

Right Ventricular Function in Cardiovascular Disease, Part I

Anatomy, Physiology, Aging, and Functional Assessment of the Right Ventricle

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In 1616, Sir William Harvey was the first to describe the importance of right ventricular (RV) function in his seminal treatise, *De Motu Cordis*: "Thus the right ventricle may be said to be made for the sake of transmitting blood through the lungs, not for nourishing them."^{1,2} For many years that followed, emphasis in cardiology was placed on left ventricular (LV) physiology, overshadowing the study of the RV. In the first half of the 20th century, the study of RV function was limited to a small group of investigators who were intrigued by the hypothesis that human circulation could function adequately without RV contractile function.³ Their studies, however, were based on an open pericardial dog model, which failed to take into account the complex nature of ventricular interaction. In the early 1950s through the 1970s, cardiac surgeons recognized the importance of right-sided function as they evaluated procedures to palliate right-heart hypoplasia. Since then, the importance of RV function has been recognized in heart failure, RV myocardial infarction, congenital heart disease and pulmonary hypertension. More recently, advances in echocardiography and magnetic resonance imaging have created new opportunities for the study of RV anatomy and physiology.

The goal of the present review is to offer a clinical perspective on RV structure and function. In the first part, we discuss the anatomy, physiology, aging, and assessment of the RV. In the second part, we discuss the pathophysiology, clinical importance, and management of RV failure.

Anatomy of the RV

Macroscopic Anatomy of the RV

In the normal heart, the RV is the most anteriorly situated cardiac chamber and lies immediately behind the sternum. In the absence of transposition of great arteries, the RV is delimited by the annulus of the tricuspid valve and by the pulmonary valve. As suggested by Goor and Lillehi,⁴ the RV can be described in terms of 3 components: (1) the inlet, which consists of the tricuspid valve, chordae tendineae, and papillary muscles; (2) the trabeculated apical myocardium;

and (3) the infundibulum, or conus, which corresponds to the smooth myocardial outflow region^{4,5} (Figure 1). In the study of congenital heart disease, this division seems to be more practical than the traditional division of the RV into sinus and conus components.⁵ Additionally, the RV can also be divided into anterior, lateral, and inferior walls, as well as basal, mid, and apical sections.⁶

Three prominent muscular bands are present in the RV: the parietal band, the septomarginal band, and the moderator band. The parietal band and the infundibular septum make up the crista supraventricularis.⁷ The septomarginal band extends inferiorly and becomes continuous with the moderator band, which attaches to the anterior papillary muscle.⁷ When abnormally formed or hypertrophied, the septomarginal band can divide the ventricle into 2 chambers (double-chambered RV).⁵ Another important characteristic of the RV is the presence of a ventriculoinfundibular fold that separates the tricuspid and pulmonary valves. In contrast, in the LV, the aortic and mitral valves are in fibrous continuity (Figure 1).

The shape of the RV is complex. In contrast to the ellipsoidal shape of the LV, the RV appears triangular when viewed from the side and crescent shaped when viewed in cross section.⁶ The shape of the RV is also influenced by the position of the interventricular septum. Under normal loading and electrical conditions, the septum is concave toward the LV in both systole and diastole.⁶ In the mature child and adult, the volume of the RV is larger than the volume of the LV, whereas RV mass is approximately one sixth that of the LV.⁸

Myofiber Architecture of the RV

The ventricles are not composed of a single muscle layer but rather of multiple layers that form a 3-dimensional (3D) network of fibers.⁵ As described by Ho and Nihoyannopoulos,⁵ the RV wall is mainly composed of superficial and deep muscle layers. The fibers of the superficial layer are arranged more or less circumferentially in a direction that is parallel to the atrioventricular (AV) groove (Figure 1).^{5,9} These fibers turn obliquely toward the cardiac apex on the sternocostal aspect and continue into the superficial myofibers of the

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(*Circulation*. 2008;117:1436-1448.)

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Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.107.653576

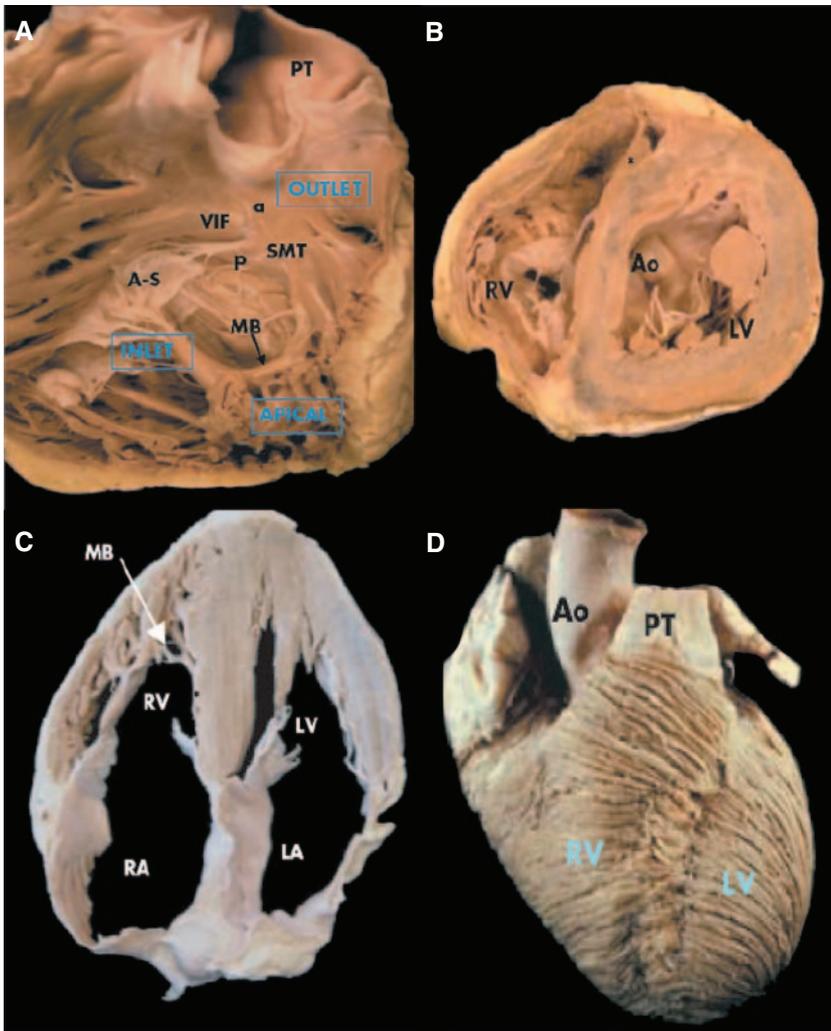


Figure 1. A, The inlet, trabeculated apical myocardium and infundibulum of the RV. The tricuspid and pulmonary valves are separated by the ventriculoinfundibular fold (VIF). B, Short-axis plane of the RV demonstrating its crescentic shape. C, The 4-chamber anatomic plane of the heart showing the moderator band (MB) and the more apical insertion of the tricuspid valve. D, Superficial muscle layer of the RV (dissection by Damian Sanchez-Quintana, University of Extremadura, Spain). SMT indicates septomarginal trabeculation with its anterior (a) and posterior (p) arm; A-S, anteriosuperior leaflet of the tricuspid valve; PT, pulmonary trunk; Ao, aorta; RA, right atrium; and LA, left atrium. Reproduced from Ho and Nihoyannopoulos⁵ with permission from the publisher. Copyright © 2006, BMJ Publishing Group Ltd.

