Stanford MEDICINE | Pediatrics
Cardiology

Right Ventricular Stroke Work Correlates With Outcomes in Pediatric Pulmonary Arterial Hypertension (PAH) Patients

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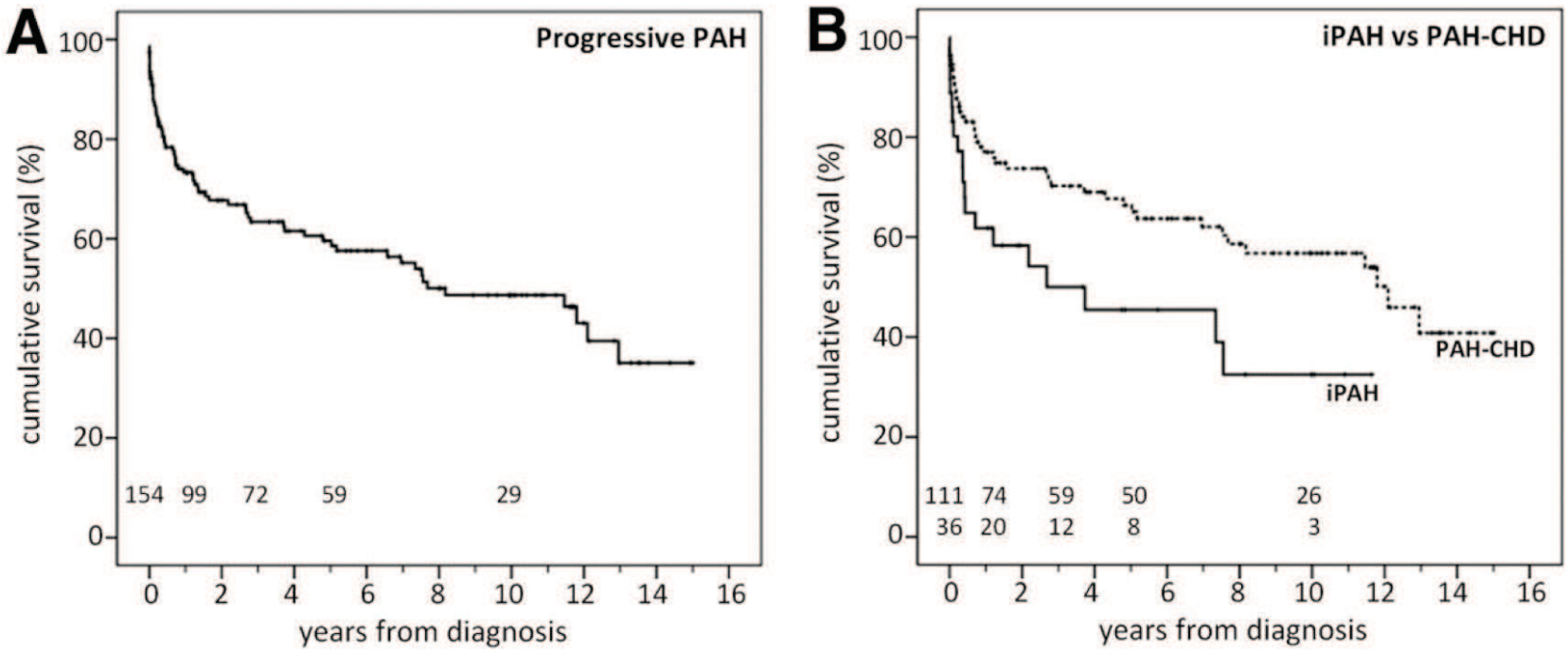
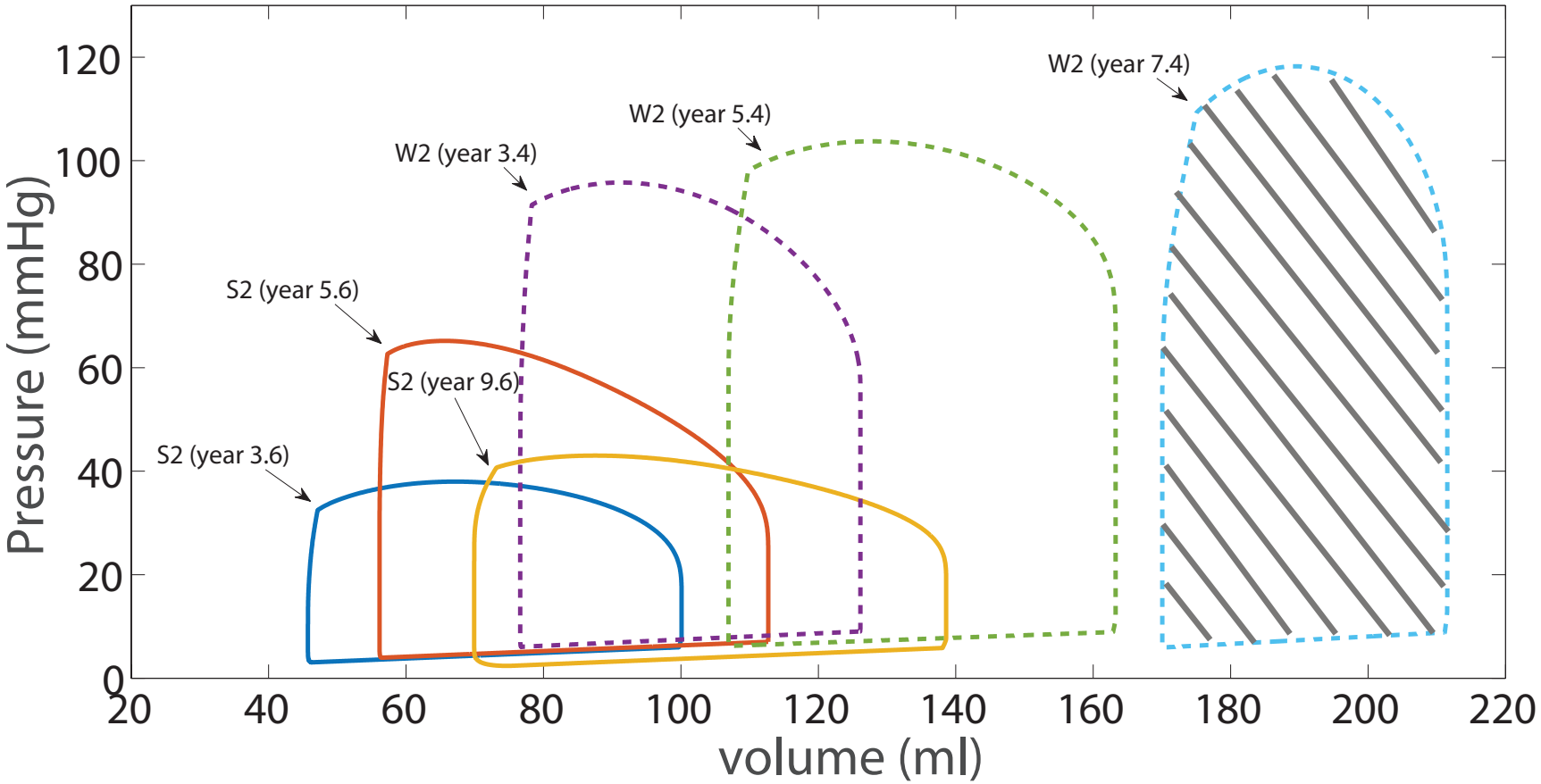
Introduction

