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Right ventricular ejection fraction as predictor of outcome in acute heart failure using RV ellipsoid model: A retrospective analysis of a prospective cross-sectional study

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Abstract

Objectives: The right ventricular (RV) function is an important prognostic factor in acute and chronic heart failure (HF). Echocardiography is an essential imaging modality with established parameters for RV function which are useful and easy to perform. However, these fail to reflect global RV volumes due to reliability on one acoustic window. It is therefore attractive to calculate RV volumes and ejection fraction (RVEF/E) using an ellipsoid geometric model which has been validated against MRI in healthy adults but not in the HF patients.

Design: This is a retrospective analysis of a prospective cross-sectional study enrolling 418 consecutive patients with symptoms of HF according to a predefined study protocol. All patients underwent echocardiographic assessment of RV function using Tricuspid Annular Plane Systolic Excursion (TAPSE) and RV fractional area change (RVFAC) and RVEF/E.

Setting: Single centre study with multiple locations for acute in-patients including high dependency units.

Participants: Patients with acute or exacerbation of chronic HF older than 18 y.o.

Main outcome measures: Ability of RVEF/E to predict patient outcomes compared with two established parameters of RV function over two-year follow-up period. Primary outcome measure was all-cause mortality.

Results: RVEF/E is equal to TAPSE & RVFAC in predicting outcome ($p \leq 0.01$ vs $p \leq 0.01$) and provides additional benefit of RV volume estimation based on standard 2D echo measurements.

Conclusions: In this study we have shown that RVEF/E derived from ellipsoid model is not inferior to well established measures of RV function as a prognostic indicator of outcome in the acute HF.

Keywords

Echocardiography, cardiology, right ventricular ejection fraction, acute heart failure, ellipsoid model

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Introduction

There has been growing evidence that right ventricular (RV) function is an important prognostic factor in acute and chronic heart failure (HF).[1–3] Moreover, RV dysfunction is associated with higher symptomatic and comorbid burden in HF with reduced and preserved ejection fraction.[4,5] It is therefore important to accurately assess RV function.

Despite a plethora of imaging tools available in clinical practice, visualizing the right heart remains challenging due to its shape, myofiber orientation and

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anterior, retrosternal position in the chest.[6,7] MRI is currently the gold standard for volumetric and functional RV assessment,[8] however due to high cost and low availability coupled with the inability of HF patients to maintain a prolonged supine position and insufficient breath holding capacity this technique is difficult to implement broadly for use in HF community. Transthoracic echocardiography (TTE) is a well-established, accurate and highly available diagnostic tool and remains the first line specialist cardiac imaging technique withknown limitations when it comes to RV volumetric and functional assessment.[8]

Tricuspid Annular Plane Systolic Excursion (TAPSE) and RV Fractional Area Change (RVFAC) are the two main TTE parameters used routinely in clinical practice. They have been shown to have prognostic value in clinical settings[4,5] and risk assessment for cardiac surgery.[9–11] They are easy to perform and largely reproducible however they are limited by reliability on a single acoustic window and lack a second orthogonal view to estimate global volumes and calculate RV ejection fraction (RVEF). Generally, TAPSE and RVFAC do not reflect the 'peristaltic' nature of RV contractions as well as radial ventricular interdependence.[12,13] Use of 3D TTE has improved the situation: RV volumes correlate well with MRI[14] but reproducibility of this technique remains center/operator dependent. Lower 3D probe availability compared to 2D TTE[15] and additional time for post-processing are the bottlenecks for wide clinical rollout. It is therefore attractive to utilize geometric models based on 2D measurements. The RV ellipsoid model[16] has been validated against MRI in healthy individuals.[17] In short, the RV volume is calculated by assuming both left and right ventricles are parts of two ellipsoids with 3 common radii which can easily be measured on standard 2D TTE. Given that cardiac remodeling affects both ventricles in other conditions including valvular HF[18,19] we have assumed that such model is valid for patients with acute HF. It is, however, not known if such estimation of RVEF provides similar prognostic value compared to conventional 2D echo parameters.

