Evaluation of the relationship between right ventricle mechanics and pulmonary artery vessel and flow dynamics in pulmonary artery hypertension by MRI

El-Sayed H Ibrahim[1], and Abubakr A Bajwa[2]

[1]*Department of Radiology, University of Florida, Jacksonville, FL, United States,* [2]*Department of Medicine, University of Florida, Jacksonville, FL, United States*

Introduction: Pulmonary artery (PA) hypertension (PAH) is characterized by elevated PA pressure (PAP), which increases the right ventricular (RV) afterload. Although PAP measurement is the gold standard for evaluating PAH, it is actually the RV condition that predicts patient survival. Despite the fact that both RV and PA are affected in PAH, there is insufficient data in literature about the relationship between these two entities in PAH. The goal of this study is to investigate the relationships between different RV-related and PA-related MRI-derived parameters in an attempt to better understand the nature of RV-PA coupling in PAH.

Methods: 25 PAH patients, confirmed by catheterization, were scanned on a 3.0-Tesla Siemens scanner. A comprehensive MRI exam was developed that lasted for 30 minutes and included: 1) Cine images covering the heart; 2) Strain-encoding (SENC) images; 3) Flow images across the main PA (MPA); 4) Flow images through the tricuspid valve. The cine images were processed to calculate: RV ejection fraction (RVEF), LVEF, ventricular volume index (VVI), ventricular mass index (VMI), RA size (= RA area on a 4-CH slice at end systole), MPA diameter (at diastole), and the newly-introduced lunar index (LI) (Fig.1). Peak RV longitudinal myocardial strain and early-diastolic strain rate were calculated from SENC images [1]. RV early-to-atrial (E/A) filling ratio was calculated from tricuspid flow images. The following parameters were calculated from PA flow images: PA pulse wave velocity (PWV) using the flow-area method [2], PA distensibility, acceleration-to-ejection (a/e) time, flow rate (during acceleration phase), and mean velocity. Furthermore, the following standard measurements in PAH were obtained: mean PAP (mPAP), pulmonary vascular resistance (PVR), tricuspid jet velocity (Tri JV), 6 minute walk (6MW), and brain natriuretic peptide (BNP). The parameters were divided into 3 groups: MRI RV parameters (RVEF, VVI, VMI, LI, RV E/A, strain, strain rate, LVEF, RA size); MRI PA parameters (MPA diameter, PWV, distensibility, a/e time, flow rate, mean velocity, PA diameter); and non-MRI measurements (mPAP, PVR, Tri JV, 6MW, BNP). Three types of statistical analysis were conducted: 1) Correlation analysis between all parameters to measure within- and across-group correlations; 2) Regression analysis to identify significant parameters, investigate within-group parameter redundancy, and study the relationship between MRI parameters and PAP; 3) Principal component analysis (PCA) to investigate data reduction in different parameter groups and identify insignificant parameters. Linear multiple regression analysis was conducted on RV and PA parameters using backward deletion modeling (mPAP is dependent variable). Regression's collinearity statistic 'tolerance' (proportion of variable's variance not accounted for by others), the model's adjusted multiple correlation coefficient squared (R^2), and ANOVA statistic F (ratio of regression to residual) were measured. Parameters' communalities were measured in PCA.