- Pulmonary arterial hypertension (PAH): PAP>25 mmHg and PVR $>$ 3 WU
- Progression is highly variable and poorly understood (5-year survival rates: 60-70%).
- Endpoints are not well characterized in children (e.g. 6MW).
- Need improved clinical markers



Van Loon et al., Circulation, 2011

- Pressure-volume (P-V) loops characterize ventricular performance.
- Right ventricular stroke work (RVSW): area enclosed by the P-V loop



- Pressure-volume (P-V) loops characterize ventricular performance.
- Right ventricular stroke work (RVSW): area enclosed by the P-V loop
- P-V loops are difficult to measure routinely.

Magnetic Resonance Imaging Analysis of Right Ventricular Pressure-Volume Loops

In Vivo Validation and Clinical Application in Patients With Pulmonary Hypertension

Titus Kuehne, MD; Sevim Yilmaz, MD; Paul Steendijk, PhD; Phillip Moore, MD; Maarten Groenink, MD; Maythem Saaed, PhD; Oliver Weber, PhD; Charles B. Higgins, MD; Peter Ewert, MD; Eckard Fleck, MD; Eike Nagel, MD; Ingram Schulze-Neick, MD; Peter Lange, MD

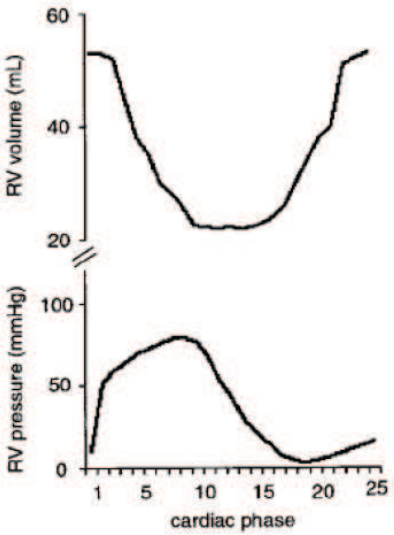


Figure 1. Representative MRI-derived volume-time and pressure-time curves of patient with RV pressure overload.

TABLE 2. Indexes of Ventricular Systolic Pump Function and Hypertrophy

	Control Group	PHT Group
RV		
EF, %	56.4±4.2	62.3±5.1*
SV, mL/m^2	33.4±3.9	28.2±4.9*
CI, L · min^{-1} · m^{-2}	2.9±0.4	2.2±0.5*
EDV, mL/m^2	59.5±4.2	46.2±5.9*
ESV, mL/m^2	26.2±2.5	18.3±3.1*
Free-wall myocardial mass, g (mg)	21.6±5.9	39.1±6.1*

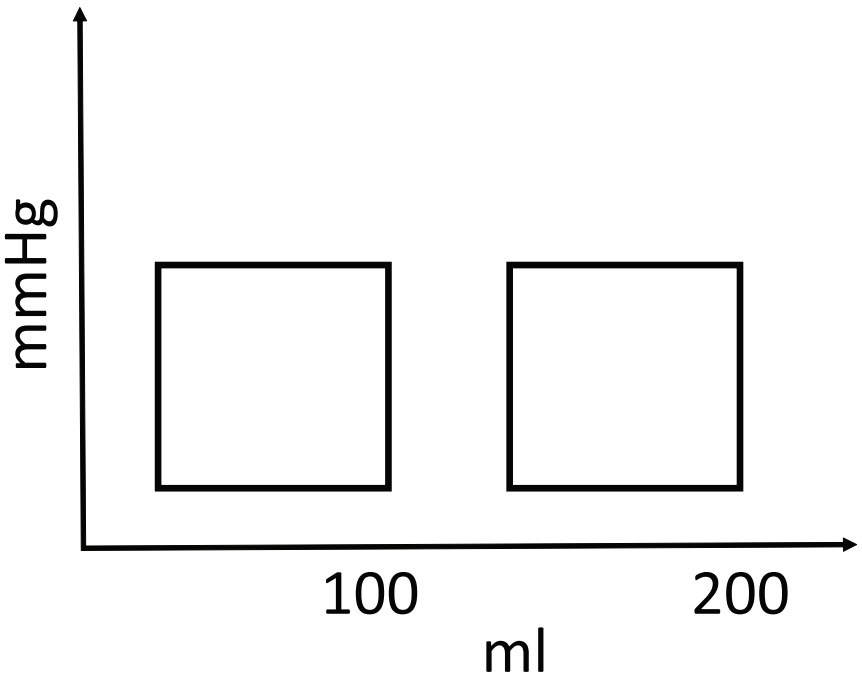
TABLE 3. Indexes of RV Contractile Function and VA Coupling

