

# The Dark Side of the Moon – Significant Disagreements between Two-Dimensional and Three-Dimensional Echocardiographic Parameters of the Right Ventricular Function in Patients with Acute Myocardial Infarction

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## ABSTRACT

**Objectives:** The present study aims to assess correlations and agreements between parameters and classification of the right ventricular (RV) function obtained by 2D echocardiography (2DE) – tricuspid annular plane systolic excursion (TAPSE), RV systolic wave velocity (S'T), fractional area change (FAC) and RV ejection fraction (3D RVEF) obtained by advanced 3D echocardiography (3DE).

**Materials and methods:** Patients admitted with acute myocardial infarction (AMI) were enrolled in the study after emergency coronary angiography. Standard 2DE and 3DE acquisitions were carried out in the first 48 hours since admission and later analysed offline by an advanced echocardiographer with five years of training in 2DE and three years of training in 3DE. Correlations between continuous echocardiographic variables were assessed using the Pearson correlation test. Patients were classified as having normal RV function or dysfunction based on current practice guidelines cut-off values and association between 2DE and 3DE parameters was assessed using the Pearson Chi-square test. Further, agreement between these categories was analysed using Cohen's  $\kappa$  test.

**Results:** Sixty-three patients (52 males, mean age  $56.8 \pm 10.3$  years) enrolled between December 2019 and June 2022 were analysed. The correlation between 3D RVEF and TAPSE, S'T and FAC was no

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statistically significant ( $r = 0.217$ ,  $p = 0.088$ ), weak ( $r = 0.385$ ,  $p < 0.001$ ) and modest ( $r = 0.482$ ,  $p = 0.002$ ), respectively. Classification of RV function by FAC was the only 2DE parameter that exhibited statistically significant agreement [ $\chi^2 (1, n=63) = 7.725$ ,  $p=0.005$ ] and association ( $k = 0.3345$ , CI  $[-0.0747, 0.5943]$ ) when compared with 3D RVEF based classification.

**Conclusions:** Our study shows that, in a population of patients with acute myocardial infarction, measurements of RV function obtained by standard 2DE have varying degrees of correlation with 3D RVEF, and the subsequent classification of RV function using current cut-off values for these parameters leads to the misclassification of a significant number of patients.

**Keywords:** acute myocardial infarction, right ventricular function, 3D echocardiography, 2D echocardiography.

## ABBREVIATIONS

2DE: 2D echocardiography  
 3DE: 3D echocardiography  
 3D RV-EDVi: 3D right ventricular indexed end-diastolic volume  
 3D RV-ESVi: 3D right ventricular indexed end-systolic volume  
 3d RV-Svi: 3D right ventricular indexed stroke volume  
 AMI: acute myocardial infarction  
 A4C: apical 4-chamber view  
 CMR: cardiac magnetic resonance  
 CVD: cardiovascular diseases  
 FAC: fractional area change  
 HF: heart failure  
 IHD: ischaemic heart disease  
 NSTEMI: non-ST segment elevation acute coronary syndromes  
 RV: right ventricle/ventricular  
 3D RVEF: right ventricular ejection fraction  
 RV-EDA: right ventricle end-diastolic area  
 RV-ESA: right ventricle end-systolic area  
 S<sub>T</sub>: right ventricular systolic wave velocity  
 STEMI: ST elevation myocardial infarction  
 TAPSE: tricuspid annular plane systolic excursion  
 TDI: tissue Doppler imaging  
 LV: left ventricle/ventricular  
 LVEF: left ventricular ejection fraction

## INTRODUCTION

Although mortality rates for cardiovascular diseases (CVD) have declined by >50% over the last three decades across member countries of the European Society of Cardiology (ESC), they remain the most common cause of mortality, with over three million deaths in the most

recent year of available data. These accounted for 40% of all deaths in females, 35% of all deaths in males and continue to be a significant burden for healthcare systems. Despite significant advances in timely diagnosis and reperfusion strategies, ischaemic heart disease (IHD) remains the most common cause of CVD death, accounting for 33% and 40% of all CVD deaths in females and males, respectively (1).

