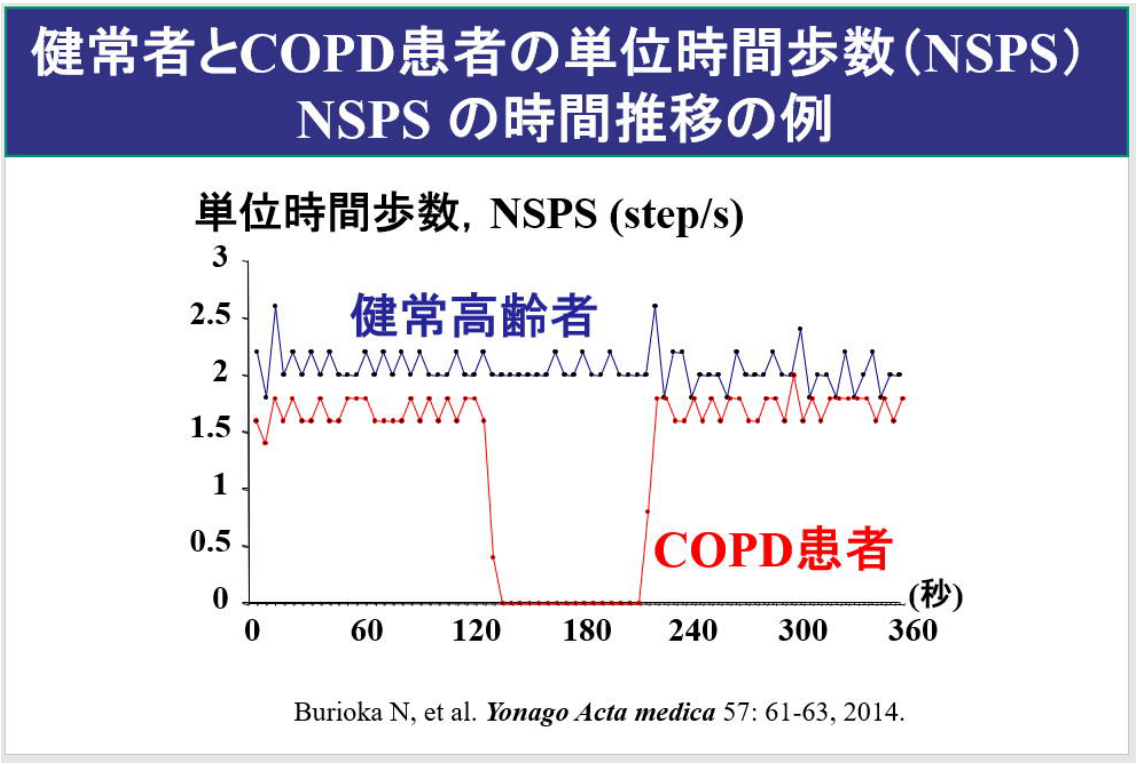
単位時間歩数の臨床応用例

時間内歩行試験が呼吸器疾患や循環器疾患患者などの運動耐容能を調べるために，広く臨床適用されている．時間内歩行試験は６分間歩行試験が一般的である．しかし，６分間歩行試験時に酸素飽和度を同時測定・確認するために，験者が被験者の横でパルスオキシメータを視認する必要があった．併歩行すると被験者の歩行ペースが験者の歩行ペースに影響されることがあった．この問題点を解決するため，短距離通信（Bluetooth）を用いてパルスオキシメータの情報を市販のタブレットに表示させるシステムを開発した．それが，「Anypal Walk」である．

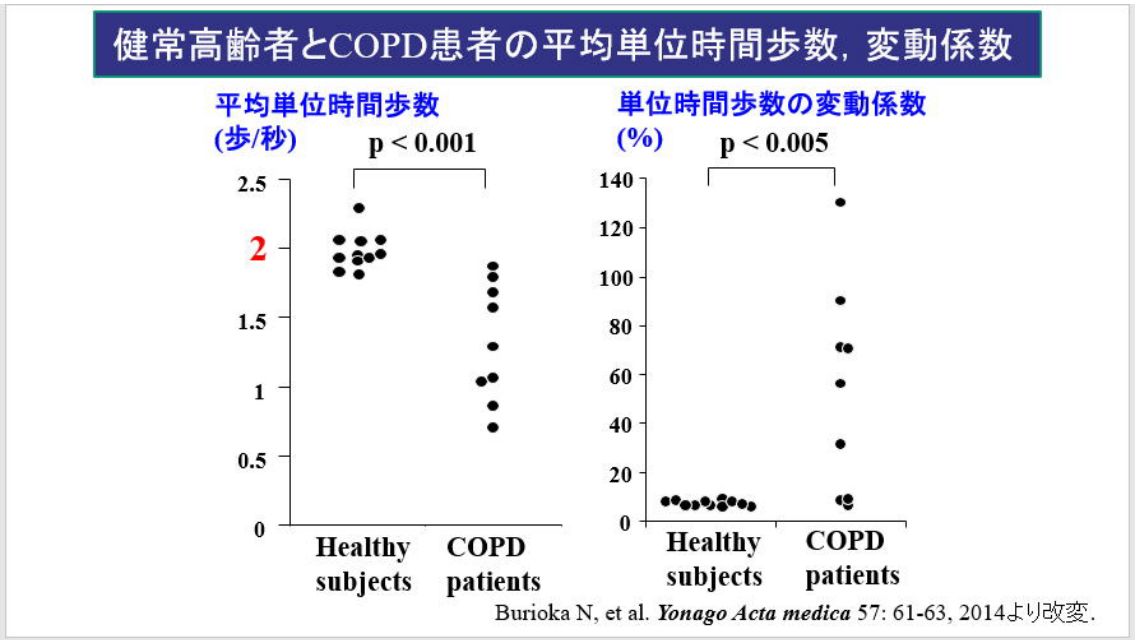
これに加えて，COPD 患者は６分間歩行試験時に息切れによって歩行停止することがある．歩行停止に関して評価法が少なかった．臨床的課題を解決するために，単位時間歩数を考案した．以下に応用例を説明する．（「Anypal Walk」は酸素飽和度，脈拍数だけではなく，３軸加速度計を内蔵しているので歩数，単位時間歩数を表示可能である）

