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Short communication

Tricuspid annular plane systolic excursion (TAPSE) in pediatric pulmonary hypertension: Integrating right ventricular ejection efficiency (RVEe) into advanced multi-parametric imaging

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ABSTRACT

The tricuspid annular plane systolic excursion (TAPSE) has evolved into one of the major echocardiographic indicators of systolic right ventricular (RV) longitudinal function in pediatric pulmonary hypertension (PH). Current RV function research in children with PH focusses on multi-parametric approaches that include TAPSE. The RV ejection efficiency (RVEe) is one of the new variables that reflects the relationship of TAPSE divided by the indexed pulmonary vascular resistance (PVRi) measured by cardiac catheterization. Here, we investigated not only RVEe, but also the ratio of TAPSE divided by pulmonary systolic arterial pressure (PASP; TAPSE/PASP ratio), and a possible association of these indices with NYHA functional class (FC) or the modified ROSS score in 42 children with PH. Both, the RVEe (TAPSE/PVRi) and the TAPSE/PASP ratio were inversely related to NYHA FC and the modified ROSS score in the pediatric PH compared. Compared to TAPSE as single measure, in both multiparametric variables (RVEe, TAPSE/PASP) more pronounced differences in subjects with different NYHA FC/modified ROSS score values were observed. Taken together, the RVEe (TAPSE/PVRi) and TAPSE/PASP ratio distinguish between NYHA FC/modified ROSS score compared to the single echocardiographic variable TAPSE, highlighting the usefulness of a multiparametric approach.

1. Introduction

The tricuspid annular plane systolic excursion (TAPSE) is used in adult cardiology since many years and in 2009, the TAPSE was established as valuable echocardiographic measure of systolic right ventricular (RV) function in the pediatric age group [1]. Since then, TAPSE has evolved into one of the major clinical indicators of systolic longitudinal RV function in pediatric pulmonary hypertension (PH) [2]. However, overreliance on a single variable has been proven to be an inadequate approach in the diagnosis or monitoring, so that current RV function research in PH patients follows multi-parametric approaches [3]. The invasively measured indexed pulmonary vascular resistance (PVRi) is a determinant of RV pressure afterload, and thus, ultimately RV systolic function. Hence, inclusion of PVRi measurements into composite variables appears to be useful for assessing the relationship between heightened RV afterload and RV function. RV ejection efficiency (RVEe) is an interesting new variable that reflects the relationship of RV function and RV afterload, where RVEe is the ratio of TAPSE over PVRi (TAPSE/PVRi) [4]. For RVEe, TAPSE we used as a surrogate for RV ejection and PVRi, derived from cardiac catheterization (CC) driving RV afterload, (PVRi = ratio of mean transpulmonary pressure gradient over pulmonary blood flow Qp, estimated by Fick principle). We hypothesized that combining RVEe (=TAPSE/PVRi ratio) and the ratio of TAPSE/pulmonary arterial systolic pressure (PASP) may reflect in detail the patients' functional capacity and hemodynamics of the individual RV to pulmonary artery unit. We therefore investigated RVEe and TAPSE/PASP ratio in 42 children with PH and their possible association with NYHA functional class (FC) and the modified ROSS score.

2. Materials and methods

The PH study group consisted of 42 children with PH (median age: 7.25; range 1.3–18.0 years; 47.6% female), with demographic data provided in Table 1. NYHA FC (or the modified ROSS score in smaller children, [5]) was determined by 2 independent pediatric

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Table 1
Demographic data of PH patients. Age of our patients at baseline is the age at inclusion in the study. Subgroups of patients (PAH-CHD, IPAH, PH-BPD) are provided. *Abbreviations*: Atrio-ventricular septal defect (AVSD); body surface area (BSA); mean pulmonary artery pressure (mPAP); pulmonary hypertension (PH); pulmonary atresia (PA); PH associated with congenital heart disease (PH-CHD); PH secondary to bronchopulmonary dysplasia (PAH-BPD); idiopathic PH (IPAH); indexed pulmonary vascular resistance (PVRi); RV, right ventricle; right ventricular outflow tract (RVOT); RVEe, RV ejection efficiency; right ventricular outflow tract velocity (RVOT VTI); systolic pulmonary artery pressure (sPAP); systolic systemic artery pressure (sSAP); tricuspid regurgitation velocity (TRV), ventricular septal defect (VSD).

