European Heart Journal - Imaging Methods and Practice (2024) **2**, qyae059
https://doi.org/10.1093/ehjimp/qyae059

ORIGINAL ARTICLE

Variability in approach to exercise stress echocardiography for diagnosis of heart failure with preserved ejection fraction: an international survey on real-world practice

Yuta Tani[1], Yogesh N.V. Reddy[2], Frederik H. Verbrugge[3,4], Jeong Hoon Yang[5,6], Kazuaki Negishi[7], Tomonari Harada[1], Kazuki Kagami[1,8], Yuki Saito[1,9], Naoki Yuasa[1], Hidemi Sorimachi[1], Fumitaka Murakami[1], Toshimitsu Kato[1], Naoki Wada[10], Hideki Ishii[1], and Masaru Obokata[1,]*

[1]Department of Cardiovascular Medicine, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan
[2]Department of Cardiovascular Diseases, Mayo Clinic, Rochester, MN 55905, USA
[3]Centre for Cardiovascular Diseases, University Hospital Brussels, Jette 1090, Belgium
[4]Faculty of Medicine and Pharmacy, Vrije Universiteit Brussels, Jette 1090, Belgium
[5]Department of Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 06351, Republic of Korea
[6]Department of Cardiology, Heart Vascular Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 06351, Korea
[7]Nepean Clinical School, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales 2747, Australia
[8]Division of Cardiovascular Medicine, National Defense Medical College, Tokorozawa, Saitama 359-8513, Japan
[9]Division of Cardiology, Department of Medicine, Nihon University School of Medicine, Tokyo 173-8610, Japan
[10]Department of Rehabilitation Medicine, Gunma University Graduate School of Medicine, Maebashi, Gunma 371-8511, Japan

Received 6 March 2024; accepted after revision 24 May 2024; online publish-ahead-of-print 12 June 2024

Abstract

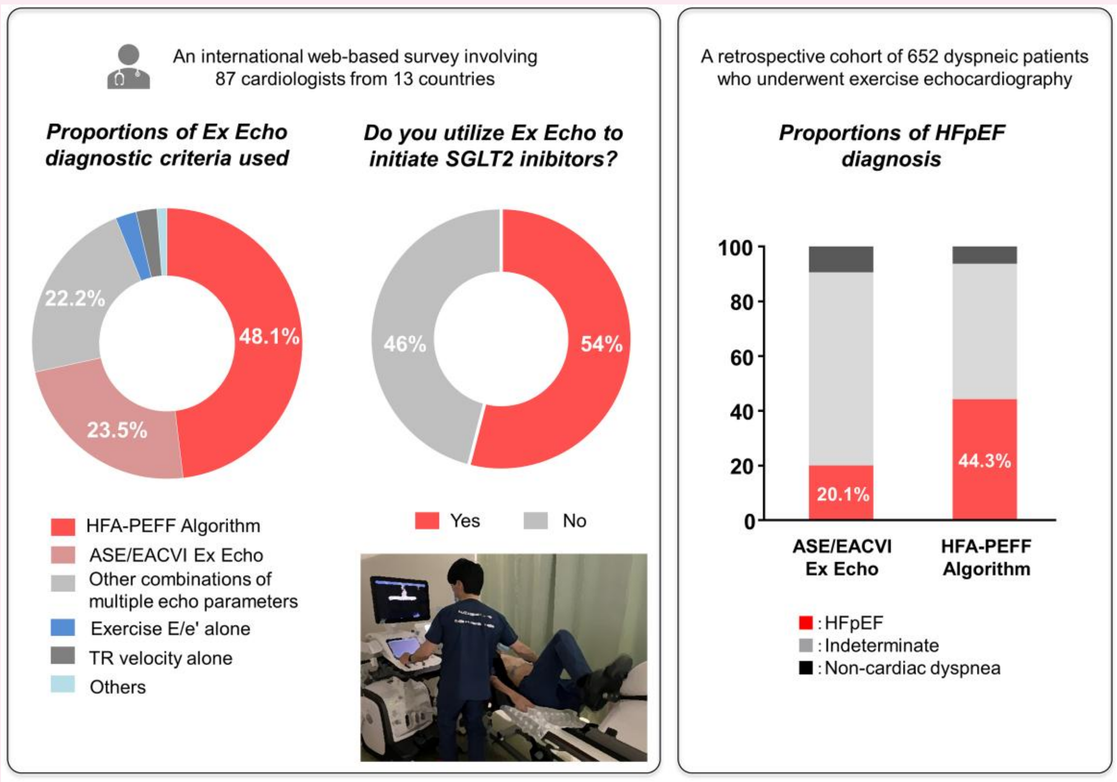
Aims The diagnosis of heart failure with preserved ejection fraction (HFpEF) remains challenging based on resting assessments. Exercise echocardiography is often used to unmask abnormalities that develop during exercise, but the diagnostic criteria have not been standardized. This study aimed to elucidate how cardiologists utilize exercise echocardiography to diagnose HFpEF in real-world practice.

Methods and results An international web-based survey involving 87 cardiologists was performed. We also performed a retrospective cross-sectional study to investigate the impact of different exercise echocardiographic diagnostic criteria in 652 dyspnoeic patients who underwent exercise echocardiography. The HFA-PEFF algorithm was the most commonly used exercise echocardiography criterion for HFpEF diagnoses (48%), followed by the ASE/EACVI criteria (24%) and other combinations of multiple parameters (22%). Among 652 patients, the proportion of HFpEF diagnosis varied substantially according to the criteria used ranging from 20.1% (ASE/EACVI criteria) to 44.3% (HFA-PEFF algorithm). Many cases (49.4–70.5%) remained indeterminate after exercise echocardiography, but only 41% of surveyed cardiologists would utilize exercise right heart catheterization to resolve an indeterminate result. Despite these diagnostic uncertainties, 54% of surveyed cardiologists would utilize exercise echocardiography results to initiate sodium–glucose co-transporter 2 inhibitors.

