



**VŠEOBECNÁ FAKULTNÍ  
NEMOCNICE V PRAZE**



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## **Prognostic Usefulness of Noninvasively Assessed Right Ventricular-Pulmonary Artery Coupling in Patients with Recently Diagnosed Unexplained LV Systolic Dysfunction**

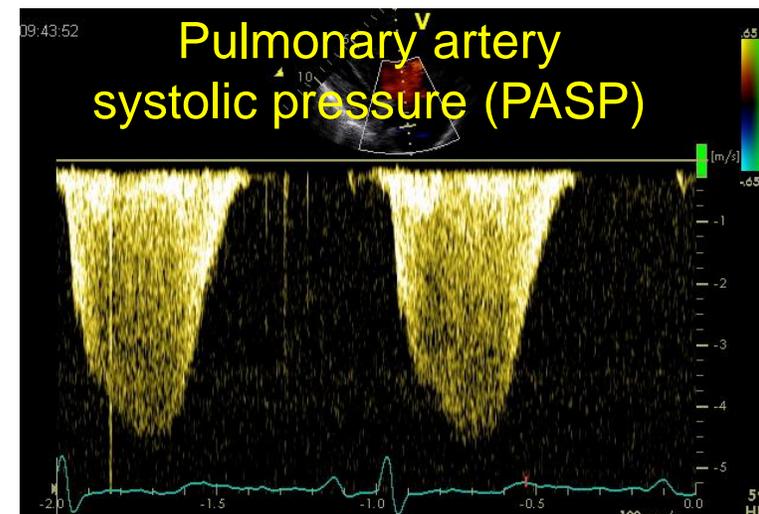
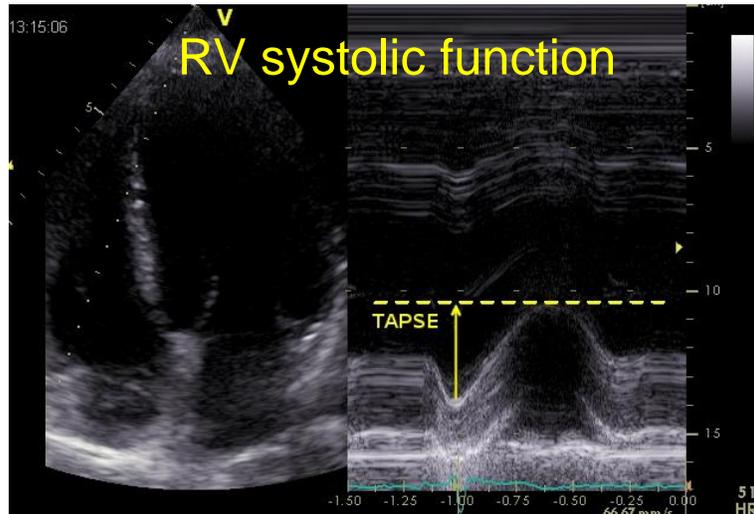
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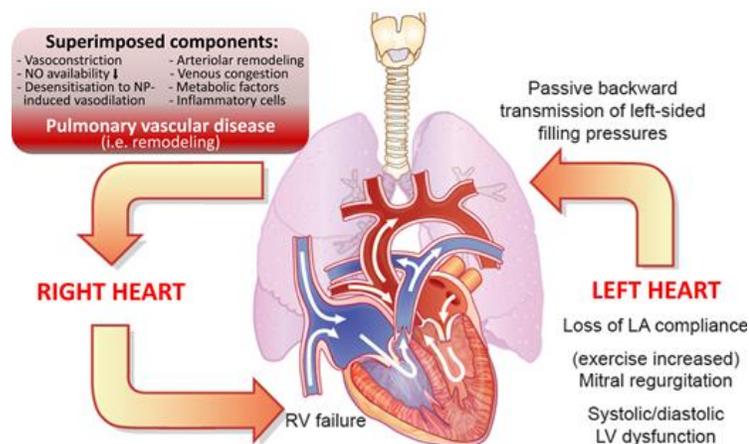
# Right Ventricular Systolic Function and Heart Failure

- **Right ventricular (RV) systolic dysfunction** is an indicator of poor prognostic course of heart failure (HF) patients, providing information over and above left ventricular (LV) systolic dysfunction.
- The prognostic role of **pulmonary hypertension (PH)**, a hemodynamic result of elevation of LV filling pressures in HF, is also well known.