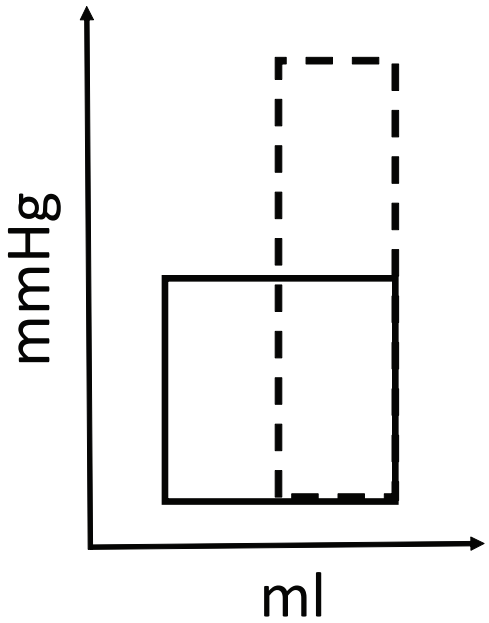
	Control Group	PHT Group
Fiber stress at end systole, mm Hg	125±23	280±31*
Fiber stress at end diastole, mm Hg	15±4	23±6
E_{max_i}, mm Hg · mL^{-1} · 100 g^{-1}	5.2±0.9	9.2±1.1*
E_a, mm Hg/mL	0.6±0.3	2.7±0.6*
E_{max}/E_a	1.9±0.4	1.1±0.3*

*Significantly different ($P<0.05$) between control and PHT groups.

Kuehne et al., Circulation, 2004

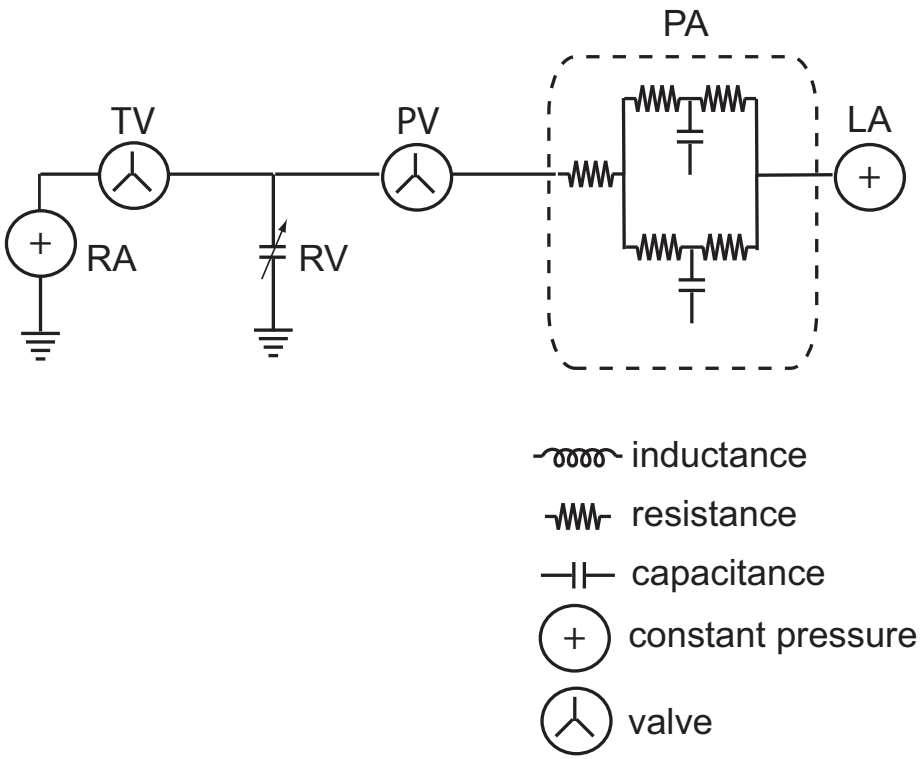
- Pressure-volume (P-V) loops characterize ventricular performance.
- Right ventricular stroke work (RVSW): area enclosed by the P-V loop
- P-V loops are difficult to measure routinely.
- Goals: assess RVSW in pediatric patients with PAH:
- $RVSW = \int_0^T P(t)V(t)dt$, $RVSW_{BSA} = \frac{RVSW}{BSA^{1.407}}$
- $RVSW_{EF} = \frac{RVSW_{BSA}}{EF}$





Methods

- Use computational modeling+routinely measured clinical data
  - Lumped parameter model (LPM): use electric circuits to model hemodynamics
  - Right heart catheterization (RHC): RV and PA pressures
  - MRI: RV volumes (EDV and ESV) and PA flow
- Tune LPM to match RHC/MRI measurements by optimization.



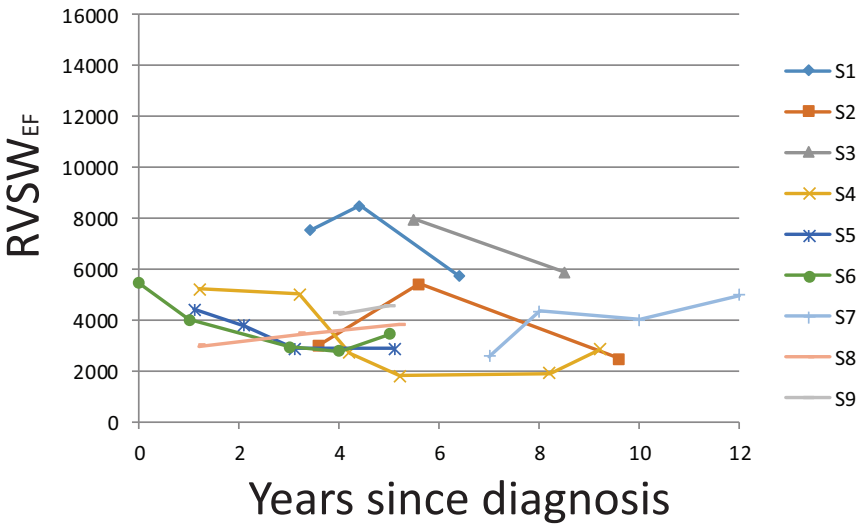
Study Design

	Stable n=9	Worsening* n=8
Male	n=4	n=4
Age (years)	10.7(4.9-16.3)	8.4(4.4-13.5)
BSA (m^2)	1.0(0.6-1.7)	0.9(0.7-1.8)
IPAH	n=5	n=7
Prostacyclin therapy	n=3	n=7
Follow-up (years)	4.2(1.2-8)	3.7(1.1-6)
PVRI ($WU \times m^2$)	6.8 (5.2-31.6)	14.8 (8.1-24.7)
RVEF (%)	48(30-55)	48(18-54)

