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The left atrium and the right ventricle: two supporting chambers to the failing left ventricle

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Abstract

Heart failure (HF) is mainly caused by left ventricular (LV) impairment of function, hence detailed assessment of its structure and function is a clinical priority. The frequent involvement of the left atrium (LA) and the right ventricle (RV) in the overall cardiac performance has recently gained significant interest with specific markers predicting exercise intolerance and prognosis being proposed. The LA and RV are not anatomically separated from the LV, while the LA controls the inlet the RV shares the interventricular septum with the LV. Likewise, the function of the two chambers is not entirely independent from that of the LV, with the LA enlarging to accommodate any rise in filling pressures, which could get transferred to the RV via the pulmonary circulation. In the absence of pulmonary disease, LA and RV function may become impaired in patients with moderate-severe LV disease and raised filling pressures. These changes can often occur irrespective of the severity of systolic dysfunction, thus highlighting the important need for critical assessment of the function of the two chambers. This review evaluates the pivotal role of the left atrium and right ventricle in the management of HF patients based on the available evidence.

Keywords Heart failure · Left atrium · Right ventricle · Prognosis · Echocardiography

Background

The clinical syndrome of heart failure (HF) has historically been understood as caused primarily by left ventricular (LV) dysfunction. Even the most recent description and classification of HF is based on LV ejection fraction, a marker of overall pump dysfunction, which categorizes the patients into three groups: HFrEF (HF with reduced EF) if LVEF < 40%, HFmrEF (HF with mid-range EF) with LVEF = 40–49%, and HFpEF (HF with preserved EF) if LVEF ≥ 50%.

Echocardiography is considered the gold standard investigation for the evaluation of HF patients [1], since it provides the main parameters, along with clinical and therapeutic information included in the prognostic scores currently used in clinical practice, such as the Seattle Heart Failure Model and the Heart Failure Survival Score [2, 3]. Recent reports have highlighted the significant limitations of using LVEF in the assessment of LV function because of its susceptibility to technical measurements errors, load dependency, poor test-retest reliability, and limited prognostic value when the measure is close to the reference range [4]. Moreover, it is crucial to consider the associated disturbances of the neighboring chambers, the left atrium (LA) and the right ventricle (RV), which are related to the primary LV disease, e.g., LA enlargement caused by progressive rise of LV filling pressures which eventually gets reflected on RV structure and function [5]. Interestingly, researchers have recently paid significant attention to the changes that take place in LA and RV in patients with HF and have reported prognostic value of the two chambers in patients with dilated cardiomyopathy which significantly exceeded that of the LV itself [6, 7].

The purpose of this review is to highlight the importance of LA and RV in the overall pathophysiology of chronic HF, and the pivotal role they play in explaining clinical findings and prognosticating such patients.

Left atrium: the early protector of LV function

The LA is anatomically linked to the LV with the two chambers sharing the mitral annulus as the insertion site of the

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longitudinal fibers which subtend the long axis function of the two chambers. This function is closely reciprocal with LV systole coinciding with LA diastole and vice versa. Because of this intimate relationship, changes in LV filling pressures have a direct effect on LA function even before any overt cavity enlargement. Indeed, studies have shown that in patients with stiff LV cavity and raised filling pressures LA intrinsic function is impaired despite completely normal cavity size.

LA mechanical function consists of three essential components: the reservoir (filling) phase, the passive emptying conduit phase, and the pumping phase, in which LA boosts LV filling by pumping 15–30% of its stroke volume during atrial systole [8]. In view of the important contribution of LA function to LV filling volume, maintaining such an integral relationship is of great importance (Fig 1). This is seen in patients with atrial fibrillation who lose LA mechanical function and its filling component of the LV which results in impaired LV function, increased filling pressures, and raised pulmonary venous pressures and symptoms. Thus, in patients with clinical conditions that affect LV structure and function as is the case with pressure afterload due to systemic hypertension and aortic stenosis, which result in progressive build-up of back pressure in the LA, early identification of myocardial dysfunction is crucial in guiding towards optimum treatment and LA pressure offloading before irreversible damage occurs and intractable arrhythmia is established [9]. It should be mentioned that the pathophysiology of LA dysfunction follows a similar pattern to that seen in the LV as described by the Frank-Starling mechanism with LA output increasing with the progressive enlargement of cavity diameter in order to maintain a normal stroke volume, up to a limit beyond which further increase in intracavity pressure results in functional decline and consequently arrhythmia.