A contemporary series of 1235 patients with acute myocardial infarction (AMI) evaluated by cardiac magnetic resonance (CMR) identified right ventricular (RV) ischaemia and infarction in 19.6% and 12.1% of patients, respectively (2). Right ventricular injury, although more common in inferior infarcts, is also present in a substantial proportion of anterior infarcts (3). Right ventricular dysfunction is associated with worse outcomes in the context of various cardiovascular diseases including myocardial infarction (2, 4, 5) and impairment of three-dimensional RV ejection fraction (3D RVEF) has been shown to carry a significantly higher risk of mortality that is independent to left ventricular ejection fraction (LVEF) (5).

Currently, the most commonly used parameters to assess RV systolic function are tricuspid annular plane systolic excursion (TAPSE), RV systolic wave velocity (S<sub>T</sub>) and fractional area change (FAC). However, these parameters may not be suited to quantify global RV function as they use a limited part of the RV or one cut-plane of the RV for measurements (6). Recent data suggest that guideline-recommended cut-off values of standard two-dimensional echocardiographic (2DE) parameters of RV systolic function are only modestly associated with 3D RVEF assessment, and the degree of RV function reclassification

varies depending on the parameter used and the underlying pathology (7).

Given these considerations, we aimed to explore the possible discordances between TAPSE, FAC,  $S'_T$  and 3D RVEF in a population of patients with AMI.  $\square$

## METHODS

### Study design and population

This is a single center prospective observational study that included patients with AMI who were hospitalized in the Department of Cardiology of the Emergency University Hospital, Bucharest, Romania, between December 2019 and June 2022.

Written informed consent for study participation was obtained separately from admission informed consent during the first 24 hours of hospitalization. The study protocol was approved by the Hospital Ethics Committee.

The following inclusion criteria were used: patients aged >18 years-old who signed an informed consent upon admission in the study; those diagnosed with AMI according to the Fourth Universal Definition of Acute Myocardial Infarction (8); and patients with sufficient image quality to perform 2DE and 3DE analysis.

The exclusion criteria used by us comprised patients with a history of heart failure (HF) or any documenter LV or RV dysfunction; those with a history of, or current, atrial fibrillation; patients with a history of significant valvular disease; and those with a history of pulmonary hypertension.

Demographic and clinical data (age, weight, height, body surface area, body mass index, cardiovascular risk factors and comorbidities) were retrieved from the clinical records obtained during hospitalization.

All patients underwent coronary angiography and subsequent standard care in accordance with the timelines and recommendations of the ESC guidelines regarding the management of ST elevation myocardial infarction (STEMI) and non-ST segment elevation acute coronary syndromes (NSTEMI/ACS) available at the time.

Two- and three-dimensional echocardiography

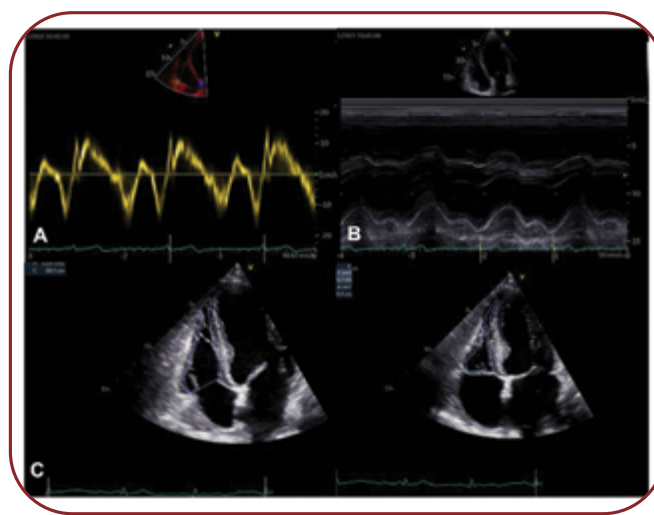
Transthoracic echocardiography examinations were performed within 48 hours of hospital admission with a state-of-the-art echocardiographic ultrasound system (Vivid E90 or Vivid E95 - GE Vingmed Ultrasound, GE Health-

care Technologies Inc.) using a M5 S probe for 2DE and a 4Vc-D probe for 3DE acquisition. Acquisition was performed by an advanced echocardiographer with five years of training in 2DE and three years of training in 3DE.

