Right Ventricle Function in Patients With Anterior Myocardial Infarction: Are We Sure it Is Not Involved?

Giuseppina Novo[a*], Ana G. Almeida[b], Domenico Nobile[a], Pierluigi Morreale[a], Khalil Fattouch[c], Daniela Di Lisi[a], Girolamo Manno[a], Patrizio Lancellotti[d], and Fausto J. Pinto[b]

From the [a] Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Italy. Cardiology Unit, University Hospital "P. Giaccone", Palermo, Italy, [b] Centro Cardiovascular da Universidade de Lisboa - CCUL, CAML, Faculdade de Medicina, Universidade de Lisboa, Portugal; Serviço de Cardiologia, Hospital Universitário de Santa Maria, CHULN, Portugal, [c] Gruppo Villa Maria Care and Research, Maria Cecilia Hospital, Cotignola, and Anthea Hospital, Bari, Italy and [d] University of Liège Hospital, GIGA Cardiovascular Sciences, Departments of Cardiology, Heart Valve Clinic, CHU Sart Tilman, Liège, Belgium.

Abstract: The right and left ventricle of heart are intimately connected by anatomical and functional links. Hence, acute changes in cardiac geometry and function can modify the performance and physiology of both sides of the heart, influencing each other. After a brief overview of the anatomy and related imaging techniques for the study of right ventricular function, we report a review-on the interesting correlation of acute anterior myocardial infarction and right ventricular function, very often underestimated. (Curr Probl Cardiol 2022;47:101277.)

Anatomy and Physiology of the Right Ventricle

Right Ventricle Anatomy

The right ventricle (RV) is a crescent-shaped chamber located anteriorly just behind the sternum with a muscle mass 6 time lower than the left ventricle (LV) and divided into 3 parts: the inlet, made-up of the

The authors have no conflicts of interest to disclose.
Curr Probl Cardiol 2022;47:101277
0146-2806/$ – see front matter
https://doi.org/10.1016/j.cpcardiol.2022.101277

tricuspid valve apparatus (leaflets, chordae tendineae and papillary muscles); the trabeculated apical myocardium; the conus or infundibulum. Anatomically the RV is delimited by the tricuspid valve annulus and the pulmonary valve. We can recognize 3 walls (anterior, lateral and inferior) and 3 sections: basal, mid, and apical. The RV has 3 typical muscular bands, the parietal, the septo-marginal, that extends inferiorly and becomes continuous with the third band, the moderator band which attaches to the anterior papillary muscle. The RV is also characterized by a ventriculo-infundibular fold, which separates the two valves tricuspid and pulmonary. A multiple network of fibres that lies in superficial and deep layers forms the RV. The superficial layer is made-up by circumferential muscle bundle parallel to the atrioventricular groove. These fibres turn obliquely toward the cardiac apex on the sternocostal aspect and continue into the superficial myofibers of the LV.[1] The deep layer is longitudinal and lined up from the base to the apex. Due to this disposition the RV and the LV are anatomically and functionally linked, which explains why LV contraction may cause a free traction of the RV wall. The interventricular septum and the pericardium also contribute to the well-known ventricular interdependence.

Vascularization and Perfusion

It is generally accepted that the perfusion of most of the RV walls is supplied by the right coronary artery (RCA) and its branches. The RCA is dominant in 85% of the population, which, in addition to supplying blood flow to the RV free wall, supplies the inferior wall of the LV and the posterior third of the septum. The conus artery supplies blood flow to the infundibulum, the acute marginal arteries to the anterior free wall and the posterior descending artery supplies the posterior third of the interventricular septum via septal branches. The other 2/3 of the interventricular septum is supplied by the septal branches of the left anterior descending artery (LAD).[2] However, there is no agreement regarding the amount of RV myocardium perfused by the left arteries. In an anatomic study, James et al. concluded that in almost a quarter of all hearts the left coronary artery supplies the perfusion of 30% of the right myocardial mass.[3] By the segmental myocardial quantification method conducted by Reig and Petit, we know that the apical segments, particularly the posteroapical segment of the RV is vascularized by the LAD and that only the 40% of the anteroapical segments of the RV, which has traditionally been considered as almost exclusively perfused by the LAD, is vascularized by the RCA.[4] These findings are also confirmed by post-mortem studies of

Andersen et al. in patient with LAD occlusion.[5] In conclusion, even if the RCA provides the perfusion of the walls of the RV, the LAD is responsible for the perfusion of almost 30% of the anterior wall of the RV and approximately 15% of its posterior wall. Due to the anatomical and physiological differences, the RV perfusion differs substantially from the LV. The RV could be considered as a low-pressure chamber that develops a lower systolic pressure than the LV and thus receives appreciable blood flow throughout the entire cardiac cycle, in contrast to the LV that receives the blood flow only in diastole due to its high systolic pressure and microvessels compression during systole. The oxygen demand of the RV is lower than the LV and in addition to higher oxygen extraction reserve, the RV is more protected from ischemia. The RV circulation has less effective pressure-flow regulation but more efficient oxygen utilization due to a reduction of the wall stiffness that occurs during a reduction of blood flow. The RV vascularization has also extensive collateral connections with the left coronary circulation; regarding the perfusion, an important role is also carried out by the Tebesian vein that may guarantee a possible retrograde perfusion from the right ventricular cavity. These differences promote the maintenance of RV oxygen supply−demand balance and provide relative resistance to ischemia-induced contractile dysfunction and infarction, but they may be compromised during acute or chronic increases in RV afterload resulting from pulmonary arterial hypertension.[6]

