Right heart evaluation and pulmonary hypertension

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The right ventricle (RV) is significantly affected in conditions characterized by increased RV after load of both cardiac and pulmonary etiology. Right ventricular ejection fraction is an independent predictor of survival in many diseases, and it has an increasingly recognized critical role in the setting of abnormal left ventricle (LV) systolic function (1-6). The complex 3D structure of the RV and the difficulty in accurately measuring RV volumes and mass by conventional imaging modalities has resulted in much less being known about the RV than the LV. The RV is of different embryologic origin than the LV and performs a very different physiologic role throughout life, despite being side-by-side with the LV in the heart.

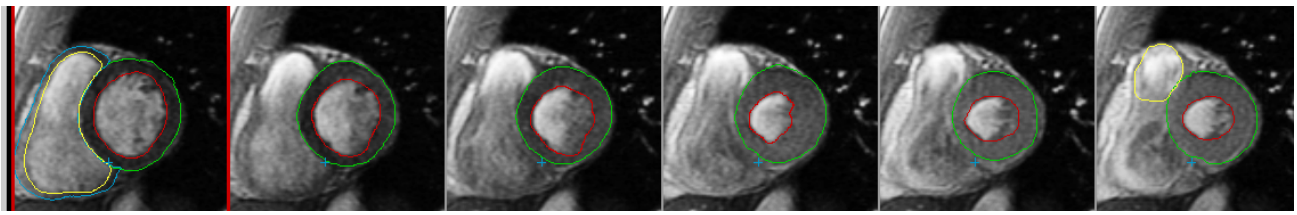
Quantification of the Right Ventricle

General considerations: Acquisitions need to cover the base to the apex. Acquisitions for quantification may either be based on a either a) a stack of transaxial images or b) a stack of short axis images in combination with 2/ 4 chamber views of the left ventricle. The latter (short axis images) are usually more convenient since the L V analysis is usually performed in conjunction with the RV.

Approximately 30 images should be acquired during the cardiac cycle using retrospective reconstruction. The general function of the LV and RV should be studied, and interpretation of both chambers and extracardiac structures should be assessed for the presence of intra- or extra-cardiac shunt that may influence the quantification. The temporal resolution of the cine sequence should be <= 50 msec. Slice thickness should be 6-8 mm or less. Slice gap should be 2-4 mm or less.

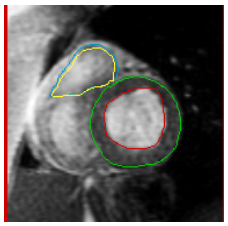
SSFP sequences are generally preferred compared to FGRE analysis. For efficiency, the observer may contour only the end systolic and end diastolic image. The RV end diastolic image is taken as that with the largest volume, and the RV end systolic image is the visually smallest volume. The discussion below will focus on the analysis of short axis images for RV volumes and mass.

Identification of the RA/ RV boundary: Due to shortening of the RV from the base towards the apex, the RA is seen on fixed image planes at the base during systole. Near end-systole, the RA is identified since it expands outward, as compared to the RV. The RV demonstrates continuous contraction inward. Note that the pulmonary outflow tract up to the pulmonary valve plane is considered part of the RV volume. In the short axis orientation, the pulmonary outflow tract is



"separate" from the RV volume due to shortening of the base towards the apex. It is extremely helpful to have completed LV volumes prior to contouring the RV.

Figure 1 depicts the sequential progression of the short axis cine images from end-diastole to end-systole. Near end-systole, the right atrium appears from within the lower part of the earlier right ventricle and expands outward as compared to the left ventricle. The right ventricle demonstrates continuous contraction inward. The opposing trend in movement during the cardiac cycle assists in demarcating the right atrium from the right ventricle. The RV also shows a relatively thicker wall compared to the RA.



Note that the pulmonary outflow tract may take-on oblique or irregular shapes (right image) rather than a round appearance in the short axis view.

Other points: In general, the RV is not contoured on slices where the LV is not also visualized and contoured. Exceptions to this are present in patients with congenital heart disease. Trabeculation of the RV is typically ignored and a smooth endocardial border is usually drawn. The reason for this is the improved reader reproducibility when a smooth endocardial border is used. The septum is considered to be the terminus of the free-wall RV contour. Total volumes are taken as the sum of volumes on individual 2d slices, accounting for the interslice gap and the slice thickness (Simpson's rule or summation of disks method).

RV diameter. RV diameter should be measured at a level approximately 1-2 cm below the triscuspid valve on a 4 chamber view.

Clinical factors affecting the right ventricle:

Cardiovascular risk factors are associated with changes in the RV mass, volumes and ejection fraction detected with cardiac MRI. In particular, RV mass is approximately 20% lower in individuals at age 80 vs age 40.

Additionally, smaller adjusted RV end diastolic volumes are associated with higher systolic blood pressure and current smoking even after adjusting for LV EDV. References values for RV structure and function are given in the table below.