This study assessed whether RVEF can provide equal prognostic value to TAPSE and RVFAC in patients presenting in the acute HF.

Methods

Database

This is a sub-analysis of MRAHF study (Mitral Regurgitation in AHF).

Over the period of 13 months (July 2016 to September 2017) patients admitted to hospital with signs or symptoms of acute HF were screened according to prespecified study protocol (appendix 1). Locations of assessment included the accident and emergency department, intensive care unit, high-dependency unit, acute medical unit, acute cardiac unit, respiratory ward and care for the elderly ward. If acute HF was considered as the primary cause of admission following physician-led clinical examination, patients were consented and recruited into the study if bedside point-of-care brain natriuretic peptide (BNP) level was raised. They underwent transthoracic echocardiography (TTE) within 24 hours of recruitment to assess cardiac function.

Patients were excluded if diagnosed with sepsis, respiratory failure secondary to pulmonary disease, stable chronic HF with an alternative diagnosis or existing in-patients at the start of recruitment. Patients in whom echocardiography was not possible (deceased, did not consent or discharged) were excluded from further analysis. All recruited patients were followed up for a period of 2 years.

Data was stored electronically and was available for review by all authors. The first and last authors developed the manuscript for submission. The design and implementation of this project and decision to submit for publication was by first and last author. Statistical analysis was carried out by independent organisation with established expertise in statistical analysis.

The study was designed by the physician-led executive committee in conjunction with Ashford & St Peter's Hospital Trust Research and Development team. The research protocol was approved by relevant institutional review boards and ethics committees and all participants gave written, informed consent.

Echocardiography

Echocardiography was performed using dedicated G.E. Vivid S70 (GE Healthcare, USA) machine. Images were stored and analysed offline using EchoPac software version 202.5 (GE Healthcare, USA). A Full dataset of images was acquired as per a predefined protocol (appendix 2). Most studies were performed by a single, accredited sonographer. The offline measurements were carried out by two experienced echocardiographers and checked by an expert imaging consultant cardiologist.

TAPSE, RVFAC were measured by standard approach[20] and RVEF using ellipsoid model were calculated.[17,21]

Using the ellipsoid model formula for RV volume is as follows:

$$RVV = \frac{\pi}{6} \times RVIT \times RVLAX \times LVD$$

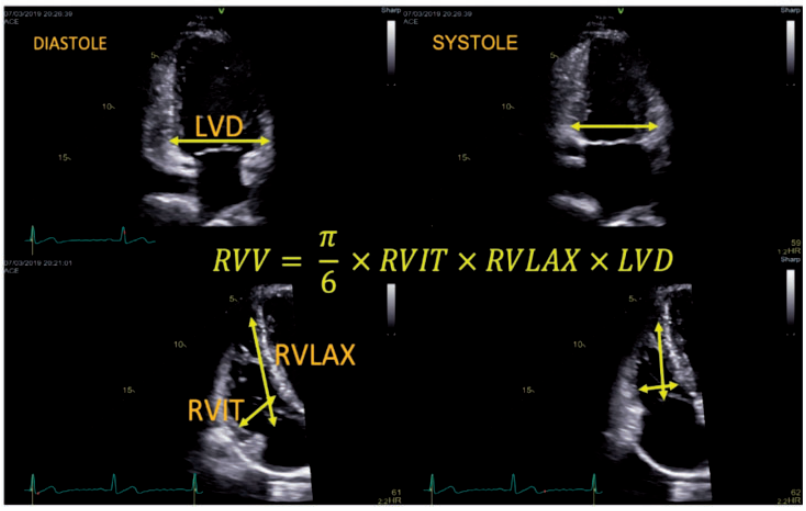

Figure 1. TTE views, measurements and formula for ellipsoid model.

This formula uses distance measurements for quantification of volume.[21] The measurements required include the right ventricular inflow tract diameter (RVIT), right ventricular long axis length (RVLAX) and the maximal outer left ventricular diameter (LVD) (Figure 1). These measurements were taken both in diastole and systole. The RVIT and the RVLAX measurements were taken from apical 4 chamber view or RV focused apical 4 chamber view and the LVD measurement taken from the apical 2 chamber view.[21] The ejection fraction was derived from the difference between these two volumes and expressed as a percentage.

