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INVITED EDITORIAL

Towards a standardized diagnostic and therapeutic pathway for suspected heart failure with preserved ejection fraction in European Dyspnoea Clinics

Jan Verwerft [1,2]*, Youri Bekhuis [1,2], and Guido Claessen [1,2]; on behalf of the X-PRESS O_2 Consortium

[1]Department of Cardiology and Jessa & Science, Jessa Hospital, Hasselt 3500, Belgium; and [2]Faculty of Medicine and Life Sciences/LCRC, UHasselt, Diepenbeek 3590, Belgium

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This editorial refers to 'The diagnostic yield of an elaborate workup for comorbidities in a real-life heart failure with preserved ejection fraction outpatient population', by S.G.J. Mourmans *et al.* https://doi.org/10.1093/eurjpc/zwaf429.

Summary of Mourmans *et al.*

In this issue of the journal, Mourmans *et al.*[1] present a well-designed prospective study evaluating the diagnostic yield of a structured comorbidity workup in 521 patients with heart failure with preserved ejection fraction (HFpEF). Their protocol included echocardiography, treadmill electrocardiogram (ECG), spirometry, 6-min walk test, ambulatory sleep studies, 24-h Holter monitoring, and an extended laboratory panel.

On average, one previously unrecognized comorbidity was identified per patient. Sleep apnoea (39%) and iron deficiency (35%) emerged as the most frequently undiagnosed conditions, while diabetes (23%), obesity (45%), and hypercholesterolaemia (36%) were often undertreated. These findings underscore the burden of comorbidities in HFpEF and highlight the potential of structured screening to identify actionable therapeutic targets.

This diagnostic yield aligns closely with findings from a Belgian multicentre dyspnoea clinic network (X-PRESS O_2 Consortium), which implemented a standardized workup in patients referred for unexplained breathlessness.[2] In that cohort of over 2000 patients with unexplained dyspnoea, a structured diagnostic pathway using score-based triage and functional testing confirmed HFpEF in 293 cases. In nearly all of these, diagnosis directly led to clinical action: cardiovascular medication was optimized in 99% (median of 3 changes per patient), 37% underwent cardiovascular interventions (most commonly ablation for atrial fibrillation), and comorbidities such as iron deficiency (40%), diabetes (35%), and obesity (31%) were actively treated. Although the impact on long-term outcomes was not assessed, both studies suggest that structured evaluation not only improves diagnostic clarity and risk stratification but also facilitates immediate, phenotype-guided management.[3,4]

Balancing between diagnostic yield and value for money

Although the comprehensive approach used by Mourmans *et al.* led to meaningful therapeutic opportunities, not all components of the workup provided comparable clinical or economic value. For example, routine Holter monitoring identified new atrial fibrillation in only 1% of cases, and spirometry rarely led to changes in clinical management.

Waist circumference—a more accurate marker of central adiposity than body mass index (BMI)—was not recorded in either the Maastricht or Belgian cohorts. This is notable given that, in PARAGON-HF, nearly all patients with HFpEF had central adiposity as assessed by waist-to-height ratio, which showed stronger associations with HF outcomes than BMI.[5]

The urine albumin-to-creatinine ratio (UACR), a low-cost and widely available marker, was incorporated into the Maastricht protocol—an important strength. Albuminuria was present in 21% of patients (UACR 3–30 mg/mmol in 17%; UACR ≥30 mg/mmol in 3%). Its inclusion enhances risk stratification and facilitates phenotype-driven comorbidity management in HFpEF. Even low-grade albuminuria independently predicts adverse outcomes in HFpEF and should be considered a diagnostic and therapeutic target in this population.[6]

In resource-limited settings, prioritizing such high-yield, low-cost tests while reserving more expensive or lower-yield diagnostics for selected patients may improve both the efficiency and clinical value of HFpEF workups.

The opinions expressed in this article are not necessarily those of the Editors of the *European Journal of Preventive Cardiology* or of the European Society of Cardiology.

