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RESEARCH ARTICLE

Exploratory evaluation of STAR and GOLD classifications in relation to physiological changes during IMT/PEP follow-up in COPD

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ABSTRACT

Exploratory evaluation of STAR and GOLD classifications in relation to physiological changes during IMT/PEP follow-up in COPD

Introduction: Inspiratory muscle training (IMT), particularly when combined with positive expiratory pressure (PEP), has been associated with improved respiratory outcomes in Chronic Obstructive Pulmonary Disease (COPD). This study aimed to explore physiological changes observed during IMT/PEP follow-up in COPD patients and to compare the associations of Global Initiative for Chronic Obstructive Lung Disease (GOLD) and Staging of Airflow Obstruction by Ratio (STAR) classifications with these changes.

Materials and Methods: Sixty-one Group E COPD patients received standard treatment and IMT/PEP therapy twice daily for 12 weeks. They were classified by GOLD and STAR systems, and assessed via pulmonary function, muscle strength, dyspnea scores, and six-minute walk test (6MWT) at baseline, week 4, and week 12. (NCT07001462).

Results: During the 12-week follow-up, significant within-patient changes were observed in Forced expiratory volume in 1 second (FEV_1), FEV_1 / Forced vital capacity, diffusing capacity for carbon monoxide (DLCO), maximal mid-expiratory flow between 25% and 75% of forced vital capacity (MEF25–75) and maximal inspiratory pressure (MIP) (all $p < 0.05$). These findings should be interpreted cautiously given the absence of a control or sham group. Dyspnea scores improved across scales (modified medical research council dyspnea, COPD Assessment Test, Borg, visual analog scale; all $p < 0.001$). STAR classification was an independent predictor of residual volume (RV) change ($p < 0.001$, $\beta = -0.660$), with strong model fit ($R^2 = 0.687$), while GOLD was not predictive ($p = 0.186$). STAR showed stronger correlations than GOLD with ΔRV ($R = -0.568$ vs. -0.506) and ΔMIP ($R = 0.495$ vs. 0.388). In multivariable regression for $\Delta 6MWT$, DLCO ($p = 0.032$) was a significant predictor.

Conclusion: In this exploratory single-arm cohort study, several physiological and symptom-related parameters changed during IMT/PEP follow-up in Group E COPD patients. STAR classification demonstrated stronger associations with selected physiological changes than GOLD classification and may warrant further evaluation in controlled studies.

Key words: COPD classification; inspiratory muscle training; pulmonary rehabilitation

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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ÖZ

KOAH'ta IMT/PEP takibi sırasında ortaya çıkan fizyolojik değişikliklerle ilişkili STAR ve GOLD sınıflamalarının keşifsel analizi

Giriş: İspiratuar kas eğitiminin (IMT), özellikle pozitif ekspiratuar basınç (PEP) ile birlikte uygulandığında, kronik obstrüktif akciğer hastalığı (KOAH)'nda solunumsal sonuçları iyileştirdiği bildirilmiştir. Bu çalışmada, KOAH hastalarında IMT/PEP takibi sırasında gözlenen fizyolojik değişikliklerin incelenmesi ve kronik obstrüktif akciğer hastalığına karşı küresel girişim (GOLD) ile orana göre hava akımı tıkanıklığının evrenmesi (STAR) sınıflamalarının bu değişikliklerle olan ilişkilerinin karşılaştırılması amaçlandı.

Materyal ve Metod: Çalışmaya Grup E, KOAH tanılı 61 hasta dahil edildi. Hastalara standart tedaviye ek olarak 12 hafta boyunca günde iki kez IMT/PEP tedavisi uygulandı. Hastalar GOLD ve STAR sınıflamalarına göre değerlendirildi. Başlangıçta, dördüncü haftada ve 12. haftada solunum fonksiyon testleri, solunum kas gücü ölçümleri, dispne skorları ve altı dakika yürüme testi (6DYT) uygulandı (NCT07001462).