# RV-Pulmonary Artery Coupling

- RV-pulmonary arterial (PA) coupling has emerged as a novel, comprehensive index that allows evaluating **RV function/contractility in relation to the underlying RV afterload**.
- Normal RV-PA coupling is maintained only when RV contractility and pulmonary vascular resistance/RV afterload are appropriately matched.
- **RV-PA uncoupling occurs when RV contractility cannot increase to match RV afterload**, resulting in RV dysfunction and right heart failure.



# RV-Pulmonary Artery Coupling

- **Invasive assessment of RV-PA coupling is still the gold standard;** however, it is highly technically difficult and expensive, thus with extremely limited applicability in clinical practice.

- **Ees/Ea ratio**

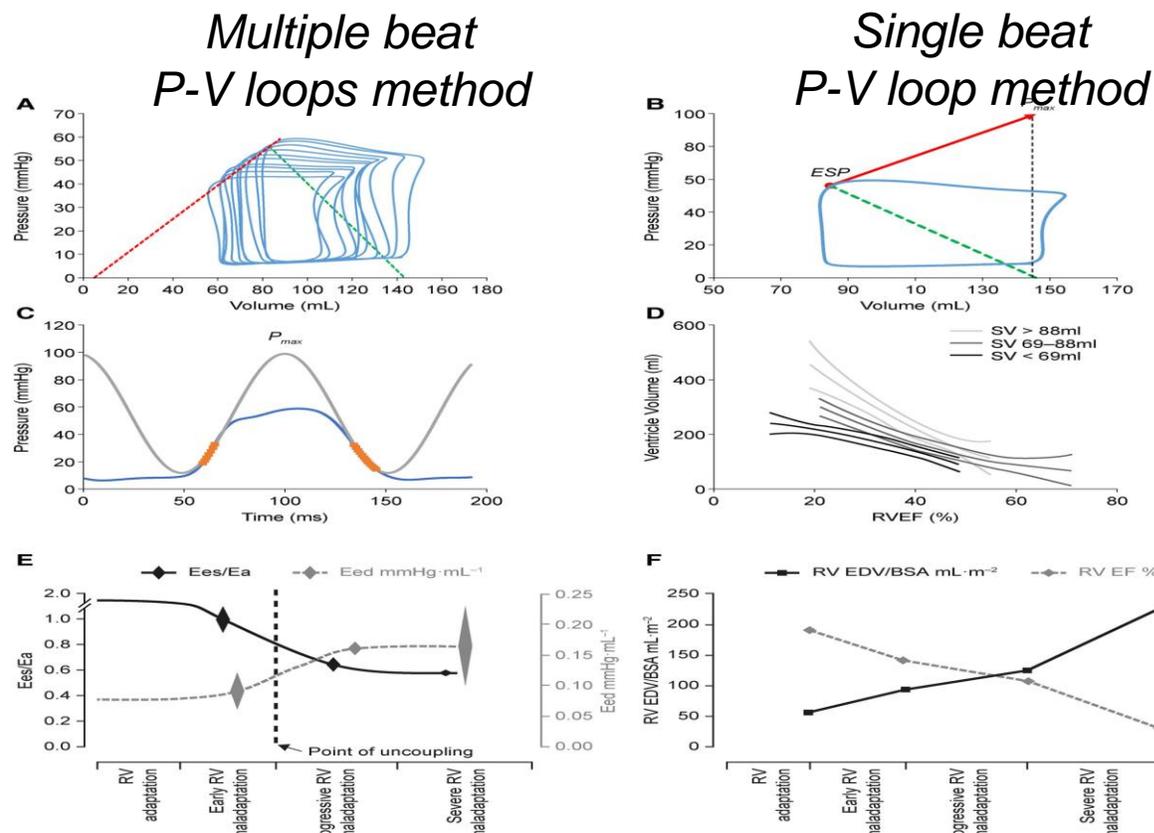
**Ees ~ RV end-systolic elastance**

Ees = RV end-systolic pressure /end-systolic volume

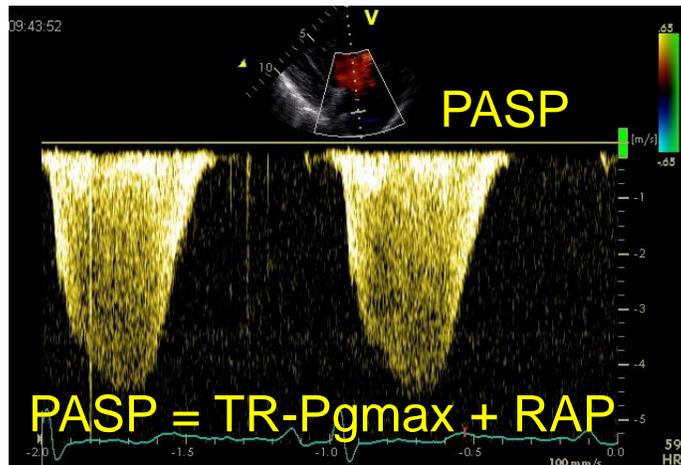
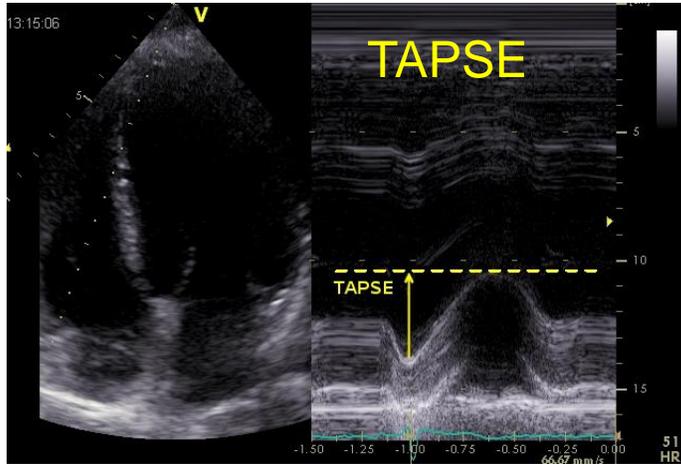
**Ea ~ arterial elastance**

Ea = RV end-systolic pressure /stroke volume

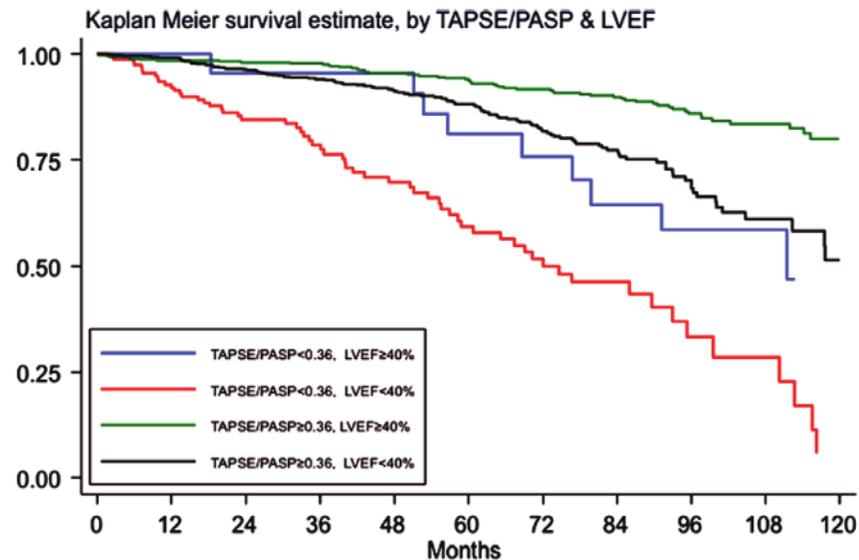
- Physiologically, Ees/Ea ratio is 1,5–2,0.



