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EDITORIAL

Advancing strategies for valvular heart disease and pulmonary hypertension: insights and perspectives

Valvular heart disease (VHD) and pulmonary hypertension (PH) are significant cardiovascular disorders with distinct yet sometimes overlapping pathophysiologies [1,2]. VHD results from structural or functional valve abnormalities caused by degenerative processes, rheumatic disease, congenital defects, or endocarditis, leading to altered hemodynamics and heart failure [3–6]. PH, defined as a mean pulmonary arterial pressure ≥20 mmHg, arises from diverse causes, including left heart disease, chronic lung disease, or idiopathic mechanisms, and can occur independently or secondary to VHD [7–10]. Advances in diagnostics, including echocardiography and pulmonary hemodynamic indices like the pulmonary artery pulsatility index (PAPi), have enhanced the assessment and stratification of both conditions [11]. Innovative therapies for PH, such as sotatercept, target vascular remodelling and complement expanding interventional options for VHD [12–18]. A thorough understanding of these conditions' interplay is essential to optimising management and improving outcomes in these complex cardiovascular disorders.

The assessment of aortic dilation and aortic regurgitation (AR) is critical for early diagnosis and management of cardiovascular diseases. A relationship between the ascending aortic diameter and the Thumb-Palm Test (TPT) has been previously established, but its evaluation using transthoracic echocardiography (TTE) in a broader population was not explored. The study by Doğan et al. included 1934 cardiology outpatients from five centres who underwent TTE between November 2022 and January 2023 [19]. TPT was assessed by measuring the distance between the thumb and palm, and ascending aortic diameter was measured by TTE. Results showed a median aortic diameter of 34 mm, with 35.5% having a diameter >36 mm, and 3.8% of patients testing positive for TPT. Significant associations were observed between TPT and both ascending aortic diameter and AR grades in univariate and multivariate analyses, highlighting its potential clinical utility.

The prevalence of secondary tricuspid regurgitation (TR) increases with age, but its mechanisms and patterns of tricuspid valve (TV) remodelling are not well understood [20]. Understanding these factors is critical for guiding patient selection for emerging therapeutic options. In older adults (60 years or older), moderate-severe TR is more common in those with underlying left or right heart abnormalities, rising from 4.5% in those without to 32.9% in those with such conditions [21]. TR severity correlates with progressive remodelling of the right heart chambers and TV, including annular dilatation, increased tenting, and leaflet elongation. Predictors of moderate-severe TR include annular dilatation ≥3.75 cm, tenting area ≥1.45 cm^2, and leaflet length ≥2.25 cm, with TR prevalence increasing from 7.2% to 64.7% as these criteria are met (Figure 1). These findings suggest that cardiac abnormalities, not ageing alone, drive TR progression and remodelling.

The accompanied editorial by Bourg et al. underscores the importance of implementing early screening protocols and embracing a multidisciplinary approach to care as key strategies to slow the progression of tricuspid regurgitation (TR), reduce associated mortality, and enhance the quality of life in elderly patients [22]. This proactive framework emphasises the integration of comprehensive echocardiographic evaluation, incorporating both the morphological parameters as identified by Abdelghani et al. and assessments of right ventricular function [21,22] (Figure 2). Coupled with the effective management of coexisting comorbidities, this approach is essential for tackling the increasing burden of TR in an ageing population.

Paravalvular leaks after mitral valve replacement occur in 7% to 17% of cases, with 1% to 5% being clinically significant and requiring intervention [23]. A 58-year-old male, with prior aortic and mitral valve replacements for rheumatic heart disease, presented with worsening dyspnoea, escalating to NewYork Heart Association (NYHA) class 4 despite medical management. Clinical examination revealed mechanical heart sounds, clear lung fields, and lower limb edoema, while diagnostic evaluation identified severe paravalvular leak and left atrial enlargement. The patient underwent transcatheter closure using a Multipurpose A1 guiding catheter and an Amplatzer Vascular Plug II device *via* a transapical approach, ensuring protection of coronary arteries. The leak was successfully sealed, and the apical puncture was closed, avoiding complications such as significant pericardial leakage. This case underscores the utility of transcatheter paravalvular leak closure as an effective, minimally invasive alternative to surgery, particularly when performed with a transapical approach in carefully selected patients. Timely intervention and a combined surgical and percutaneous strategy are crucial for optimal outcomes.