LV.^{5,9} The deep muscle fibers of the RV are longitudinally aligned base to apex. In contrast to the RV, the LV contains obliquely oriented myofibers superficially, longitudinally oriented myofibers in the subendocardium, and predominantly circular fibers in between. This arrangement contributes to the more complex movement of the LV, which includes torsion, translation, rotation, and thickening.^{5,9}

The continuity between the muscle fibers of the RV and LV functionally binds the ventricles together and represents the anatomic basis of free ventricular wall traction caused by LV contraction. This continuity also contributes, along with the interventricular septum and pericardium, to ventricular interdependence.⁹

Distinguishing Anatomic Features of the RV

Although the RV is usually located on the right side of the heart and connects with the pulmonary circulation, the anatomic RV is defined by its structure rather than by its position or connections. The morphological features that best differentiate anatomic RV, LV, or indeterminate ventricle include the following: (1) the more apical hinge line of the septal leaflet of the tricuspid valve relative to the anterior leaflet of the mitral valve; (2) the presence of a moderator band; (3) the presence of more than 3 papillary muscles; (4)

the trileaflet configuration of the tricuspid valve with septal papillary attachments; and (5) the presence of coarse trabeculations.^{5,7} Prominent trabeculations in the systemic ventricle can also be seen in congenitally corrected transposition of great arteries (anatomic RV) or in noncompaction of the LV.

Physiology

The primary function of the RV is to receive systemic venous return and to pump it into the pulmonary arteries. Under normal circumstances, the RV is connected in series with the LV and is, therefore, obligated to pump on average the same effective stroke volume.

Mechanical Aspects of Ventricular Contraction

RV contraction is sequential, starting with the contraction of the inlet and trabeculated myocardium and ending with the contraction of the infundibulum (approximately 25 to 50 ms apart).⁹ Contraction of the infundibulum is of longer duration than contraction of the inflow region.⁹

The RV contracts by 3 separate mechanisms: (1) inward movement of the free wall, which produces a bellows effect; (2) contraction of the longitudinal fibers, which shortens the long axis and draws the tricuspid annulus toward the apex; and (3) traction on the free wall at the points of attachment

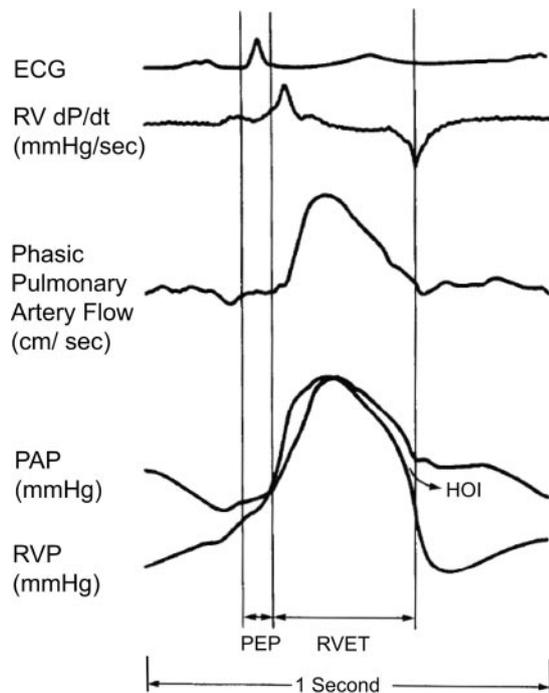


Figure 2. Simultaneously recorded ECG, RV analog signal of pressure development (dP/dt), phasic pulmonary artery flow, pulmonary artery pressure (PAP), and RV pressure (RVP) in the human subject. PEP indicates preejection period; RVET, RV ejection time; and HOI, hangout interval. Reproduced from Dell'Italia and Walsh,¹² copyright © 1988, with permission from Elsevier.

secondary to LV contraction.⁶ Shortening of the RV is greater longitudinally than radially.¹⁰ In contrast to the LV, twisting and rotational movements do not contribute significantly to RV contraction. Moreover, because of the higher surface-to-volume ratio of the RV, a smaller inward motion is required to eject the same stroke volume.⁶

RV Hemodynamics

Under normal conditions, the RV is coupled with a low-impedance, highly distensible pulmonary vascular system. Compared with the systemic circulation, pulmonary circulation has a much lower vascular resistance, greater pulmonary artery distensibility, and a lower peripheral pulse wave reflection coefficient.⁹

Under normal conditions, right-sided pressures are significantly lower than comparable left-sided pressures.¹¹ RV pressure tracings show an early peaking and a rapidly declining pressure in contrast to the rounded contour of LV pressure tracing (Figure 2).¹² RV isovolumic contraction time is shorter because RV systolic pressure rapidly exceeds the low pulmonary artery diastolic pressure. A careful study of hemodynamic tracings and flow dynamics also reveals that end-systolic flow may continue in the presence of a negative ventricular-arterial pressure gradient (Figure 2).^{9,12} This interval, which is referred to as the hangout interval, is most likely explained by the momentum of blood in the outflow tract.¹²

Cardiodynamics

RV systolic function is a reflection of contractility, afterload, and preload. RV performance is also influenced by heart

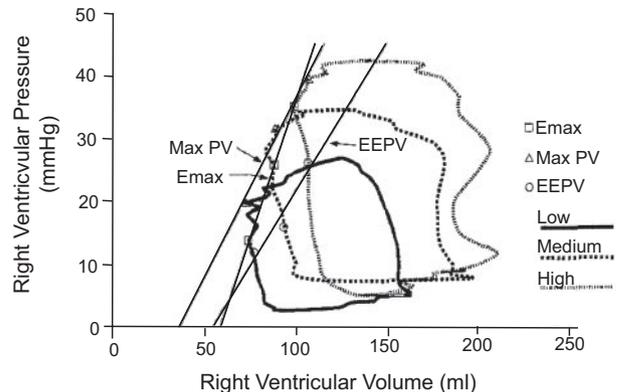


Figure 3. Pressure-volume loops of the RV under different loading conditions. The slope of maximum time-varying elastance (Emax), maximum pressure-volume ratio (Max PV), and end-ejection pressure/volume (EEPV) are displayed on the graph. Reproduced from Dell'Italia and Walsh,²⁰ copyright © 1988, with permission from the European Society of Cardiology.

rhythm, synchrony of ventricular contraction, RV force-interval relationship, and ventricular interdependence.^{13–16} Significant valvular regurgitation or shunt physiology should always be considered because they can decrease effective cardiac output.⁹

The complex relationship between RV contractility, preload, and afterload can be better understood with the help of pressure-volume loops. Pressure-volume loops depict instantaneous pressure-volume curves under different loading conditions. For the LV, Suga et al¹⁷ showed that the end-systolic pressure-volume relationship can be approximated by a linear relationship. The slope of this relationship is referred to as ventricular elastance. Because of its relative load independence, many investigators consider ventricular elastance as the most reliable index of contractility.¹⁸

