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Effect of Collaboration between a Community Pharmacist and Physical Therapist on Patients with COPD

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Patients with chronic obstructive pulmonary disease (COPD) have difficulty inhaling bronchodilator medication due to dyspnea. We investigated whether collaboration between community pharmacists and physical therapists at a respiratory clinic (COLLAB) that provides breathing exercises and inhalation instructions to COPD patients resulted in improved breathing techniques and respiratory indices.

Indices including the breathing technique scores of exhalation, inhalation, inspiratory length, and breath hold (poor 0, good 8); forced expiratory volume in one second (FEV_1); COPD assessment test (CAT) score (good 0, poor 40); and six-minute walk test (6MWT) were measured at 0 and 3 months after COLLAB.

Thirty-nine patients participated in the study. The median breathing technique score improved significantly in patients with stages Ⅰ and Ⅱ COPD (0-month 6.0 vs 3-month 8.0, $P < 0.001$) and patients with stages Ⅲ and Ⅳ COPD (0-month 3.0 vs 3-month 7.0, $P < 0.001$). The median 6MWT increased to a greater extent in patients with stages Ⅰ and Ⅱ COPD and improved the breathing techniques score (4 – 8 points) more than in patients with a slightly improved score (0 – 3 points) (48 m vs 0 m, $P = 0.005$). Patients with stages Ⅲ and Ⅳ COPD also had a greater increase in the median FEV_1 (0.02 L vs –0.10 L, $P = 0.013$) and decrease in the median CAT score (–3.0 vs 1.0, $P = 0.024$).

COLLAB improved the breathing technique scores, with patients achieving significant improvement in techniques having improved clinical indices. Therefore, COLLAB is important to achieve the full effect of inhalation medication in COPD patients.

Key words —— inhalation instructions, pharmacist, physical therapist, chronic obstructive pulmonary disease

Introduction

The mortality rate of patients with chronic obstructive pulmonary disease (COPD) is high worldwide. According to a 2019 survey by the World Health Organization (https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death, 10 July, 2022), COPD is the third leading cause of death, with its mortality expected to increase as the population ages.

The treatment of COPD consists of a combination of drug and non-drug therapies such as respiratory rehabilitation and smoking cessation.[1)] Bronchodilators administered by an inhaler are the main therapeutic agents for treating COPD. However, > 50% of COPD patients have an incorrect inhalation technique, resulting in increased frequency of acute exacerbations of COPD.[2)] The factors that contribute to an incorrect inhalation technique include increased age, advanced COPD, and the absence of personal instructions from a professional regarding the correct use of the inhaler.[3, 4)] Respiratory rehabilitation consists of breathing exercises such as abdominal breathing and strength training that improve dyspnea and increase exercise tolerance.[5, 6)]

The main pathological manifestation of COPD is dyspnea due to inadequate inspiratory effort

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causing reduced inhalation of therapeutic agents.[7] We hypothesized that if breathing exercises (pursed lip breathing and abdominal breathing) given by physical therapists were combined with instructions on inhalation technique (device operation and breathing technique) provided by pharmacists, this may result in improved inhalation flow rate and ensure sufficient delivery and effectiveness of inhaled drugs. This collaboration between the physical therapists and pharmacists was defined as COLLAB. To the best of our knowledge there are no reports on the results of combining respiratory rehabilitation with inhalation training and therefore little is known on the effects of the combination on a patient's inhalation techniques and therapeutic efficacy.

The aims of the study were to evaluate whether intervention in inhalation technique based on COLLAB improved device operation and breathing techniques (exhalation, inhalation, inspiratory length, and breath hold), and to investigate differences in the degree of change in indices of therapeutic effects, such as respiratory function and respiratory symptoms, between 'well improved' and 'slightly improved' groups. Because COPD patients require different treatment strategies depending on the severity of their respiratory function,[1] we examined indices of therapeutic effectiveness, grouped according to COPD stage. We also evaluated the effect of COLLAB on respiratory function by assessing whether respiratory function changed from the time the community pharmacist provided inhalation instructions (before COLLAB) to the end of the study (after COLLAB).

Methods

1. Collaboration between pharmacists and physical therapists

The study design is shown in **Fig 1**. The study consisted of two arms: evaluation of changes in respiratory function indices before and after COLLAB (Study 1), and evaluation of changes in inhalation technique, respiratory function, and indices of therapeutic effects after COLLAB (Study 2). The study protocol was approved by the ethics committee of Tokushima Bunri University in December 2019 and January 2021 (No. R1-38 and R2-36). All patients provided written, informed consent for the study.

