Research Article

Effectiveness of education intervention carried out by clinical pharmacist on quality of life of patients with COPD: A randomized controlled trial

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a disease affecting the patient's ability to perform normal daily physical and social activities, thereby affecting their quality of life (QoL). The aim of this study was to evaluate the effectiveness of education intervention carried out by clinical pharmacists on COPD patients' QoL. A randomized, controlled trial was conducted at Department of Screening Respiratory Function, University Medical Center, Ho Chi Minh City, Vietnam from December 2017 to May 2018. Patients aged 40 years or older, who were diagnosed with COPD and agreed to participate were included in this study. Selected patients were randomized into two groups, the intervention group (IG) and the non-intervention group (NIG). The clinical pharmacist intervention program included education about COPD knowledge, medication usage, inhaler technique, the importance of medication adherence and smoking cessation, lifestyle adjustments, recognition and prevention of possible adverse drug effects. Participants were followed up by monthly telephone calls. Patients' QoL was measured by the validated Vietnamese version of the Clinical COPD Questionnaire (CCQ). The main outcome was the difference in QoL scores between IG and NIG after the three-month follow-up. After three months, the number of patients in the IG and in the NIG was 73 and 68, respectively. The total CCQ score improved significantly after the pharmacist intervention (0.81 ± 0.54 in the IG vs. 1.24 ± 0.81 in the NIG, $p < 0.001$). Our study suggests that clinical pharmacist-led education can improve COPD patients' QoL.

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common disease of the respiratory system, which is one of the major causes of morbidity and mortality worldwide[1]. COPD continues to increase in both developed and developing countries[2]. Vietnam is predicted to have the highest COPD prevalence (6.7%) in the Asia-Pacific region[3]. Patients with COPD commonly suffer critical health problems such as reduced quality of life (QoL) and increased economic burden.

COPD has been described as "10% medication and 90% education"[4]. Management of COPD is complex, included behavioral and lifestyle changes such as smoking cessation, proper use of inhalation technique, adherence to exercise therapy and optimal,

medication adherence[5]. Pharmacists can help patients to understand their condition, the importance of prescribed medications and lifestyle changes to improve their QoL and clinical outcomes[6].

Some previous studies have demonstrated that pharmacist-led educational interventions may improve the health outcomes of patients with COPD[6]. However, in Vietnam, treatment for COPD is mainly provided by doctors or nurses, while pharmacist-led education remains largely under-used across the healthcare system. One reason is the critical shortage of the quantity and quality of pharmacists in Vietnam[7], particularly clinical pharmacists. Therefore, this study aimed to evaluate the effectiveness of education interventions implemented by pharmacists involving face-to-face and telephone counseling on COPD patients' QoL.

2. MATERIALS AND METHODS

2.1. Study settings

This was a parallel – group, randomized, controlled trial with a 3 month follow – up.

2.2. Participants

According to the following inclusion and exclusion criteria:

2.2.1. Inclusion criteria

- Patients diagnosed with COPD, who visited the Department of Screening Respiratory Function, University Medical Center, from December 15, 2017 to May 15, 2018.
- Aged 40 years or older.
- Patients who accepted to participate in the study.

2.2.2. Exclusion criteria

- Patients with insufficient personal information or did not provide a contact address.
- Patients who had an impaired cognitive situation or dementia.
- Patients who did not have or could not use a mobile phone/telephone.

2.3. Sample size

The required sample size for each group was calculated using the following formula:

$$n = \frac{2C}{ES^2} = \frac{2C}{(\frac{\Delta}{\sigma})2}$$

C = 7.85 (α = 0.05, reliability 95%, β = 0.2 and power = 0.8). σ is the standard deviation of the mean QoL score by the Clinical COPD Questionnaire. Δ is the difference in QoL score between the intervention group (IG) and the non-intervention group (NIG). According to the study of Le Khac Bao, σ was 1.0[8]. The desired Δ was 0.5. Therefore, the minimum sample size for each group was 63. In this study, we selected 92 patients in the IG and 93 patients in the NIG.

