# Handgrip Strength During Admission for COPD Exacerbation: Impact on Further Exacerbation Risk

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**Research Article**

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## Abstract

# Background:

Low handgrip strength (HGS) is independently associated with a higher exacerbation risk in smokers with stable chronic obstructive pulmonary disease (COPD); however, the relationship between HGS on admission for COPD exacerbation admission and further exacerbation risk remains unclear. This study aimed to investigate the relationship between HGS and further exacerbation risk in patients admitted for COPD exacerbation.

# Methods:

We enrolled patients admitted for COPD exacerbation between January 2018 and June 2019 who underwent HGS measurement within 3 days after admission. The primary endpoint was exacerbations within 12 months after the index admission. We analyzed the relationships among demographics, HGS, pulmonary function parameters, and acute exacerbation events.

# Results:

Among 43 enrolled patients, 31 (72.1%) presented HGS weakness (22.1 ± 4.1 kg). Forced expiratory volume in one second ($FEV_1$) and $FEV_1$ percentage of predicted value ($FEV_1$ predicted%) were significantly lower in patients with HGS weakness (0.82 ± 0.20 vs. 1.59 ± 0.77, p = 0.018; 36.2 ± 10.4% vs. 66.3 ± 22.2, p = 0.004, respectively). Moreover, patients with HGS weakness were more likely to have severe GOLD grade IV (19.4% vs. 8.3%, p = 0.002). Finally, patients with HGS weakness showed a significantly higher rate of emergency room visits within 6, 9, and 12 months after the index admission (0.81 ± 1.30 vs. 0.08 ± 0.29, p = 0.045; 1.26 ± 1.59 vs. 0.17 ± 0.38, p = 0.019; 1.48 ± 1.86 vs. 0.25 ± 0.62, p = 0.027, respectively).

# Conclusions:

HGS weakness measured upon admission for COPD exacerbation was associated with a higher risk of further exacerbation.

# Trial registration:

ClinicalTrials.gov Identifier: NCT04885933

## Background

Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation, which is caused by the complex interactions among exposure to noxious particles or gases and various host factors, including genetic inheritance, airway hyperresponsiveness, or inadequate lung development[1, 2]. COPD has caused a progressive health burden worldwide mostly due to increasing exposure to noxious particles and the aging population [3]. In Taiwan, the estimated COPD prevalence in individuals aged > 40 years was approximately 6% in 2013 [4]. Moreover, in 2013, chronic airway diseases were the seventh leading mortality cause in Taiwan, with an annual mortality rate of 33.2 per 100,000 population [5].

COPD not only presents lung function impairment but also extrapulmonary complications resulting from systemic inflammation that extends from chronic airway inflammation, including cardiovascular diseases, osteoporosis, and muscle atrophy. Previous studies have shown that skeletal muscle dysfunction increases the risk of COPD morbidity and mortality [6]. Compared with healthy individuals, patients with COPD show reduced strength of skeletal and respiratory muscles [7–9]. Hamilton et al. reported that 70% of patients with chronic lung disease present with quadriceps muscle weakness [10]. Moreover, patients with moderate-to-severe COPD present with a 20–30% decrease in the quadriceps femoris muscle strength [9, 11, 12]. The impairment degree of limb muscle strength is correlated with COPD severity [12]. Regarding ventilatory muscle function, patients with COPD present with a 30–40% decrease in the maximal diaphragm strength, which is represented by the maximal transdiaphragmatic pressure [8, 11].

Handgrip strength (HGS), which is a simple bedside hand muscle strength parameter, not only directly represents hand muscle strength but also is a good surrogate measurement for overall muscle strength [13, 14]. Specifically, in patients with COPD, HGS is correlated with the strength of other muscles, including the quadriceps and respiratory muscles [11, 15]. Not only the representative of muscle strength, the degree of the HGS impairment is associated with a decline in forced expiratory volume in one-second percentage of predicted value ($FEV_1$% of predicted value) and COPD Global Initiative for Chronic Obstructive Lung Disease (GOLD) grading [16] [17]. Moreover, Martinez et al. found that a 1-kg reduction in HGS was associated with an increased risk of exacerbation by 5% in stable COPD[18, 19].