Statistical analysis

Socio-demographic and baseline characteristics were summarised as preserved vs impaired RVEF groups and overall for the complete analysis set. Categorical variables were reported as numbers and percentages and between-groups comparisons compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were reported as means and standard deviations or as medians and interquartile ranges and compared using Student's t test or the Mann-Whitney U test.

Receiver Operator Curve (ROC) analyses were carried out on RVEF/E, TAPSE and RVFAC. The optimum cut-off for prediction 24-month mortality was estimated by identifying the sensitivity and specificity associated with the maximum Youden Index.

24-month mortality analysis was carried out by constructing unstratified Kaplan-Meier survival curves for RVEF/E, RVFAC and TAPSE using ROC cut-offs. Hazard ratios were estimated using an unadjusted Cox regression model, with statistical significance being assessed using the logrank test.

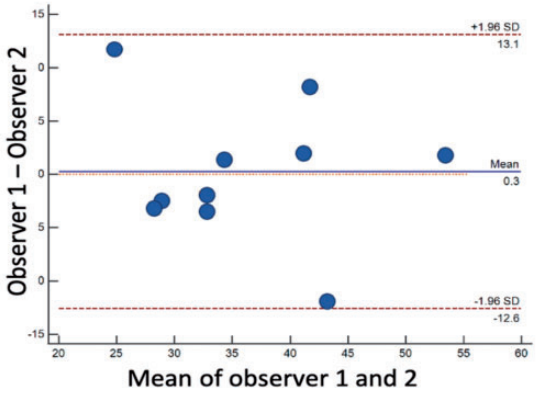

Figure 2. Bland-Altman plot demonstrating acceptable inter-observer variability.

Inter and intra observer agreement of ellipsoid model was assessed using the Bland-Altman plot.

Results

The Bland-Altman plot showed good reproducibility of ellipsoid model in calculation of RVEF/E (Figure 2).

From the ROC curves (Figure 3) for TAPSE, RVFAC and RVEF/E the cut-offs between preserved and impaired RV function were determined based on best combination of sensitivity and specificity as described in methods. For TAPSE a cut off was 1.6 cm ($P \leq 0.09$) (HR 1.48, CI 1.08–2.02, $P \leq 0.05$), for RVFAC - 38.2% ($P \leq 0.11$) (HR 1.48, CI 1.09–2.03, $P \leq 0.01$) and for RVEF/E - 46.9% (≤ 0.05) (HR 1.48 CI 1.09–2.02, $P \leq 0.01$).