2.4. Study process

Sampling took place in the Department of Screening Respiratory Function, University Medical Center, while the follow-up was conducted via monthly phone calls. Selected patients were randomized into two groups, IG and NIG, using a list composed by the website www.random.org. Three pharmacists took part in the sampling, interviewing, and follow-up process. Before we started the study, the three pharmacists were trained on the consultation process by the principal investigator, then they passed the oral test checked by the scientific committee, including the head of clinical pharmacy department and a simulated patient to ensure the consistency between the three pharmacists.

The NIG patients only received usual hospital outpatient care by the doctors and nurses. In addition to usual care, the IG patients were educated by the clinical pharmacist about COPD knowledge, medication usage, inhaler technique, the importance of medication adherence and smoking cessation, lifestyle adjustments, recognition and prevention of possible adverse drug effects (ADEs). This information was provided based on the Global Initiative for Chronic Obstructive Lung Disease 2017 (GOLD 2017)[9] and the Guidelines for diagnosis and treatment of chronic obstructive pulmonary disease of the Ministry of Health – Vietnam (2015)[10].

The counselling sessions were carried out in IG patients at the hospital and lasted about 20 – 30 minutes. Patient education materials about medications and lifestyle changes, especially on how to use the inhaler device were prepared and distributed to patients for reinforcing the content delivered through counselling, patients were allowed to take a copy

to their home. These patients would receive follow-up telephone calls by the clinical pharmacist at the 1st, 2nd, 3rd month after the first meeting. During 20 minutes of each telephone counselling, the pharmacist asked the IG patients about the treatment effects, explained the possible ADEs, reinforced the education, recommended the patients about adjusting their lifestyles and reminded when the patients should visit their doctor.

At the beginning of the study, baseline data for all participating patients were collected by pharmacist included demographic measures, disease characteristics, respiratory medications. QoL scores based on the validated Vietnamese version of the Clinical COPD Questionnaire (CCQ)[11] were also calculated for all patients, at the beginning of the study at the hospital, and 1st, 2nd, 3rd month after they joined the study by telephone. Higher CCQ score denotes a lower quality of life.

2.5. Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS) Program, version 20.0. Patient's data were presented as mean ± S.D., median (interquartile range 25- 75%) or percentage. The comparison of percentages between the IG and the NIG were assessed using the Chi-square test. The T-test or Mann Whitney test was used to test for significant differences in QoL scores and the mean change (Δ) in QoL score three months after the intervention. The possible associated factors (intervention, age, body mass index, smoking status, pack – year, education level, living area, GOLD classification, COPD duration, combination route (yes/no), number of comorbidities, error in inhaler technique (defined as "Yes" if a participant had at least one incorrect step of inhaler usage and "No" if all steps were correct) on the change in QoL

Table 1. Baseline characteristics of patients in the two study groups

Characteristics		Group		p value
		IG (n = 92)	NIG (n = 93)	
Gender (Male)		91 (98.9%)	90 (96.8%)	0.317
Mean Age		63.80 ± 9.96	66.08 ± 8.67	0.100
40–60		31 (33.7%)	20 (21.5%)	0.064
≥ 60		61 (66.3%)	73 (78.5%)	
BMI (kg/m²)		21.49 ± 3.24	21.83 ± 3.55	0.491
Education level	Illiterate	1 (1.1%)	1 (1.1%)	0.641
	Primary	25 (27.2%)	31 (33.3%)	
	Secondary	31 (33.7%)	22 (23.7%)	
	High school	26 (28.3%)	27 (29.0%)	
	University/college	9 (9.8%)	11 (11.8%)	
	Postgrad	0 (0%)	1 (1.1%)	
Living area	Rural	58 (63.0%)	54 (58.1%)	0.488
	Urban	34 (37.0%)	39 (41.9%)	
Smoking status	Non - smoker	3 (3.3%)	4 (4.3%)	0.921
	Former smoker	63 (68.5%)	64 (68.8%)	
	Current smoker	26 (28.3%)	25 (26.9%)	
Pack - year		34.91 ± 18.59	36.73 ± 18.90	0.535
GOLD classification	A	5 (5.4%)	5 (5.4%)	0.409
	B	27 (29.3%)	29 (31.2%)	
	C	18 (19.6%)	10 (10.8%)	
	D	42 (45.7%)	49 (52.7%)	
COPD duration (year)		3.88 ± 3.80	4.63 ± 4.52	0.421
Comorbidities	Yes	78 (84.8%)	69 (74.2%)	0.075
	Hypertension	43 (46.7%)	42 (45.2%)	0.830
	Gastritis	15 (16.3%)	14 (15.1%)	0.815
	Ischemic heart disease	10 (10.9%)	12 (12.9%)	0.669
Total CCQ score		1.73 ± 0.95	1.57 ± 1.05	0.140
Symptom score		2.16 ± 1.11	1.90 ± 1.08	0.128
Functional state score		1.54 ± 1.10	1.53 ± 1.32	0.552
Mental state score		1.23 ± 1.56	0.98 ± 1.60	0.109