However, HSG measurement in these previous studies mostly was for patients with stable COPD. Respiratory discomfort and physical weakness could negatively affect HGS on admission for acute exacerbation of COPD (AECOPD)[20]. To our knowledge, there has been scarce studies on the relationship between HGS and further exacerbation risk in patients admitted with AECOPD. This prospective study aimed to investigate the relationship between HGS and further exacerbation risk in patients admitted for AECOPD.

# Methods

# Designs and participants

We enrolled patients aged > 45 years who were admitted for AECOPD. COPD was defined as an obstructive ventilatory defect ($FEV_1/FVC < 0.7$) based on pulmonary function tests along with smoking for > 15 pack-years or a history of noxious gas exposure or the clinical impression by attending physicians in case spirometry data were missing. Acute exacerbation was defined as acute worsening of respiratory symptoms that results in additional therapy. We excluded patients with heart failure; permanent pacemaker or implantable cardioverter-defibrillator [21]; significant fluid retention, including edema, pleural effusion, or ascites; morbid obesity with BMI > 34 [22]; use of noninvasive positive-pressure ventilators (NIPPV) use upon admission; structural lung defects, including significant tuberculosis sequelae, bronchiectasis, and pneumoconiosis; and re-admission for AECOPD within 1 month.

Participants received standard care based on the clinical judgments of attending physicians. HGS measurements were performed upon admission or within 3 days if admission at the weekend. The COPD assessment test (CAT) questionnaire was simultaneously administered. Data regarding exacerbation occurrence with emergency room visits or even admission were obtained at three-month intervals through outpatient clinic follow-up visits, medical record or telephone interviews. The CAT questionnaire was re-administered at the third post-discharge month. The primary end-points were acute exacerbations leading to emergency room visits or readmission within 12 months after admission. This study was approved by the Institutional Review Board of Far Eastern Memorial Hospital (FEMH-10699-E). In addition, participants had to sign informed consents before initiating the study.

# Handgrip strength measurement

HGS measurements were performed by using a dynamometer (North Coast Hydraulic Hand Dynamometer, North Coast Medical Inc., Morgan Hill, CA). The patient was seated with the wrist neutrally positioned and the elbow flexed at 90 degree[23]. For patients who were unable to sit, HGS measurements were obtained while lying in bed at 30° with supported elbows. HGS was measured by the dominant hand of participants three times with the interval of at least one minute. The highest value was used in our analyses. HGS weakness (HGSw) was defined based on the guidelines of the European Working Group on Sarcopenia in Older People (EWGSOP)[24]. The patients were divided into the HGSw and non-HGSw groups, with cut-off HGS values of < 30 kg in men and < 20 kg in women.

# Measurement of skeletal muscle mass

Skeletal muscle mass was assessed using a foot-to foot bioelectrical impedance analyzer (BIA) (TBF-410-GS Tanita, Japan). It was measured, following by the manufacture's instruction.

# Sarcopenia definition

Sarcopenia was defined based on EWGSOP recommendations as follows: skeletal muscle index (skeletal muscle mass/height$^2$, SMI) of men was less than 8.87 kg/m$^2$ and that of women was < 6.42 kg/m$^2$ in conjugated to HGS weakness[24]

# Pulmonary function test

Pulmonary spirometry data, including FEV1, forced vital capacity (FVC), and FEV1/FVC, were collected within 12 months before admission according to electronic medical record. All presented data were post-bronchodilator data.

# Statistical Analysis

All statistical analyses were used IBM SPSS statistics Version 19. Categorical and continuous variables were compared using the chi-square and Mann-Whitney U tests, respectively. One-way analysis of variance (ANOVA) was used for between-group comparison of pulmonary obstruction severity, which was graded using the GOLD classification [25]. Statistical significance was set as $P < 0.05$.

# Results

There were 111 participants admitted for AECOPD who were potentially eligible. After screening based on the exclusion criteria and willingness to participate, we finally enrolled 43 participants (Fig. 1). Table 1 presents the demographic characteristics of the participants. Among the 43 participants, 31 (72.1%) participants belonged to HGSw group. The HGS was significantly lower in HGSw than non-HGSw group(22.1 ± 4.1 vs. 33.7 ± 3.1 kg, $p < 0.001$). There were no between-group differences in age; sex; and comorbidities, including hypertension, diabetes, and heart diseases (coronary artery disease and valvular heart disease) (Table 1). However, compared with the HGSw group, the non-HGSw group had more active smokers (9.7% vs. 50%, $p = 0.003$). As expected, BMI and SMI were significantly higher in the non-HGSw group than in the HGSw group (25.8 ± 3.6 vs. 22.3 ± 4.2, $p < 0.001$; 18.8 ± 1.3 vs. 16.5 ± 1.8, $p < 0.001$, respectively).