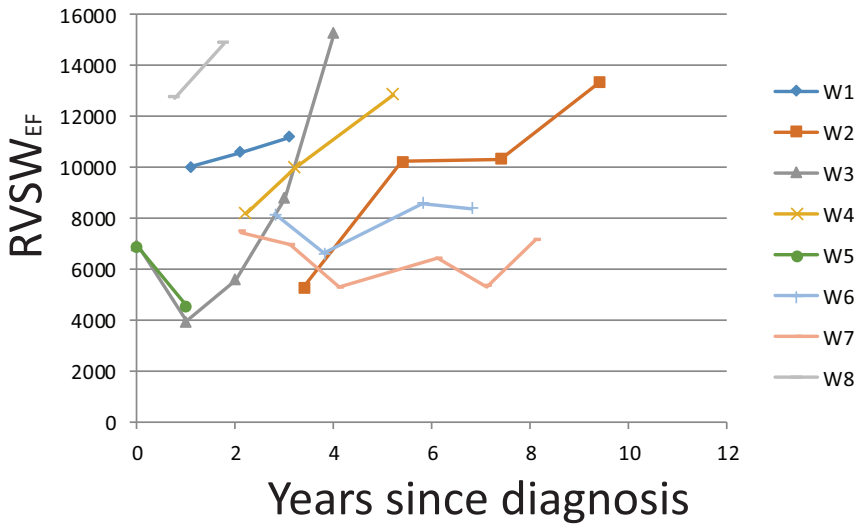
- Inclusion criteria
  - Age<18
  - IPAH or PAH-CHD
  - multiple paired RHC/MRI (n≥2)
- 17 patients with 61 data points
- *Clinical worsening: death, listed or considered for transplantation, poor hemodynamic responses to maximal therapy

Results

a) Stable



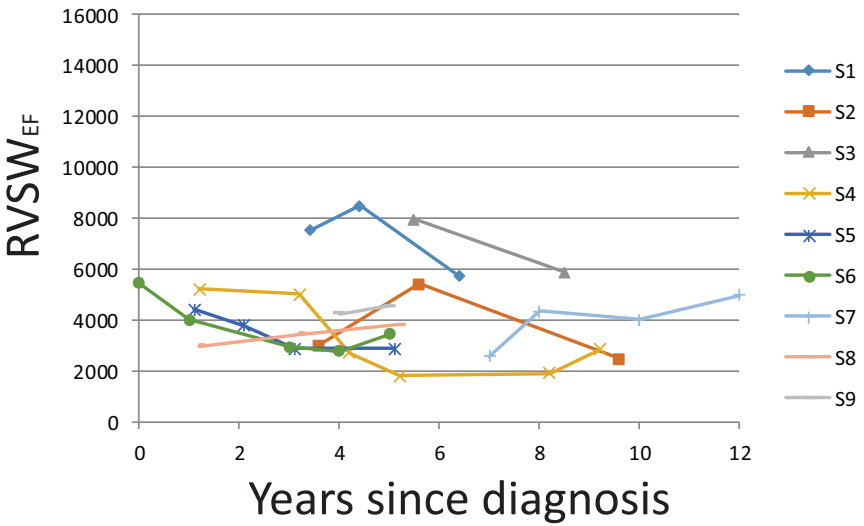
b) Worsening



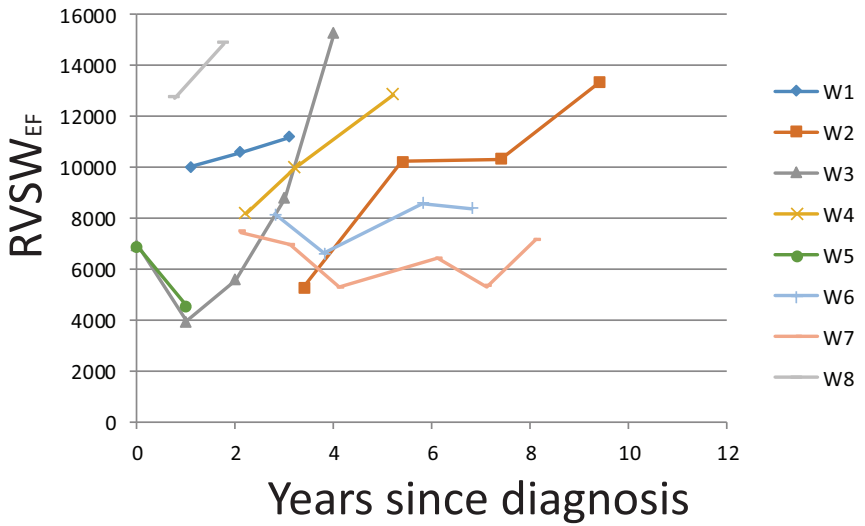
- Patients with clinical worsening have increased RVSW.