Subclinical hypothyroidism (SCH), defined by normal peripheral thyroid hormone levels with mildly elevated TSH levels, is associated with increased arterial stiffness [24]. This study by Evsen et al. compared 33 newly diagnosed SCH patients with 34 age- and gender-matched healthy controls using echocardiography and oscillometric arteriography. SCH patients showed significantly lower aortic strain and distensibility ($p < 0.001$) and higher pulse wave velocity (PWV) and augmentation index (AIx)

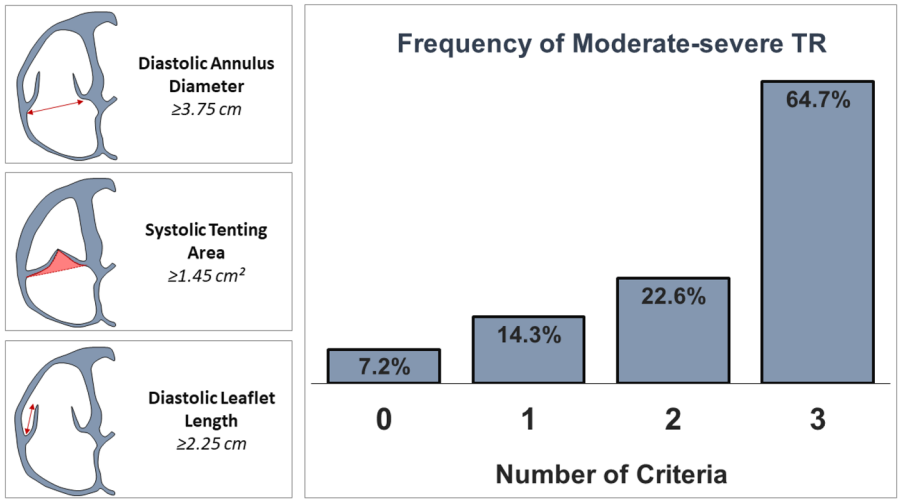

Figure 1. Three criteria of tricuspid valve remodelling (on the left-hand side) and the frequency of moderate-severe TR according to the number of criteria fulfilled [from reference 21].

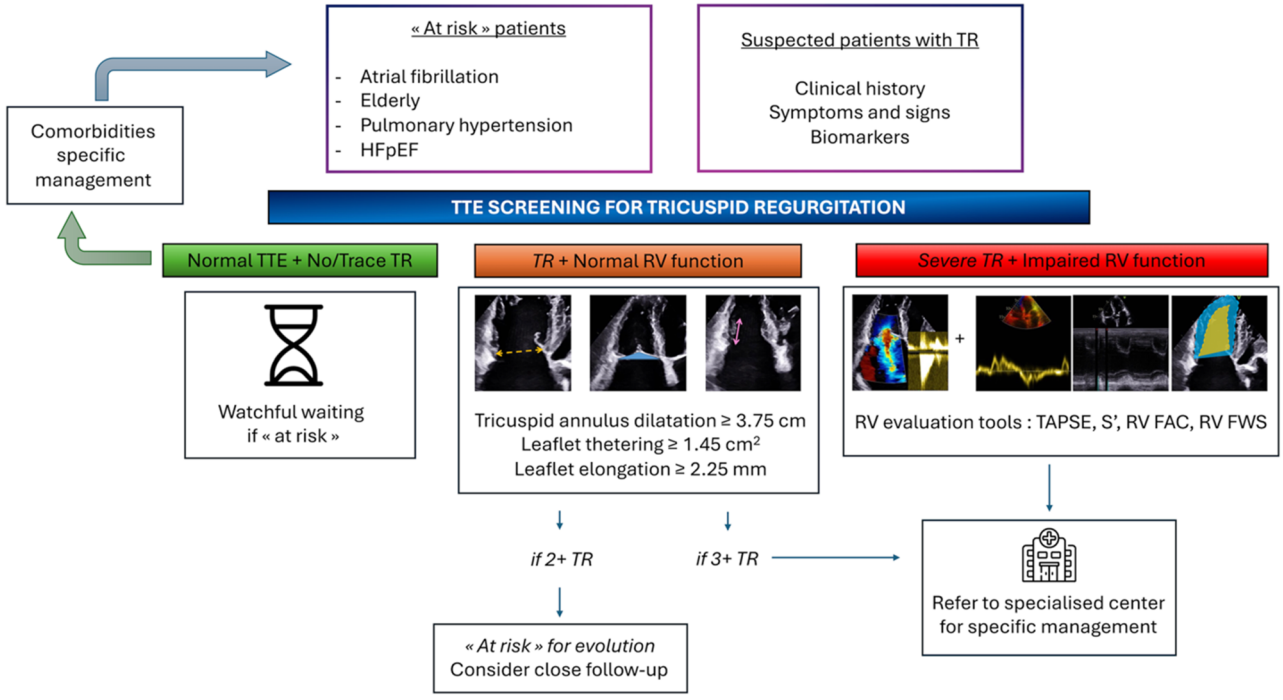

Figure 2. Proposed algorithm for the secondary TR in elderly based on TTE morphologic parameters as proposed by Abdelghani et al. and according to right ventricular function. HFpEF, heart failure with preserved ejection fraction; TR, tricuspid regurgitation; TTE, TransThoracic echocardiography; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; FAC, fractionnal area change; FWS, free wall strain [from reference 22].