Bulgular: On iki haftalık takip süresince birinci saniyedeki zorlu ekspiratuar hacim (FEV_1), FEV_1 /zorlu vital kapasite, karbonmonoksit difüzyon kapasitesi (DLCO), zorlu hayati kapasitenin %25 ila %75'i arasındaki maksimum ekspirasyon ortası akım hızı (MEF25–75) ve maksimum nefes alma basıncı (MIP) değerlerinde hasta içi anlamlı değişiklikler saptandı (tüm $p < 0,05$). Bununla birlikte, kontrol veya yalancı tedavi grubunun bulunmaması nedeniyle bu bulgular dikkatli yorumlanmalıdır. Dispne skorlarında da tüm ölçeklerde (Modifiye Tıbbi Araştırma Konseyi, KOAH değerlendirme testi, Borg ve görsel analog skala) anlamlı iyileşme gözlemlendi (tüm $p < 0,001$). STAR sınıflaması, rezidüel volüm (RV) değişiminin bağımsız belirleyicisi olarak bulundu ($\beta = -0,660$; $p < 0,001$) ve modelin açıklayıcılığı yüksekti ($R^2 = 0,687$); buna karşın GOLD sınıflaması anlamlı bulunmadı ($p = 0,186$). STAR sınıflaması, ΔRV ($r = -0,568$ 'e karşı $-0,506$) ve ΔMIP ($r = 0,495$ 'e karşı $0,388$) ile GOLD sınıflamasına göre daha güçlü korelasyonlar gösterdi. Çok değişkenli regresyon analizinde, 6DYT değişiminin ($\Delta 6DYT$) bağımsız belirleyicisi DLCO düzeyi olarak saptandı ($p = 0,032$).

Sonuç: Bu keşifsel, tek kollu kohort çalışmasında Grup E KOAH hastalarında IMT/PEP takibi sırasında çeşitli fizyolojik ve semptomlarla ilişkili parametrelerde değişiklikler gözlemlenmiştir. STAR sınıflaması, seçilmiş fizyolojik değişikliklerle GOLD sınıflamasına göre daha güçlü ilişkiler göstermiştir. Bu bulguların doğrulanması ve klinik öneminin ortaya konulabilmesi için kontrollü çalışmalara ihtiyaç vardır.

Anahtar kelimeler: KOAH sınıflandırması; solunum kası eğitimi; akciğer rehabilitasyonu

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a prevalent and progressive respiratory disorder characterized by persistent airflow limitation and systemic manifestations. Primarily linked to tobacco exposure, COPD significantly impairs exercise capacity and quality of life (1,2). In addition to pharmacologic therapies, non-pharmacologic interventions such as pulmonary rehabilitation (PR) and respiratory muscle training are essential components of comprehensive disease management (2). Among these, inspiratory muscle training (IMT) has emerged as a promising adjunct aimed at improving inspiratory muscle function, reducing dyspnea, and enhancing physical performance (3).

IMT has shown significant benefits, particularly in COPD patients with reduced inspiratory muscle strength. When applied with adequate intensity and duration, it improves oxygen delivery to respiratory muscles and contributes to enhanced exercise performance, reduced symptom burden, and improved gas exchange capacity (4). However, the magnitude of improvement varies considerably among individuals, indicating that patient-specific factors likely influence the response (5). Identifying which subgroups benefit most from IMT is therefore essential for targeted and effective rehabilitation strategies.

To aid in clinical phenotyping and management, classification systems such as the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and the more recently proposed Staging of Airflow Obstruction by Ratio (STAR) have been utilized to stratify disease severity (2,6). While the GOLD system combines spirometric data with symptoms and exacerbation history, the STAR classification offers a physiology-based framework centered on the Forced expiratory volume in 1 second (FEV_1)/Forced vital capacity (FVC) ratio. Recent studies have suggested that the STAR system may show closer associations with physiological impairment and selected rehabilitation-related outcomes (7,8).

The primary aim of this study was to evaluate the three-month physiological effects of IMT/positive expiratory pressure (PEP) therapy in patients with COPD and to compare how GOLD and STAR classifications predict these changes. By identifying patient characteristics associated with the most favorable response to IMT, this study aimed to enhance the precision of PR strategies. Additionally, we aimed to explore the comparative predictive value of GOLD and STAR classifications in forecasting multi-dimensional treatment outcomes in COPD.

MATERIALS and METHODS

Study design

This prospective study was conducted between July 2023 and April 2025 at the Department of Pulmonary Medicine, Atatürk University Medical Faculty Hospital. We included patients with a confirmed diagnosis of Group E COPD, as defined by the GOLD 2024 criteria. Eligibility required a post-bronchodilator FEV₁/FVC ratio below 70%, along with an modified medical research council (mMRC) score ≥2 or COPD assessment test (CAT) score ≥10, and at least two exacerbations or one COPD-related hospitalization in the previous year. Ethics approval was obtained from the Clinical Research Ethics Committee of Atatürk University Faculty of Medicine (Protocol No: B.30.2ATA.0.01.00/487; Date: 06.07.2023). All participants gave written informed consent. The study was supported by the Atatürk University Scientific Research Projects Commission (Project Number: 13001). This study was designed as a prospective single-arm pre-post intervention study, as the primary objective was to evaluate within-patient physi-

ological changes following IMT/PEP therapy and to compare the predictive performance of GOLD and STAR classifications rather than to establish treatment superiority. Therefore, the study was not designed to establish causal treatment efficacy or superiority over standard care. A flow diagram summarizing patient enrollment, exclusions, and follow-up is provided in Figure 1.