Finally, the LA acts also as a watershed between the LV and the pulmonary circulation. In advanced stages of chronic HF, LA function dramatically worsens, so a greater hemodynamic load stresses the pulmonary vasculature, promoting remodeling and leading to the development of pulmonary hypertension (PH). Chronically increased pulmonary vascular resistance (PVR) and stiffness would eventually represent a pressure afterload on the RV, which is the first step for the development of RV dysfunction then eventually, failure. This phenomenon suggests that strategies to optimize LA function or to prevent its deterioration may mitigate the progression to pulmonary vascular and right heart dysfunction and improve outcome in HF patients, particularly HFpEF [10].

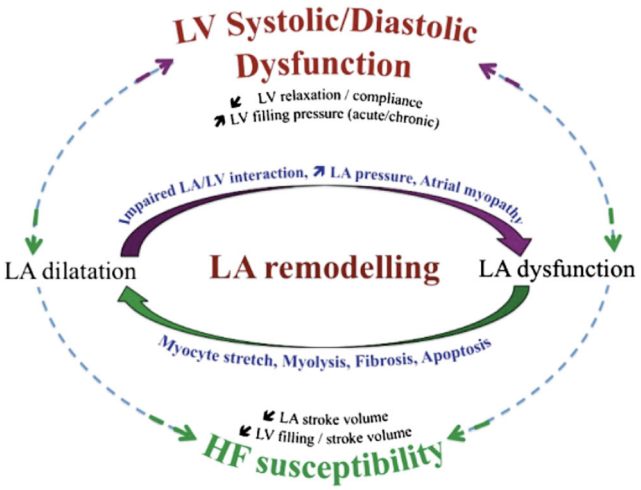

Fig. 1 Relationship between left atrial (LA) remodeling, left ventricular (LV) function, and heart failure (HF). Lancellotti et al. Eur J Heart Fail. 2014;16(10):1047–8

Right ventricle: the last barrier to prevent end-stage HF

The RV is anatomically and physiologically different from the other cardiac chambers. Its primary function is to pump systemic venous return through the pulmonary circulation. Since the two ventricles are anatomically connected, they pump almost the same stroke volume [6]. The RV is less muscular than the LV thus, is more sensitive to afterload alterations.

RV performance depends on myocardial contractile function, preload, and afterload, and is influenced by heart rhythm, intraventricular synchrony, and ventricular interdependence. The normal contraction time delay between the inlet and outflow tract compartments of the RV is important in maintaining its overall performance. RV/LV functional interdependence also plays an essential role in optimizing RV function, both in systole and diastole with LV systolic pressure almost four times that of RV. In pressure- or volume-overload, RV dilation increases intrapericardial pressure and shifts the interventricular septum to the left, altering LV geometry and preload, thus reducing cardiac output [11]. RV adaptation to pressure overload occurs via cavity dilatation and myocardial hypertrophy with the resulting spherical geometry and its impact on raised wall stress. Nevertheless, RV is incapable of sustaining pressure overload over a long time, hence the process of enlargement and proliferation of cardiomyocytes which is accompanied by neuro-hormonal signaling, oxidative stress, and inflammation with extracellular matrix synthesis. These changes eventually affect RV morphology and its diastolic and systolic function and provide the background for electrical instability and loss of contractile force, leading to the right HF (Fig. 2) [5]. It must be mentioned that the most common cause of right-sided HF is left-sided HF [12], since pulmonary venous pressure and contraction of small pulmonary arteries increase the PVR, reducing the highly afterload-dependent RV pump-function and consequently, the stroke volume. Therefore, although the chronic HF syndrome usually emerges from a failing LV, secondary RV dysfunction also contributes to the development of the syndrome and worsening of symptoms. The association

