FAKULTNÍ NEMOCNICE® OLOMOUC

Lékařská fakulta
Univerzita Palackého v Olomouci

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

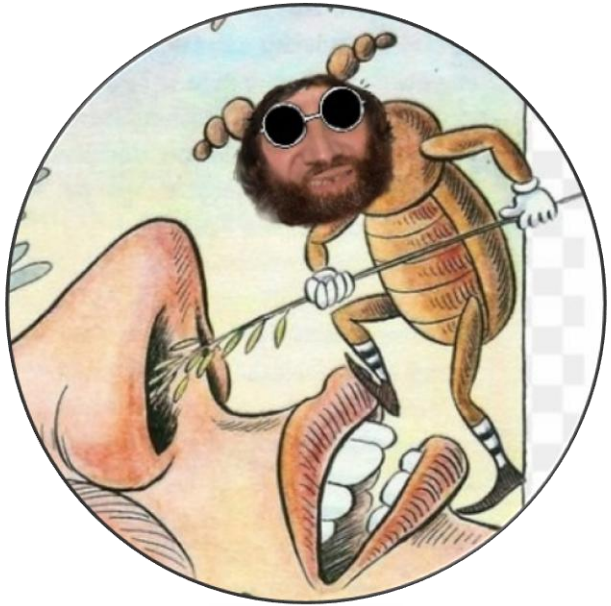
Na co se soustředit v diagnostice a léčbě pacientů s PH:
OVLIVNĚNÍ HEMODYNAMIKY A FUNKCE PRAVÉ KOMORY

Martin Hutyra

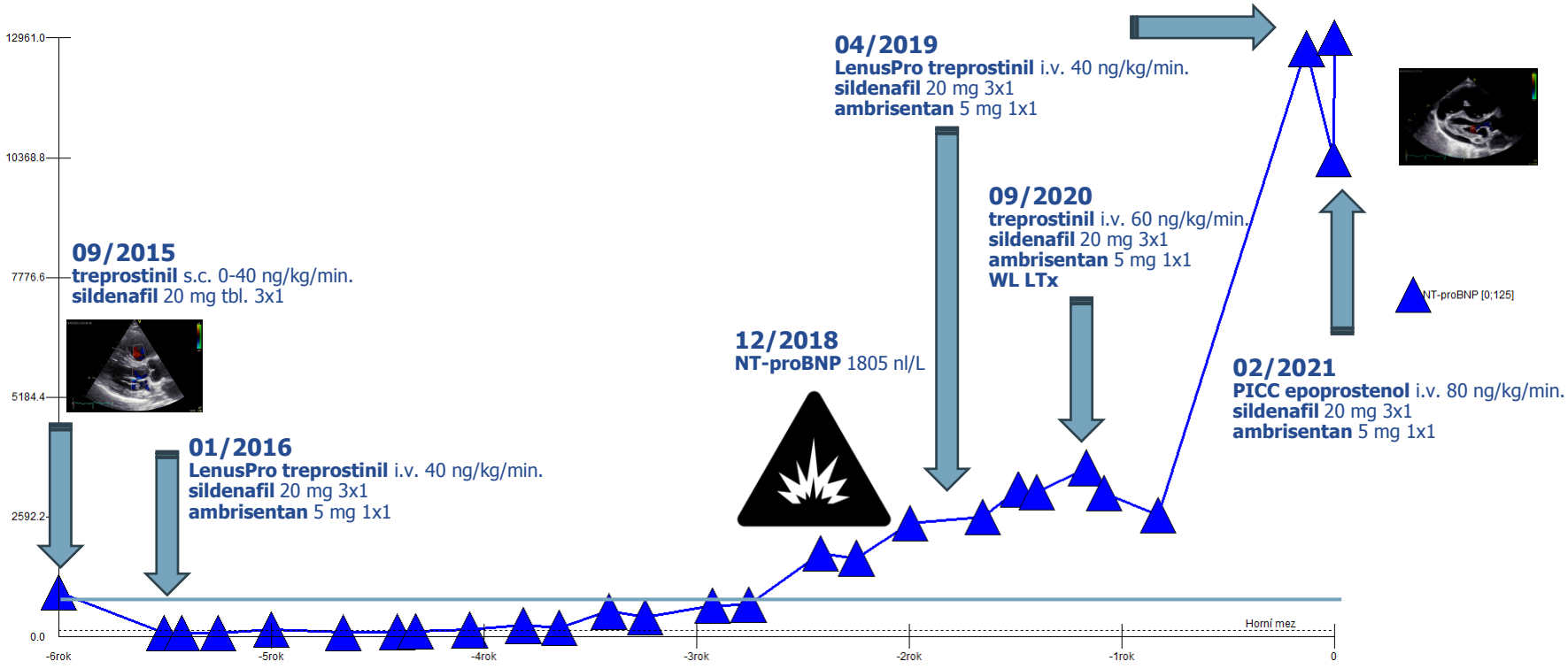
4.–7. KVĚTNA 2024 | VELETRHY BRNO
XXXII.
VÝROČNÍ SJEZD
ČESKÉ KARDIOLOGICKÉ
SPOLEČNOSTI

O čem to bude?

1. Význam pravé komory u plicní arteriální hypertenze.
2. Jak na hodnocení její funkce a morfologie?
3. Jaké jsou terapeutické možnosti ovlivnění afterloadu/preloadu pravé komory a její morfologie/funkce a jak můžeme pravou komoru monitorovat?
4. Je reverzní remodelace pravé komory dostatečný terapeutický cíl plicní arteriální hypertenze?



NT-proBNP



09/2015
treprostinil s.c. 0-40 ng/kg/min.
sildenafil 20 mg tbl. 3x1

01/2016
LenusPro treprostinil i.v. 40 ng/kg/min.
sildenafil 20 mg 3x1
ambrisentan 5 mg 1x1

12/2018
NT-proBNP 1805 nl/L

04/2019
LenusPro treprostinil i.v. 40 ng/kg/min.
sildenafil 20 mg 3x1
ambrisentan 5 mg 1x1

09/2020
treprostinil i.v. 60 ng/kg/min.
sildenafil 20 mg 3x1
ambrisentan 5 mg 1x1
WL LTx

01/2021
PICC epoprostenol i.v. 80 ng/kg/min.
sildenafil 20 mg 3x1
ambrisentan 5 mg 1x1
WL LTx

02/2021
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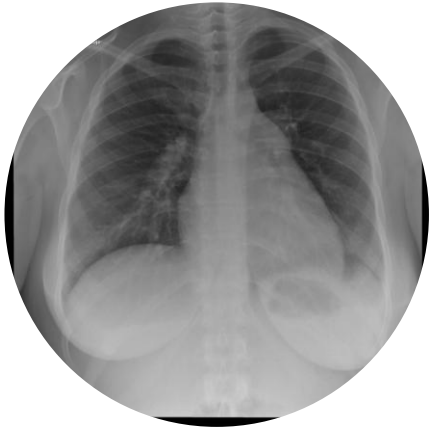
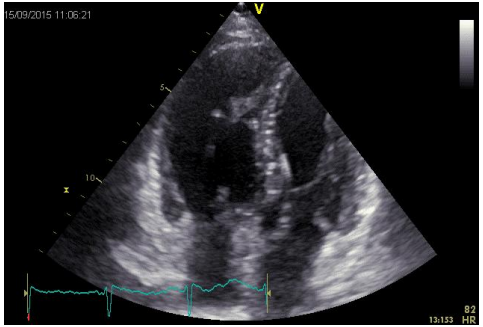
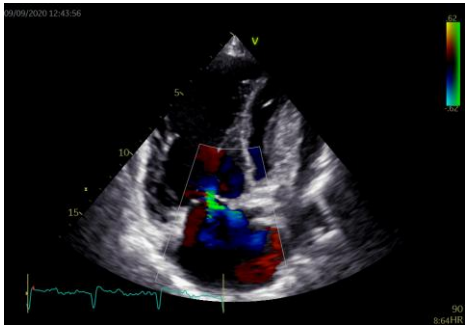
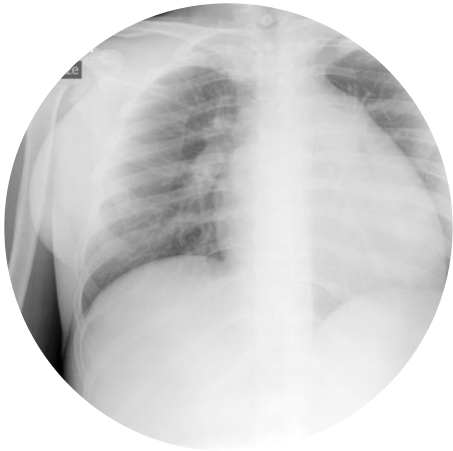
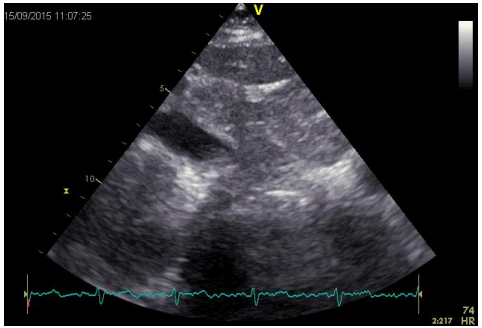
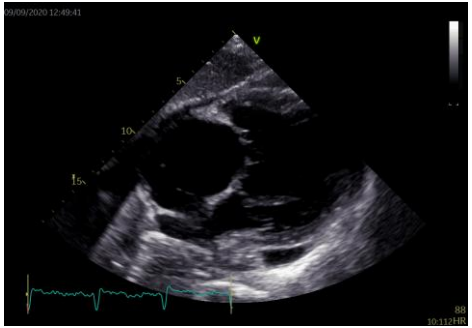
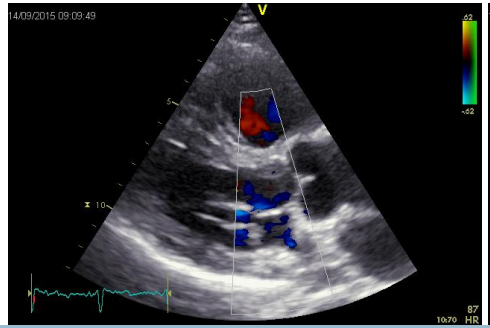
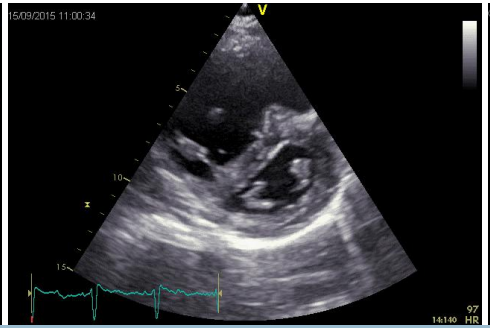
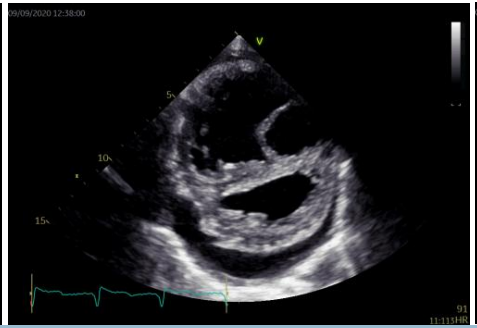
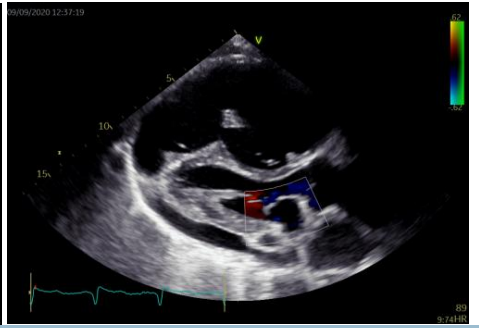
ambrisentan 5 mg 1x1

Význam pravé komory u plicní arteriální hypertenze.