The patients were recruited at month 0 of COLLAB. Informed consent was provided by opting out of the FEV_1 survey before starting COLLAB, due to the survey being started after patient enrolment. Before COLLAB, inhalation instructions were given once a month at the pharmacy, while respiratory rehabilitation was conducted two to four times a month at the clinic. At the pharmacy, the pharmacist first checked the patient's inhalation technique without the use of the inhalation training device, and then provided instructions on how to use the device when experiencing inhala-

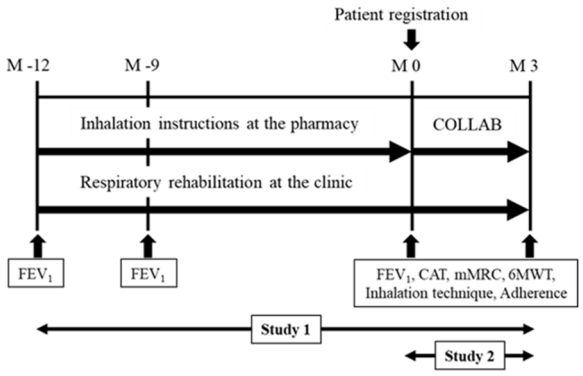

Fig 1 Overview of the study protocol
CAT: COPD assessment test, FEV_1: forced expiratory volume in one second, mMRC: modified Medical Research Council, 6MWT: six-minute walk test.

tion problems. At the clinic, the physical therapist guided the patient through practice breathing exercises such as pursed lip breathing and abdominal breathing, and exercise therapy such as lower limb strength training.

After COLLAB, the pharmacist visited the rehabilitation room at the clinic, usually monthly, to provided inhalation instructions that incorporated breathing techniques in collaboration with the physical therapist. The first step for inhalation instructions was to exhale slowly using pursed lip breathing while the second step was to inhale deeply through the mouth using abdominal breathing. The aim was to achieve sufficient inhalation for air to reach the lower lung. Specifically, the pharmacist first had the patient practice their inhalation technique using an inhalation training device and then explained the device operation and breathing technique using the device. The physical therapist then instructed the patient about posture during inhalation and had them practice breathing techniques, such as pursed lip breathing and abdominal breathing. The COLLAB instructions were repeated immediately if the pharmacist and physical therapist considered that the patient still had problems operating the device or with their breathing technique. After COLLAB, the physical therapist provided continuous respiratory rehabilitation two to four times a month.

2. Participants

The inclusion criteria for study enrolment were: 1) COPD patients who had attended the Yamaji Respiratory Medicine Clinic between February 2020 and May 2021, 2) patients who had used an inhaled drug and received respiratory rehabilitation at the clinic and inhalation instruction at Star Pharmacy for longer than 12 months, 3) patients who had not changed their inhaled drug 1 month before the start of COLLAB (–1 month), and 4) patients who provided informed consent. After COLLAB, patients were excluded from the analysis if they 1) had an acute illness (*eg*, pneumonia, influenza, or other infectious disease), 2) had a change in the type of inhaled drug, 3) did not receive medical attention, 4) had respiratory rehabilitation discontinued, and 5) did not complete the study protocol.

3. Outcomes and data analyses

(1) Study 1

FEV_1 was evaluated at –12, –9, 0, and 3 months after initiation of COLLAB, with the data analyzed as changes from –12 months.

(2) Study 2

Inhalation technique, adherence, respiratory function, respiratory symptoms, and exercise tolerance were evaluated at 0 and after 3 months of COLLAB. Inhalation technique was evaluated by distinguishing between "device operation" and "breathing technique" (**Table 1**), according to the inhalation instruction evaluation chart of the Gunma Inhalation Therapy Study Group.[8] Operation of the device was evaluated at two levels: "can do" and "cannot do". Breathing technique was evaluated using four items: "exhalation", "inhalation", "inspiratory length" and "breath hold" at three levels: "can do", "can manage" and "cannot do" with a possible total score between 0 – 8 points. Inhalation was evaluated as "inspiratory force" using a dry powder inhaler (DPI) and "inspiratory synchronization" using either a pressurized metered dose inhaler (pMDI) or soft mist inhaler (SMI). The inspiratory force was checked to determine whether the inhalation training device sounded, while inspiratory synchronization was checked to determine whether inspiration was well synchronized. Inhalation length was

Table 1 Evaluation chart for the device operation and breathing technique scores

Index	0 month	3 months
Device operation score	☐ Can do (1 point) ☐ Cannot do (0 point)	☐ Can do (1 point) ☐ Cannot do (0 point)
Breathing technique score		
Exhalation	☐ Can do (2 points) ☐ Can manage (1 point) ☐ Cannot do (0 point)	☐ Can do (2 points) ☐ Can manage (1 point) ☐ Cannot do (0 point)
Inhalation Inspiratory force Inspiratory synchronization	☐ Can do (2 points) ☐ Can manage (1 point) ☐ Cannot do (0 point)	☐ Can do (2 points) ☐ Can manage (1 point) ☐ Cannot do (0 point)
Inspiratory length	☐ Longer than 2 sec. (2 points) ☐ 1 to 2 sec. (1 point) ☐ Less than 1 sec. (0 point)	☐ Longer than 2 sec. (2 points) ☐ 1 to 2 sec. (1 point) ☐ Less than 1 sec. (0 point)
Breath hold	☐ Can do (2 points) ☐ Can manage (1 point) ☐ Cannot do (0 point)	☐ Can do (2 points) ☐ Can manage (1 point) ☐ Cannot do (0 point)