Standard two-dimensional (2D) acquisition was made following a protocol of ECG-gated 2D loops using the parasternal, apical and subxiphoid views. Datasets were digitally stored in raw-data format and analysed offline using commercially available dedicated software (EchoPAC version 203, GE Vingmed, GE Healthcare Technologies Inc.).

Tricuspid annular plane systolic excursion was obtained analysing M-mode acquisition with the cursor placed on the lateral tricuspid annulus in the apical four-chamber view (A4C) optimised for the RV. TAPSE values of 17 mm and higher were considered normal. Area values were obtained from A4C view optimised for the RV. These values were then used to calculate FAC and values of 35% and higher were considered normal. Right ventricular systolic wave velocity ( $S'_T$ ) was measured from tissue Doppler imaging (TDI) waveforms obtained from placing the cursor at the lateral tricuspid annulus in A4C view optimised for the RV (Figure 1). Values of 10 mm/s and higher were considered normal. Cut-off values used were according to current guidelines (9).

Three-dimensional (3D) images were obtained using views optimised for the left and right heart. Full volume 3D datasets were recon-



**FIGURE 1.** 2DE parameters of right ventricular function:  $S'_T$  (panel A), TAPSE (panel B), FAC (panel C) TAPSE=tricuspid annular plane systolic excursion;  $S'_T$ =right ventricular systolic wave velocity; FAC=fractional area change

structed using ECG gating from sequences of six cardiac cycles. Analysis was carried out offline using semiautomated commercially available software packages (3D RV Quantification, EchoPAC version 203, GE Vingmed, GE Healthcare Technologies Inc). We quantified 3D right ventricular indexed end-diastolic volume (3D RV-EDVi), end-systolic volume (3D RV-ESVi), stroke volume (3d RV-SVi) and ejection fraction (3D RVEF).

Statistical analysis

Statistical analysis was performed using SPSS (ver. 26, IBM). Continuous variables were expressed as mean±SD and categorical variables as frequencies and percentages. Normal distribution of variables was verified using bot statistical tests (Shapiro-Wilk test) and graphical methods (Q-Q plots, standard boxplots). Correlations between continuous echocardiographic variables were assessed using the Pearson correlation test.

Patients were then divided into groups describing normal RV function and RV dysfunction based on cut-off values both for each standard 2DE parameter and 3D RVEF. Association between each of the 2DE parameter derived categories and 3D RVEF derived categories was assessed using the Pearson Chi-square test. Further, agreement between these categories was analyzed using Cohen's k test. Sankey diagrams (Python ver 3.12.4) were constructed to visualize agreements between classifications obtained by standard 2D parameters and 3D RVEF. □

RESULTS

Study population

A total of 63 Caucasian patients were included between December 2019 and June 2022. The study population consisted mainly of male patients (n=52, 82.5%) with a mean age of 56.8 (±10.3) years. Patients were mainly admitted for STEMI (n=43, 68.3%) and the majority of them (n=54, 85.7%) received timely reperfusion or revascularization through percutaneous coronary intervention. Culprit lesions were most frequently located on the left anterior descending (n=25, 39.68%) and right coronary (n=24, 38.1%) arteries. The most frequently observed comorbidities were dyslipidaemia (n=61, 96.8%), hypertension (n=44, 69.8%) and smoking (n=38, 60.3%). Population characteristics are detailed in Table 1.

