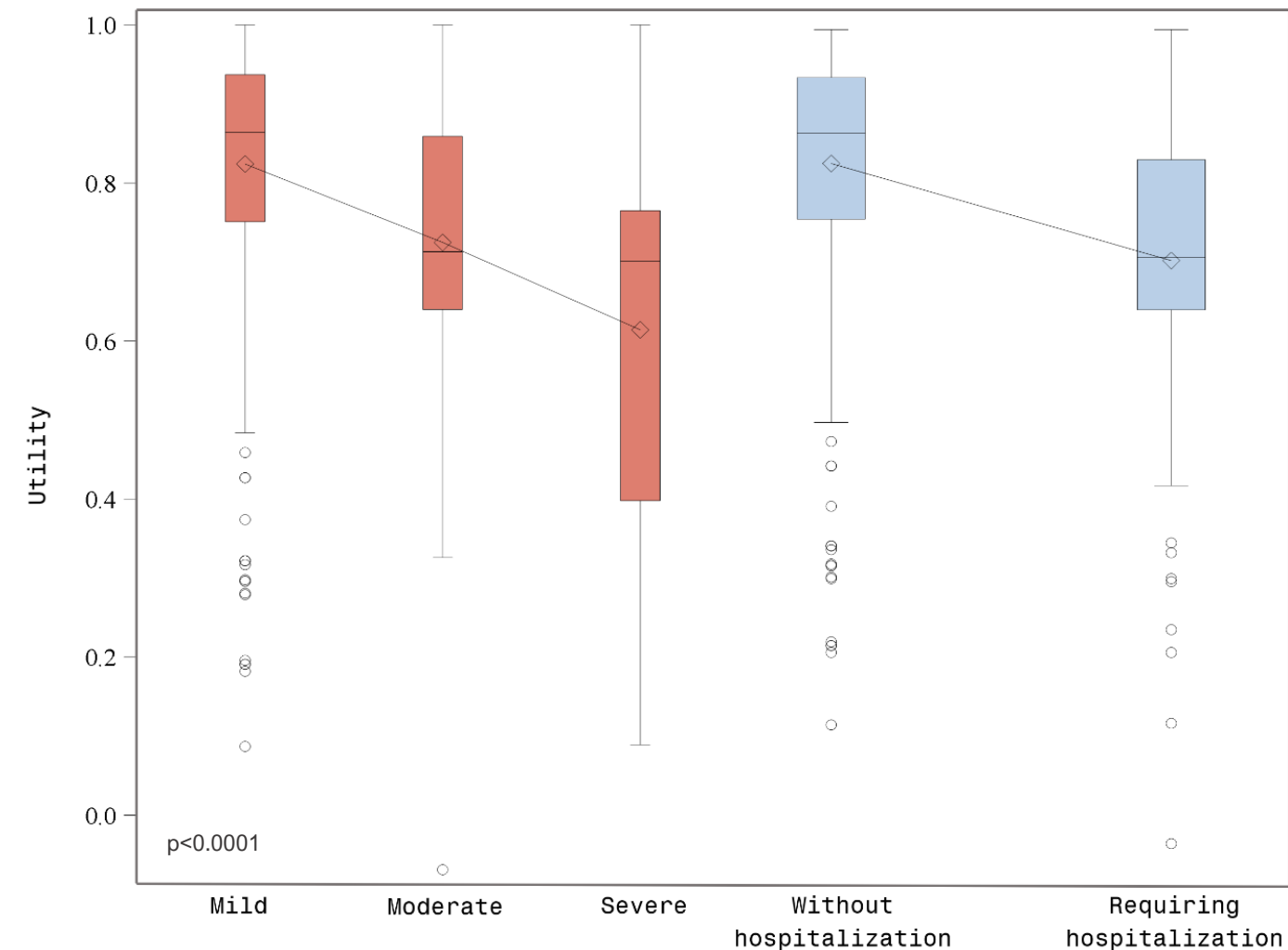

Fig. 4 Quality of life expressed as unadjusted utility value based on the EQ- 5D by COVID- 19 severity and hospitalization status. Scoring higher in the adherence to an inhaled medication application technique was associated with significantly improved EQ- 5D utility (p<0.0001). EQ- 5D, EuroQol-5 Dimension. A- AppIT, adherence to an inhaled medication application technique.

CONCLUSIONS

Asthma patients with COVID-19 who struggle with proper inhaler use experience greater declines in lung function and overall health compared to those who use their inhalers correctly. Mistakes in inhalation technique increase the risk of severe COVID-19 and negatively affect quality of life. The study's findings suggest that inhaled corticosteroids (ICS) may offer protection against severe COVID-19, as effective inhaler use is crucial in supporting this protective effect.

References: (1) Halpin DMG, Singh D, Hadfield RM. Inhaled corticosteroids and COVID-19: a systematic review and clinical perspective. Eur Respir J. 2020 May 1;55(5). (2) Vytrisalova M, Hendrychova T, Touskova T, Zimcikova E, Vlcek J, Nevoranek L, et al. Breathing Out Completely Before Inhalation: The Most Problematic Step in Application Technique in Patients With Non-Mild Chronic Obstructive Pulmonary Disease. Front Pharmacol. 2019;10. (3) Plaza V, Giner J, Rodrigo GJ, Dolovich MB, Sanchis J. Errors in the Use of Inhalers by Health Care Professionals: A Systematic Review. Journal of Allergy and Clinical Immunology: In Practice. 2018;6(3). (4) Capstick TGD, Clifton IJ. Inhaler technique and training in people with chronic obstructive pulmonary disease and asthma. Vol. 6, Expert Review of Respiratory Medicine. 2012.