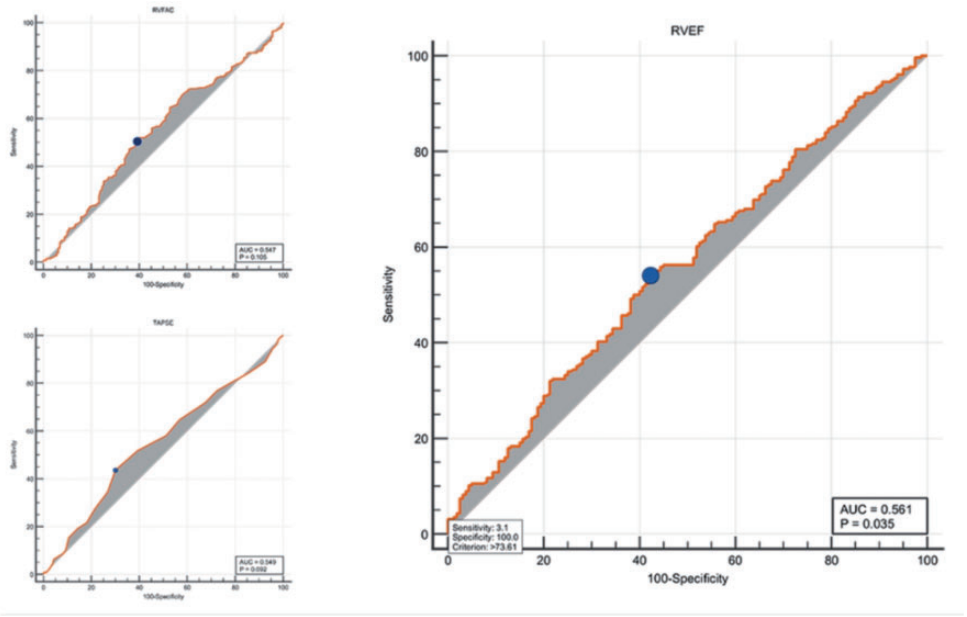

Figure 3. ROC curves used to establish optimum cut-offs for preserved and impaired RV function from maximum Youden index.

Baseline characteristics of the entire cohort are summarised in Table 1. The data for patients with preserved and reduced RVEF showed well matched age and co-morbid profile. RVEF was able to separate patients with higher BNP level ($p \leq 0.0001$) and lower systolic BP ($p \leq 0.002$). As expected TAPSE and RVFAC were significantly reduced in patients with impaired RVEF.

All three parameters of RV function (TAPSE, RVFAC and RVEF/E) were similar in predicting long term outcomes (Figure 4) and reached equal statistical significance ($p \leq 0.01$) at 2 year follow-up. The mortality rate for both TAPSE and RVFAC was 43.95% compared with RVEF/E which was 44.29%.

Discussion

In this study we have shown that RVEF derived from this ellipsoid model is not inferior to well established measures of RV function as a predictor of outcome in acute HF. Additionally, it provides the advantage of estimation of RV diastolic and systolic volumes utilizing readily available 2D measurements. The intra/inter-observer agreement was good in this study, with the element of a learning curve in these assessments; reproducibility of a novel technique is vital to validate usefulness in daily clinical practice.

TAPSE proved to be useful when predicting outcomes and survival despite being an angle dependent, single view measure of long axis function. The cut-off for TAPSE produced from ROC analyses corroborated established values in national and international guidelines[8,20] and in agreement with other studies on HF.[1,5]

RVFAC considers radial RV free wall function with less dependence on angulation of the probe but could be miscalculated in foreshortened views. Nevertheless, it has shown to be a useful risk assessment tool for cardiac surgery[9,11] and important prognostic marker in HF with preserved ejection fraction group.[22] It is recognised broadly by national and international echo guidelines[20,23] but HF experts are still evaluating appropriateness of RVFAC for HF guidelines.[8] The cut-off established in this study was marginally higher but within 2 SD of the accepted cut-off of 35%.

There have been numerous attempts to introduce geometrical models for estimation of RV volumes since the early 1990s.[24] A few have been validated in patients with congenital heart disease and pulmonary arterial hypertension. These early studies showed steps forward in estimating and even predicting RV volumes, this necessitated validation of these models in adult cohorts due to a differing dataset and orientation in paediatric echo studies.[25,26] The ellipsoid model is a more recent example which has been validated against gold standards in normal adult individuals. This model underestimates RV volumes when compared with MRI however this is generally the tendency with echocardiography.[17,23,27] Despite this RVEF from both modalities are comparable.[21]

Given the intricate relationship between left and right ventricular chambers with fixed RV myocardial insertion points we have speculated that alterations to LV geometry will be accompanied with similar changes

Table 1. Baseline characteristics.