Mean age, BMI, pack – year, COPD duration, total CCQ score, symptom score, functional state score, mental state score were compared using t-test or Mann-Whitney test. Rates of gender, age group, education level, smoking status, GOLD classification, comorbidities were Chi – square test.
Abbreviation. BMI, Body Mass Index; GOLD, Global Initiative for Chronic Obstructive Lung Disease;

Table 2. Baseline medication usage in the two study groups

		Group		p value
		IG (n = 92)	NIG (n = 93)	
Administration	Combination route	66 (71.7%)	72 (77.4%)	0.375
	Inhalation	26 (28.3%)	21 (22.6%)	
Percentage of prescribed inhalation drug	SABA	13 (14.1%)	15 (16.1%)	0.705
	LABA	23 (25.0%)	25 (26.9%)	0.770
	LAMA	41 (44.6%)	44 (47.3%)	0.708
	SABA/SAMA	57 (62%)	59 (63.4%)	0.835
	LABA/LAMA	3 (3.3%)	2 (2.2%)	0.641
	ICS/LABA	27 (29.3%)	30 (32.3%)	0.668
	SMART	36 (39.1%)	31 (34.4%)	0.505
Percentage of prescribed oral drug	LABA	3 (3.3%)	3 (3.2%)	0.989
	OCS	4 (4.3%)	6 (6.5%)	0.527
	Theophylline	43 (46.7%)	49 (52.7%)	0.418
	Mucolytic agents	25 (27.2%)	30 (32.3%)	0.449
	Antibiotic	6 (6.5%)	11 (11.8%)	0.212
	LTRA	9 (9.8%)	8 (8.6%)	0.781
	PPI	9 (9.8%)	3 (3.2%)	0.070
Inappropriate inhaler technique		84 (91.3%)	86 (92.5%)	0.771

Rates of administration route, percentage of prescribed inhalation drug, percentage of prescribed oral drug were compared using Chi – square test (or Fisher exact test).
Abbreviation. SABA, Short-Acting Beta-Agonists; LABA, Long-Acting Beta-Agonists; LAMA, Long Acting Muscarinic Antagonist; SAMA, Short Acting Muscarinic Antagonist; ICS, Inhaled corticosteroids; SMART, Single Maintenance and Reliever Therapy; OCS, Oral corticosteroids; LTRA, Leukotriene Receptor Antagonists; PPI, Proton Pump Inhibitors.

scores was evaluated by multivariate linear regression analysis. Results were presented as Per Protocol (PP) analysis for the remaining sample after 3-month follow-up. We also considered an Intention-to-treat (ITT) analysis with baseline characteristics of all participants at randomization. In case a patient was lost to follow up, we assumed that the QoL at the 3-month interval was unchanged. A p-value of < 0.05 was considered statistically significant.

3. RESULTS

A total of 185 patients were enrolled for our study, included 92 patients in the IG and 93 patients in the NIG. Of these, 141 patients completed follow-up (73 in IG and 68 in NIG).