Physiology

The RV output is essentially equal to that of the LV. However, the RV differs from the LV in many aspects. The RV may be considered a high-volume and low-pressure pump and its afterload is significantly lower than the LV due to the low diastolic pulmonary artery pressure, in contrast to the aorta's, so that the hemodynamic effects of alterations in RV compliance are fundamentally different when compared to the LV. In fact, pulmonary vascular resistances and hydraulic impedance are lower and compliance higher. The differences in load have important implications for the pattern of ventricular ejection and for its termination. The LV pressure-volume loop is characterized by a square or rectangular loop while the RV pressure-volume loop adopts a trapezoidal shape, because ejection occurs early after the onset of pressure rise.[7] The consequence of this behaviour is a much lower capacity to resist to changes in afterload. The compliance of the pulmonary circulation, unlike the aorta, is distributed over the entire pulmonary circulation, not only on the central

pulmonary arteries.[8,9] Therefore, in case of exaggerated increase in RV pressure, considering low level of pulmonary arterial diastolic pressure, the pulmonary arterial valve opens, resulting in forward flow into the pulmonary artery during late diastole.[10] As a result, the pattern of transtricuspid flow may be normal despite significant abnormalities of diastolic compliance, although during this period the RV is acting as a passive conduit between the right atrium and pulmonary artery, rather than as an elastic chamber. This pattern of antegrade diastolic pulmonary arterial flow is an indicator of restrictive physiology.[10,11]

The Close Connection Between Right and Left Ventricle

Ventricular Interdependence

The RV and the LV are intimately connected by anatomical and functional links (Figure 1). Regarding anatomical links, namely the pericardium, the shared myocardium fibres and the electrical system, the contribution of the RV output to the LV perfusion and functional factors. The anatomic relationship of the RV and LV, including their interlacing muscle bundles, the interatrial septum, the interventricular septum and the shared coronary blood flow set up a continuous interplay between both ventricles. Therefore, acute or chronic hemodynamic changes could affect the perfusion of both ventricles. LV hypertrophy and dilatation could compress the RV, resulting in diminished RV function, and cardiac failure.[12] An immediate increase in RV pressure after an increase in LV volume was found in the isolated rabbit heart. In fact, a volume and pressure loading of one ventricle decrease the output and function of the contralateral ventricle as demonstrated in other animal models.[13,14] This diastolic interaction seems to be mediated by the pericardium. However, it is not the only cause of interaction because the effect is not completely abolished in the absence of the pericardium. The interventricular septum is an additional factor for ventricular function interplay. In the case of volume expansion, Frank-Starling mechanism is activated in the interventricular septum and the increase in right and left ventricular end-diastolic pressures is not mediated by a shift in septal position but rather by the restraining effect of the pericardium. From the studies of acute pulmonary hypertension in animal models, leftward shift of the interventricular septum plays an important role in the mechanism of ventricular interaction.[15,16] An increase in total systemic peripheral resistance increases the afterload of the LV and RV and, through a mechanism of ventricular interaction, a parallel upward shift of the RV diastolic

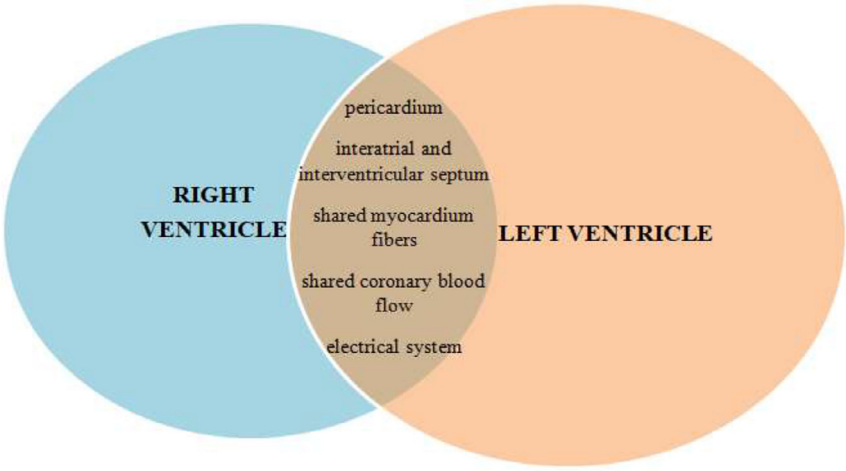

FIG 1. Close anatomical and functional correlations between right and left ventricle.

pressure-volume relationship occurs.[15,16] The probable mechanism is mediated by lengthening of the distance between the septum and the RV free wall as demonstrated by the analysis of biplane orthogonal regional RV end-diastolic dimensions. In the intact circulation, when acute alterations in arterial and venous pressures affect all 4 heart chambers simultaneously and total cardiac volume is varied, pericardial restraint rather than shifting of the interventricular septum may be the predominant mechanism mediating these changes in passive diastolic properties of the ventricles.[16] On the other hand, damage of the RV could be fully offset by the LV contraction that contributes directly to RV systolic function.[17] LV or the interventricular septum may assist RV function in the absence of RV free wall contraction as demonstrated by Sawatini et al.[18] The authors reported that the RV free wall patch moved toward the interventricular septum during systole, thereby reducing RV volume. LV contraction contributes to the generation of RV systolic pressure via the mechanical coupling of the ventricles, a contribution usually masked by the near synchrony of LV and RV contraction.[19] These data are also confirmed by other studies demonstrating that over half of the external work performed by the RV is a direct consequence of LV shortening, presumably through deformation of the RV free wall contiguous with that of the LV.[20-23] In this review, we report an interesting overview of correlation between RV and LV, in particular in the setting of acute anterior myocardial infarction, with important implications from a diagnostic, prognostic and therapeutic point of view.