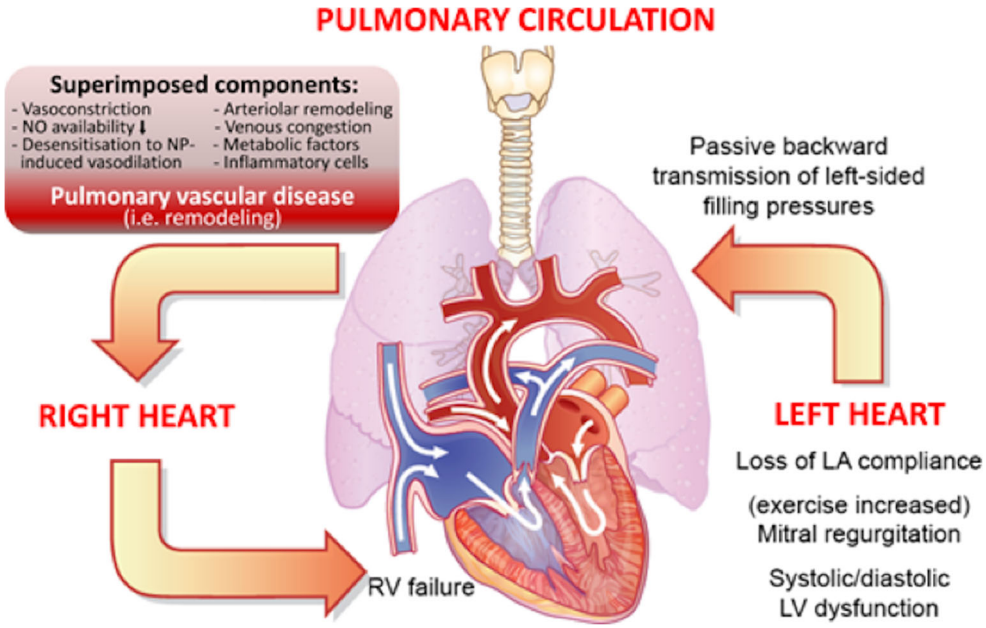

Fig. 2 Cardiopulmonary interaction and pathobiology of pulmonary hypertension (PH) in left ventricular (LV) heart failure (HF), which slightly leads to RV ischemia and progressive RV failure. NO, nitric oxide; NP, natriuretic peptides. Rosenkranz S et al. European Heart Journal (2016) 37, 942–954

of severe LV and RV failure is often found in patients with end-stage HF, with limited treatment options [11].

Pulmonary hypertension and RV-PA uncoupling

RV dilation and dysfunction can be related to the same LV intrinsic pathology, e.g., dilated or restrictive cardiomyopathy. Also, patients with LV dysfunction after myocardial infarction or HF and/or elevation of pulmonary pressures are at increased risk for RV dysfunction or even failure [13], particularly when there is increased RV afterload. In clinical practice, PVR is the most important determinant of RV afterload, thus, RV maladaptive remodeling in HF is often the consequence of post-capillary PH [14]. However, other factors play important roles, multiple interactions between an increased afterload and an abnormal autocrine, paracrine, and neuroendocrine signaling ultimately lead to RV-pulmonary arterial (RV-PA) uncoupling [15]. RVF occurs when the contractile function of the hypertrophied RV is insufficient to compensate for the increase in PVR resulting from LV and LA chronically elevated pressures, hence RV-PA uncoupling. Although RV-PA uncoupling is now recognized as a critical event leading to RVF, its temporal relationship with the onset of RVF remains unclear [16]. These facts make evaluation of the right heart–pulmonary circulation based on RV volumes and EF significantly limited since the global RV response to hemodynamic changes is influenced not only by RV intrinsic performance but also by preload and afterload [17]. For this reason, it could be useful to evaluate RV-PA E_{es}/E_a coupling as the hemodynamic definition of the matching between RV contractility (end-systolic elastance—E_{es}) and PA afterload (effective arterial elastance—E). E_{es}/E_a uncoupling has been shown to be due to a disproportionate increase in E_a and inability to augment contractility (E_{es}) [18]. Recently, Ghio et al. have shown that evaluating RV-PA coupling improved prognostic stratification in a cohort of 1663 patients with HF, according to the phenotype of LV dysfunction (HFrEF, HFpEF) [19].