Demographic data			n or median (range)
All PH patients	Fulfilled inclusion criteria	(n)	42
	Female (%)	(n)	19 (47.6)
	Age at baseline (range)	(Years)	7.25 (1.28–17.95)
	Body weight (range)	(kg)	21.0 (5.7–72.0)
	Body length (range)	(cm)	128 (48–185)
	BSA range	(m^2)	0.88 (0.39–1.92)
	NYHA-FC/ROSS score	I (n)	17
		II (n)	17
		III (n)	8
PH medication	Bosentan	(n)	3
	Bosentan + Sildenafil	(n)	7
	Macitentan	(n)	7
	Macitentan + Sildenafil	(n)	10
	Sildenafil	(n)	13
	Calcium antagonists	(n)	2
	Selexipag	(n)	3
PAH-CHD		(n)	23
	TRV	(m/s)	4.0 (3.2–5.0)
	sPAP/sSAP	(%)	73 (40–105)
	mPAP	(Mean ± range; mm Hg)	38 (27–56)
	PVRi	(Mean ± range; WU)	4.1 (2.2–17.8)
	RVEe		0.35 (0.04–0.82)
	TAPSE/PASP ratio		0.02 (0.01–0.04)
Diagnosis	AVSD	(n)	10
	VSD	(n)	9
	PA with VSD	(n)	3
IPAH		(n)	13
	TRV	(m/s)	4.3 (3.3–5.4)
	sPAP/sSAP	(%)	90 (42–119)
	mPAP	(Mean ± range; mm Hg)	46 (29–90)
	PVRi	(Mean ± range; WU)	8.6 (2.8–19.9)
	RVEe		0.17 (0.06–0.77)
	TAPSE/PASP ratio		0.02 (0.01–0.05)
PH-BPD		(n)	6
	TRV	(m/s)	3.5 (3.1–4.3)
	sPAP/sSAP	(%)	64 (40–88)
	mPAP	(Mean ± range; mm Hg)	35 (27–54)
	PVRi	(Mean ± range; WU)	6.0 (3.4–15.5)
	RVEe		0.19 (0.08–0.56)
	TAPSE/PASP ratio		0.02 (0.02–0.05)

cardiologists. At enrollment, all patients were in a clinically stable condition without any change of medication in the preceding 12 weeks. Tricuspid regurgitation velocity (TRV) > 2.8 m/s was considered a cut-off to define elevated pulmonary pressure in the absence of pulmonary stenosis [6]. The echocardiographic estimation of PASP is based on the peak velocity of the jet of TR (omitting the adding of the real right atrial v-wave). All children with echocardiographically suspected (and later confirmed PH underwent cardiac catheterization. PH was defined as a mean pulmonary artery pressure (mPAP) ≥25 mm Hg at rest, a pulmonary capillary wedge pressure (PCWP) ≤15 mm Hg, and a pulmonary vascular resistance (PVR) >3 mm WU × m^2 [iWU], [7]. In those PH patients, PASP and indexed PVR (PVRi = WU × m^2) were invasively determined and calculated, respectively. The TAPSE was measured with M-mode in the apical 4-chamber view [1].

Group comparisons for continuous variables were analyzed using Kruskal Wallis H-test. Associations were expressed by the Spearman's rank correlation coefficient (ρ = Spearman's rho, a nonparametric measure for associations). Effect sizes for Krusakal Wallis H-test (η^2) were calculated to compare the results. Age adjusted TAPSE z-scores were calculated according to Koestenberger et al. [1]. A *p*-value of <5% ($p < 0.05$) was considered significant. This study complies with the institutional guidelines related to patient confidentiality and research ethics including institutional review board approval. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the *International Journal of Cardiology*.

3. Results

In 42 pediatric PH patients TAPSE ranged from 0.5 to 2.15 (median 1.5; age specific TAPSE z-score: median: −3.3, range: −6.8–0.71). Median PASP level was 64 mm Hg (range 38–120) and median PVRi level 6.2 WU (range: 2.2–19.9).

We found a negative correlation between TAPSE and CC-derived PVRi (ρ = −0.557, $p < 0.001$) and between TAPSE and PASP (ρ = −0.350, $p < 0.001$).

The TAPSE/PASP ratio decreased ($p < 0.001$, $\eta^2 = 0.062$) with increasing NYHA functional class (FC)/modified ROSS score, i.e. an indicator of disease severity [median (IQR): NYHA FC 1: 0.032 (0.024–0.040), NYHA FC 2: 0.022 (0.020–0.023), NYHA FC 3: 0.014 (0.011–0.016)] (Fig. 1a, Supplemental Fig. 1a).