* Corresponding author. Tel: +32 11 87 11 87, Email: jan.verwerft@jessazh.be

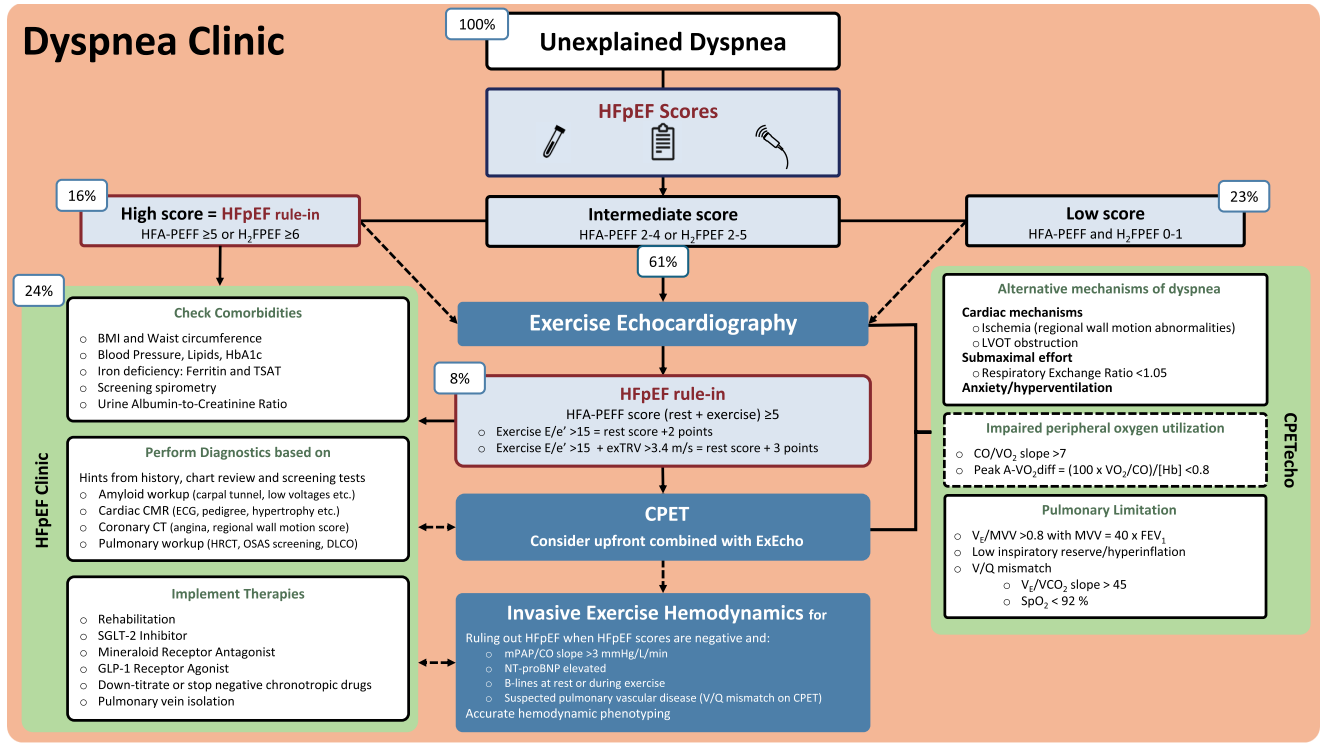

Figure 1 Proposed diagnostic flowchart for the evaluation of patients with unexplained dyspnoea in a multidisciplinary dyspnoea clinic. Patients are initially triaged using the HFA-PEFF or H_2FPEF scores. Those with intermediate scores undergo exercise echocardiography to improve diagnostic precision. If heart failure with preserved ejection fraction is confirmed (based on resting and/or exercise scores), patients are referred to an heart failure with preserved ejection fraction clinic for phenotype-driven comorbidity screening and tailored therapeutic interventions. Cardiopulmonary exercise testing, preferably combined with echocardiography (CPETecho), is recommended for patients with persistent diagnostic uncertainty. This approach also enables the identification of alternative causes of dyspnoea, including pulmonary, peripheral, and behavioural mechanisms. Invasive exercise haemodynamic testing may be considered in select cases when non-invasive assessments are inconclusive. HFpEF, heart failure with preserved ejection fraction; HFA-PEFF, Heart Failure Association diagnostic algorithm for HFpEF; H_2FPEF, Clinical HFpEF score (Heavy, Hypertensive, AF, Pulmonary hypertension, Elder, Filling pressure); 6MWT, 6-min walk test; ECG, electrocardiogram; CMR, cardiac magnetic resonance; TSAT, transferrin saturation; HbA1c, glycated haemoglobin; UACR, urine albumin-to-creatinine ratio; DLCO, lung diffusion capacity for carbon monoxide; HRCT, high-resolution computed tomography; OSAS, obstructive sleep apnoea syndrome; CPET, cardiopulmonary exercise testing; CPETecho, combined cardiopulmonary exercise testing and echocardiography; exTRV, exercise tricuspid regurgitation velocity; E/e', mitral inflow to annular velocity ratio; CO/VO_2, cardiac output to oxygen consumption; a-vO_2diff, arteriovenous oxygen difference; [Hb], haemoglobin concentration; VE/VCO_2, ventilatory efficiency slope; MVV, maximal voluntary ventilation; FEV_1, forced expiratory volume in 1 s; SpO_2, peripheral oxygen saturation; mPAP/CO, mean pulmonary artery pressure to cardiac output slope.

Integrating heart failure with preserved ejection fraction clinics within dyspnoea clinics

Although the Maastricht cohort consisted of patients with an established HFpEF diagnosis, the authors clarify that diagnoses were made in the context of a broader dyspnoea clinic, using HFA-PEFF or H_2FPEF scoring systems (*Figure 1*). This reflects the ideal model: HFpEF clinics should operate as integrated modules within multidisciplinary dyspnoea clinics, not as isolated units.