* Corresponding author. E-mail: obokata.masaru@gunma-u.ac.jp

Conclusion In real-world practice, exercise echocardiographic criteria utilized across cardiologists vary, which meaningfully impacts the frequency of HFpEF diagnoses, with indeterminate results being common. Despite these diagnostic uncertainties, many cardiologists initiate pharmacotherapy based on exercise echocardiography. The lack of consensus on universal diagnostic criteria for exercise echocardiography and approaches to indeterminate results may limit the delivery of evidence-based treatment for HFpEF.

Graphical Abstract



Keywords diagnosis • exercise stress echocardiography • heart failure with preserved ejection fraction • questionnaire • survey

Introduction

Recent clinical trials have shown convincing beneficial effects of pharmacotherapy in heart failure with preserved ejection fraction (HFpEF), such as sodium–glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP1-) agonists.[1–3] This makes its correct and early identification more important.[4] Nevertheless, the diagnosis of HFpEF among people with chronic dyspnoea but without overt congestion remains challenging and relies on the demonstration of objective evidence of elevated left ventricular (LV) filling pressures by diagnostic tests such as natriuretic peptide or standard echocardiography.[5–8] Importantly, LV filling pressures are often normal in patients with HFpEF at rest but increase abnormally during physiological stress, such as exercise.[7,9–11] Recent guidelines recommend using exercise stress testing to detect such haemodynamic abnormalities during exercise in cases of diagnostic uncertainty based on resting assessments,[12–14] and exercise stress echocardiography (i.e. diastolic stress echocardiography) being non-invasive is often used for the identification of occult HFpEF.[7,10,15–19] However, universal exercise protocols and diagnostic criteria have not been established. As a result, their application in clinical practice may vary widely, affecting the diagnosis (or prevalence) and ultimately the management of HFpEF.

Accordingly, our main objective was to investigate the current practice of exercise stress echocardiography by collecting opinions from various cardiologists via a web-based international survey. We also performed a cross-sectional study to determine the impact of different diagnostic criteria on the proportion of HFpEF diagnoses using a large cohort of individuals undergoing exercise echocardiography.

Methods

An international survey for exercise stress echocardiography

This international web-based survey was designed to determine current practices regarding exercise stress echocardiography for the evaluation of HFpEF or dyspnoea. A group of HF or echocardiography specialists (Y.N.V.R., F.H.V., J.H.Y., K.N., T.H., and M.O.) developed and edited the survey, which included 16 individual questions (see Supplementary data online, *Supplementary Materials*). The survey was distributed to cardiologists through social networking services (SNS) [X (former Twitter) and Facebook] of the Echocardiography Laboratory, Gunma University Hospital, the Japanese Association of Young Echocardiography Fellow (JAYEF), and individual investigators. The questionnaire was also emailed to investigators' colleagues. This survey was approved by the Ethics Board of the Gunma University Hospital (HS2023-057). The data underlying this article cannot be shared publicly due to the privacy of individuals who participated in the study.

A cross-sectional study

To investigate the impact of different criteria on HFpEF diagnosis, we performed a retrospective cross-sectional study. Consecutive series of 865 patients who were referred to the Gunma University echocardiographic laboratory for exercise stress echocardiography for the evaluation of unexplained dyspnoea between September 2019 and November 2023 were identified. We excluded patients without symptoms, current or previously documented reduced ejection fraction (EF < 50%), significant left-sided valvular heart disease (>moderate regurgitation, >mild stenosis); infiltrative, restrictive, or hypertrophic cardiomyopathy, non-group II pulmonary hypertension (PH), those younger than 20 years old, those who did not perform ergometer exercise echocardiography, and duplicate cases. This study was also approved by our Institutional Review Board with a waiver of informed consent (HS2023-118).

Details of the exercise stress echocardiographic examination in our laboratory are described previously.[10,17,18] Briefly, all patients underwent semi-supine ergometer exercise, starting with a 20 watts (W) load for 5 min, with 20 W-increments in 3 min to participants' exhaustion (Angio imaging, Lode B.V., Groningen, Netherlands). Echocardiographic images were recorded at baseline and at all stages of exercise to obtain *trans*-mitral inflow, mitral annular tissue velocities, tricuspid regurgitation (TR) velocity, and LV outflow pulse Doppler time–velocity integral.

The diagnosis of HFpEF was coded using different schemes: the recommendations from the American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) for the assessment of LV diastolic dysfunction;[14] and the HFA-PEFF diagnostic algorithm from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC).[13] The diagnosis of HFpEF was first coded from resting echocardiographic data using the ASE/EACVI recommendations for the assessment of elevated LV filling pressure (see Supplementary data online, *Figure S1A*). Then, exercise stress echocardiography was considered abnormal (i.e. HFpEF) when all of the following criteria were met: septal E/e′ > 15 during exercise, exercise TR velocity >2.8 m/sec, and septal e′ velocity at baseline is <7 cm/sec (see Supplementary data online, *Figure S1B*).[14] The results were normal (non-cardiac dyspnoea) when septal E/e' ratio was <10 with exercise and peak TR velocity was <2.8 m/sec with exercise. If either the resting or exercise result was positive, the diagnosis of HFpEF was coded.

The HFA-PEFF algorithm calculates a score based on resting echocardiography and natriuretic peptide levels (0–6 points, Step 2). A score ≥5 points was defined as HFpEF while a score of <2 was considered as non-cardiac dyspnoea. Among patients with intermediate scores (2–4 points), two or three points were added depending on the E/e' ratio and TR velocity during exercise stress echocardiography (Step 3). A diagnosis of HFpEF was coded if the combined score from Step 2 to Step 3 was ≥5 points (see Supplementary data online, *Figure S2*).[13]

The reproducibility of E/e' and TR velocity during peak exercise was assessed in 30 randomly selected patients. Intra- and inter-observer agreement was evaluated after the same observer and another experienced reader repeated the analysis using intraclass correlation coefficients (ICCs).

Statistical analysis

Data are reported as mean (standard deviation), median (interquartile range: IQR), or number (%) unless otherwise noted. Between-group differences were compared using the χ^2 test. Within-group differences were compared by paired *t*-test or Wilcoxon signed rank test. All tests were two-sided, with statistical significance set at $P < 0.05$. All statistical analyses were performed using JMP 17.1.0 (SAS Institute, Cary, NC, USA).