	All patients (n = 418)	Impaired RVEF < 46.8 (n = 210)	Preserved RVEF ≥ 46.8 (n = 208)	p-value*
Demographics				
Age, mean (sd),y	78.7 (11.7)	78.4 (12.6)	79.0 (10.8)	0.621
Gender (male), n (%)	222 (53.1)	119 (56.6)	103 (49.5)	0.144
Race, n (%)				
White	390 (93.3)	196 (93.3)	194 (93.3)	0.979
BAME	28 (6.7)	14 (6.7)	14 (6.7)	
BMI, mean: kg/m^2 (sd)	28.6 (8.06)	28.5 (8.90)	28.7 (7.12)	0.819
Comorbidities n (%)				
Coronary artery disease	152 (36.4)	73 (34.8)	79 (38.01)	0.495
Hypertension	232 (55.5)	116 (55.2)	116 (55.8)	0.913
Diabetes	130 (31.1)	60 (28.6)	70 (33.7)	0.262
Chronic Kidney Disease	189 (45.2)	92 (43.8)	97 (46.6)	O.562
COPD	61 (14.6)	31(14.8)	30 (14.4)	0.922
Cerebrovascular disease	64 (15.3)	27 (12.9)	37 (17.8)	0.162
Presentation				
NYHA class,n (%)				
II	37 (8.9)	15 (7.1)	22 (10.6)	0.217
III	161 (38.5)	79 (37.6)	82 (39.4)	0.143
IV	220 (52.6)	116 (55.2)	104 (50.0)	0.284
ECG findings				
Sinus rhythm, n (%)	163 (39.0)	76 (36.2)	87 (41.8)	0.235
AF, n (%)	192 (45.9)	105 (50.0)	87 (41.8)	0.092
Paced, n (%)	39 (9.3)	18 (8.6)	21 (10.1)	O.592
Other rhythm, n (%)	18 (4.3)	8 (3.8)	10 (4.8)	0.253
Echocardiography				
RV Volume, ml mean (sd)				
Diastole	102.6 (52.4)	103.4 (50.8)	99.7 (50.3)	0.457
Systole	56.9 (38.2)	59.3 (36.2)	52.4 (36.6)	0.054
RA size (systole), cm^2 mean (sd)	24.4 (8.8)	24.5 (8.6)	24.2 (8.9)	0.710
TAPSE, mm mean (sd)	15.5 (5.0)	14.1 (4.6)	17.0 (4.9)	<0.0001
RVFAC, % mean (sd)	46.5 (15.6)	44.8 (15.6)	49.0 (15.8)	0.009
Observations				
BPs, mmHg mean (sd)	136 (26.4)	132 (24.0)	140 (28.2)	0.002
BPd, mmHg mean (sd)	76 (16.9)	75 (17.4)	76 (16.5)	0.357
HR, bpm mean (sd)	89 (27.2)	90 (27.5)	89 (26.9)	0.703
SpO_2. % mean (sd)	95.0(3.78)	95.0 (3.81)	94.9 (3.75)	0.825
Biochemistry				
Haemoglobin, g/L mean (sd)	122.5 (21.76)	122.3 (21.30)	122.8 (22.25)	0.817
Creatinine, μmol/L mean (sd)	120.0 (73.44)	115.4 (58.98)	124.8 (85.48)	0.190
eGFR, ml/min/l.73m^2 mean (sd)	48.3 (14.56)	49.0 (14.12)	47.6 (14.99)	0.322
CRP, mg/dl mean (sd)	29.5 (42.74)	33.3 (43.70)	25.7 (41.53)	0.083
BNP, ng/L mean (sd)	1363 (1254.2)	1646 (1336.9)	1078 (1096.2)	<0.0001

*p-values are estimated using N-1χ^2 for proportions and independent samples t-test for continuous variables.

to RV volumes in HF. Differential changes to RV geometry have been documented previously in patients with pulmonary hypertension including severe MR[18] as well as in mildly hypertensive patients.[19] The former is more pertinent to this study and poses a risk for over encumbering RVEF/E as a driver of mortality rather than significant MR in this study group. This highlights a potentially significant confounder. However, this should be investigated more rigorously and is therefore out of the scope of this paper. Utilising multiple views we have ensured maximal RV width diameter to improve accuracy for RV volume assessment mimicking data acquisition for 3D TTE RV datasets.[7] An advantage of this method is that it does not require full visualization of the entire lateral aspect of the RV free wall in apical 4 chamber view which is relevant for dataset acquisition time in acutely unwell patients.[17]