Interestingly, despite having markedly different ventricular geometry and hemodynamics, many studies showed that the RV also follows a time-varying elastance model (Figure 3).^{19,20} Because of the different shape of RV pressure-volume curves, maximal RV elastance better reflects RV contractility than does the end-systolic elastance commonly used in LV pressure-volume interpretation.²⁰ On the basis of the study by Dell'Italia and Walsh,²⁰ the normal maximal RV elastance is 1.30 ± 0.84 mm Hg/mL. Although maximal RV elastance is the most reliable index of RV contractility, some studies have outlined limitations in the RV time-elastance model, such as nonlinearity, variability in slope values, and afterload dependency.²¹

RV afterload represents the load that the RV has to overcome during ejection. Compared with the LV, the RV demonstrates a heightened sensitivity to afterload change (Figure 4).^{22,23} Although in clinical practice, pulmonary vascular resistance (PVR) is the most commonly used index of afterload, PVR may not reflect the complex nature of ventricular afterload. A more complete model would ideally take into account the static and dynamic components of pulmonary vascular impedance as well as potential valvular or intracavitary resistive components.⁹

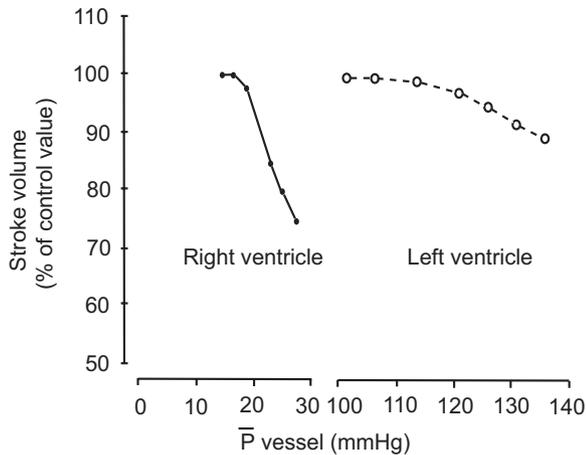


Figure 4. The response of the RV and LV to experimental increase in afterload. Reproduced from MacNee²² with permission from the publisher. Copyright © 1994, the American Thoracic Society.

RV preload represents the load present before contraction. Within physiological limits, an increase in RV preload improves myocardial contraction on the basis of the Frank-Starling mechanism. Beyond the physiological range, excessive RV volume loading can compress the LV and impair global ventricular function through the mechanism of ventricular interdependence.²³ Compared with LV filling, RV filling normally starts before and finishes after. RV isovolumic relaxation time is shorter, and RV filling velocities (E and A) and the E/A ratio are lower. The respiratory variations in RV filling velocities are, however, more pronounced.^{6,24} Many factors influence RV filling, including intravascular volume status, ventricular relaxation, ventricular chamber compliance, heart rate, passive and active atrial characteristics, LV filling, and pericardial constraint.²⁵ The filling period is also an important determinant of ventricular preload and function. As demonstrated by Dell'Italia,¹³ the RV follows a force-interval relationship in which stroke volume increases above baseline after longer filling periods, as seen in postextrasystolic beats. On the basis of the sarcomere length-pressure curve relationship, RV compliance is believed to be greater than LV compliance.^{26,27} Also, in general, the pericardium imposes greater constraint on the thinner, more compliant, low-pressure RV.⁹

Heart Rhythm and Dyssynchrony

Maintenance of sinus rhythm and AV synchrony is especially important in the presence of RV dysfunction. For example, atrial fibrillation or complete AV block are poorly tolerated in acute RV myocardial infarction, acute pulmonary emboli, or chronic RV failure.¹⁴

RV dyssynchrony refers to the concept of suboptimal coordination of RV mechanical function. RV dyssynchrony could potentially lead to reduced cardiac output or increased filling pressures. The effects of “resynchronization therapy” in patients with RV failure and congenital heart disease have been assessed recently in a multicenter international study (n=103).²⁸ Dubin and colleagues²⁸ demonstrated that resynchronization therapy was associated with improvement in RV

ejection fraction (RVEF) in patients with congenital heart disease with either systemic or pulmonic RV.

Ventricular Interdependence

Ventricular interdependence refers to the concept that the size, shape, and compliance of 1 ventricle may affect the size, shape, and pressure-volume relationship of the other ventricle through direct mechanical interactions.¹⁶ Although always present, ventricular interdependence is most apparent with changes in loading conditions such as those seen with respiration or sudden postural changes.¹⁶ Ventricular interdependence plays an essential part in the pathophysiology of RV dysfunction.

Systolic ventricular interdependence is mediated mainly through the interventricular septum. The pericardium may not be as important for systolic ventricular interdependence as it is for diastolic ventricular interdependence.^{15,16} Experimental animal studies showed that approximately 20% to 40% of RV systolic pressure and volume outflow results from LV contraction.¹⁶ Moreover, in the presence of scarring of the RV or replacement with a noncontractile patch, the septum is able to maintain circulatory stability as long as the RV is not dilated.²⁹

The evidence for diastolic ventricular interdependence is well established and based on many experimental and clinical studies.^{16,30} In acute RV pressure- or volume-overload states, dilatation of the RV shifts the interventricular septum toward the left, alters LV geometry, and increases pericardial constraint. As a consequence, the LV diastolic pressure-volume curve shifts upward (decreased distensibility), which potentially leads to a decreased LV preload, an increased LV end-diastolic pressure (usually a mild increase), or low cardiac output states. Acute RV dilatation has also been shown to lead to a decrease in LV elastance.^{9,16} Conversely, LV volume or pressure overload has also been shown to shift upward the RV diastolic pressure-volume relationship and to redistribute RV filling into late diastole.^{30,31}

Perfusion of the RV

The blood supply of the RV varies according to the dominance of the coronary system. In a right-dominant system, which is found in ≈80% of the population, the right coronary artery supplies most of the RV.^{9,32} The lateral wall of the RV is supplied by the marginal branches of the RV, whereas the posterior wall and the inferoseptal region are supplied by the posterior descending artery. The anterior wall of the RV and the anteroseptal region are supplied by branches of the left anterior descending artery. The infundibulum derives its supply from the conal artery, which has a separate ostial origin in 30% of cases. The separate ostium explains the preservation of infundibular contraction in the presence of proximal right coronary occlusion.^{9,32}

In the absence of severe RV hypertrophy or pressure overload, proximal right coronary artery flow occurs during both systole and diastole.³³ However, beyond the RV marginal branches, diastolic coronary blood flow predominates.⁷ The relative resistance of the RV to irreversible ischemic injury may be explained by (1) its lower oxygen consumption, (2) its more extensive collateral system, especially from