Clinical Implications of RV-LV Interaction

Acute changes in cardiac geometry can modify the functional performance of both sides of the heart. For instance, during an acute pulmonary hypertensive crisis, severe LV systolic and diastolic dysfunction occurs in the setting of sudden RV dilation. RV afterload is increased and overall contractile performance becomes increasingly dependent on the systolic ventricular interaction because with high RV afterload, the oblique septal fibres are more efficient mechanically than the free wall transverse fibres. On the other side, increase in LV afterload such as aortic constriction or using vasopressor therapy leads to increase in RV stroke volume via the crosstalk mechanism discussed earlier.[24,25] Above and beyond the effects of altered geometry, it is also likely that changes in electromechanical function contribute to the adverse ventricular interactions in pulmonary arterial hypertension. RV ejection is abbreviated in this condition, but the overall duration of RV systole is prolonged, contracting well into LV diastole, impeding LV filling. The reduction in RV output further compromises pulmonary venous return to the LV and again a vicious cycle can evolve. Indeed, a simple ratio of the systolic-to-diastolic filling time (S/D ratio) has been shown to have prognostic significance in children with pulmonary arterial hypertension.[26] A more obvious relationship is shown by the increase in pulmonary artery pressure and RV afterload, in cases of raised LV end diastolic pressure due to LV systolic dysfunction. Consequently, both global LV and RV performance are reduced with impaired systolic ventricular interaction, even if the RV is not directly involved in the disease process causing LV systolic dysfunction. With a progressive dilatation of the LV and increased sphericity, the septal fibres become less oblique, reducing their mechanical advantages, and further impairing RV contractile function, with associated tricuspid regurgitation and a vicious cycle of RV enlargement with further reduction in the oblique septal fibres. In addition to the systolic interaction of the LV on the RV, when the RV is enlarged and stretches the pericardium, pericardial and RV diastolic pressures may become markedly increased and this can result in constraint to filling of the LV by the pericardium (pericardial constraint) and by the RV via the interventricular septum (diastolic ventricular interaction). Thus, RV systolic dysfunction frequently coexists with LV systolic dysfunction. As is well known RV systolic dysfunction being a negative prognostic marker of outcome in patients with LV systolic disease and heart failure. Therefore, all therapeutic interventions for LV systolic disease need to take close consideration of these hemodynamic interactions and the impact on the RV.[27]

Echocardiographic Evaluation of the RV Function

Recently, the right heart function has become a topic of greater interest, in contrast with the LV that has always been the most important clinically. Magnetic resonance imaging (MRI) nowadays remains the gold standard for the evaluation of the RV but the high costs and its low availability often limit its use. However, echocardiography keeps its role for the RV diagnosis especially in the initial evaluation, according to published recommendations.[28,29] Other imaging techniques as CT, PET and right sided heart catheterization are reserved for very specific situations.

The assessment of the RV by echocardiography could be challenging due to several inherent difficulties such as its retrosternal position, complex shape and absence of clear landmarks allowing the standardization of views.[30] A correct approach to the RV should include both qualitative and quantitative parameters. This could be obtained by 2D evaluation and most recently by 3D and strain imaging. The essential image windows and views required for a correct assessment of size, systolic and diastolic function of the RV are: apical 4-chamber; RV-focused apical 4-chamber and modified apical 4-chamber; left parasternal long- and short-axis, left parasternal RV inflow, and subcostal.[28] The parameters that could be obtained from these views are listed in Table 1.

RV Systolic Function

Using conventional echo-Doppler, and to reduce inter-reader variability, the following quantitative variables of RV systolic function should be obtained: TAPSE, RVFAC, peak systolic velocity of the tricuspid annulus (S'), RIMP.

TAPSE measures the longitudinal systolic motion of the RV below the tricuspid valve annulus. This method has several limitations as translational motion of the heart that can overestimate its value, a correct angle is essential and moreover, it is not reliable in patients with wall motion abnormalities. A value <17 mm is abnormal.[28]

RVFAC is defined as (end diastolic area - end systolic area)/ end diastolic area x 100. It is obtained by tracing the RV endocardium in systole and diastole. The accuracy of the method is limited by the quality of the image especially the delineation between endocardium and trabeculated myocardium. Values of RVFAC $<35\%$ are considered abnormal.[29,30]

S' is assessed using pulsed wave tissue Doppler with the sample volume placed at the lateral tricuspid annulus or in the basal region of the free wall of the RV. S' measures the displacement during cardiac cycle. A s' value <9.5 cm is accepted as abnormal.[30]

TABLE 1. Main studies regarding evaluation of right ventricle function in patients with anterior myocardial infarction: characteristics and limitations

Main studies regarding evaluation of right ventricle function in patients with anterior myocardial infarction			
Study	**Characteristics**	**Limitations**	**Ref.**
Mittal et al.	14 patients with anterior AMI vs 14 normal person. Standard TTE and PW tissue Doppler imaging examination of LV and RV was performed	Limited number of patients, consideration of an isolated lesion, no use of more advanced techniques (strain imaging echocardiography, CMR)	47
Hsu et al.	60 consecutive patients with anterior AMI divided into 2 groups according to infarct location vs 10 (control group). Standard TTE and PW tissue Doppler imaging examination of LV and RV was performed	No use of more advanced techniques (strain imaging echocardiography, CMR)	48
Caplin et al.	20 patients (10 whit AMI and 10 with inferior myocardial infarction). Standard TTE and PW tissue Doppler imaging examination of LV and RV was performed	Limited number of patients, no use of more advanced techniques (strain imaging echocardiography, CMR)	49
Maheshwari et al.	30 patients (25 patients with isolated LAD occlusion, 5 patients with LAD + LCx occlusion). Standard TTE and PW tissue Doppler imaging examination of LV and RV was performed	Limited number of patients, no use of more advanced techniques (strain imaging echocardiography, CMR)	50
Sonmez et al.	44 patients with AMI vs 20 patients were selected for the control group. The individual myocardial velocity, strain, and strain rate values for evaluation of RV and LV function	Limited number of patients, No use of CMR	51
Jensen et al.	50 patients with AMI. CMR was performed immediately after successful PCI. The prevalence of right ventricular involvement detected with ECG and echocardiography was compared with the prevalence detected with cardiac MRI, which was the reference standard.	Limited number of patients, CMR was performed for patients with ST-segment elevation MI and successful restoration of epicardial blood flow by coronary intervention, and	57

(*continued*)

TABLE 1. (*continued*)

Main studies regarding evaluation of right ventricle function in patients with anterior myocardial infarction			
Study	**Characteristics**	**Limitations**	**Ref.**
		the results may be different after non reperfused and non-ST-elevation MI.	

