

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Authors: Thank you very much for your time and effort to edit the manuscript.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>. As a letter to the editor, would you please discuss at least one related article published in WJCC?

Authors: We thank the Company Editor-in-Chief for the important comments. References have been updated with recent research articles. In addition, we have added and discussed the following papers from the *World Journal of Clinical Cases* (Rezende PC, et al. World J Clin Cases 2015, 3(2):163-170. / Zhang JF, et al. Ultrasonographic assessment of cardiac function and disease severity in coronary heart disease. World J Clin Cases 2021, 9(28):8366-8373.) Please see below:

“In addition, phenotypic heterogeneity often occurs and in complex diseases, like coronary artery disease (CAD). In CAD a spectrum of phenotypes is observed related among others to disease onset and stability (e.g., acute, or stable, recent onset or chronic, fatal, or not), extent of coronary lesions (e.g., number of vessels involved, plaque composition and burden) and the severity of LV structural and functional abnormalities (e.g., presence of LV dysfunction or lack thereof) [Rezende PC, et al. World J Clin Cases 2015, 3(2):163-170. / Zhang JF, et al. World J Clin Cases 2021, 9(28):8366-8373.]”

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This letter is well written and I agree with the authors that HFpEF is complex and represents a group of distinct disease (accepting that more than one can exist in any one patient) My major concern with the article is that for some reason is focuses on Machine Learning – only to then say that ML currently has no role to play. If this review is about the lack of robustness of current ML approaches then the title should reflect this and the introductory paragraphs should mention ML so that the reader aware of the focus of the letter earlier.

Authors: We thank the Reviewer for the instructive comments. Accordingly, discussion about Machine Learning has been updated. Please see below:

“It has been suggested that in the realm where machine learning (ML) algorithms may aid in our understanding of phenotypically heterogeneous diseases, HFpEF may be an ideal domain in which to apply ML. ML is based on neural networks which are series of nodes or artificial neurons that are processing elements forming a series of hidden layers. Within each node there is a set of inputs, weight, and a bias value. As an input enters the node, it gets multiplied by a weight value and the resulting output is either observed or passed to the next layer in the neural network. In other words, weight is the parameter within a neural network that transforms input data within the network's hidden layers. Recent studies have reported the promising role of ML for the identification of HFpEF as well as its distinct phenotypic subgroups (Unterhuber M, Rommel K-P, Kresoja K-P, Lurz J, Kornej J, Hindricks G, Scholz M, Thiele H, Lurz P. Deep learning detects heart failure with preserved ejection fraction using a baseline electrocardiogram. *Eur Heart J - Digital Health* 2021; 2 (4):699–703. DOI: <https://doi.org/10.1093/ehjdh/ztab081> / Segar MW, et al. *Eur J Heart Fail.* 2020;22(1):148-158 / Woolley RJ, et al. *Eur J Heart Fail.* 2021;23(6):983-991). Nevertheless, further research is needed to establish these findings in larger cohorts.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Some comparative analysis and description can be made between common HF and HFpEF in the article. Some related references can be added.

Authors: We thank the Reviewer for the valuable comments. Please see below:

“HF is a heterogeneous syndrome in which functional and structural parameters change dynamically during disease progression in a patient-specific fashion. Therefore, HF can be

regarded as a spectrum of phenotypes. Each HF phenotype is the result of a patient-specific trajectory wherein the heart remodels towards concentric hypertrophy (i.e. HFpEF), eccentric hypertrophy (i.e. HF with reduced LVEF), or a combination of both. The way of entry and the subsequent path of the trajectory depend on the patient's risk factors, comorbidities, and disease modifiers (Triposkiadis F, et al. Eur Heart J. 2019 Jul 1;40(26):2155-2163. / De Keulenaer GW, Brutsaert DL. Circulation. 2009 Jun 23;119(24):3044-6.)