Inspiratory force is evaluated using a dry powder inhaler (DPI). Inspiratory synchronization is evaluated using a pressurized metered dose inhaler (pMDI) and soft mist inhaler (SMI).

evaluated at three levels: "longer than 2 seconds", "1 to 2 seconds", and "less than 1 second". Adherence was classified into four levels according to the report of Saito[9]: "I use the drug approximately as directed", "I sometimes delay the use of the drug", "I sometimes forget to use the drug", or "I sometimes reduce or discontinue the drug at my own discretion". We defined "I use the drug approximately as directed" as the "adherent group" and the other three responses as the "non-adherent group".

Respiratory function was assessed using spirometry to measure FEV_1 as an index of airflow limitation. Two tests were used to assess respiratory symptoms, the COPD assessment test (CAT)[10] and the modified Medical Research Council (mMRC) test.[11] The CAT uses a questionnaire to assess the effect of COPD status on the patient's health and daily life activities and includes 8 items (cough, phlegm, chest tightness, breathlessness, limited activities, confidence leaving home, sleeplessness, and energy) scored on a scale of 0 to 5. A total score of 0 indicates good function and 40 indicates poor function. The mMRC uses a questionnaire to assesses the effect of dyspnea (shortness of breath) on daily life and is graded from 0 (good) to 4 (poor). The six-minute walk test (6MWT) was used to assess exercise tolerance.

For COPD staging, the analyses were classified into Stages I and II and Stages III and IV. We defined a difference in breathing technique total score of 0 – 3 points during the 3 months of COLLAB as the "slightly improved group" and 4 – 8 points as the "well improved group". We compared the difference in FEV_1, CAT score, and 6MWT values over the 3 months of COLLAB in the two groups.

(3) Statistical Analyses

The paired data of continuous variables in the two groups were compared using the Wilcoxon signed-rank test, while comparison of three or more groups used the Friedman test and Wilcoxon signed-rank test (Holm method). Analysis of two groups of continuous values was carried out using the Mann-Whitney *U*-test, while analysis of the

corresponding frequencies used the McNemar test. The level of statistical significance was set at *P*-values < 0.05. EZR version 1.37[12] was used for the statistical analyses.

Results

A total of 44 patients were enrolled in the study, with all providing informed consent. Of these 44 patients, 5 were excluded (acute exacerbation due to pneumonia $n = 3$, discontinued respiratory rehabilitation $n = 2$) leaving 39 patients in the analysis. The characteristics of the 39 patients at 0 months of COLLAB are shown in **Table 2**. 34 patients (87.2%) were male and 5 patients (12.8%) were female, with a median (interquartile range) age of 78.0 years (72.0 – 81.5). COPD staging was stage I in 6 patients (15.4%), stage II in 14 patients (35.9%), stage III in 14 patients (35.9%), and stage IV in 5 patients (12.8%). Of the 28 (71.8%) patients who used DPI as their inhaler device, more than half (23 patients, 59.0%) used Ellipta®.

(1) Study 1

The changes in FEV_1 at –12, –9, 0, and 3 months of COLLAB are shown in **Fig 2**. The median (interquartile range) FEV_1 at each time point was 1.14 (0.87 – 1.50), 1.08 (0.86 – 1.58), 1.16 (0.82 – 1.55), and 1.25 (0.89 – 1.55), respectively. The differences between the groups were not significant ($P = 0.536$).

(2) Study 2

The device operation and breathing technique scores, FEV_1, CAT score, and 6MWT at 0 and 3 months of COLLAB, grouped according to COPD stage are shown in **Table 3**. Device operation was correct in all patients at both 0 and 3 months of COLLAB. The total scores (median and interquartile range) at 0 month for breathing technique were 6.0 (3.0 – 7.0) for Stages I and II and 3.0 (1.0 – 5.0) for Stages III and IV, with lower individual scores in Stages III and IV, especially for exhalation and inspiratory length scores with a median of 0.0. Comparison of data collected at 0 and 3 months of COLLAB showed that the total

Table 2 Patient characteristics at month 0 of COLLAB

Characteristics		Subjects (n = 39)	
Age (yr)		78.0	(72.0 – 81.5)
Gender	Male	34	(87.2)
	Female	5	(12.8)
FEV_1 (L)		1.18	(0.86 – 1.57)
COPD stage	Ⅰ	6	(15.4)
	Ⅱ	14	(35.9)
	Ⅲ	14	(35.9)
	Ⅳ	5	(12.8)
Home oxygen therapy		8	(20.5)
Type of devices			
DPI		28	(71.8)
Ellipta®		23	(59.0)
Breezhaler®		4	(10.3)
Turbuhaler®		1	(2.6)
SMI		10	(25.6)
pMDI		5	(12.8)
Use of two types of devices		4	(10.3)

The data are expressed as numbers with the percentage in parentheses. Age and FEV_1 are expressed as the median with the interquartile range in parentheses. FEV_1: forced expiratory volume in one second, DPI: dry powder inhaler, SMI: soft mist inhaler, pMDI: pressurized metered dose inhaler.