1. **Význam pravé komory u plicní arteriální hypertenze.**
2. Jak na hodnocení její funkce a morfologie?
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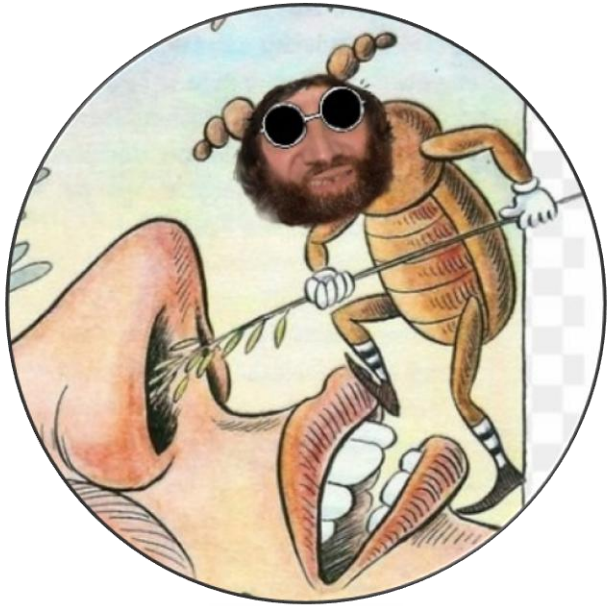
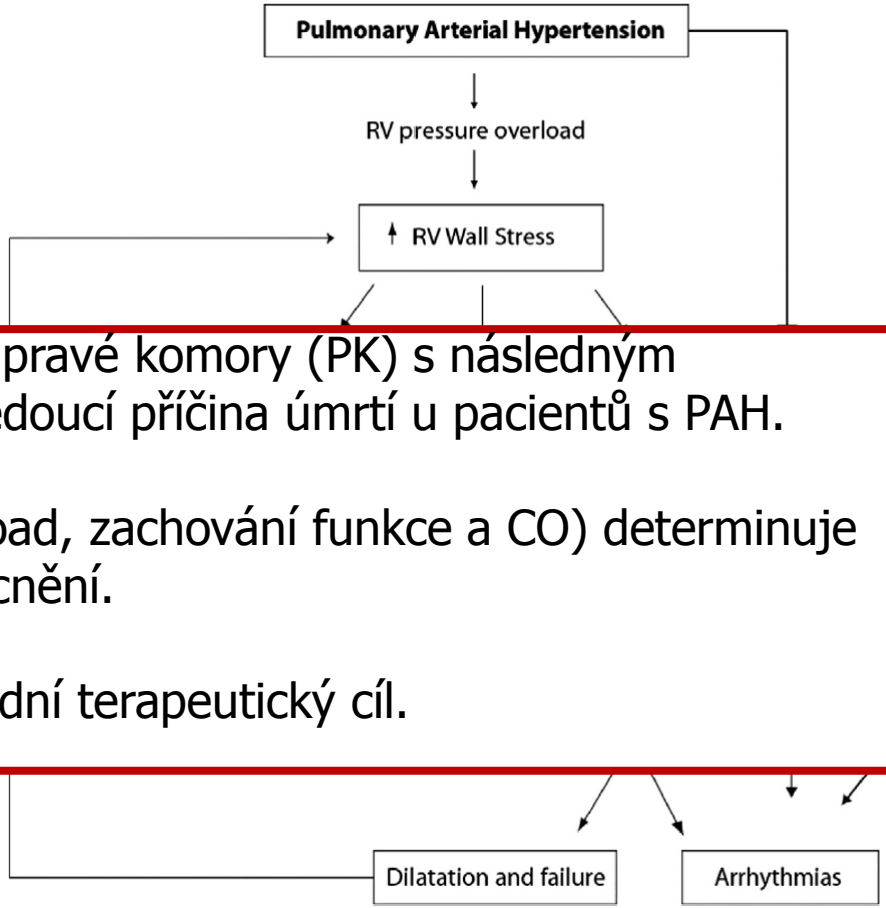


Pravá komora u PAH

- An **afterload mismatch** - increased RV afterload, driven by increased PVR, leads to right heart failure.
- At an early stage, the RV adapts to the increased afterload to preserve stroke volume (**homeometric adaptation**), followed by an **heterometric adaptation** when the latter gets exhausted



- Vyčerpání kompenzačních mechanismů pravé komory (PK) s následným pravostranným srdečním selháním je vedoucí příčina úmrtí u pacientů s PAH.
- Funkce PK (adaptace na zvýšený afterload, zachování funkce a CO) determinuje funkční status a klinický průběh onemocnění.
- Zachování/zlepšení funkce PK jako zásadní terapeutický cíl.

characterized by **uncoupling of the RV to the pulmonary circulation**

Vonk-Noordegraaf A et al. JA Am Coll Cardiol 2013; Vol. 62, No. 25, Suppl D; D22–33;

Miotti C et al. J Clin Med 2021, 10, 619.

Co je standardem měření V-A couplingu?

= RV Ees/PA Ea

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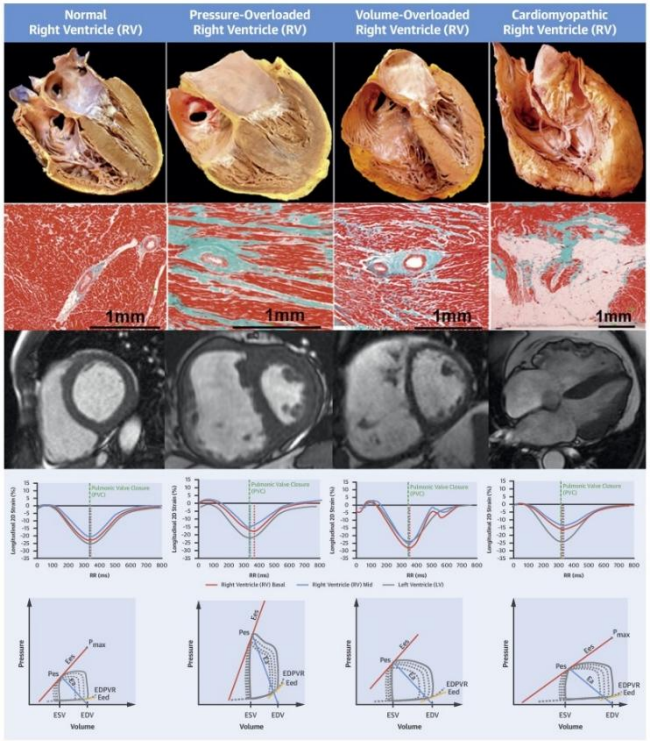
THE PRESENT AND FUTURE

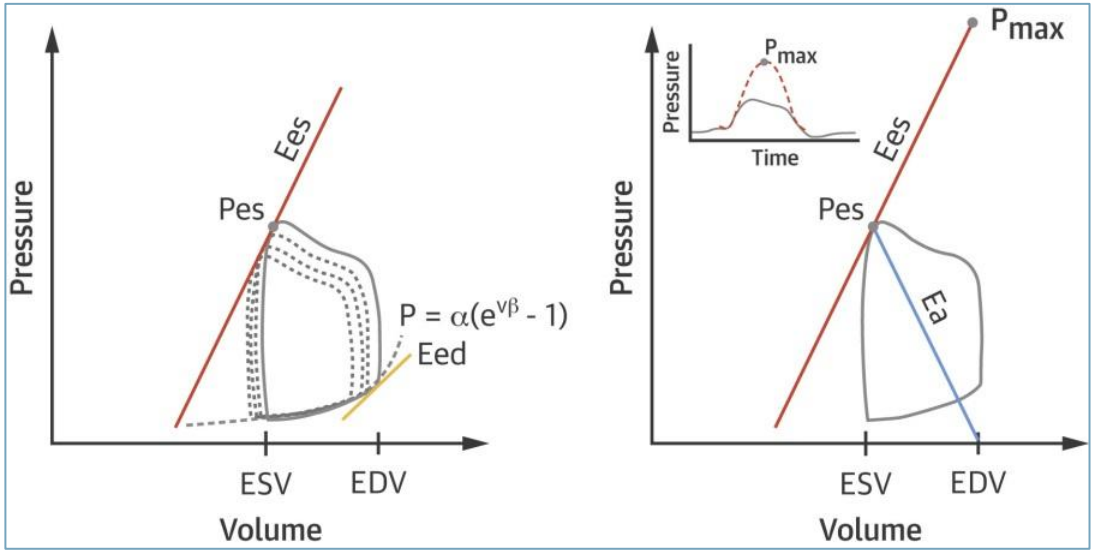
JACC STATE-OF-THE-ART REVIEW

Anatomy, Function, and Dysfunction of the Right Ventricle

JACC State-of-the-Art Review

Javier Sanz, MD,[a,b] Damián Sánchez-Quintana, MD, PsD,[c] Eduardo Bossone, MD, PsD,[d] Harm J. Bogaard, MD, PsD,[e] Robert Naeije, MD, PsD[f]



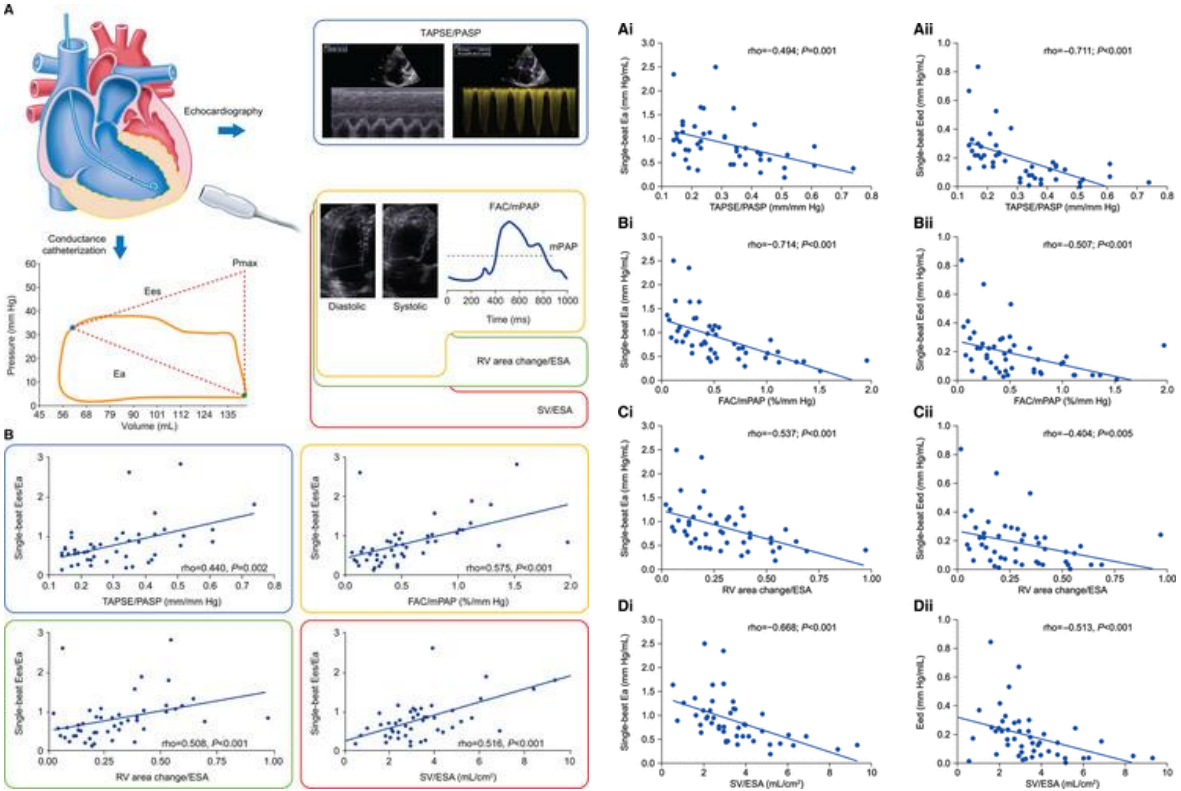


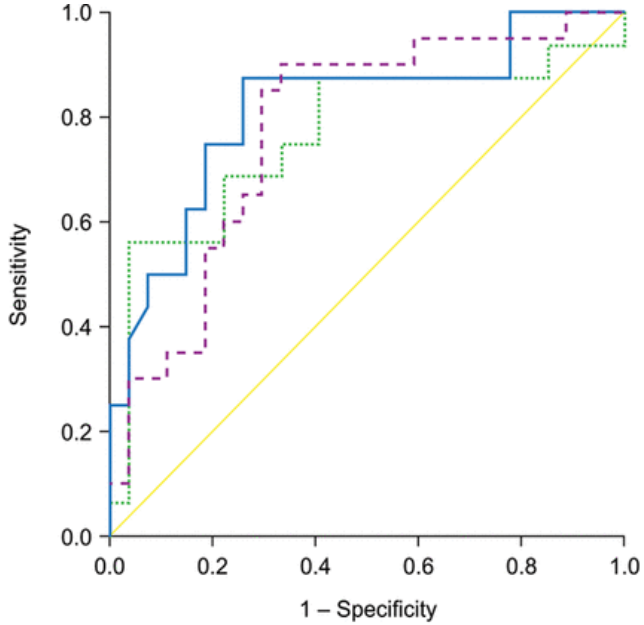
Sanz, J. et al. J Am Coll Cardiol. 2019;73(12):1463–82.

Circulation: Cardiovascular Imaging
Volume 12, Issue 9, September 2019
https://doi.org/10.1161/CIRCIMAGING.119.009047

ORIGINAL ARTICLE

Validation of the Tricuspid Annular Plane Systolic Excursion/Systolic Pulmonary Artery Pressure Ratio for the Assessment of Right Ventricular-Arterial Coupling in Severe Pulmonary Hypertension





Variable	AUC	Standard error	Cut-off	Sensitivity	Specificity
TAPSE/PASP	0.816	0.071	0.3095 mm/mm Hg	87.5%	75.9%
FAC/mPAP	0.766	0.083	0.7071 %/mm Hg	65.0%	96.3%
SV/ESA	0.776	0.070	2.93 mL/cm²	90.0%	66.7%

Tello K. Circulation: Cardiovascular Imaging. Validation of the Tricuspid Annular Plane Systolic Excursion/Systolic Pulmonary Artery Pressure Ratio for the Assessment of Right Ventricular-Arterial Coupling in Severe Pulmonary Hypertension, Volume: 12, Issue: 9, DOI: (10.1161/CIRCIMAGING.119.009047)

Jak na hodnocení její funkce a morfologie?