Intervention Protocol

All participants received standard pharmacologic treatment for COPD based on GOLD 2024 guidelines. Additionally, patients were instructed to perform home-based IMT combined with PEP using a dual-function device (BIO Breathe, Korea). The device consists of integrated IMT and PEP compartments with adjustable pressure dials and can be used with either a mask or a mouthpiece. Following in-person instruction by a respiratory therapist, patients initiated therapy with 15-minute sessions twice daily over a 12-week period. Pressure loads were titrated biweekly: IMT pressures started at 10 cmH₂O and were increased up to 40 cmH₂O as tolerated, while

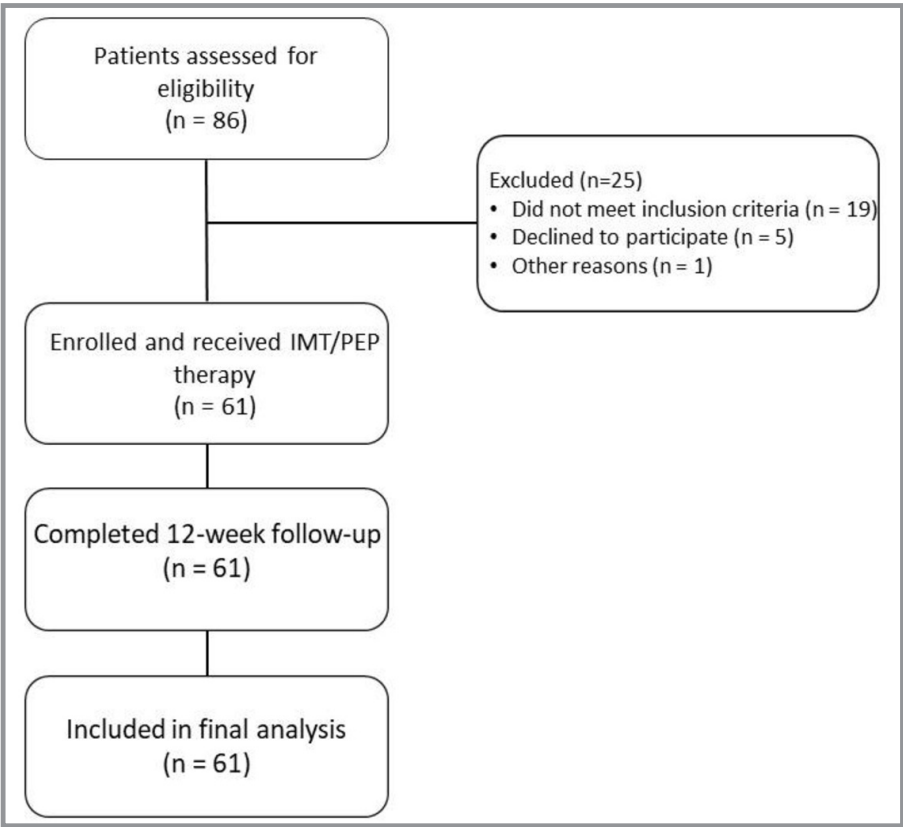


Figure 1. Flow diagram of patient enrollment, exclusion, follow-up, and inclusion in the final analysis. IMT: Inspiratory muscle training, PEP: Positive expiratory pressure.

PEP pressures ranged from 5 to 20 cmH₂O depending on airway clearance needs and individual tolerance.

Measurements and Follow-Up

Pulmonary function tests (PFT), including spirometry, whole-body plethysmography, diffusing capacity for carbon monoxide (DLCO), and respiratory muscle strength testing [maximal inspiratory pressure (MIP) and maximum expiratory pressure (MEP)], were conducted at baseline, week 4, and week 12 by a single experienced technician. Testing adhered strictly to ATS/ERS 2019 guidelines (9). Participants were advised to avoid smoking, alcohol, heavy meals, and vigorous physical activity for a defined period before testing. Ambient temperature and barometric pressure corrections were applied during calibration.