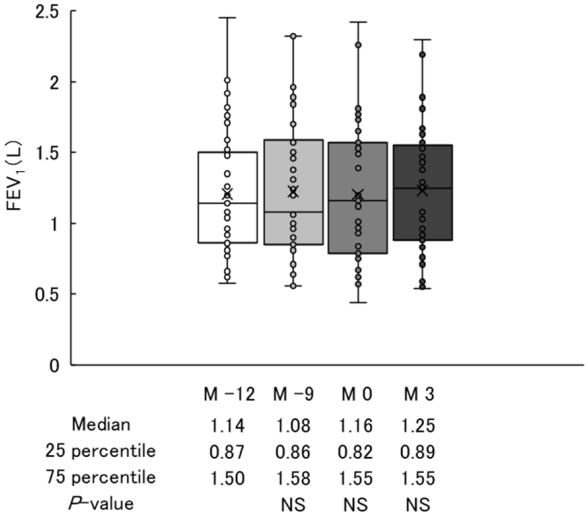

Fig 2 Changes in FEV_1 before and after COLLAB

FEV_1 was evaluated at –12, –9, 0, and 3 months after initiation of COLLAB, with the data analyzed for changes from –12 months. The *P*-values were calculated using the Friedman test and the Wilcoxon signed-rank test (Holm method). FEV_1: forced expiratory volume in one second, NA: not significant.

Table 3 Measurements of device operation, breathing technique, and therapeutic outcomes at months 0 and 3 of COLLAB, grouped by COPD stage

Index	COPD stages Ⅰ and Ⅱ (n = 20)			COPD stages Ⅲ and Ⅳ (n = 19)		
	M 0	M 3	P-value	M 0	M 3	P-value
Device operation score	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)	NA	1.0 (1.0 – 1.0)	1.0 (1.0 – 1.0)	NA
Breathing technique score						
Total	6.0 (3.0 – 7.0)	8.0 (7.0 – 8.0)	< 0.001	3.0 (1.0 – 5.0)	7.0 (5.5 – 8.0)	< 0.001
Exhalation	2.0 (1.0 – 2.0)	2.0 (2.0 – 2.0)	0.019	0.0 (0.0 – 1.5)	2.0 (2.0 – 2.0)	0.001
Inhalation	1.0 (1.0 – 2.0)	2.0 (2.0 – 2.0)	< 0.001	1.0 (0.0 – 1.0)	2.0 (2.0 – 2.0)	< 0.001
Inspiratory length	2.0 (1.0 – 2.0)	2.0 (2.0 – 2.0)	0.007	0.0 (0.0 – 1.0)	2.0 (1.0 – 2.0)	< 0.001
Breath hold	0.5 (0.0 – 2.0)	2.0 (1.8 – 2.0)	0.017	1.0 (0.0 – 1.5)	2.0 (1.0 – 2.0)	0.004
FEV_1 (L)	1.55 (1.41 – 1.76)	1.55 (1.37 – 1.72)	0.681	0.79 (0.68 – 0.98)	0.89 (0.72 – 0.10)	0.84
CAT score	9.0 (6.8 – 15.5)	6.5 (4.8 – 12.3)	0.011	14.0 (9.0 – 18.0)	10.0 (7.5 – 17.5)	0.121
6MWT (m)	312 (269 – 344)	324 (261 – 361)	0.551	312 (198 – 377)	326 (208 – 385)	0.528

The data are expressed as the median with the interquartile range in parentheses. The P-values were calculated using the Wilcoxon signed rank test. Inhalation including inspiratory force was evaluated using a dry powder inhaler (DPI) and inspiratory synchronization by a pressurized metered dose inhaler (pMDI) and soft mist inhaler (SMI). NA: not applicable, FEV_1: forced expiratory volume in one second, CAT: COPD assessment test, 6MWT: six-minute walk test.

