Effects of Modified Diaphragmatic Training on Gastroesophageal Reflux Disease Questionnaire Score, Diaphragmatic Excursion, and Maximum Inspiratory Pressure in Adults with Gastroesophageal Reflux Disease After COVID-19: A Single-Blinded Randomized Control Trial

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ABSTRACT

Background: *Although diaphragmatic training has been shown to improve gastroesophageal reflux disease (GERD) symptoms, its effectiveness in adults with GERD after COVID-19 has not been evaluated. This study examined the effectiveness of modified diaphragmatic training (MDT) on GERD questionnaire (GERDQ) score, diaphragmatic excursion, and maximum inspiratory pressure (MIP) in adults with GERD after COVID-19.* ***Methods:*** *This single-blinded randomized control trial was conducted at Persahabatan Hospital from February to April 2023. The medical records of 364 patients with persistent gastrointestinal symptoms were evaluated; among these potential participants, 302 had symptoms before, and 62 after, COVID-19 infection. Fifty of these patients fulfilled the study inclusion and exclusion criteria and were randomly assigned to the intervention (n = 25) or control (n = 25) groups. Four weeks of diaphragmatic training were followed by MDT or standard diaphragmatic training. A follow-up assessment was conducted 30 days after the beginning of the training.* ***Results:*** *The GERDQ score was significantly decreased in the pre–post-intervention group (10.44 ± 2.00 vs 1.84 ± 2.17) and the control group (8.64 ± 0.57 vs 3.32 ± 1.49), with p < 0.001. The intervention group showed* *significant improvements in the right diaphragmatic excursion (RDE) (44% vs 11.87%), left diaphragmatic excursion (LDE) (46.61% vs 13.62%), and MIP (75.26% vs 23.97%) compared with the control group.* ***Conclusion:*** *MDT in adults after COVID-19 with GERD enhanced diaphragmatic excursion and MIP and decreased symptoms of gastroesophageal reflux by 8.60 points of GERDQ. Respiratory symptoms and other side effects were comparable between the groups.*

Keywords**:** *COVID-19, diaphragmatic training, gastroesophageal reflux disease questionnaire score, diaphragmatic excursion, maximal inspiratory pressure.*

INTRODUCTION

The COVID-19 pandemic has led to significant survivor disability in various organ systems, including the respiratory and gastrointestinal systems.[1] Though COVID-19 primarily affects the respiratory system, a recent report suggests that it can also lead to gastrointestinal symptoms. A high prevalence of gastrointestinal symptoms in patients with COVID-19 has been reported, including diarrhea, nausea, and vomiting.[2] COVID-19 is known to cause systemic inflammation that leads to skeletal muscle dysfunction, including myositis. Such impacts on respiratory muscle tissues, including the diaphragm as the primary respiratory muscle, can cause disability of both the respiratory and gastrointestinal systems. The crural diaphragm is crucially linked to the lower esophageal sphincter (LES), a muscular valve at the junction between the esophagus and stomach.[3] The LES normally functions to prevent the reflux of gastric contents into the esophagus.[4] The diaphragm helps maintain LES integrity through support and pressure regulation. Diaphragmatic dysfunction can weaken the LES, compromising the barrier to gastric content reflux. This can contribute to gastric acid and other stomach contents flowing more easily back into the esophagus, and thus development or worsening of gastroesophageal reflux disease (GERD) symptoms.

Hosseini et al. demonstrated the benefits of diaphragmatic training in various respiratory conditions.[5] However, the effectiveness of modified diaphragmatic training (MDT) with precise strengthening load and intensity has not been explored for improving GERD symptoms and related parameters in COVID-19. We hypothesized that MDT would improve diaphragmatic excursion, maximum inspiratory pressure (MIP), LES tone, the anti-reflux barrier, and GERD symptoms. The six-domain GERD questionnaire (GERDQ) has been validated to assess GERD symptom severity and quality of life and is diagnostic of GERD at a score cutoff ≥ 8.[6]

MIP measures inspiratory muscle strength using a respiratory power meter, with a minimal clinically important difference of 17.2 cmH2O.[7,8] Strengthening the respiratory muscles, specifically the diaphragm, may reduce GERD symptoms and respiratory dysfunction. The diaphragmatic excursion is measured using ultrasound imaging, by monitoring diaphragm movement during inspiration and expiration. Improvement is considered an excursion $\geq$ 2 cm,[9,10] indicating enhanced diaphragmatic strength and respiratory muscle function that may improve GERD management.