Table 1. Comparison of Normal RV and LV Structure and Function

Characteristics	RV	LV
Structure	Inflow region, trabeculated myocardium, infundibulum	Inflow region and myocardium, no infundibulum
Shape	From the side: triangular ⁹ cross section: crescentic	Elliptic ⁹
End-diastolic volume, mL/m ²	75±13 (49–101) ⁸	66±12 (44–89) ⁸
Mass, g/m ²	26±5 (17–34) ⁸	87±12 (64–109) ⁸
Thickness of ventricular wall, mm	2 to 5 ^{5,6}	7 to 11 ⁶
Ventricular pressures, mm Hg	25/4 [(15–30)/(1–7)] ¹¹	130/8 [(90–140)/(5–12)] ¹¹
RVEF, %	61±7 (47–76) ⁸ >40–45*	67±5 (57–78) ⁸ >50*
Ventricular elastance (E _{max}), mm Hg/mL	1.30±0.84 ²⁰	5.48±1.23 ¹⁸
Compliance at end diastole, mm Hg ⁻¹	Higher compliance than LV ^{26†}	5.0±0.52×10 ⁻²⁽²⁷⁾
Filling profiles	Starts earlier and finishes later ↑ lower filling velocities ⁶	Starts later and finishes ⁶ earlier, higher filling velocities
PVR vs SVR, dyne · s · cm ⁻⁵	70 (20–130) ¹¹	1100 (700–1600) ¹¹
Stroke work index, g/m ² per beat	8±2 (1/6 of LV stroke work) ⁹	50±20 ¹¹
Exercise reserve	↑ RVEF ≥5% ⁹	↑ LVEF ≥5% ³⁷
Resistance to ischemia	Greater resistance to ischemia ⁹	More susceptible to ischemia ⁹
Adaptation to disease state	Better adaptation to volume overload states ⁹	Better adaptation to pressure overload states ⁹

PVR indicates pulmonary vascular resistance; SVR, systemic vascular resistance; and ↑, increase.

*Lower range of normal RV function used in clinical practice; lower value of normal described with radionuclide angiography.

†Mainly based on sarcomere length–pressure curve relationship, limited data on end-diastolic passive compliance in humans.

the moderator band artery, a branch of the first septal perforator that originates from the left anterior descending coronary artery, and (3) its ability to increase oxygen extraction.³⁴

Regulation of RV Function

The mechanisms that can acutely regulate RV as well as LV function include heart rate, the Frank-Starling mechanism and the autonomic nervous system. The autonomic nervous system has a differential effect on the inflow and outflow region of the RV. In fact, weak vagal stimulation, which causes bradycardia, prolongs the normal sequence of activation, whereas sympathetic stimulation may abolish the usual delay or even reverse the sequence of contraction in these 2 regions of the RV.⁹ The inflow and outflow regions may also differ in their response to sympathetic activation or inotropic stimulation; animal and human studies have suggested that the inotropic response of the infundibulum may be greater than that of the inflow tract.^{35,36} As will be discussed in the second part of this series, numerous studies also describe the role of the renin-angiotensin-aldosterone system, natriuretic peptides, the endothelin system, tumor necrosis factor, and inflammation in patients with RV dysfunction. Table 1 summarizes important anatomic and physiological characteristics of the RV.^{5,6,8,9,11,18,20,26,27,37}

Embryology and Aging

A basic understanding of embryology is helpful in the study of cardiovascular and congenital heart disease. The RV and RV outflow tract are derived from the anterior heart field, whereas the LV and the atrial chambers are derived from the

primary heart field.³⁸ Transcription factors such as HAND1 and HAND2 appear to play an important role in chamber-specific heart formation.³⁹ The sinus part of the RV is derived from the ventricular portion of the primitive cardiac tube, whereas the infundibulum is derived from the conus cordis. In the anatomic LV, subaortic conal absorption occurs, which explains the absence of an infundibular component as well as mitral-aortic continuity.⁹ Under normal conditions, the dextroventricular loop positions the anatomic RV to the right and the anatomic LV to the left. The complex spiral development of the outflow tracts explains the characteristic “crisscross” relationship between right and left outflow tracts, with the RV outflow tract being located anteriorly and to the left of the LV outflow tract.^{6,7}

The RV undergoes significant changes with aging, especially after birth and during infancy. In the fetus, cardiovascular physiology is characterized by a high-resistance pulmonary circulation; a low-resistance systemic circulation; a large, nonrestrictive ductus arteriosus; right-to-left flow across the foramen ovale; equal pulmonary arterial and aortic pressure; and hypoxemia.^{40–42} RV and LV free-wall thickness and force development are equal throughout fetal life, and the interventricular septum is midline and flat throughout the cardiac cycle.^{40–42} After birth and in infancy, RV hypertrophy regresses, and the heart remodels to the typical postnatal heart with a crescent-shaped RV and an elliptic LV. With aging, several changes occur in the RV and the pulmonary vascular system. The pulmonary artery pressure and vascular resistance mildly increase with normal aging, most probably secondary to an increase in arterial stiffness of the pulmonary vasculature.^{43,44} RVEF remains relatively well

