

## New York Heart Association class is strongly associated with mortality beyond heart failure in symptomatic women

Online publish-ahead-of-print 21 December 2020

Cardiovascular disease is the leading cause of mortality in women worldwide.<sup>1</sup> The New York Heart Association's (NYHA) functional classification was specifically designed to estimate the general condition of heart failure patients<sup>2</sup> and to indicate their mortality risk.<sup>3</sup> Its use is now being extended to include complaints of chest pain, dyspnoea, and fatigue.<sup>4</sup>

New York Heart Association classification is easy to determine, and it is often used at outpatient cardiology clinics to assess risk. However, risk stratification tools for cardiovascular disease are mainly investigated in men. Therefore, cardiologists often find it

difficult to estimate risk in the growing population of symptomatic women referred by general practitioners. Since the association between NYHA class and mortality may differ between sexes and patient domains,<sup>3,5</sup> we studied this association in more than 9000 individuals visiting one of 13 outpatient cardiology clinics during 2007 and 2018.

We extracted data from the electronic health records of individuals visiting a clinic for the first time with complaints of chest pain, dyspnoea, or fatigue, with a documented NYHA class. Mortality was assessed by linking our data to the national database, Statistics Netherlands. We estimated survival functions using the Kaplan–Meier curves and Cox proportional hazards regression analysis (adjusted for age and SCORE). The UMCU Medical Research Ethical Committee judged that the Dutch Medical Research Involving Human Subjects Act does not apply to the data collection used for this study.

Of 9011 selected individuals, 4782 (53%) were female of whom 1450 were referred for

dyspnoea, 2801 for chest pain, and 531 for fatigue. New York Heart Association Classes I, II, and III–IV (out of IV) were documented in these women: 2196 (46%), 2077 (43%), and 509 (11%), respectively; in the 4229 men, this distribution was 2114 (50%), 1688 (40%), and 428 (10%), respectively (Figure 1B). After a median of 8 years' follow-up, 354 (7%) women and 415 (10%) men had died.

Survival analysis showed that a higher NYHA class was associated with mortality in all women (Figure 1A). Multivariate Cox regression analysis confirmed that mortality risk increased with higher NYHA class in women (NYHA Class II vs. I hazard ratio (HR) 1.7, 95% confidence interval (CI) 1.3–2.3; NYHA Class III–IV vs. I HR 3.9, 95% CI 2.8–5.5). This association became stronger after adjustment for SCORE (NYHA Class II vs. I HR 3.3, 95% CI 2.2–4.9, NYHA Class III–IV vs. I HR 7.8, 95% CI 4.9–12.2). Results were similar in men (NYHA Class II vs. I HR 3.3, 95% CI 2.3–4.6, NYHA Class III–IV vs. I HR 7.1, 95% CI 4.8–10.5). Furthermore, NYHA class was associated with a higher mortality risk in all complaint groups in women in NYHA class II (chest pain HR 1.4, 95% CI 0.8–2.2, dyspnoea HR 1.2, 95% CI 0.7–2.1, fatigue HR 0.9, 95% CI 0.4–2.1) and NYHA Class III–IV (chest pain: HR 2.4, 95% CI 1.3–4.6, dyspnoea HR 2.6, 95% CI 1.5–4.6, fatigue HR 2.5, 95% CI 1.0–6.0).

Thus, functional grading of complaints with NYHA classification provides important information on mortality risk in women presenting with a variety of cardiac complaints, beyond diagnosed heart failure. It indicates higher mortality risk in women suffering from NYHA Class III–IV complaints who may therefore warrant close attention.