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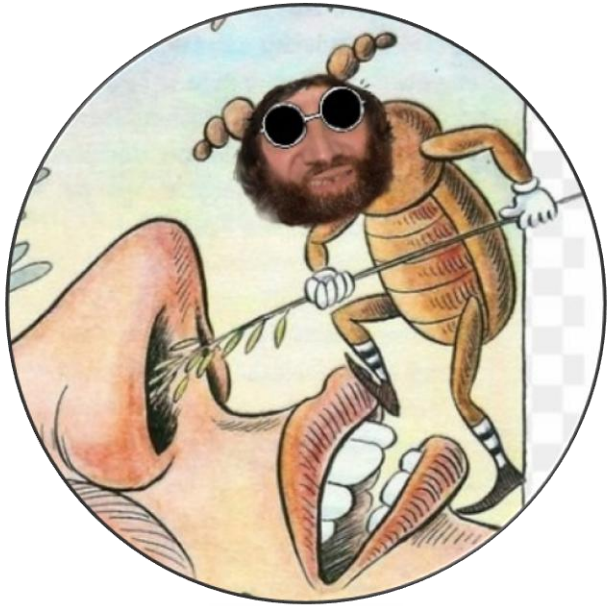
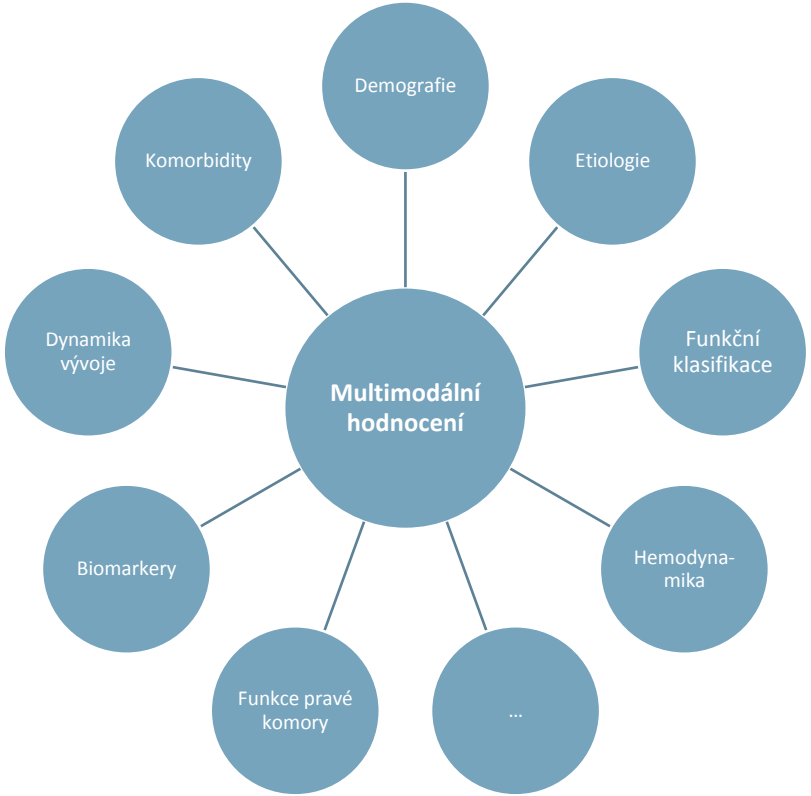


Multimodální hodnocení

žádný izolovaný prognostický faktor neposkytuje dostatečnou diagnostickou a prognostickou informaci

nutnost pravidelné komplexní reevaluace

- přítomnost známek **klinického zhoršení** oproti minulé vizitě
  - je případné klinické zhoršení způsobeno *progresí PAH* nebo jiným *konkomitantním onemocněním*
- **funkce pravé komory** – stabilita a adekvátnost
- dosažení stavu spojeného s **dobrou dlouhodobou prognózou** (kritéria nízkého rizika)



Poměr TAPSE/PASP

significant marker of **ventriuloarterial coupling**

- index of in vivo RV shortening in the longitudinal axis versus developed force in patients with HF
- non-invasive, indirect measurement of RV contractile function and RV-pulmonary arterial coupling
- validated against the ratio of end-systolic to arterial elastances (Ees/Ea)
- directly compared with P-V loop measures of ventriculoarterial coupling (invasively measured)

validated as an important **clinical and prognostic parameter** in patients

- *with **heart failure with and without pulmonary hypertension***
- *with **combined post- and pre-capillary PH*** (even after adjusting for other echocardiographic or hemodynamic prognostic indicators)

promising echocardiographic parameter derived from **routinely measured indices**, fully applicable on the **daily basis routine**, with variation coefficient for intra and interobserver agreements is about 1%

Cut-off value:

- 0.55 mm/mmHg - probability of PH
- 0.32 mm/mmHg - low-risk status in patients with PAH
- 0.19 mm/mmHg - high mortality risk in patients with PAH

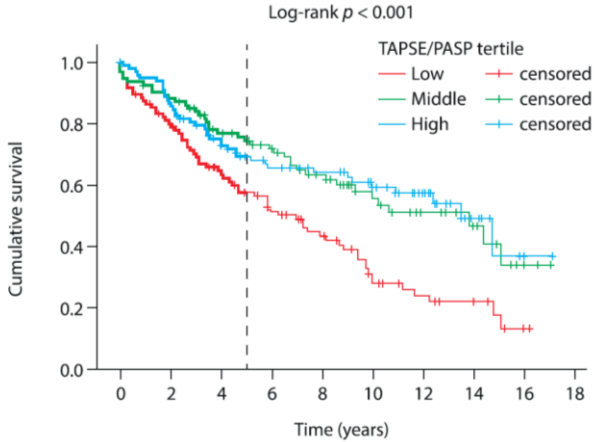
Tello K et al. Int J Cardiol . 2018 Sep 1;266:229-235.

Tello K et al. Int J Cardiol 2018

290 patients with PAH

associated with hemodynamics and functional class

independently associated with overal mortality
(even after adjusting for other echocardiographic
or hemodynamic prognostic indicators)



Tello K et al. Circ Cardiovasc Imaging 2019

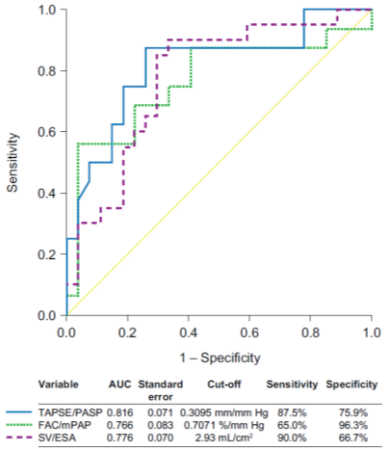
52 patients with PAH and CTEPH

TAPSE/PASP correlated with Ees/Ea and end-diastolic elastance

TAPSE/PASP <0.31 mm/mm Hg

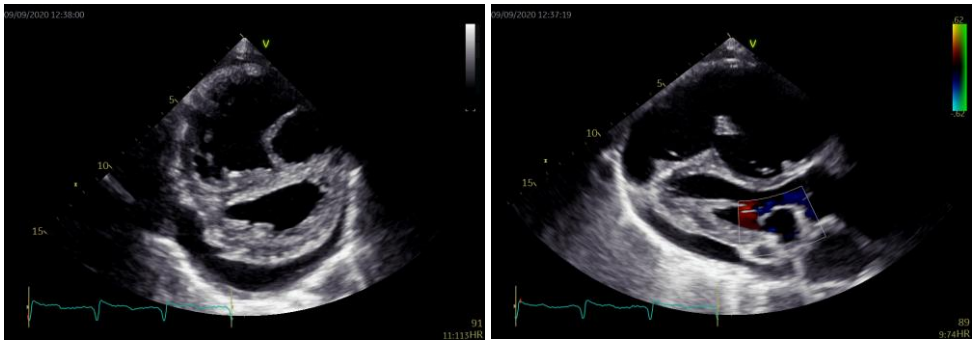
significantly worse prognosis

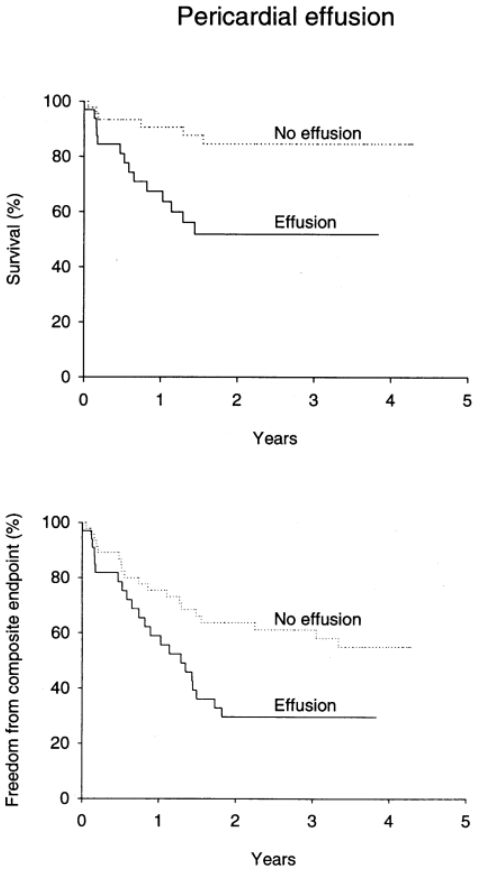
discriminated RV-arterial uncoupling (Ees/Ea <0.805) - sensitivity: 87.5%; specificity: 75.9%



Perikardiální výpotek

- nejčastěji uváděný echokardiografický prognostický faktor u PAH
- způsoben zvýšením tlaku v PS, který omezuje venózní a lymfatickou drenáž myokardu - odraz diastolické dysfunkce PK
- až 40-50 % pacientů s těžkou PAH
- korelace s prognózou, tolerancí zátěže, hemodynamickou závažností
- známka **pokročilého** onemocnění
- CAVE *jiná etiologie* perikardiálního výpotku (pacienti se systémovým onemocněním pojiva)





Raymond RJ et al. J Am Coll Cardiol 2002 Apr 3;39(7):1214-9

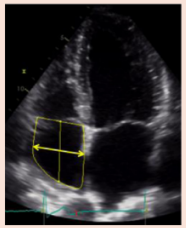
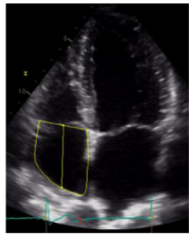
Plocha pravé síně

- dilatace pravé síně je důsledkem chronického zvýšení tlaků v PK a z něj vyplývající dysfunkce PK s postupným nárůstem plnících tlaků, tj. tlaků v pravé síni
- ke zvýšení tlaků v pravé síni přispívá také trikuspidální regurgitace

- apikální 4-dutinová projekce
- end-systola
  plocha PS maximální
  (měření od linie trikuspidálního anulu ke stropu PS, tedy mimo oblast mimo Tri chlopní a anulem)

- patologické hodnoty plochy
  > 18 cm^2

Table 12 Recommendations for the echocardiographic assessment of RA size

Parameter and method	Echocardiographic imaging	Advantages	Limitations
Linear dimensions. The minor axis of the right atrium should be measured in the apical four-chamber view as the distance between the lateral RA wall and interatrial septum, at the midatrial level defined by half of RA long axis	2D-guided linear measurements 	• Easy to obtain • Established normal values	• Single dimension only • Assumes that RA enlargement is symmetrical • View dependent
Area. Measured in the apical four-chamber view at end-systole, on the frame just prior to tricuspid valve opening, by tracing the RA blood-tissue interface, excluding the area under the tricuspid valve annulus.	2D view 	• More representative of actual RA size than linear dimensions • Established normal values	• Need of a dedicated view to avoid RA foreshortening • Assumes a symmetrical shape of the cavity • View dependent

Lang RM et al. J Am Soc Echocardiogr 2015 Jan;28(1):1-39.e14.

BMJ Open

Association between right atrial area measured by echocardiography and prognosis among pulmonary arterial hypertension: a systematic review and meta-analysis

Ke Liu ,[1] Chunhua Zhang,[2] Bingyu Chen,[3] Mingfeng Li,[4] Peican Zhang[4]

Table 2 Values of right atrial area or right atrial area index and HR with 95% CI from the publications included in the meta-analysis

Authors	Right atrial size	Changing amplitude	Events (n)		HR (95% CI)	
			All-cause mortality	Composite endpoint	All-cause mortality	Composite endpoint
RAA (cm^2, m±SD)						
Moceri *et al*[15]	21.1±6.1	Per 10 cm^2	19	NA	3.59 (1.92 to 6.72)	
Park *et al*[26]	22.5±9.4	Per 9.4 cm^2	12	20	1.36 (0.85 to 2.18)	1.45 (1.02 to 2.05)
Murata *et al*[27]	18±5	Per 1 cm^2	NA	19	NA	1.20 (1.06 to 1.34)
Badagliacca *et al*[28]	31±10	Per 1 cm^2	NA	54	NA	1.04 (1.01 to 1.06)
Stepnowska *et al*[31]	29±11(died) vs 19±6 (survival)	Per 1 cm^2	9	NA	1.08 (1.02 to 1.14)	NA
Bai *et al*[32]	28.2±7.3 (with events) vs 17.9±4.2 (without events)	Per 1 cm^2	NA	20	NA	1.13 (1.08 to 1.18)
Kawamukai *et al*[33]	18.0±8.0 (with events) vs 19.8±6.9 (without events)	Per 1 cm^2	NA	18	NA	0.97 (0.90 to 1.02)
RAAI (cm^2/m, m±SD)						
Raymond *et al*[14]	19.9±6.6	Per 5 cm^2	20	41	1.54 (1.13 to 2.10)	1.33 (1.06 to 1.66)
Mathai *et al*[24]	14.0±5.5	Per 1 cm^2	25	NA	1.11 (1.02 to 1.19)	NA
Haddad *et al*[25]	NA	Per 5 cm^2	NA	27	NA	1.81 (1.44 to 2.28)
Mazurek *et al*[29]	13.0±4.4	Per 1 cm^2	18	NA	0.98 (0.62 to 1.56)	NA
Amsallem *et al*[30]	12.1±4.7	Per 4.7 cm^2	NA	88	NA	1.37 (1.20 to 1.57)

NA, not available; RAA, right atrial area; RAAI, right atrial area index.

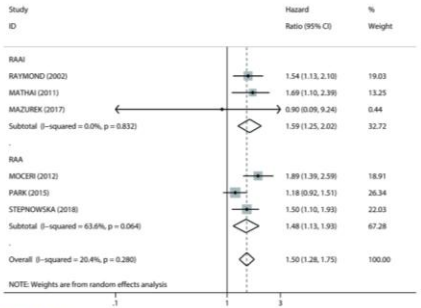


Figure 2 Forest plot comparing the unadjusted HRs of RAA/RAAI for all-cause mortality pooled from included studies. RAA, right atrial area; RAAI, right atrial area index.