Results

a) Stable



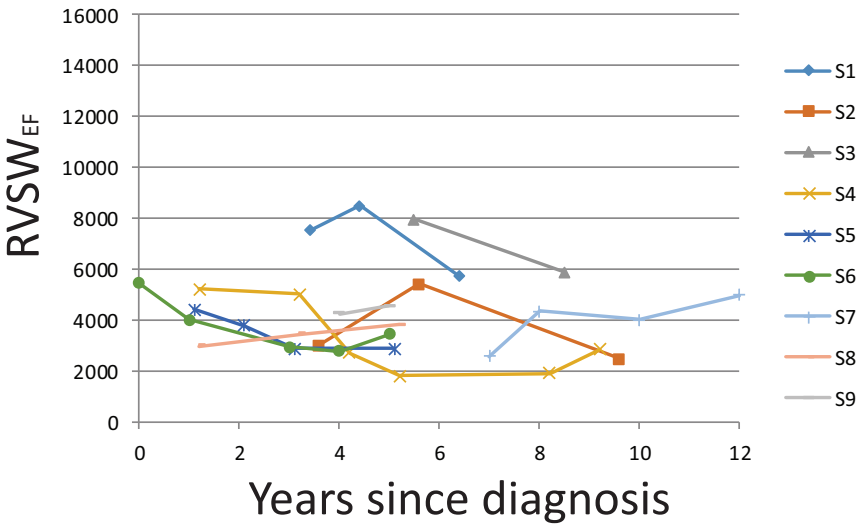
b) Worsening



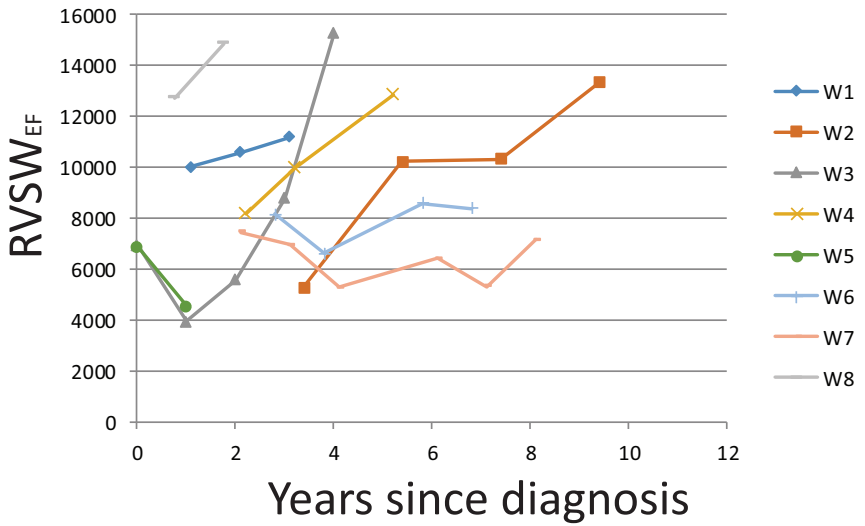
- Patients with clinical worsening have increased RVSW.
- Quantities of interest are grouped and compared by outcomes (stable vs clinical worsening) within 2 years following RHC/MRI.

Results

a) Stable

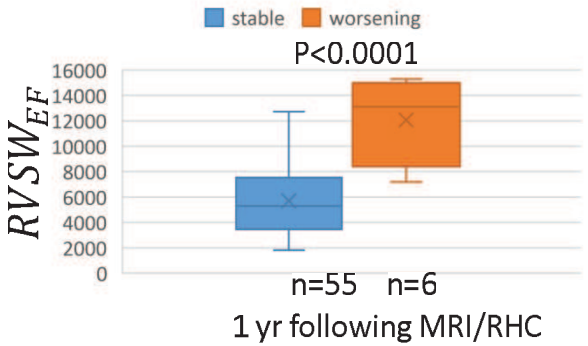


b) Worsening

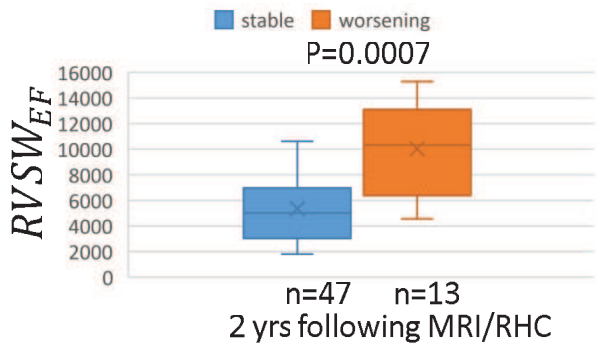


- Patients with clinical worsening have increased RVSW.
- Quantities of interest are grouped and compared by outcomes (stable vs clinical worsening) within 2 years following RHC/MRI.
- A linear mixed model is used to test the associations between predictors and outcomes.

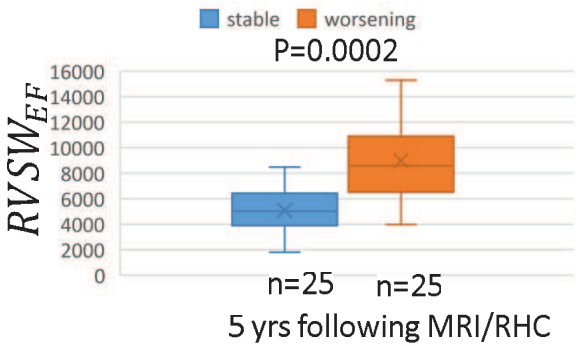
a)


stable
worsening
P<0.0001
$RVSW_{EF}$
16000
14000
12000
10000
8000
6000
4000
2000
0
n=55 n=6
1 yr following MRI/RHC

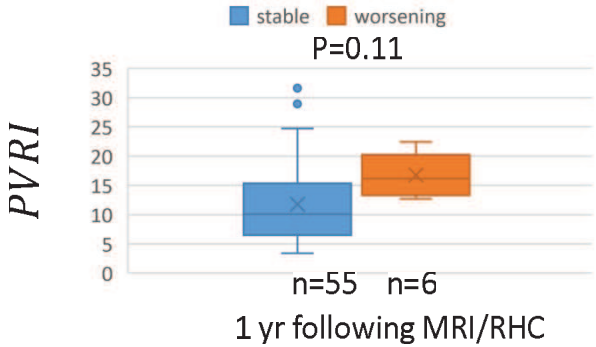
b)


stable
worsening
P=0.0007
$RVSW_{EF}$
16000
14000
12000
10000
8000
6000
4000
2000
0
n=47 n=13
2 yrs following MRI/RHC

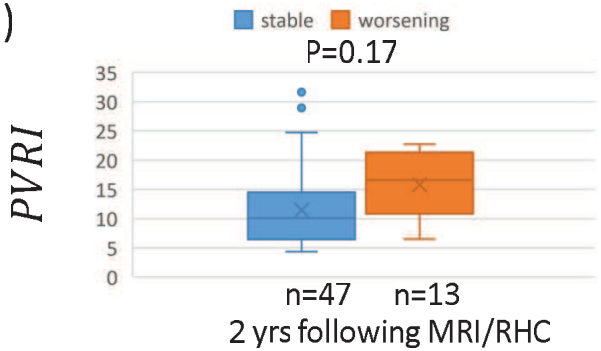
c)


stable
worsening
P=0.0002
$RVSW_{EF}$
16000
14000
12000
10000
8000
6000
4000
2000
0
n=25 n=25
5 yrs following MRI/RHC

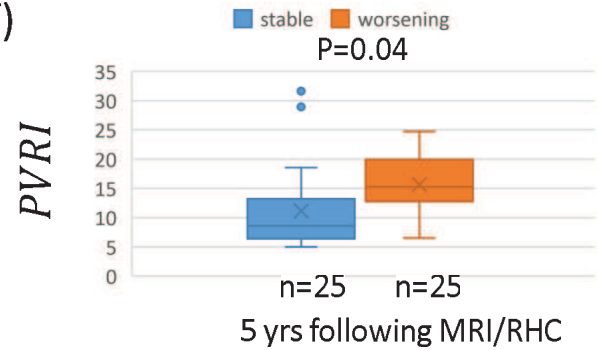
d)


stable
worsening
P=0.11
$PVRI$
35
30
25
20
15
10
5
0
n=55 n=6
1 yr following MRI/RHC