単位時間歩数を利用すると，
・被験者の歩行パターン・歩行ペースが直感的に把握できる
・歩行試験中の停止が分かる
・歩行試験の歩行停止を含めた歩行状況，酸素飽和度の変化などをいわゆる「魚拓」のように記録を残せる．

１．健常高齢者と COPD 患者の違い

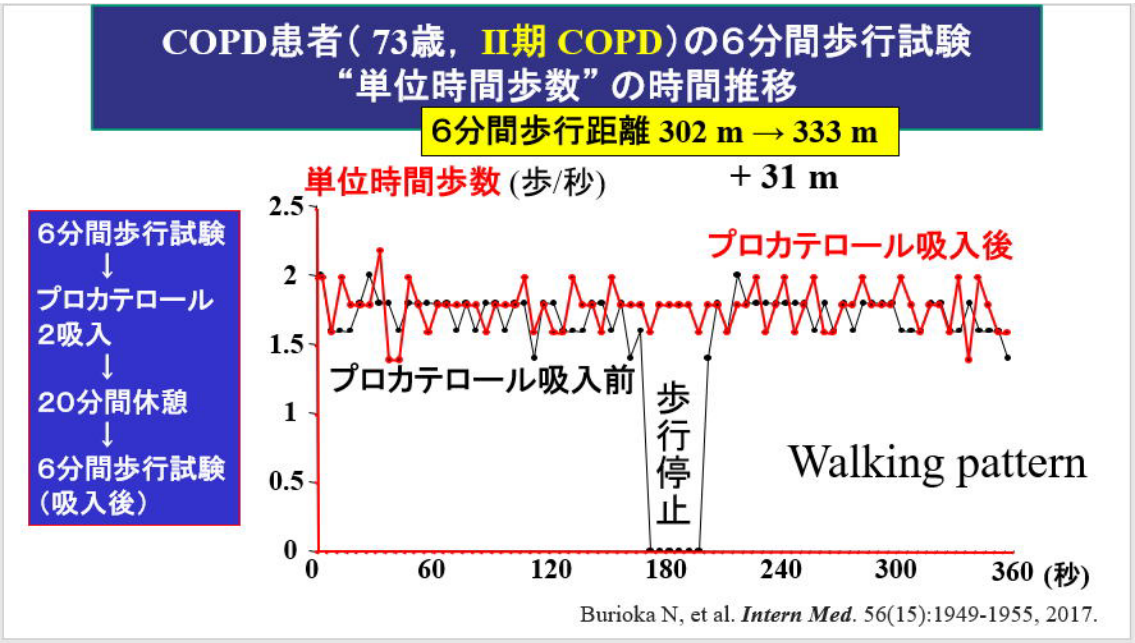


縦軸に単位時間歩数，横軸に時間をとって時間推移を描写する．
健常高齢者は，平均１秒間に２歩進む．一方 COPD 患者は１秒間の歩数が小さく，中途で息切れのため休憩して単位時間歩数が０になっている時間帯があるのが分かる．