|                                                | Total (n=63) |
|------------------------------------------------|--------------|
| Baseline demographic characteristics           |              |
| Age, years                                     | 56.86 ± 10.3 |
| Gender, male                                   | 52 (82.5)    |
| BMI, kg/m <sup>2</sup>                         | 28.57 ± 3.14 |
| BSA, m <sup>2</sup>                            | 1.98 ± 0.21  |
| AMI type and revascularization                 |              |
| ST-segment elevation myocardial infarction     | 43 (68.3)    |
| Non-ST-segment elevation myocardial infarction | 20 (31.7)    |
| Percutaneous coronary intervention, n (%)      | 54 (85.7)    |
| Culprit coronary arteries                      |              |
| Left anterior descending, n (%)                | 25 (39.68)   |
| Right coronary, n (%)                          | 24 (38.1)    |
| Left circumflex, n (%)                         | 6 (9.52)     |
| Other, n (%)                                   | 8 (12.7)     |
| Risk factors and medical history               |              |
| History of smoking, n (%)                      | 38 (60.3)    |
| Diabetes, n (%)                                | 16 (25.4)    |
| Hypertension, n (%)                            | 44 (69.9)    |
| Obesity, n (%)                                 | 21 (33.3)    |
| Dyslipidaemia, n (%)                           | 61 (96.8)    |
| Peripheral artery disease, n (%)               | 1 (1.6)      |
| Chronic kidney disease, n (%)                  | 17 (27.0)    |

TABLE 1. Demographic and clinical characteristics

TABLE 2. Echocardiographic measurements

| 2D echocardiographic parameters          |              |
|------------------------------------------|--------------|
| TAPSE, mm                                | 20.49 ± 3.6  |
| RV-EDAi, cm <sup>2</sup> /m <sup>2</sup> | 7.67 ± 2.01  |
| RV-ESAi, cm <sup>2</sup> /m <sup>2</sup> | 4.45 ± 1.34  |
| FAC, %                                   | 41.9 ± 10    |
| S <sub>T</sub> , cm/s                    | 13.05 ± 2.38 |
| 3D echocardiographic parameters          |              |
| 3D RV-EDVi                               | 39.7 ± 10.5  |
| 3D RV-ESVi                               | 20.38 ± 7.7  |
| 3D RV-SVi                                | 19.54 ± 6.26 |
| 3D RVEF                                  | 48.83 ± 8.48 |

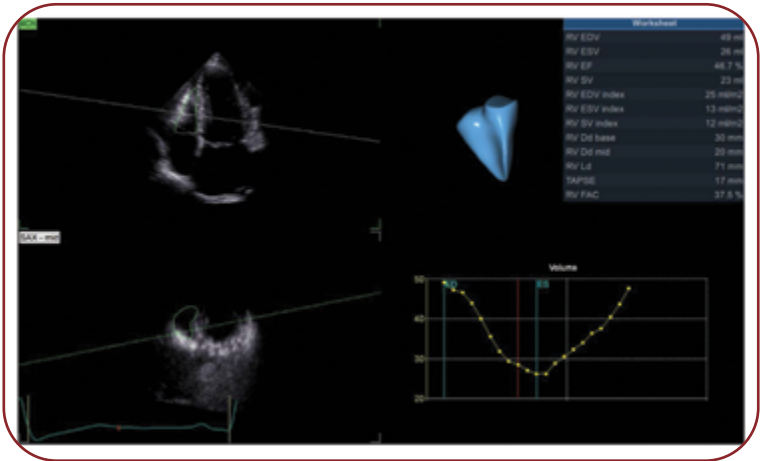


FIGURE 2. 3D RVEF quantification using 3D RVQ tool in Echopac v.203 (GE Vingmed, GE Healthcare Technologies Inc.) 3D RVEF=three-dimensional right ventricular ejection fraction

Distribution of echocardiographic data

Given the size of the sample, normal distribution of echocardiographic variables was verified using



the Shapiro-Wilk test and visualised by normal Q-Q plots. According to the Shapiro-Wilk test, only  $S'_T$  ( $p=0.269$ ), FAC ( $p=0.369$ ) and 3D RVEF ( $p=0.555$ ) had a normal distribution. However, inspection of Q-Q normal plots revealed that TAPSE values also exhibited a normal distribution, the test value ( $p=0.016$ ) probably being altered due to one significant outlier (Figure 1).

### Comparison between 2DE and 3DE parameters

Mean values for TAPSE,  $S'_T$ , FAC and 3D RVEF are shown in Table 2. Scatter plots were generated for visualization (Figure 2) and correlation was tested using the Pearson r-test. When comparing TAPSE with 3D RVEF there was no significant correlation between the two parameters ( $r=0.217$ ,  $p=0.088$ ).  $S'_T$  showed a weak but statistically significant correlation with 3D RVEF values ( $r=0.385$ ,  $p < 0.001$ ), while FAC had showed a modest statistically significant correlation ( $r=0.482$ ,  $p=0.002$ ).