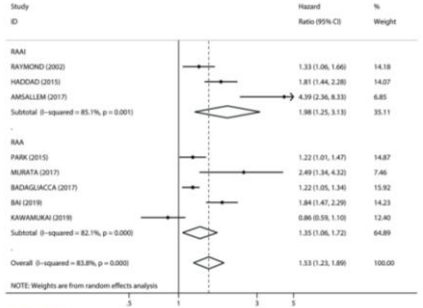


Figure 3 Forest plot comparing the unadjusted HRs of RAA/RAAI for the composite point pooled from included studies. RAA, right atrial area; RAAI, right atrial area index.

- Twelve studies with a 1085 patients with PAH (mean follow-up time 9.2 months - 5.0 years)
- Patients with PAH with enlarged RAA/RAAI were associated with poor prognosis.
- The risk of **all-cause mortality** in patients with PAH was found to statistically increase by 50% for every 5-unit increase in RAA/RAAI (HR 1.50, 95%CI 1.28 to 1.75)
- The risk of the **composite endpoint** significantly increased by 53% for every 5-unit increase in RAA/RAAI (HR 1.53, 95%CI 1.23 to 1.89, p<0.001).

Longitudinální funkce PK

European Heart Journal – Cardiovascular Imaging (2015) 16, 233–271
doi:10.1093/ehjci/jev014
POSITION PAPER

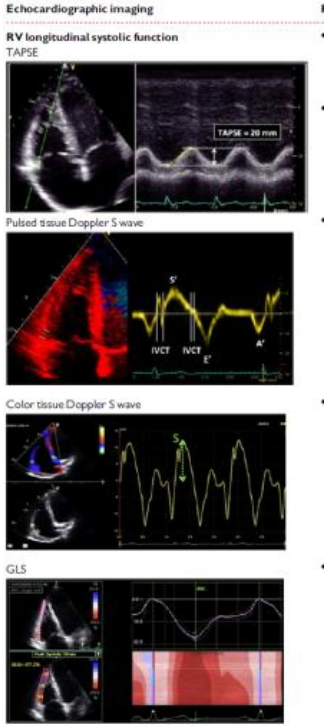
Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

Tricuspid annular plane systolic excursion (TAPSE) reflects longitudinal shortening of the RV. TAPSE is measured in the A4C by placing an M-mode cursor on the lateral tricuspid annulus and measuring the peak distance travelled by this reference point during systole. A greater distance travelled during systole implies greater RV systolic function, with the normal reference limit being a TAPSE of ≥1.7 cm.

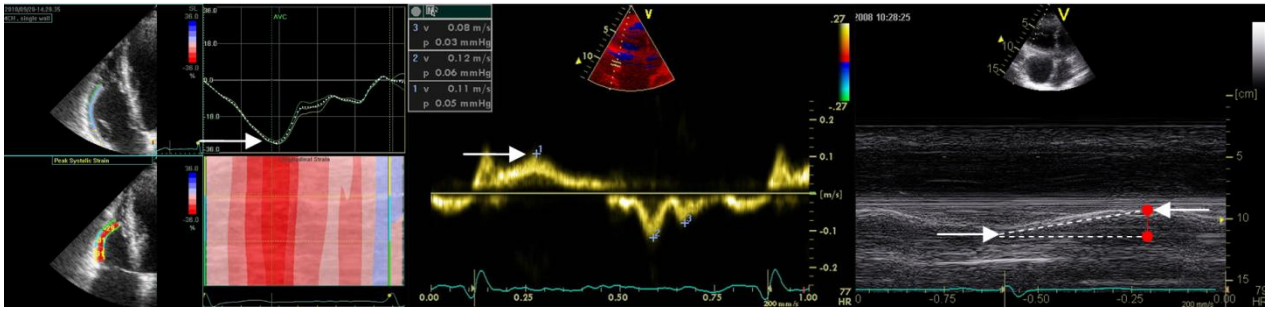
The primary limitation of TAPSE is that it only represents one component of RV motion within one single segment of RV myocardium. The RV may be frankly dysfunctional despite relatively preserved TAPSE, as in some cases of severe pulmonary arterial hypertension. Alternatively, the RV function may be globally preserved despite significantly reduced TAPSE, as often seen after cardiac surgery. In healthy individuals, TAPSE correlates with RV size.

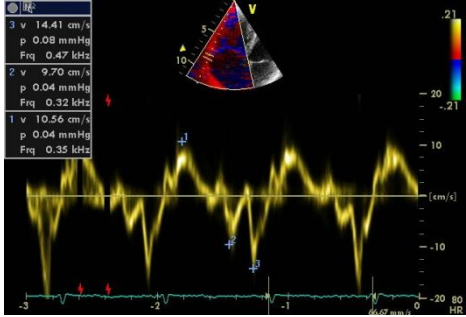
Two common sources of error with TAPSE are:

1. Not placing the M-mode cursor parallel to the plane of longitudinal motion, which results in angle-dependent underestimation of TAPSE.
2. Incorrectly measuring the magnitude of displacement from the M-mode image.



Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1.





Tricuspid annular velocity reflects the longitudinal velocity of the tricuspid annulus during systole.

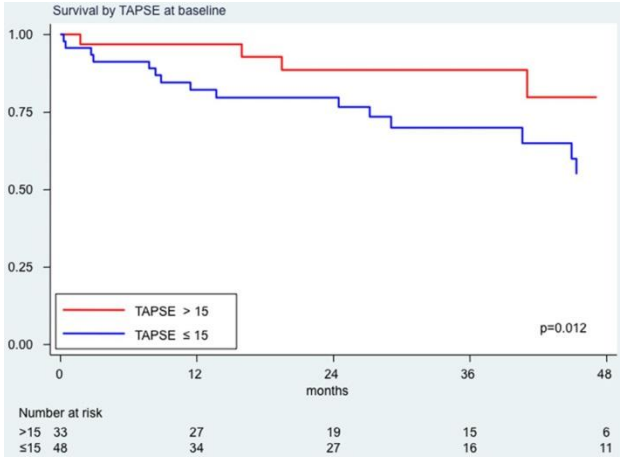
S' is measured in the A4C by placing a tissue Doppler cursor on the lateral tricuspid annulus and measuring the peak velocity of this reference point during systole. Care should be taken to measure the peak of the ejection waveform and not the earlier isovolumetric contraction waveform.

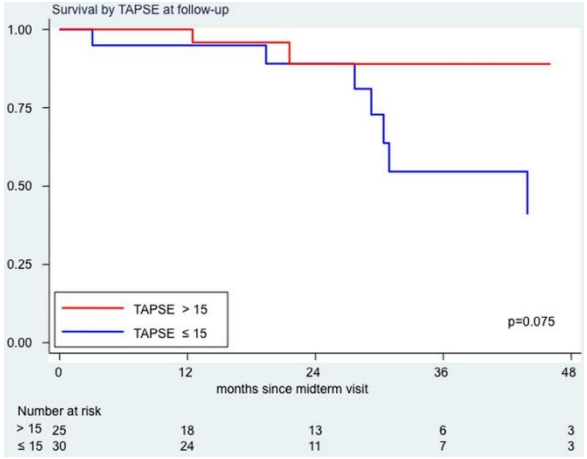
A greater velocity during systole implies greater RV systolic function, with the **normal reference limit** being an S' of ≥9.5 cm/s. Both pulsed tissue Doppler and color-coded tissue Doppler can be used to measure S', although the color-coded method yields mean velocities that are usually slightly lower.

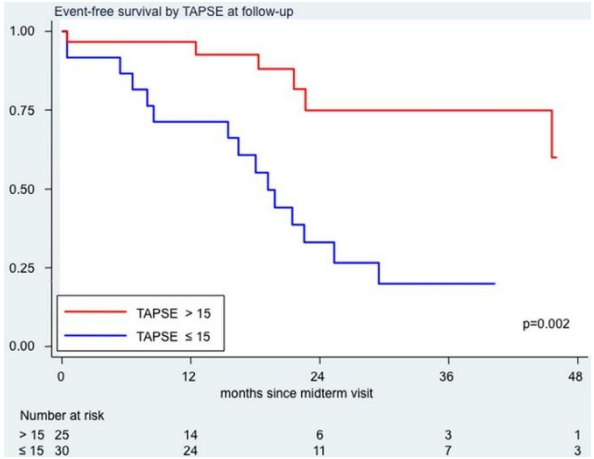
The **advantages and limitations** are the same as TAPSE:

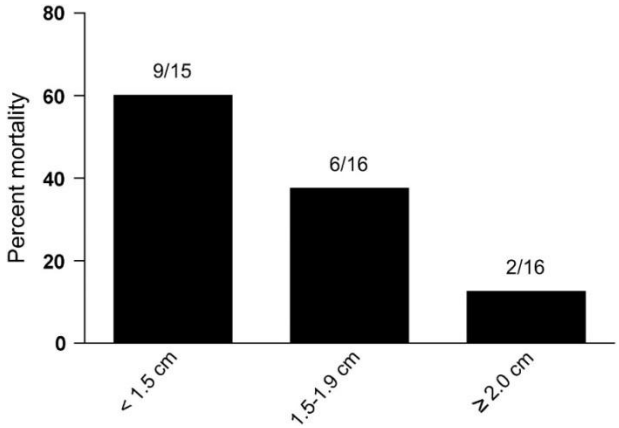
1. S' is simple to perform and has prognostic data, yet it is angle-dependent and only represents the longitudinal annular component of RV motion.
2. S' has been shown to correlate with CMR-derived RVEF and predicts outcomes in patients with pulmonary hypertension, inferior myocardial infarction, chronic heart failure, and arrhythmogenic RV cardiomyopathy (ARVC).

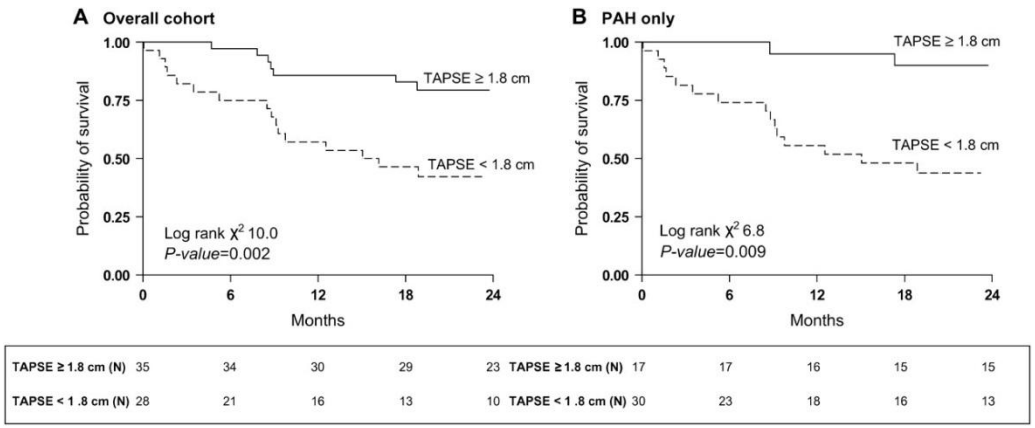
Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1.











Ghio S et al. Open Heart 2016 May 9;3(1):e000408.

Forfia PR et al. Am J Respir Crit Care Med 2006 Nov 1;174(9):1034-41.

Frakční změna plochy PK

Fractional area change (FAC) is the % change in RV area from diastole to systole, a two-dimensional surrogate for RV EF, and thereby reflects the systolic function of the inflow and apical portions of the RV. FAC encompasses longitudinal shortening as well as radial thickening and the contribution of the septum.

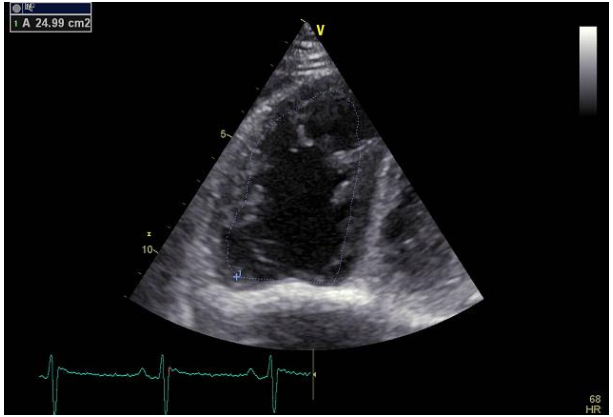
FAC = [(end-diastolic RV area – end-systolic RV area)/end-diastolic RV area] x 100

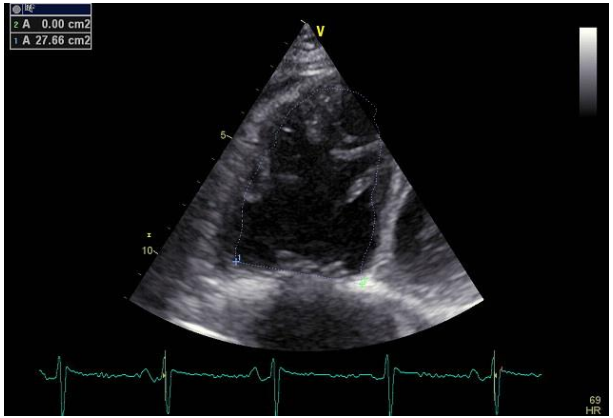
The normal reference limit for FAC is ≥35%.

The primary challenge and main limitation of FAC is the accurate tracing of the true RV endocardial border.