Table 1 Characteristics of the participants

	***n* = 87**
Region, n (%)	
East Asia (Japan, South Korea)	65 (75%)
Europe (Belgium, France, Germany, Italy, Portugal, Spain)	18 (21%)
North America (USA)	3 (3%)
Others	1 (1%)
Specialty and subspecialty,[a] n (%)	
General cardiologist	43 (49%)
Echocardiography specialist	63 (72%)
Heart failure specialist	59 (68%)
Other cardiovascular imaging specialist	2 (2%)
EP specialist	1 (1%)
Interventional cardiologist	10 (11%)
Others	2 (2%)
Experience of ESE, n (%) (n = 86)	
0–1 years	8 (9%)
2–5 years	27 (32%)
6–10 years	26 (30%)
>10 years	25 (29%)
Number of ESE performed at practicing hospital per year, n (%)	
1–50 cases	32 (37%)
51–100 cases	17 (19%)
101–300 cases	24 (28%)
301–500 cases	6 (7%)
>500 cases	8 (9%)
Percentage of ESE for HFpEF or dyspnoea	
0%	4 (5%)
1–25%	41 (47%)
26–50%	12 (14%)
51–75%	22 (25%)
76–100%	8 (9%)
RA pressure estimation method during ESE[a], n (%) (n = 81)	
Use resting RAP value	33 (41%)
Measure IVC-based RAP during exercise	27 (33%)
Use fixed value (e.g. 10 mmHg)	22 (27%)
Measure IVC-based RAP in the recovery	10 (12%)
Measure peripheral venous pressure	2 (2%)
Others	1 (1%)

EP, Electrophysiology; ESE, exercise stress echocardiography; HFpEF, heart failure with preserved ejection fraction; IVC, inferior vena cava; RAP, right atrial pressure; RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation; and USA, United States of America.
[a]Multiple answers allowed.

Results

The international survey

Characteristics of participants

A total of 87 cardiologists from 71 hospitals in 13 countries participated in this survey during ∼5 weeks from 10 August to 19 September 2023. The characteristics of the participants are shown in *Table 1*. The largest number of participants was from Japan (64%), followed by Belgium, Italy, and South Korea (*Table 1*). Nearly half of the participants (44%)

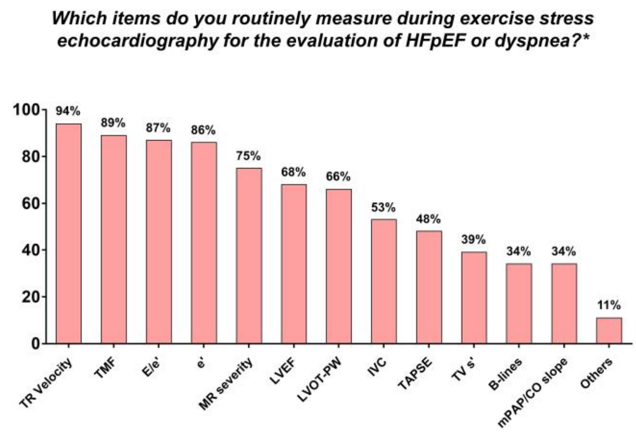


Figure 1 Frequency of echocardiographic variables measured during exercise stress echocardiography. *Multiple answers allowed. Values are expressed as percentages. E/e', the ratio of early diastolic mitral inflow to mitral annular tissue velocities; HFpEF, heart failure with preserved ejection fraction; IVC, inferior vena cava; LVEF, left ventricular ejection fraction; LVOT-PW, left ventricular outflow tract pulse wave Doppler; mPAP/CO slope, the slope of estimated pulmonary artery mean pressure to cardiac output; MR, mitral regurgitation; TAPSE, tricuspid annular plane systolic excursion; TMF, *trans*-mitral inflow velocity pattern; TR, tricuspid regurgitation; and TV s', systolic tissue velocity at the lateral tricuspid valve.

were practicing at hospitals with more than 100 exercise stress echocardiography cases per year. Sixty-three participants (72%) were echocardiography specialists and 59 (68%) were heart failure specialists (*Table 1*). More than half of the participants (59%) had ≥6 years of experience with exercise stress echocardiography.

Echocardiographic variables measured during exercise

Figure 1 demonstrates echocardiographic variables routinely measured during exercise echocardiography at the surveyed cardiologists' medical centre. TR velocity, *trans*-mitral inflow velocity, E/e' ratio, and mitral e' velocity were assessed in more than 85% of the participants. Several cutoff values of TR velocity during exercise are proposed for an HFpEF diagnosis.[12–14] Of the participants who answered with a single cutoff value ($n = 78$), the most commonly proposed cutoff for exercise TR velocity was 3.3 m/sec (49%), followed by 2.8 m/sec (17%) and 3.4 m/sec (10%; *Figure 2*). Similarly, an estimated right ventricular systolic pressure (eRVSP) during the exercise of 60 mmHg was the most frequently used cutoff value for an HFpEF diagnosis (28%), followed by 50 mmHg (17%) and 35 mmHg (15%; *Figure 2*). Thirty-three (41%) participants responded that they would use resting right atrial (RA) pressure value when estimating exercise RVSP (*Table 1*). The severity of mitral regurgitation was also assessed in most of the participants (75%). One-third of the participants reported that they would obtain mPAP/CO slope or ultrasound B-lines during exercise.

