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Olivier Huttin, Nicolas Girerd

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e'VM ALGORITHM:

A NEW EVIDENCE-BASED ECHOCARDIOGRAPHIC APPROACH TO PREDICT HEART FAILURE

Olivier Huttin, Nicolas Girerd

The diagnosis of heart failure (HF) is often straightforward in patients with overt clinical symptoms of HF (AHA stage C and D HF) related to volume overload and acutely or chronically increased cardiac and venous pressures (1). However, in the setting of the epidemic of HF, in particular HF with preserved ejection fraction (HFpEF), we need to prevent HF rather than diagnosing the latter at late/symptomatic stages which are only moderately accessible to treatment. However, to do so, an efficient prediction tool is needed in order to identify patients at high risk of subsequent progression to overt HFpEF (2). To achieve this goal, we may need to change the approach used in this field, targeting the prediction of hard outcomes such as incidental HFpEF using innovative methodological approaches (3).

Pre-symptomatic diastolic dysfunction (DD) has been previously defined as subjects with DD and normal systolic function without congestive heart failure (4). Given that the process of LV myocardial remodeling begins before the onset of symptoms, guidelines place special emphasis on the detection of subclinical DD and the timely identification of patients who are at high risk of developing overt HF (5). However, the identification of these high-risk patients represents a challenge in the absence of symptoms. An echocardiography-centered risk stratification is a scalable approach that can provide a direct assessment of diastolic patterns

and left ventricular and atrial remodeling (6). There is growing evidence regarding the relevance of early diagnosis of these patients using echocardiographic measurement of DD (7). Notwithstanding, how to best use echocardiography to detect patients at the highest risk for HF still remains a matter of debate.

The head-to-head comparison of currently available echocardiographic algorithms have highlighted wide differences in the prevalence of DD, ranging from 10 to 30% mainly according to the echocardiographic algorithm used (8)(9)(10). In a large population cohort, we recently reported that the prevalence of DD was 1.3% using the 2016 ASE/EACVI recommendations (4) as opposed to 5.7 to 8.8% using previous DD algorithms (11–14). These large variations in the prevalence of DD based solely on its definition should be a source of great concern, and may explain why echocardiography does not change the management of asymptomatic individuals. Most importantly, despite the impetus to use echocardiography as a new marker for preclinical DD screening, there is actually a low level of evidence regarding the most commonly-used algorithm of echocardiographic grading of diastolic dysfunction (14)(13). Indeed, the current ASE/EACVI algorithm was derived from an expert consensus rather than a data-driven approach (15) which probably limits its impact/diffusion. As emphasized previously, truly evidence-based grading systems are needed (16). The most pragmatic and widely accepted approach is probably outcome-based (i.e. adopting an echocardiographic algorithm that predicts hard outcomes). Such hard outcomes do exist for DD: it is the occurrence of HFpEF as defined by the need for an unplanned hospitalization for HF with normal EF in a population of patients without HF at baseline. Using the data of a large cohort of patients with baseline echocardiographic data and available follow-up with a sizeable number of the aforementioned outcome, an evidence-based echocardiographic algorithm reaching a high level of evidence could be constructed.

Building algorithms identifying DD remain nonetheless challenging given the multiplicity of available echocardiographic indices and their intrinsic correlation. In addition, echocardiographic variables can interact with one another; e.g. one parameter can be useful only in a portion of patients. This level of complexity is difficult to manage using classical statistical modeling. In contrast, machine learning-based approaches such as clustering can be particularly effective in identifying homogenous groups of patients (i.e. phenotypes) that can subsequently be predicted using other machine learning techniques (such as decision trees or random forests). Using this approach, our group recently proposed a machine learning-based algorithm that could be useful in a routine clinical setting(17) (Figure). This approach goes beyond DD since all echocardiographic variables are considered. The output of such approach is the identification of echocardiographic phenotypes/archetypes in which patients can be classified.

Using this approach, we identified 3 distinct echocardiographic phenotypes using k-means clustering in the first generation of the STANISLAS cohort (N=827), aged 60 ± 5 at the time of echocardiographic assessment, namely: “mostly normal (N)”, “diastolic changes (D)”, and “diastolic changes with structural remodeling (D/S)”. The D phenotype comprised mainly women and featured increased levels of inflammatory biomarkers, whereas the D/S phenotype, comprising predominately men, displayed the highest values of left ventricular mass, volume and remodeling biomarkers. We built a simple decision tree, based on e', atrial/ventricular volumes and ventricular mass, that adequately classified patients across the 3 echocardiographic phenotypes. This simple algorithm was termed the “e'VM” algorithm (Figure 1). When applying this algorithm in our validation cohort (the Malmö Preventive Project cohort - N=1,396), conducted in a very different setting, the “diastolic abnormalities” and “structural remodeling” phenotypes were found to be significantly associated with the risk of HF onset during follow-up, even after adjusting for the ARIC score (a clinical HF risk

score). A more advanced algorithm, based on random forest is available in GitLab (https://gitlab.com/cic-p/echocardio_clustering).