Symptom and functional assessments included the mMRC dyspnea scale, CAT, Modified Borg Scale, and a visual analog scale (VAS). The 6-minute walk test (6MWT) was performed in a standardized 30-meter corridor after a 15-minute rest. Oxygen saturation and heart rate were measured before and after the test using fingertip pulse oximetry. Participants recorded device usage in daily diaries, and biweekly telephone calls were made to reinforce adherence and monitor for adverse events.

Safety and tolerability were monitored throughout the study period. No serious adverse events related to IMT/PEP therapy were reported. The intervention was well tolerated, and no participants discontinued the program due to device-related discomfort or safety concerns.

Exclusion Criteria

Patients with unstable cardiac disease, recent thoracic or abdominal surgery, cognitive or psychiatric impairment, or any contraindication to PFT or 6MWT were excluded. Specific exclusions included severe aortic stenosis, uncontrolled arrhythmias, orthopedic disability, and room-air PaO₂ < 40 mmHg or PaCO₂ > 70 mmHg. Patients who had experienced a COPD exacerbation within the previous two weeks were deferred until clinical stability was achieved.

Outcomes

The primary outcome of the study was the change in MIP after 12 weeks of IMT/PEP therapy. Secondary outcomes included changes in residual volume (RV), 6MWT distance, dyspnea-related symptom scores, and spirometric parameters, including FEV₁, FEV₁/

FVC, and DLCO. In addition, the study assessed the predictive performance of the GOLD and STAR classifications for post-intervention physiological changes. The primary and secondary outcomes reported in this manuscript are consistent with those specified in the ClinicalTrials.gov registration (NCT07001462).

Statistical Analysis

Data analysis was conducted using SPSS version 27.0 (IBM Corp., Armonk, New York). Normality of continuous variables was assessed using the Shapiro-Wilk test. As most variables showed non-normal distributions, non-parametric tests were employed. Pre- and post-treatment comparisons were made using the Wilcoxon signed-rank test. Correlations between classification scores and changes in pulmonary function parameters were analyzed using Spearman's rank correlation coefficient.

As the regression analyses were intended to explore associations between baseline characteristics and treatment-related changes, the multivariable models were considered exploratory rather than confirmatory. Multicollinearity among predictors was assessed using variance inflation factor and tolerance statistics. Multivariable linear regression models were constructed to identify independent predictors of change in MIP, RV, and 6MWT distance. Covariates included baseline pulmonary metrics, classification stages, and muscle strength measures. A p-value < 0.05 was considered statistically significant throughout the analysis. Given the exploratory nature of the study and the consistency of effects across related physiological and clinical outcomes, no formal adjustment for multiple comparisons was applied.

RESULTS

Median age of the patients in our study was 59 (40-78). Forty-nine (80.3%) of the patients were male. The most common comorbidity among the patients was hypertension, observed in 15 (24.6%). According to the GOLD staging, the ratio of patients in stages 1-2-3-4 was 26.2-37.7-19.7-16.4, respectively, and according to the STAR staging, it was 26.2-24.6-24.6-24.6 (Cohen kappa value 0.344) (Table 1).

Changes in PFT, 6MWT, dyspnea and symptom assessment scales, and MIP and MEP values before and after IMT/PEP treatment are shown in Table 2. Accordingly, a statistically significant increase was observed in FEV₁/FVC, FEV₁, maximal mid-expiratory flow between 25% and 75% of forced vital capac-

Table 1. Demographic characteristics, comorbidities, and stages of patients according to GOLD and STAR

Characteristics	COPD Patients (n= 61) Median (Min-Max)
Demographic characteristics	
Age (years)	59 (40–78)
BMI (kg/m ²)	26 (18–39)
Male sex, n (%)	49 (80.3)
Comorbidities	
Hypertension, n (%)	15 (24.6)
Diabetes mellitus, n (%)	10 (16.4)
Coronary artery disease, n (%)	3 (4.9)
Cerebrovascular disease, n (%)	2 (3.3)
Disease staging	
GOLD stage (1–2–3–4), %	26.2 – 37.7 – 19.7 – 16.4
STAR stage (1–2–3–4), %	26.2 – 24.6 – 24.6 – 24.6
Agreement between GOLD and STAR classifications was assessed using Cohen's kappa coefficient ($\kappa=0.344$), indicating fair agreement. GOLD: Global obstructive lung disease, STAR: Staging of airflow obstruction by ratio.	

ity (MEF25-75), and DLCO values after treatment ($p= <0.001$, 0.001, 0.002, <0.001 respectively). A significant increase was noted only in the MIP level during muscle strength assessment ($p= <0.001$). Additionally, a significant improvement was observed in modified Borg, mMRC, VAS, and CAT scores of dyspnea and symptom assessment scales after treatment ($p= <0.001$ for all).