AMI, acute myocardial infarction; CMR, cardiac magnetic resonance; LAD, left anterior descending; LCx , left circumflex artery; LV, left ventricle; MI, myocardial infarction; PCI, percutaneous coronary intervention; PW, pulse – wave; RV; right ventricle; TTE, transthoracic echocardiography.

RIMP is defined as: isovolumetric relaxation time - isovolumic contraction time / RV ejection time. RIMP is obtained by tissue Doppler velocity (TD) or pulse wave velocity of the RV inflow and outflow. Irregular heart rates and elevated right atrium pressure could affect the isovolumetric relaxation time. Abnormal values are <0.43 measured by pulse wave and <0.54 measured by TD.[30]

Despite the utility of the above parameters TAPSE, RVFAC, RIMP are affected by changes in RV load without change in myocardial contractility. This means that they do not reflect the innate myocardial function.[31]

RV3D EF (assessed from the equation RV end-diastolic volume – RV end-systolic volume / RV end-diastolic volume) provides a global measure of RV systolic performance that is more independent from the operator, but this variable is dependent from other factors beyond the contractility, being affected by loads, interventricular changes affecting septal motion, poor acoustic windows, and irregular rhythms. The RV3D EF has shown good correlation with MRI. The volumetric semi-automated border detection approach is the recommended method.[30-33] RV EF of <45% usually reflects abnormal RV systolic function, even if these values are age- and gender-specific.

Finally, myocardial strain and strain rate are additional indices of RV performance that may be obtained by echocardiography. The term strain refers to change in myocardial deformation, and it is expressed as percentage. This deformation over the time is defined strain rate. These indices may be measured by Doppler tissue imaging or, preferably, by speckle-tracking technique since this one is independent of Doppler angle and of ventricular loads. Among the types of strain evaluated noninvasively, the most clinically useful seems to be longitudinal strain that

refers to the percentage of systolic shortening of the long axis RV free wall compared with diastole.[30] Global longitudinal strain reflects the average strain of the RV free wall and septal segments with mean normal values cutoff of > - 20%.[28]

RV Diastolic Function

For the RV diastolic function assessment, the same parameters employed for the left chamber are used such as Doppler velocities of the transtricuspid flow (E, A, and E/A), tissue Doppler velocities of the tricuspid annulus (E0, A0, E0/A0) deceleration time, and IVRT and RA size. Tricuspid E/A ratio <0.8 suggests impaired relaxation, a tricuspid E/A ratio of 0.8-2.1 with an E/E0 ratio >6 or diastolic flow predominance in the hepatic veins suggests pseudonormal filling, and a tricuspid E/A ratio >2.1 with a deceleration time <120 ms suggests restrictive filling (as does late diastolic antegrade flow in the pulmonary artery).[29]

Which is the Best Technique?

Few studies have compared RV echocardiographic parameters to MRI,[34-36] which is accepted as gold-standard for volumes and ejection fraction. Therefore, due to the lack of evidence in literature, there is no consensus as to the best echocardiographic technique to evaluate the RV function. A combination of different approaches could be useful for overall evaluation of the RV.[30]

Anterior Acute Myocardial Infarction and Right Ventricle: State of Art

AMI is defined as evidence of myocardial injury with necrosis in a clinical setting consistent with myocardial ischaemia.[37] As well known, AMI could be also defined according to the wall of the ventricle affected by the ischemia as anterior, septal, antero-lateral, posterior, postero-lateral and RV infarction. This is valuable information for the clinician because treatment and complications of an anterior wall infarction, for instance, is different than those of an inferior wall infarction. Short-term and long-term effects of an anterior wall infarction are usually more severe than those of an inferior wall infarction[38] Historically, it is a general assumption that the anterior infarction does not involve the RV. However, this is not supported by anatomical and functional considerations.[40-58] In addition, RV

involvement is an independent predictor of major cardiac adverse events.[43] In clinical practice low importance has been deserved to the RV during initial evaluation of the patients with acute settings of the anterior STEMI. Few studies have assessed the RV involvement in anterior STEMI and his clinical impact. We summarize below the state of art of the right ventricular function in patients with anterior STEMI. The association of RV and inferoseptal AMI is well established. However, the mechanisms underlying the occurrence of RV involvement in association with anterior MI are not clarified. In fact, the RV undergoes major histopathological morphological alterations following anterior infarction, as discussed previously.[39-42] In a post-mortem study, Cabin et al. found that in a series of 97 hearts with anterior infarction 13 also presented a RV myocardial infarction involving 10%-50% of the circumference of the RV free wall from base to apex.[39] In anteroseptal infarction RV involvement in a similar percentage was also found by Tahirkheli et al.[40] Bodi et al. confirmed RV involvement by MRI studies in patients with anterior AMI.[42,43] A significant apoptosis in the RV myocardium cells was found in patients with cardiac remodelling after AMI even when ischemic involvement on the RV wall is not suspected.[44]

Animal Models

The RV function was previously studied in animal models. In a swine model, Bonand et al. also found RV microvascular obstruction in patients with LAD obstruction associated with severe histopathological changes in the affected part of the RV.[41] Lancaster et al.[45] induced a total LAD obstruction in 12 pigs by percutaneus transcatheter plug placement in the mid portion of the artery and they found by echocardiography a small rim of the RV free wall adjacent to the septum and the RV apex necrosis involvement, an increase in the end diastolic pressures in both ventricles and an increase in RV peak systolic pressure. They also found that the half time of the isovolumic relaxation of the RV was prolonged and there was a reduction in the ejection fraction of both ventricles. There was no change in either right or LV dP/dt These data suggest a RV diastolic and systolic dysfunction as the result of an anteroseptal myocardial infarction.[45] In an acute LAD embolization sheep models, Jerzewski et al.[46] analysing the end systolic pressure-volume relationship obtained by MRI and RV catheterization, found a reduction of both RV and LV systolic function as indicated by substantial rightward shifts of ESPVR. They

also found an increase in septum and the RV free wall length, which could be responsible for the reduction of the RV systolic function.

