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## **The new era of evidence-based echocardiographic algorithms using artificial intelligence**

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Artificial intelligence (AI) is expected to broadly reshape medical practice, potentially improving clinician decision-making, facilitating disease diagnosis and reducing readmission and mortality rates (1,2). In the field of cardiovascular medicine, medical AI studies can benefit from a substantial amount of data sources encompassing medical histories, physical examinations, laboratory tests, as well as the wealth of data stemming from cardiovascular imaging (mainly echocardiography and cardiac MRI). Today, cluster analysis (i.e., unsupervised machine learning), a branch of medical AI, can identify underlying disease patterns, indicative of severity or mechanistic phenotypes in patients with heterogenous characteristics that were previously undiscernible to the human eye (3,4).

An ischemic event impairs ventricular contractile function and stiffens the ventricle in patients with heart failure (HF). An ensuing inflammatory response may further reduce diastolic function (5). In addition, comorbidities such as hypertension, diabetes mellitus or renal disease can further increase the risk of developing cardiac remodeling. As coronary artery disease (CAD) increases the risk of mortality in patients with HF (6), identifying “high-risk” patterns of cardiac structure and function is urgently needed to personalize patient management in this specific population.

Congruent with this thinking, in this issue of the *International Journal of Cardiology*, Du et al. report the use of unsupervised cluster analysis based on echocardiographic data from >5,000 patients with chronic HF and comorbid CAD, leading to intriguing findings of echocardiographic patterns associated with a high risk of mortality (7). The investigators enrolled patients who were diagnosed with chronic HF and CAD in Shanxi Province, China. Of the 5,126 included patients, standard echocardiographic variables (*i.e.*, right and left cardiac structure, left ventricular systolic and diastolic function parameters) were incorporated in a latent cluster analysis. Among the 3 identified echocardiographic phenotypes, 34% were included in the cluster labeled “eccentric hypertrophy” which had the greatest left ventricular (LV) mass indexed by body surface area (LVMI) and smallest relative wall thickness (RWT). The cluster labeled “concentric hypertrophy” (20%) had the largest RWT, with mostly normal systolic and diastolic function parameters. The last cluster with the largest number of patients (46%) was labeled “diastolic decline”. Patients in the eccentric hypertrophy group were more often men and had a more frequent history of myocardial infarction and more severe HF, whereas those in the concentric hypertrophy group were more often women and had a more frequent prevalence of hypertension and atrial fibrillation. Decision tree analysis revealed LVMI, LV ejection fraction, RWT and E/A ratio as the

most relevant variables for predicting echocardiographic phenotypes, independent of clinical covariates. Furthermore, their echocardiographic phenotypes were able to discriminate patients' mortality risk, showing a worse prognosis for the patients with the "eccentric hypertrophy" followed by patients with the "diastolic decline" and "concentric hypertrophy" phenotypes, respectively.

This study is unique in that it focuses specifically on patients with both HF and CAD. Since echocardiograms are often performed in the management of this high-risk population, the suggested "EFVMD" algorithm could be broadly applied to identify patients with a high risk of death and those requiring further therapeutic intensification. To some extent, these results are in line with our recently published e'VM algorithm on echocardiographic data of the STANISLAS French populational cohort. Indeed, the e'VM algorithm enabled identifying a "diastolic changes" pattern and a "diastolic changes with structural remodeling" pattern. The fact that diastolic patterns and remodeling patterns are able to identify the disease process both very early on (i.e., in the STANISALS cohort) as well as much later (i.e., in the present ischemic heart failure cohort) suggests that this may be a biological feature that is intrinsic to cardiology itself. The genetic and biological determinants of these pleiotropic patterns should be explored in greater depth in the future as it may relate to therapeutic targets.

Although the results presented by Du et al. are clinically relevant and their echocardiographic algorithm may facilitate its application in clinical practice, further studies will be needed to generalize the results on a global scale. The major limitation of clustering analysis is that clusters identified in a population may be mostly appropriate in this initial group of patients; therefore, external validation of cluster patterns in other cohort studies is mandatory to obtain a sufficient level of evidence to modify clinical practice and guidelines (8). In addition, echocardiographic variables which were incorporated into this cluster analysis were categorized by guideline-recommended cut-off points, albeit with somewhat arbitrary values, which may limit overall generalizability. While the EFVMD algorithm has the great advantage of being simple, it did mislabel the “concentric hypertrophy” phenotype in approximately one third of patients. Furthermore, events related to myocardial dysfunction might change during the natural course of this disease, confounded by a “stunned myocardium” or drug effects.

Despite the above unanswered questions, the article by Du et al. represents a significant step toward echocardiogram-based risk stratification in patients with HF and CAD. Unraveling the underlying patterns of cardiac structure and function alterations may be of great value in better understanding the pathophysiological mechanism as well

as lead to better stratification of this high-risk population. In addition, it should be emphasized that this machine learning approach to cardiovascular imaging is a game changer since it allows integrating a vast number of variables (numerous echocardiographic variables in this instance) and provides a simple algorithm than can help clinicians categorize patients. The huge advantage of AI is its ability to integrate different variables into algorithms, whereas previous multi-variable algorithms were constructed by experts based solely on single-marker studies. This new approach is likely to translate into more stable algorithms recommended by the guidelines (since they would be anchored in generalizable evidence). This new framework should enable to tangibly reshape the way we progress in the field of cardiovascular imaging (Figure). In our view, this may represent a major step forward toward indisputable evidence-based guidelines that would attract great support and probably be universally applied (9): We believe this paradigm shift will ultimately result in AI evidence-driven CV imaging recommendations.

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## AI FRAMEWORK TO ACHIEVE EVIDENCE-DRIVEN GUIDELINES IN CV IMAGING