Table 4 Adherence and mMRC at months 0 and 3 of COLLAB, grouped by COPD stage

Index			COPD stages Ⅰ and Ⅱ (n = 20)			COPD stages Ⅲ and Ⅳ (n = 19)		
			M 3		P-value	M 3		P-value
			Adherent	Non-adherent		Adherent	Non-adherent	
Adherence	M 0	Adherent	14	0	0.134	13	0	0.48
		Non-adherent	4	2		2	4	
			M 3		P-value	M 3		P-value
			Grade 0 – 1	Grade 2 – 4		Grade 0 – 1	Grade 2 – 4	
mMRC	M 0	Grade 0 – 1	8	1	0.131	5	2	1.000
		Grade 2 – 4	6	5		1	11	

The data are expressed as numbers. The P-values were calculated using the McNemar test. mMRC: modified Medical Research Council.

score for breathing technique improved significantly at each COPD stage, from a median of 6.0 to 8.0 in Stages I and II ($P < 0.001$) and from 3.0 to 7.0 in Stages III and IV ($P < 0.001$). Breathing technique categories of exhalation, inhalation, inspiratory length, and breath hold also improved significantly following COLLAB. The CAT score improved significantly from a median of 9.0 to 6.5 only in Stages I and II COPD ($P = 0.011$). FEV_1 and 6MWT did not improve significantly in any COPD stage.

Adherence and mMRC scores at 0 and 3 months of COLLAB grouped by COPD stage are shown in **Table 4**. Twelve patients (30.8%) were non-adherent, with 6 classified as "I sometimes forget to use the drug", 4 as "I sometimes delay the use of the drug", and 2 as "I sometimes reduce or discontinue the drug at my own discretion". Although the adherence score showed no significant improvement, 4 of 6 patients (66.7%) in Stages I and II and 2 of 6 patients (33.3%) in Stages III and IV improved from poor adherence at 0 months to good adherence at 3 months. The mMRC score improved from Grade 2 – 4 at 0 months to Grade 0 – 1 at 3 months in each COPD stage, although these change were not statistically significant.