($p < 0.05$) compared to controls, despite similar age, gender, and BMI. These findings indicate that SCH contributes to aortic stiffness independent of other cardiovascular risk factors. The oscillometric method, due to its simplicity and clinical applicability, proved valuable for assessing arterial stiffness. Identifying increased aortic stiffness in SCH patients may help in early detection of cardiovascular risks.

Postoperative gastrointestinal complications (GICs) are serious and potentially fatal in patients undergoing aortic arch surgery, necessitating reliable prediction tools. A retrospective analysis of 3063 patients identified 157 with GICs, and a prediction model was developed based on six key risk factors: hypertension, ASA classification, preinduction MAP, aortic cross-clamp time, CPB time, and intraoperative red blood cell transfusion [25]. Patients with GICs experienced higher mortality rates, prolonged ICU and hospital stays, and were stratified into four risk categories. The model was validated internally, showing promise for clinical application, though external validation is

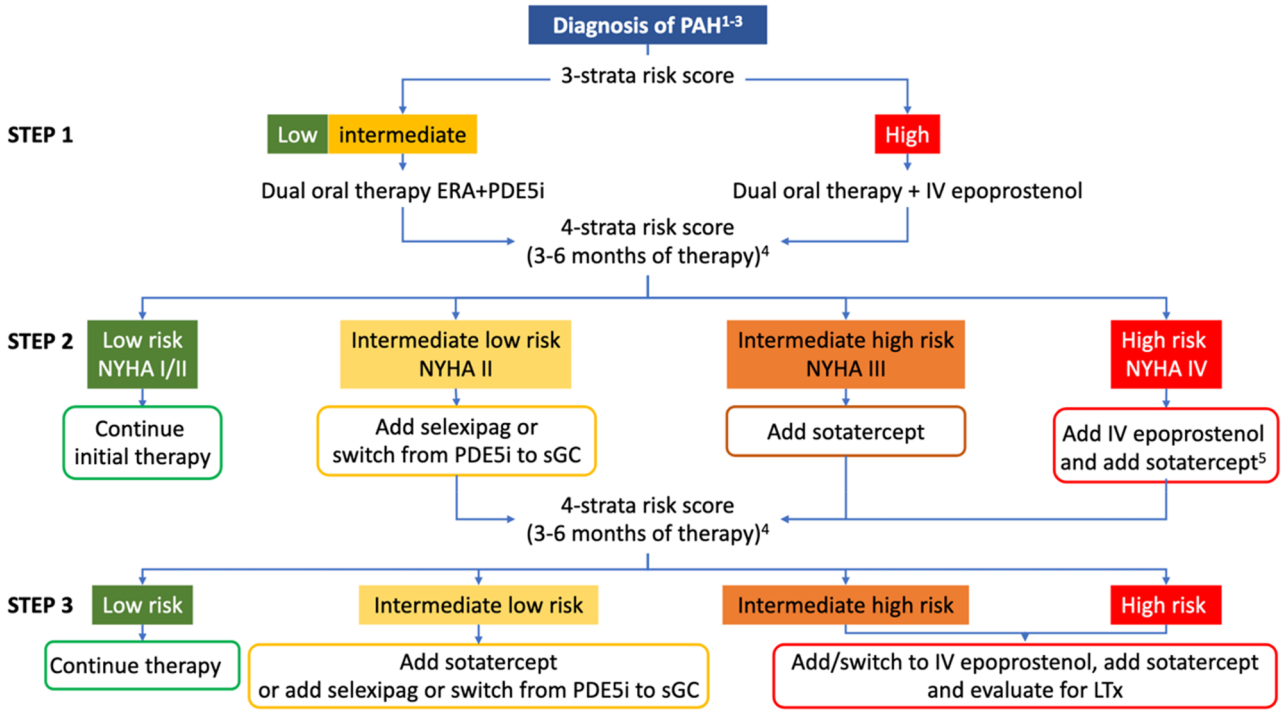

Figure 3. Proposed algorithm for the use of sotatercept in Belgium [from reference 12]. 1. Efficacy established in idiopathic PAH, heritable PAH, PAH associated with systemic sclerosis, or PAH associated with corrected CHD, all with few cardiopulmonary comorbidities (mean age 48–50 years). 2. Patient preferences should be considered at every step. 3. Patients should be considered for inclusion in a study with a novel agent when appropriate. 4. Patients should be reassessed sooner in case of deterioration or clinical event. 5. Add sotatercept after reaching maximal tolerated dose of epoprostenol.

needed before widespread use. This tool may assist in early identification and intervention for high-risk patients.