Diagnostic criteria of HFpEF by exercise stress echocardiography

Of 81 participants who responded, nearly half of the participants (48%) reported that they use the HFA-PEFF algorithm (i.e. exercise avg. E/e' ≥ 15 and exercise TR velocity >3.4 m/sec) for the diagnosis of HFpEF, followed by the ASE/EACVI criteria (23%; i.e. exercise avg. E/e' > 14, exercise TR velocity >2.8 m/sec, and septal e' velocity at baseline <7.0 cm/sec) or other combinations of multiple parameters (22%; *Figure 3*). In participants who reported using multiple echocardiographic parameters, two would use the combination of *trans*-mitral inflow velocity pattern and TR velocity and other two would use the combination of *trans*-mitral inflow velocity pattern, E/e' ratio, and TR velocity, while the remaining would use other combinations (e.g. E/e' ratio, TR velocity, mPAP/CO slope, ultrasound B-lines, inferior vena cava, etc.). Some cardiologists answered that they diagnose HFpEF based on a single echocardiographic parameter (exercise E/e' ratio, $n = 2$; and exercise TR velocity, $n = 2$). A comparison of responses from Asia and Europe reveals that the HFA-PEFF algorithm was used more frequently in Asia than in Europe (54.8% in Asia vs. 23.5% in Europe) while the use of the ASE/EACVI criteria was similar (24.2% in Asia vs. 23.5% in Europe). The use of other combinations of multiple parameters was more commonly used in Europe than in Asia (16.1% in Asia vs. 47.1% in Europe).

Questionnaires for therapeutic implication of exercise echocardiography and invasive cardiopulmonary exercise test

Of 84 participants who answered, the majority ($n = 45$, 54%) would initiate SGLT2 inhibitors based on the results of exercise stress echocardiography. Approximately half of all participants ($n = 52\%$) reported that invasive cardiopulmonary exercise tests are available in their hospitals. Two-thirds of the participants (64%) responded that they would consider an invasive exercise haemodynamic test if concern for PAH was present, followed by negative exercise echocardiographic results but high suspicion for HFpEF (55%), low diagnostic quality examination (e.g. poor image quality; 45%), and intermediate exercise echocardiographic results (41%; *Figure 4*).

Results of the retrospective cross-sectional study

The final cohort of the retrospective cross-sectional study included 652 subjects. Overall, patients were elderly and predominantly women (59.4%), with multiple cardiac and metabolic comorbidities, but only modestly elevated natriuretic peptide levels (*Table 2*). On average, LV end-diastolic volume and mass index, LA volume, and eRVSP were normal, with a borderline elevation of E/e' ratio at rest. During exercise, E/e' ratio and eRVSP were significantly increased, with a modest increase in mitral e' velocity (all $P < 0.0001$).

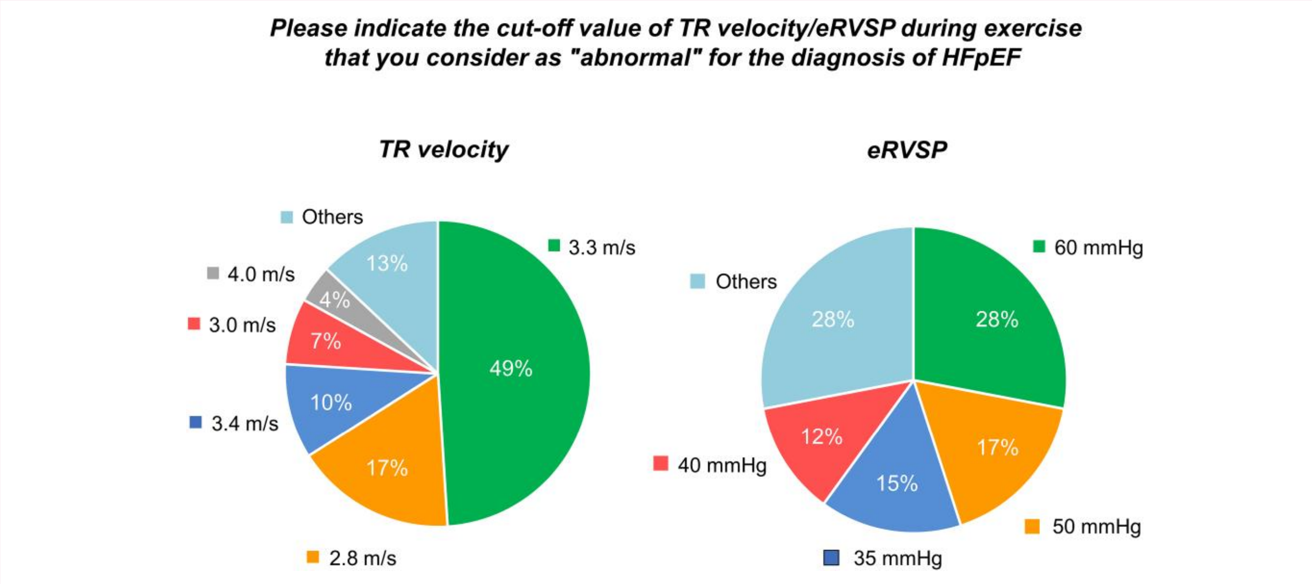


Figure 2 Cutoff values of TR velocity and estimated right ventricular pressure during exercise for HFpEF diagnoses. Values are expressed as percentages. eRVSP, estimated right ventricular systolic pressure; and other abbreviations as in *Figure 1*.