Compared with TAPSE and S', FAC was found to correlate best with the reference standard of CMR-derived RVEF *(r=0.80)*.

1. In substudies from the SAVE and VALIANT trials, 416 and 522 patients with **AMI** and evidence of LV dysfunction underwent complete echocardiographic assessment. Four independent predictors of subsequent all-cause mortality were identified: age, Killip classification, LV ejection fraction, and FAC; with FAC <35 percent carrying an adjusted hazard ratio of 3.56.
2. In the **Multidisciplinary Study of Right Ventricular Dysplasia**, FAC was found to be significantly reduced in probands compared with normal controls. The revised ARVC Task Force Criteria list FAC ≤33% as a major diagnostic criterion and FAC 34-40% as a minor criterion





Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1.

hodnotí longitudinální i radiální komponentu kontrakce PK

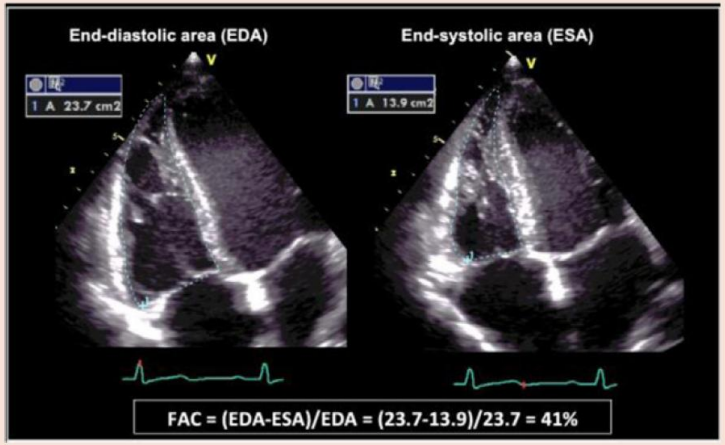
dobrá korelace s EF PK hodnocenou pomocí MR – prognostický význam

nepostihuje podíl výtokového traktu PK na celkovou systolickou funkci PK

horší reproducibilita – obtížnější detekce endokardu

RV global systolic function

FAC



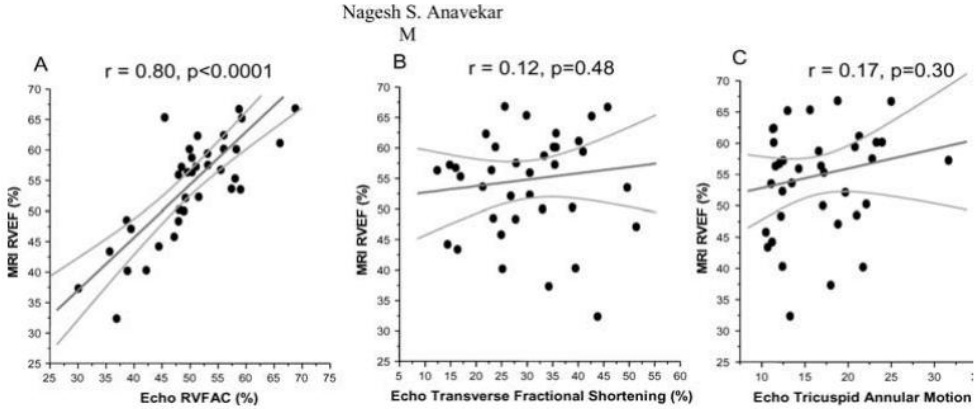


Figure 2. *Relationship between MRI-derived RVEF and echo-derived (**A**) RVFAC, (**B**) TFS, and (**C**) TAM. (n(36).*

Lang RM et al. J Am Soc Echocardiogr 2015 Jan;28(1):1-39.e14.

Anavekar NS et al. Echocardiography 2007 May;24(5):452-6.

Table 3. Cox Proportional-Hazards Analysis for Modeling Mortality in Patients with Pulmonary Arterial Hypertension

	Univariable Analysis		Multivariable Analysis	
	HR (95% Confidence Interval)	*P* Value	HR (95% Confidence Interval)	*P* Value
Women	1.80 (1.20–2.69)	0.004	...	...
Hypertension	0.36 (0.23–0.57)	<0.001	...	...
LA diameter, mm	0.96 (0.92–0.99)	0.022	...	...
E/A ratio	0.39 (0.22–0.69)	0.001	...	...
PA dilatation	6.28 (2.57–15.35)	<0.001	3.52 (1.35–9.19)	0.010
TR velocity, m/s	1.72 (1.39–2.13)	<0.001	...	...
Moderate–severe TR	13.62 (9.48–19.58)	<0.001	11.99 (5.15–27.93)	<0.001
RV systolic function*	6.42 (3.26–12.65)	<0.001	...	...
RV dilatation	6.34 (3.22–12.49)	<0.001	...	...
RV FAC, %	0.92 (0.89–0.95)	<0.001	0.97 (0.93–0.99)	0.038
PEf	3.67 (2.59–5.19)	<0.001	1.67 (1.17–2.39)	0.005
EID	5.74 (3.25–10.13)	<0.001	...	...
EIS	3.19 (2.41–4.24)	<0.001	...	...
MPI	10.72 (5.89–19.52)	<0.001	...	...
TAPSE, mm	0.95 (0.91–0.99)	0.011	...	...
RA volume	1.01 (1.004–1.008)	<0.001	...	...
IVC diameter, mm	1.05 (0.99–1.10)	0.070	...	...
IVRT	1.01 (1.01–1.02)	<0.001	...	...
PVR	0.90 (0.83–0.98)	0.019	...	...
RVOT AT, ms	0.99 (0.982–0.999)	0.031	...	...
Hemodynamic data				
RAP, mm Hg	1.11 (1.07–1.15)	<0.001	1.07 (1.03–1.11)	0.001
PASP, mm Hg	1.01 (1.01–1.02)	<0.001	...	...
PVR, dyn/s·per cm^{-5}	1.33 (1.27–1.39)	<0.001	1.10 (1.05–1.16)	<0.001
CI, L/min per m^2	0.16 (0.13–0.21)	<0.001	0.32 (0.24–0.43)	<0.001

Data are expressed as the mean value±SD or number (percentage) of patients. CI indicates cardiac index; E/A ratio, mitral inflow ratio; EID, left ventricular eccentricity index in end diastole; EIS, left ventricular eccentricity index in end systole; FAC, fractional area change; HR, hazard ratio; IVC, inferior vena cava; IVRT, isovolumic relaxation time; LA, left atrial; MPI, myocardial performance index; PA, pulmonary artery; PASP, PA systolic pressure; PEf, pericardial effusion; PVR, pulmonary vascular resistance; RA, right atrial; RAP, RA pressure; RV, right ventricle; RVSP, RV systolic pressure; TAPSE, tricuspid annular plane systolic excursion; RVOT AT, RV outflow tract acceleration time; and TR, tricuspid regurgitation.

*Normal and mild impairment of RV systolic function compared with moderate and severe dysfunction.

Pulmonary Arterial Hypertension

Echocardiographic and Hemodynamic Predictors of Survival in Precapillary Pulmonary Hypertension

Seven-Year Follow-Up

Julia Grapsa, MD, PhD; Maria Carmo Pereira Nunes, MD, PhD; Timothy C. Tan, MD, PhD; Ines Zimbarra Cabrita, PhD; Taryn Coulter, MSc; Benjamin C.F. Smith, MSc; David Dawson, MSc; J. Simon R. Gibbs, MD; Petros Nihoyannopoulos, MD

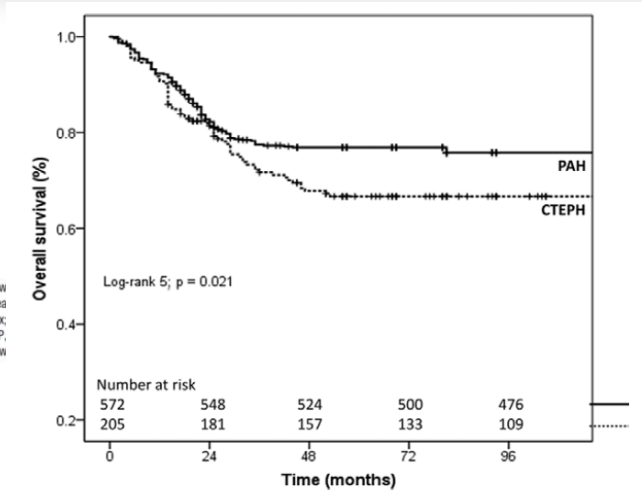


Figure 3. Kaplan–Meier Survival for both the groups: cause 1, pulmonary arterial hypertensive patients (PAH); cause 2, chronic thromboembolic pulmonary hypertensive patients (CTEPH). Kaplan–Meier plots for 4 echocardiographic indices.

Grapsa J et al. Circ Cardiovasc Imaging 2015 Jun;8(6):e002107

Strain PK

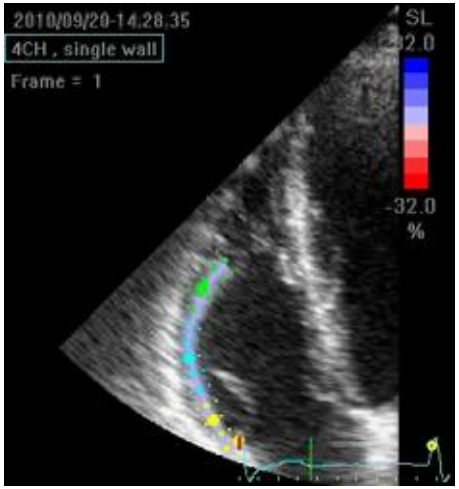
2D strain imaging is defined as the % change in myocardial deformation (RV longitudinal shortening). Strain is currently measured principally by the speckle-tracking (non-angle-dependent) approach.

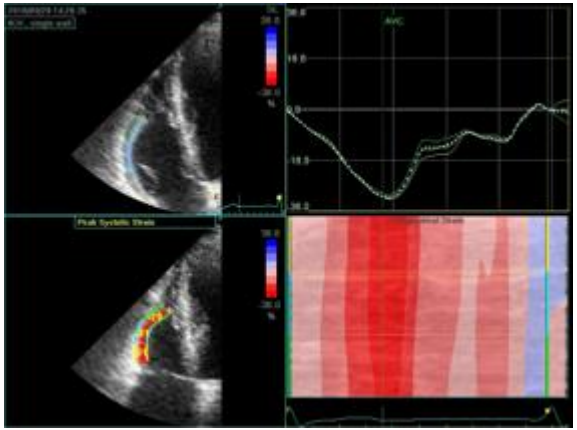
Potential pitfalls include technical challenges in image acquisition and analysis (need for high frame rates, high signal-to-noise, experienced observers for reproducible measurements).

Contemporary speckle-tracking algorithms have enhanced reproducibility and are beginning to yield **clinically relevant** observations:

1. In a large cohort of 575 patients with pulmonary arterial hypertension, free wall longitudinal strain by 2D speckle tracking was predictive of functional capacity and 18-month mortality.
2. In 200 patients with heart failure and seemingly normal RV systolic function (TAPSE >16 mm), a substantial proportion of patients was found to have abnormal RV free wall strain indicative of subclinical RV dysfunction, which was in turn predictive of death and hospitalization.
3. To identify signs of RV infarction in patients presenting with acute myocardial infarction, RV free wall strain was superior to conventional echocardiographic parameters.

The **normal reference limit** for 2DS of the RV free wall is -23%/-20%.





ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2019) 20, 475–484
doi:10.1093/ehjci/jey120

Prognostic value of right ventricular longitudinal strain in patients with pulmonary hypertension: a systematic review and meta-analysis

Hugo G. Hulshof[1], Thijs M.H. Eijsvogels[1,2], Geert Kleinnibbelink[1,2], Arie P. van Dijk[3], Keith P. George[2], David L. Oxborough[2], and Dick H.J. Thijssen[1,2]*

Figure 2 Forrest plot summarizing the effect of a (relative) reduction of RVLS on a combined endpoint of mortality and PH-related events in PH patients. The red squares present the weighted effect size and the black lines the 95% CIs. The size of the red squares indicate the weight of the study.

Eleven studies; 1169 patients with PH (67% female, 0.6–3.8 years follow-up).

combined endpoint (mortality and PH-related events) - higher risk with a

relative reduction of RVLS of 19% [HR 1.22, 95% confidence interval (CI) 1.07–1.40]

all-cause mortality - higher risk with a ***relative reduction of RVLS of 22%*** [HR 2.96, 95% CI 2.00–4.38]

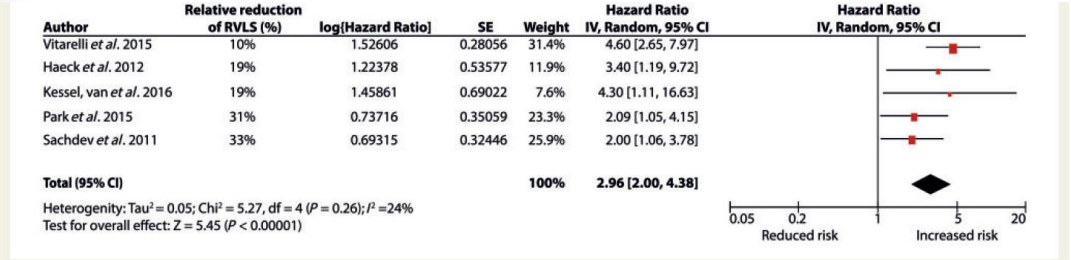


Figure 3 Forrest plot summarising the effect of a (relative) reduction of RVLS on all-cause mortality in PH patients. The red squares present the weighted effect size and the black lines the 95% CIs. The size of the red squares indicate the weight of the study. The black diamond presents the mean weighted HR.