LA dilation and dysfunction and its prognostic value in chronic HF

LA remodeling and dysfunction due to high filling pressures often represents the crucial point of transition to symptomatic HF [20]. The coexistence of LA mechanical, endocrine, and regulatory failure (global LA failure) is associated with an increased risk for incident atrial fibrillation, poor exercise tolerance, and increased morbidity and mortality [6]. LA size can be assessed by echocardiography, considering LA volume indexed (LAVI) for BSA (body surface area) to make meaningful comparisons between patients [21], with a normality cut-off value of 34 mL/m^2. According to the latest American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) recommendations [22], LAVI could be used in a grading system to estimate LV filling pressures (non-invasively), which proved its reliability in the multicenter prospective Euro-Filling Study [23]. LAVI has also been found to be an independent prognostic marker for many pathologic conditions [24–26]. It has also been found to correlate with clinical outcome in patients with HF in a meta-analysis having shown a baseline LAVI increase of 10 mL/m^2 associated with a 22% increased adjusted hazard ratio (HR) of all-cause mortality [27]. In a cohort of 1148 patients with systolic HF from the recent Warfarin versus Aspirin in Reduced Ejection Fraction (WARCEF) trial, after adjustment for demographics and clinical covariates, moderate or severe LA enlargement was significantly associated with all-cause mortality (HR 1.6

and 2.7, respectively), CV mortality (HR 1.7 and 3.3), and HF hospitalization (HR 2.3 and 2.6) [28]. Moreover, in different studies, LAVI provided additive prognostic information compared with exercise tolerance parameters in patients with chronic HF [29] over and above clinical and other echocardiographic variables in predicting mortality in patients with suspected HF referred from the community (Fig. 3) [30].

HFpEF

Although irrespective of EF patients with HF present with similar signs and symptoms, characteristics of LA mechanical dysfunction seem to be different between HFpEF and HFrEF. In a study comparing two groups at identical mean LA pressure, HFrEF patients had larger LA volumes, whereas HFpEF patients had higher LA peak pressures, lower minimal, pressures and higher stiffness [10]. LA size also differed in its prognostic power between the two syndromes [31], despite its recent use as an imaging marker of diastolic dysfunction in patients with HFpEF [32]. Carlino et al. in the Emergency Department found that, in the presence of lung ultrasonography positivity, EF ≤ 40% is a good tool to identify acute HFrEF, while LA dilation expands the spectrum of recognizable acute HF allowing the identification of acute HFpEF [33]. Since, currently, no effective therapy for HFpEF is available, assessment of LA size seems a reliable tool to follow up the evolution of HFpEF for optimum recognition of patients at increased risk and for the prevention of irreversible LA remodeling.

LA strain

In addition to changes in LA volume during different phases of the cardiac cycle, LA reservoir, conduit, and booster pump