Methods for improving GERD symptoms and diaphragmatic function may assist healthcare professionals in implementing targeted rehabilitation management of GERD in their patients with a disability after COVID-19. infection. Thus, the aim of this single-blinded randomized controlled trial (RCT) was to examine the effectiveness of MDT for improving GERDQ score, diaphragmatic excursion, and MIP in adults with GERD after COVID-19 infection.

METHODS

For this single-blinded RCT, participants were not given any information about their treatment allocation. Single blinding was applied to the examiners during ultrasonography of the diaphragm and respirometer. **Figure 1** shows a flow chart of participants' recruitment according to the principles of the Declaration of Helsinki and Consolidated Standards of Reporting Trials (CONSORT). All participants consented to study participation, after which they were randomized with a 1:1 ratio using stratified block randomization to avoid selection bias, with random block sizes. An independent statistician in our randomization center used Sealed Envelop Ltd registered in England and Wales number 04338315, software-generated tables to assign participants to the intervention (n = 25) or control (n = 25) group. For concealment, each participant was assigned a sequential code number by a researcher who was not involved in the study. The participants underwent training based on their code number. After approval by the ethics committee of the Faculty of Medicine at Universitas Indonesia (protocol number: 22-11-1417) and registration with ClinicalTrials.gov (ID: NCT05833243), CONSORT procedures were used to conduct the study.

Eligible participants were aged 18 – 60 years, diagnosed with moderate COVID-19 infection less than six months before study participation, and had a GERDQ score ≥ 8. Potential participants were excluded if they: used a ventilator; had cardiac disease, uncontrolled chronic respiratory disease, a history of abdominal or back surgery, a severe postural disorder, HIV/AIDS, or an autoimmune disease; were pregnant or breastfeeding; had used dyslipidemia medication for > 1 year; or had used a prokinetic agent regularly for > 4 months. The study commenced in February and ended in April 2023. All participants were recruited based on a review of their medical records at the Persahabatan Hospital in Jakarta, Indonesia.

Both groups participated in a four-week diaphragmatic training program, with five once-daily training sessions per week, without receiving any standard GERD therapy. The intervention group received MDT as a strengthening diaphragm exercise, combining standard diaphragmatic training with an inspiratory muscle trainer (IMT); in this group, the load gradually increased from 60% of the patient's MIP each week. The control group received standard or conventional diaphragmatic training. MIP, evaluated by microRPM, and GERDQ score were administered on the first day of each training week. The diaphragmatic excursion was measured using ultrasonography for baseline and final follow-up week 4. This training protocol has been registered with Indonesia's intellectual property right (HAKI) number EC00202319527.

The confounding variable in this study is the patient's sex and baseline MIP already adjusted with multivariate analysis with a 0.05 significance level and 80% study power with a 0.67 effect size rate.

All statistical analyses were performed using SPSS version 26. A 95% confidence interval (CI) was used to measure effect size. Categorical data are presented as mean ± standard deviation (SD). Descriptive demographic data are also presented as totals and percentages. Normally distributed data were analyzed using unpaired t tests. When data were not normally distributed, the Mann–Whitney test was used. Mixed repeated-measures analysis of variance with Bonferroni correction was used to test intervention effects.

RESULTS

Frame sampling, conducted from hospital medical record data, retrieved 364 patients who had persistent gastrointestinal symptoms within six months of study inclusion after they recovered from a moderate COVID-19 infection. This study was designed based on the flow diagram in the revised CONSORT statement (**Figure 1**). No serious adverse events were reported during the study period.

The baseline characteristics of 50 consecutive participants who had gastrointestinal symptoms within six months after COVID-19 infection, and who met the other inclusion criteria, are described in **Table 1**. There were significant differences in demographic data sex and baseline MIP and GERDQ score differences between the intervention and control groups. The participants' mean age was 37.6 ± 9.66 years in the intervention group vs. 36.2 ± 10.23 years in the control group. The mean body mass index was 27.17 ± 6.06 kg/m2 in the intervention group vs. 25.49 ± 3.91 kg/m2 in the control group. There were two intervention group participants who smoked. No control group participant had any comorbidities; four intervention group participants had controlled asthma. No participant had moderate–severe obstructive or restrictive lung function.