Right Ventricular Dysfunction in Systemic Sclerosis–Associated Pulmonary Arterial Hypertension

Ryan J. Tedford, James O. Mudd, Reda E. Girgis, Stephen C. Mathai, Ari L. Zaiman, Traci Housten-Harris, Danielle Boyce, Benjamin W. Kelemen, Anita C. Bacher, Ami A. Shah, Laura K. Hummers, Fredrick M. Wigley, Stuart D. Russell, Rajeev Saggar, Rajan Saggar, W. Lowell Maughan, Paul M. Hassoun, and David A. Kass

Originally published 24 Jun 2013 | https://doi.org/10.1161/CIRCHEARTFAILURE.112.000008 | Circulation: Heart Failure. 2013;6:953–963

Other version(s) of this article

Abstract

Background—

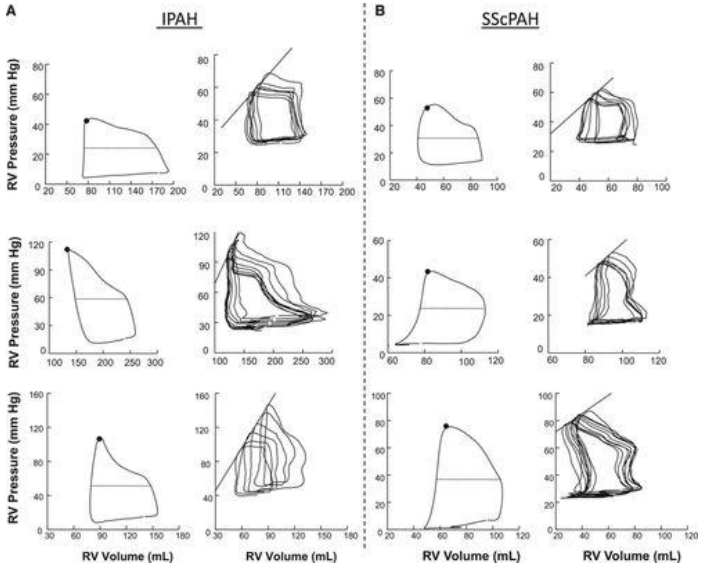
Systemic sclerosis–associated pulmonary artery hypertension (SScPAH) has a worse prognosis compared with idiopathic pulmonary arterial hypertension (IPAH), with a median survival of 3 years after diagnosis often caused by right ventricular (RV) failure. We tested whether SScPAH or systemic sclerosis–related pulmonary hypertension with interstitial lung disease imposes a greater pulmonary vascular load than IPAH and leads to worse RV contractile function.

Methods and Results—

We analyzed pulmonary artery pressures and mean flow in 282 patients with pulmonary hypertension (166 SScPAH, 49 systemic sclerosis–related pulmonary hypertension with interstitial lung disease, and 67 IPAH). An inverse relation between pulmonary resistance and compliance was similar for all 3 groups, with a near constant resistance×compliance product. RV pressure–volume loops were measured in a subset, IPAH (n=5) and SScPAH (n=7), as well as SSc without PH (n=7) to derive contractile indexes (end-systolic elastance [E_{es}] and preload recruitable stroke work [M_{sw}]), measures of RV load (arterial elastance [E_a]), and RV pulmonary artery coupling (E_{es}/E_a). RV afterload was similar in SScPAH and IPAH (pulmonary vascular resistance=7.0±4.5 versus 7.9±4.3 Wood units; E_a=0.9±0.4 versus 1.2±0.5 mm Hg/mL; pulmonary arterial compliance=2.4±1.5 versus 1.7±1.1 mL/mm Hg; P>0.3 for each). Although SScPAH did not have greater vascular stiffening compared with IPAH, RV contractility was more depressed (E_{es}=0.8±0.3 versus 2.3±1.1, P<0.01; M_{sw}=21±11 versus 45±16, P=0.01), with differential RV-PA uncoupling (E_{es}/E_a=1.0±0.5 versus 2.1±1.0; P=0.03). This ratio was higher in SSc without PH (E_{es}/E_a=2.3±1.2; P=0.02 versus SScPAH).

Conclusions—

RV dysfunction is worse in SScPAH compared with IPAH at similar afterload, and may be because of intrinsic systolic function rather than enhanced pulmonary vascular resistive and pulsatile loading.



Right ventricular (RV) pressure–volume loops in 6 patients, 3 with (**A**) idiopathic pulmonary arterial hypertension (IPAH) and 3 with (**B**) systemic sclerosis–associated pulmonary artery hypertension (SScPAH).
Steady-state loops (**left**) in both cohorts show RV pressure rising throughout ejection and peaking at end-systole, consistent with increased RV afterload from PAH. The black dot identifies the end-systolic pressure–volume point, and the dashed line mean loop width (stroke volume).
E_a was determined by the ratio of end-systolic pressure to SV. In the loops generated during Valsalva maneuver (**right**), the data are all shifted upward because of the rise in intrathoracic pressure, but while this is held, phase 2 of the Valsalva maneuver results in a beat-to-beat decline in filling volume, various PV relations including the end-systolic pressure–volume relationship (black line). The slope is end-systolic elastance (E_{es}).

Jaké jsou terapeutické možnosti ovlivnění afterloadu/preloadu pravé komory a její morfologie/funkce a jak můžeme pravou komoru monitorovat?

1. Význam pravé komory u plicní arteriální hypertenze.
2. Jak na hodnocení její funkce a morfologie?
3. **Jaké jsou terapeutické možnosti ovlivnění afterloadu/preloadu pravé komory a její morfologie/funkce a jak můžeme pravou komoru monitorovat?**
4. Je reverzní remodelace pravé komory dostatečný terapeutický cíl plicní arteriální hypertenze?

Riziková stratifikace u PAH

Stanovení prognózy → Výběr optimální terapie → Monitorace terapeutické odpovědi → Načasování eskalace terapie

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5–20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[a]
WHO-FC	I, II	III	IV
6MWD[c]	>440 m	165–440 m	<165 m
CPET	Peak VO_2 >15 mL/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 mL/min/kg (35–65% pred.) VE/VCO_2 slope 36–44	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope >44
Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mmHg Moderate or large pericardial effusion
cMRI[e]	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37% SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mmHg CI ≥2.5 L/min/m^2 SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 L/min/m^2 SVI 31–38 mL/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 L/min/m^2 SVI <31 mL/m^2 SvO_2 <60%

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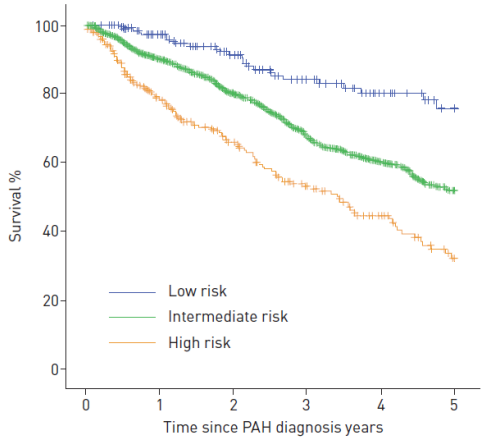

Table 18 Variables used to calculate the simplified four-strata risk-assessment tool

Determinants of prognosis	Low risk	Intermediate–low risk	Intermediate–high risk	High risk
Points assigned	1	2	3	4
WHO-FC	I or II[a]	-	III	IV
6MWD, m	>440	320–440	165–319	<165
BNP or NT-proBNP,[a] ng/L	<50 <300	50–199 300–649	200–800 650–1100	>800 >1100

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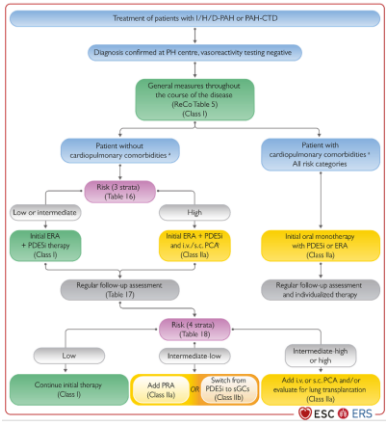
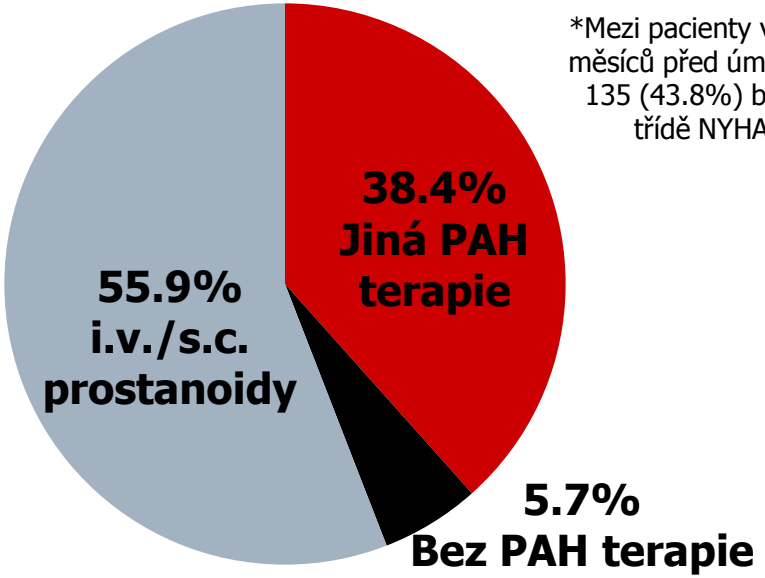


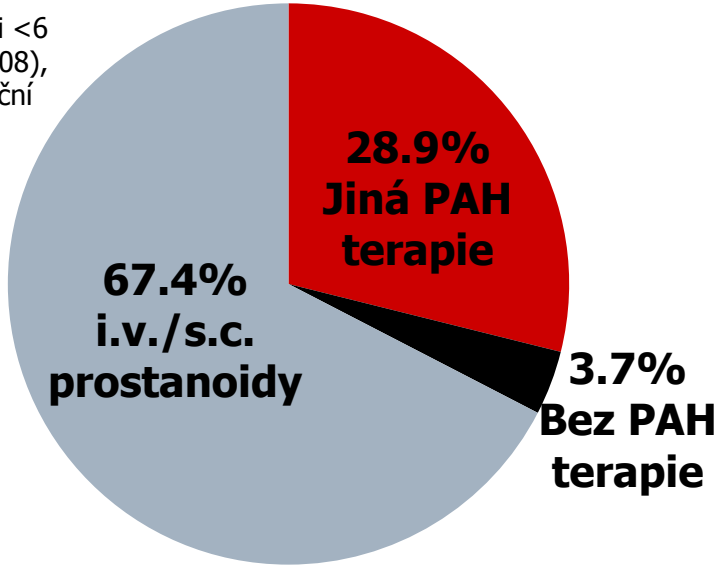
Léčba PAH v době úmrtí

Všichni pacienti (*n* = 487)



*Mezi pacienty vyšetřenými <6 měsíců před úmrtím (*n* = 308), 135 (43.8%) bylo ve funkční třídě NYHA/WHO IV.

NYHA IV* pacienti (*n* = 135)

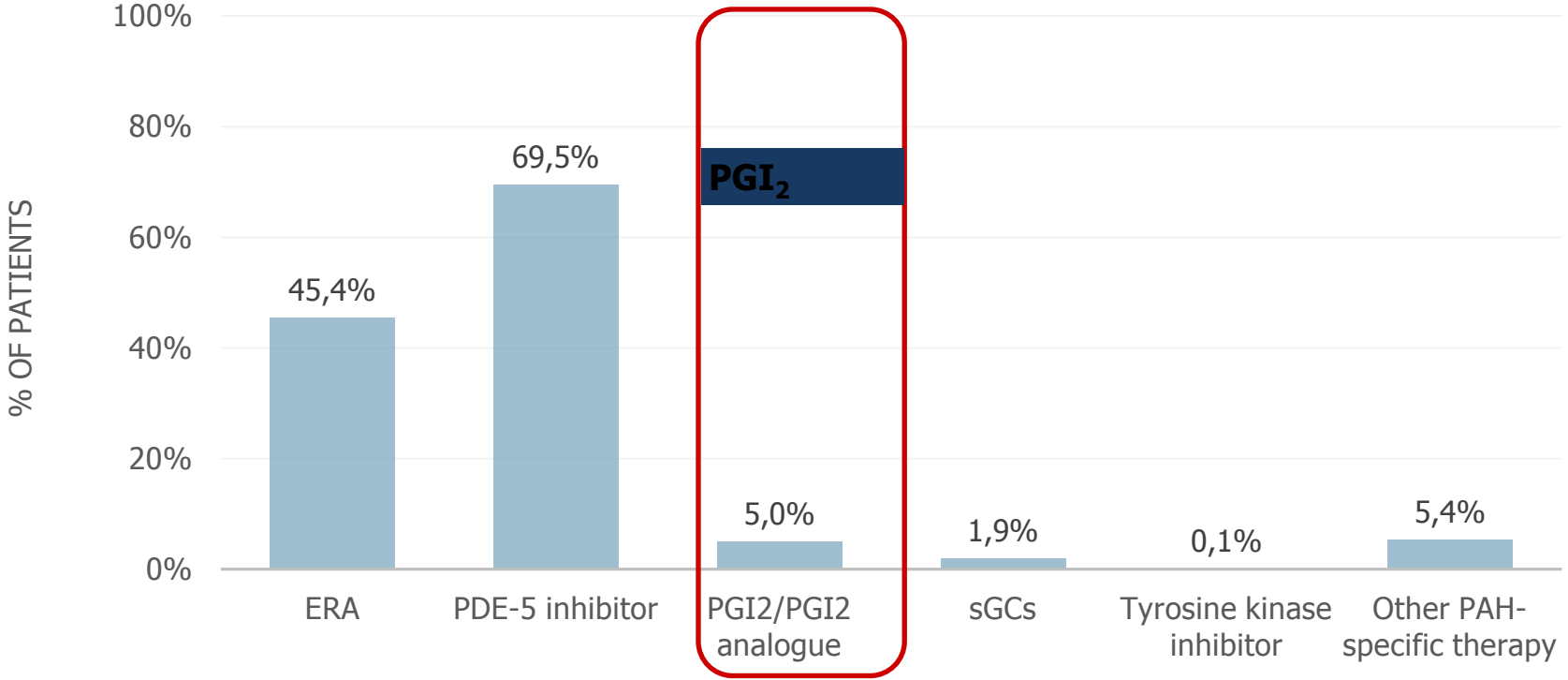


V době úmrtí souvisejícího s PAH :

- U **všech pacientů**, téměř polovina (44.1%) neužívalo parenterální prostanoidy
- U **NYHA/WHO IV pacientů**, téměř třetina (32.6%) neužívalo parenterální prostanoidy

Farber HW, *et al. J Heart Lung Transplant* 2013; 32:1114-22.