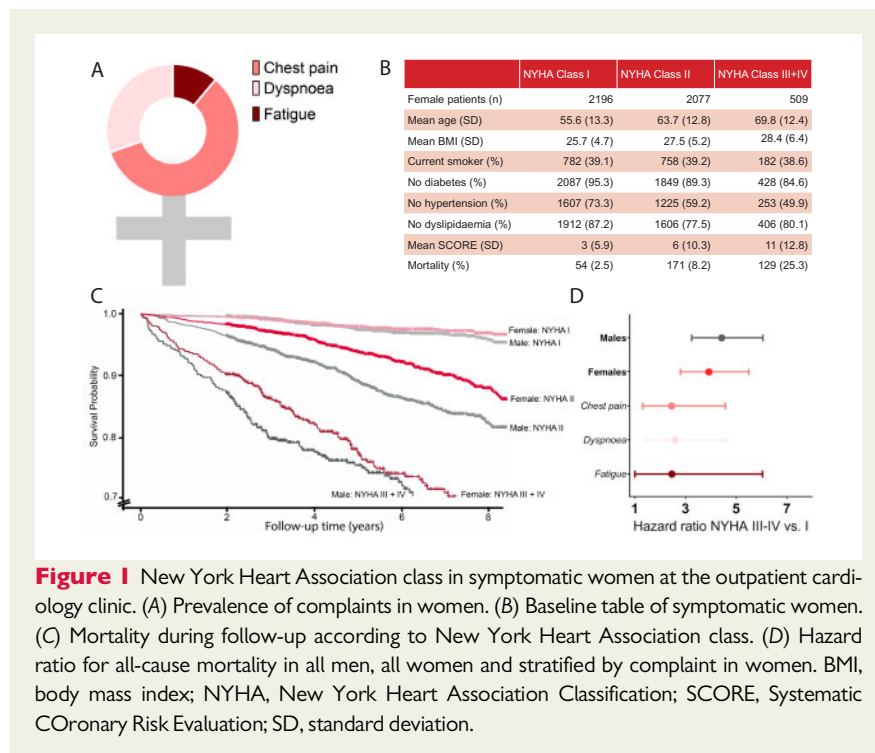
## Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

**Conflict of interest:** none declared.

## Funding

The DCVA (2020B004—IMPRESS), an ERC consolidator grant (866478—UCARE), and



**Figure 1** New York Heart Association class in symptomatic women at the outpatient cardiology clinic. (A) Prevalence of complaints in women. (B) Baseline table of symptomatic women. (C) Mortality during follow-up according to New York Heart Association class. (D) Hazard ratio for all-cause mortality in all men, all women and stratified by complaint in women. BMI, body mass index; NYHA, New York Heart Association Classification; SCORE, Systematic COronary Risk Evaluation; SD, standard deviation.

<sup>†</sup>The first two authors contributed equally to the study.

the Dutch Heart Foundation (2018B017—CVON-AI).

## References

1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP et al Heart disease and stroke statistics—2020 update: a report from the American Heart Association. *Circulation* 2020;**141**: E139–E596.
2. Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels*, 9th edn. Boston: Little, Brown & Co; 1994.
3. Kajimoto K, Sato N. Investigators of the Acute Decompensated Heart Failure Syndromes (ATTEND) Registry. Sex differences in New York Heart Association Functional Classification and survival in acute heart failure patients with preserved or reduced ejection fraction. *Can J Cardiol* 2020;**36**:30–36.
4. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Drazner MH et al 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;**62**: e147–e239.
5. Ghali JK, Krause-Steinrauf HJ, Adams KF, Khan SS, Rosenberg YD, Yancy CW et al Gender differences in advanced heart failure: insights from the BEST study. *J Am Coll Cardiol* 2003;**42**:2128–2134.

**Klaske R. Siegersma**<sup>1,2†</sup>,  
**Floor Groepenhoff**<sup>1,3†</sup>,  
**N. Charlotte Onland-Moret**<sup>4</sup>,  
**Igor I. Tulevski**<sup>5</sup>, **Leonard Hofstra**<sup>2,5</sup>,  
**G. Aernout Somsen**<sup>5</sup>, and  
**Hester M. Den Ruijter**<sup>1\*</sup>

<sup>1</sup>Laboratory of Experimental Cardiology,  
 University Medical Center Utrecht, Utrecht

University, Utrecht, The Netherlands;  
<sup>2</sup>Department of Cardiology, Location VUmc,  
 Amsterdam University Medical Centres,  
 Amsterdam, The Netherlands; <sup>3</sup>Central  
 Diagnostic Laboratory, University Medical  
 Center Utrecht, Utrecht University, Utrecht,  
 The Netherlands; <sup>4</sup>Department of  
 Epidemiology, Julius Center for Health  
 Sciences and Primary Care, University Medical  
 Center Utrecht, Utrecht University, Utrecht,  
 The Netherlands; and <sup>5</sup>Department of  
 Cardiology, Cardiology Centers of the  
 Netherlands, Utrecht, The Netherlands

\*Corresponding author. Tel: (0031) 088  
 75657654,

Email: [H.M.denRuijter-2@umcutrecht.nl](mailto:H.M.denRuijter-2@umcutrecht.nl)