Human Models

One of the few studies on the RV function in association with LAD occlusion in humans was conducted by Mittal et al.[47] in 14 patients with anterior AMI due to the isolated occlusion of proximal LAD diagnosed by coronary angiography. RCA disease and other comorbid conditions that could have impact on RV function were excluded. Detailed 2-dimensional, M-mode echocardiography, pulse wave Doppler and DTI of LV and RV were performed. These patients with anterior AMI due to isolated occlusion of LAD had impairment of diastolic DTI parameters in all segments of the RV. Impairment of the systolic DTI parameters was seen along the tricuspid annulus and at the lateral and anterior wall of the RV. The presence of common myocardial fibres encircling the 2 ventricles and leading to myocardial interaction, could explain these observations.[47] In another study, Hsu et al.[48] investigate the effect of different infarction sites on RV function in patients with a first acute ST-elevation MI without concomitant RV infarction. They assessed the RV in 60 patients after successful primary percutaneous coronary interventions that were divided into 2 groups: group I consisted of 35 patients with anterior (including anteroseptal) wall infarction and group II included 25 patients with inferior (including inferior and inferolateral) wall infarction. Ten healthy individuals served as the control group. All patients underwent a 2D echocardiography and a pulsed-wave TDI study within 72 hours after undergoing primary PCI. This study demonstrated that in patients with inferior wall AMI without associated RV infarction, the peak early diastolic velocity of the tricuspid annulus was significantly reduced and the tricuspid E/Em ratio was higher compared with healthy controls; the remaining echocardiographic parameters of RV function did not differ from those in the controls. However, the anterior AMI resulted in a greater extent of RV functional changes, including the systolic (reflected by TAPSE), diastolic (reflected by tricuspid annular Em velocity and right ventricle relaxation time and global aspects (reflected by RIMP) compared with the healthy subjects, even though successful primary PCI had been performed. These data suggest that RV function might be affected discrepantly after an episode of AMI with different infarct locations, with greater changes of global RV function occurring in patients with anterior wall infarction but not in patients with inferior wall infarction without concomitant RV infarction, in whom only the RV diastolic

function was altered. The results of this study demonstrate that in patients with a first acute STEMI who have received successful primary PCI, global RV function may be affected discrepantly depending on the infarction sites. For patients with inferior infarction without associated RV infarction, most echocardiographic indicators of RV function are like those in healthy subjects except for RV diastolic function. On the contrary, the alteration of global RV function is more pronounced in patients with anterior wall infarction. Ventricular interaction seems to explain the discordance only partially.[48]

In another study Caplin et al.[49] demonstrated that RV dysfunction commonly occurs after both anterior and inferior MI. Right and left ventricular functional impairment are related after anterior MI, but are interrelated after inferior MI. The different effects of anterior and inferior myocardial infarction on RV function may be explained by differences in septal and free wall involvement. They studied the relationship of global and regional right and left ventricular function during the acute phase after a first MI in 20 patients by first pass radionuclide angiography. The RV ejection fraction did not differ significantly between the groups, but LV ejection fraction was significantly depressed after anterior myocardial infarction. There was evidence of RV dilatation and impaired RV transit time (defined as duration of radionuclide activity in the right ventricle) in the group with inferior infarction. Five patients with anterior infarction and 6 with inferior infarction had abnormal RV ejection fractions. RV wall motion abnormalities concerned the septum, in the group with anterior infarction, and the right ventricle free wall in the group with inferior infarction. The relation between right and left ventricular ejection fractions was markedly different in the 2 groups. In the group with anterior infarction there was a significant linear correlation between right and left ventricular ejection fraction, whereas in the group with inferior infarction there was no association. Thus, RV dysfunction occurs after both anterior and inferior myocardial infarction.[49] Maheshwari et al.[50] demonstrated that even in patients with isolated LV AMI, there is RV dysfunction due to ventricular interdependence. They compared Simpson's RV ejection fraction with RIMP to predict RV function in 2 groups of patients with isolated LV anterior myocardial infarction. Group 1 consisted of 25 patients with significant stenosis of proximal LAD with a patent first septal perforator (S_1). Group 2 was composed of 25 patients with significant stenosis of both LAD and left circumflex artery. Both groups had fully patent RCA. RIMP value determined using pulsed Doppler echocardiography was 0.40 ± 0.19 in healthy subjects. However, RIMP was increased in both subgroups of LV-AMI with significant increase in

group 2 ($P < 0.005$) as compared to group 1 patients ($P < 0.01$). Simpson's RV ejection fraction was not significantly different between the 2 groups.[51] For the first time, Sonmez et al.[51] evaluated RV regional function in patients who were successfully treated for their first anterior MI, using a strain and strain rate imaging tissue Doppler method, observing that both systolic and diastolic functions were affected after anterior STEMI. The patient group included 44 patients who had experienced their first anterior MI and had undergone successful percutaneous coronary intervention and 20 patients for the control group (selected by patients who had undergone coronary angiography in any centre and had a normal coronary artery or insignificant coronary stenosis <50%). The myocardial velocity, strain, and strain rate values of each basal, mid, and apical segment were obtained. The RV myocardial velocities of the patient's group were significantly decreased with respect to all 3 velocities in the control group. The peak and mean strain and strain rate values of the right mid and apical ventricular segments in the patient group were significantly lower than those of the control group (excluding the right ventricular basal strain and strain rate). The main finding of the present study was that a significant decrease in TDI-based myocardial velocities and S/SR values of the RV. The mid and apical RV segments were affected by LV infarction, whereas there was no change in classical TDI velocity findings. S/SR imaging is currently a very important echocardiographic modality for revealing subclinical myocardial damage.[51]