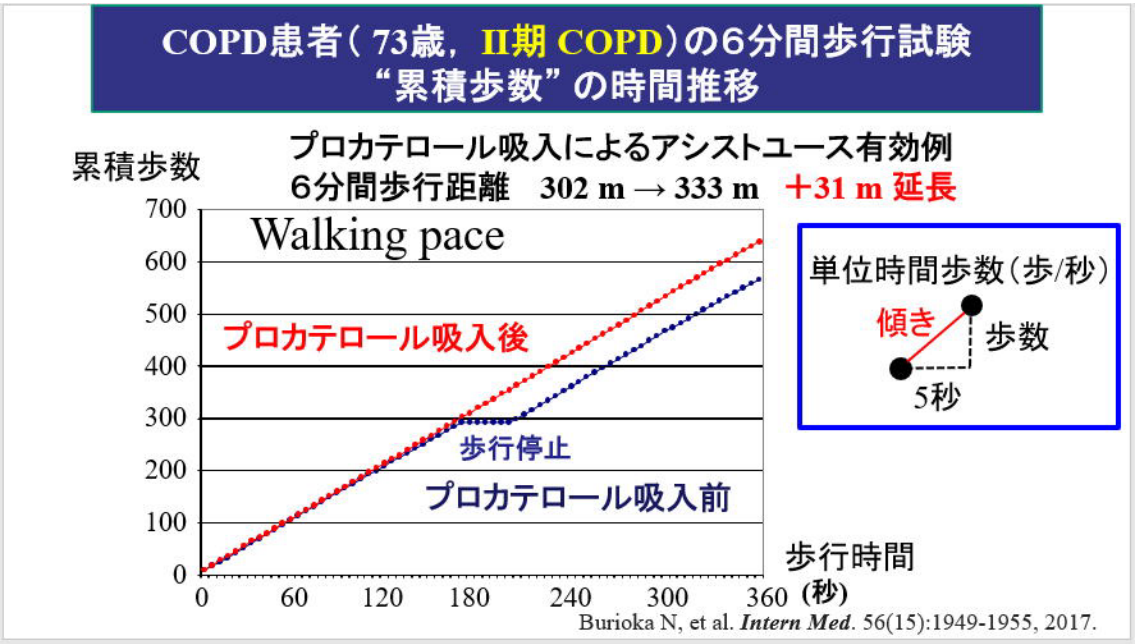
歩行停止すると単位時間歩数の変動係数が大きくなる．

２．短時間作用性気管支拡張薬，プロカテロールの吸入前後の歩行パターン，歩行ペースの違い



歩行パターンの違いが直感的に分かる．

上記症例では，プロカテロール吸入によって動的肺過膨張が改善し，歩行停止がなくなり６分間歩行距離が延びたと思われる．



縦軸を累積歩数にすると歩行ペースが客観的に分かる．歩行停止以外では傾きが吸入前後でほぼ同じであり，客観的に６分間歩行試験が行われたと推測される．

歩行停止以外の「累積歩数－時間」の傾きが吸入前後で大きく異なっている場合，６分間歩行試験に何らかの外的要因が加わった可能性も疑うべきである．

INTERNAL MEDICINE

□ ORIGINAL ARTICLE □

A Modified Method for Examining the Walking Pattern and Pace of COPD Patients in a 6-min Walk Test Before and After the Inhalation of Procaterol

Naoto Burioka[1], Sachiko Nakamoto[1], Takashi Amisaki[2], Takuya Horie[1] and Eiji Shimizu[3]

Abstract

Objective The 6-min walk test (6MWT) is a simple test that is used to examine the exercise tolerance and outcomes in patients with chronic obstructive pulmonary disease (COPD). Although the 6MWT is useful for assessing exercise tolerance, it is difficult to evaluate time-dependent parameters such as the walking pattern. A modified 6MWT has been devised to assess the walking pattern by calculating the number of steps per second (NSPS). This study was performed to investigate walking pattern of COPD patients in the modified 6MWT before and after a single inhalation of the short-acting β_2-agonist procaterol.

Methods Nine male COPD patients participated in this study. The 6MWT was performed before and after the inhalation of procaterol hydrochloride. A digital video recording of the 6MWT was made. After the 6MWT, the number of steps walked by the subject in each 5-s period was counted manually with a hand counter while viewing the walking test on the video monitor.

Results After the inhalation of procaterol, the 6-min walking distance increased significantly in comparison to baseline ($p<0.01$). The mean NSPS was also significantly increased after the inhalation of procaterol in comparison to baseline ($p<0.01$). The walking pattern was displayed on a graph of time versus NSPS, and the walking pace was shown by a graph of time versus cumulative steps.

Conclusion The analysis of the COPD patients' walking test performance and their walking pattern and pace in the 6MWT may help to evaluate the effects of drug treatment.

Key words: β_2-agonist, chronic obstructive pulmonary disease, 6-min walk test, procaterol, steps

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Introduction

The 6-min walk test (6MWT) has been used to evaluate the functional capacity and to predict mortality in patients with chronic respiratory disease (1, 2). This test assesses the maximum distance that a patient can walk during a 6-min period (3). Although the test is simple, it is useful for measuring clinical improvement in response to pulmonary rehabilitation and drug therapy (4).

Chronic obstructive pulmonary disease (COPD) is one of the most important respiratory diseases and is associated with a high mortality rate (5). Physical activity and the number of steps walked per day are strong predictors of all-cause mortality in COPD patients (6, 7). The functional status of COPD patients is examined by performing lung function tests and timed walking tests such as the 6MWT. In COPD patients, exercise causes dynamic lung hyperinflation and an increase in the end-expiratory lung volume (EELV) due to the trapping of air due to decreased elastic recoil, which occurs secondarily to the destruction of the alveoli and the narrowing of the small airways (8-10). The inspiratory capacity (IC) of COPD patients is significantly decreased during the 6MWT (11). The decrease in the IC of

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Table 1. Pulmonary Function of Male COPD Patients (n=9).

	before	after procaterol inhalation
FVC (L)	2.56 ± 0.73	2.80 ± 0.77
FEV_1 (L)	1.21 ± 0.52	1.38 ± 0.68
FEV_1/FVC (%)	46.7 ± 12.3	47.5 ± 13.3
FEV_1 %pred. (%)	56.6 ± 25.2	62.0 ± 28.1

Values are the mean ± standard deviation.

FVC: forced vital capacity

FEV_1: forced expiratory volume in one second

COPD patients was significantly attenuated and the 6-min walking distance (6MWD) was increased after the inhalation of the short-acting β_2-agonist procaterol hydrochloride in comparison to patients who inhaled a placebo (11).