30 (69.7%) participants had pulmonary function data. Among them, 21 (67.7%) and 9 (75%) participants were in the HGSw and non-HGSw groups, respectively (Table 2). There was no significant between-group difference in the presence of lung function data. All the lung function data were FEV1/FVC < 0.70, which was consistent with the diagnostic criteria of lung function for COPD. $FEV_1$, $FEV_1$ predicted %, forced vital volume (FVC), and FVC predicted % were significantly lower in the HGSw group than in the non-HGSw group. The FEV1 predicted % of the HGSw group was 36.2 ± 10.4 %. Moreover, 12 (57.1%) and 6 (28.6%) patients with HGWs were GOLD grade III and IV, respectively. On the other hand, the $FEV_1$ predicted% of the non-HGSw group was 66.3 ± 22.2% ($p = 0.004$). Further, 7 (77.8%) participants in the non-HGWs group were GOLD I & II. There was significant difference in the severity of GOLD grade between HGSw and non-HGSw groups($p = 0.002$).

There was no significant between-group difference in the CAT score at admission ($CAT_{ad}$)and 3 months after index admission ($CAT_{3m}$)(Table 3). Compared with $CAT_{ad}$, $CAT_{3m}$ was significantly decreased, no matter of total population, HGSw or non-HGSw groups ($p = 0.002$, 0.025, and 0.024, respectively.) However, the $CAT_{3m}$ was not significantly lower in the non-HGSw group (10.2 ± 4.3) than in the HGSw group (13.8 ± 5.9, $p = 0.272$). Significantly clinical difference between $CAT_{ad}$ and $CAT_{3m}$ was defined as the difference with equal or more than 2. It was not significantly different between HGSw and non-HGSw

groups (35.5% vs. 41.7%, p = 0.757). Compared with non-HGSw group, the HGSw group showed significantly higher rates of emergency room visits within 6 (0.81 ± 1.30 vs. 0.08 ± 0.29, p = 0.045), 9 (1.26 ± 1.59 vs. 0.17 ± 0.38, p = 0.019), and 12 months after index admission (1.48 ± 1.86 vs. 0.25 ± 0.62, p = 0.027). Although it did not achieve significant differences in the readmission rates at 6, 9, and 12 months between HGSw and non-HGSw groups(Table 3, Fig. 2). However, the HGSw group showed a tendency of more re-admission within 9 (0.77 ± 1.38 vs. 0.08 ± 0.29) p = 0.064) and 12 months (0.94 ± 1.56 vs. 0.08 ± 0.29, p = 0.062) than non-HGSw group .

# Discussion

Martinez et al. reported HGS was associated with exacerbation risk in cross-sectional and longitudinal analyses [18]. However, the relationship of inpatient HGS measurement with further exacerbation risk was little investigated. Regarding physical weakness and respiratory distress in admission, HGS assessment is rarely recommended at acute stage of AECOPD admission, though there is small-scale studies reported about HGS in intensive care and respiratory failure[26]. We observed an association of HGSw with emergency department visits within 6 to 12 months after index admission, which could be possibly related to higher admission rates in the subsequent 9 to 12 months. This suggests that HGSw could be associated with the risk of further AECOPD requiring medical emergency or admission care.

In addition, we observed an association between HGSw in inpatients with AECOPD and the degree of airway flow limitation ($FEV_1$). Approximately 85% of patients with HGSw were classified as GOLD grade III or IV. Consistent with our findings, the Korean National Health and Nutrition Examination Survey (KNHANES) on 5,303 participants aged > 40 years reported a significant association of HGSw with the degree of pulmonary function impairment, measured by FEV1% of the predicted value, which was independent of age, height, and smoking habit[17]. The present study reported an association of HGS with lung function and GOLD grading.

The exacerbation risk is associated with the exacerbation history within the previous year and COPD GOLD grading [27]. However, we observed no between-group difference in the exacerbation history in the previous year. The airflow limitation degree could confound the relationship between HGSw and further exacerbation. However, lung function tests are not routinely recommended in the acute stage of AECOPD [1]. Lung function might be underestimated in the acute stage of patients showing insufficient effort and cooperation due to physical weakness. A similar concern could be associated with HGS. Nonetheless, even without data regarding lung function tests, the present study showed that inpatient HGS measurement might be a predictor of further exacerbation.

