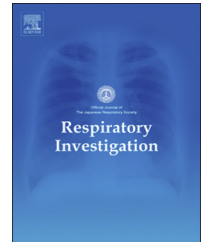




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## Original article

# Home-based pulmonary rehabilitation in patients with inoperable or residual chronic thromboembolic pulmonary hypertension: A preliminary study



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## ABSTRACT

**Background:** Management of chronic thromboembolic pulmonary hypertension (CTEPH) has recently improved because of advances in pulmonary endarterectomy (PEA), balloon pulmonary angioplasty (BPA), and disease-targeted medications. However, patients with inoperable CTEPH or persistent pulmonary hypertension (PH) after these interventions continue to exhibit impaired exercise capacity and limited quality of life (QOL).

**Methods:** Eight patients with inoperable or residual CTEPH (mean age,  $64 \pm 12$  years; WHO functional class II/III, 6/2; mean pulmonary artery pressure,  $47 \pm 13$  mmHg) in stable condition and receiving disease-targeted medications participated in a 12-week home-based pulmonary rehabilitation program (muscle strength training, respiratory exercises, and walking) with supervised hospital sessions from March 2012 to January 2014. Efficacy parameters were prospectively evaluated at baseline and at completion of the 12-week program.

**Results:** After completion of the pulmonary rehabilitation program, the 6-minute walking distance (6MWD) ( $33.3 \pm 25.1$  m), St. George's Respiratory Questionnaire activity score, quadriceps force, and 7-day physical activity level were significantly improved compared with baseline. All subjects completed the rehabilitation program. Although one patient experienced presyncope during the in-hospital exercise sessions, no other severe adverse events or complications of pulmonary rehabilitation were observed.

**Conclusions:** These findings suggest that home-based pulmonary rehabilitation with closely supervised sessions may safely improve exercise capacity, leg muscle strength, general activity in daily life and health-related QOL in CTEPH patients.

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## 1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by obstruction of the pulmonary arteries by unresolved organized thrombi. Patients with untreated CTEPH may develop severe pulmonary hypertension (PH) and right heart failure with a poor prognosis [1]. Although pulmonary endarterectomy (PEA) is a promising treatment for CTEPH with surgically accessible thrombi, PEA is not effective or contraindicated in certain cases, such as CTEPH with peripherally located organized thrombi, in which PEA is associated with a lower rate of improvement of pulmonary hemodynamics and higher mortality [2–5]. Recently, new pulmonary arterial hypertension (PAH)-specific therapies (e.g., endothelin-receptor antagonists, phosphodiesterase type 5 inhibitors) [6,7] and/or balloon pulmonary angioplasty (BPA) [8,9] have been reported to improve hemodynamics and survival rates in inoperable or residual CTEPH patients. Nevertheless, such optimized therapies for CTEPH patients remain insufficient for achieving a normal exercise capacity and health-related quality of life (QOL) [10].

Safety of physical exercise in patients with PH is of general concern, because PH patients may experience presyncope or syncope immediately after exercise [11]. In particular, in more severely affected PH patients, many doctors recommend the avoidance of physical exercise because of concern about sudden cardiac arrest [12]. To date, studies in European countries have reported exercise to improve the peak oxygen consumption, World Health Organization (WHO) functional class, and 6-minute walking distance (6MWD) in patients with various forms of PH [13–16]. These reports have concluded that exercise programs with close monitoring (3-weeks in-hospital training and 12-weeks home rehabilitation) can be safely conducted in PH patients [13–16], although one study revealed that exercise is not completely harmless [15]. Therefore, exercise programs may provide useful and safe supplementary treatment of disease-targeted medication in patients with inoperable or residual CTEPH. However, most previous reports (other than one study [17]) have not focused on patients with CTEPH. Additionally, studies of pulmonary rehabilitation for PH have not been performed in Japan.

The purpose of the present study was to evaluate the efficacy and safety of pulmonary rehabilitation in Japanese patients with inoperable CTEPH or persistent PH after intervention. As the first preliminary study of home-based pulmonary rehabilitation for Japanese CTEPH outpatients, the protocol was started using a low-dose home-based training program with supervised sessions in the hospital, and the

study population included outpatients who had been stable for at least three months and were receiving optimized medical therapy.

## 2. Materials and methods

### 2.1. Study population and design

We prospectively evaluated outpatients with inoperable or residual CTEPH who were stable and undergoing treatment with disease-targeted medication and who participated in a 12-week home-based pulmonary rehabilitation program at Chiba University Hospital from March 2012 to January 2014. The diagnosis of CTEPH was based on published criteria and made at least one year before entry into the study [2,11,18]. CTEPH was defined as a mean pulmonary arterial pressure (PAP) of  $\geq 25$  mmHg with a normal wedge pressure on the right heart catheterization in patients with symptoms such as dyspnea on exertion for  $>6$  months. Lung perfusion scans were also required to demonstrate segmental or larger defects concomitant with normal ventilation scans. Chronic thromboembolic findings were confirmed on pulmonary angiography.

The subjects with CTEPH were eligible to participate if they reported dyspnea on exertion leading to limitations in daily activities (Medical Research Council [MRC] grade  $\geq 2$ ). The inclusion criteria were an age between 18 and 80 years and a WHO functional class of II–IV. The patients were required to be stable and compensated with optimized medical therapy, including warfarin, diuretics, PAH-targeted agents, and nasal administration of oxygen, for at least three months before entering the study. Individuals with other unstable/severe pulmonary disease or cardiac, orthopedic, or neurological disorders limiting exercise performance were excluded.

All patients were under the care of an experienced pulmonologist (NT). The medical treatment remained unchanged and was continued during the rehabilitation program. The study was approved by the Human Ethics Review Committee of Chiba University Graduate School of Medicine (Approval date: December 2, 2011; Approved #: 1259), and the subjects provided written informed consent prior to participation.

### 2.2. Outcome measures

Baseline measurements included age, gender, body mass index, time since diagnosis, use of long-term oxygen therapy,

Abbreviations: CTEPH, chronic thromboembolic pulmonary hypertension; PH, pulmonary hypertension; PEA, pulmonary endarterectomy; PAH, pulmonary arterial hypertension; BPA, balloon pulmonary angioplasty; QOL, quality of life; WHO, World Health Organization; 6MWD, 6-minute walking distance; 6MWT, 6-minute walk test; PAP, pulmonary arterial pressure; MRC, Medical Research Council; TRPG, tricuspid regurgitation pressure gradient; sPAP, systolic pulmonary arterial pressure; BNP, brain natriuretic peptide; BDI, baseline dyspnea index; TDI, transition dyspnea index; QF, quadriceps force; HF, handgrip force; ADL, activities of daily living; NRADL, Nagasaki University Respiratory ADL Questionnaire; SGRQ, St. George's Respiratory Questionnaire

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