



## Pulmonary function impairment in patients with chronic heart failure: Lower limit of normal versus conventional cutoff values



Armine G. Minasian, MD<sup>a,\*</sup>, Frank J.J. van den Elshout, MD, PhD<sup>a</sup>,  
P.N. Richard Dekhuijzen, MD, PhD<sup>b</sup>, Petra J.E. Vos, MD, PhD<sup>a</sup>,  
Frank F. Willems, MD, PhD<sup>c</sup>, Paul J.P.C. van den Bergh, MD<sup>c</sup>,  
Yvonne F. Heijdra, MD, PhD<sup>b</sup>

<sup>a</sup> Department of Pulmonary Diseases, Rijnstate Hospital, Wagnerlaan 55, 6815 AD Arnhem, The Netherlands

<sup>b</sup> Department of Pulmonary Diseases, Radboud University Nijmegen Medical Center, Geert Grooteplein-Zuid 10, 6525 GA Nijmegen, The Netherlands

<sup>c</sup> Department of Cardiology, Rijnstate Hospital, Wagnerlaan 55, 6815 AD Arnhem, The Netherlands

### ARTICLE INFO

#### Article history:

Received 3 February 2013

Received in revised form

25 March 2014

Accepted 29 March 2014

#### Keywords:

Chronic heart failure

Conventional cutoff values

Lower limit of normal

Prevalence

Pulmonary function impairment

### ABSTRACT

**Objective:** To determine the prevalence of pulmonary function abnormalities in patients with chronic heart failure (HF) according to recent American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines using the lower limit of normal (LLN) compared to conventional cutoff values.

**Background:** Recent ATS/ERS guidelines recommend the use of the LLN instead of the conventional cutoff values to define pulmonary function impairment to avoid misclassification of patients. However, studies addressing the prevalence of pulmonary function abnormalities according to both definitions in patients with chronic HF are lacking.

**Methods:** In this prospective cross-sectional study, 164 chronic HF outpatients (age  $68 \pm 10$  years, 78% men, 88% New York Heart Association class I–II) with left ventricular ejection fraction  $< 40\%$  underwent spirometry and measurement of diffusing capacity. Body plethysmography was performed in patients with abnormal spirometry results.

**Results:** Diffusion impairment and airway obstruction were found in 44–58% and 26–37% of the patients, respectively, depending on the definition used (LLN versus conventional cutoff values,  $p < 0.05$ ). However, restriction was infrequent, irrespective of the definition used (7% versus 5%, respectively,  $p > 0.05$ ). The LLN identified fewer patients with abnormal lung function, whereas the conventional cutoff values classified more patients with diffusion impairment, airway obstruction, or a mixed category. Twenty-seven percent of patients were misclassified by the conventional cutoff values.

**Conclusion:** Pulmonary function abnormalities, especially diffusion impairment and airway obstruction, were highly prevalent in patients with chronic HF. Conventional cutoff values classified more patients with diffusion impairment, airway obstruction, or a mixed category compared to the LLN.

© 2014 Elsevier Inc. All rights reserved.

### Introduction

Isolated or combined pulmonary function abnormalities, such as restriction, diffusion impairment, and to a lesser extent airway

obstruction are common in patients with chronic heart failure (HF)<sup>1–7</sup> and can contribute to the perception of dyspnea<sup>8</sup> and exercise intolerance.<sup>8–12</sup> Reported prevalence rates vary between 41% and 93% for diffusion impairment,<sup>13–19</sup> between 21% and 55% for

**Abbreviations:** ACE-I, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin receptor blocker; ATS/ERS, American Thoracic Society/European Respiratory Society; BMI, Body mass index; CABG, Coronary artery bypass grafting; COPD, Chronic obstructive pulmonary disease; CRT, Cardiac resynchronization therapy; ECCS, European Community for Coal and Steel; FEF<sub>50</sub>, Forced expiratory flow at 50% of forced vital capacity; FEV<sub>1</sub>, Forced expiratory volume in 1s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HF, Heart failure; IC, Inspiratory capacity; ICD, Implantable cardioverter defibrillator; LLN, Lower limit of normal; LVEF, Left ventricular ejection fraction; LVSD, Left ventricular systolic dysfunction; NT-pro-BNP, N-terminal pro-B natriuretic peptide; NYHA,