Kaymaz et al. [28] reported a significant association of upper limb muscle strength with exercise capacity, dyspnea sensation, and quality of life in patients with severe COPD. Impaired upper limb muscle strength might be indicative of HGS weakness. Consistent with this, HGS is significantly associated with exacerbation rates and the severity of airflow obstruction among patients with stable COPD [16–19]. In addition to upper limb muscle strength, HGS is associated with lower limb strength and the 6-minute walk

distance [11]. HGS weakness was also reported to associate with increased mortality risk [29]. We observed a correlation of HGS weakness with the risk COPD re-exacerbation rates in need of emergency care from half to one year, and it possibly increased re-admission rate of exacerbation. HGS weakness of inpatients, admitted due to AECOPD, might be a predictor of exacerbation risk in the coming one year even in the status of lacking lun. Upper limb training, which could improve arm function and reduce symptoms in patients with COPD, should be considered for patients with HGSw and difficulties in daily arm activities [30–32]. Therefore, the HGS of inpatients might not only provide additional treatment clues regarding pulmonary rehabilitation but also act as a follow-up parameter.

However, this study has several limitations. First, we assessed a small sample size that may not be representative of the real population. There is a need for future large-scale studies to yield more comprehensive results. Second, HGS measurement is heavily reliant on the patients' comprehension since it should be executed in cooperative patients with clear consciousness. Third, we excluded patients with apparent fluid overload and severe exacerbation under NIPPV use on admission, which may not reflect the real population.

# Conclusions

In conclusion, we observed that HGSw in inpatients with AECOPD was associated with a higher risk of further exacerbations. HGS could provide a simple bedside measurement parameter for inpatients with AECOPD who are not immediately feasible for pulmonary function tests upon admission.

# Abbreviations

Handgrip strength (HGS)

Chronic obstructive pulmonary disease (COPD)

Forced expiratory volume in one second ($FEV_1$)

Body mass index (BMI)

Acute exacerbation of COPD (AECOPD)

Noninvasive positive pressure ventilators (NIPPV)

COPD assessment test (CAT)

European Working Group on Sarcopenia in Older People (EWGSOP)

Bioelectrical impedance analyzer (BIA)

Skeletal muscle index (SMI)

Forced vital volume (FVC)

HGS weakness (HGSw)

Korean National Health and Nutrition Examination Survey (KNHANES)

# Declarations

### Ethics approval and consent to participate

The Institutional Review Board of Far Eastern Memorial Hospital approved this study (IRB 106099-E). Participants had to sign Informed consent before initiating the study.

### Consent for publication

Not applicable.

### Availability of data and materials

The data that support the findings of this study are available from the corresponding author, [P.H.W], upon reasonable request.

### Competing interests

All authors declare no financial, professional, or other personal interests of any nature or kind in a related product, service, and/or company.


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### Authors' contributions

Chi-Tai Lee: Conceptualization, Methodology, Validation, Investigation, Resources, Writing - Original Draft

Ping-Huai Wang: Conceptualization, Methodology, Validation, Resources, Writing - Review & Editing, Funding acquisition


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# Tables

Table 1 Demographic characteristics of the participants

| | Total (n = 43) | HGSw (n = 31) | non-HGSw (n = 12) | p |
|---|---|---|---|---|
| Gender(M/F) | (40/3) | 28/3 | 12/0 | 0.364 |
| Age | 72.3 ± 9.2 | 75.2 ± 7.3 | 65.1 ± 9.8 | 0.333 |
| Smoking (+/-/ex) n(%) | 9/3/31(20.9/7/72.1) | 3/3/25(9.7/9.7/80.6) | 6/0/6(50/0/50) | 0.003 |
| Hypertension n(%) | 18(41.9) | 14(45.2) | 4(33.3) | 0.363 |
| CVA n(%) | 1(2.3) | 1(3.2) | 0(0) | 0.721 |
| DM n(%) | 8(18.6) | 5(16.1) | 3(25.0) | 0.393 |
| Heart disease n(%) | 10(23.3) | 7(22.6) | 3(25.0) | 0.579 |
| CAD | 8(18.6) | 5(16.1) | 3(25.0) | |
| VHD | 2(4.6) | 2(6.4) | 0(0) | |
| CKD n(%) | 1(2.3) | 1(3.2) | 0(0) | 0.721 |
| Cancer n(%) | 2(4.7) | 2(6.5) | 0(0) | 0.515 |
| Exacerbation in previous year | 0.67 ± 1.36 | 0.74 ± 1.53 | 0.50 ± 0.80 | 0.974 |
| BMI ($kg/m^2$) | 23.3 ± 4.3 | 22.3 ± 4.2 | 25.8 ± 3.6 | <0.001 |
| SMI ($kg/m^2$) | 17.2 ± 2.0 | 16.5 ± 1.8 | 18.8 ± 1.3 | <0.001 |
| HGS (kg) | 25.3 ± 6.5 | 22.1 ± 4.1 | 33.7 ± 3.1 | <0.001 |