Score-based triage, integrating laboratory parameters, echocardiographic indices, and clinical features, offers a logical starting point. However, these scores, while specific, lack sensitivity, particularly for early-stage HFpEF. Many patients with HFpEF remain undiagnosed if assessment is limited to resting evaluation alone.[7]

This limitation is underscored by our own findings from the Belgian X-PRESS O_2 Consortium, where approximately one-third of patients with unremarkable resting evaluations were subsequently diagnosed with HFpEF only after exercise echocardiography.[8] These observations reinforce the need for exercise-based diagnostic modalities to confirm HFpEF and differentiate it from alternative causes such as pulmonary disease or deconditioning.

Rethinking functional assessment

In the Maastricht Dyspnoea Clinic, functional assessment relied on multiple separate tests—treadmill exercise ECG, spirometry, and the 6-min walk test. Each yields partial information; however, this stepwise strategy is time-consuming and fails to provide integrated insight into exercise physiology.

Among available modalities, exercise echocardiography—highly specific though modestly sensitive—is now recommended as the preferred dynamic test to unmask HFpEF when resting evaluations are inconclusive.[9,10]

In cases where diagnostic uncertainty persists, cardiopulmonary exercise testing (CPET) adds mechanistic insight into ventilatory, circulatory, and metabolic performance. However, CPET alone cannot reliably distinguish between central and peripheral limitations.[10]

A combined approach—CPETecho—offers a single-session, integrative evaluation (*Figure 1*). It captures pulmonary pressures, stroke volume reserve, gas exchange efficiency, and peripheral oxygen extraction in real time, thereby improving diagnostic clarity in complex presentations.[10,11]

Merging multiple standalone tests into an integrated CPETecho strategy may streamline diagnostic pathways, reduce delays, and enhance the patient experience—without substantial additional cost or complexity, beyond the perceived barriers associated with organizational change. Ultimately, the structured approach developed in Maastricht provides a strong foundation for implementing more integrated, mechanism-based functional assessment.