Baseline characteristics of two study groups

There was no statistically significant difference between the two groups at baseline, included demographic measures and disease characteristics ($p > 0.05$). The majority were males (98.9% in IG vs. 96.8% in NIG) with low educational level (under university) and lived in rural areas. Most patients were elderly, the mean age was 63.80 ± 9.96 in IG and 66.08 ± 8.67 in NIG. The majority of the study participants were current or former smokers, the pack – years was estimated to be 34.91 ± 18.59 in IG and 36.73 ± 18.90 in NIG. IG and NIG were also matched for

duration of COPD (3.88 ± 3.80 vs. 4.63 ± 4.52), mean %FEV$_1$ (53.18 ± 20.82 vs. 54.62 ± 17.57). Most patients belonged to GOLD B or D class (75% in IG vs. 83.9% in NIG), and more than half of the participants reported different comorbidities which included hypertension, gastritis, ischemic heart disease, and other conditions (Table 1).

Medication Characteristics in the Study

The treatment medications were similar between the two groups. In this study, the combination route (e.g., the inhalation and oral route) was common (71.7% in IG vs. 77.4% in NIG). All patients in this study were prescribed inhaled medication, in which, ICS/LABA combination was the most frequently prescribed medicine (68.4% in IG vs. 66.6% in NIG), followed by SABA/SAMA and LAMA. In cases of non-inhaled drugs, theophylline and mucolytic agents were widely used. The medication usage of participants was represented in Table 2. A significantly high number of patients had at least one error in inhaler techniques (91.3% in IG vs. 92.5% in CG).

Outcomes after the 3-month follow-up

At baseline, the patients in both the IG and the NIG were found to have similar scores in QoL parameters including total CCQ scores and its domains - Symptoms, Functional state and Mental state ($p > 0.05$) (Table 1).

Table 3. Outcomes after the 3 month follow-up

Outcome after 3 months	Group		p value*
	IG (n = 73)	NIG (n = 68)	
Total CCQ score	0.81 ± 0.54	1.24 ± 0.81	**0.001**
Symptom score	1.09 ± 0.82	1.54 ± 0.97	**0.004**
Functional state score	0.85 ± 0.62	1.29 ± 0.97	**0.011**
Mental state score	0.17 ± 0.38	0.57 ± 1.13	**0.026**
Δ Total CCQ score	$(- 0.90) \pm 0.65$	$(- 0.26) \pm 0.74$	**< 0.001**
Δ Symptom score	$(- 1.05) \pm 0.90$	$(- 0.29) \pm 0.98$	**< 0.001**
Δ Functional state score	$(- 0.68) \pm 0.85$	$(- 0.18) \pm 0.86$	**0.001**
Δ Mental state score	$(- 1.03) \pm 1.42$	$(- 0.39) \pm 1.33$	**0.002**
Inappropriate inhaler technique	21 (28.8%)	66 (97.1%)	**< 0.001**

* Mann-Whitney test
Δ score = score after 3 months – baseline score

CCQ scores after the 3-month follow-up were shown in Table 3. The mean CCQ score in IG was significantly lower than that in NIG (0.81 ± 0.54 vs. 1.24 ± 0.81, $p < 0.001$). It means the QoL improved significantly after pharmacist intervention. The scores of three domains, included Symptoms, Functional state and Mental state in the IG were also significantly lower than those in NIG ($p < 0.05$). The best improvement was noted in the Mental state domain (0.17 ± 0.38 in IG vs 0.57 ± 1.13 in NIG, $p = 0.026$). In particular, the change (Δ) in QoL score in IG was significantly higher than that in the NIG, not only with respect to the total CCQ scores (($- 0.90) \pm 0.65$ in IG vs. ($- 0.26) \pm 0.74$ in NIG, $p < 0.001$) but also with respect to the three domains scores ($p < 0.05$). In addition, the result of multiple regression analysis showed that the pharmacist intervention really improved the QoL in patients with COPD ($\beta = -0.687$, $p < 0.001$) (Table 4). At the end of the trial, the percentage of patients with error in inhaler techniques was significantly lower in the IG compared to the NIG (28.8% in IG vs. 97.1% in NIG) (Table 4).