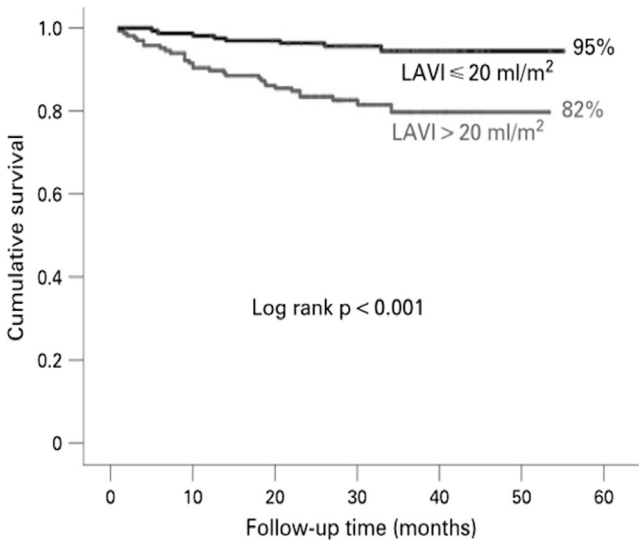

Fig. 3 Kaplan-Meier survival curves in patients with suspected HF demonstrating a normal versus an increased left atrial volume index (LAVI). Lim TK, Dwivedi G, Hayat S, et al. Heart 2009;95:1172–1178

functions may be accurately measured with strain imaging using speckle tracking echocardiography (STE) [34], which is an emerging noninvasive method for the quantification of LA function. A reduction in LA strain mirrors the presence of a stiff cavity due to fibrosis secondary to maladaptive remodeling [35, 36]. LA reservoir function has recently gained particular interest. It is influenced by both LV systolic function and the intrinsic LA compliance and has been shown to play an important role in disease progression, e.g., atrial fibrillation, acute myocardial ischemia, and HF. In 86 patients with HFpEF, enrolled in the Karolinska Rennes (KaRen) biomarker prospective substudy, ST2 levels were shown to inversely associate with global LA strain ($r = 0.30$, $P = 0.009$), but not with LA size, LV geometry, and systolic or diastolic LV function ($P > 0.05$ for all). Also, LA strain predicted death and hospitalization independent of the degree of LV remodeling or dysfunction [37]. Even among patients with normal LAVI, those with abnormal LA strain were significantly more likely to have New York Heart Association (NYHA) functional class III or IV symptoms or experience a HF hospitalization within 2 years [38]. Furthermore, LA reservoir strain proved to be a more accurate predictor of LVEDP than the E/e′ ratio in patients with various degrees of impairment of LVEF. In 308 HFpEF patients prospectively enrolled and longitudinally followed for 13.8 months, abnormal LA reservoir, conduit, and booster pump strains were associated with increased events (CV hospitalization and all-cause mortality), and worse reservoir strain was associated with reduced cardiac output and decreased peak oxygen consumption (VO2), over and above LV strain [39]. In addition, in a cohort of 83 symptomatic hospitalized patients, LA reservoir strain < 17.5% was found to be 89% sensitive and 55% specific for diagnosing HFpEF [39], comparable to the ability of LA strain to accurately diagnose new-onset HFpEF in the outpatient setting. Caravita et al. reported a case of HFpEF secondary to a stiff LA, in which the invasive hemodynamic assessment showed pathognomonic tall V-waves in the wedge pressure in the absence of mitral regurgitation and with a near-normal QRS-gated and pre-V-wave pressure, indicating that LV diastolic dysfunction was not a major issue. The completion of the study with STE revealed very low LA strain values, compatible with a stiff and non-compliant chamber [40].

Despite the overwhelming evidence for the important clinical application of LA strain, it has its limitations. STE needs good image quality and frame rates of ~ 50–70 for accurate tracking and to avoid speckle decorrelation. Thus, the location of the atrium, which reduces the signal to noise ratio, the thin atrial wall, the presence of the appendage, the atrial septal abnormalities, and the pulmonary veins make LA deformation analysis challenging. In addition, there is a lack of consensus about which regions to include in calculating global strains. Thus, although the available evidence strongly suggests that, in patients with HFpEF, LA strain may aid in its diagnosis and

prognostic assessment, robust outcome data from large prospective trials are needed to confirm the additive predictive ability of LA function before these measurements could be widely accepted. Also needed is the standardization of equipment and analytic techniques and further investigations to determine the impact on clinical outcome of therapies designed to assess LA reverse-remodel and improve its cavity function [38].