A proposal for integration and European consensus

We propose a tiered, resource-sensitive model in which HFpEF clinics are embedded within broader dyspnoea clinics. Structured triage using HFA-PEFF or H_2FPEF algorithms can standardize referrals and guide functional testing.

Exercise echocardiography is recommended for patients with intermediate or high HFpEF probability. Where feasible, combining CPET and echocardiography in a single session (CPETecho) enhances diagnostic precision and workflow efficiency. In other centres, a stepwise approach remains a valid and pragmatic alternative.

To reduce delays and promote timely, phenotype-driven care, diagnostic workup and therapeutic initiation (guideline-directed medical therapy and comorbidity management) should be closely integrated. While basic risk profiling is essential in all patients, extended comorbidity screening is best reserved for confirmed HFpEF cases, guided by therapeutic relevance.

This approach avoids unnecessary testing, streamlines diagnosis, and supports more accurate labelling. A Europe-wide consensus on minimal diagnostic requirements and functional testing modalities would promote consistency and quality of care across centres. We encourage collaborative action from national cardiovascular societies, the European Association of Preventive Cardiology (EAPC), and European Society of Cardiology (ESC) working groups to co-develop such a framework.

Conflict of interest: none declared.

Collaborators

The X-PRESS O_2 Consortium

Maarten Falter MD[a,b,c], Youri Bekhuis MD[a,b,c,d], Wouter L'Hoyes MD[e,f], Mauricio Milani MD PhD[a,g,h], Sarah Hoedemakers MD[a,b], Lucie Soens MD[i,j], Sara Moura-Ferreira MD[a,b], Sebastiaan Dhont MD[b,k], Rik Pauwels MD[a,b,c,d], Annemie Jacobs MD[e], Stephanie De Schutter MD[l,m], Boris Delpire MD[a,b,d], Hannah Van Belle[c,d], Sarah Stroobants[a,b], Siddarth Jogani[a,b], Simon Vanhentenrijk[a,b], Sibel Altintas[a,b], Johan Verbeeck PhD[n], Jan Stassen MD PhD[a,b], Andreas B. Gevaert MD PhD[l,m], Philippe Debonnaire MD PhD[e], Alexander Van de Bruaene MD PhD[c,d], Philippe B. Bertrand MD PhD[b,k], Lieven Herbots MD PhD[a,b], Ruta Jasaityte MD PhD[a,b], Frederik H. Verbrugge MD PhD MSc[i,j], Guido Claessen MD PhD[a,b,c], Jan Verwerft MD PhD[a,b]

[a]Jessa Hospital, Department of Cardiology and Jessa & Science, Hasselt, Belgium; [b]UHasselt, Faculty of Medicine and Life Sciences/LCRC, Diepenbeek, Belgium; [c]Department of Cardiovascular Sciences, KU Leuven, Belgium; [d]Department of Cardiovascular Diseases, UZ Leuven, Belgium; [e]Department of Cardiology, Sint-Jan Hospital, Bruges, Belgium; [f]Department of Cardiology, Imelda Hospital, Bonheiden, Belgium; [g]UHasselt, Faculty of Rehabilitation Sciences, Rehabilitation Research Center, Diepenbeek, Belgium; [h]University of Brasilia, Health Sciences and Technologies Graduate Program, Brasilia, Brazil; [i]Centre for Cardiovascular Diseases, University Hospital Brussels, Jette, Belgium; [j]Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel, Brussels, Belgium; [k]Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium; [l]Research Group Cardiovascular Diseases, GENCOR Department, University of Antwerp, Antwerp, Belgium; [m]Department of Cardiology, Antwerp University Hospital (UZA), Edegem, Belgium; and [n]DSI, I-Biostat, UHasselt, Diepenbeek, Belgium

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