The results of differences in breathing tech-

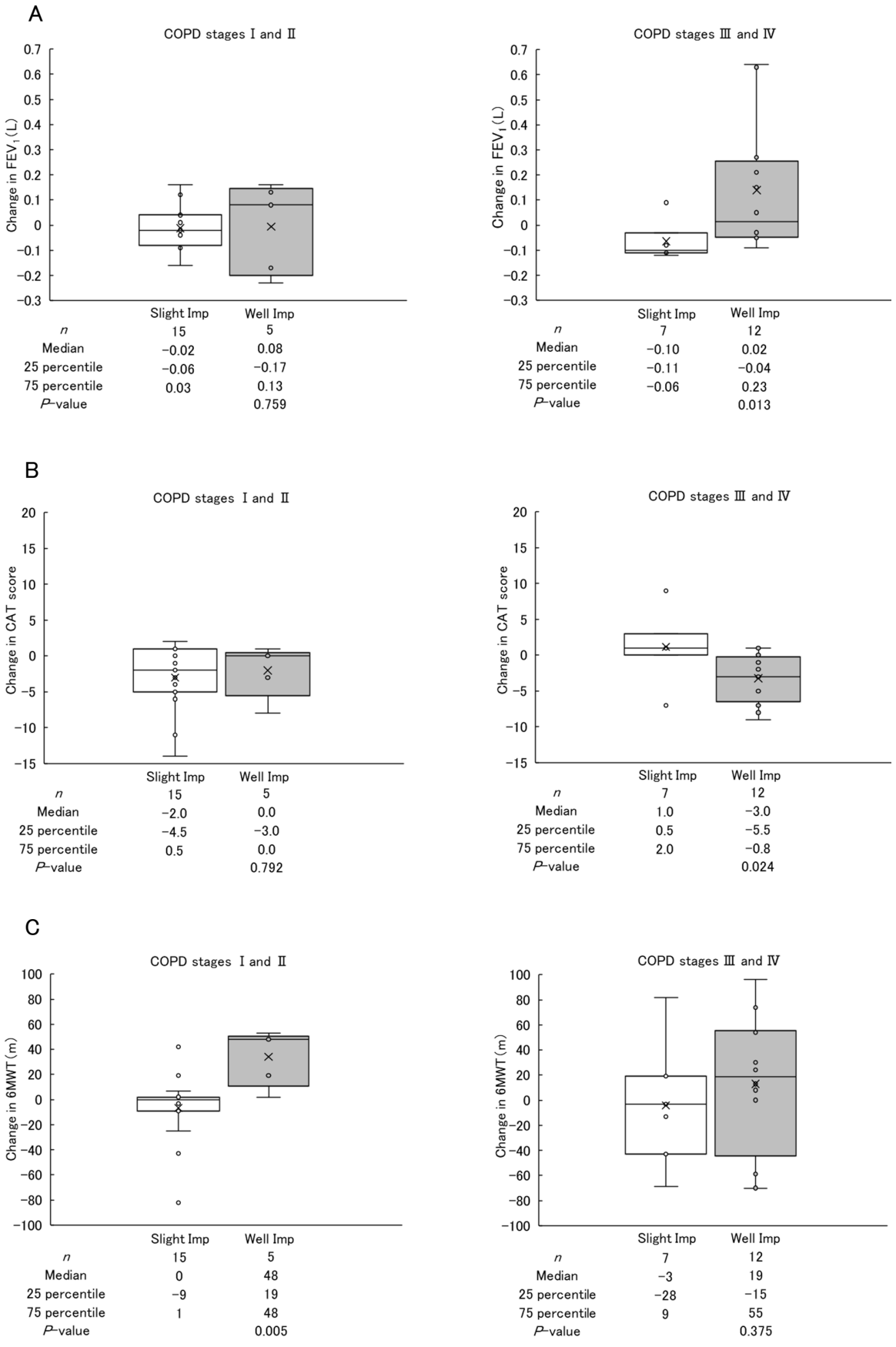

Fig 3 Changes in the clinical measurements for each breathing technique improvement group

A, B, and C show the changes in FEV_1, CAT score, and 6MWT during the 3 months of COLLAB, respectively. Slight Imp represents a difference in the breathing technique total score of 0 – 3 points and Well Imp represents a difference in the score of 4 – 8 points during the 3 months of COLLAB. The *P*-values were calculated using the Mann-Whitney *U*-test. CAT: COPD assessment test, FEV_1: forced expiratory volume in one second, Slight imp: slightly improved group, Well imp: well improved group, 6MWT: six-minute walk test.

nique total score during 0 – 3 months of COLLAB are shown in **Fig 3**. In patients with stages I and II COPD, the group with a slight improvement in breathing technique had a significant increase in median 6MWT compared with that in the well improved group (0 m vs 48 m, respectively, P = 0.005). However, no improvement was observed in FEV_1 and CAT. In patients with stages III and IV COPD, there were significant improvements in FEV_1 (–0.10 vs 0.02, P = 0.013) and CAT (1.0 vs –3.0, P = 0.024) during the three months of COLLAB, but no improvement in 6MWT.

Discussion

This study showed that COLLAB improved breathing technique scores, such as exhalation and inspiratory length, regardless of the COPD stage. Compared with the group with a slight improvement in breathing technique, the well improved group had a significant improvement in 6MWT in stages I and II COPD patients and FEV_1 and CAT scores in stages III and IV COPD patients. The device operation score showed that all the patients were able to operate the inhalation device correctly at 0 months of COLLAB, indicating that the inhalation instructions provided by the pharmacist prior to COLLAB had taught the patients how to operate the device but did not adequately teach breathing techniques. This finding emphasizes that incorporation of breathing methods in inhalation instructions is important for improving therapeutic effects.

The present study was designed to combine inhalation instructions provided by a pharmacist with breathing exercises provided by a physical therapist that included reviewing posture during inhalation, pursed lip breathing, and abdominal breathing. COPD patients may not be able to inhale an adequate dose of drug due to dyspnea. Our study showed that at the start of COLLAB, patients with advanced stages III and IV COPD had lower breathing technique scores than those with stages I and II COPD. This difference was especially apparent for exhalation and inspiratory length, with median scores of 0. At least half of the patients were not able to exhale at all, with an inspiratory length of < 1 second. In this regard, Sakano[13] reported that an inspiration length of > 1 second with appropriate inspiratory force was necessary to obtain the effect of inhaled drugs. Our data showed that even indices of therapeutic effect, such as FEV_1 and CAT score, improved in stages III and IV COPD patients who had a marked improvement in breathing technique. Compared to stage I and II COPD patients, stage III and IV COPD patients have severely impaired respiratory function. It may therefore be very important to improve breathing techniques by repeating COLLAB to ensure adequate inspiratory flow rate and the medication effectiveness of the inhaled drugs.

This study was designed to promote collaboration between a physical therapist not usually involved in inhalation instructions and a pharmacist not involved in respiratory rehabilitation so that both provided inhalation instructions. Iwashiro[14] reported on the principals of collaboration between pharmacists, nurses, and physical therapists to provide inhalation instructions, but did not mention how collaboration affected inhalation techniques and respiratory function. Sato also reported that physical therapists who provided inhalation instructions during respiratory rehabilitation improved some respiratory functions (Sato T, Effect of comprehensive pulmonary rehabilitation in the maintenance phase, 46th *J Jpn Physic Ther Ass*, May 2011, Miyazaki. doi: 10.14900/cjpt.

2010.0.DbPI1373.0.). Recently, a wide variety of inhalation devices have become available, with different devices requiring different inhalation techniques, resulting in increased misuse of inhaled drugs by patients.[15] Device operation was good prior to COLLAB for all patients in the study, although their breathing techniques subsequently improved following collaboration with the physical therapist. Collaboration between pharmacists and physical therapists is therefore essential for providing helpful instructions on device operation and breathing techniques.