New York Heart Association; PCI, Percutaneous coronary intervention; PEF, Peak expiratory flow; PFTs, Pulmonary function tests; % pred., Percent predicted; PY, Pack-years; TLC, Total lung capacity; TLCOc, Transfer factor for carbon monoxide corrected for hemoglobin concentration; VA, Alveolar volume; VC, Largest vital capacity.

\* Corresponding author. Department of Pulmonary Diseases, Rijnstate Hospital, P.O. Box 9555, 6800 TA Arnhem, The Netherlands. Tel.: +31 (0) 6 55890546, fax: +31 (0) 88 005 6124.

E-mail address: [aminasian@rijnstate.nl](mailto:aminasian@rijnstate.nl) (A.G. Minasian).

restriction,<sup>13–17,20</sup> and between 14% and 60% for airway obstruction.<sup>13–18,20,21</sup> These varying rates across the studies can be partly explained by the usually small number of patients included and differences in study population as well as diagnostic criteria used to define pulmonary function abnormalities. All studies except for one<sup>20</sup> have used conventional cutoff values to define an abnormality. However, the 80% predicted value (i.e. diffusing capacity or total lung capacity <80% predicted) and the fixed ratio of 0.7 (i.e. forced expiratory volume in 1s to forced vital capacity (FEV<sub>1</sub>/FVC) < 0.7) that are traditionally used may misclassify more than 20% of patients leading to false-positive diagnosis in the elderly and underdiagnosis in younger patients.<sup>22</sup> This is explained by the physiological decrease of the FEV<sub>1</sub>/FVC ratio with age because the FEV<sub>1</sub> declines more rapidly with age than the FVC in normal subjects.<sup>23</sup> Furthermore, the frequently used 80% predicted value has neither statistical nor physiological validity.<sup>24</sup> To avoid misclassification, recent American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines<sup>25</sup> recommend the use of statistically derived lower limit of normal (LLN) values that are based on the normal distribution and that classify the bottom 5% of the healthy population as abnormal. However, studies using the LLN values to assess the prevalence of pulmonary function abnormalities in patients with HF are lacking. Therefore, the purpose of this study was to determine the prevalence of pulmonary function abnormalities according to recent ATS/ERS guidelines using the LLN in comparison to conventional cutoff values in outpatients with chronic HF.

## Methods

### Study design and participants

This study was part of a larger prospective cross-sectional study evaluating the prevalence of chronic obstructive pulmonary disease (COPD) in patients with chronic HF ([ClinicalTrials.gov](http://ClinicalTrials.gov) Identifier NCT01429376). All patients visiting two outpatient cardiology departments of a large hospital in The Netherlands were screened for inclusion between October 2009 and December 2010. Inclusion criteria were chronic HF<sup>26</sup> with left ventricular systolic dysfunction (LVSD), i.e. left ventricular ejection fraction (LVEF) <40%, and New York Heart Association class (NYHA) I–IV. Chronic HF was defined according to the European Society of Cardiology guidelines as a clinical syndrome with symptoms and signs typical of HF and objective evidence of a structural or functional abnormality of the heart at rest.<sup>26</sup> Echocardiography was performed in patients without a recent (≤6 months) echocardiography to confirm persisting LVSD. Patients who were not able to cooperate or undergo reliable spirometry according to ERS standards for acceptability and reproducibility<sup>27</sup> or who had a history of asthma were excluded. Other exclusion criteria were malignancy with a poor prognosis (survival <6 months) and participation in another study. For the current study we also excluded patients with known pulmonary, pleural (with exception of pleural effusion due to HF), neuromuscular, collagen vascular, or other diseases that could affect pulmonary function. Patients with a body mass index (BMI) above 35 were excluded from the restriction prevalence analysis.

