The right heart in HFpEF
Insights from a cardiac magnetic resonance study

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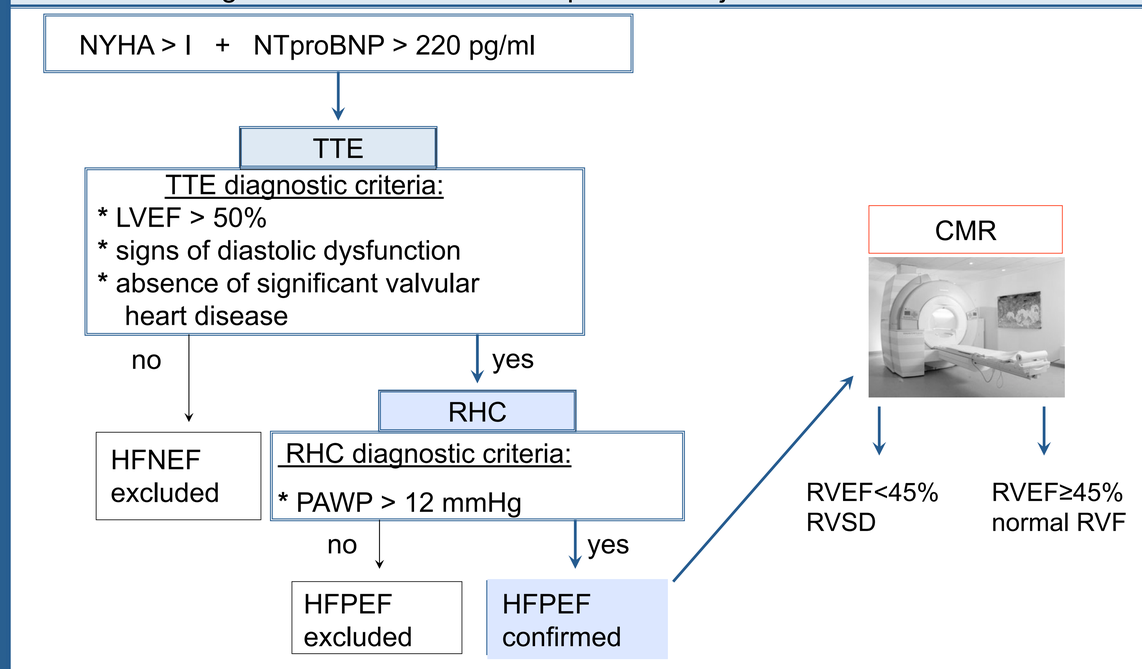
Background:

Cardiovascular magnetic resonance imaging (CMR) is the gold-standard technique for the assessment of right ventricular function. Recent data indicate that right ventricular ejection fraction (RVEF) <45% by CMR is a strong predictor of outcome in patients with dilated cardiomyopathy[1]. However, the prognostic significance of RVEF in heart failure with preserved ejection fraction (HFpEF) is unknown.