### Patients' classification based on cut-off values

Patients were dichotomized as per current guideline recommended cut-off values in those with either normal RV function or RV dysfunction. When using standard 3DE parameters, normal RV function was found in 82.5% ( $n=52$ ) of subjects, 85.7% ( $n=54$ ) and 76.2% ( $n=48$ ) for TAPSE,  $S'_T$  and FAC, respectively. Classification by 3D RVEF identified 63.5% ( $n=40$ ) of patients as having normal RV function (Table 3).

### Comparison of classifications obtained by 2DE and 3DE parameters

Cross-reference was done between categories obtained by each 2DE parameter individually and 3D RVEF. When comparing TAPSE with 3D RVEF, 41.3% ( $n=26$ ) of patients were misclassified, with 30.2% ( $n=19$ ) of them having been initially identified with normal RV function, despite a below cut-off 3D RVEF value (Table 4, Figure 3). There was no statistically significant association between the two classifications [ $\chi^2$  (1,  $n=63$ ) = 0,  $p=0.991$ ]. Further analysis using Cohen's k test did not show any significant agreement between the two methods [ $k=0.0143$ , CI (-0.2959, 0.3246)].

When considering  $S'_T$ , misclassification was seen in 34.9% ( $n=22$ ) of cases, with 28.6%

**TABLE 3.** Classification of patients based on guideline cut-off values

| Parameter      | Normal function | RV dysfunction |
|----------------|-----------------|----------------|
| TAPSE, n (%)   | 52 (82.5)       | 11 (17.5)      |
| $S'_T$ , n (%) | 54 (85.7)       | 9 (14.3)       |
| FAC, n (%)     | 48 (76.2)       | 15 (23.8)      |
| 3D RVEF, n (%) | 40 (63.5)       | 23 (36.5)      |

**TABLE 4.** Crosstabulation of categories obtained by TAPSE and 3D RVEF

|       |             |            | 3D RVEF |             | Total  |
|-------|-------------|------------|---------|-------------|--------|
|       |             |            | Normal  | Dysfunction |        |
| TAPSE | Normal      | Count      | 33      | 19          | 52     |
|       |             | % of Total | 52.4%   | 30.2%       | 82.5%  |
|       | Dysfunction | Count      | 7       | 4           | 11     |
|       |             | % of Total | 11.1%   | 6.3%        | 17.5%  |
| Total |             | Count      | 40      | 23          | 63     |
|       |             | % of Total | 63.5%   | 36.5%       | 100.0% |