In order to investigate whether or not the loss-to-follow-up proportion (> 20%) affected our findings, we performed three analyses. In the first one, referred as ITT analysis, results of multivariate regression analysis in all patients at randomization (n = 185) showed that intervention program was associated with a positive change in QoL ($\beta = -0.540$, $p < 0.001$) (Supplemental Table 1). In the second and third analysis, we assessed if there were any differences in the baseline characteristics between remaining patients and loss-to-follow-up patients after three months in the two groups. The result showed that, no statistically differences in baseline demographic features or CCQ scores between remaining patients and loss-to-follow-up patients in IG and NIG after three months were detected (Supplemental Table 2 and 3, respectively).

4. DISCUSSION

There was no statistically significant difference between the two study groups with respect to demographic measures and disease characteristics, medication characteristics and baseline QoL scores ($p > 0.05$).

After the 3 month follow-up, the IG's mean CCQ score had clinically significant improvement (more than 0.4 points change in CCQ[12]; $p < 0.05$) when compared with the NIG's. The QoL improvement in the IG had been shown in all three domains (Symptoms, Functional state and Mental state) of the CCQ scores ($p < 0.05$). The results of multivariate linear regression also reaffirmed the positive relationship between a pharmacist's education and intervention and an improvement in a patient's QoL ($p < 0.001$). As a result, this study has demonstrated the effectiveness of a pharmacist's consultation in improving QoL of COPD patients.

Table 4. Factors associated with the change in QoL scores after the 3-month follow-up with PP analysis

Factor	Changes in QoL scores (Δ)	β	p value*
Intervention		- 0.691	**< 0.001**
Combination route	Δ total CCQ score	- 0.375	**0.010**
Current/Former smoker		0.836	**0.013**

The factors, including age, body mass index, pack – year, education level, living area, GOLD classification, COPD duration, number of comorbidities, error in inhaler technique, that did not associate with the change in QoL were not mentioned in the table 4. *Multivariate linear regression

In some previous studies, Khdour et al.[13], Wei et al.[14], Xin et al.[15], Suhaj et al.[16] had also reached a similar conclusion about the value of clinical pharmacist-led patient education. All these authors used St George's Respiratory Questionnaire (SGRQ) to access COPD patients' QoL. The SGRQ is an airways disease-specific questionnaire that examines three domains: symptoms (8 items), activity (16 items), and impacts (26 items). Ställberg[17] showed that CCQ and SGRQ overall scores correlated strongly (r = 0.84). The correlation between Symptoms domains of SGRQ and CCQ was moderately (r = 0.70). There was also a good correlation between the Impacts and Mental State domains. They also supported that the Functional State domain of CCQ corresponds to the Activity domain of SGRQ. In our study, we used CCQ, because it is shorter and easier to complete than SGRQ, allows data to be quickly collected and processed, and is thus suitable for use in practice.

Khdour et al.[13] investigated the impact of a clinical pharmacy-led disease and medicine management programme on QoL of patients with COPD. Intervention patients received education on disease state, medications and inhaler techniques from a clinical pharmacist, while in the control group, patients received usual hospital outpatient care from doctor and nursing staff. Patients were followed up at 6 and 12 months during a scheduled visit. QoL of patients in IG was significantly improved at the 12-month follow-up point.

Wei et al.[14] investigated whether pharmaceutical care could improve health-related quality of life in patients with COPD. The clinical pharmacist was mainly responsible for individualized education and a series of telephone counselling for 6 months. At the end of the study, scores on symptoms and impacts domains in the pharmaceutical care group were significantly improved compared with those in the control group (40.68 ± 18.59 vs. 47.25 ± 20.96, p = 0.032; 32.19 ± 19.22 vs. 41.36 ± 25.66, p = 0.018, respectively).

Xin et al.[15] study was conducted in 2015 to access the impact of the pharmacist-managed clinic (PMC) on QoL in COPD patients. The PMC consisted of individualized education and a comprehensive pharmaceutical care program for patients provided by a clinical pharmacist. After 12 months, the total SGRQ scores improved significantly after the PMC intervention (42.7 ± 3.2 vs. 52.4 ± 5.2, p < 0.05), and the scores of three domains of symptoms, activities, and impacts in the PMC group were significantly improved. The best improvement was noted in the impacts domain (30.8 ± 2.4 vs. 43.2 ± 5.4, p < 0.05).