In another study, Marmor et al.[52] showed that in patients with anterior MI there was persistent regional and global impairment of LV function but only transient impairment of the RV, whereas inferior infarction was associated with severe, persistent regional and global impairment of the RV. In fact, in 22 patients who had anterior MI, the global RV ejection fraction was decreased reflecting a uniform depression of function without localized abnormalities and returned to normal by the tenth day. The authors hypothesised that RV function may be depressed after anterior infarction on a simple mechanical basis: impaired, RV contractility secondary to increased afterload in the pulmonary vascular system, that could play a partial role in its transient dysfunction. This hypothesis is partly supported by finding of a significant correlation between the right and left ventricular ejection fractions measured within the first 48 hours after anterior infarction. It is possible that abnormalities in septal contraction due to septal necrosis or ischemia accompanying anterior infarction also contribute to the decrease in RV ejection fraction. However, the regional ejection fraction of the septal segment of the left ventricle does not correlate with the degree of initial RV impairment or its improvement

during convalescence.[52] In contrast to the above-mentioned studies, Tobinick et al.[53] demonstrated that RV ejection fraction is well-preserved in anterior infarct. They measured RV and LV ejection fraction by radionuclide angiography in patients with MI. In 24 acute anterior or lateral infarction patients RV ejection fraction was normal, while LV ejection fraction was reduced. In 19 patients with acute inferior infarction and depressed LV ejection fraction, 7 patients had reduced RV ejection fraction. In another study conducted by Ozturk et al.,[54] echocardiograms were used to determine the RIMP, LV myocardial performance index (LIMP), tricuspid E/A, tricuspid deceleration time and the LV diastolic and systolic diameters in 116 patients divided in 3 subgroups based on the polymorphism of the ACE gene with a first acute anterior MI. RVMPI and LVMPI were significantly prolonged in patients with deletion/deletion (DD) polymorphism of the ACE gene.[54] The first study that addressed the follow up in patients with transmural LV MI was conducted by Hirose et al.[55] They studied 27 patients who underwent cine-computed tomography during the first year after an initial Q-wave MI, 14 with anterior and 13 with inferior LV infarction. They showed that post-myocardial infarction remodelling after initial infarction involved a biventricular process. In the group with anterior MI, progressive and significant increases in global LV and RV chamber volumes were shown to occur despite insignificant changes in global LV and RV ejection fractions. LV dilatation can also occur after inferior LV infarction but is accompanied by only minimal changes in RV volume. So, global changes occur in both LV and RV volumes during the first year after an initial infarction regardless of infarct location, but the magnitude of these changes was greater after anterior than inferior wall LV infarction.[55] In the few studies on the prognostic implications of RV involvement in acute LV myocardial infarction showed that RV involvement was a strong independent predictor of major cardiac adverse events, and that RV function provides strong prognostic information in patients treated with primary percutaneous coronary intervention for AMI.[56-58] Figure 2 resume a close interdependence between anterior acute myocardial infarction and right ventricle function.

Despite these interesting scientific evidence, studies that have been reviewed in this article present some limits. Most of them included a limited number of patients with no clear exclusion criteria. Moreover, no data about prognosis, lab tests, are available in these studies in patients with RV involvement after AMI. No studies were conducted with a complete protocol of evaluation of the RV as guidelines suggest. Table 1 summarizes the main studies, their characteristics and limitations.

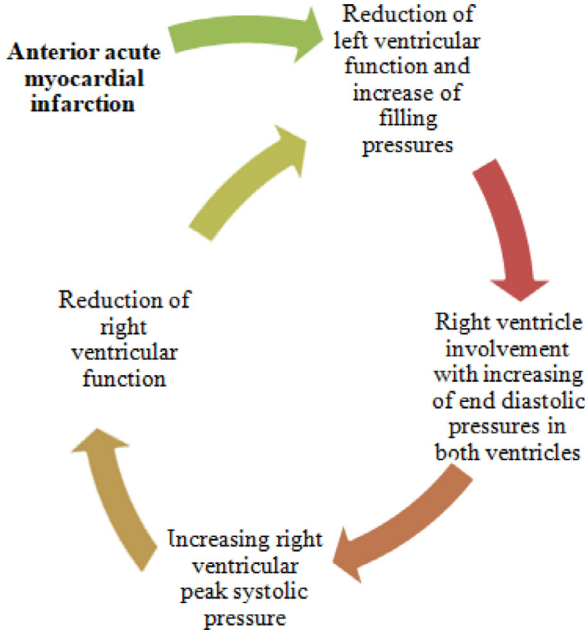

FIG 2. Anterior acute myocardial infarction and right ventricle function: a vicious circle.

Conclusion

The analysis of the literature shows that the involvement of the RV in the setting of anterior myocardial infarction has been found in many studies. Anatomical and physiological aspects as pericardium, the shared myocardium fibres, the electrical system, their interlacing muscle bundles, the interatrial septum, the interventricular septum and the shared coronary blood flow creating continuous interplay between both ventricles, can explain this involvement and also have clinical impact. Furthermore, over half of the external work performed by the RV is a direct consequence of LV shortening, presumably through deformation of the RV free wall contiguous with that of the LV. However, the studies reviewed in this article present some limits. In conclusion further studies wither of patient, complete protocol of RV echocardiographic evaluation and severe exclusion criteria are needed to confirm a RV involvement in the setting of anterior myocardial infarction especially in patients with isolated LAD obstruction.

Financial Interest

No financial interest in this manuscript.