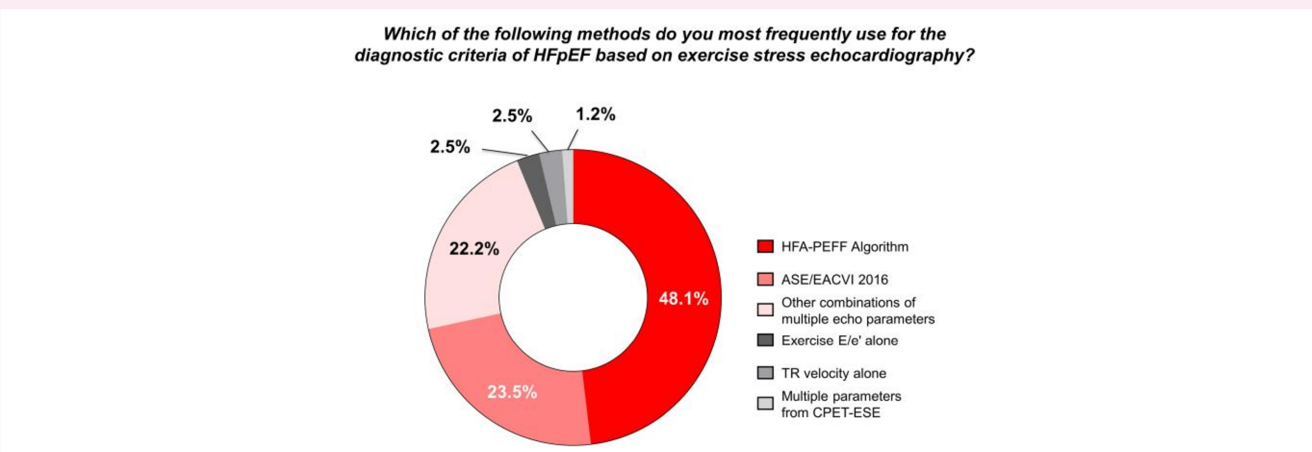


Figure 3 Proportions of most frequently used diagnostic criteria for HFpEF by exercise stress echocardiography. Values are expressed as percentages. ASE/EACVI, the American Society of Echocardiography/European Association of Cardiovascular Imaging; CPET-ESE, cardiopulmonary exercise test and exercise stress echocardiography; HFA-PEFF, the Heart Failure Association Pre-test assessment, echocardiography and natriuretic peptide, functional testing, final aetiology; and other abbreviations as in *Figure 1*.

Figure 5 shows the frequency of HFpEF diagnosis according to different diagnostic criteria. The rate of HFpEF diagnosis was the lowest ($n = 55$, 8.4%) when the ASE/EACVI resting criteria were applied. The addition of the ASE/EACVI-based exercise echocardiography criteria to the resting ASE/EACVI assessments resulted in a modest increase in HFpEF diagnosis ($n = 131$, 20.1%), with a large number of indeterminate cases ($n = 460$, 70.5%). When the resting HFA-PEFF algorithm (Step 2) was applied, the rate of HFpEF diagnosis was increased to 31.7% ($n = 207$), but a large number of cases remained inconclusive (2–4 points; $n = 404$, 62.0%). The frequency of HFpEF diagnosis was increased to 44.3% ($n = 289$), with a decreased rate of indeterminate cases ($n = 322$, 49.4%).

The intra-observer ICCs for exercise E/e' ratio and TR velocity were 0.87 and 0.87, respectively. The corresponding inter-observer ICCs were 0.83 and 0.93, respectively.

Discussion

The diagnosis of HFpEF remains challenging. Current guidelines recommend exercise stress echocardiography for the evaluation of HFpEF, but it remains unclear how it is performed in real-world clinical practice and how the results are interpreted to guide treatment. This study is

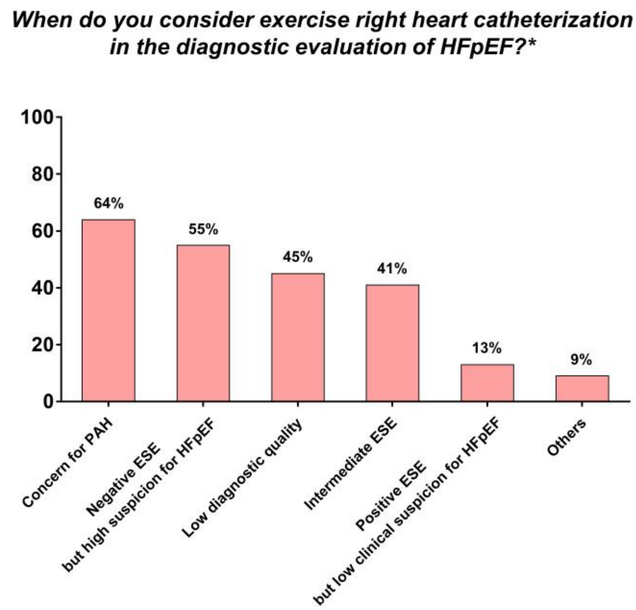


Figure 4 Indications for exercise right heart catheterization for the diagnosis of HFpEF. *Multiple answers allowed. Values are expressed as percentages. ESE, exercise stress echocardiography; PAH, pulmonary artery hypertension; and other abbreviations as in *Figure 1*.

the first investigation to determine the current practice of exercise stress echocardiography by collecting worldwide opinions from cardiologists via a web-based international survey. The main findings are as follows: (i) the exercise echo diagnostic criteria utilized for HFpEF diagnosis differed among individual cardiologists, with the HFA-PEFF algorithm and the ASE/EACVI criteria being the two most frequently used criteria; (ii) the prevalence of HFpEF diagnoses in patients with dyspnoea differed substantially depending on the criteria that were used; (iii) more than half of the participating cardiologists indicated that they would start SGLT2 inhibitors based on the results of exercise stress echocardiography; and (iv) indeterminate results were common in our retrospective cohort, and less than half of cardiologists would refer for confirmatory exercise right heart catheterization in the presence of indeterminate results. These data provide important clinical implications: they point out inconsistencies in the worldwide evaluation of HFpEF with exercise stress echocardiography, and they emphasize the need for universal protocol and diagnostic criteria to maximize its utility in clinical practice.

Variety of echocardiographic parameters measured during exercise

The diagnosis of HFpEF is challenging among patients with euvolemia because cardiac congestion is difficult to evaluate non-invasively and many patients develop abnormal haemodynamics only during physiological stress, such as exercise.[4–11] Recent guidelines emphasize the importance of exercise stress testing to detect such abnormalities,[12–14] and exercise stress echocardiography has been increasingly advocated as an initial test to enhance the diagnosis of HFpEF.[7,10,15–19] However, there are no universal protocols, measurements, or diagnostic criteria for exercise stress echocardiography for the evaluation of HFpEF. This may affect the quality of the test and ultimately clinical management.