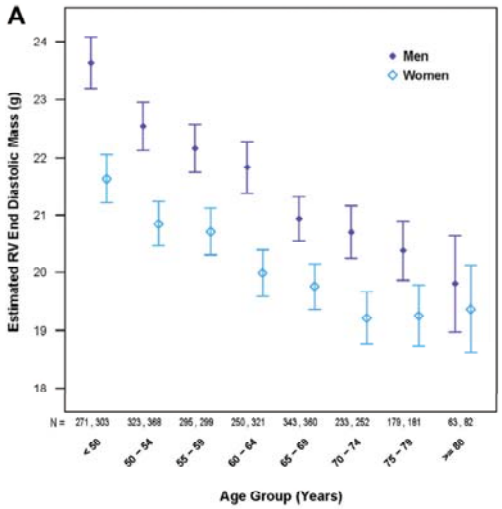


Figure 1. The relationship between age and RV mass in normal subjects. From Kawut et al, Circulation 2011:123

<u>Normal Right ventricle volumes and systolic function determined by MRI</u>

Men

STUDY	End-diastolic volume (ml)	End-systolic volume (ml)	Stroke Volume (ml)	Ejection fraction %	Mass (gm)
Prakken et al	125.5	61.5	-	51.3	12.1
Tandri et al	142.4	54.3	88.3	62	-
MESA 2000	142.7	47.7	95.0	66.7	23.3
Alfakih et al	TGE 160.4	67.8	92.7	57.6	-
	SSFP 176.5	79.3	97.8	55.1	
Maceira et al	163	57	106	66	66
Sandstede	131	53	-	60	52
Lorenz et al	157	63	95	60	50

Women

STUDY	End-diastolic volume (ml)	End-systolic volume (ml)	Stroke Volume (ml)	Ejection fraction (%)	RV Mass (gm)
Prakken et al	105	49	-	53.7	10.5
Tandri et al	110.2	35.1	75	69	-
MESA 2000	109.7	31.8	77.9	71.3	19.3
Alfakih et al	TGE 117.4	44.5	72.9	61.8	-
	SSFP 130.6	52.3	78.3	59.8	
Maceira et al	126	43	83	66	48
Sandstede	100	33	-	69	39
Lorenz et al	106	40	66	63	40

Prototype diseases of the RV:

Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C) is one of the most arrhythmogenic forms of inherited cardiomyopathy and a frequent cause of sudden death in the young. Affected individuals typically present between the second and fourth decade of life with arrhythmias coming from the right ventricle. Pathogenic mutations in genes encoding the cardiac desmosome can be found in approximately 60% of index patients, leading to our current perception of ARVD/C as a

desmosomal disease. Although ARVD/C is known to preferentially affect the right ventricle, early and/or predominant left ventricular involvement is increasingly recognized. Diagnosis is made by combining multiple sources of diagnostic information as prescribed by the "Task Force" criteria. Abnormalities in cardiac structure and function are present in the majority of patients at the time of their clinical presentation. CMR is an ideal technique in ARVD/C workup, as it provides comprehensive information on cardiac morphology, function, and tissue characterization in a single investigation. Prevention of sudden cardiac death using implantable cardioverter-defibrillators is the most important management consideration.

Table . Revised 2010 Task Force Criteria for ARVD/C*

1	**Global or regional dysfunction and structural alterations**		
	Major		
		2D Echo Criteria	
			Regional RV akinesia, dyskinesia, or aneurysm AND 1 of the following measured at end diastole: - PLAX RVOT ≥ 32 mm (PLAX/BSA ≥ 19 mm/m^2), or - PSAX RVOT ≥ 36 mm (PSAX/BSA ≥ 21 mm/m^2), or - Fractional area change ≤ 33%
		CMR criteria	
			Regional RV akinesia or dyskinesia or dyssynchronous RV contraction AND 1 of the following: RV EDV/BSA ≥ 110 mL/m^2 (male) or ≥ 100 mL/m^2 (female) RV ejection fraction ≤ 40%
		RV angiography criteria	
			Regional RV akinesia, dyskinesia, or aneurysm
	Minor		
		2D Echo Criteria	
			Regional RV akinesia or dyskinesia or dyssynchronous RV contraction AND 1 of the following measured at end diastole: - PLAX RVOT ≥29 to <32 mm (PLAX/BSA ≥16 to <19 mm/m^2), or - PSAX RVOT ≥32 to <36 mm (PSAX/BSA ≥18 to <21 mm/m^2), or - Fractional area change > 33% ≤ 40%
		CMR criteria	
			Regional RV akinesia or dyskinesia or dyssynchronous RV contraction AND 1 of the following - RV EDV/BSA ≥110 to 110 mL/m^2 (male) or ≥90 to 100mL/m^2 (female) - RV ejection fraction >40 to ≤ 45%
2	**Tissue characterization of wall**		
	Major		
		Residual myocytes < 60% by morphometric analysis (or < 50% if estimated), with fibrous replacement of the RV free wall myocardium in ≥1 sample, with or without fatty	

replacement of tissue on endomyocardial biopsy

Minor

Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated), with fibrous replacement of the RV free wall myocardium in ≥1 sample with or without fatty replacement of tissue on endomyocardial biopsy