Suhaj et al.[16] study evaluated the effectiveness of clinical pharmacist intervention by laying emphasis on the importance of medication compliance, need for smoking cessation, simple exercise, proper use of inhaler devices and need for timely follow-up by pulmonary medicine department on QoL in COPD patients. The QoL score in the intervention group was significantly lower than that in the control group (60.40 vs. 68.50, respectively) (p < 0.001). This denoted a higher QoL in the intervention group.

The similarity between results of our study and other previous studies was derived from the same research design − randomized controlled trials with pharmacist's intervention, the same method intervention based on patient face-to-face education as well as the same education materials about the pathophysiology of COPD, medicine usage, inhaler technique, the importance of medication adherence, ADE recognition and prevention, and lifestyle adjustments (smoking cessation, healthy diet, exercises). Furthermore, the regularity of monitoring and reminding patients about medication usage and treatment adherence is the key to achieving effectiveness, despite a short follow-up time.

Although many previous studies supported the positive impact of pharmacists on improving the QoL of COPD patients, studies of Jarab et al.[18] and Tommelein et al.[6] yielded different results. Jarab et al.'s study showed some improvement in total SGRQ score and its subscales at the 6-month assessment in the intervention group; however, the improvement in QoL failed to reach statistical significance (p > 0.05)[17]. Meanwhile, Tommelein et al. used the EuroQol five-dimension questionnaire (EQ-5D) to accessed patient's QoL and did not find a significant difference in health status between intervention group (0.72 ± 0.24) and control group (0.73 ± 0.25) after 3 months (p = 0.19)[6]. The disagreement between these conclusions and ours may stem from dissimilarities in demographic characteristics (gender, duration of COPD, age) and frequency of patient access. In particular, while in our study, 97.8% were men, the rate of men gender was lower in Tommelein et al.'s and Jarab et al.'s studies (66.1% and 40.6%, respectively). Female patients are more

concerned about health than men, so they have complied with medications and have higher QoL from the beginning, so the intervention does not affect them much. Besides, patients in both studies had a longer duration of COPD than ours. The longer the duration of the disease, the more familiar the patient is with controlling the disease, so the effect of the intervention will not be evident. In addition, Tommelein et al's study selected patients aged 50 and older, the average age of these patients was higher than ours. The older the patient, the lower the ability to remember, the lower the effectiveness of the intervention through education. Finally, the frequency of monitoring in Tommelein et al.'s and Jarab et al.'s studies was less regular than ours. The high frequency of repeated consultation can help to increase COPD control, belief in pharmacotherapy, and optimize inhaler usage skills, therefore increase patients' QoL. In Tommelein et al. study, patients in the intervention group received a protocol-defined two-session intervention; one session at the start of the study and one session at the 1 month follow-up visit, while in Jarab et al. study, patients were only counseled at the beginning of the study and re-evaluated at the 6 month follow-up.

Our study showed that pharmacist-led counselling significantly improved QoL of COPD patients after 3 months. To the best of our knowledge, this is the first randomized controlled study in Vietnam that demonstrates the important role of patient education by clinical pharmacists on QoL of patients with COPD. The findings are envisaged to assist in the development of pharmacist advice models for prevention and management of chronic respiratory diseases in Vietnam.

In our study, in addition to pharmacist interventions, the results of multivariate regression analysis showed that a combination route and smoking status also affected patients' QoL scores in the third month. All patients in our study were prescribed inhalers, the addition of oral medication (mainly theophylline and mucolytic agents) helped improve the patient's symptoms and health condition, thereby improving patients' QoL. Former/current smoking factor reduced the QoL of COPD patients. In patients diagnosed with COPD, cigarette smoke worsened the progression of the disease with persistent respiratory inflammation, thereby leading to an increase in respiratory symptoms and lung function abnormalities. Cigarette smoke also increased secretion of mucus along with reduced lung defense mechanisms, paving the way for infection and acute exacerbations of COPD[19].