REFERENCES

1. Haddad F, Hunt SA, Rosenthal DN, et al. Right ventricular function in cardiovascular disease, part I: anatomy, physiology, aging, and functional assessment of the right ventricle. *Circulation* 2008;117:1436–48.
2. Agur AMR, Dalley AF, Moore KL. Clinically Oriented Anatomy. Lippincott Williams & Wilkins; English 2017 ISBN: 9781496354044.
3. James TN. Anatomy of the coronary arteries in health and disease. *Circulation* 1965;32:1020–33. Dec.
4. Reig J, Petit M. Perfusion of myocardial segments of the right ventricle: role of the left coronary artery in infarction of the right ventricle. *Clin Anat* 2001;14:142–8.
5. Andersen HR, Falk E, Nielsen D. Right ventricular infarction: frequency, size and topography in coronary heart disease: a prospective study comprising 107 consecutive autopsies from a coronary care unit. *J Am Coll Cardiol* 1987:1223–32.
6. Crystal GJ, Pagel PS. Right ventricular perfusion: physiology and clinical implications. *Anesthesiology* 2018;128:202–18.
7. Greyson CR. The right ventricle and pulmonary circulation: Basic concepts. *Rev Esp Cardiol.* 2010;63:81–95.
8. Tedford RJ, Hassoun PM, Mathai SC, et al. Pulmonary capillary wedge pressure augments right ventricular pulsatile loading. *Circulation* 2012;125:289–97.
9. Lankhaar JW, Westerhof N, Faes TJ, et al. Pulmonary vascular resistance and compliance stay inversely related during treatment of pulmonary hypertension. *Eur Heart J* 2008;29:1688–95.
10. Cullen S, Shore D, Redington A. Characterization of right ventricular diastolic performance after complete repair of tetralogy of Fallot. Restrictive physiology predicts slow postoperative recovery. *Circulation.* 1995;91:1782–9.
11. Gatzoulis MA, Clark AL, Cullen S, et al. Right ventricular diastolic function 15 to 35 years after repair of tetralogy of Fallot. Restrictive physiology predicts superior exercise performance. *Circulation* 1995;91:1775–81.
12. Bernheim D. De l'asystolie veineuse dans l'hyper trophie du coeur gauche par stenose concomitante du ventricule droit. *Rev Med.* 1910;39:785.
13. Henderson Y, Prince AL. The relative systolic discharges of the right and left ventricles and their bearing on pulmonary congestion and depletion. *Heart.* 1914;5:217–26.
14. Molaug M, Stokland O, Ilebekk A, et al. Myocardial function of the interventricular septum. Effects of right and left ventricular pressure loading before and after pericardiotomy in dogs. *Circ Res.* 1981;49:52–61.
15. Dell'Italia LJ, Walsh RA. Right ventricular diastolic pressure-volume relations and regional dimensions during acute alterations in loading conditions. *Circulation.* 1988;77:1276–82.
16. Santamore WP, Dell'Italia LJ. Ventricular interdependence: significant left ventricular contributions to right ventricular systolic function. *Prog Cardio Vasc Dis.* 1998;40:289–308.
17. Santamore WP, Lynch PR, Heckman JL, et al. Left ventricular effect on right ventricular developed pressure. *J Appl Physiol* 1976;41:925–30.

18. Sawatani S, Mandell C, Kusaba E. Ventricular performance following ablation and prosthetic replacement of right ventricular myocardium. *Trans Am Soc Artif Intern Organs* 1974;20 B:629–36.
19. Feneley MP, Gavaghan TP, Baron DW, Branson JA, Roy PR, Morgan JJ. Contribution of left ventricular contraction to the generation of right ventricular systolic pressure in the human heart. *Circulation* 1985;71:473–80.
20. Damiano RJ, Jr, La Follette P, Jr, Cox JL, et al. Significant left ventricular contribution to right ventricular systolic function. *Am J Physiol.* 1991;261:H1514–24.
21. Hoffman D, Sisto D, Frater RW, et al. Left-to-right ventricular interaction with a oncontracting right ventricle. *J Thorac Cardiovasc Surg* 1994;107:1496–502.
22. Brookes C, Ravn H, White P, et al. Acute right ventricular dilatation in response to ischemia significantly impairs left ventricular systolic performance. *Circulation* 1999;100:761–7.
23. Gan C, Lankhaar JW, Marcus JT, et al. Impaired left ventricular filling due to right-to-left ventricular interaction in patients with pulmonary arterial hypertension. *Am J Physiol Heart Circ Physiol.* 2006;290:H1528–33.
24. Belenkie I, Horne SG, Dani R, et al. Effects of aortic constriction during experimental acute right ventricular pressure loading. Further insights into diastolic and systolic ventricular interaction. *Circulation* 1995;92:546–54.
25. Apitz C, Honjo O, Friedberg MK, et al. Beneficial effects of vasopressors on right ventricular function in experimental acute right ventricular failure in a rabbit model. *Thorac Cardiovasc Surg* 2012;60:17–23.
26. Alkon J, Humpl T, Manlhiot C, et al. Usefulness of the right ventricular systolic to diastolic duration ratio to predict functional capacity and survival in children with pulmonary arterial hypertension. *Am J Cardiol.* 2010;106:430–6.
27. Schwarz K1, Singh S, Dawson D, Frenneaux MP. Right ventricular function in left ventricular disease: pathophysiology and implications. *Heart Lung Circ* 2013;22:507–11.
28. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Ecocardiography and European Association of Cardiovascular imaging. *J Am soc echocardiogr* 2015;28:1–39.
29. Rudski LG, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;23:685–713.
30. Dutta T, Aronoe WS. Ecocardiographic evaluation of the right ventricle: clinical implication. *Clin Cardiol.* 2017;40(8):542–8.
31. Dandel M, Hetzer R. Echocardiographic assessment of the right ventricle: Impact of the distinctly load dependency of its size, geometry and performance. *Int J Cardiol* 2016;221:1132–42.
32. Shimada YJ, Shiota M, Siegel RJ, Shiota T. Accuracy of right ventricular volumes and function determined by three-dimensional echocardiography in comparison with