Baseline MIP differed significantly between the groups ($p < 0.05$; **Table 2**) Thus, both baseline MIP and sex were used as covariates in other group comparisons. There were statistically significant differences between the intervention and control groups from the first through fourth training weeks ($p < 0.001$). The mean MIP difference between baseline and final follow-up week 4 was statistically significant (32.12 ± 13.15 cmH_2O in the intervention group vs. 13.28 ± 6.59 cmH_2O in the control group).

As shown in **Table 3**, there were statistically significant within-group differences between the right diaphragmatic excursion (RDE) and left diaphragmatic excursion (LDE) (both, $p < 0.001$). The mean RDE after the end of week 4 was 6.84 ± 0.92 cm in the intervention group vs 5.57 ± 0.95 cm in the control group; the mean LDE was 6.48 ± 0.78 cm in the intervention group vs 5.33 ± 0.90 cm in the control group. Mean baseline to final follow-up week 4 differences for both diaphragmatic excursions were statistically significant: 2.09 ± 0.29 cm vs. 0.59 ± 0.48 cm ($p < 0.001$) for RDE and 2.06 ± 0.39 cm vs. 0.64 ± 0.51 cm ($p < 0.001$) for LDE.

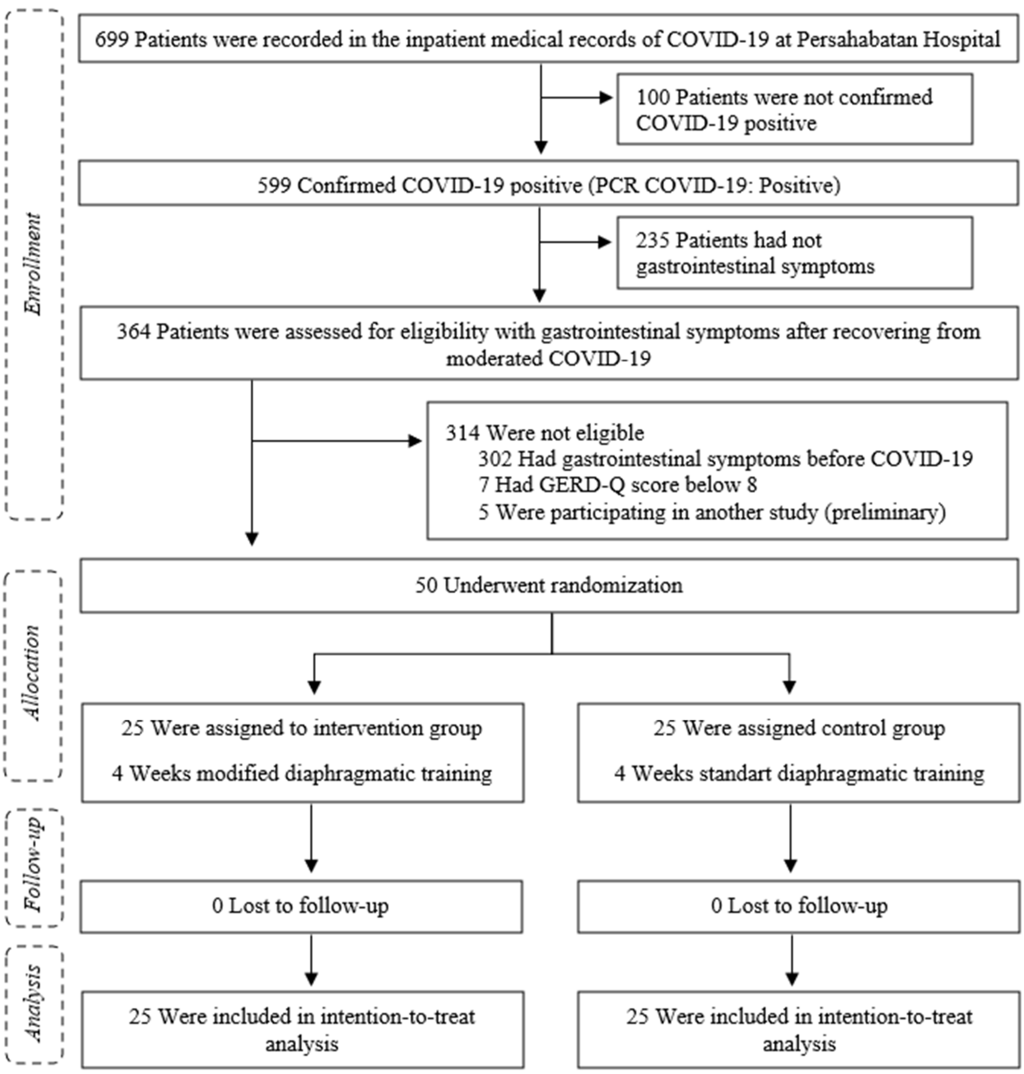

Figure 1. Flow chart of participant enrollment, allocation, follow-up, and analysis according to Consolidated Standards of Reporting Trials (CONSORT) principles.