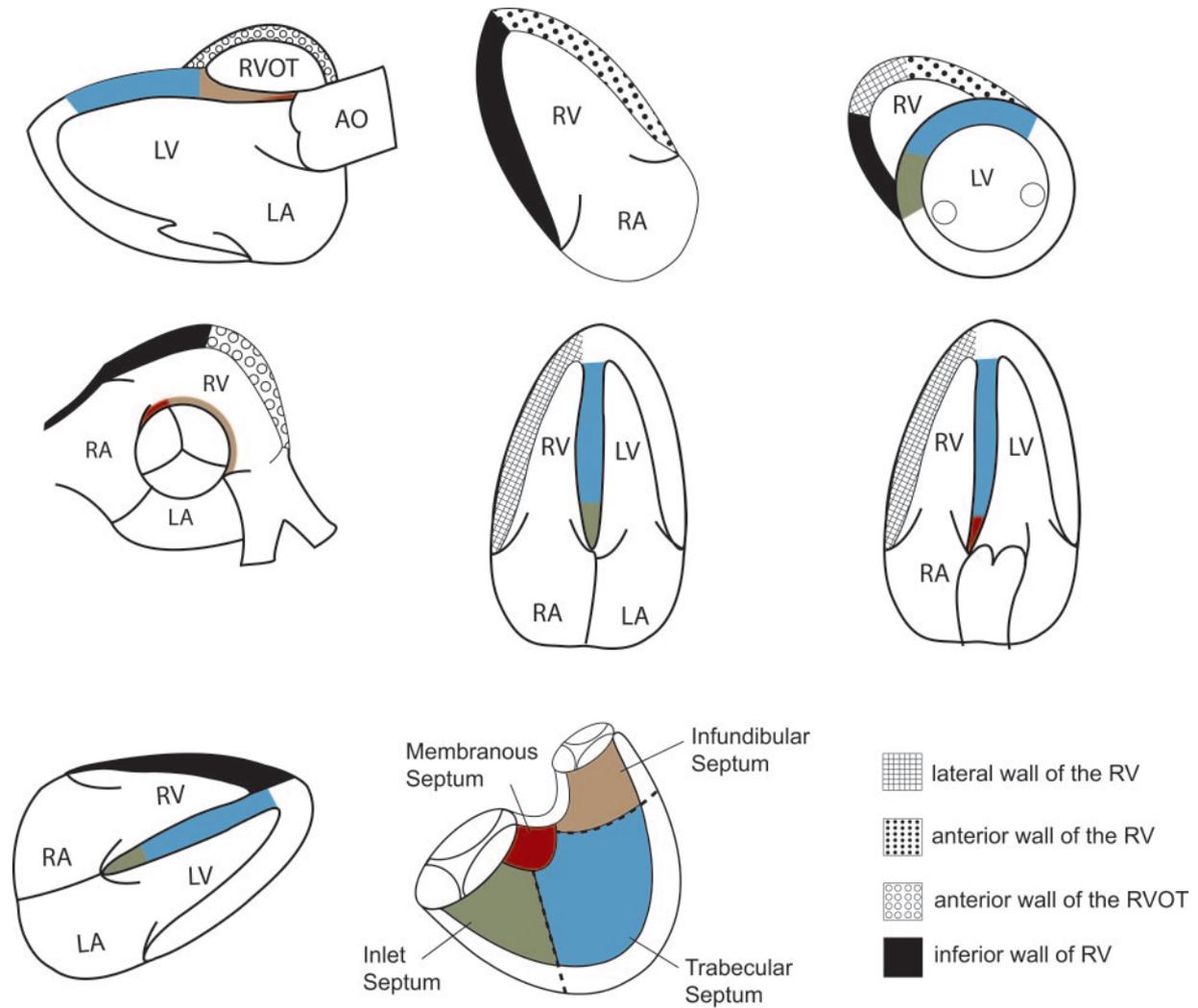


Figure 5. Segmental anatomy of the RV as shown in representative echocardiographic views. The colors indicate the different subdivisions of the interventricular septum. RVOT indicates RV outflow tract; AO, aorta; LA, left atrium; and RA, right atrium. Adapted from Weyman⁶ with permission from the publisher. Copyright © 1994, Lippincott Williams & Wilkins.

preserved with aging, as does LV ejection fraction. RV diastolic function changes with time. Doppler indices, reflective of flow pattern, demonstrate a reduced early RV diastolic filling, increased late filling, and reduced myocardial diastolic velocities.⁴⁵ These changes are analogous to changes in LV diastolic filling profiles. Changes in RV systolic reserve with exercise have not been well studied but most likely parallel the small decline seen in LV systolic reserve.⁴⁶

Assessment of the RV

Overview of RV Assessment

Evaluation of RV structure and function in patients with cardiopulmonary disorders is an essential component of clinical management. Although there have been significant improvements in cardiac imaging, many factors contribute to the challenges of RV assessment. These include (1) the complex geometry of the RV; (2) the limited definition of RV endocardial surface caused by the heavily trabeculated myocardium; (3) the retrosternal position of the RV, which can limit echocardiographic imaging windows; and (4) the marked load dependence of indices of RV function.⁶

The RV can be studied with many imaging and functional modalities. In clinical practice, echocardiography is the mainstay of evaluation of RV structure and function. Compared with other modalities, it offers the advantages of versatility and availability. Also, Doppler-derived indices of RV function, such as the myocardial performance index and tricuspid annular isovolumic acceleration (IVA), are emerging as promising parameters of RV function. Figure 5 summarizes the segmental anatomy of the RV in different echocardiographic views.⁶ Cardiac magnetic resonance imaging (MRI) is increasingly used as a standard tool in the evaluation of RV structure and function. MRI is the most accurate method for assessing RV volume. With careful attention to detail, diastolic and systolic volumes can be determined and used to calculate ejection fraction. In addition, MRI flow studies are used to estimate forward flow through semilunar valves and AV valves, which allows accurate calculation of regurgitant fractions, cardiac output, and shunt fraction. In the future, MRI could also have a potential role in assessing the physiological characteristics of pulmonary arterial flow. Radionuclide-based techniques provide reliable and geomet-

rically independent assessments of RVEF. Radionuclide-based time activity curves are also useful in the quantification of shunts. Cardiac catheterization provides direct hemodynamic data and allows accurate assessment of pulmonary vascular resistance. Pulmonary angiography and coronary angiography can further delineate important anatomic and functional characteristics. Compared with CT angiography, pulmonary angiography may be limited in its assessment of proximal lamination but has a relative benefit in assessing distal obstruction. Analysis of RV function by pressure-volume loops is useful because it quantifies various determinants of RV function such as RV elastance, dP/dt , ventricular compliance, stroke work, and preload recruitable stroke work. Currently, the conductance catheter is the most frequently used method to construct pressure-volume loops. This catheter contains a high-fidelity pressure sensor and up to 12 electrodes to measure RV electrical conductance, from which instantaneous RV chamber volume is determined.⁴⁷ Compared with LV conductance studies, RV conductance studies are technically more challenging because of the difficulty in obtaining reliable ventricular volumes.

Assessment of RV Structure

A change in RV shape and volume can be the first sign of RV dysfunction, pressure or volume overload, or arrhythmogenic RV dysplasia. A comprehensive assessment of RV structure should include the study of (1) RV volume, (2) RV shape and internal architecture, (3) RV hypertrophy and mass, (4) tissue characterization, and (5) assessment for potential masses (Table 2).^{6,8,48–50}

To be accurate, volume assessment should always take into account the complex shape of the RV. Furthermore, the infundibulum should be included in the volume measurement because it can account for as much as 25% to 30% of RV volume.⁵¹ The simplest and most routinely used method for assessing RV volume includes linear dimensions and areas obtained from single tomographic echocardiographic planes. The best correlations between single-plane measurements and RV volumes have been obtained with the maximal short-axis dimension and the planimetered RV area (in the 4-chamber view).⁶ Significant overlap has been noted, however, between normal and volume-overloaded conditions, especially for mild to moderate enlargement.⁶ In an effort to be more accurate, different approaches have been sought to directly measure RV volume. These include the area-length method and Simpson's rule approach. In 2-dimensional echocardiography, numerous studies showed that the area-length method that uses an ellipsoid or pyramidal model correlates better with RV volume than Simpson's rule.⁶ The main difficulty seen with the application of Simpson's rule to 2-dimensional echocardiographic images is obtaining 2 appropriate orthogonal views with a common long axis. Three-dimensional echocardiography is a promising technique that could lead to more accurate assessment of RV volume. However, visualization of the anterior wall and inclusion of the infundibulum in a simple model remain difficult, which explains the variable correlations with MRI and cast models.^{6,51,52} MRI is considered the most reliable method for measuring RV volumes. By acquiring parallel and contiguous tomographic

Table 2. Structural Characteristics of the RV

Feature	Criteria (Reference)	Interpretation
Dilatation	Volume >101 mL/m ²⁽⁶⁾	Volume overload
	RV max SAX >43 mm ⁽⁶⁾	Pressure overload
	RVEDA/LVEDA >2/3 ⁽⁶⁾	Intrinsic myocardial disease
D-shaped LV	Eccentricity index >1 ^{(49)*}	RV pressure or volume overload
		Diastolic D-shape LV suggests volume overload
		Systolic D-shape LV suggests pressure overload
Hypertrophy	Mass >35 g/m ²⁽⁶⁾	Pressure-overloaded RV
	RV inferior wall >5 mm ⁽⁶⁾	Hypertrophic cardiomyopathy, infiltrative disease; exclude double-chambered RV
Aneurysm	Localized RV dilatation ⁽⁶⁾	ARVD; RVMI; localized absence of pericardium
TV septal insertion	Septal insertion >1 cm or 8 mm/m ²⁽⁵⁰⁾	Consider Ebstein's anomaly
Delayed enhancement	Area of delayed contrast uptake and washout in MRI	Suggests myocardial fibrosis
Fatty infiltration	High-intensity signal on MRI	Consider ARVD

RV max SAX indicates RV maximal short-axis diameter; RVEDA/LVEDA, ratio of RV to LV end-diastolic area; ARVD, arrhythmogenic RV dysplasia; RVMI, RV myocardial infarction; and TV, tricuspid valve.