In this international survey, we obtained opinions from cardiologists, the majority of whom had ≥6 years of experience with exercise echocardiography. We found that *trans*-mitral inflow velocity, mitral e' velocity, E/e' ratio, and TR velocity were the four most frequently obtained parameters during exercise echocardiography. This may be related to the current consensus statements,[12–14] but data to support the accuracy and optimal combination of imaging parameters to estimate LV filling pressures during exercise remain limited.[20] Some studies have demonstrated robust correlations of exercise echocardiographic parameters (e.g. E/e' ratio, TR velocity) with invasively measured data,[7,21–23] but others have not reproduced these favourable correlations.[20,24] There is no agreement concerning cutoff values of diagnostic variables and they are based on expert consensus opinion.[12–14] In fact, our survey found that cutoff values of TR velocity or estimated RVSP varied widely among physicians (*Figure 2*). The current study reveals the important, previously unrecognized limitations of exercise stress echocardiography. Other important limitations also exist: an isolated increase in TR velocity is not sufficient to diagnose HFpEF because it may be caused by precapillary pulmonary arterial hypertension or a normal hyperdynamic response to exercise in the absence of LV diastolic dysfunction.[12] In addition, TR velocity alone cannot account for increased RA pressure during exercise. In our survey, many cardiologists reported using resting or fixed RA pressure to estimate RA pressure during exercise. This may lead to serious underestimation of RA and RVSP, and thus HFpEF diagnosis.[21,23] Recent studies have demonstrated the potential utility of emerging parameters such as ultrasound B-lines and mPAP/CO slope,[18,25–27] and further investigations are required on the combined accuracy of these multiple parameters.

The diversity of diagnostic criteria and its adverse effects

The primary limitation of exercise stress echocardiography for the evaluation of HFpEF is the lack of validated diagnostic criteria.[18] To address the impact of different diagnostic criteria in real-world practice, we combined the international survey and cross-sectional study. Our survey demonstrated that the diagnostic criteria used varied significantly among individual cardiologists (*Figure 3*). Overall, the HFA-PEFF

Table 2 Baseline characteristics

	***n* = 652**
Age (years)	70.4 ± 12.3
Female, *n* (%)	387 (59.4%)
Body mass index (kg/m^2)	23.9 ± 5.1
Comorbidities	
Coronary artery disease, *n* (%)	58 (9%)
Diabetes mellitus, *n* (%)	136 (21%)
Hypertension, *n* (%)	479 (73%)
Atrial fibrillation, *n* (%)	148 (23%)
COPD, *n* (%)	52 (8%)
H_2FPEF score (points)	2 (2, 4)
Medications (n = 647)	
ACEI, ARB, or ARNI, *n* (%)	236 (36%)
Beta-blockers, *n* (%)	137 (21%)
Loop diuretics, *n* (%)	140 (22%)
MRA, *n* (%)	65 (10%)
SGLT2 inhibitors, *n* (%)	47 (7%)
Laboratories	
BNP (pg/mL), *n* = 272	51 (20, 120)
NT-proBNP (pg/mL), *n* = 434	157 (78, 492)
Creatinine (mg/dL), *n* = 617	0.78 (0.66, 0.98)
Vital signs	
Heart rate (bpm)	72 ± 14
Systolic BP (mmHg), *n* = 643	128 ± 19
Resting echocardiography	
LV end-diastolic volume (mL), *n* = 625	72 ± 26
LV mass index (g/m^2), *n* = 641	83 ± 23
LV ejection fraction (%)	63 ± 7
LA volume index (mL/m^2), *n* = 645	29 (22, 39)
E-wave (cm/sec), *n* = 651	70 ± 22
Mitral e' (cm/sec), *n* = 650	6.4 ± 1.9
E/e' ratio (septal), *n* = 649	11.7 ± 4.7
eRVSP (mmHg), *n* = 615	22 ± 8
Exercise echocardiography	
Peak (W)	55 ± 24
Peak mitral e' (cm/sec), *n* = 650	8.7 ± 2.5
Peak E/e' ratio (septal), *n* = 649	13.8 ± 5.3
Peak eRVSP (mmHg), *n* = 607	42 ± 13

Data are mean ± SD, median (interquartile range), or *n* (%).
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers; ARNI, angiotensin-receptor–neprilysin inhibitors; BNP, B-type natriuretic peptide; BP, blood pressure; COPD, chronic obstructive pulmonary disease; E/e' ratio, the ratio of early diastolic mitral inflow to mitral annular tissue velocities; eRVSP, estimated right ventricular systolic pressure; LA, left atrial; LV, left ventricular; MRA, mineralocorticoid-receptor antagonists; NT-pro BNP, N-terminal pro B-type natriuretic peptide; and SGLT2, sodium–glucose co-transporter-2.

algorithm and the ASE/EACVI criteria were the two most frequently used criteria. Differences in the frequency were observed between Asia and Europe, but most importantly, the proportion of HFpEF diagnoses in patients with dyspnoea differed substantially according to the diagnostic criteria used (*Figure 5*). Although the accuracy of these two diagnostic criteria is beyond the scope of the current study due to the lack of the gold standard of invasive exercise haemodynamic test, the large difference in the proportion of HFpEF or indeterminate diagnosis caused by the different diagnostic criteria used suggests that appropriate treatment may not be delivered to patients in clinical practice. Indeed, our survey revealed that the majority of cardiologists would initiate SGLT2 inhibitors based on the results of exercise stress echocardiography. Further studies are warranted to establish an evidence-based criterion for exercise stress echocardiography to diagnose HFpEF with definitive ascertainment of HFpEF or non-cardiac dyspnoea status by the gold standard of invasive exercise haemodynamic testing.

Future perspectives

In this cross-sectional study, a large proportion of patients were classified as intermediate/indeterminate, especially by current exercise criteria, an issue that contributes to the diagnostic challenges for HFpEF by exercise stress echocardiography. Invasive exercise haemodynamic test is the gold standard test to diagnose or rule out HFpEF.[6,13] Notably, less than half of cardiologists surveyed would consider an exercise right heart catheterization with an inconclusive exercise echocardiogram result, suggesting further clarification of this category and optimal approach is needed. In addition, invasive haemodynamic exercise testing is not available in many hospitals worldwide and the optimal approach to diagnosis in these settings from an indeterminate exercise echocardiogram is uncertain. As such, further studies are needed to develop and validate the optimal exercise echocardiography criteria for the diagnosis of HFpEF.