Table 1. Baseline characteristics of participants in the intervention and control groups.

Baseline characteristic	Group	
	Intervention (n = 25)	Control (n = 25)
Age (years)	37.6 ± 9.66	36.2 ± 10.23
Sex		
Male	7 (28%)	18 (72%)
Female	18 (72%)	7 (28%)
Body mass index (kg/m^2)	27.17 ± 6.06	25.49 ± 3.91
Smoking status		
Not smoking	24 (96%)	24 (96%)
Smoking	1* (4%)	1** (4%)
Using prokinetic agent		
No	23 (92%)	25 (100%)
Yes (< 1 month)	2 (8%)	0
Comorbidity		
No comorbidity	21 (84%)	25 (100%)
Comorbidity	4*** (16%)	0
Lung function (spirometry)		
Obstructive		
No obstruction	21 (84%)	22 (88%)
Mild obstruction	4 (16%)	3 (12%)
Restrictive		
No restriction	18 (72%)	19 (76%)
Mild restriction	7 (28%)	6 (24%)
MIP (cmH_2O)	42.68 (16,46)	55.40 (20,33)
Diaphragmatic excursion (cm)		
RDE	4.75 ± 0.98	4.97 ± 0.93
LDE	4.42 ± 0.86	4.70 ± 0.85
GERDQ Score	10.44 ± 2.00	8.64 ± 0.57

Data reported as mean ± SD or numbers (%).
*Moderate Brinkman index: 352.0; **Moderate Brinkman index: 350.0; ***Controlled asthma

Table 2. Between-group comparisons of weekly MIP values.

	Intervention group mean ± SD	Control group mean ± SD	Adjusted difference* (95% CI)	P value
Baseline	42.68 ± 16.46	55.40 ± 20.33		0.019
1st week	55.68 ± 17.23	58.52 ± 21.23	11.84 (7.31 to 16.38)	<0.001*
2nd week	64.48 ± 18.94	62.40 ± 21.34	17.03 (11.11 to 22.94)	<0.001*
3rd week	70.12 ± 20.11	64.76 ± 21.16	22.08 (15.21 to 28.95)	<0.001*
Final follow-up week 4	74.80 ± 20.33	68.68 ± 21.25	22.39 (15.54 to 29.25)	<0.001*

*Generalized linear model, adjusted for baseline MIP and sex

Table 3. Within-group comparison of diaphragmatic excursion values.

	Intervention group	Control group	Adjusted difference** (95% CI)	P value
RDE				
Baseline	4.75 ± 0.98	4.97 ± 0.93	–0.39 (–0.99 to 0.21)	0.416
Final follow-up week 4	6.84 ± 0.92	5.57 ± 0.95	1.15 (0.56 to 1.75)	<0.001**
Change between time	2.09 ± 0.29*	0.59 ± 0.48*		<0.001**
LDE				
Baseline	4.42 ± 0.86	4.70 ± 0.85	–0.42 (–0.96 to 0.11)	0.260
Final follow-up week 4	6.48 ± 0.78	5.33 ± 0.90	1.01 (0.48 to 1.54)	<0.001**
Change between time	2.06 ± 0.39*	0.64 ± 0.51*		<0.001**

*Bonferroni correction generalized linear model
**Generalized linear model, adjusted for sex

There was a statistically significant between-group difference in baseline GERDQ score ($p < 0.001$; **Table 4**). Thus, we used baseline GERDQ score and sex as covariates in other group comparisons. GERDQ scores during the first, second, and third weeks did not differ significantly. During week four, there was a significant GERDQ score difference between the intervention (1.84 ± 2.17) and control (3.32 ± 1.49) groups ($p < 0.001$). The mean GERDQ score post- to pre-intervention difference was –8.60 ± 3.08 for the intervention group and –5.32 ± 1.41 for the control group.