In the multivariable regression analysis for the change in RV (ΔRV), both STAR stage and the RV/ Total lung capacity (TLC) ratio emerged as significant independent predictors (STAR: $\beta= -0.660$, $p<0.001$; RV/TLC: $\beta= -0.526$, $p<0.001$), whereas GOLD stage and other physiological parameters were not statistically significant. The model explained approximately 68.7% of the variance in ΔRV ($R^2=0.687$) (Table 3).

The multivariable regression analysis evaluating the effects of STAR and GOLD staging, respiratory function test parameters, and respiratory muscle strength on changes in MIP (ΔMIP) following IMT/PEP therapy

Table 2. Comparison of PFT, 6MWT, MIP, MEP, dyspnea, and symptom scales of COPD patients before and after IMT/PEP

	Before IMT Treatment (n= 61) Median (Min-Max)	After IMT Treatment (n= 61) Median (Min-Max)	p
FEV ₁ /FVC	51.7 (31-70.4)	58.2 (39.1-73.3)	<0.001
FEV ₁ (Lt)	1.5 (0.92-3.6)	1.92 (0.59-3.82)	0.001
FEV ₁ (%)	56 (26-105)	77 (21-114)	<0.001
FVC (Lt)	3.1 (2.07-5.69)	3.66 (1.1-5.48)	0.09
FVC (%)	96 (52-141)	109 (31-138)	0.12
MEF25-75	18 (11-54)	30 (7-71)	0.002
RV (Lt)	3.4 (0.39-6.59)	2.84 (1.9-6.49)	0.19
RV (%)	155 (18-395)	143 (79-368)	0.11
TLC (Lt)	6.8 (3.53-10.2)	6.8 (4.43-9.9)	0.33
TLC (%)	112 (73-208)	110 (82-119)	0.2
RV/TLC (Lt)	49.1 (6.78-84.1)	47.9 (29.1-83.8)	0.28
RV/TLC (%)	138 (21-248)	119 (41.1-215)	0.14
MIP (cmH ₂ O)	50 (20-122.3)	68.1 (12.1-127.4)	<0.001
MIP (%)	54 (23-143)	74 (13-145)	<0.001
MEP (cmH ₂ O)	73.8 (12.4-144.3)	75.3 (33-161.8)	0.1
MEP (%)	53 (20-116)	56 (35-123)	0.08
DLCO (%)	82 (49-139)	103 (48-140)	<0.001
SO ₂ (%)	89 (75-94)	92 (85-97)	<0.001
Pulse (/min)	83 (55-114)	85 (70-117)	0.02
Respiratory Rate (/min)	16 (16-18)	16 (16-17)	0.9
Modified Borg Scale	5 (4-7)	4 (3-5)	<0.001
MMRC	3 (2-3)	1 (1-2)	<0.001

Table 2. Comparison of PFT, 6MWT, MIP, MEP, dyspnea, and symptom scales of COPD patients before and after IMT/PEP (continue)

	Before IMT Treatment (n= 61) Median (Min-Max)	After IMT Treatment (n= 61) Median (Min-Max)	p
MMRC	3 (2-3)	1 (1-2)	<0.001
VAS	6 (4-7)	4 (2-6)	<0.001
6MWT (meter)	361 (231-576)	401 (340-590)	0.07
CAT	20 (16-23)	17 (14-18)	<0.001

FEV₁: Forced expiratory volume in 1 second, FVC: Forced vital capacity, MEF25-75: Midexpiratory flow rate between 25% and 75%, RV: Residual volume, TLC: Total lung capacity, MIP: Maximum inspiratory pressure, MEP: Maximum expiratory pressure, DLCO: Diffusion lung capacity of carbon monoxide, MMRC: Modified medical research council dyspnea, VAS: Visual analog score, 6MWT: 6 minutes walking test, CAT: COPD Assessment Test.

is presented in Table 4. In this model, baseline MIP and the RV/TLC ratio showed significant inverse associations with Δ MIP (baseline MIP: $\beta = -0.480$, $p = 0.004$; RV/TLC: $\beta = -0.468$, $p = 0.001$), which likely

reflects a ceiling effect rather than a true predictive relationship. The model explained approximately 66.1% of the variance in Δ MIP ($R^2 = 0.661$).