Limitations

The current investigation has certain limitations. Although this survey was open access, distribution of the survey through SNS might be limited to reach a wide range of cardiologists worldwide. For example, physicians who were not on SNS would have been excluded from the study. Because the survey was targeted to cardiologists who perform exercise echocardiography, the number of participants was relatively small, with a limited number of countries. Half of the participating cardiologists were practicing in Japan, which might limit the generalizability of the results. Many surveyed cardiologists might practice at specialized centres, which also introduced bias. The retrospective nature of the cross-sectional study might introduce selection bias. The cross-sectional study did not address the diagnostic accuracy of the two diagnostic schemes. We did not assess advanced echocardiographic parameters, such as LV and RV longitudinal strain. The percentage of cardiologist responses regarding the prescription of SGLT2 inhibitors should be interpreted in light of the fact that exercise echocardiography was not an inclusion criterion in the two large clinical trials of SGLT2 inhibitors.[1,2] Nevertheless, this is the first investigation to determine the current real-world practice of exercise stress echocardiography for the diagnosis of HFpEF.

Conclusion

In real-world practice, exercise echocardiography criteria used for HFpEF diagnosis vary among cardiologists, even among those with years of experience with exercise echocardiography. While many cardiologists consider initiating SGLT2 inhibitors based on the results of exercise stress echocardiography, the frequency of HFpEF diagnoses varies substantially depending on the diagnostic criteria used. The lack of universal diagnostic criteria may limit the delivery of appropriate treatment to patients with HFpEF. Further studies are needed to establish the optimal protocol and diagnostic criteria for the diagnosis of HFpEF.

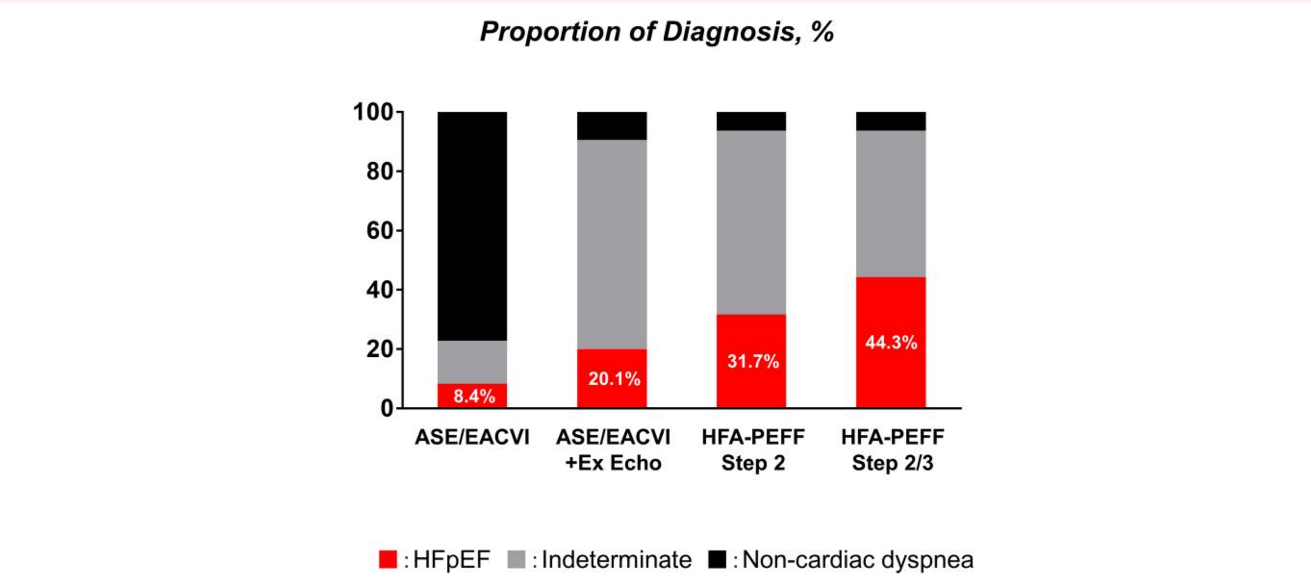


Figure 5 Proportion of HFpEF diagnosis according to the different diagnostic criteria. Values are expressed as percentages. Ex, exercise; and other abbreviations as in *Figures 1* and *3*.

Consent

This study was approved by our Institutional Review Board (HS2023-057 and HS2023-118) with a waiver of informed consent.

Supplementary data

Supplementary data are available at *European Heart Journal - Imaging Methods and Practice* online.

Acknowledgements

Dr Obokata received research grants from the Fukuda Foundation for Medical Technology, Mochida Memorial Foundation for Medical and Pharmaceutical Research, Nippon Shinyaku, Takeda Science Foundation, Japanese Circulation Society, Japanese College of Cardiology, AMI Inc., Nippon Boehringer-Ingelheim, JSPS KAKENHI (21K16078), and AMED (23jm0210104h0002). Dr Harada received research grants from the Bayer Academic Support.

Funding

None declared.

Conflict of interest: Dr Obokata received speaker honoraria from Novartis, Otsuka Pharmaceutical, AstraZeneca, and Nippon Boehringer-Ingelheim. Dr Ishii received lecture fees from AstraZeneca Inc., Bayer Pharmaceutical Co., Ltd, Boehringer-Ingelheim Japan, Bristol-Myers Squibb Inc., Daiichi-Sankyo Pharma Inc., MSD K.K., Mitsubishi Tanabe Pharma Co., Ltd, Mochida Pharmaceutical Co., Ltd, Novartis Japan, and Pfizer Japan Inc.

Data availability

Due to ethical restrictions imposed by the Ethics Committee and to protect the privacy of individuals, raw data cannot be publicly shared.

Lead author biography

Yuta Tani is a physical therapist and is currently enrolled in a doctoral programme at the Gunma University Graduate School of Medicine. He has been active in clinical research and his research interests include heart failure, especially heart failure with preserved ejection fraction (HFpEF). From the viewpoint of a physical therapist, Yuta Tani focuses on the evaluation and management of HFpEF.