The present study showed that patients with stages I and II COPD in the well improved group for breathing technique had an increase in the 6MWT 3 months after COLLAB, whereas those with stages III and IV COPD did not. Because the 6MWT as a measure of exercise tolerance is affected by both respiratory function and low extremity muscle strength,[16, 17] patients with stages III and IV COPD have severely reduced physical activity, skeletal muscle dysfunction, sarcopenia, and nutritional deficits.[18] These abnormalities would not have been expected to improve during the three-month study period.

We observed that stages I and II COPD patients were the only group with a significant improvement in CAT score during the three months of COLLAB, whereas FEV_1 and 6MWT did not improve in any COPD stage. On the other hand, no significant improvement in mMRC and adherence score was observed after three months of COLLAB. The reason for this lack of improvement in mMRC may be that shortness of breath is the most common symptom of COPD and persists longer after treatment than cough and sputum symptoms.[19] Twelve patients (30.8%) were non-adherent in the study, a rate lower than the 70% reported by a study in Germany which included patients who used inhaled drugs.[20] The current study enrolled patients who had been receiving respiratory rehabilitation for more than 12 months and may have fully understood the need for inhalers at the time of enrolment, resulting in their good adherence.

No differences were observed in FEV_1 between the period of –12 months when pharmacists provided inhalation instructions and after 3 months of COLLAB. COPD patients have a greater decline in respiratory function over time than that observed in normal subjects, with Vestbo[21] reporting a mean decline in FEV_1 of 33 mL per year and that 38% of patients lost more than 40 mL per year. In contrast, our study showed similar median and 25 and 75 percentile values for FEV_1 from –12 to 3 months that did not deteriorate, possibly reflecting the effect of medication therapy and respiratory rehabilitation. However, the study did not clarify the effect of COLLAB on FEV_1.

This study had some limitations. First, it could not prove the direct effect of COLLAB because we did not measure the inhalation technique using device operation and breathing technique scores at the pharmacy prior to COLLAB and therefore could not compare changes in these scores after COLLAB. In addition, FEV_1, the only parameter that could be compared before and after COLLAB, did not deteriorate or improve. Comparisons of clinical effects before and after COLLAB may also have been affected over time. Therefore, further research including a comparative control group is needed to evaluate the specific effects of COLLAB. Second, the study was conducted in one medical institution and one pharmacy and enrolled only a small number of patients (n = 39), which necessitated careful interpretation of the results. Third, the study did not measure the time required for inhalation

instruction. It is possible that COLLAB takes more time than inhalation instruction, which was only carried out by pharmacists at the pharmacy. Future research is needed to measure the time required for COLLAB.

Despite these limitations, the study showed that inhalation instructions incorporating breathing exercises, provided by collaboration between pharmacists and physical therapists, improved breathing techniques such as exhalation and inspiratory length regardless of the COPD stage. The study also demonstrated that FEV_1, an index of therapeutic effect, improved in patients whose breathing technique was well improved compared with those with only a slight improvement in technique. This finding indicated that collaborative intervention to improve breathing techniques may increase FEV_1 by ensuring a sufficient inspiratory flow rate of the inhaled drug. Further research is needed to confirm the effectiveness of inhalation instructions that incorporate breathing techniques provided by collaboration between pharmacists and physical therapists.

Conflict of Interest

The authors declare no conflict of interest.