Results: Fig.2 shows color-coded correlation map between all parameters. In regression analysis in RV group, the following parameters were eliminated in this order: RV E/A, RA size, LVEF, RVEF, strain rate, VVI. The resulting model consisted of: lunar index (p (significance) = 0.001, β (standardized regression coefficient)=-0.41, tolerance = 0.48), VMI (p=0.012, β=-0.32, tolerance=0.37), strain (p=0.012, β=0.32, tolerance=0.36). The model's R^2=0.88, ANOVA statistic F=59.6, model significance < 0.005. In regression analysis on PA group, the following parameters were eliminated in this order: distensibility, a/e time, MPA diameter. The resulting model consisted of: PWV (p=0.003, β=-0.45, tolerance=0.42), mean velocity (p=0.007, β=0.36, tolerance=0.34), flow rate (p=0.06, β=0.23, tolerance=0.37). The model's R^2=0.88, ANOVA F = 60.4, model significance < 0.005. Finally, regression analysis was conducted on both PA and RV parameters (as one group) for estimating mPAP. The following parameters were eliminated in this order: LVEF, velocity mean, distensibility, RA size, a/e time, RV E/A, strain rate, VMI, LI, PWV. The resulting model consisted of: RVEF (p=0.004, β=-0.32, tolerance=0.38), MPA diameter (p=0.001, β=0.23, tolerance=0.43), flow rate (p=0.002, β=0.25, tolerance=0.35), VVI (p=0.015, β=-0.19, tolerance=0.33), strain (p=0.04, β=-0.16, tolerance=0.31). The model's R^2=0.96, ANOVA F=115, model significance < 0.005. PCA analysis was conducted on RV group. It resulted in two components (variances = 56.88% and 14.88%). Parameters' communalities were: RVEF=0.789, VVI=0.77, VMI=0.804, LI=0.852, RV E/A=0.723, strain=0.679, strain rate=0.638, LVEF=0.485, RA size=0.521. Components were: c1 = [0.888, -0.813, -0.897, 0.919, 0.039, 0.805, 0.796, -0.19, -0.074] and c2 = [-0.024, 0.33, -0.01, -0.091, 0.85, -0.179, -0.064, 0.67, -0.98] (factors in same order as communalities). PCA factor analysis was conducted on parameters in PA group. It resulted in one component (variance = 76.83%). Parameters' communalities were: PWV=0.811, distensibility=0.777, a/e time=0.736, flow rate=0.75, mean velocity=0.849, PA diameter=0.749. Component was: c1=[0.9, -0.881, -0.858, 0.866, 0.921, 0.865]. Finally, PCA analysis was conducted on the non-MRI measurements group. It resulted in two components (variances = 61.77% and 20.21%). Parameters' communalities were: mPAP=0.954, PVR=0.926, Tri JV=0.823, 6MW=0.668, BNP=0.722. Components were: c1 = [0.975, 0.962, 0.754, -0.326, 0.267] and c2 = [-0.056, 0.001, 0.31, 0.75, 0.807].

Discussion: The results showed different degrees of correlations between analyzed parameters (Fig.2). Results from correlation analysis are in agreement with regression and PCA analyses. Strongly correlated within-group parameters reflected data redundancy, which can be excluded from analysis without much affecting the results. Data redundancy comes in agreement with basic understanding of the nature of these parameters and PAH development process. Weakly correlated parameters reflected the parameters' non-specificity or insignificance within its group. These results come in agreement with our understanding about the parameters' roles in PAH. For example, although E/A<1 reflects diastolic dysfunction, E/A>1 does not necessarily mean normal function; it occurs also in pseudonormal and restrictive cases, which necessitates its interpretation with other parameters in consideration. In RV-PA analysis, VVI, VMI, LI, strain and strain rate in the RV group showed strong correlations with all PA parameters; RVEF showed moderate correlation with all PA parameters; and RV E/A, LVEF, and RA size showed weak correlations with PA parameters. The strongest correlation occurred between VMI and flow rate. From redundancy analysis, the significant parameters could be reduced to: RV group (LI, VMI, strain) and PA group (PWV, mean velocity, flow rate). In conclusion, RV and PA are coupled and their functions are negatively affected in PAH. Therefore, both entities should be evaluated and interpreted together in PAH for more understanding of the disease pathophysiology and better diagnosis and treatment.

References: [1] Youssef et al, JCMR 2008; 10:1-10. [2] Peng et al, JMRI 2006; 24:1303-1310.

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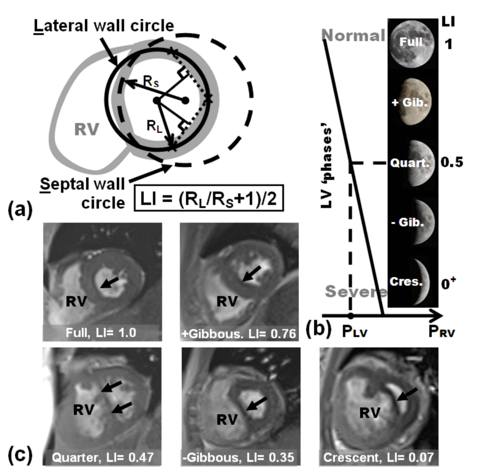

Figure 1. Lunar index (LI) for measuring septal wall curvature. (a) Three points marked on the lateral wall at early diastole to determine the circle that passes through them (and its radius RL). Same process is repeated for septal wall to determine Rs, which is positive and negative for convex and concave curvatures (seen from the RV). LI ranges from +1 for (normal) full-circle LV to almost 0 for (severe) crescent-like LV. (b) Similarity with moon phases. (c) Images of patients with different conditions.