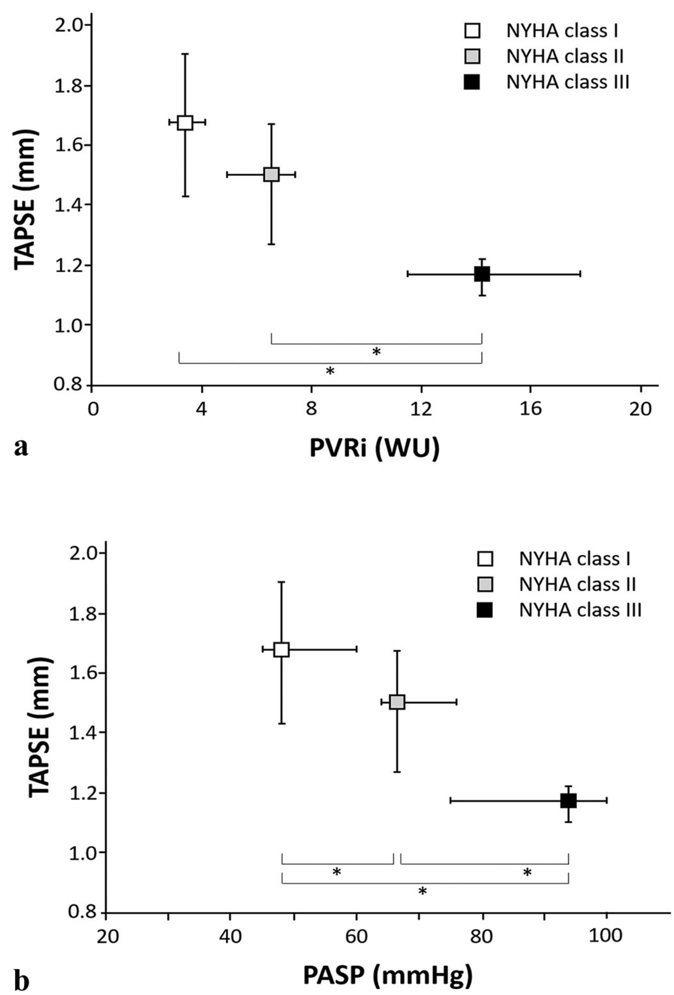

Fig. 1. (a) Median CC-derived RVEe (RVEe = TAPSE/PVRi) distribution according to NYHA FC/modified ROSS score. Error bars: IQR. (b) Median TAPSE-to-PASP ratio distribution according to NYHA FC/modified ROSS score. Error bars: IQR. *Abbreviations*: CC, cardiac catheterization; RVEe, right ventricular ejection efficiency, New York Heart Association (NYHA); PASP, pulmonary arterial systolic pressure; PVR, pulmonary vascular resistance; TAPSE, tricuspid annular plane systolic excursion; IQR, interquartile range.

Moreover, the lowest RVEe (TAPSE/PVRi ratio) values ($p < 0.001$, $\eta^2 = 0.53$) were observed in the most severely compromised PH children, i.e. those with NYHA FC 3 [n = 8; TAPSE/PVRi: 0.09 (0.07–0.11)], followed by NYHA FC 2 [n = 17; TAPSE/PVRi: 0.23 (0.21–0.28)] and NYHA FC 1 [n = 17; TAPSE/PVRi: 0.48 (0.35–0.63)], respectively (Fig. 1b, Supplemental Fig. 1b).

With higher NYHA FC/modified ROSS score (i.e., lower functional capacity), TAPSE ($p = 0.001$, $\eta^2 = 0.24$) decreased, while PASP ($p < 0.001$, $\eta^2 = 0.64$), and CC-derived PVRi [$p < 0.001$, $\eta^2 = 0.58$; NYHA FC 1: 3.4 (2.8–4.1), FC 2: 6.6 (4.9–7.4), FC 3: 14.2 (11.5–17.8) increased (Supplemental Fig. 2).

4. Discussion

TAPSE is vastly independent of heart rate (HR) and can be determined even at high heart rate, making this echocardiographic variable especially suitable for children [1]. Meanwhile, TAPSE is an accepted parameter to measure systolic RV function in children with PH for which normal reference values are available. Nowadays, the research focus trends towards multiparametric approaches that combines the information of the TAPSE (systolic RV function) with afterload parameters. Determining the RVEe (TAPSE/PVRi ratio) and the TAPSE/PASP ratio avoids overreliance on a single parameter and as such is in line with multi-parametric approach in pediatric echocardiography. Both RVEe (TAPSE/PVRi ratio) and the TAPSE/PASP ratio have been demonstrated to be useful for a detailed evaluation of RV function in adult populations [3, 8]. Based on our results in a mid-sized pediatric PH cohort, we propose that the RVEe and TAPSE/PASP ratio may provide a comprehensive assessment of RV contractile state that adds to the information offered by either variable considered separately. The combined information of RV systolic function and afterload (=RVEe) can provide new insights into the physiological determinants of RV function and stress in pediatric PH. Despite the rather small sample size in our study, we found that with worsening (increasing) NYHA FC, the single variables investigated i.e. age specific TAPSE z-scores ($p = 0.001$) decreased, while the PASP ($p < 0.001$), and the CC-derived PVRi ($p < 0.001$) increased. The multiparametric variables TAPSE/PASP ratio and RVEe were inversely related to NYHA FC/modified ROSS score in our children with PH. Compared to TAPSE as single measure, both RVEe and TAPSE/PASP ratio revealed more pronounced differences (effect size; η^2) between children of different NYHA FC/modified ROSS score values.

5. Conclusion

By using a multiparametric echocardiographic approach, we found that RVEe (=TAPSE/PVRi) and TAPSE/PASP ratio to be inversely correlated with NYHA FC/modified ROSS score in our 42 PH children, therefore suggesting that the inclusion of these novel multiparametric approaches provides a comprehensive estimation of RV contractile capacity in conditions with high afterload. As both above ratios correlate well with functional capacity (NYHA FC/modified ROSS score) in our pediatric PH cohort and outperforms the single variable TAPSE, RVEe (=TAPSE/PVRi) and TAPSE/PASP ratio can add valuable information on clinical outcome and mortality in future studies. We therefore promote prospective investigations into the prognostic implications of echocardiographic RVEe and TAPSE/PASP ratio in pediatric PH, with or without therapeutic intervention.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.07.013.

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Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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