FIGURE 1. Diagnosis of heart failure with preserved ejection fraction



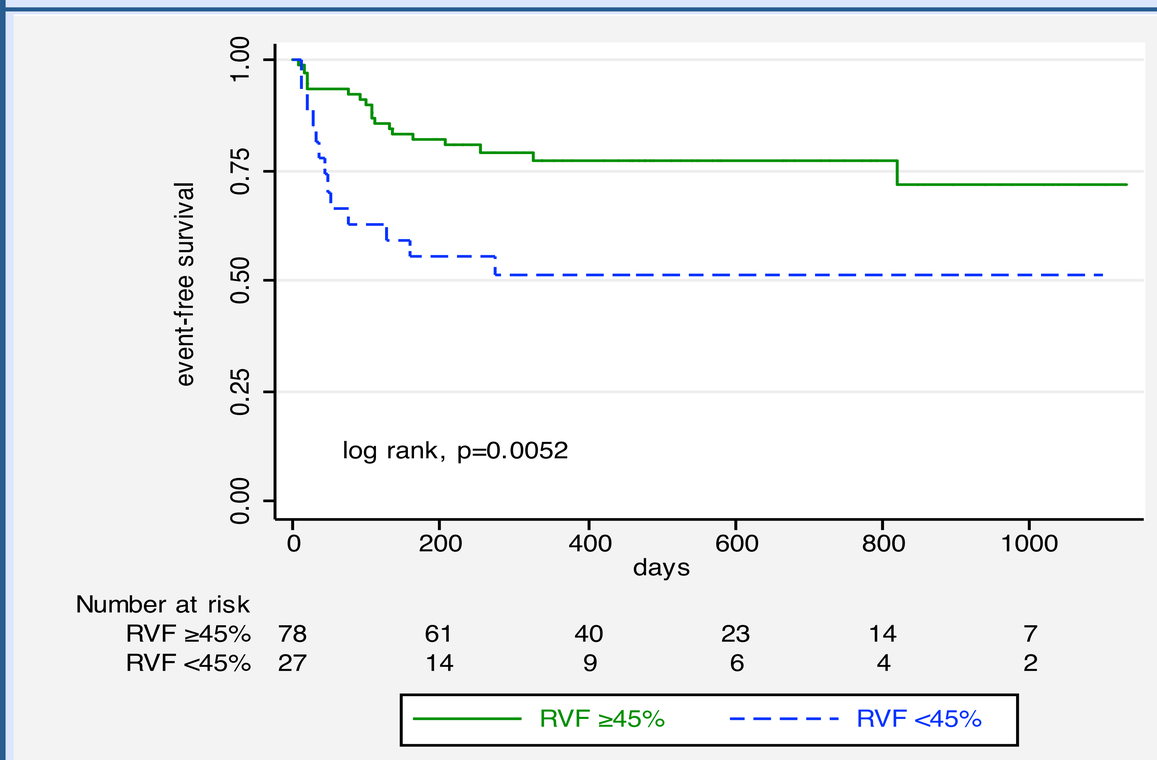
NYHA, New York Heart Association; NT-proBNP, N-terminal brain natriuretic peptide; TTE, transthoracic echocardiogram; LVEF, left ventricular ejection fraction; RHC, right heart catheter; PAWP, pulmonary artery wedge pressure. CMR: cardiovascular magnetic resonance imaging, RVEF: right ventricular ejection fraction,

TABLE 2. Univariate and multivariate cox regression

	univariate analysis				multivariate analysis			
variable	Haz. Ratio	p -value	[95% CI]		Haz. Ratio	p -value	[95% CI]	
NYHA functional class	5.33	0.01	1.62	17.55				
RSVD	2.66	0.01	1.30	5.44	4.85	0.00	1.97	11.92
Diabete melitus	3.86	0.00	1.81	8.24	3.99	0.00	1.65	9.65
Body mass index	1.02	0.52	0.96	1.08				
Age	1.03	0.15	0.99	1.07				
6- minute walk distance, m	0.99	0.00	0.99	1.00				
Systolic blood pressure, mmHg	0.99	0.38	0.97	1.01				
Diastolic blood pressure, mmHg	1.00	0.78	0.97	1.02				
Heart rate, bpm	0.99	0.38	0.96	1.02				
sPAP, mmHg,PAP	1.04	0.00	1.03	1.06				
mPAP	1.08	0.00	1.04	1.12				

RSVD: right ventricular systolic dysfunction, sPAP: sytolic pulmonary arterial pressure, mPAP: mean pulmonary arterial pressure, CI: confidence interval

Figure 2. Kaplan-Meier analysis. Patients were stratified according the presence of right ventricular systolic dysfunction; RVF indicates right ventricular function.



Methods:

Between December 2010 and September 2013 105 HFpEF patients were prospectively enrolled. At baseline, all patients underwent CMR imaging in addition to invasive and non-invasive testing. Right ventricular systolic dysfunction (RVSD) was defined as RV ejection fraction <45% (Figure 1). Endpoints were defined as hospitalization for heart failure and/or death for cardiac reason.