*The eccentricity index measures the degree of septal displacement and is defined as the ratio of the minor axis diameter of the LV parallel to the septum to that perpendicular to it.

images with high temporal resolution, MRI obviates the need for geometric assumptions. Volume is then calculated by summing the volume of each slice with Simpson's rule.

Assessment of RV Function

The load dependence of many of the indices of RV function and the difficulty in constructing and analyzing RV pressure-volume loops render the study of RV function particularly challenging. In this section, we will review noninvasive and invasive indices of contractility, preload, and afterload in the context of clinical practice.

Selected Indices of RV Contractility

An ideal index of contractility should be independent of afterload and preload, sensitive to change in inotropy, independent of heart size and mass, easy and safe to apply, and proven to be useful in the clinical setting.⁵³ In clinical practice, RVEF is the most commonly used index of RV contractility. Although widely accepted, RVEF is highly dependent on loading conditions and may not adequately reflect contractility. Because the RV chamber is larger than the LV chamber, RVEF is, under normal conditions, lower than LV ejection fraction. The normal range of RVEF varies between 40% and 76% depending on the methodology used. MRI is the most accurate method for measuring RVEF. According to Lorenz and colleagues,⁸ the normal value of RVEF is $61 \pm 7\%$, ranging from 47% to 76%. RV images can be acquired in the short-axis or axial direction. Alfakih and colleagues⁵⁴ demonstrated that the axial orientation resulted

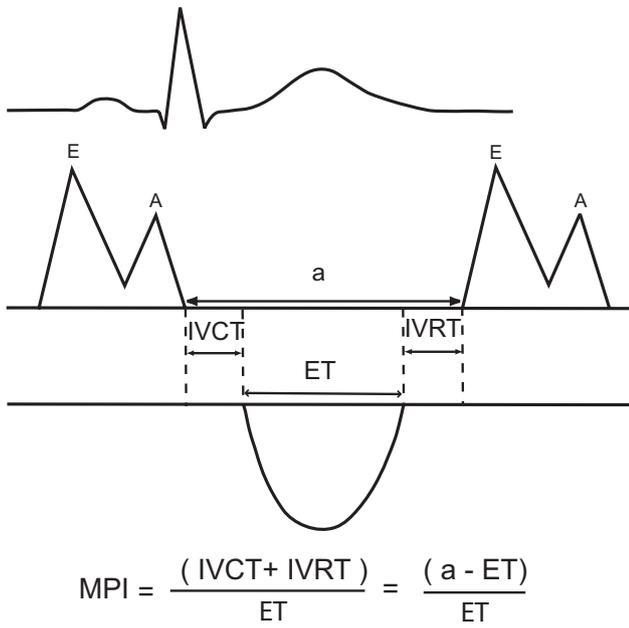


Figure 6. The RV myocardial performance index (MPI). E indicates the rapid filling velocity; A, atrial filling velocity; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; and ET, ejection time.

in a better intraobserver and interobserver reproducibility than the short-axis orientation. The lower limit of radionuclide-derived normal RVEF ranges from 40% to 45%.⁵⁵ Radionuclide angiography can be completed with either first-pass or equilibrium techniques. Both techniques have the advantage of being independent of geometric assumption and have been validated extensively. The first-pass technique has the disadvantage of having a lower count density, whereas the equilibrium technique has difficulty separating the right atrium from the RV.⁵⁵ Echocardiography is less accurate than the 2 previously mentioned methods. Two-dimensional assessment of RVEF with Simpson's rule and the area-length method showed moderate correlation with radionuclide- or MRI-derived RVEF (correlations ranging from 0.65 to 0.80).⁶ In the clinical setting, 3D echocardiography has also shown variable correlations with RVEF. Difficulties that still need to be overcome include delineation of the anterior wall and identification of the infundibular plane. RV fractional area change represents the ratio of systolic area change to diastolic RV area. It is measured in the 4-chamber view and can be incorporated systematically into the basic echocardiographic study. In end-stage pulmonary disease, a good correlation has been reported between RV fractional area change and RVEF.⁵⁶

Tricuspid annular plane systolic excursion is another useful quantitative measurement of RV systolic performance. This method reflects the longitudinal systolic excursion of the lateral tricuspid valve annulus toward the apex. It is usually measured with M-mode imaging in the 4-chamber view.⁵⁷ Studies showed moderate correlation between tricuspid annular plane systolic excursion and RVEF measured by radionuclide angiography.⁵⁸

RV myocardial performance index, which is the ratio of isovolumic time intervals to ventricular ejection time, has

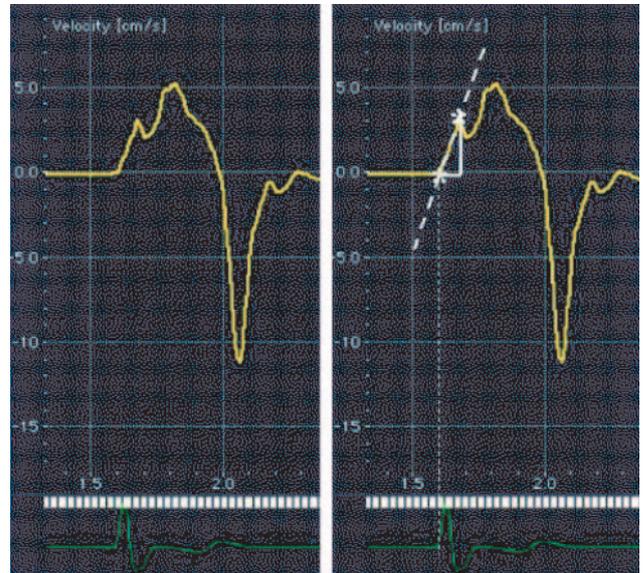


Figure 7. Tissue Doppler echocardiography spectral curve at the level of the tricuspid annulus. The isovolumic myocardial acceleration is calculated as the difference between baseline and peak velocity (stars) during isovolumic contraction divided by their time interval. Reproduced from Vogel et al⁶⁴ with permission from the publisher. Copyright © 2004, the American College of Cardiology Foundation.

been described as a nongeometric index of global ventricular function (Figure 6).⁵⁹ RV myocardial performance index appears to be relatively independent of preload, afterload, and heart rate and has been useful in assessing patients with congenital heart disease and pulmonary hypertension.^{60–62} The normal value of this index is 0.28 ± 0.04 , and it usually increases in the presence of RV systolic or diastolic dysfunction. Recently, Yoshifuku and colleagues⁶² described pseudo-normalized values in acute and severe RV myocardial infarction, which can probably be explained by a decrease in isovolumic contraction time associated with an acute increase in RV diastolic pressure.