**Abbreviations:** BMI, body mass index; CKD, chronic kidney disease; CVA, cerebrovascular accident; DM, diabetes mellitus; ex, ex-smoker; F, female; HGS, handgrip strength; HGSw, handgrip strength weakness; M, male; SMI, smooth muscle index

Table 2: Post-bronchodilator lung function test and COPD GOLD stage of the participants

| | Total (n = 43) | HGSw (n = 31) | non-HGSw (n = 12) | p |
|---|---|---|---|---|
| PFT exam | 30(69.7) | 21(67.7) | 9(75.0) | |
| FVC | 2.0 ± 0.81 | 1.82 ± 0.69 | 2.65 ± 0.81 | 0.017 |
| FVC predicted % | 63.9 ± 18.8 | 56.2 ± 14.1 | 77.0 ± 21.6 | 0.023 |
| $FEV_1$ | 1.05 ± 0.56 | 0.82 ± 0.20 | 1.59 ± 0.77 | 0.018 |
| $FEV_1$ predicted % | 45.2 ± 20.2 | 36.2 ± 10.4 | 66.3 ± 22.2 | 0.004 |
| $FEV_1$/FVC (%) | 52.1 ± 12.7 | 50.0 ± 12.5 | 57.0 ± 12.4 | |
| GOLD grade | | | | 0.002 |
| I (n) | 2 | 0 | 2 | |
| II (n) | 9 | 4 | 5 | |
| III (n) | 13 | 12 | 1 | |
| IV (n) | 7 | 6 | 1 | |

**Abbreviation** $FEV_1$: forced expiratory volume in one second; $FEV_1$ predicted %: forced expiratory volume in one-second percentage of predicted value; FVC: forced vital volume; FVC predicted %: forced vital capacity percentage of predicted value; GOLD: global initiative of chronic obstructive lung disease; HGS, handgrip strength; HGSw, handgrip strength weakness; PFT: pulmonary function test

Table 3: CAT score on admission and after three months, as well as the rate of emergency room visits and admissions within three, six, and twelve months after index admission.

| | Total (n = 43) | HGSw (n = 31) | non-HGSw (n = 12) | p |
|---|---|---|---|---|
| $CAT_{ad}$ | 16.6 ± 4.3 | 16.7 ± 4.3 | 16.5 ± 4.7 | 0.817 |
| $CAT_{3m}$ | 12.9 ± 5.6 | 13.8 ± 5.9 | 10.2 ± 4.3 | 0.272 |
| $CAT_{ad-3m}$≧2 n(%) | 16(37.2) | 11(35.5) | 5(41.7) | 0.737 |
| $ER_{3m}$ | 0.20 ± 0.46 | 0.26 ± 0.51 | 0.08 ± 0.29 | 0.279 |
| $Admission_{3m}$ | 0.20 ± 0.51 | 0.26 ± 0.58 | 0.08 ± 0.29 | 0.364 |
| $ER_{6m}$ | 0.60 ± 1.15 | 0.81 ± 1.30 | 0.08 ± 0.29 | 0.045 |
| $Admission_{6m}$ | 0.34 ± 0.81 | 0.45 ± 0.93 | 0.08 ± 0.29 | 0.188 |
| $ER_{9m}$ | 0.95 ± 1.44 | 1.26 ± 1.59 | 0.17 ± 0.38 | 0.019 |
| $Admission_{9m}$ | 0.58 ± 1.21 | 0.77 ± 1.38 | 0.08 ± 0.29 | 0.064 |
| $ER_{12m}$ | 1.13 ± 1.69 | 1.48 ± 1.86 | 0.25 ± 0.62 | 0.027 |
| $Admission_{12m}$ | 0.69 ± 1.38 | 0.94 ± 1.56 | 0.08 ± 0.29 | 0.062 |