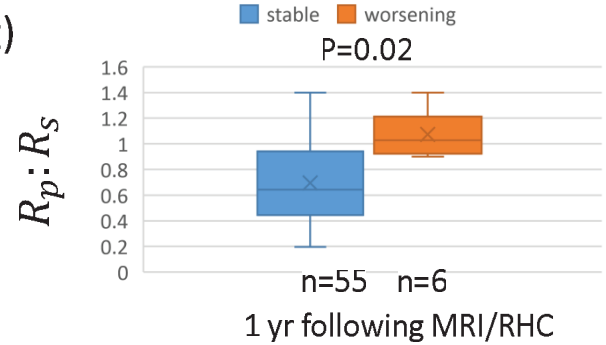
e)


stable
worsening
P=0.17
$PVRI$
35
30
25
20
15
10
5
0
n=47 n=13
2 yrs following MRI/RHC

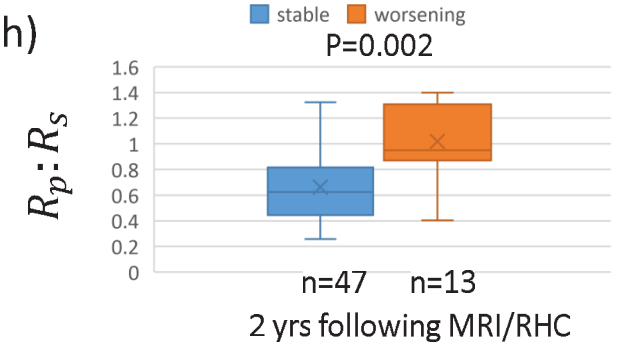
f)


stable
worsening
P=0.04
$PVRI$
35
30
25
20
15
10
5
0
n=25 n=25
5 yrs following MRI/RHC

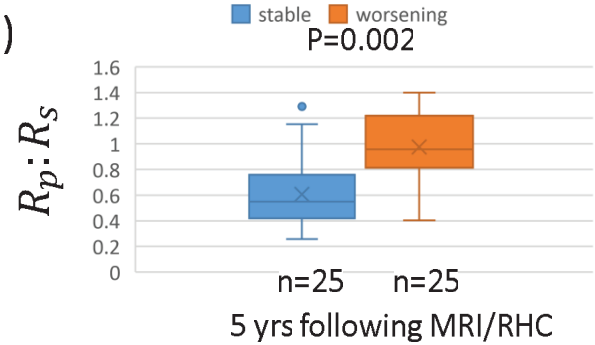
g)


stable
worsening
P=0.02
$R_p:R_s$
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
n=55 n=6
1 yr following MRI/RHC

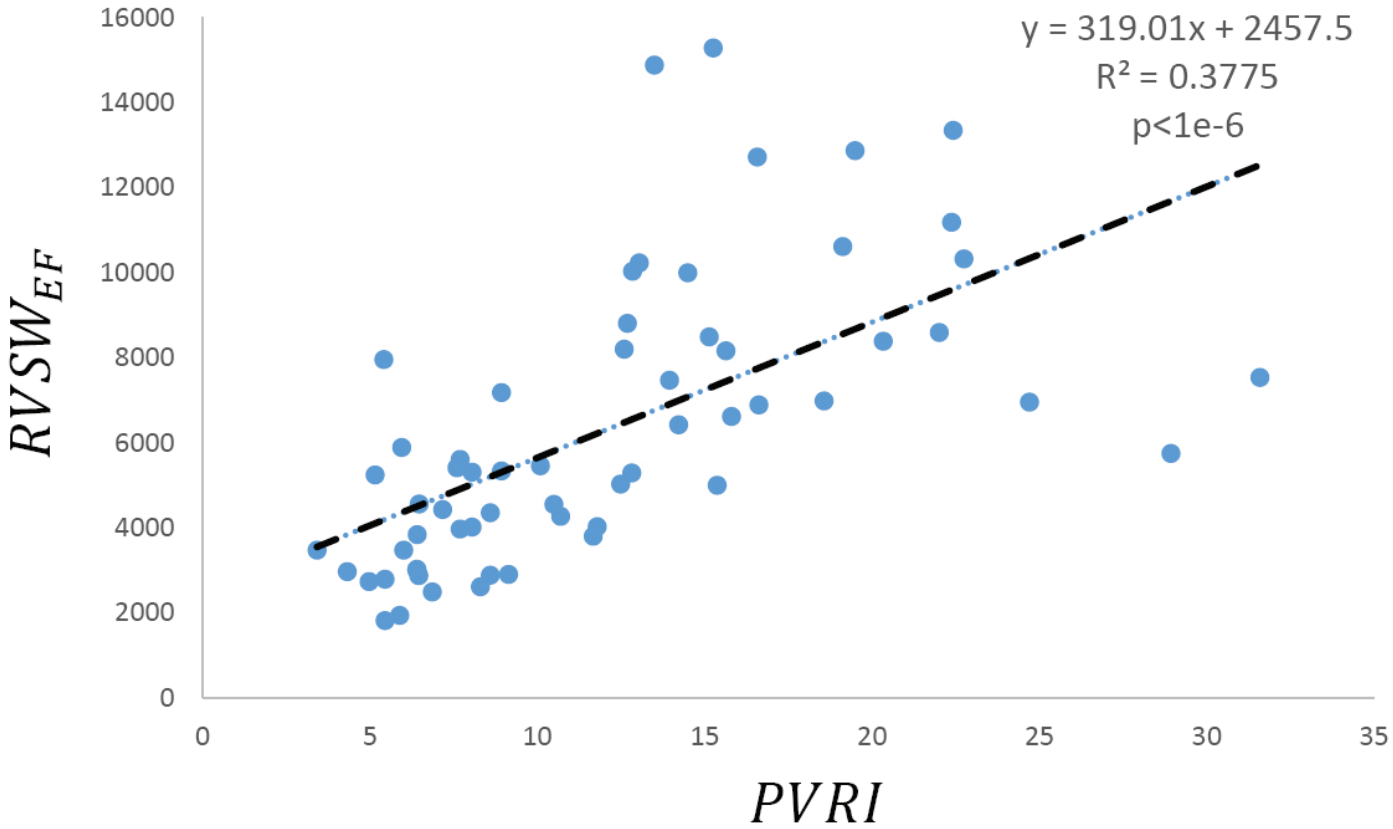
h)


stable
worsening
P=0.002
$R_p:R_s$
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
n=47 n=13
2 yrs following MRI/RHC