However, many COPD patients cannot walk for 6 minutes without stopping and may have to rest several times during the 6MWT due to dyspnea (12). Their walking pace and resting time may influence the results of the 6MWT, because oxygen desaturation can be improved by resting. Although the conventional 6MWT is useful for assessing the general exercise tolerance, it is difficult to evaluate time-dependent parameters such as the instantaneous walking speed. A modified 6MWT has been developed to examine the walking pattern by determining the number of steps per second (NSPS) (12). In the present study, we assessed the effect of a single dose of inhaled procaterol on the improvement of the walking distance, the resting time, and the walking pattern and pace (as NSPS) in COPD patients who performed the 6MWT.

Materials and Methods

Patients

Nine male patients with COPD (72.9±6.0 years) participated in this study. Spirometry was performed before and after the inhalation of 20 μg of procaterol hydrochloride (Meptin™, Otsuka Pharmaceutical, Tokyo, Japan) using a pulmonary function testing system (Chestac-7800, Chest, Tokyo, Japan) on another day (Table 1). The severity of airflow limitation in COPD was classified according to forced expiratory volume in one second (FEV_1) after the inhalation of a bronchodilator (5). Five of the 9 patients inhaled tiotropium, 3 patients inhaled tiotropium and salmeterol, and 1 patient inhaled formoterol with budesonide, regularly. Patients who had experienced unstable angina or myocardial infarction during the previous month, those who had a resting heart rate of more than 120 bpm, a resting systolic blood pressure of more than 180 mmHg or a diastolic pressure of more than 100 mmHg, orthopedic or neurologic conditions were excluded from the study (3). The present study was approved by the ethics boards of Tottori University and Hitachi Memorial Hospital (No. 1845). All of the participants gave their written informed consent.

Study protocol

The baseline 6MWT was performed before the inhalation of procaterol. The subjects performed the baseline 6MWT and then inhaled 20 μg of procaterol using a spacer device. After resting on a chair for 20 minutes, the patients performed the 6MWT again. The 6MWT was performed in a flat corridor of 54 m in length at Tottori University Hospital or Hitachi Memorial Hospital; the other technical aspects of the 6MWT were in accordance with the published guidelines (3). Arterial blood oxygen saturation was measured by pulse oximetry (SpO_2) with a finger sensor (Pulsox 300i, Konica-Minolta, Tokyo, Japan) and was continuously recorded during the test. The pulse oximetry variables were analyzed using the DS-5 Pulsox software program (Konica-Minolta). The severity of dyspnea was subjectively assessed before and after the 6MWT using a modified Borg scale (13). It has been reported that at least 2 practice walks should be performed before the 6MWT since training influences the results of the test (14, 15). The patients performed at least 2 practice walks on another day prior to the actual test because dyspnea and fatigue could have influenced the results of the 6MWT if they had practiced on the same day. The patients were allowed to sit on a chair to rest during the test, if needed, and resumed walking themselves when they had recovered. The duration of each rest was measured with a stopwatch. All of the walking tests were recorded on digital video and the 6MWD was measured.

The calculation of the number of steps per second (NSPS)

The NSPS is a new index (12); it is defined as the steps walked in A-second period divided by A, where A is a divisor of 360. We used A=5 (5-s interval) in the present study. The mean NSPS is calculated using the following formula:

$$\text{Mean NSPS} = \frac{\lfloor total\ steps\ in\ 360 \rfloor}{360} = \frac{\lfloor total\ steps\ in\ 360 \rfloor \div 5}{360 \div 5}$$

$$= \frac{\{\lfloor steps\ in\ 0 < t \leq 5 \rfloor + \lfloor steps\ in\ 5 < t \leq 10 \rfloor + \cdots + \lfloor steps\ in\ 355 < t \leq 360 \rfloor\} \div 5}{72}$$

$$= \frac{\sum_{k=1}^{72} \{\lfloor steps\ in\ 5(k-1) < t \leq 5k \rfloor \div 5\}}{72} = \frac{\sum_{k=1}^{72} NSPS_k}{72},$$

where ⌊ ⌋ is the floor function, and $NSPS_k$ is the value of NSPS at the k-th 5-s interval (k=1,2,3,..., 72). $NSPS_k$ shows the slope of time versus the cumulative steps in 5-s (12).

The number of steps walked by a subject in each 5-s period was counted manually with a hand counter while viewing the walking test on the video monitor. The walking speed (m/s) was considered to be the average step length (m/step) × NSPS (step/s) (12). The NSPS was calculated as the number of steps walked in a 5-s period divided by 5, and this calculation was performed for 72 consecutive periods (360 s ÷ 5 s) in each subject. Because the NSPS is proportional to the walking speed, it usually decreases when a patient walks more slowly and falls to zero if the patient

Table 2. Results of the 6-min Walk Test (6MWT) before and after Inhalation of Procaterol (n=9).

	First 6MWT	Second 6MWT after procaterol inhalation	p value
6-min distance (m)	258.7 ± 124.0	293.4 ± 115.6	p<0.01 *
Total no. of steps	473.6 ± 153.9	526.1 ± 135.6	p<0.02 *
Resting HR before test (min^{-1})	91.5 ± 10.5	92.3 ± 9.1	p>0.43 *
Mean length of a step (m)	0.52 ± 0.09	0.54 ± 0.09	p>0.10 *
Mean NSPS (step/s)	1.32 ± 0.43	1.46 ± 0.38	p<0.01 *
Total resting time (s)	85 (20.3 - 149.8) †	59 (13.3 - 104.8) †	p<0.05 **
Borg scale after 6MWT	3.0 (1.8 - 4.2) †	3.0 (1.9 - 4.1) †	p>0.99 **
Lowest SpO_2 (%)	88.7 ± 5.1	88.2 ± 5.5	p>0.45 *
Mean SpO_2 (%)	91.4 ± 3.7	91.3 ± 3.8	p>0.75 *

HR: heart rate

Values are the mean ± standard deviation or median (interquartile range) †.