Tissue Doppler imaging, which measures myocardial velocities, also allows quantitative assessment of RV systolic function. Systolic tissue Doppler signal of the tricuspid annulus (St) has been studied as an index of RV function in patients with heart failure. Peak systolic values <11.5 cm/s identified the presence of ventricular systolic dysfunction (RVEF $<50\%$) with a sensitivity and specificity of 90% and 85%, respectively.⁶³

IVA represents a new tissue Doppler-derived parameter of systolic performance. It is calculated by dividing the maximal isovolumic myocardial velocity by the time to peak velocity: $IVA = \text{maximum velocity} / \text{time to peak}$ (Figure 7).⁶⁴ Vogel and colleagues studied the value of myocardial IVA in a closed-chest animal model during modulation of preload, afterload, contractility, and heart rate. Their study showed that IVA reflects RV myocardial contractile function and is less affected by preload and afterload within a physiological range than either the maximum first derivative of RV pressure development ($dp/dt \text{ max}$) or ventricular elastance.⁶⁴ Two clinical studies confirmed its value in congenital heart disease, ie, after repair of tetralogy of Fallot and in transposition

Table 3. Selected Indices of RV Contractility

Functional Parameters	Normal Value	Load Dependence*	Clinical Utility
RVEF, %	61±7% (47%–76%) ⁸ >40%–45%	+ + +	Clinical validation, wide acceptance Prognostic value in cardiopulmonary disorders ⁹
RVFAC, %	>32% ⁴⁸	+ + +	Good correlation with RVEF Prognostic value in MI and bypass surgery ⁴⁸
TAPSE, mm	>15 ⁴⁸	+ + +	Simple measure not limited by endocardial border recognition: Good correlation with RVEF
Sm annular, cm/s	>12 ⁶³	+ + +	Good sensitivity and specificity for RVEF <50% ⁶³
Strain	Basal: 19±6 ⁶⁸ Mid: 27±6 Apical: 32±6	+ + +	Correlates with stroke volume ^{69,70}
Strain rate, s ⁻¹	Basal: 1.50±0.41 ⁶⁸ Mid: 1.72±0.27 Apical: 2.04±0.41	+ +	Correlates with contractility ^{69,70}
RVMPI	0.28±0.04 ⁵⁹	+ +	Global nongeometric index of systolic and diastolic function, prognostic value PH, CHD ^{60–62}
dP/dt max, mm Hg/s	100–250 ⁹	+ +	Not a reliable index of contractility ⁶⁶ More useful in assessing directional change when preload accounted for
IVA, m/s ²	1.4±0.5 ⁶⁴	+	Promising new noninvasive index of contractility, studies in CHD ^{64,65}
Maximal RV elastance, mm Hg/mL	1.30±0.84 ²⁰	+	Most reliable index of contractility ⁹

RVFAC indicates RV fractional area change; MI, myocardial infarction; TAPSE, tricuspid annular plane systolic excursion; Sm, tissue Doppler maximal systolic velocity at the tricuspid annulus; RVMPI, RV myocardial performance index; PH, pulmonary hypertension; and CHD, congenital heart disease.

*Should be viewed as a general indication of load dependence.

of the great arteries.^{64,65} Further validation of this new index is being actively pursued.

dP/dt max is also used as an index of RV contractility. As demonstrated by numerous studies, RV dP/dt max is significantly affected by loading conditions and cannot be used as a reliable index of contractility.⁶⁶ It may, however, be useful in assessing directional change in response to therapy.

As discussed earlier, maximum ventricular elastance is considered by many investigators as the best index of contractility.²⁰ Because conductance catheterization is invasive and time consuming, it is predominantly used as a research tool for assessment of ventricular function.⁶⁵ More recently, single-beat estimation of RV elastance with the maximal pressure of isovolumic beat has been validated in the clinical setting. This method could potentially simplify the measure of ventricular elastance.⁶⁷ Table 3 compares different indices of RV systolic function.^{8,9,20,48,59–70}

Patterns of RV Segmental Dysfunction

In pulmonary embolism, McConnell and colleagues⁷¹ described a distinct pattern of RV dysfunction, characterized by severe hypokinesia of the RV mid free wall, with normal contraction of the apical segment. Compared with several other conditions, the finding showed a sensitivity of 77% and a specificity of 94% for pulmonary embolism. Recently, Casazza and colleagues⁷² also recognized this pattern of ventricular dysfunction in patients with acute RV myocardial infarction.

In RV myocardial infarction, the pattern of segmental dysfunction depends on the culprit artery. With involvement

of the right coronary artery proximal to the marginal branches (in a right-dominant coronary system), segmental hypokinesia is seen in the lateral and inferior wall. With involvement of the posterior descending artery, hypokinesia is usually limited to the inferior segments. In anterior myocardial infarction involving the left anterior descending coronary artery, RV hypokinesia is usually limited to the anterior wall.

In patients with arrhythmogenic RV dysplasia who meet the Task Force diagnostic criteria for this condition, Yoerger and colleagues⁷³ showed that RV enlargement and decreased RV function occur frequently. Regional wall-motion abnormalities occurred in 79% of probands; the apex (72%) and the anterior wall (70%) were the most common sites of these abnormalities.⁷³

RV Diastolic Parameters and Estimation of Preload

Because RV diastole is composed of many phases, it cannot be described by a single parameter. The different parameters used in the study of RV diastole include (1) RV end-diastolic or right atrial pressures, (2) RV volume, (3) RV filling profiles, (4) relaxation-phase indices (dP/dt minimum and the time constant of isovolumic pressure decay), and (5) passive chamber characteristics such as compliance (Table 4).^{11,25,48,74–77}

Right atrial pressure or RV end-diastolic pressure can be measured directly during right-heart catheterization or estimated noninvasively by assessing inferior vena cava diameter and collapse index.⁴⁸ The annular tricuspid E/e ratio and annular tissue Doppler relaxation time have also shown moderate correlation with right atrial pressure.⁷⁸ Assessment of RV preload is

Table 4. Selected Indices of RV Function

Index	Normal Values	Clinical Utility-Comment
Diastolic parameters		
Pressures, mm Hg	RAmean: 3 (1–5) ¹¹ RVEDP: 4 (1–7)	High values suggest diastolic dysfunction
Inferior vena cava	≤1.7 cm, CI ≥50% ⁴⁸	Estimates RA pressure: (mm Hg)* IVC ≤1.7 cm, CI ≥50%: 0–5 IVC >1.7 cm, CI ≥50%: 6–10 IVC >1.7 cm, CI <50%: 10–15 IVC >1.7 cm, fixed: ≥15
Diastolic E/A velocity ratio	1.50±0.3 ²⁵	RV diastolic profiles have not been well correlated with chamber compliance or ventricular pressures; E/A >2 and DT <160 ms suggest restrictive physiology
E deceleration time, ms	198±23 ²⁵	
Hepatic vein S/D velocity ratio	>1 in sinus rhythm ⁷⁴ <1 in AF	Reversal of systolic flow seen in severe diastolic dysfunction or severe TR
Diastolic pulmonary flow	Absent	Presence suggests “restrictive” physiology in TOF ⁷⁵
End-diastolic compliance	not well defined	Limited data available in humans
Ventricular interdependence		
Respiratory variation in E velocity	Tricuspid: ≤15% inspiratory ↑ Mitral: ≤10% inspiratory ↓ ⁷⁶	Increased respiratory variations seen in constriction (TΔ ≥40%, MΔ ≥25%) or tamponade (TΔ ≥80%, MΔ ≥40%) ⁷⁶
Valvular function		
Tricuspid regurgitation	<1/4	VC >7 mm and hepatic vein S reversal in severe TR ⁷⁷
Tricuspid valve gradient, mean, mm Hg	<2	Gradient >5 mm Hg and area <1 cm ² in severe TS ⁷⁷
Pulmonary regurgitation	<1/4	RF >40% suggests severe PR ⁷⁷ ; PHT ≤100 ms in moderate-severe PR (TOF)
Pulmonary peak gradient, mm Hg	Maximal gradient <25 (upper limit of normal)	Maximal gradient 50–80 mm Hg suggests moderate PS and peak gradient >80 mm Hg suggests severe PS ⁷⁷