References

1) The Japanese Respiratory Society (JRS), The JRS Guidelines for the Management of Chronic Obstructive Pulmonary Disease 2018, Medical Review, Tokyo, 2018.
2) Molimard M, Raherison C, Lignot S, Balestra A, Lamarque S, Chartier A, Droz-Perroteau C, Lassalle R, Moore N, Girodet PO, Chronic obstructive pulmonary disease exacerbation and inhaler device handling: real-life assessment of 2935 patients, *Eur Respir J*, 2017, **49**, 1601794. doi: 10.1183/13993003.01794-2016.
3) Wieshammer S, Dreyhaupt J, Dry Powder Inhalers: Which Factors Determine the Frequency of Handling Errors?, *Respiration*, 2008, **75**, 18-25.
4) Pothirat C, Chaiwong W, Phetsuk N, Pisalthanapuna S, Chetsadaphan N, Choomuang W, Evaluating inhaler use technique in COPD patients, *Int J Chron Obstruct Pulmon Dis*, 2015, **8**, 1291-1298.
5) Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, Hill K, Holland AE, Lareau SC, Man WD, Pitta F, Sewell L, Raskin J, Bourbeau J, Crouch R, Franssen FM, Casaburi R, Vercoulen JH, Vogiatzis I, Gosselink R, Clini EM, Effing TW, Maltais F, van der Palen J, Troosters T, Janssen DJ, Collins E, Garcia-Aymerich J, Brooks D, Fahy BF, Puhan MA, Hoogendoorn M, Garrod R, Schols AM, Carlin B, Benzo R, Meek P, Morgan M, Rutten-van Mölken MP, Ries AL, Make B, Goldstein RS, Dowson CA, Brozek JL, Donner CF, Wouters EF; ATS/ERS Task Force on Pulmonary Rehabilitation, An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation, *Am J Respir Crit Care Med*, 2013, **188**, e13-e64.
6) Rochester CL, Vogiatzis I, Holland AE, Lareau SC, Marciniuk DD, Puhan MA, Spruit MA, Masefield S, Casaburi R, Clini EM, Crouch R, Garcia-Aymerich J, Garvey C, Goldstein RS, Hill K, Morgan M, Nici L, Pitta F, Ries AL, Singh SJ, Troosters T, Wijkstra PJ, Yawn BP, ZuWallack RL; ATS/ERS Task Force on Policy in Pulmonary Rehabilitation, An Official American Thoracic Society/European Respiratory Society Policy Statement: Enhancing Implementation, Use, and Delivery of Pulmonary Rehabilitation, *Am J Respir Crit Care Med*, 2015, **192**, 1373-1386.
7) Jarvis S, Ind PW, Shiner RJ, Inhaled therapy in elderly COPD patients; time for re-evaluation?, *Age Ageing*, 2007, **36**, 213-218.
8) Majima K, What is required of pharmacists in the future, and the goal of co-operation between hospital pharmacies and community pharmacies, *J Jp Soc Resp Care Rehab*, 2013, **23**, 53-58.
9) Saito I, Medication compliance and blood pressure control, *Journal of Blood Pressure*, 2006, **13**, 1019-1025.
10) Tsuda T, Suematsu R, Kamohara K, Kurose M, Arakawa I, Tomioka R, Kawayama T, Hoshino T, Aizawa H, Development of the Japanese version of the COPD Assessment Test, *Respir Investig*, 2012, **50**, 34-39.
11) Bestall JC, Paul EA, Garrod R, Garnham R, Jones

PW, Wedzicha JA, Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease, *Thorax*, 1999, **54**, 581-586.

12) Kanda Y, Investigation of the freely available easy-to-use software 'EZR' for medical statistics, *Bone Marrow Transplant*, 2013, **48**, 452-458.

13) Sakano M, Contribution to Inhalation Therapy by Pharmacists Based on Scientific Evidence, *Jpn J Pharm Health Care Sci*, 2009, **36**, 635-647.

14) Iwashiro M, Pulmonary rehabilitation in elderly patients, *Jp Soc Resp Care Rehab*, 2008, **18**, 223-226.

15) Bosnic-Anticevich S, Chrystyn H, Costello RW, Dolovich MB, Fletcher MJ, Lavorini F, Rodríguez-Roisin R, Ryan D, Wan Yau Ming S, Price DB, The use of multiple respiratory inhalers requiring different inhalation techniques has an adverse effect on COPD outcomes, *Int J Chron Obstruct Pulmon Dis*, 2016, **12**, 59-71.

16) Gosselink R, Troosters T, Decramer M, Peripheral muscle weakness contributes to exercise limitation in COPD, *Am J Respir Crit Care Med*, 1996, **153**, 976-980.

17) Takahashi H, Factors influencing exercise capacity in patients with COPD, *J Jp Soc Resp Care*, 2002, **11**, 420-423.

18) Ueki J, Kozu R, Ohdaira T, Katsura H, Kurosawa H, Ando M, Sano Y, Sano E, Ishikawa A, Takahashi H, Kitagawa C, Tamaki A, Sekikawa K, Yoshikawa M, Tsuda T, Pulmonary Rehabilitation in Japan: A position statement from the Japan Society for Respiratory Care and Rehabilitation, the Japanese Society of Respiratory Physical Therapy, and the Japanese Respiratory Society, *J Jp Soc Resp Care Rehab*, 2017, **27**, 95-114.

19) Setoguchi Y, Izumi S, Nakamura H, Hanada S, Marumo K, Kurosaki A, Akata S, Survey to determine the efficacy and safety of guideline-based pharmacological therapy for chronic obstructive pulmonary disease patients not previously receiving maintenance treatment, *Expert Opin Pharmacother*, 2015, **16**, 2271-2281.

20) Mueller S, Wilke T, Bechtel B, Punekar YS, Mitzner K, Virchow JC, Non-persistence and non-adherence to long-acting COPD medication therapy: A retrospective cohort study based on a large German claims dataset, *Respir Med*, 2017, **122**, 1-11.

21) Vestbo J, Edwards LD, Scanlon PD, Yates JC, Agusti A, Bakke P, Calverley PM, Celli B, Coxson HO, Crim C, Lomas DA, MacNee W, Miller BE, Silverman EK, Tal-Singer R, Wouters E, Rennard SI; ECLIPSE Investigators, Changes in forced expiratory volume in 1 second over time in COPD, *N Engl J Med*, 2011, **365**, 1184-1192.