*: Paired t-test, **: Wilcoxon matched-pairs signed-rank test

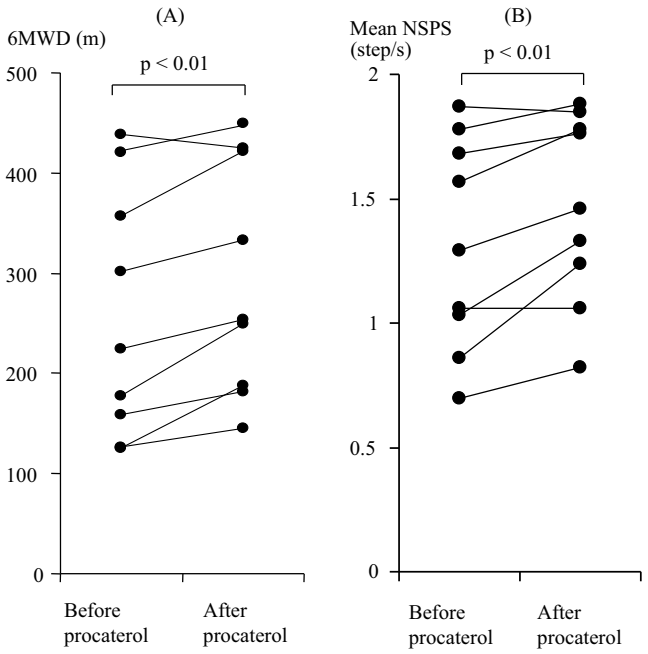

Figure 1. The 6-min walking distance (6MWD) and the mean of number of steps per second (NSPS) before and after the inhalation of procaterol. (A) The inhalation of procaterol significantly increased the mean 6MWD. (B) The mean NSPS was also significantly increased after the inhalation of procaterol.

stops walking (12).

Statistical analysis

The results are presented as the median (interquartile range) or mean ± SD. Comparisons were performed using the Wilcoxon matched-pairs signed-rank test or the paired *t*-test. The StatFlex software program was used to perform the statistical analyses (StatFlex, ViewFlex, Tokyo, Japan). p values of <0.05 were considered to indicate statistical significance.

Results

With regard to the severity of airflow limitation in our COPD patients, 3 patients were classified as Global initiative for chronic Obstructive Lung Disease (GOLD) 1 (predicted FEV_1 (%) ≥80%), 2 patients were classified as GOLD 2 (50% to <80%), 3 patient were GOLD 3 (30% to <50%), and 1 patient was classified as GOLD 4 (<30%) (5). The height, weight and body mass index of the 9 COPD patients were 1.58±0.06 m, 51.6±9.2 kg and 20.7±4.2 kg/m^2, respectively. Table 1 shows the results of a pulmonary function test before and after the inhalation of procaterol on another day. Table 2 shows the results of the 6MWT before and after the inhalation of procaterol. After a single inhalation of procaterol, the 6MWD was significantly longer in comparison to baseline (Fig. 1A). An increase of >30 m in the 6MWD is considered to be the minimal clinical important difference (MCID) for the patients with chronic respiratory disease (1, 2). After the inhalation of procaterol, the 6MWD changed by more than 30 m in 4 of the 9 COPD patients. The resting heart rate was not significantly changed in comparison to that before the 6MWT. The total number of steps in 6 minutes was significantly increased by the inhalation of procaterol, but the mean step length did not change (Table 2). Six of the 9 patients had to rest on a chair during the baseline 6MWT. The median (range) number of rests before and after the inhalation of procaterol was 1 (0-3) and 1 (0-3), respectively. Although the number of rests was almost same, the total resting time was significantly shorter after the inhalation of procaterol (Table 2). The mean NSPS showed a significant increase after the inhalation of procaterol in comparison to the baseline value (Fig. 1B). On the other hand, the lowest SpO_2 and mean SpO_2 values were not significantly different after the inhalation of procaterol. There was no significant difference in the modified Borg scale values after the 6MWT before and after the inhalation of procaterol (Table 2).