Abbreviation: $Admission_{3m}$: admission during three months after index admission; $Admission_{6m}$: admission during six months after index admission; $Admission_{9m}$: admission during six months after index admission; $Admission_{12m}$: admission during 12 months after index admission; CAT: chronic obstructive pulmonary disease assessment test; $CAT_{ad}$: CAT on admission; $CAT_{3m}$: CAT three months after index admission; $CAT_{ad-3m}$: the difference of $CAT_{ad}$ minus $CAT_{3m}$ ; $ER_{3m}$: emergency room visits during three months after index admission; $ER6_{m}$: emergency room visit during six months after index admission; $ER9_{m}$: emergency room visit during six months after index admission; $ER_{12m}$: emergency room visit during 12 months after index admission; HGS, handgrip strength; HGSw, handgrip strength.

# Figures

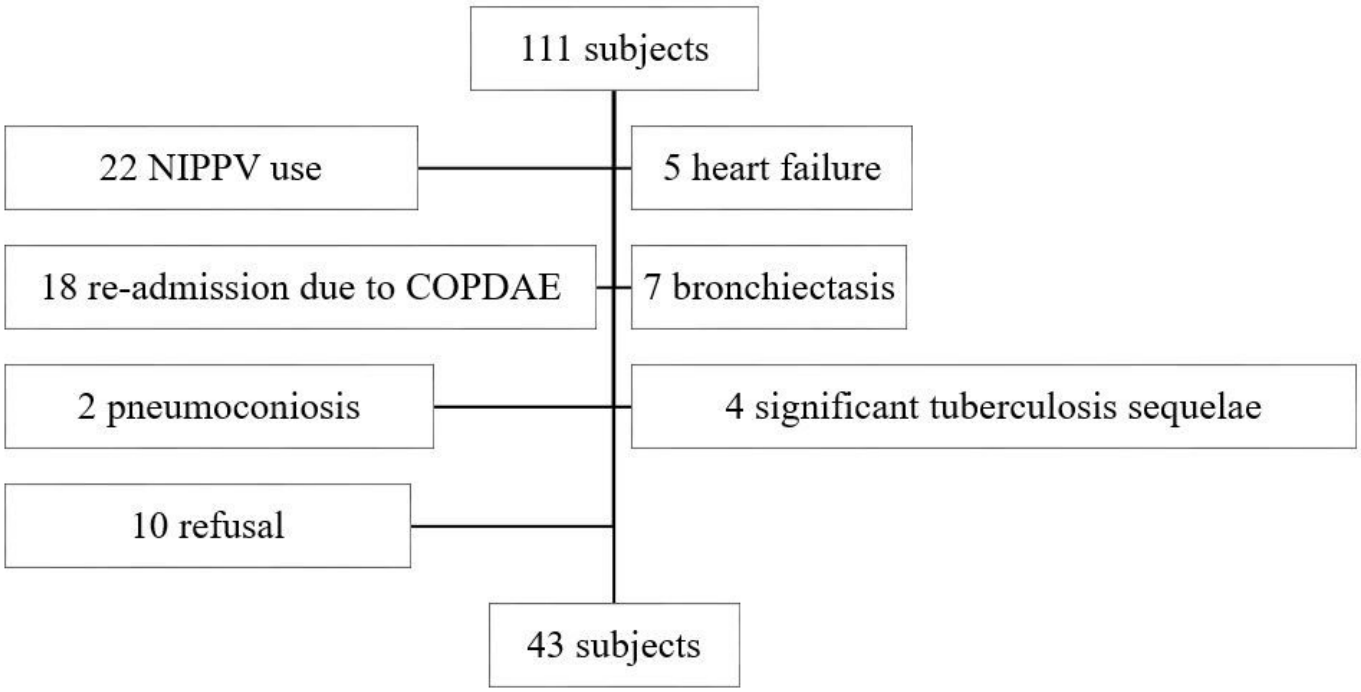
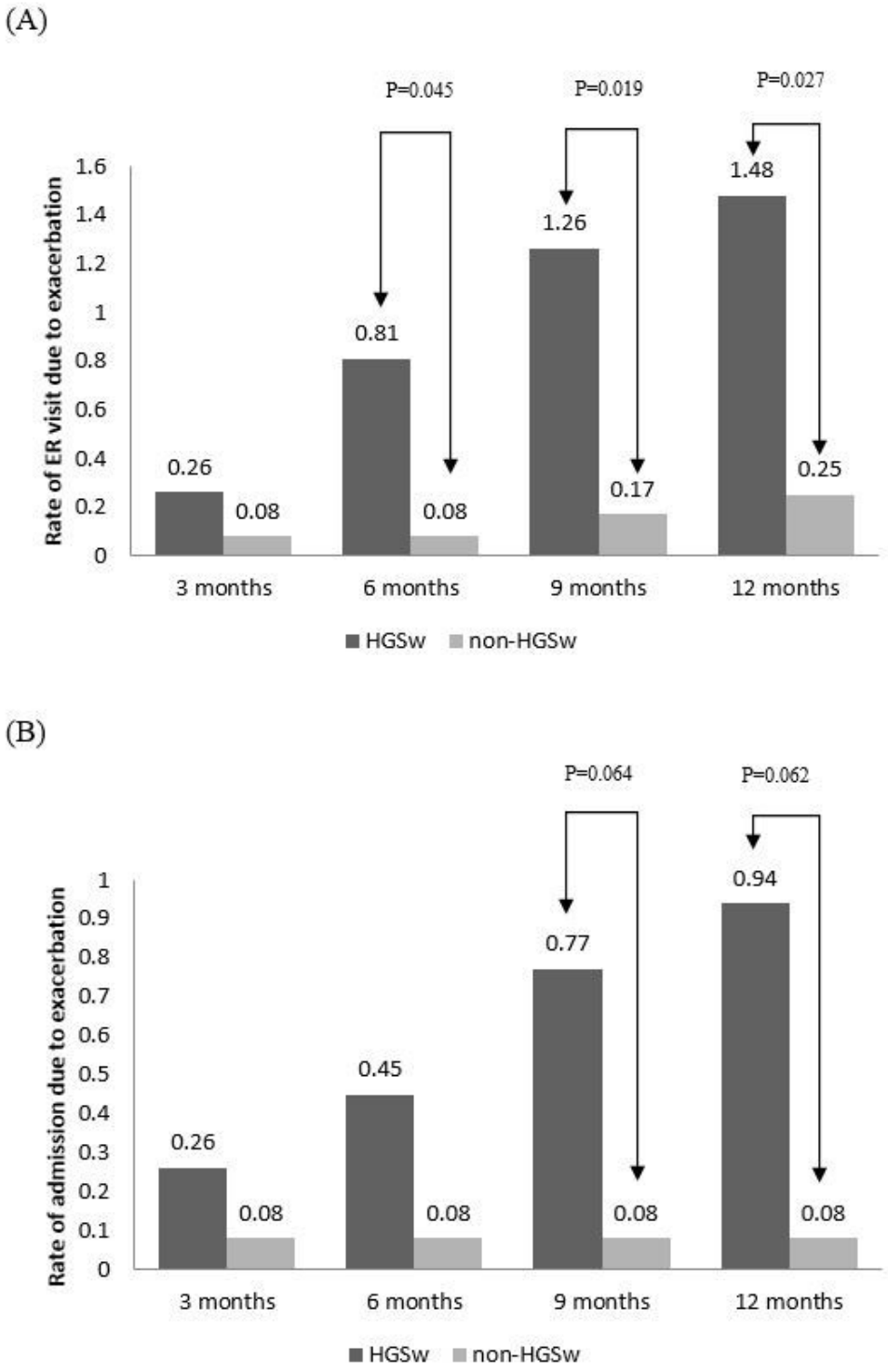



**Figure 1**

Flowchart of inclusion of study participants




## Figure 2

Rate of exacerbations requiring emergency room visit and admission within three, six, nine, and twelve months of the index admission. Abbreviation: ER: emergency room; HGSw: handgrip strength weakness (A)The rates of emergency room visits within 6, 9, and 12 months after index admission were significantly higher in the HGSw group than in the non-HGSw group. (B)There was a non-significant tendency of more re-admissions within 9 and 12 months in the HGSw group than in the non-HGSw group.