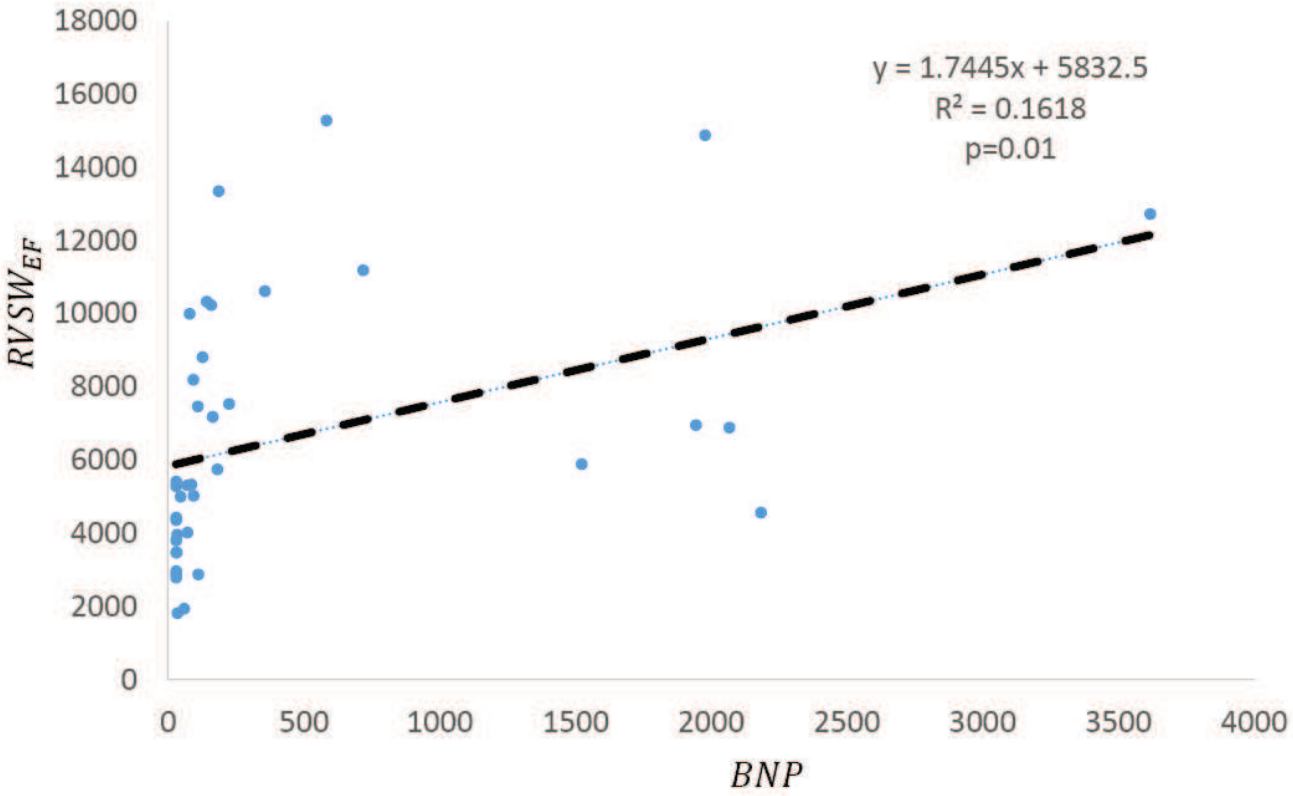
i)


stable
worsening
P=0.002
$R_p:R_s$
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
n=25 n=25
5 yrs following MRI/RHC

Results


y = 319.01x + 2457.5
R² = 0.3775
p<1e-6
$RVSW_{EF}$
$PVRI$
16000
14000
12000
10000
8000
6000
4000
2000
0
0
5
10
15
20
25
30
35