Fig. 2A shows an example of the walking pattern and

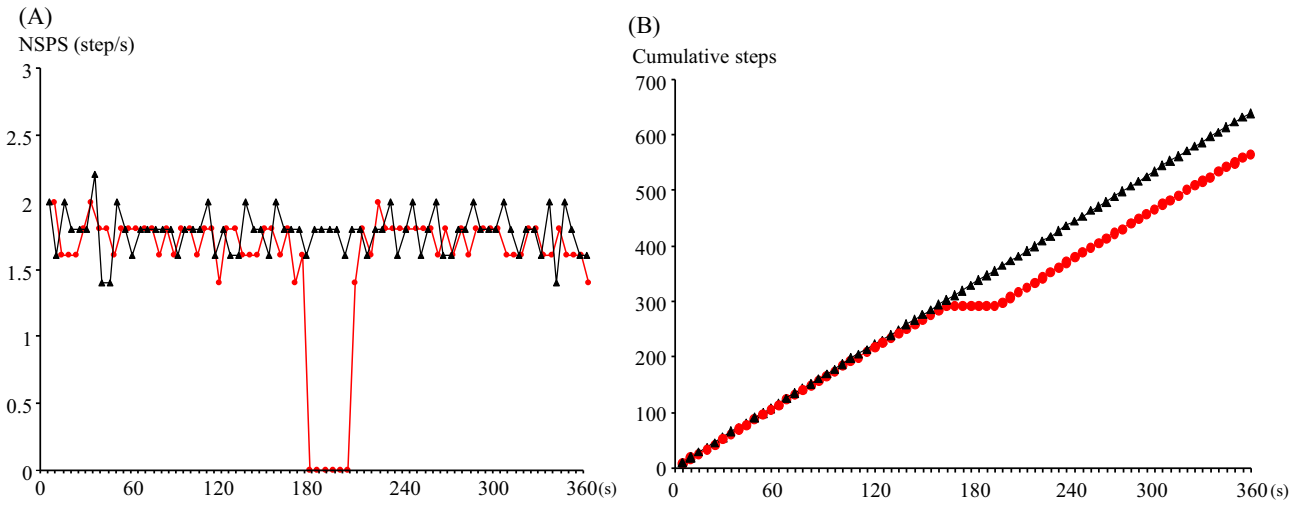

Figure 2. Determining the walking pattern and pace from the number of steps per second (NSPS) and the cumulative steps before and after the inhalation of procaterol. The patient was a 73-year-old man with COPD. Although the patient walked 302 m in the 6-min walk test (6MWT) with 32 s of rest before the inhalation of procaterol (closed circle), he could walk 332.5 m without a rest after the inhalation of procaterol (closed triangle). The walking pattern is clearly displayed on this graph of time versus NSPS (A). During the 6MWT, the NSPS falls to zero each time the patient stops walking. The cumulative number of steps is shown as a function of time for each test (B). The slope indicates the walking pace. This patient walked at the same pace before and after the inhalation of procaterol, except for during rest periods.

pace (as the NSPS) in a 73-year-old patient with moderate COPD. The 6MWD improved by 30.5 m following the inhalation of procaterol. Note that NSPS falls to zero when the patient stops walking. The patient rested for a total of 32-s before the inhalation of procaterol (Fig. 2A). After the inhalation of procaterol, this patient could walk for 6 minutes without rest. Fig. 2B shows the numbers of the cumulative steps during the 6MWT for the same patient. The results of the two tests (before and after the inhalation of procaterol) shared a common slope (except for during the rest periods), and the slope was constant (Fig. 2B), which suggested that, with the exception of the rest periods, the walking pace was almost the same during the 6MWT. The mean NSPS before and after the inhalation of procaterol in the 6MWT was 1.57 and 1.78 (step/s), respectively. The mean NSPS is increased by a decrease in the rest time and/or an increase in the walking pace. In this case, the inhalation of procaterol led to a decrease in the rest time, resulting in an increase in the mean NSPS. Figs. 3 and 4 show that when the resting time was decreased by the inhalation of procaterol, the 6MWD was improved by more than 30 m after the inhalation of procaterol.

Fig. 5A shows an example of the increase in the walking pace after the inhalation of procaterol. This 68-year-old patient could walk in 6-minute without a rest. Fig. 5B shows a graph of time versus the cumulative steps during the 6MWT. The slope increased after the inhalation of procaterol (Fig. 5B), which suggests that the walking pace increased during the 6MWT. The mean NSPS before and after the inhalation of procaterol in the 6MWT was 1.78 and 1.88 (step/s), respectively. In this case, the increase in the walking pace following the inhalation of procaterol might have resulted in an increase in the mean NSPS; however, a placebo study will be necessary. The results in 5 participants in whom the improvement in the 6MWD was <30 m after the inhalation of procaterol are not shown.

Discussion

The present study demonstrated that a single inhalation of procaterol significantly prolonged the 6MWD, and shortened the total resting time or increased the walking pace during the 6MWT, suggesting that the inhalation of procaterol may be useful for improving the exercise performance of COPD patients undertaking this test. In addition, the steps per second and the cumulative steps were effective measures for analyzing the changes in the walking pattern and pace after the inhalation of procaterol in COPD patients. Determining the number of steps walked per unit time and the consideration of the total resting time during the 6MWT may be important when assessing the functional status before and after drug treatment because some COPD patients cannot walk continuously for 6-minute without resting.

In COPD patients, exercise causes an increase in the EELV along with an increase of ventilation, which is known as dynamic lung hyperinflation (8-10). A significant relationship has been reported between dynamic lung hyperinflation and dyspnea during exercise in COPD patients (8). Several reports have also shown that the pretreatment of COPD patients with inhaled procaterol improves dynamic