LA parameters as markers of CRT-response

A novelty in the field of HF is that the study of LA dimensions and function could independently predict clinical outcome in mildly symptomatic HF patients treated with cardiac resynchronization therapy (CRT) device.

Stefan et al. found that LAVI alteration after CRT implantation improved prediction of positive clinical response compared with changes in LV volume. In a multivariate analysis, smaller LA diameter and milder mitral regurgitation remained independent predictors of super-response to CRT [41]. Also, Imamura T et al. showed smaller LAVI (odds ratio (OR), 36.67; $P = 0.001$), together with complete left bundle branch block, as good predictors of response in 67 patients with advanced HF receiving CRT-D [42]. It is the results of CRT that exert pronounced reverse remodeling effect on LA, which may provide a better clinical response to CRT. These findings suggest that baseline and follow-up measures of LA should be routinely used in the evaluation of patients undergoing CRT-D implantation. By the same token, peak LA strain has been shown to improve significant identification of CRT responders [43]. Peak LA strain less than 10% predicted higher rates of death or HF hospitalization in a CRT population [44]. Such increasing popularity of the use of LA indexes in CRT practice has awakened interest in its regular use and improvements in spatial and temporal resolution, automation and other attempts to reduce variability, and standardization among platforms and vendors [38].

Right ventricular dysfunction: a strong prognosticator in chronic HF

RV morphology and its position in the chest make cross-sectional echocardiographic assessment suboptimal particularly for quantification of its global function. M-mode measurement of tricuspid annular plane systolic excursion (TAPSE) or tissue Doppler parameter E/E′ are traditionally used to evaluate RV inlet systolic function, but they represent only a regional approach to the complex shape of the whole chamber. Also, TAPSE is relatively load- and angle-dependent. RV fractional area change (RVFAC), calculated as RV (end-diastolic area—end systolic area)/end-diastolic area, with a standard value > 35%, is a feasible quantitative alternative to analyze RV systolic function and correlates with RV EF measured by cardiac magnetic resonance (CMR) [45]. In a recent study, lower RVFAC predicted RVEF [32], a finding that was not reproduced in other retrospective studies [46, 47]. In patients with advanced chronic HF, LVEF loses its prognostic power, whereas RV ejection fraction (RVEF) proved to be an independent predictor of survival in patients with moderate-to-severe HF [44]. A consistent number of studies confirmed the unique value of RV as a prognosticator in patients with advanced chronic HF [48, 49].

Advances in imaging modalities improved assessment of RV function

As is the case with LA, STE has been applied in the assessment of RV regional myocardial deformation. Compared to Doppler techniques, STE is angle-independent and more user-friendly, but it requires excellent image quality. It provides rapid and simultaneous quantification of both regional and global lateral RV systolic function measuring RV longitudinal strain (RVLS) since longitudinal lateral (free-wall) RV function generates 80% of the RV stroke volume [50]. RV strain imaging is increasingly used in showing function impairment suggesting microvascular ischemia or myocardial disarray related to the cavity dilation [51]. RVLS has been shown to provide incremental prognostic value over and above LV function in a cohort of ambulatory patients with systolic chronic HF [52]. Furthermore, in a prospective echocardiographic study, RVLS was a better predictor of major adverse cardiac events than other indexes of RV systolic function (TAPSE and S′) or LV function (LVEF and E/E'), preserving its association with the primary outcome even when all clinical, laboratory, and echocardiographic variables were added to the model [53].

We too have found a close negative correlation between free-wall RVLS and RV stroke work index (RVSWI), which is the hemodynamic parameter commonly used for the invasive assessment of RV function in patients waiting for heart transplantation [54]. Moreover, by a comparison between RV and LV echocardiographic variables as predictors of outcome in patients referred for heart transplantation, we demonstrated that the best overall predictor of outcome was free-wall RVLS (Fig. 4). It showed a strong correlation with event-free survival rate with a cut-off value of free-wall RVLS = − 15% [55]. In a cross-sectional study including 54 patients with ischemic HFrEF divided in subgroups according to cardiopulmonary exercise testing (CPET), among two- and three-dimensional (2D and 3D) echocardiographic indexes, reduced RV strain more accurately reflected severe impairment of the RV performance (area under curve, AUC of 0.83), although other parameters such as RVFAC, TAPSE, and 3D RVEF were also associated with exercise capacity [56].