# TAPSE/PASP Ratio



- **Noninvasive measure of RV-PA coupling**  
(~ an index of the length-force relationship).
- **A large body of evidence** has arisen outlining the **prognostic role of** echocardiographically assessed RV-PA coupling, i.e. **TAPSE/PASP ratio**, in **chronic and acute HF patients (HFREF, HFPEF)**.



# Aim of our Study

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- To assess the prognostic usefulness of TAPSE/PASP ratio in symptomatic patients with recently diagnosed unexplained LV systolic dysfunction.

# Study Cohort

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- Retrospective analysis
- 133 patients with recently diagnosed unexplained LV systolic dysfunction (55±11 years, 72 % males) with HF symptoms lasting <6 months referred to our institution between April 2007–November 2013 for further evaluation.
- In all patients, endomyocardial biopsy (EMB) was performed.
- Median follow-up of 5 years

# Inclusion and Exclusion Criteria

## Inclusion criteria

- **History of HF symptoms < 6 months**
- **LV EF < 40% persisting after at least 1 week of conventional HF therapy**

## Exclusion criteria

- Significant coronary artery disease
- Moderate or severe primary valvular disease
- Haemodynamically significant congenital heart disease
- Atrial fibrillation/flutter with ventricular rate >100bpm
- Uncorrected metabolic or endocrine disorder
- History of alcohol or drug abuse
- History of cardiotoxic oncologic treatment
- Family history of DCM; peripartal onset

# Clinical, ECG and Laboratory Characteristics

Number of subjects	133
Age (years)	55 [46,61]
Gender (women)	37 (27.8%)
SBP (mmHg)	116±17
Heart rate (beats/min)	81±14
HF symptoms duration (days)	56 [28,123]
NYHA class I/II/III/IV (class)	4/25/45/57
Arterial hypertension	52 (39.1%)
Diabetes mellitus	17 (12.7%)
eGFR (mL/min/1.73m <sup>2</sup> )	78±18
Sinus rhythm	124 (93.2%)
Atrial fibrillation	9 (7%)
LBBB	25 (18.7%)
BNP (pg/mL)	405 [198,789]
TnI (ug/L)	0.05 [0.03,0.16]

Variables expressed as means and standard deviations, median [25<sup>th</sup>, 75<sup>th</sup> percentile] or as a count and percentage of subjects; *BNP* B-type natriuretic peptide; *eGFR* glomerular filtration rate; *HF* heart failure; *LBBB* left bundle branch block; *NYHA* New York Heart Association; *SBP* systolic blood pressure; *TnI* troponin I

# Baseline Echocardiographic Parameters

Number of subjects	133
LVEDD (mm)	68±7
LVESD (mm)	59±8
LVEDV (mL)	199 [159,239]
LVESV (mL)	143 [113,176]
LVEF (%)	28 ±7
E (m/s)	0.77 ±0.26
e' (cm/s)	7 [5,8]
Mitral regurgitation (grade)	2 [1,2.5]
LAV (mL)	97 [73,122]
RVEDD (mm)	36 [32,41]
TAPSE (mm)	18 [15,21]
Tricuspid regurgitation (grade)	1 [1,1.5]
RA area (cm <sup>2</sup> )	18 [15,22]
RAP (mmHg)	3 [3,8]
PASP (mmHg)	36 [27,47]
TAPSE/PASP	0.54±0.27

Variables are expressed as means and standard deviations or median [25<sup>th</sup>, 75<sup>th</sup> percentile];

*E* peak early diastolic velocity;

*e'* peak early diastolic mitral annular velocity;

*LAV* left atrial volume;

*LVEDD* left ventricular end-diastolic diameter;

*LVEDV* left ventricular end-diastolic volume;

*LVESD* left ventricular end-systolic diameter;

*LVESV* left ventricular end-systolic volume;

*LVEF* left ventricular ejection fraction;

*PASP* pulmonary artery systolic pressure;

*RA area* right atrial area;

*RAP* right atrial pressure;