DISCUSSION

This study found that 4-week MDT was effective for improving GERDQ score, diaphragmatic excursion, and MIP in adults with GERD after COVID-19 infection. Bogariu et al. described potential disabilities among COVID-19 survivors, particularly in the respiratory and gastrointestinal systems.[1] According to Hosseini et al., diaphragmatic breathing exercises can help reduce gastric reflux symptoms and improve quality of life over time.[5]

According to a statement by the American Thoracic Society, respiratory muscle function can be assessed with a portable, handheld oral respiratory pressure meter (MicroRPM, CareFusion Micro Medical, Kent, United Kingdom) to test MIP, and sonography can be used to test diaphragmatic excursion.[11]

Bostanci et al. reported an improvement in MIP among healthy male smokers after training for four weeks with a targeted IMT load.[12] According to Iwakura et al., the minimal clinically important difference for MIP is 17.2 cmH2O.[8] Herein, MIP increased significantly in both groups, with a greater improvement in the intervention group 75,26% (32.12 ± 13.15) compared with the control group 23,97% (13.28 ± 6.59; $p < 0.001$).

Ultrasound is a well-understood, rapid, noninvasive procedure used to assess diaphragmatic excursion in a variety of settings.[13] The lower normal limit for a diaphragmatic excursion during maximal inspiratory effort is 3.6 cm in women and 4.7 cm in men.[11] Cheng et al. found that diaphragmatic training significantly impacts diaphragmatic excursion in nonobese male patients with chronic obstructive pulmonary disease.[14] Diaphragmatic excursion herein improved in both the intervention and control groups 44% vs 11,87% (2.09 ± 0.29 and 0.59 ± 0.48, respectively, for RDE; 46,61% vs 13,62% (2.06 ± 0.39 and 0.64 ± 0.51), respectively, for LDE; both $p < 0.001$).

GERDQ score ≥ 8 indicates a diagnosis of GERD symptoms.[15] The crural diaphragm, which is affected by systemic and local inflammation during COVID-19, may weaken LES integrity and worsen GERD symptoms.[3] Diaphragmatic training may thus strengthen the crural diaphragm and improve both GERD symptoms and GERDQ scores. At the first weekly follow-up, both intervention and control group showed improvements compared to their baseline scores. Intervention group exhibited a substantial increase of 3.36, and the control group also improved, with a change of 2.40. In the subsequent weeks, intervention group's progress continued, with changes of 2.28, 1.60, and 1.36 for the 2nd, 3rd, and final weeks, respectively. The control group maintained a consistent improvement with changes of 1.08, 1.24, and 0.6 for the same weekly periods. Herein, there was a significant improvement in GERDQ score after diaphragmatic training, with a mean change

Table 4. Between-group comparison of weekly GERDQ scores.

	Intervention group mean ± SD	Control group mean ± SD	Adjusted difference* (95% CI)	P value
Baseline	10.44 ± 2.00	8.64 ± 0.57		<0.001
1st week	7.08 ± 2.14	6.24 ± 1.17	–0.78 (–1.77 to 0.21)	0.119*
2nd week	4.80 ± 1.96	5.16 ± 1.60	–1.09 (–2.36 to 0.18)	0.091*
3rd week	3.20 ± 2.53	3.92 ± 1.41	–0.81 (–2.31 to 0.68)	0.279*
Final follow-up week 4	1.84 ± 2.17	3.32 ± 1.49	–1.72 (–3.09 to –0.35)	0.015*