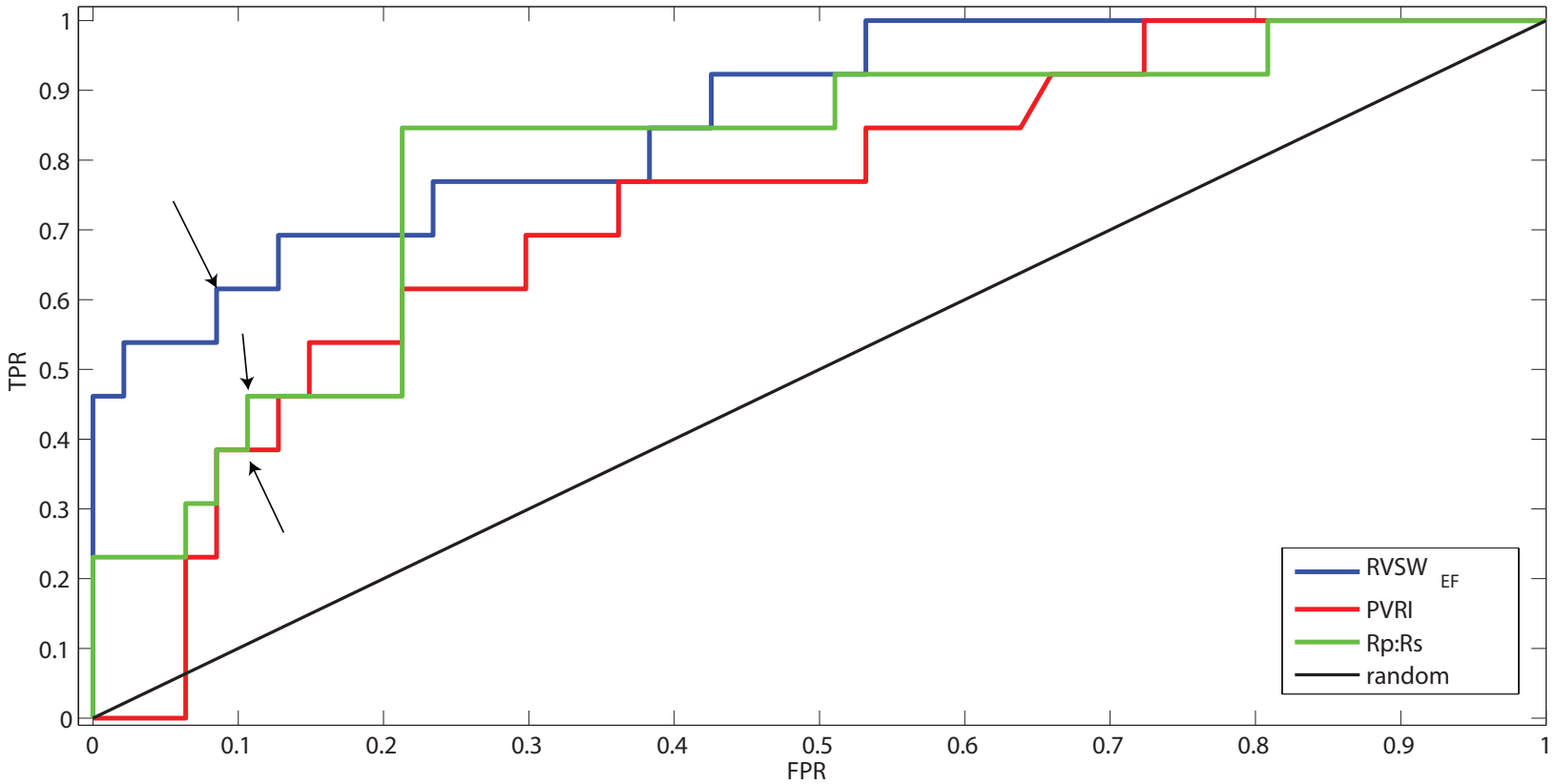
Results



- $RVSW_{EF}$ is an independent predictor.

Receiver operating characteristic (ROC)

- TPR: true positive rate=sensitivity, FPR: false positive rate=1-specificity
- RVSW outperforms PVRI and Rp:Rs for predicting worsening 2 years following RHC/MRI (AUC: 0.86 vs 0.74 vs 0.79).
- Cutoff values for 90% spec. RVSW=8593,PVRI=19, Rp:Rs=1.1



Receiver operating characteristic (ROC)

	1 year following MRI/RHC				
	$RVSW_{EF}$	PVRI	Rp:Rs	EF	EDVI
AUC	0.93	0.78	0.83	0.83	0.88
Cutoff values	10027	22	1.29	37%	126
Sensitivity	0.67	0.2	0.17	0.67	0.83
	2 years following MRI/RHC				
	$RVSW_{EF}$	PVRI	Rp:Rs	EF	EDVI
AUC	0.86	0.74	0.79	0.74	0.76
Cutoff values	8593	19	1.1	37%	125
Sensitivity	0.62	0.39	0.38	0.38	0.54
	5 years following MRI/RHC				
	$RVSW_{EF}$	PVRI	Rp:Rs	EF	EDVI
AUC	0.85	0.78	0.83	0.69	0.73
Cutoff values	8160	19	1.1	34%	122
Sensitivity	0.6	0.32	0.36	0.24	0.44

Discussion

ar disease

ORIGINAL ARTICLE

RV stroke work in children with pulmonary arterial hypertension: estimation based on invasive haemodynamic assessment and correlation with outcomes

Michael V Di Maria,[1] Adel K Younoszai,[1] Luc Mertens,[2] Bruce F LandeckII,[1] D Dunbar Ivy,[1] Kendall S Hunter,[3] Mark K Friedberg[2]

RVSW=mPAPxSV
Cath derived mPAP
Echo derived SV

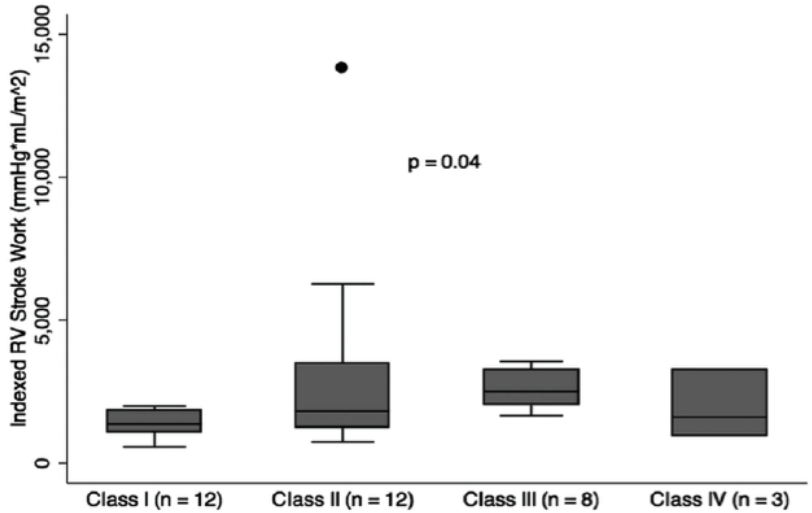


Figure 1 Indexed RV stroke work (RVSW) by WHO class. When grouped by WHO heart failure class, there was a significant difference in indexed RVSW (p=0.04). RVSW appeared to trend upward in WHO classes 1, 2, and 3, but showed a decline in WHO class 4. Box plots presented here feature the median as a horizontal line within the box, while the box itself represents the IQR (25–75th); the 'whiskers' represent the bounds of the extreme values in which Q3+1.5(Q3-Q1) and Q1–1.5*(Q3-Q1), respectively, and single points are, therefore, outliers.

- RVSW is associated with WHO classification.
- RVSW is reduced in class IV.
- RVSW was not found be superior to PVRI.
- RVSW by mPAPxSV might underestimate RVSW by up to 35%.

Di Maria et al., Heart, 2014

Conclusions

- Patient specific RVSW and P-V loops can be modeled easily.
- RVSW correlates with symptomatic/disease worsening in pediatric PAH.
- RVSW outperforms PVRI and Rp:Rs for predicting clinical worsening in pediatric patients with PAH.
- Future studies will include validation and a larger cohort of patients.
- Translate computational modeling into clinical practice: a web site/mobile app based risk calculator for PAH patients.