3 **Repolarization abnormalities**

Major

Inverted T waves in right precordial leads (V1, V2, and V3) or beyond in individuals >14 yrs of age (in the absence of complete RBBB QRS ≥ 120 ms)

Minor

Inverted T waves in V1 and V2 in individuals >14 yrs of age (in the absence of complete RBBB) or in V4, V5, and V6

Inverted T waves in leads V1, V2, V3, and V4 in individuals >14 years of age in the presence of a complete RBBB

4 **Depolarization / conduction abnormalities**

Major

Epsilon wave (reproducible low-amplitude signals between end of QRS complex to onset of T wave) in the right precordial leads (V1 - V3)

Minor

Late potentials by SAECG in ≥1 of 3 parameters in the absence of a QRSd of ≥110 msec on standard ECG:

- Filtered QRS duration (fQRS) ≥ 114 msec
- Duration of terminal QRS < 40 microV ≥ 38 ms
- Root-mean-square voltage of terminal 40 ms ≤20 micro V

Terminal activation duration ≥55 ms measured from the nadir of the end of all depolarization deflections including R', in V1, V2, or V3 in absence of complete RBBB

5 **Arrhythmias**

Major

Nonsustained or sustained VT of LBBB morphology with superior axis

Minor

Nonsustained or sustained VT of RVOT configuration, LBBB morphology with inferior axis or of unknown axis

> 500 PVCs per 24 hours on Holter monitoring

6 **Family History**

Major

ARVD/C in first degree relative who meets Task Force Criteria

ARVD/C confirmed pathologically at autopsy or surgery in first degree relative

Identification of pathogenic mutation categorized as associated or probably associated with ARVD/C in the patient under evaluation

Minor

	History of ARVD/C in first degree relative in whom it is not possible to determine whether the family member meets Task Force Criteria Premature sudden death (<35 years of age) due to suspected ARVD/C in a first degree relative ARVD/C confirmed pathologically or by current Task Force Criteria in second-degree relative

* adapted from reference #20.

Abbreviations: ARVD/C: Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy, BSA: body surface area, CMR: cardiac magnetic resonance, ECG: electrocardiogram, EDV: end-diastolic volume, LBBB: left bundle branch block, PLAX: parasternal long axis, PSAX: parasternal short axis, RV: right ventricular, RVOT: right ventricular outflow tract, SAECG: signal-averaged electrocardiogram, VT: ventricular tachycardia.

Pulmonary hypertension (PH) is a complex chronic disorder of the pulmonary circulation that encompasses a wide variety of etiologies. It is diagnostically and therapeutically challenging and usually carries a poor prognosis (7, 8). Elevated pressure and resistance in the pulmonary vascular bed lead to progressive right ventricular structural and functional remodeling that result in right heart failure and ultimately death. While definite PH diagnosis requires invasive measurements through right-heart catheterization (RHC), close repeated right ventricular (RV) functional and structural monitoring is substantial as a major determinant of symptoms and survival (9, 10).

Echocardiography is the most widely available tool for PH patients follow up. However, the technique carries several limitations that could impair accurate evaluation of RV performance (e.g. operator dependence , patient dependent echo window) (11). Cardiac magnetic resonance (CMR) imaging is considered a standard of reference for the anatomical and functional assessment of the right ventricle. It is an accurate and reproducible tool for measurement of RV global function (12-14). MR myocardial tagging techniques, including conventional tagging and Fast-SENC, provide a detailed analysis of regional myocardial deformation (15-17). Furthermore, using delayed contrast enhancement (DE) imaging, scar burden can be accurately quantified.

Using CMR, different patterns of DE have been described in association with various myocardial ischemic and non ischemic pathologies (18-20). A number of these pathologies have demonstrated altered regional deformation at the scar sites (21, 22). Recently, the presence of DE in association with PH has been typically described in the LV septum at the RV insertion sites.

Recent MR studies have demonstrated the role of LV septal bowing caused by overloaded RVon the LV filling thus reducing LV performance. Furthermore, Vonk-Noordegraaf et al used MR tagging to reveal interventricular mechanical asynchrony in PAH patients caused by prolonged RV systolic contraction compared to LV. Using DCE, areas of scarring were detected at the RV septal insertions often extending into the interventricular septum correlating with RV functional indices. Noninvasive functional and anatomic assessment of pulmonary circulation can be achieved using MRA and phase contrast techniques. Recently, a study by Sanz et al showed good correlation of phase contrast-acquired indices

including pulmonary artery area, flow velocity, and arterial strain with mean pulmonary artery pressure and pulmonary vascular resistive index acquired by catheterization. In addition, ultrafast MR imaging techniques using 3-dimensional parallel imaging tracking a small dose intravenous bolus allow qualitative and quantitative assessment of pulmonary perfusion thus providing a radiation-free diagnostic tool compared with nuclear imaging. Thus, CMR can provide a noninvasive 1-stop assessment of cardiopulmonary unit in PAH.

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