*Generalized linear model, adjusted for GERDQ score baseline and sex

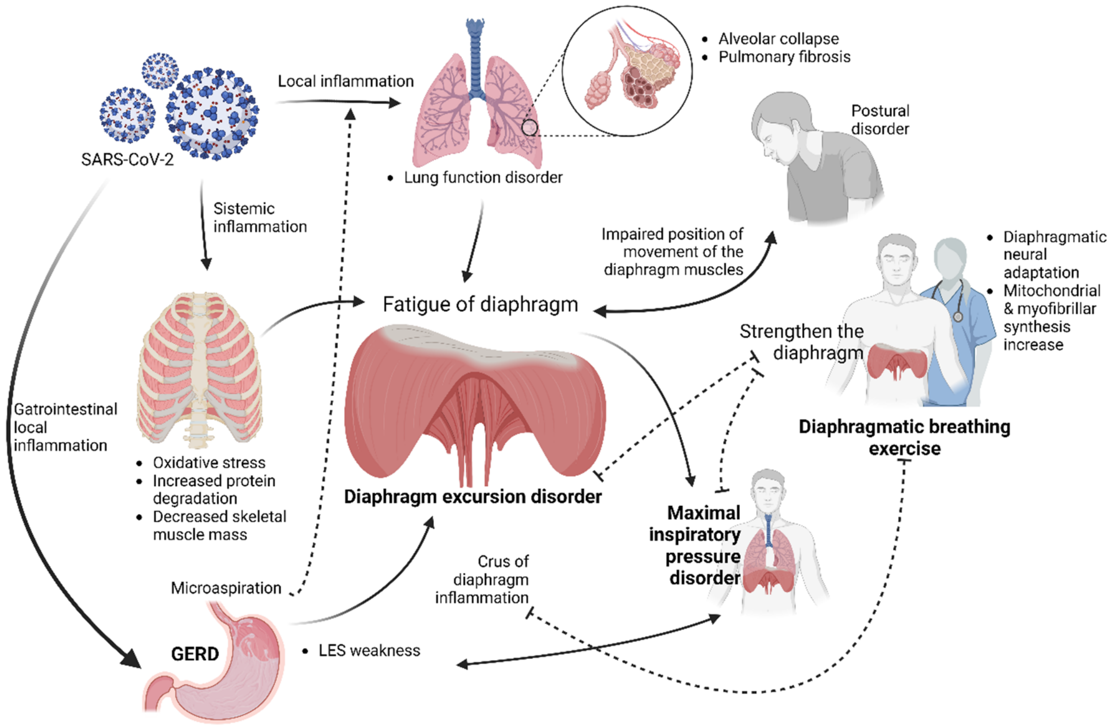

Figure 2. Mechanism of Diaphragm Exercise Therapy Effects in COVID-19 Patients with GERD Assessed by Maximum Inspiratory Pressure, Diaphragm Excursion, and GERDQ Score

of 8.6 ± 3.08 in the intervention group and 5.32 ± 1.41 in the control group (both $p < 0.001$). This finding may improve our understanding of the pathophysiology of GERD during and after COVID-19, and that diaphragmatic training may be therapeutic.

The administration of modified diaphragm training in post-inflammatory diaphragm dysfunction due to severe COVID-19 is expected to improve GERD symptoms (reducing GERDQ scores) by enhancing diaphragm function through improved diaphragm muscle strength, indicated by increased maximum inspiratory pressure and diaphragm excursion (**Figure 2**). The improvement in diaphragm function (particularly the crural side) is believed to increase lower esophageal sphincter tone and prevent gastroesophageal reflux. Prolonged local lung inflammation leads to a long-term effect of lung fibrosis, which continues if not treated with anti-fibrotic medication, resulting in decreased lung function.

Strengths and Limitations

There was no selection bias herein, as participation was 100% among eligible patients. The sample size was fulfilled. Randomization and concealment were adequate. Follow-up was complete, with no missing data. All baseline data were equal between the groups, except for sex and pre-intervention MIP and GERD, which differed significantly. MIP and diaphragm excursion, measurements and GERDQ scores results were validly and reliably collected by certified examiners.

Nevertheless, this study was not without several limitations. There was an unequal sex distribution between the groups. Multiple data analyses were controlled with a general linear model and Bonferroni corrections. Although the intervention duration sufficed for diaphragmatic muscle strength training, other parameters may require a longer time period to be effective.

These findings have external validity suitable for the target population and have great generalizability. MDT may be administered with video assistance and used independently by patients across healthcare contexts or as a home-based exercise.

CONCLUSION

This RCT indicates that four weeks of MDT in adults with GERD after COVID-19 infection can improve diaphragmatic excursion and MIP and decrease gastroesophageal reflux symptoms. No serious adverse events were reported in either group. These findings provide valuable insights into GERD rehabilitation management in adults after COVID-19 infection.

ACKNOWLEDGMENTS

This was a dissertation study in partial fulfillment of the requirements of the Doctoral Program of Medical Science at the Universitas Indonesia.

Appreciation to study participants, research team organizers, and examiners in this research.

CONFLICT INTERESTS

The author declares no conflict of interest in this research.

FUNDING

This study was funded by the Universitas Indonesia, Jakarta. (Hibah PUTI Q2 NKB- 1253/ UN2.RST/HKP.05.00/2022).

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