CMR is considered the noninvasive gold standard for the estimation of RV volumes and EF, but there are several limitations related to its everyday clinical use. It is not widely

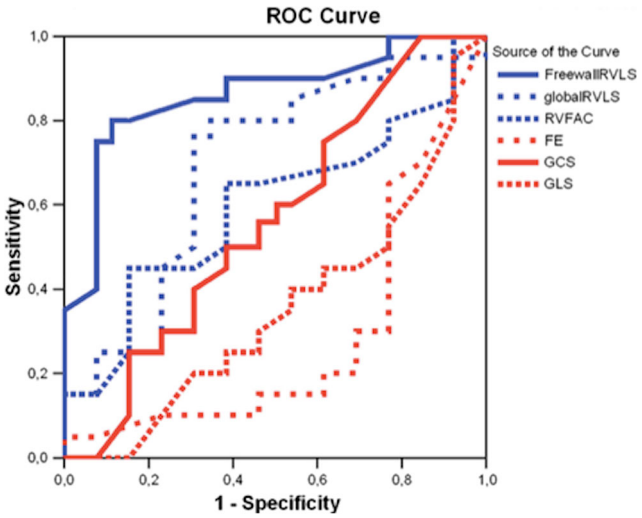

Fig. 4 Receiver operating characteristic (ROC) curves for the overall performance of free-wall RVLS, global RVLS, RVFAC, LVEF, LV global longitudinal strain (GLS), and LV global circumferential strain (GCS) for the prediction of cardiovascular events in patients referred for heart transplantation. Cameli M et al. Am J Cardiol 2013;112:1778e1784

available, it can be time-consuming to perform, it is costly, and it is contraindicated in some conditions including pacemakers and mechanical valves. However, echocardiography is now challenging CMR and many studies have validated its use for RV volume measurements. 2D-STE and 3D echocardiography are angle-independent, fast, less load-dependent, and more accurate compared to basic echocardiography. They allow accurate evaluation of RV volumes and RVEF with results comparable to CMR measurements [57, 58]. Thus, new echocardiographic methods could represent the first line methods for the evaluation of the RV structure and function in HF patients. Some authors claim that 3D evaluation is the most promising tool for future evaluation of the RV since it overcomes the challenge of complex RV geometry, but it still tends to underestimate its volumes (end-diastolic, end-systolic, and stroke volume) compared with CMR [17]. RV function has also been suggested to be measured by cardiac computed tomography (CT) using a novel 3D volumetric segmentation tool by applying a dedicated biphasic injection protocol. The RV EF from CT is a closer surrogate of right atrial pressure than TAPSE. Cardiac CT is fast and reliable and could be a valuable alternative modality to CMR for the evaluation of RV function [59], but there is still small evidence about its technical applicability, validity, and radiation exposure.