#	Parameter	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	PWV	1.00																			
2	disten	-0.82	1.00																		
3	a/e t	-0.69	0.70	1.00																	
4	flow r	0.77	-0.64	-0.78	1.00																
5	vel_m	-0.77	0.79	0.85	-0.75	1.00															
6	PA dim	0.78	-0.70	-0.67	0.66	-0.82	1.00														
7	RVEF	-0.57	0.55	0.54	-0.73	0.52	-0.50	1.00													
8	VVI	0.67	-0.73	-0.72	0.70	-0.73	0.64	-0.70	1.00												
9	VMI	0.61	-0.46	-0.62	0.82	-0.63	0.53	-0.86	0.63	1.00											
10	LI	-0.71	0.74	0.61	-0.73	0.69	-0.72	0.70	-0.85	-0.62	1.00										
11	RV E/A	0.16	-0.16	-0.15	0.04	-0.14	-0.03	0.02	0.24	-0.07	-0.28	1.00									
12	strain	-0.67	0.66	0.63	-0.67	0.61	-0.70	0.69	-0.79	-0.71	0.76	-0.13	1.00								
13	strain r	-0.65	0.68	0.60	-0.72	0.60	-0.43	0.63	-0.71	-0.70	0.63	-0.04	0.54	1.00							
14	LVEF	0.32	-0.33	-0.39	0.34	-0.53	0.44	-0.32	0.29	0.26	-0.37	0.21	-0.19	-0.19	1.00						
15	RA Sz	0.19	-0.21	-0.03	0.31	-0.25	0.24	-0.43	0.37	0.28	-0.44	-0.09	-0.16	-0.23	0.15	1.00					
16	mPAP	0.82	-0.77	-0.76	0.87	-0.79	0.79	-0.85	0.87	0.84	-0.88	0.10	-0.86	-0.70	0.35	0.35	1.00				
17	PVR	0.73	-0.70	-0.69	0.80	-0.70	0.70	-0.89	0.84	0.85	-0.84	0.16	-0.85	-0.63	0.30	0.37	0.97	1.00			
18	Trc j.v.	0.53	-0.43	-0.57	0.69	-0.55	0.60	-0.49	0.60	0.67	-0.61	0.11	-0.69	-0.49	0.29	0.14	0.73	0.71	1.00		
19	6MW	-0.36	0.27	0.13	-0.15	0.34	-0.48	0.21	-0.42	-0.07	0.38	0.05	0.43	0.18	-0.08	-0.14	-0.37	-0.29	-0.28	1.00	
20	BNP	0.16	0.01	-0.21	0.42	0.11	0.10	-0.06	0.07	0.39	-0.03	-0.25	-0.15	-0.09	-0.44	0.08	0.18	0.20	0.20	0.20	1.00
		PWV	disten	a/e t	flow r	vel_m	PA dim	RVEF	VVI	VMI	LI	RV E/A	strain	str. r	LVEF	RA Sz	mPAP	PVR	Trc j.v.	6MW	BNP

Abbreviations: 6MW = six minutes walk; β = standardized regression coefficients; a/e t = acceleration to ejection time; BNP = brain natriuretic peptide ; RVEF = RV ejection fraction (EF); disten = distensibility; flow r = flow rate ; LVEF = LV EF; Meas = measurements ; mPAP = mean PA pressure; PA dim = main PA diameter ; PVR = pulmonary vascular resistance; PWV = pulse wave velocity; r = correlation coefficient; RA Sz= right atrium area (# pixels) on a 4-ch view at end-systole; RV E/A = RV early to atrial filling ratio; STR = strong; strain = RV peak longitudinal myocardial strain ; strain r = early-diastolic strain rate; Trc j.v. = tricuspid jet velocity; vel_m = mean velocity; LI = lunar index (septal curvature ratio); VMI = ventricular mass index; VVI = ventricular volume index; WK = weak.

Organization (Blocks)

	PA	RV	Meas
PA	[1]		
RV	[4]	[2]	
Meas	[5]	[6]	[3]

Correlation

WK	0.0 ≤ |r| < 0.2
	0.2 ≤ |r| < 0.4
	0.4 ≤ |r| < 0.6
	0.6 ≤ |r| < 0.8
STR	0.8 ≤ |r| < 1.0

Regression (mPAP)

WK	0.0 ≤ |β| < 0.1
	0.1 ≤ |β| < 0.2
	0.2 ≤ |β| < 0.3
	0.3 ≤ |β| < 0.4
STR	0.4 ≤ |β| < 0.5

pars redund.

Figure 2. Color-coded correlation, regression, and data reduction map between CMR pulmonary artery (PA) parameters (red), CMR right ventricular (RV) parameters (yellow), and non-CMR measurements (blue) in PAH. The map is divided into blocks of different parameter groups (see organization key on top-right). Correlations coefficient cells are color coded according to the scale on the right. The parameter names (bottom) are color coded based on regression coefficients as shown on the scale on the right. Within-group redundant parameters are given the same color on the left. mPAP is the dependent variable in regression and data reduction analyses.