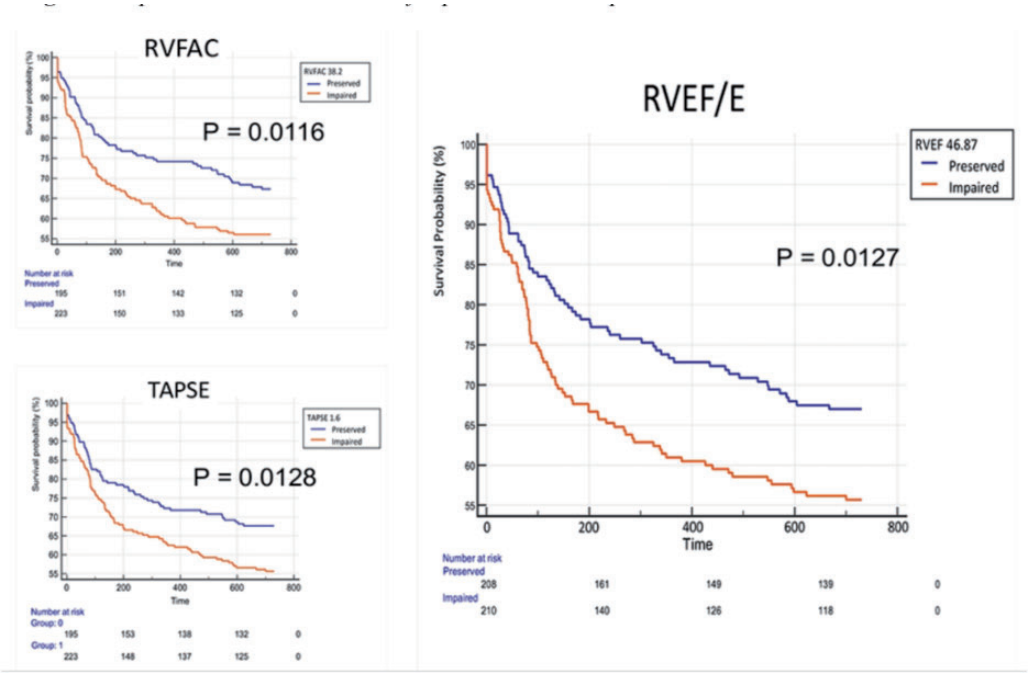

Figure 4. Kalpan-Meier survival curves for preserved and impaired RVEF, TAPSE and RVFAC.

To our knowledge, this is the only study validating the clinical application of this model in the HF patient group. The stringent inclusion/exclusion criteria for this study and small number lost for full two-year follow-up provided us with a robust cohort of patients presenting with acute HF to validate both standard and new TTE parameters of RV function. Such volumetric calculations, which can be performed at the bedside open doors to assessing other parameters such as proportionality of tricuspid regurgitation for surgical workup at lower cost and higher availability.

Limitations

This ellipsoid model has been investigated in small numbers of healthy individuals and compared with MRI. We were unable to validate calculated volumes in similar way, but RVEF has been calibrated against broadly accepted echo parameters derived from the same dataset. It has demonstrated similarly strong prognostic value in predicting long-term outcome in patients with HF. Subject to validation against MRI this model can easily be incorporated in standard protocols and provide valuable volumetric RV analysis at the clinical frontline.

Conclusions

The RV has a role in driving HF in previous studies,[1,2,4,5] this study has shown RVEF/E predicts outcome in acute HF patients whilst estimating RV volumes. With good reproducibility between observers this technique could be used where 3D TTE facilities and experience is scarce.

Declaration of conflicting interests

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Guarantor

Aigul Baltabaeva.

Contributorship

Contributorship statement was provided with article submission.EA prepared the manuscript, performed echocardiographic studies, collected study data, assisted with methodology design and constructed diagrams.OL performed echocardiographic studies and assisted with methodology.JB performed in depth statistical analyses and constructed statistical figures.MB collected mortality data and assisted with methodology.AB provided study concept, finalised study design and manuscript as well as decision to submit for publication.

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Supplemental material

Supplementary material for this article is available online.

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