Table 3. Multivariate regression analysis of STAR, GOLD staging, respiratory function test parameters, and MIP and MEP levels on RV changes after IMT treatment

Model	Unstandardized coefficients		Standardized coefficients	t	p	95.0% Confidence interval for B	
	B	Std. Error				Lower bound	Upper bound
(Constant)	4.194	1.010		4.154	<0.001	2.170	6.218
STAR stage	-0.703	0.161	-0.660	-4.367	<0.001	-1.026	-0.380
GOLD stage	0.249	0.186	0.213	1.339	0.186	-0.124	0.623
RV/TLC (Lt)	-0.015	0.004	-0.526	-4.031	<0.001	-0.022	-0.008
MIP (cmH ₂ O)	-0.009	0.007	-0.180	-1.174	0.246	-0.024	0.006
MEP (cmH ₂ O)	-0.006	0.005	-0.174	-1.334	0.188	-0.016	0.003
DLCO (%)	-0.003	0.007	-0.046	-0.376	0.709	-0.017	0.012

GOLD: Global obstructive lung disease, STAR: Staging of airflow obstruction by ratio, RV: Residual volume, TLC: Total lung capacity, MIP: Maximum inspiratory pressure, MEP: maximum expiratory pressure, DLCO: Diffusion lung capacity of carbon monoxide.

Table 4. Multivariable regression analysis of STAR, GOLD staging, respiratory function test parameters, and MIP and MEP levels on MIP change after IMT treatment

Model	Unstandardized coefficients		Standardized coefficients	t	p	95.0% Confidence interval for B	
	B	Std. Error				Lower bound	Upper bound
(Constant)	33.923	14.601		2.323	0.024	4.651	63.196
STAR stage	3.216	2.329	0.216	1.381	0.173	-1.453	7.885
GOLD stage	5.317	2.694	0.324	1.974	0.054	-0.084	10.719
RV/TLC (Lt)	-0.186	0.054	-0.468	-3.469	0.001	-0.293	-0.078
MIP (cmH ₂ O)	-0.326	0.107	-0.480	-3.032	0.004	-0.541	-0.110
MEP (cmH ₂ O)	0.143	0.068	0.283	2.104	0.06	0.007	0.279
DLCO (%)	-0.110	0.106	-0.132	-1.036	0.305	-0.323	0.103

GOLD: Global obstructive lung disease, STAR: Staging of airflow obstruction by ratio, RV: Residual volume, TLC: Total lung capacity, MIP: Maximum inspiratory pressure, MEP: maximum expiratory pressure, DLCO: Diffusion lung capacity of carbon monoxide.

Table 5. Multivariate regression analysis of STAR, GOLD staging, respiratory function test parameters, and changes in MIP and MEP levels in 6MWT after IMT treatment							
Model	Unstandardized coefficients		Standardized coefficients	t	p	95.0% Confidence interval for B	
	B	Std. Error	Beta			Lower bound	Upper bound
(Constant)	64.832	71.615		0.905	0.369	-78.747	208.410
STAR stage	-9.029	11.422	-0.150	-0.791	0.433	-31.929	13.871
GOLD stage	9.360	13.215	0.141	0.708	0.482	-17.134	35.854
RV/TLC (Lt)	0.233	0.263	0.145	0.888	0.379	-0.293	0.759
MIP (cmH ₂ O)	0.083	0.527	0.030	0.158	0.875	-0.974	1.140
MEP (cmH ₂ O)	0.239	0.333	0.118	0.719	0.476	-0.428	0.906
DLCO (%)	-1.150	0.521	-0.341	-2.206	0.032	-2.195	-0.105

GOLD: Global obstructive lung disease, STAR: Staging of airflow obstruction by ratio, RV: Residual volume, TLC: Total lung capacity, MIP: Maximum inspiratory pressure, MEP: maximum expiratory pressure, DLCO: Diffusion lung capacity of carbon monoxide.