5. CONCLUSIONS

Our study demonstrated that the clinical pharmacist educational intervention, including providing knowledge about COPD, face-to-face training in inhaler technique, counselling on medicine usage and ADE prevention, as well as regular reminders about medication adherence, improved patients' QoL. Therefore, clinical pharmacist can be good support for patients in the COPD management.

6. ACKNOWLEDGMENTS

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Supplemental Table 1: Factors associated with the change in QoL scores after the 3-month follow-up with ITT analysis (n=185)

Factor	Changes in QoL scores (Δ)	β	p value*
Intervention		- 0.540	**< 0.001**
Combination route	Δ total CCQ score	- 0.257	**0.029**
Current/Former smoker		0.586	**0.037**

The factors, including age, body mass index, pack – year, education level, living area, GOLD classification, COPD duration, number of comorbidities, error in inhaler technique, that did not associate with the change in QoL were not mentioned in the Supplemental Table 1.
*Multivariate linear regression

Supplemental Table 2: Baseline characteristics of patients lost to follow-up and remaining after 3 months in the IG (n= 92)

Characteristics		Overall (n=92)	Group Loss-to-follow-up IG (n = 19)	3rd month remaining IG (n = 73)	p value
Gender (Male)		91 (98.9%)	18 (94.7%)	73 (100%)	0.050
Mean Age		63.80 ± 9.96	64.11 ± 9.44	63.73 ± 10.15	0.883
40–60		31 (33.7%)	6 (31.6%)	25 (34.2%)	0.827
≥ 60		61 (66.3%)	13 (68.4%)	48 (65.8%)	
BMI (kg/m^2)		21.49 ± 3.24	20.64 ± 2.65	21.71 ± 3.36	0.201
Education level	Illiterate	1 (1.1%)	1 (5.3%)	0 (0%)	
	Primary	25 (27.2%)	7 (36.8%)	18 (24.7%)	
	Secondary	31 (33.7%)	5 (26.3%)	26 (35.6%)	0.239
	High school	26 (28.3%)	4 (21.1%)	22 (30.1%)	
	University/ college	9 (9.8%)	2 (10.5%)	7 (9.6%)	
	Postgrad	0 (0%)	0 (0%)	0 (0%)	
Living area	Rural	58 (63.0%)	13 (68.4%)	45 (61.6%)	0.586
	Urban	34 (37.0%)	6 (31.6%)	28 (38.4%)	
Smoking status	Non - smoker	3 (3.3%)	1 (5.3%)	2 (2.7%)	
	Former smoker	63 (68.5%)	11 (57.9%)	52 (71.2%)	0.519
	Current smoker	26 (28.3%)	7 (36.8%)	19 (26.0%)	
Pack - year		34.91 ± 18.59	32.37 ± 16.28	35.58 ± 19.18	0.506
GOLD classification	A	5 (5.4%)	2 (10.5%)	3 (4.1%)	
	B	27 (29.3%)	6 (31.6%)	21 (28.8%)	0.656
	C	18 (19.6%)	4 (21.1%)	14 (19.2%)	
	D	42 (45.7%)	7 (36.8%)	35 (47.9%)	
COPD duration (year)		3.88 ± 3.80	3.66 ± 3.10	3.93 ± 3.97	0.934
Comorbidities	Yes	78 (84.8%)	14 (73.7%)	64 (87.7%)	0.131
	Hypertension	43 (46.7%)	6 (31.6%)	37 (50.7%)	0.137
	Gastritis	15 (16.3%)	3 (15.8%)	12 (16.4%)	0.946
	Ischemic heart disease	10 (10.9%)	0 (0%)	10 (13.7%)	0.087
Inappropriate inhaler technique		84 (91.3%)	17 (89.5%)	67 (91.8%)	0.751
Total CCQ score		1.73 ± 0.95	1.79 ± 1.09	1.71 ± 0.92	0.843
Symptom score		2.16 ± 1.11	2.21 ± 1.16	2.14 ± 1.10	0.817
Functional state score		1.54 ± 1.10	1.61 ± 1.20	1.52 ± 1.08	0.873
Mental state score		1.23 ± 1.56	1.34 ± 1.85	1.21 ± 1.49	0.918

Mean age, BMI, pack – year, COPD duration, total CCQ score, symptom score, functional state score, mental state score were compared using t-test or Mann-Whitney test. Rates of gender, age group, education level, smoking status, GOLD classification, comorbidities were Chi – square test.

