Commentary to the Article Metabolic Syndrome and the Risk of Preclinical Heart Failure: Insights after 17 Years of Follow-Up from the STANISLAS Cohort

Ethan Yen-Hua Teng^a Karen Chia-Wen Liao^b Yi-Cheng Chang^{c, d, e}

^aBiological Programs for Younger Scholar, Academia Sinica, Taipei, Taiwan; ^bBiological Sciences Division, University of Chicago, Chicago, IL, USA; ^cDepartment of Internal Medicine, National Taiwan University, Taipei, Taiwan; ^dGraduate Institute of Medical Genetics and Proteomics, National Taiwan University, Taipei, Taiwan; ^eInstitutes of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

According to the contemporary professional consensus, heart failure (HF) is not an organic pathological diagnosis, but a clinical syndrome defined by symptoms and signs [1]. Associated with a high disability rate and an approximately 60% mortality rate within 5 years of diagnosis, HF represents a major and escalating public health problem. As a result, it is important to identify people at high-risk and conduct effective preventive interventions [2].

Preclinical HF indicates asymptomatic myocardial dysfunction. The AHA/ACC classification of Stage A is defined as those at high risk for HF but without structural heart disease or symptoms of HF. Stage B includes those with structural heart disease, but without signs or symptoms of HF. Stage B can be further delineated into two groups, those with preserved ejection fraction ($\geq 50\%$) and those with reduced ejection fraction ($< 50\%$). Once symptomatic, the patient will be classified as Stage C. Preclinical HF is associated with significantly high rate to progress into clinical (Stage C) HF [3]. About 35% of Stage A HF individual progresses to Stage B HF in 4 years [3].

The SuiviTemporaireAnnuel Non-Invasif de la Santé des LorrainsAssurésSociaux (STANISLAS) cohort is a single-center familial longitudinal cohort comprising

1,006 families (4,295 participants) from the Nancy region of France, who were recruited during 1993–95 [4, 5]. Totally four visits have been performed during an interval of 5–7 years. The implementation of the fourth visit enabled follow-up at 18–23 years of this cohort population. The study allows the long-term evaluation of clinical, biological, and morphological data [4, 5]. To this date, over a hundred publications on the STANISLAS cohort have appeared, and more than 600 demographic and laboratory data have been collected from each individual at the beginning of all three recruitments.

Previous prospective cohort studies have clearly shown the correlation between metabolic syndrome and HF [6, 7]. This report added another precious piece of evidence showing obesity and hypertension are strong contributors to preclinical HF. After a median of 17 years of follow-up, participants with baseline metabolic syndrome and those who developed metabolic syndrome were associated with an increased risk of preclinical HF. Particularly, elevated waist circumference and hypertension appeared to be the most associated with preclinical HF development independent of the level of NT-proBNP [8].

Ethan Yen-Hua Teng and Karen Chia-Wen Liao contributed equally.

Since there are significantly different baseline characteristics, confounding factors still may exist after adjustment. Even so, the STANISLAS cohort study is internationally the only longitudinal family cohort of subjects who are presumed to be healthy and gave us an excellent insight into the relationship between metabolic syndrome and HF [8].

It is quite interesting to notice that the overall incidence of preclinical HF is 46–68% at the end of follow-up, which may be related to the inclusion of NT-proBNP in the diagnosis of preclinical HF. NT-proBNP is a good biomarker for diagnosing HF in patients presenting to the emergency department with symptoms and is useful in the setting of uncertainty to support the clinical diagnosis, establishing prognosis or disease severity of acute decompensated HF [9]. Each increase in BNP by 100 pg/mL is associated with a 35% increase in relative risk of mortality [9]. However, in an outpatient setting, biomarker-guided, with either BNP or NT-proBNP, HF therapy is of uncertain benefit in clinical practice and therefore not advised [10]. The utility of serial measurement of BNP or

NT-proBNP to reduce HF hospitalization or mortality is also not well-established [10]. Furthermore, the interpretation of NT-proBNP concentrations in the presence of comorbidity such as pulmonary and renal diseases should be cautious [10].

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

We received no funds.

Author Contributions

Ethan Yen-Hua Teng and Karen Chia-Wen Liao wrote the manuscript; Yi-Cheng Chang critically revised and reviewed the manuscript.

References

- 1 Authors/Task Force Members; McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2022; 24(1):4–131.
- 2 McMurray JJ, Stewart S. Epidemiology, aetiology, and prognosis of heart failure. *Heart*. 2000;83(5):596–602.
- 3 Young KA, Scott CG, Rodeheffer RJ, Chen HH. Progression of preclinical heart failure: a description of stage A and B heart failure in a community population. *Circ Cardiovasc Qual Outcomes*. 2021;14(5):e007216.
- 4 Ferreira JP, Girerd N, Bozec E, Mercklé L, Pizard A, Bouali S, et al. Rationale and design of the fourth visit of the STANISLAS cohort: a familial longitudinal population-based cohort from the Nancy region of France. *Int J Epidemiol*. 2018;47(2):395–j.
- 5 Visvikis-Siest S, Siest G. The STANISLAS Cohort: a 10-year follow-up of supposed healthy families. Gene-environment interactions, reference values and evaluation of biomarkers in prevention of cardiovascular diseases. *Clin Chem Lab Med*. 2008;46(6):733–47.
- 6 Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. *Circulation*. 2005;112(20):3066–72.
- 7 Perrone-Filardi P, Paolillo S, Costanzo P, Savarese G, Trimarco B, Bonow RO. The role of metabolic syndrome in heart failure. *Eur Heart J*. 2015;36(39):2630–4.
- 8 Sharma A, Razaghizad A, Ferreira JP, Machu JL, Bozec E, Girerd N, et al. Metabolic syndrome and the risk of preclinical heart failure: insights after 17 years of follow-up from the STANISLAS Cohort. *Cardiology*. 2022 Feb 23. Epub ahead of print.
- 9 Nah EH, Kim SY, Cho S, Kim S, Cho HI. Plasma NT-proBNP levels associated with cardiac structural abnormalities in asymptomatic health examinees with preserved ejection fraction: a retrospective cross-sectional study. *BMJ Open*. 2019;9(4):e026030.
- 10 Chow SL, Maisel AS, Anand I, Bozkurt B, de Boer RA, Felker GM, et al. Role of biomarkers for the prevention, assessment, and management of heart failure: a scientific statement from the American Heart Association. *Circulation*. 2017;135(22):e1054–91.