Podíl pacientů léčených jednotlivými třídami specifických léků PAH v době randomizace



COMPERA. Annual report: Prospective registry of newly initiated therapies for pulmonary hypertension 2014.

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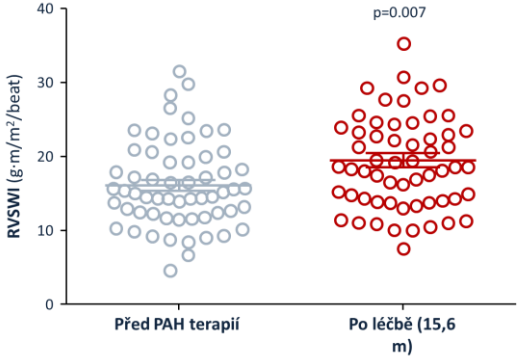
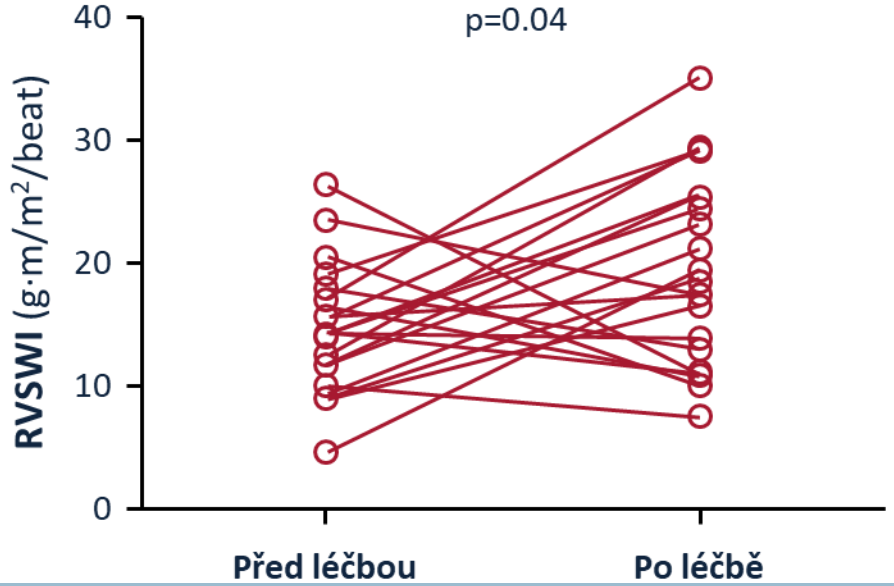
JACC Heart Fail. 2013 August 1; 1(4): 300–307. doi:10.1016/j.jchf.2013.05.004.

Prostanoids But Not Oral Therapies Improve Right Ventricular Function in Pulmonary Arterial Hypertension

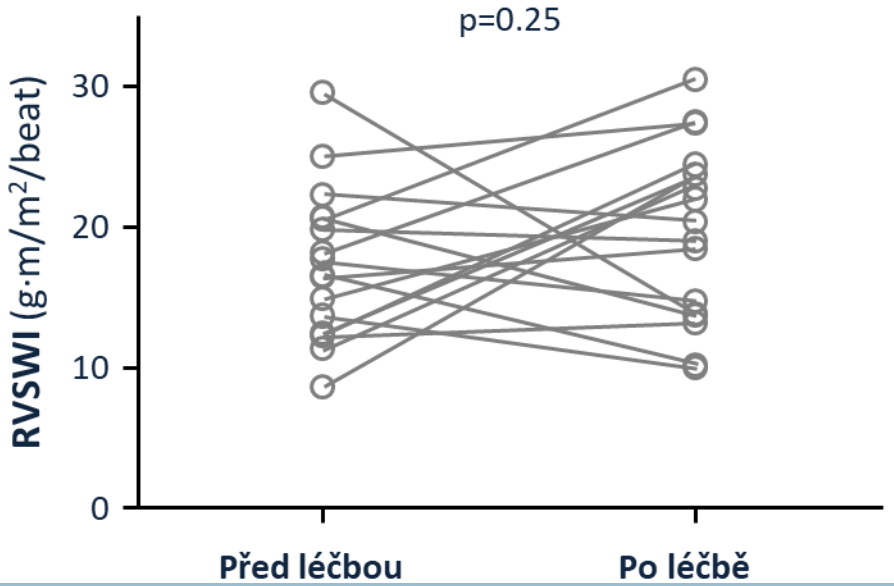
Evan L. Brittain, MD*, Meredith E. Pugh, MD, MSCI†, Lisa A. Wheeler, BS†, Ivan M. Robbins, MD†, James E. Loyd, MD†, John H. Newman, MD†, Eric D. Austin, MD, MSCI‡, and Anna R. Hemnes, MD†



Terapie prostanoidy



Perorální terapie



HR, heart rate; PAH, pulmonary arterial hypertension; PAP, pulmonary arterial pressure; RAP, right atrial pressure; RHC, right heart catheterisation; RV, right ventricle; RVSWI, right ventricular stroke work index
Brittain et al. *JACC Heart Fail*. 2013;1:300-307

Contents lists available at ScienceDirect

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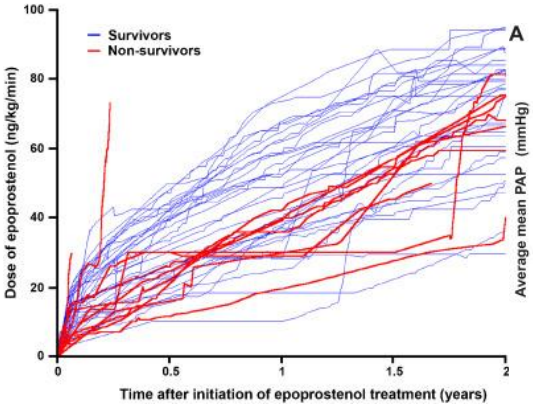
journal homepage: www.elsevier.com/locate/jjcc

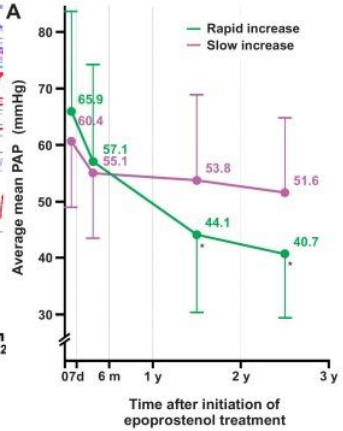
Original article

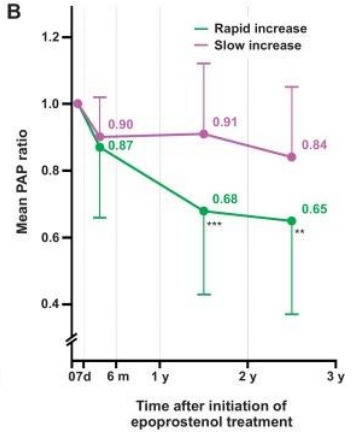
Rapid and high-dose titration of epoprostenol improves pulmonary hemodynamics and clinical outcomes in patients with idiopathic and heritable pulmonary arterial hypertension

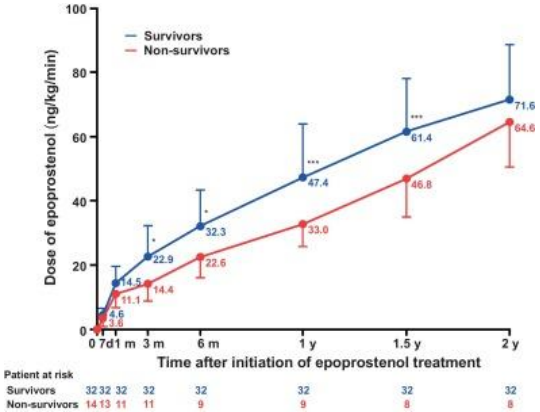
Naoto Tokunaga (MD)[a,b,c], Aiko Ogawa (MD, PhD)[b], Hiroshi Ito (MD, PhD, FJCC)[c], Hiromi Matsubara (MD, PhD)[a,b,*]

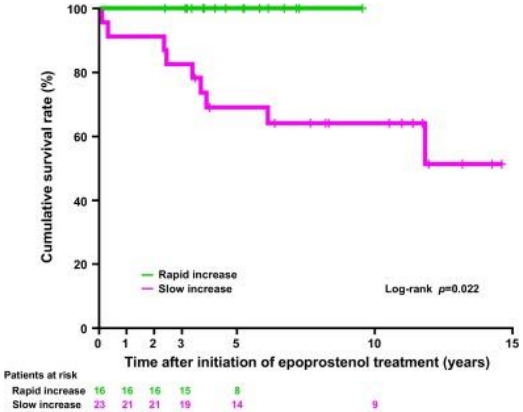
	Survivors (n=32)	Non-survivors (n=14)	p value
Baseline			
Age, years	28 ± 9	31 ± 9	0.301
Female, n (%)	24 (75)	10 (71)	1.000
BMI, kg/m^2	21.5 ± 4.6	21.7 ± 4.1	0.849
HPAH, n (%)	10 (31)	1 (7)	0.133
WHO FC, n (%)			
III	21 (66)	3 (21)	0.01
IV	11 (34)	11 (79)	
HR, bpm	79 ± 17	93 ± 13	0.010
6MWD, m	337 ± 85	206 ± 144	0.006
BNP, pg/ml	334 ± 370	454 ± 250	0.272
mPAP, mmHg	63 ± 15	62 ± 14	0.850
CO, l/min	3.5 ± 1.1	2.7 ± 1.4	0.066
PVR, dyn s cm^{-5}	1414 ± 579	1779 ± 746	0.107
Diagnosis-oral PAH-targeted drugs, days	222 ± 475	413 ± 680	0.279
Diagnosis-epoprostenol, days	473 ± 698	1010 ± 979	0.080
Concomitant PAH-targeted drugs, n (%)			
Endothelin receptor antagonist	15 (47)	7 (50)	1.000
PDE-5 inhibitor	10 (31)	4 (29)	1.000
Post-treatment			
Duration of epoprostenol therapy, days	2609 ± 1325	968 ± 1190	<0.001
Maximum dose of epoprostenol, ng/kg/min	105.2 ± 39.3	78.9 ± 67.3	0.191





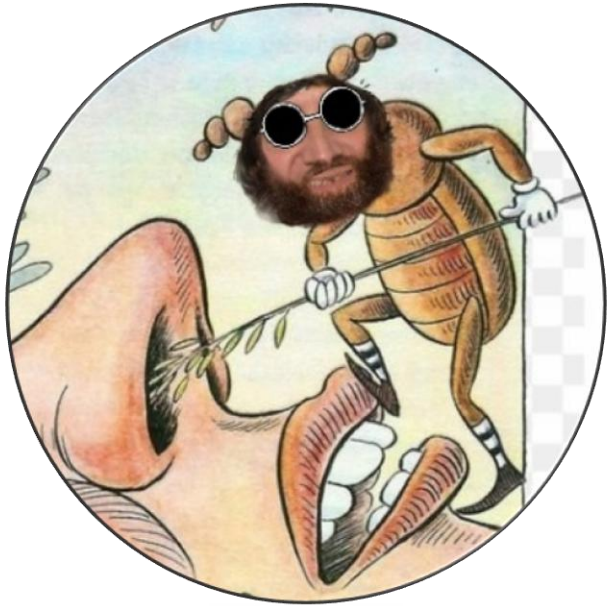






Je reverzní remodelace pravé komory dostatečný terapeutický cíl plicní arteriální hypertenze?

1. Význam pravé komory u plicní arteriální hypertenze.
2. Jak na hodnocení její funkce a morfologie?
3. Jaké jsou terapeutické možnosti ovlivnění afterloadu/preloadu pravé komory a její morfologie/funkce a jak můžeme pravou komoru monitorovat?
4. **Je reverzní remodelace pravé komory dostatečný terapeutický cíl plicní arteriální hypertenze?**



Reverzní remodelace PK

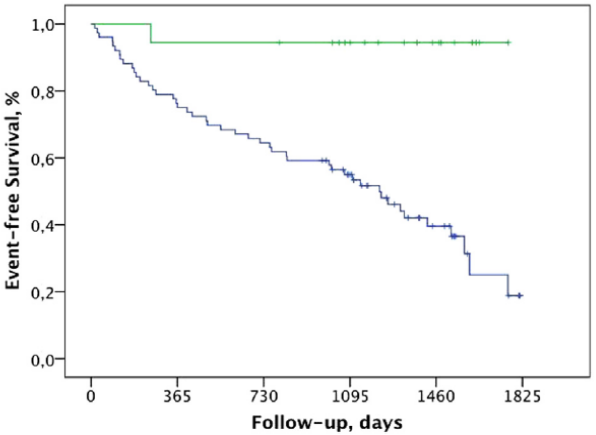


Figure 6 Event-free survival of patients with right heart reverse remodeling (green line; echo score, 4–4.5) compared with patients without right heart reverse remodeling (blue line; echo score, < 4): 94%, 94%, and 94% vs 75%, 55%, and 24% after 1, 3, and 5 years of follow-up, respectively, from the 1-year re-evaluation (p = 0.0001).