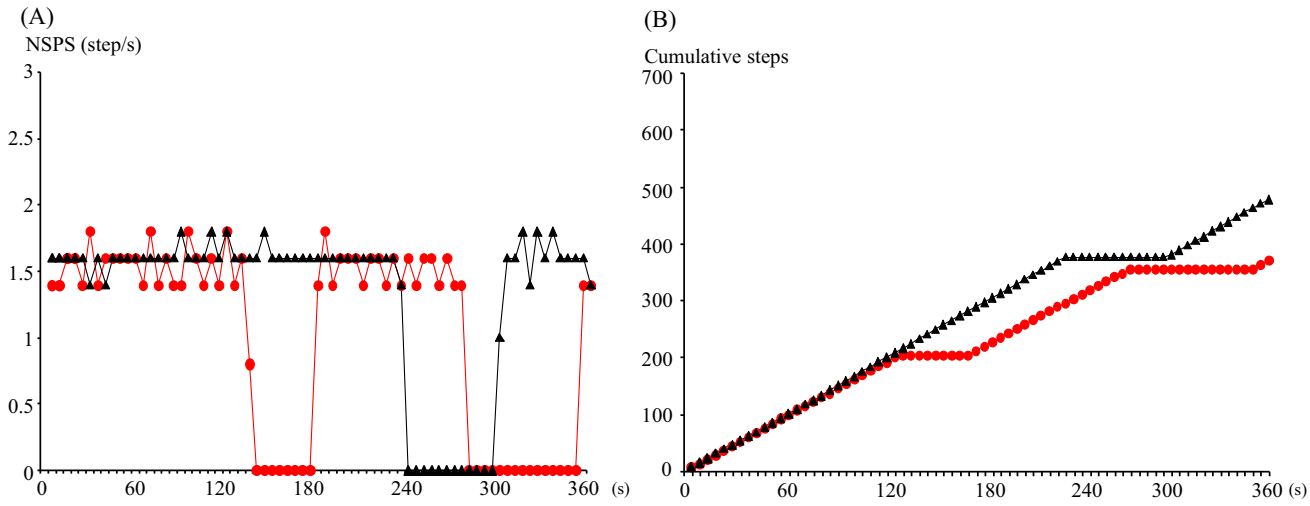

Figure 3. **Determining the walking pattern and pace from the number of steps per second (NSPS) and the cumulative steps before and after the inhalation of procaterol. The patient was an 80-year-old man with COPD. Although the patient walked 177 m in the 6-min walk test (6MWT) with 114 s of rest before the inhalation of procaterol (closed circle), he could walk 249.5 m with 62 s of rest after the inhalation of procaterol (closed triangle) (A). The cumulative number of steps is shown as a function of time for each test (B). The slope indicates the walking pace. This patient walked at the same pace before and after the inhalation of procaterol, except for during rest periods.**

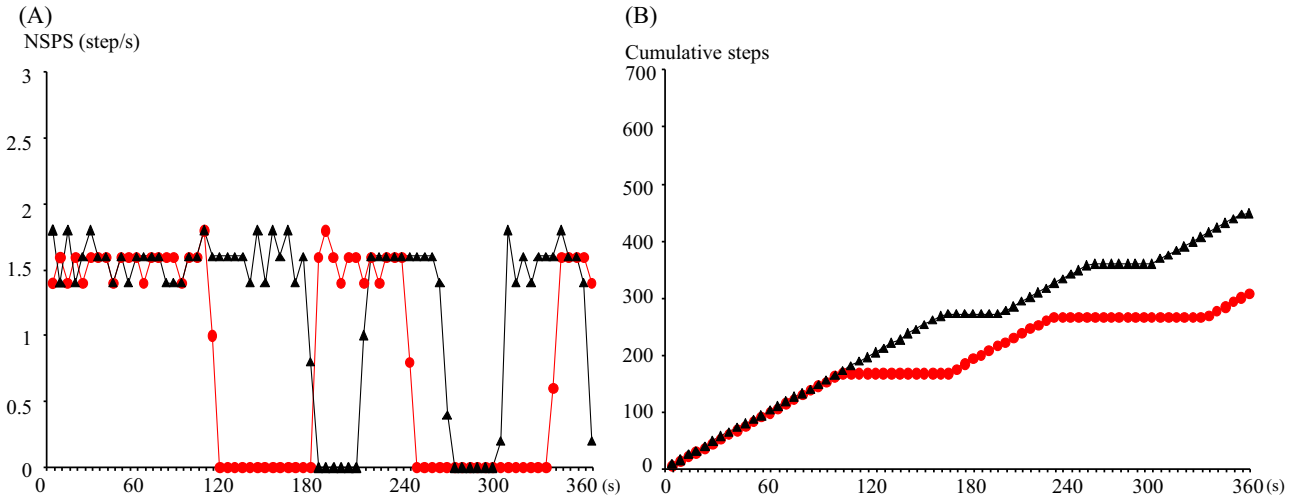

Figure 4. **Determining the walking pattern and pace from the number of steps per second (NSPS) and the cumulative steps before and after the inhalation of procaterol. The patient was an 81-year-old man with COPD. Although the patient walked 125 m in the 6-min walk test (6MWT) with 158 s of rest before the inhalation of procaterol (closed circle), he could walk 188 m with 77 s of rest after the inhalation of procaterol (closed triangle) (A). The cumulative number of steps is shown as a function of time for each test (B). The slope indicates the walking pace. This patient walked at the same pace before and after the inhalation of procaterol, except for during rest periods.**

lung hyperinflation and exercise tolerance (10, 11, 16-18). A previous report also indicated that the inhalation of formoterol increased the 6MWD (19). In addition, Fujimoto et al. reported that dynamic lung hyperinflation secondary to hyperventilation reduced the IC in COPD patients, while the IC was increased by the inhalation of procaterol (10). Moreover, the use of procaterol has been shown to improve both the exercise tolerance and health-related quality of life (16). In the present study, the 6MWD was significantly increased after the inhalation of procaterol. It is reported that a >30-m increase in the 6MWD represents the minimal clinically important difference (MCID) for COPD patients (1, 2). The 6MWD changed by >30 m following the inhalation of procaterol in 4 of the 9 COPD patients. In a graph of time versus cumulative steps, 3 of the 4 patients who showed an improvement of >30 m after the inhalation of procaterol