magnetic resonance imaging: a meta-analysis study. *J Am Soc Echocardiogr.* 2010;23:943–53.
33. Sugeng L, Mor-Avi V, Weinert L, et al. Multimodality comparison of quantitative volumetric analysis of the right ventricle. *JACC Cardiovasc Imaging.* 2010;3:10–8.
34. Wang J, Prakasa K, Bomma C, et al. Comparison of novel echocardiographic parameters of right ventricular function with ejection fraction by cardiac magnetic resonance. *J Am Soc Echocardiogr* 2007;20:1058–64.
35. Li Y, Wang Y, Zhai Z, et al. Real-time three-dimensional echocardiography to assess right ventricle function in patients with pulmonary hypertension. *PLoS One* 2015;10: e0129557.
36. Focardi M, Cameli M, Carbone SV, et al. Traditional and innovative echocardiographic parameters for the analysis of right ventricular performance in comparison with cardiac magnetic resonance. *Eur Heart J Cardiovasc Imaging* 2015;16:47–52.
37. Ibanez B, James S, Agewall S, et al. ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:119–77.
38. Stone PH, Raabe DS, Jaffe AS. Prognostic significance of location and type of myocardial infarction: independent adverse outcome associated with anterior location. *J Am Coll Cardiol* 1988;11:453–63.
39. Cabin HS, Clubb KS, Wackers FJ, Zaret BL. Right ventricular myocardial infarction with anterior wall left ventricular infarction: an autopsy study. *Am Heart J* 1987;113:16–23.
40. Tahirkheli NK, Edwards WD, Nishimura RA, Holmes DR, Jr. Right ventricular infarction associated with anteroseptal myocardial infarction: a clinicopathologic study of nine cases. *Cardiovasc Pathol* 2000;9:175–9.
41. Bonanad C, Ruiz-Sauri A, Forteza MJ, et al. Microvascular obstruction in the right ventricle in reperfused anterior myocardial infarction. Macroscopic and pathologic evidence in a swine model. *Thromb Res* 2013;132:592–8.
42. Bodi V, Sanchis J, Mainar L, et al. Right ventricular involvement in anterior myocardial infarction: a translational approach. *Cardiovasc Res* 2010;87:601–8.
43. Jensen CJ, Jochims M, Hunold P, Sabin GV, Schlosser T, Bruder O. Right ventricular involvement in acute left ventricular myocardial infarction: prognostic implications of MRI findings. *AJR Am J Roentgenol* 2010;194:592–8.
44. Abbate A, Bussani R, Sinagra G, et al. Right ventricular cardiomyocyte apoptosis in patients with acute myocardial infarction of the left ventricular wall. *Am J Cardiol* 2008;102:658–62.
45. Lancaster LD, Kern KB, Morrison DA, Olajos M, Goldman S. Changes in right ventricular relaxation during acute anterior myocardial infarction in pigs. *Cardiovasc Res* 1989;23:46–52.
46. Jerzewski A, Steendijk P, Pattynama PM, Leeuwenburgh BP, de Roos A, Baan J. Right ventricular systolic function and ventricular interaction during acute

embolisation of the left anterior descending coronary artery in sheep. *Cardiovasc Res* 1999;43:86–95.
47. Mittal SR. Right ventricular function in isolated occlusion of left anterior descending coronary artery. *J Assoc Physicians India* 2012;60:24–6.
48. Hsu SY, Lin JF, Chang SH. Right ventricular function in patients with different infarction sites after a first acute myocardial infarction. *Am J Med Sci* 2011;342:474–9.
49. Caplin JL, Dymond DS, Flatman WD, Spurrell RA. Global and regional right ventricular function after acute myocardial infarction: dependence upon site of left ventricular infarction. *Br Heart J* 1987;58:101–9.
50. Maheshwari M, Mittal SR. Right ventricle myocardial performance index versus simpson's right ventricle ejection fraction in patients with isolated left ventricle anterior myocardial infarction. *Heart Views* 2013;14:68–71.
51. Sonmez O, Kayrak M, Altunbas G, et al. Right ventricular involvement in anterior myocardial infarction: a tissue Doppler-derived strain and strain rate study. *Clinics.* 2013;68:1225–30. Sao Paulo.
52. Marmor A, Geltman EM, Biello DR, Sobel BE, Siegel BA, Roberts R. Functional response of the right ventricle to myocardial infarction: dependence of the site of left ventricular infarction. *Circulation* 1981;64:1005–11.
53. Tobinick E, Schelbert HR, Henning H, et al. Right ventricular ejection fraction in patients with acute anterior and inferior myocardial infarction assessed by radionuclide angiography. *Circulation* 1978;57:1078–84.
54. Ozturk O, Ulgen MS, Tekes S, Ozturk U, Toprak N. Influence of angiotensin-converting enzyme I/D gene polymorphism on the right ventricular myocardial performance index in patients with a first acute anterior myocardial infarction. *Circ J* 2005;69:211–5.
55. Hirose K, Shu NH, Reed JE, Rumberger JA. Right ventricular dilatation and remodeling the first year after a initial transmural wall left ventricular myocardial infarction. *Am J Cardiol* 1993;72:1126–30.
56. Bussani R, Abbate A, Biondi-Zoccai GG, et al. Right ventricular dilatation after left ventricular acute myocardial infarction is predictive of extremely high peri-infarctual apoptosis at postmortem examination in humans. *J Clin Pathol* 2003;56:672–6.
57. Jensen CJ, Jochims M, Hunold P, Sabin GV, Schlosser T, Bruder O. Right ventricular involvement in acute left ventricular myocardial infarction: prognostic implications of MRI findings. *AJR Am J Roentgenol* 2010;194:592–8.
58. Antoni ML, Scherptong RW, Atary JZ, et al. Prognostic value of right ventricular function in patients after acute myocardial infarction treated with primary percutaneous coronary intervention. *Circ Cardiovasc Imaging* 2010;3:264–71.