TAPSE, RVFAC, and RVEF are all load-dependent, so they are not direct indexes of intrinsic RV contractility. Afterload may be evaluated as ventricular-vascular coupling, which considers both resistive and pulsatile components and describes total RV afterload than PVR alone. Measures of coupling are of particular interest for the identification of subclinical right-sided HF. Pressure-volume relations provide the most reliable information on RV-PA coupling. Despite their clinical value, especially in the field of PH, measurements of effective Ea, maximal end-systolic elastance (Emax), and coupling from pressure-volume loops are not routinely performed because of technical complexity. RV-PA coupling parameters have already been tried using noninvasive techniques. Two-dimensional Doppler echocardiography allows the calculation of combined indexes such as TAPSE/sPAP (systolic pulmonary artery pressure) [60], TAPSE/PVR [61], or RV strain/sPAP [62], which have been shown to be associated with prognosis in HF and in patients with PH. However, these parameters consider only the steady component of RV afterload. 3D Echocardiographic parameters showed a good correlation with reference right heart catheterization-CMR indexes and increasing levels of PVR in 90 patients with suspected PH [17]. Nochioka et al., in the Atherosclerosis Risk in Communities (ARIC) Study, showed that in 1004 patients with mean age 76 ± 5 years, RV EF, RVEF/sPAP, and RVLS were each progressively lower across advancing American College of Cardiology Foundation/American Heart Association HF stages. Particularly, among participants free of HF at baseline, lower RVEF and worse RV-PA coupling (i.e., lower RVEF/PASP ratio) were both associated with incident HF or death independent of LVEF and N-terminal pro-BNP [63].

RV function and LVAD as destination therapy

In patients with intractable HF, LV assist device may represent the last management option. The device imposes hemodynamic stress to the RV, which is load-dependent, so it is rarely followed by complete RV recovery and severe postoperative RVF occurs in 25% of cases, associated with high patient mortality. RV function represents the most common short- and long-term mortality and morbidity determinant after LVAD implantation [64] and many of these patients eventually need a right VAD (RVAD) implantation. As long-term RVADs are unavailable, treatment of irreversible RVF is limited to heart transplantation. Implantation of a temporary mechanical RV support simultaneously with LVAD implantation in high-risk patients for postoperative RVF can avoid permanent biventricular VAD (BVAD) support and improve outcome since LVADs provide better survival rates and quality of life than BVADs [65, 66]. Thus, it could be important to identify patients who definitely need a BVAD or a temporary RVAD in addition to the LVAD preoperatively or at least intraoperatively. Moreover, in primary left-sided systolic HF, the PDE-5 inhibitor sildenafil, can acutely and also chronically reduce the PVR, enhancing the patient's exercise capacity with mild systemic vascular effects [67]. In patients with RV dysfunction, RV preconditioning with the calcium-sensitizer levosimendan shortly before LVAD implantation can improve clinical outcome and survival.

Strategies to achieve better outcome in patients receiving LVAD should include better risk stratification for RVF prior to LVAD placement as well as a clear discussion about eligibility for LVAD destination therapy of patients ineligible for transplant [68]. RV function evaluation is the most important element for the prediction of success of LVAD therapy in patients with advanced chronic HF [46]. For clinical decision-making, it appears more reliable to use complex quantitative scoring systems including quantification of different risk factors for post-LVAD RVF and measures of RV geometry, function, and load [12]. However, the application of risk-score models currently available had equivocal results. With the exception of CMR, RV imaging has poor accuracy. In the last years, echocardiographers expanded their view with the application of 3D technology and strain imaging in order to get further insight into abnormal RV function states [68]. STE could aid in the decision-making process to RVLS association with an increased risk of RV failure among patients undergoing LVAD implantation was enlightened in several studies [69, 70], providing additive benefit on top of clinical risk scores [46]. These considerations put significant stress on researchers to create a risk-score model with a good efficacy in the prognostic stratification of patients with end-stage HF which could help clinicians in the selection of patients for destination therapy with LVAD and in the prevention of postoperative complications due to RVF.

Conclusions

An accurate diagnostic and prognostic evaluation of patients with chronic HF cannot be without the analysis of LA and RV function. The clearer understanding of LA and RV physiopathology and their close relationship with LV function established their pivotal role in chronic HF, irrespective of EF. The two chambers act as a double consecutive barrier to limit the consequences of LV myocardial damage, as has recently been shown by their prognostic accuracy in such patients. In clinical practice, the markers of LA and RV structure and function measurements should be factored during therapeutic decision-making. A mindful combination of the recent findings could help clinicians to optimize the limited therapeutic resources available for these patients and to provide the best-individualized therapy. Finally, a continuous flow of investigations in this field is needed to overcome some limitations of the existing models.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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