Among asymptomatic middle-aged individuals, echocardiographic data-driven classification, based on the e'VM algorithm, allowed identifying profiles with different long-term HF risk. This simple algorithm could help in providing an evidence-based echocardiographic approach for risk stratifying patients who undergo echocardiography in routine practice. Echocardiographic exams are routinely performed in a number of asymptomatic individuals, for example in hypertensive patients as recommended by the ACC/AHA in patients with slightly elevated natriuretic peptides, i.e. BNP>50 pg/mL.

The adequacy of this innovative algorithm should be assessed by other teams to maximize its impact (i.e. if its added value is similar in the hands of other teams). In fact, we would be thankful that our algorithm be tested in a variety of settings in order to maximize its generalizability !

Which preventive strategy to use in these high-risk patients still remains an open question. On a case-by-case evaluation, we believe that an optimized follow-up and possibly cardiovascular preventive treatment could be proposed to patients in the highest-risk categories of the e'VM algorithm. In addition, we believe that future trials targeted at preventing HF could use the e'VM as an inclusion criteria. In this respect, sodium-glucose cotransporter 2 inhibitors (SGLT2i) could represent strong candidates given their important preventive effect in the field of diabetes. In addition, MRAs have recently been shown to feature noteworthy antifibrotic properties in a pre-HF setting and whether the e'VM algorithm could identify patients with the highest benefit of MRA is to be tested.

The proposed e'VM echocardiographic algorithm is an important addition to preventive cardiology and can be the basis of a new segmentation of asymptomatic patients.

REFERENCES

1. Bhatia RS, Tu JV, Lee DS, Austin PC, Fang J, Haouzi A, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. *N Engl J Med*. 2006 Jul 20;355(3):260–9.
2. Juillière Y, Venner C, Filippetti L, Popovic B, Huttin O, Selton-Suty C. Heart failure with preserved ejection fraction: A systemic disease linked to multiple comorbidities, targeting new therapeutic options. *Arch Cardiovasc Dis*. 2018 Dec;111(12):766–81.
3. Schrub F, Oger E, Bidaut A, Hage C, Charton M, Daubert JC, et al. Heart failure with preserved ejection fraction: A clustering approach to a heterogenous syndrome. *Arch Cardiovasc Dis*. 2020 Jul;113(6–7):381–90.
4. Wan S-H, Vogel MW, Chen HH. Pre-clinical diastolic dysfunction. *J Am Coll Cardiol*. 2014 Feb 11;63(5):407–16.
5. Heart Failure Society Of America. Executive summary: HFSA 2006 Comprehensive Heart Failure Practice Guideline. *J Card Fail*. 2006 Feb;12(1):10–38.
6. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Eur J Echocardiogr J Work Group Echocardiogr Eur Soc Cardiol*. 2009 Mar;10(2):165–93.
7. Kane GC, Karon BL, Mahoney DW, Redfield MM, Roger VL, Burnett JC, et al. Progression of left ventricular diastolic dysfunction and risk of heart failure. *JAMA*. 2011 Aug 24;306(8):856–63.
8. Redfield MM, Jacobsen SJ, Burnett JC, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA*. 2003 Jan 8;289(2):194–202.
9. Lam CSP, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2011 Jan;13(1):18–28.
10. Kuznetsova T, Herbots L, López B, Jin Y, Richart T, Thijs L, et al. Prevalence of Left Ventricular Diastolic Dysfunction in a General Population. *CLINICAL PERSPECTIVE*. *Circ Heart Fail*. 2009 Mar 1;2(2):105–12.
11. Appleton CP. Doppler assessment of left ventricular diastolic function: the refinements continue. *J Am Coll Cardiol*. 1993 Jun;21(7):1697–700.
12. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. *Circulation*. 2000 Oct 10;102(15):1788–94.
13. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Eur J Echocardiogr J Work Group Echocardiogr Eur Soc Cardiol*. 2009 Mar;10(2):165–93.

14. Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *Eur Heart J*. 2007 Oct;28(20):2539–50.
15. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr*. 2016 Apr;29(4):277–314.
16. Fraser AG, Girerd N. Cardiovascular imaging “guidelines” - High time for a paradigm shift. *Int J Cardiol*. 2021 Apr 15;329:246–8.
17. Preud’homme G, Duarte K, Dalleau K, Lacomblez C, Bresso E, Smaïl-Tabbone M, et al. Head-to-head comparison of clustering methods for heterogeneous data: a simulation-driven benchmark. *Sci Rep*. 2021 Feb 18;11(1):4202.