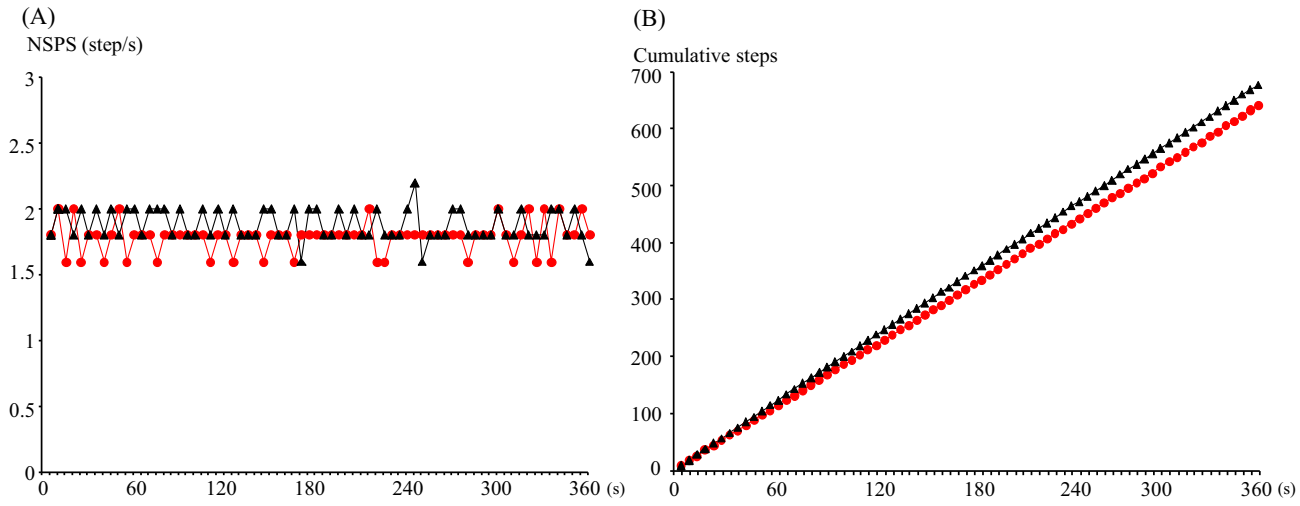

Figure 5. Determining the walking pattern and pace from the number of steps per second (NSPS) and the cumulative steps before and after the inhalation of procaterol. The patient was a 68-year-old man with COPD. Although the patient walked 356.5 m in a 6-min walk test (6MWT) without a rest before the inhalation of procaterol (closed circle), he could walk 422 m after the inhalation of procaterol (closed triangle) (A). The cumulative number of steps is shown as a function of time for each test (B). The slope indicates that the walking pace was increased by the inhalation of procaterol.

showed a shorter total rest time, and the walking pace of one patient increased during the 6MWT. Thus, the increase in the 6MWD after the inhalation of procaterol might be a clinically relevant effect in 4 patients.

Although Golpe et al. found that exercise-related oxygen desaturation during the test was not an independent predictor in a multivariate analysis (20), the 6MWT has been reported to predict mortality in COPD patients (20-22). However, patients with moderate or severe COPD frequently rest during the 6MWT, as was noted in the present study, and exercise-related oxygen desaturation could improve after resting. In this study, the modified Borg scale after the 6MWT, the lowest SpO_2, and the mean SpO_2 were not significantly changed by the inhalation of procaterol. This suggests that our COPD patients walked as far as possible until they needed to rest during both tests, and recovered SpO_2, resulting in no significant change in dyspnea or in the lowest or mean SpO_2 values. Thus, it is important to take the rest time during the 6MWT into consideration when assessing the changes in SpO_2 and desaturation during exercise. The previous reports did not clarify importance of a number of points, including the number of rests and the total resting time. The NSPS value, which decreases with rest during the 6MWT, can be used to evaluate the impact of resting in the 6MWT. An analysis of the walking pattern and pace during the 6MWT would be useful in clinical studies on COPD medications.

The total steps walked during the 6MWT is reported to be useful for assessing the exercise capacity of patients with chronic heart disease (23, 24). We have developed a modified 6MWT, in which the walking pattern is examined by counting steps (12), allowing the walking pattern of COPD patients to be displayed on a graph of time versus NSPS. In addition, the walking pace could be displayed by a graph of time versus cumulative steps because $NSPS_k$ (k=1,2,3,..., 72) shows a slope in 5-s (12). Moreover, it has been reported that a 3-dimensional accelerometer can accurately detect steps while a subject is walking (23, 24), and evaluate daily physical activity (25). If a pulse oximetry system that incorporates a 3-dimensional accelerometer that can accurately count steps is developed, the device could record SpO_2 continuously, compute the NSPS, and plot a graph of time versus NSPS automatically to display the walking pattern during the 6MWT.

The present study is associated with several limitations, with the most obvious being its relatively small sample size. Furthermore, we did not investigate a random sample of COPD patients who showed a spectrum of disease severity or use a placebo. Further studies that include a placebo group will be needed to clarify the effects of pretreatment with inhaled procaterol on the exercise performance of COPD patients (26) and the usefulness of our new modified 6MWT with NSPS in assessing the response to drug treatment and the efficacy of pulmonary rehabilitation.

The authors state that they have no Conflict of Interest (COI).

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