*RVEDD* right ventricular end-diastolic diameter

*TAPSE* tricuspid annular plane systolic excursion

# Endomyocardial Biopsy Findings

PCR focused on viruses (NAS)	133
-positive endomyocardial biopsy	69 (52%)
EM focused on viruses (NAS)	133
-positive endomyocardial biopsy	82 (62%)
Dallas criteria (NAS)	133
- active or borderline myocarditis +	3 (2%)
IH criteria for myocarditis (NAS)	128
-positive	22 (17%)
HLA DR (NAS)	109
-grade 0/1/2/3	35/35/19/20
LCA (NAS)	86
-positive cells (counts)	5[2,8]
CD3 (NAS)	122
-positive cells (counts)	3[1,5]
CD 68 (NAS)	85
-positive cells (counts)	1[0,3]

Variables expressed as means and standard deviations, median [25<sup>th</sup>, 75<sup>th</sup> percentile]

or as a count and percentage of subjects;

*CD* cluster of differentiation;

*EM* electron microscopy;

*HLA* Human Leucocyte Antigen DR isotype;

*LCA* leucocyte common antigen;

*NAS* number of subjects available for analysis;

*PCR* polymerase chain reaction

*Immunohistochemical criteria for myocarditis:*

≥14 leucocytes/mm<sup>2</sup>

and ≥7 CD 3 positive T-lymphocytes/mm<sup>2</sup>

# Univariate predictors of mortality

	<b>HR</b>	<b>95%CI</b>	<b>p</b>
RA area (cm <sup>2</sup> )	1.09	1.02-1.17	0.008
RAP (mmHg)	1.1	1-1.21	0.043
TR severity	1.79	1.11-2.9	0.017
E/e'	1.08	1.01-1.17	0.036
PR interval (ms)	1.02	1-1.03	0.009
logBNP	1.58	1.01-2.46	0.043
CD 68+ cells in EMB	1.15	1.03-1.3	0.016

**TAPSE/PASP**

**0.25**

**0.03-2.23**

**0.215**

*BNP* B-type natriuretic peptide; *CD 68+ cells in EMB* macrophages in endomyocardial biopsy; *E* peak early diastolic velocity; *e'* peak early diastolic mitral annular velocity; *PASP* pulmonary artery systolic pressure; *RA area* right atrial area; *RAP* right atrial pressure; *TAPSE* tricuspid annular plane systolic excursion, *TR* tricuspid regurgitation

# Multivariate predictors of mortality

	<b>OR</b>	<b>95%CI</b>	<b>p</b>
PR interval	1.02	1.006-1.035	0.00575
logBNP	2.02	1.14-3.56	0.01557
RA area	1.097	1.007-1.196	0.03499

*BNP* B-type natriuretic peptide; *RA area* right atrial area

# Univariate predictors of mortality/ HF hospitalizations/heart transplant

	OR	95%CI	p
PR interval	1.01	1.00-1.02	0.0344
Elevated RAP	2.44	1.04-5.74	0.0412
RA area	1.07	1.01-1.13	0.029
CRP	1.021	1.001– 1.03	0,033

**TAPSE/PASP**

**0.73**

**0.16-3.42**

**0.689**

*BNP* B-type natriuretic peptide; *CRP* C-reactive protein; *PASP* pulmonary artery systolic pressure;  
*RA area* right atrial area; *RAP* right atrial pressure; *TAPSE* tricuspid annular plane systolic excursion

**In multivariate analysis, none of the parameters have been shown  
to be statistically significant predictor.**

# TAPSE/PASP and mortality/ HF hospitalizations/heart transplant in pts with PH

- **41 pts with PASP  $\geq$  40 mmHg** (33 % of all study cohort)

- **Mortality – univariate analysis**

TAPSE/PASP      OR 0.69      95%CI 0.0001-983      p=0.92

- **Mortality/HF hospitalizations/heart transplant – univariate analysis**

TAPSE/PASP      OR 0.59      95%CI 0.001-365      p=0.87

# Conclusions

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- Baseline TAPSE/PASP ratio was not associated with subsequent 5-year survival/HF hospitalizations/heart transplantation in our cohort of unselected symptomatic patients with recently diagnosed unexplained LV systolic dysfunction.
- Among echocardiographic parameters, RA area appears to be a significant echocardiographic predictor of 5-year survival in these individuals.



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**Thanks a lot for your attention**