Supplemental Table 3: Baseline characteristics of patients lost to follow-up and remaining after 3 months in the NIG (n= 93)

Characteristics		Overall (n=93)	Group		p value
			Loss-to-follow-up NIG (n = 25)	3rd month remaining NIG (n = 68)	
Gender (Male)		90 (96.8%)	25 (100%)	65 (95.6%)	0.286
Mean Age		66.08 ± 8.67	64.60 ± 9.32	66.62 ± 8.43	0.323
40–60		20 (21.5%)	6 (24.0%)	14 (20.6%)	0.723
≥ 60		73 (78.5%)	19 (76.0%)	54 (79.4%)	
BMI (kg/m^2)		21.83 ± 3.55	21.89 ± 3.10	21.81 ± 3.73	0.920
Education level	Illiterate	1 (1.1%)	0 (0%)	1 (1.5%)	0.499
	Primary	31 (33.3%)	6 (24.0%)	25 (36.8%)	
	Secondary	22 (23.7%)	9 (36.0%)	13 (19.1%)	
	High school	27 (29.0%)	8 (32.0%)	19 (27.9%)	
	University/ college	11 (11.8%)	2 (8.0%)	9 (13.2%)	
	Postgrad	1 (1.1%)	0 (0%)	1 (1.5%)	
Living area	Rural	54 (58.1%)	13 (52.0%)	41 (60.3%)	0.472
	Urban	39 (41.9%)	12 (48.0%)	27 (39.7%)	
Smoking status	Non - smoker	4 (4.3%)	1 (4.0%)	3 (4.4%)	0.987
	Former smoker	64 (68.8%)	17 (68.0%)	47 (69.1%)	
	Current smoker	25 (26.9%)	7 (28.0%)	18 (26.5%)	
Pack - year		36.73 ± 18.90	37.88 ± 16.48	36.31 ± 19.82	0.497
GOLD classification	A	5 (5.4%)	0 (0%)	5 (7.4%)	0.375
	B	29 (31.2%)	9 (36.0%)	20 (29.4%)	
	C	10 (10.8%)	4 (16.0%)	6 (8.8%)	
	D	49 (52.7%)	12 (48.0%)	37 (54.4%)	
COPD duration (year)		4.63 ± 4.52	4.40 ± 4.60	4.72 ± 4.52	0.651
Comorbidities	Yes	69 (74.2%)	18 (72.0%)	51 (75.0%)	0.769
	Hypertension	42 (45.2%)	12 (48.0%)	30 (44.1%)	0.739
	Gastritis	14 (15.1%)	2 (8.0%)	12 (17.6%)	0.249
	Ischemic heart disease	12 (12.9%)	2 (8.0%)	10 (14.7%)	0.392
Inappropriate inhaler technique		86 (92.5%)	23 (92.0%)	63 (92.6%)	0.916
Total CCQ score		1.57 ± 1.05	1.73 ± 1.01	1.51 ± 1.07	0.241
Symptom score		1.90 ± 1.08	2.11 ± 1.02	1.82 ± 1.10	0.251
Functional state score		1.53 ± 1.32	1.71 ± 1.27	1.46 ± 1.34	0.302
Mental state score		0.98 ± 1.60	1.02 ± 1.79	0.96 ± 1.54	0.996

Mean age, BMI, pack – year, COPD duration, total CCQ score, symptom score, functional state score, mental state score were compared using t-test or Mann-Whitney test. Rates of gender, age group, education level, smoking status, GOLD classification, comorbidities were Chi – square test.