Patients were classified as having stable HF in the absence of hospitalization due to progression of HF within 3 months, change in diuretics within 1 month, 3% or more weight gain within 3 days, and more than 50% increase of N-terminal pro-B natriuretic peptide (NT-pro-BNP) within 1 month when the baseline NT-pro-BNP was 100 pmol/L or higher or more than 100 pmol/L increase of NT-pro-BNP within 1 month when baseline NT-pro-BNP was below 100 pmol/L.<sup>28</sup>

### Measurements and data collection

At baseline, a first blood sample was taken for the measurement of NT-pro-BNP. One month later, the participants visited the hospital for an interview with the investigator and several examinations, including height and weight measurement, pulmonary function tests (PFTs), a chest radiograph, and a second blood sample (hemoglobin, NT-pro-BNP). Additional data were collected from medical records and personal interviews. Smoking status was defined as never (<100 cigarettes in a lifetime), former (≥3 months ago), or current smoker (<3 months). Smoking pack-years (PY) were based only on the tobacco cigarette history, and one PY was defined as smoking twenty cigarettes a day for one year.

### Pulmonary function tests

All participants underwent pre-bronchodilator spirometry (MasterLab Pro, Jaeger, Würzburg, Germany) and measurement of the transfer factor of the lungs for carbon monoxide (TLCO). TLCO was measured with standard single-breath technique and was corrected for the subject's hemoglobin concentration (TLCOc). Body plethysmography was only performed in patients with airway obstruction and/or signs of restriction on spirometry including FVC and/or largest VC <LLN and/or <80% predicted, since patients with normal spirometry results were not expected to have abnormal findings of body plethysmography. PFTs were performed by trained and certified operators using standard techniques and according to the ERS standards for acceptability and reproducibility.<sup>27</sup> The European Community for Coal and Steel (ECCS) reference equations were used to calculate predicted values.<sup>27</sup>

Diffusion impairment was defined as TLCOc < LLN (ATS/ERS)<sup>25</sup> and <80% predicted (conventional cutoff value). Restriction was defined as total lung capacity (TLC) < LLN (ATS/ERS)<sup>25</sup> and <80% predicted (conventional cutoff value). Airway obstruction was defined as FEV<sub>1</sub>/VC <LLN (ATS/ERS)<sup>25</sup> and FEV<sub>1</sub>/FVC <0.7 (conventional cutoff value).<sup>29</sup> LLN was regarded as the lower fifth percentile of the frequency distribution of a healthy reference population and it was calculated by subtracting 1.64 times the residual standard deviation from the predicted value based on the ECCS reference equations. Severity of diffusion impairment and airway obstruction using the LLN criteria was categorized according to ATS/ERS guidelines<sup>25</sup> and severity of airway obstruction using the fixed ratio of 0.7 was categorized according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.<sup>29</sup>

### Chest radiographs

Standard posterior-anterior and lateral chest radiographs were performed and evaluated for the presence or absence of cardiomegaly (cardiothoracic ratio >0.5), congestion (alveolar edema, pleural effusion, Kerley-B lines, and/or redistribution of pulmonary blood flow) and conditions that belonged to the exclusion criteria. Independent radiologists qualitatively assessed the chest radiographs with an overall clinical impression.

### Ethical considerations

The study was approved by the regional Research Ethics Committee Arnhem-Nijmegen in The Netherlands ([ClinicalTrials.gov](http://ClinicalTrials.gov) Identifier NCT01429376) and complies with the Declaration of Helsinki. All patients gave written informed consent.

Download English Version:

<https://daneshyari.com/en/article/5868951>

Download Persian Version:

<https://daneshyari.com/article/5868951>

[Daneshyari.com](https://daneshyari.com)