References

1. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, Hernandez AF *et al.* Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med* 2022;**387**:1089–98.
2. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Böhm M *et al.* Empagliflozin in heart failure with a preserved ejection fraction. *N Engl J Med* 2021;**385**:1451–61.
3. Kosiborod MN, Abildstrøm SZ, Borlaug BA, Butler J, Rasmussen S, Davies M *et al.* Semaglutide in patients with heart failure with preserved ejection fraction and obesity. *N Engl J Med* 2023;**389**:1069–84.
4. Albani S, Zilio F, Scicchitano P, Musella F, Ceriello L, Marini M *et al.* Comprehensive diagnostic workup in patients with suspected heart failure and preserved ejection fraction. *Hellenic J Cardiol* 2024;**75**:60–73.
5. Borlaug BA. Evaluation and management of heart failure with preserved ejection fraction. *Nat Rev Cardiol* 2020;**17**:559–73.
6. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple, evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction. *Circulation* 2018;**138**:861–70.
7. Obokata M, Kane GC, Reddy YNV, Olson TP, Melenovsky V, Borlaug BA. Role of diastolic stress testing in the evaluation for heart failure with preserved ejection fraction: a simultaneous invasive-echocardiographic study. *Circulation* 2017;**135**:825–38.
8. Obokata M, Reddy YNV, Borlaug BA. Diastolic dysfunction and heart failure with preserved ejection fraction: understanding mechanisms by using noninvasive methods. *JACC Cardiovasc Imaging* 2020;**13**:245–57.

9. Borlaug BA, Nishimura RA, Sorajja P, Lam CSP, Redfield MM. Exercise hemodynamics enhance diagnosis of early heart failure with preserved ejection fraction. *Circ Heart Fail* 2010;**3**:588–95.
10. Harada T, Obokata M, Kagami K, Sorimachi H, Kato T, Takama N *et al.* Utility of E/e' ratio during low-level exercise to diagnose heart failure with preserved ejection fraction. *JACC Cardiovasc Imaging* 2022:S1936-878X(22)00666-0.
11. Litwin SE, Komtebedde J, Hu M, Burkhoff D, Hasenfuß G, Borlaug BA *et al.* Exercise-induced left atrial hypertension in heart failbjure with preserved ejection fraction. *JACC Heart Fail* 2023;**11**:1103–17.
12. Lancellotti P, Pellikka PA, Budts W, Chaudhry FA, Donal E, Dulgheru R *et al.* The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 2017;**30**:101–38.
13. Pieske B, Tschöpe C, De Boer RA, Fraser AG, Anker SD, Donal E *et al.* How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur Heart J* 2019;**40**:3297–317.
14. 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* 2016;**29**:277–314.
15. Pugliese NR, De Biase N, Del Punta L, Balletti A, Armenia S, Buralli S *et al.* Deep phenotype characterization of hypertensive response to exercise: implications on functional capacity and prognosis across the heart failure spectrum. *Eur J Heart Fail* 2023;**25**: 497–509.
16. Verwerft J, Soens L, Wynants J, Meysman M, Jogani S, Plein D *et al.* Heart failure with preserved ejection fraction: relevance of a dedicated dyspnoea clinic. *Eur Heart J* 2023;**44**:1544–56.
17. Takizawa D, Harada T, Obokata M, Kagami K, Sorimachi H, Yuasa N *et al.* Pathophysiologic and prognostic importance of cardiac power output reserve in heart failure with preserved ejection fraction. *Eur Heart J Cardiovasc Imaging* 2024; **25**:220–8.
18. Kagami K, Obokata M, Harada T, Sorimachi H, Yuasa N, Saito Y *et al.* Incremental diagnostic value of post-exercise lung congestion in heart failure with preserved ejection fraction. *Eur Heart J Cardiovasc Imaging* 2023;**24**:553–61.
19. Saito Y, Obokata M, Harada T, Kagami K, Wada N, Okumura Y *et al.* Prognostic benefit of early diagnosis with exercise stress testing in heart failure with preserved ejection fraction. *Eur J Prev Cardiol* 2023;**30**:902–11.
20. Obokata M, Borlaug BA. The strengths and limitations of E/e' in heart failure with preserved ejection fraction. *Eur J Heart Fail* 2018;**20**:1312–4.
21. Obokata M, Kane GC, Sorimachi H, Reddy YNV, Olson TP, Egbe AC *et al.* Noninvasive evaluation of pulmonary artery pressure during exercise: the importance of right atrial hypertension. *Eur Respir J* 2020;**55**:1901617.
22. Talreja DR, Nishimura RA, Oh JK. Estimation of left ventricular filling pressure with exercise by Doppler echocardiography in patients with normal systolic function: a simultaneous echocardiographic-cardiac catheterization study. *J Am Soc Echocardiogr* 2007; **20**:477–9.
23. Yang JH, Harada T, Choi KH, Kato T, Kim D, Takama N *et al.* Peripheral venous pressure-assisted exercise stress echocardiography in the evaluation of pulmonary hypertension during exercise in patients with suspected heart failure with preserved ejection fraction. *Circ Heart Fail* 2022;**15**:e009028.
24. Santos M, Rivero J, McCullough SD, West E, Opotowsky AR, Waxman AB *et al.* E/e' ratio in patients with unexplained dyspnea lack of accuracy in estimating left ventricular filling pressure. *Circ Heart Fail* 2015;**8**:749–56.
25. Saito Y, Obokata M, Harada T, Kagami K, Sorimachi H, Yuasa N *et al.* Disproportionate exercise-induced pulmonary hypertension in relation to cardiac output in heart failure with preserved ejection fraction: a non-invasive echocardiographic study. *Eur J Heart Fail* 2023;**25**:792–802.
26. Pugliese NR, De Biase N, Gargani L, Mazzola M, Conte L, Fabiani I *et al.* Predicting the transition to and progression of heart failure with preserved ejection fraction: a weighted risk score using bio-humoural, cardiopulmonary, and echocardiographic stress testing. *Eur J Prev Cardiol* 2021;**28**:1650–61.
27. Gargani L, Pugliese NR, De Biase N, Mazzola M, Agoston G, Arcopinto M *et al.* Exercise stress echocardiography of the right ventricle and pulmonary circulation. *J Am Coll Cardiol* 2023;**82**:1973–85.