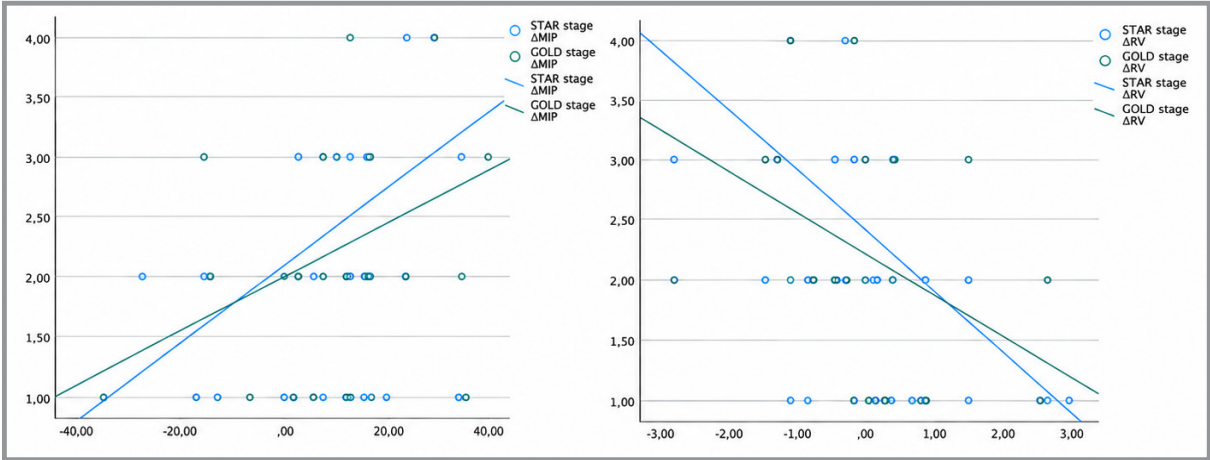


Figure 2. Scatterplots illustrating the correlations between STAR and GOLD classifications and changes in maximal inspiratory pressure (Δ MIP) and residual volume (Δ RV). Correlations were assessed using Spearman's rank correlation coefficient, with correlation coefficients (R) and corresponding p-values indicated.

The multivariable regression analysis evaluating the effects of STAR and GOLD staging, respiratory function test parameters, and respiratory muscle strength on changes in 6MWT (Δ 6MWT) following IMT/PEP therapy is presented in Table 5. In this model, DLCO emerged as the only significant independent predictor of Δ 6MWT ($\beta = -0.341$, $p = 0.032$). The model explained approximately 41.0% of the variance in 6MWT improvement ($R^2 = 0.410$).

As illustrated in Figure 2, STAR classification showed stronger correlation with both Δ MIP and Δ RV levels compared to GOLD. It was noted that the correlations of Δ MIP and Δ RV with the STAR score were statistically more significant than those of GOLD staging

($R = 0.495$, $p < 0.001$, $R = -0.568$, $p < 0.001$, $R = 0.388$, $p < 0.001$, $R = -0.506$, $p < 0.001$, respectively).

DISCUSSION

In this study, we evaluated the effects of a three-month IMT/PEP follow-up in Group E COPD patients. Significant changes were observed in MIP, whereas reductions in RV did not reach statistical significance at the group level. Although 6MWT distance numerically increased, the change did not reach statistical significance. STAR staging showed stronger associations with RV and MIP changes than GOLD classification. While the overall change in RV did not reach statistical significance at the group level, substantial inter-individual variability was observed. In this context,

STAR classification was able to discriminate patients who exhibited greater reductions in RV, supporting its potential value at the individual level rather than as a determinant of mean group change. Given the single-arm study design, these findings should be interpreted as within-patient physiological changes rather than definitive evidence of causal superiority over standard care.

COPD is a heterogeneous disease characterized by progressive airflow limitation that affects not only the respiratory system but also other organ systems, leading to reduced exercise capacity and impaired quality of life (10). As the disease progresses, symptoms such as dyspnea, cough, and sputum production intensify, accompanied by a decline in physical performance (11). While pharmacological therapies may alleviate respiratory symptoms, their effect on exercise capacity remains limited (12). This decline in exercise tolerance often results in functional dependency and social isolation. For this reason, current guidelines emphasize PR as an integral part of COPD management, particularly in Groups B and E. PR has been shown to improve exercise capacity, enhance quality of life, and increase the threshold for dyspnea (13).