RAmean indicates mean right atrial pressure; RVEDP, RV end-diastolic pressure; IVC, inferior vena cava; CI, collapse index; RA, right atrial; E, rapid filling velocity of the RV; A, end-diastolic ventricular filling corresponding to the atrial contraction; DT, deceleration time; S/D, systolic to diastolic ratio of hepatic vein flow; AF, atrial fibrillation; TR, tricuspid regurgitation; TOF, tetralogy of Fallot; T, tricuspid; M, mitral; VC, venae contracta; TVG, tricuspid valve gradient; TS, tricuspid stenosis; PR, pulmonary regurgitation; RF, regurgitant fraction; PHT, pressure half-time; and PS, pulmonary stenosis.

*Athletes can have a dilated IVC without increased pressure. There exists variability in IVC size thresholds used in the literature.

more challenging. Although RV volume usually represents a reliable index of preload, RV volume may not always reflect sarcomeric length or predict response to fluid therapy.²⁰ Also, although right atrial pressure and RV end-diastolic pressure are often used as surrogates for RV preload, many studies showed that pressure and volume are not linearly related. More recently, in the intensive care setting, dynamic respiratory changes in right atrial pressure and dynamic changes in arterial pulse pressure have been shown to be better markers of fluid responsiveness than catheter-derived RV end-diastolic volume or absolute values of pressures.⁷⁹

RV chamber compliance or stiffness has not been studied extensively in humans owing to the difficulty in obtaining accurate and simultaneous estimation of RV volume. Therefore, correlations between RV filling profiles and chamber characteristics are not well established. In tetralogy of Fallot, however, diastolic pulmonary flow during atrial systole has been described as indicating decreased ventricular compliance or restrictive physiology.⁷⁵ The time constant of isovolumic pressure decay and dP/dt minimum have been shown to have marked load dependence and are not used routinely in the study of ventricular diastology.⁸⁰

Assessment of RV Afterload

Pulmonary vascular resistance is the most commonly used index of RV afterload in clinical practice; however, a more complete understanding of afterload should take into account resistive, capacitive, inertial, and pulse-reflection properties of the pulmonary vasculature, as well as potential outflow or ventricular resistive component.⁹ Models of the pulmonary vasculature that integrate passive and dynamic components of vascular impedance are being actively investigated.

Assessment of Ventricular Interdependence

Assessment of ventricular interdependence is helpful in differentiating restrictive from constrictive physiology, both of which can present with right-sided heart failure. Ventricular interdependence may be clinically assessed by considering (1) the degree of reciprocal respiratory change in ventricular filling profiles, (2) ventricular coupling (in dimension or pressure), or (3) abnormal septal motions. In assessing ventricular interdependence, it is also important to consider the effects of ventricular dysfunction on the pressure-volume relationship and function of the other ventricle.

Strain and Strain Rate Analysis

Strain is defined as the degree of deformation of an object, whereas strain rate represents the speed at which strain occurs.⁸¹ In echocardiography, RV longitudinal strain can be assessed reliably from apical views, whereas radial strain is difficult and is hampered by near-field artifacts and extremely small computational distance. Theoretically, MRI could provide highly reproducible data on RV myocardial deformation not only in the longitudinal and radial directions but also in the circumferential direction. At this moment, however, few data are available on RV MRI strain. In mathematical models and in experimental studies, longitudinal strain appears to correlate best with changes in stroke volume, whereas longitudinal strain rate is more related to local contractile function and appears to be more independent of loading.⁷⁰

Evaluation of RV Dyssynchrony

The study of RV dyssynchrony is in its early stages, but several groups are currently investigating specific ECG (QRS duration) and mechanical criteria of RV dyssynchrony. Echocardiographic indices of dyssynchrony are assessed by measuring time delay in mechanical activity between segments. At this time, areas that can be assessed by tissue Doppler imaging are limited to the septum-RV free wall. MRI could theoretically have the advantage of assessing 3D indices of dyssynchrony.

Cardiac Rhythm and the RV

Cardiac rhythm plays an essential role in RV function. Atrial fibrillation can severely compromise RV function. In addition, ventricular tachycardia can originate from the RV in a variety of disorders, such as arrhythmogenic RV dysplasia, RV myocardial infarction, left bundle-branch block, idiopathic ventricular tachycardia, or after surgical repair of congenital disease.⁸² Although ventricular tachycardia that arises from the RV usually has a left bundle-branch block morphology, most ventricular tachycardia with this morphology arises from a paraseptal LV location.⁸²

Cardiac Markers

Recent studies showed that serum levels of B-type natriuretic peptide may be useful in diagnosing RV failure associated with pulmonary hypertension, congenital heart disease, or pulmonary disease.^{83–85} In pulmonary arterial hypertension, an elevated B-type natriuretic peptide level at baseline (>150 pg/mL) and follow-up (>180 pg/mL) has been associated with worse survival.⁸³ Elevated troponin levels have also been associated with worse outcome in pulmonary embolism and pulmonary hypertension.^{86,87}

Conclusion and Future Directions

A proper understanding of RV physiology requires knowledge of ventricular contractility, preload, and afterload, as well as ventricular interdependence and pericardial constraint. Because of its complex shape and marked load dependence, the study of the RV remains challenging. New and promising noninvasive indices of contractility include tissue Doppler IVA and RV myocardial performance index. In the future, advances in cardiac imaging are expected in the

field of 3D echocardiography, strain imaging, diffusion tensor MRI imaging, and tissue characterization. These could lead to the discovery of new noninvasive indices of contractility and chamber compliance and to a better understanding of ventricular remodeling.

Acknowledgments

We gratefully acknowledge the insightful comments of Patrick Fisher, DO, PhD, André Denault, MD, and Michel White, MD, as well as the assistance of Thu Anh Vu, BSc, and Victoria Joven, BSc. We are also grateful for the educational support of the Vera Moulton Wall Center.

Disclosures

None.

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KEY WORDS: imaging ■ heart failure ■ ventricles ■ aging ■ contractility ■ echocardiography ■ physiology

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Circulation. 2008;117:1436-1448

doi: 10.1161/CIRCULATIONAHA.107.653576

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

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