TABLE 1. Baseline characteristics

	normal RVF		reduced RVF		all patients		p-value
Number of patients (%)	78	(74.3)	27	(25.7)	105		
Age	69.88±	8.90	71.81±	10.44	70.38±	9.31	0.36
Male gender, n (%)	28.21	(22)	8	(30)	30	(29)	0.89
History of AF, n (%)	52.56	(41)	20	(74)	61	(58)	0.05
Diabtes mellitus, n (%)	41.03	(11)	11	(41)	43	(41)	0.98
Smoking, n (%)	34.62	(27)	11	(41)	38	(36)	0.57
CAD, n (%)	17.95	(14)	7	(26)	21	(20)	0.38
Hypertension, n (%)	96.15	(75)	27	100	102	(97)	0.31
BMI	30.35±	6.14	29.51±	6.10	30.13±	6.11	
Heart rate, bpm	69.04±	11.27	76.07±	18.54	70.87±	13.79	
Blood pressure, mmHg							
systolic	139.83±	19.78	135.84±	20.83	138.79±	20.03	0.37
diastolic	78.97±	12.82	79.67±	14.42	79.15±	13.18	0.81
NYHA functional class							0.02
I	0	0.00	0	0.00	0	0.00	
II	28	35.90	5	18.52	33	31.43	
III	48	61.54	18	66.67	66	62.86	
IV	2	2.56	4	14.81	6	5.71	
6 min walking test, meters	341.80±	119.62	290.23±	119.85	328.52±	121.21	0.060
CMR data:							
LV-end diastolic diameter, mm	47.27±	5.13	47.30±	7.18	47.28±	5.69	0.99
LV-end diastlic volume, mL	122.46±	33.33	136.85±	69.82	126.16±	45.62	0.16
LV-end systolic volume, mL	79.05±	23.30	70.70±	39.47	76.88±	28.41	0.19
LV mass	111.98±	34.55	117.4±	40.33	113.41±	36.01	0.51
LV ejection fraction, %	66.25±	9.99	54.63±	10.97	63.20±	11.42	0.00
RV-end diastolic diameter	38.55±	6.54	43.56±	8.95	39.85±	7.53	0.00
Interventricuar septum, mm	11.18±	2.16	11.74±	2.22	11.33±	2.18	0.25
Left atrial diameter, mm	64.40±	8.82	66.19±	9.52	64.87±	8.99	0.38
Left atrial area, cm²	30.60±	8.56	32.79±	12.24	31.15±	9.59	0.32
Right atrial diamter, mm	64.34±	8.29	66.44±	9.89	64.89±	8.73	0.28
Right atrial area, cm²	28.24±	9.01	30.44±	9.18	28.80±	9.06	0.30
RV-ejection fraction, %	56.47±	8.15	38.44±	5.03	51.84±	10.87	0.00
RV-end diastolic volume, mL	153.68±	124.85	178.96±	93.92	160.00±	117.96	0.35
RV-stroke volume, mL	80.43±	23.45	75.15±	44.88	79.10±	30.14	0.44

LV: left ventricle, RV: right ventricle

Results:

Patients were followed for 434 ± 325 days, during which 31 had a cardiac event (hospitalization for heart failure and/or death for cardiac reason).

RVSD was present in 27 (25.71%) patients.

By univariate Cox analysis RVSD (p=0.007), NYHA functional class (p=0.006), 6-minute-walking-distance (p<0.001), diabetes (p<0.001), and invasively measured systolic (p<0.001) and mean pulmonary artery pressures (p<0.001) were significantly associated the primary endpoint (Table 2).

By multivariable analysis only RVSD (HR 4.852, CI 1.97 - 11.92, p=0.001) and diabetes (HR 3.99, CI 1.65 - 9.65 p= 0.002) remained significant predictors of cardiac events (Table 2).

In addition, patients with RVSD had a significantly higher resting heart rate (p= 0.022), more advanced NYHA functional class (p= 0.016) and shorter 6-minute-walking-distance (t-test p= 0.016).

By Kaplan Meier analysis, outcome was significantly worse in patients with RVSD (log rank, p=0.0052), Figure 2.

Conclusion:

Although HFpEF is considered a disease of the left ventricle, respective LV functional parameters are not related with outcome. In contrast, RVSD is significantly associated with clinical status and prognosis of HFpEF patients. Assessment of RVSD by CMR seems important for risk-stratification of these patients.

1 Gulati, A. *et al.* The prevalence and prognostic significance of right ventricular systolic dysfunction in nonischemic dilated cardiomyopathy. *Circulation* **128,** 1623–1633 (2013).