Respiratory muscle training, particularly IMT, is recognized as a key component of PR in COPD. Previous studies have demonstrated that IMT improves inspiratory muscle strength, functional capacity, and pulmonary function parameters (14). Recently, devices combining IMT with PEP have been developed to enhance usability and patient adherence while maintaining airway patency during both inspiration and expiration (14). However, studies focusing on the effectiveness of IMT/PEP combinations remain scarce (15). Existing research primarily focuses on IMT alone and has shown that it reduces exertional dyspnea and increases exercise tolerance (16). Some studies have reported that while both IMT and IMT/PEP improve MIP, significant improvements in MEP occur only with IMT/PEP, likely due to alternating training of both inspiratory and expiratory muscles (15,17). These findings align with our study, which demonstrated increases in both MIP and MEP after IMT/PEP therapy, although only the MIP increase reached statistical significance (14,18). In addition, changes in FEV_1 , DLCO, exercise performance, and symptom scores suggest potential multidimensional physiological and symptomatic changes during follow-up (15). However, the magnitude of the improvements observed in FEV_1 and DLCO should be interpreted cau-

tiously. Repeated PFT may be influenced by normal measurement variability, improved familiarity with test procedures, and greater patient cooperation during follow-up. These factors may have contributed to the observed changes, particularly in the absence of a control group, and therefore the improvements cannot be attributed solely to the IMT/PEP intervention.

STAR demonstrated stronger associations with changes in RV and MIP than GOLD in both correlation and regression analyses. Given that STAR is derived from the FEV_1/FVC ratio, which closely reflects the degree of airflow obstruction, its relationships with lung mechanics-related outcomes likely represent physiological coherence rather than causal independence. In the multivariable model for RV change, STAR remained a significant independent predictor, whereas GOLD staging was not predictive. Overall, the model accounted for a substantial proportion of the variability in RV change. These observations suggest that physiology-based classification may be more sensitive to treatment-related changes in respiratory mechanics than symptom-based staging systems. As the analyses were associative in nature and did not involve formal comparisons of predictive accuracy, the findings should be interpreted as hypothesis-generating.

An additional finding of this study was that the RV/TLC ratio independently predicted both changes in RV and MIP. RV/TLC is a well-recognized marker of static hyperinflation and reflects the mechanical load imposed on the inspiratory muscles. Patients with higher baseline hyperinflation may therefore derive greater physiological benefit from interventions targeting respiratory mechanics, such as IMT/PEP. This observation further supports the role of lung volume-based parameters in identifying patients most likely to respond to targeted respiratory muscle training.

Although RV is not routinely considered a primary target in COPD rehabilitation, reductions in hyperinflation are closely associated with improvements in dyspnea, inspiratory muscle function, and exercise tolerance. From this perspective, the ability of STAR to identify patients who experience greater reductions in RV may have practical implications for identifying individuals more likely to show physiological changes during IMT/PEP follow-up. Significant changes were observed in MIP, MEF25–75, FEV_1/FVC , dyspnea scores, and oxygen saturation during follow-up. However, given the absence of a control

or sham group, these observations should not be interpreted as definitive evidence of treatment efficacy. In addition, reductions in RV and increases in 6MWT distance did not reach statistical significance at the group level. While the regression model for 6MWT demonstrated modest explanatory power ($R^2=0.410$), STAR classification showed stronger associations with selected physiological changes than GOLD classification. Taken together, these findings suggest that STAR classification may provide additional physiological insight during IMT/PEP follow-up in COPD patients.

This study has several limitations. The relatively small sample size and single-center design may limit the generalizability of the findings. In addition, the number of predictors included in the multivariable models relative to the sample size may have increased the risk of overfitting; therefore, these findings should be considered exploratory and require validation in larger cohorts. In addition, the absence of a control or sham group limits the ability to attribute observed changes specifically to IMT/PEP therapy, as repeated testing effects, natural symptom variability, or concurrent standard medical treatment may also have contributed to the findings. Adherence was monitored using patient diaries and telephone follow-up, while objective device-based adherence and achieved training pressures were not systematically recorded. Finally, the STAR classification is not yet incorporated into major international guidelines, which may affect its immediate clinical applicability. However, focusing on a clinically high-risk Group E population allowed for a more homogeneous assessment of physiological changes during IMT/PEP follow-up.

In this exploratory prospective cohort study, several physiological and symptom-related parameters changed during IMT/PEP follow-up in patients with Group E COPD. STAR classification showed closer associations with selected physiological changes than GOLD classification. Controlled studies are needed to determine whether these observations reflect true treatment-related effects and to clarify the clinical utility of STAR-guided rehabilitation strategies.

Ethical Committee Approval: This study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 51, Date: 06.07.2023).

Peer-review: Externally peer-reviewed.

CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Conception/Design : BK, AA, MBC

Analysis/Interpretation : AA, LJ

Data Acquisition: AA, LJ

Writing : BK, MBC, SMC

Revision and Correction : SMC, AA

Final Approval: BK, MBC

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