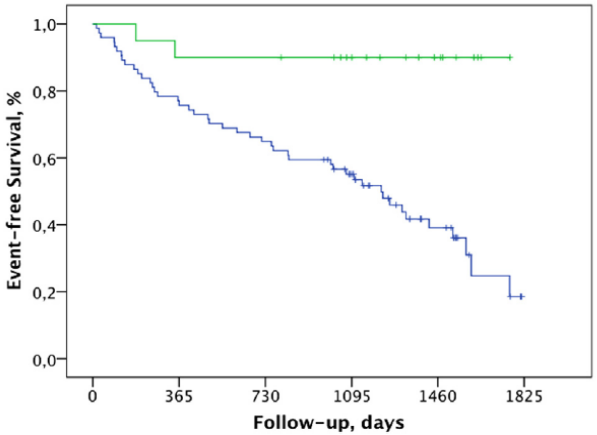


Figure 7 Event-free survival of patients with right heart reverse remodeling (green line) compared with patients without right heart reverse remodeling RHRR (blue line), defined by the presence of the upper tertile of all 3 echo parameters: 88%, 83%, and 83% vs 76, 55%, and 23% after 1, 3, and 5 years of follow-up, respectively, from the 1-year reevaluation (p = 0.001).

decrease in RV enddiastolic area (RVEDA) [-2,45 cm^2 (sensitivity 93 %; specificity 40 %)], **right atrial (RA) area** [-1.30 cm^2 (sensitivity 75 %; specificity 63 %)], **and left ventricular systolic eccentricity index (LV-EIs)** [-0.12 (sensitivity 88 %; specificity 44 %)]

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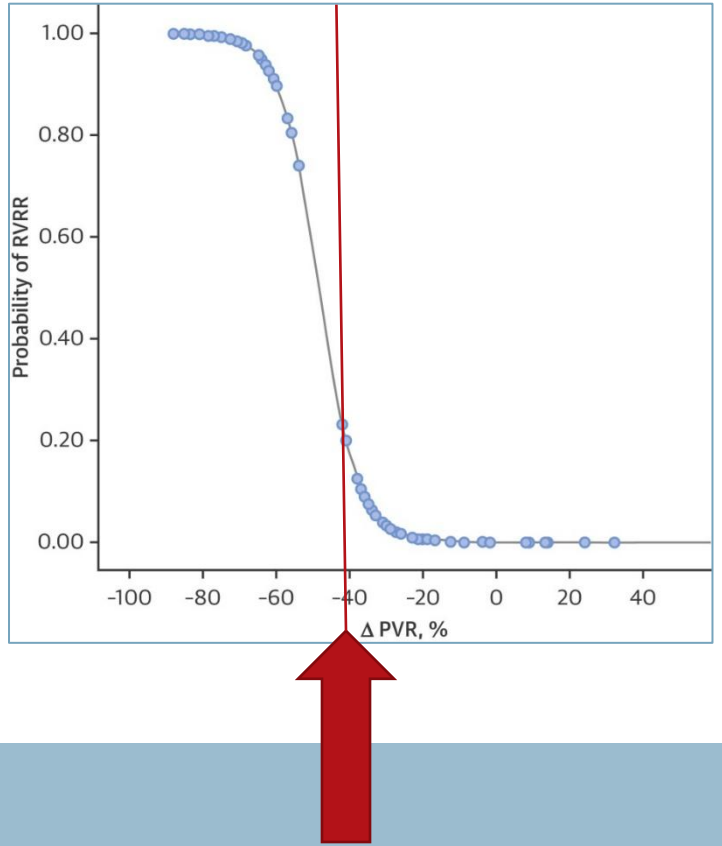
The Official Publication of the International Society for Heart and Lung Transplantation

FEATURED PAPERS | VOLUME 37, ISSUE 2, P195-205, FEBRUARY 01, 2018

Prognostic relevance of right heart reverse remodeling in idiopathic pulmonary arterial hypertension

Roberto Badagliacca, MD, PhD • Roberto Poscia, MD, PhD • Beatrice Pezzuto, MD • ...
Roberto Torre, RN, MSN • Francesco Fedele, MD • Carmine Dario Vizza, MD • Show all authors

Published: October 02, 2017 • DOI: https://doi.org/10.1016/j.healun.2017.09.026 • Check for updates



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Pulmonary Hypertension

Progressive Right Ventricular Dysfunction in Patients With Pulmonary Arterial Hypertension Responding to Therapy

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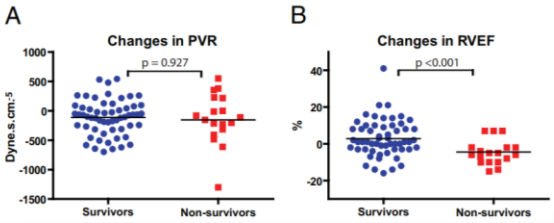
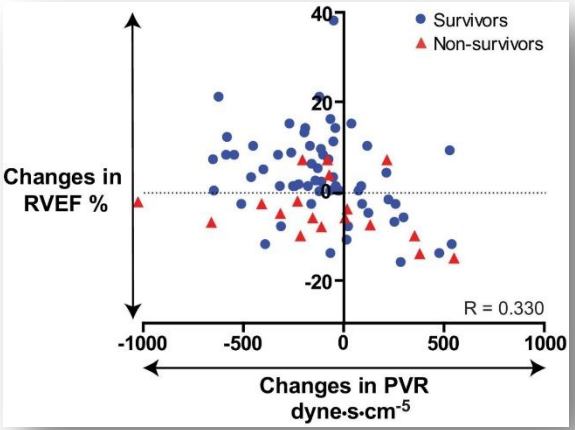
Amsterdam, the Netherlands; and Richmond, Virginia





Odhad systolického tlaku v plicnici - trikuspidální regurgitační gradient

základní parametr pro screening PH pomocí echokardiografie

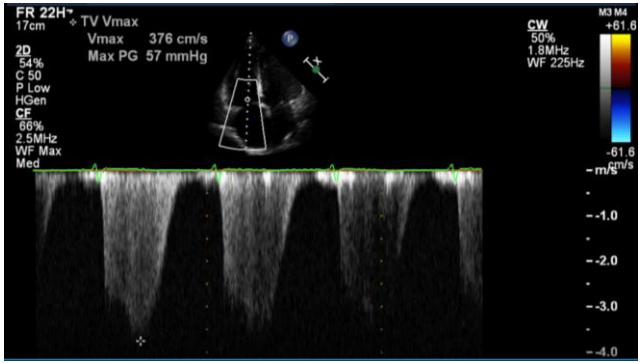
pro **hodnocení prognózy a rozhodnutí o terapii nemá význam**

vzestup odhadovaného sPAP nemusí nutně ukazovat progresi onemocnění, pokles odhadovaného sPAP nemusí nutně odpovídat zlepšení PAP

invazivně měřený mPAP má rovněž poměrně malý prognostický význam (kromě responderů akutní vazoreaktivity)

Tabulka 4A – Pravděpodobnost zjištění plicní hypertenze echokardiografickým vyšetřením symptomatických pacientů s podezřením na plicní hypertenzi

Maximální rychlost proudu krve při nedomykavosti trojcípé chlopně (m/s)	Přítomnost jiných „známek PH" při echokardiografickém vyšetření[a]	Možnost plicní hypertenze podle echokardiografického vyšetření
≤ 2,8 nebo neměřitelná	Ne	Nízká
≤ 2,8 nebo neměřitelná	Ano	Středně vysoká
2,9–3,4	Ne	
2,9–3,4	Ano	Vysoká
> 3,4	Není nutno provádět	



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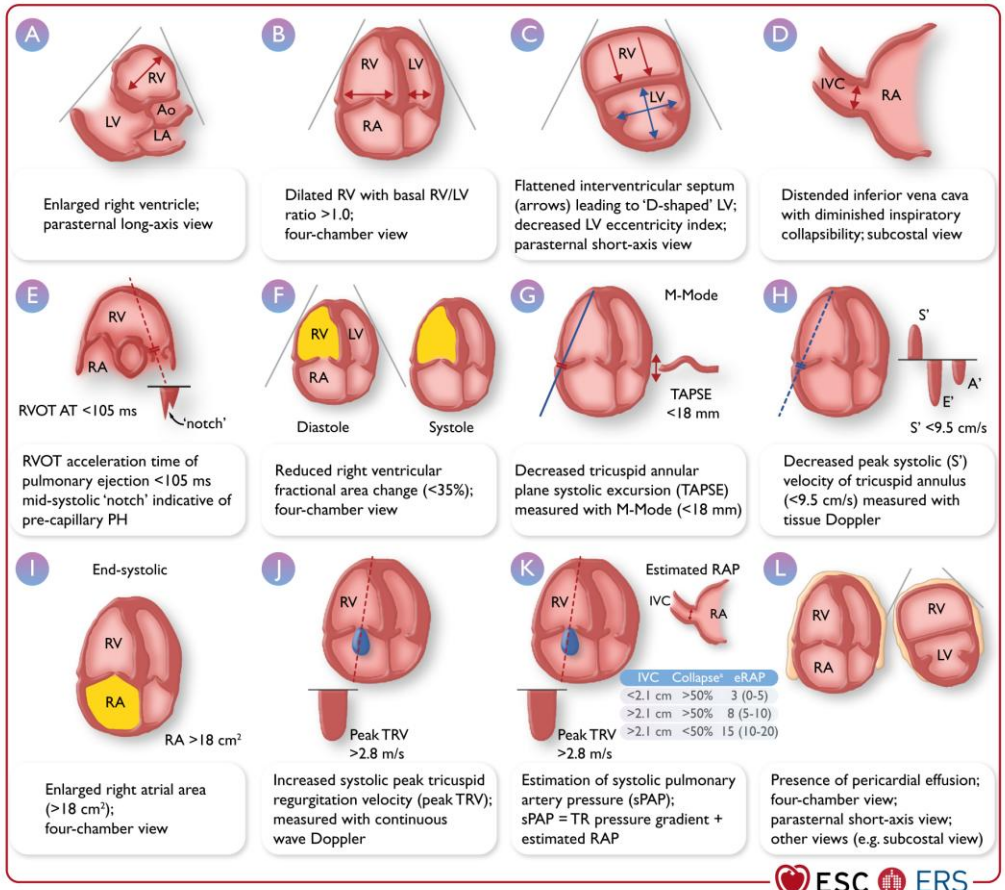
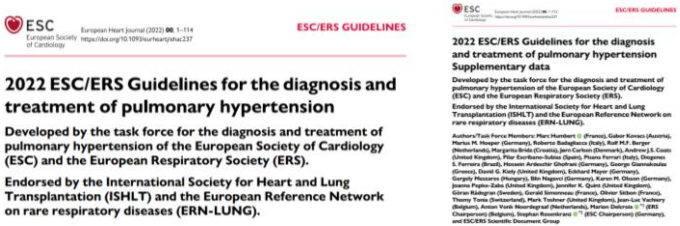



ESC European Society of Cardiology
European Heart Journal (2022) 00, 1–114
https://doi.org/10.1093/eurheartj/ehac237
ESC/ERS GUIDELINES

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

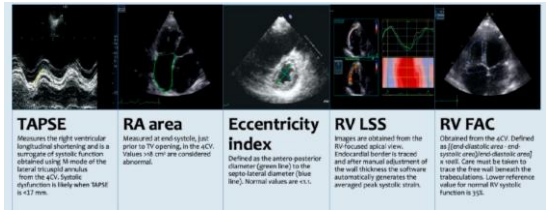
Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG).

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension
Supplementary data

A: The ventricles	B: Pulmonary artery	C: Inferior vena cava and RA
RV/LV basal diameter/ area ratio >1.0	RVOT AT <105 ms and/or mid-systolic notching	IVC diameter >21 mm with decreased inspiratory collapse (<50% with a sniff or <20% with quiet inspiration)
Flattening of the interventricular septum (LVEI >1.1 in systole and/or diastole)	Early diastolic pulmonary regurgitation velocity >2.2 m/s	RA area (end-systole) >18 cm^2
TAPSE/sPAP ratio <0.55 mm/mmHg	PA diameter >AR diameter PA diameter >25 mm	

Závěry

1. Vyčerpání kompenzačních mechanismů pravé komory (PK) s následným pravostranným srdečním selháním je vedoucí příčina úmrtí u pacientů s PAH.
2. Funkce PK (adaptace na zvýšený afterload, zachování funkce a CO) determinuje funkční status a klinický průběh onemocnění.
3. Multimodalitní hodnocení morfologie a funkce pravé komory je důležitou součástí každého echokardiografického vyšetření.
4. Dysfunkce PK je u SScPAH ve srovnání s iPAH při identickém afterloadu horší a může být způsobena spíše vlastní systolickou funkcí než zvýšenou rezistencí plicních cév a pulzatilním zatížením. Tato zjištění naznačují klinicky silentní dysfunkci myokardu PK, která může předcházet manifestní PAH a může sloužit jako důležitý cíl pro specifickou léčbu.
5. Zachování/zlepšení funkce PK jako zásadní terapeutický cíl.



DĚKUJEME ZA POZORNOST

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