Right ventricular (RV) overload is a critical factor influencing risk stratification and management in acute pulmonary embolism (APE), as it reflects the hemodynamic burden placed on the heart. Early detection of RV dysfunction or dilatation (RVD) is essential for guiding treatment decisions, including the need for thrombolysis or advanced therapies [10]. While transthoracic echocardiography (TTE) is a valuable diagnostic tool, electrocardiography (ECG) remains a widely accessible and rapid method for initial assessment. Recent studies have proposed a new ECG parameter, terminal D1S+D3R (T-D1S+D3R), as a potential marker for diagnosing APE. The study by Başyiğit et al. investigated the relationship between the T-D1S+D3R ECG pattern and RV dilatation (RVD) in 267 APE patients who underwent echocardiography [26]. Among 72 patients with RVD and 139 without, the T-D1S+D3R pattern was significantly more common in the RVD group (70.8% vs. 18.0%, $p<0.001$). Logistic regression identified T-D1S+D3R, V1-3/4 ST-segment elevation, and frontal QRS-T angle as independent predictors of RVD in APE patients. These findings highlight the utility of the T-D1S+D3R parameter in detecting RVD and guiding APE management.

In heart failure with preserved ejection fraction (HFpEF), identifying reliable predictors of mortality is crucial for improving patient outcomes [27–31]. The pulmonary artery pulsatility index (PAPi) has emerged as a significant prognostic marker, shown to independently predict mortality in HFpEF patients undergoing right heart catheterisation [11]. A PAPi value below 2.84 demonstrated 76.2% sensitivity and 77% specificity in predicting mortality, with lower values associated with worse outcomes. Beyond HFpEF, PAPi and right ventricular stroke work index (RVSWi) are established indicators of right ventricular dysfunction in heart failure, both influenced by right atrial pressure (RAP). However, their correlation with RAP has been understudied. In a retrospective observational study of 70 heart failure patients, Spearman's rank correlation revealed that decreased PAPi, but not RVSWi, was significantly associated with elevated RAP across both preserved and reduced ejection fraction groups. These findings underscore the prognostic value of PAPi in heart failure and highlight its potential utility in routine monitoring and risk stratification, especially given its stronger correlation with RAP compared to RVSWi.

Pulmonary arterial hypertension (PAH) is a progressive and rare condition characterised by remodelling of small pulmonary vessels, leading to increased pulmonary vascular resistance, right ventricular failure, and ultimately death [7]. Despite advances in therapies targeting the endothelin, nitric oxide/cGMP, and prostacyclin pathways, these treatments primarily act as vasodilators and fail to address the underlying vascular remodelling, leaving PAH incurable [7]. As a result, research has increasingly focused on exploring novel pathways to develop disease-modifying therapies. Sotatercept, a ligand trap targeting multiple proteins within the TGF-β superfamily, represents a promising breakthrough in this field [12]. Recently approved in the United States for the treatment of PAH, sotatercept

offers a unique mechanism of action as an anti-remodelling agent rather than a simple vasodilator. The safety and efficacy of subcutaneous sotatercept have been rigorously evaluated in two multicentre, placebo-controlled randomised controlled trials. These studies demonstrated significant and consistent improvements across key endpoints, including exercise capacity, pulmonary hemodynamics, quality of life, and the delay of clinical worsening in PAH patients. Importantly, sotatercept has shown an acceptable safety profile, though it carries risks of telangiectasia and alterations in platelet counts and haemoglobin levels. These findings highlight its potential to fill a critical gap in the current therapeutic landscape by addressing the structural changes in pulmonary vasculature that drive disease progression. Sotatercept's introduction represents a shift in PAH treatment strategies, combining the benefits of vascular remodelling inhibition with existing vasodilatory therapies. This review evaluates the emerging evidence on sotatercept and considers its potential impact from a Belgian healthcare perspective, emphasising its role in future PAH management (Figure 3). With further clinical adoption and long-term monitoring, sotatercept may redefine the therapeutic paradigm for this challenging disease.

In this issue of Acta Cardiologica, several focus images highlighting interesting cases have also been reported [32–37].

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