**TABLE 5.** Crosstabulation of categories obtained by  $S'_T$  and 3D RVEF

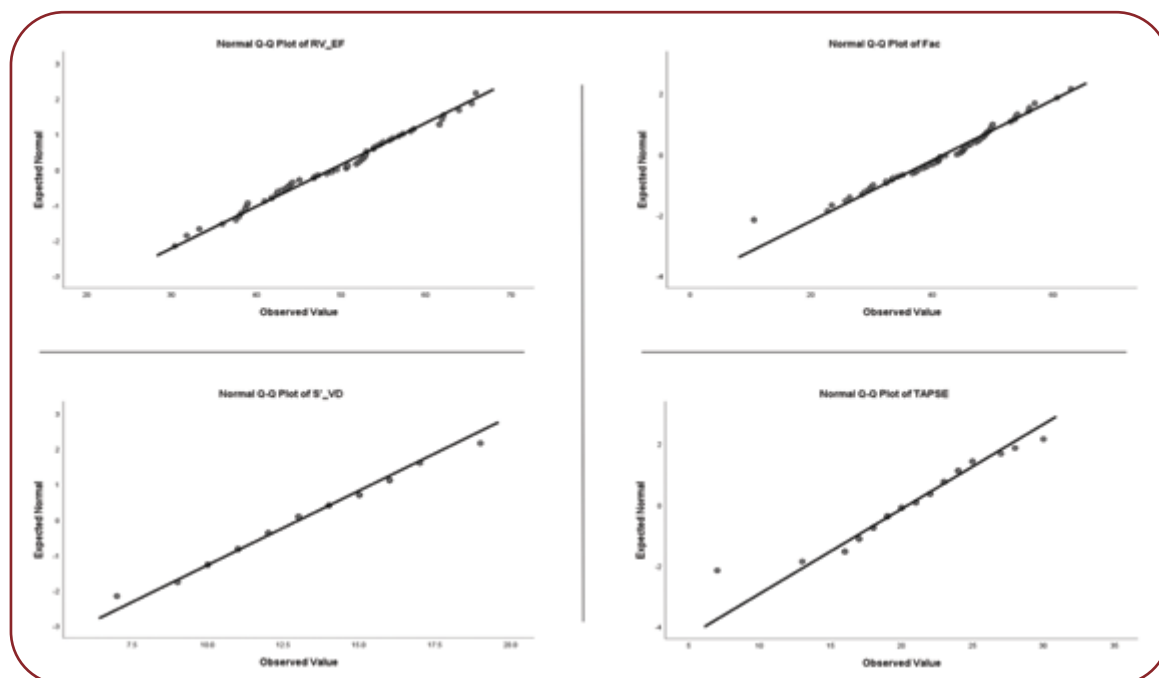
|       |             |            | 3D RVEF |             | Total  |
|-------|-------------|------------|---------|-------------|--------|
|       |             |            | Normal  | Dysfunction |        |
| S'r   | Normal      | Count      | 36      | 18          | 54     |
|       |             | % of total | 57.1%   | 28.6%       | 85.7%  |
|       | Dysfunction | Count      | 4       | 5           | 9      |
|       |             | % of total | 6.3%    | 7.9%        | 14.3%  |
| Total |             | Count      | 40      | 23          | 63     |
|       |             | % of total | 63.5%   | 36.5%       | 100.0% |

**TABLE 6.** Crosstabulation of categories obtained by FAC and 3D RVEF

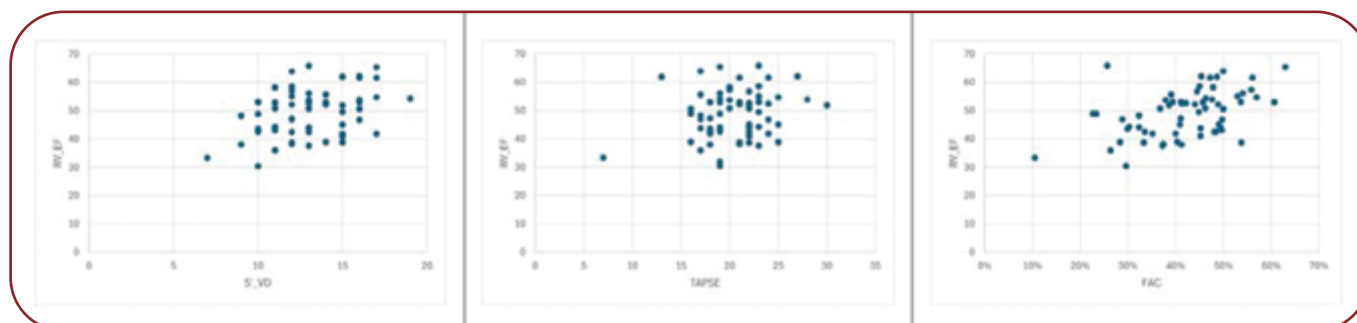
|       |             |            | 3D RVEF |             | Total  |
|-------|-------------|------------|---------|-------------|--------|
|       |             |            | Normal  | Dysfunction |        |
| FAC   | Normal      | Count      | 35      | 13          | 48     |
|       |             | % of total | 55.6%   | 20.6%       | 76.2%  |
|       | Dysfunction | Count      | 5       | 10          | 15     |
|       |             | % of total | 7.9%    | 15.9%       | 23.8%  |
| Total |             | Count      | 40      | 23          | 63     |
|       |             | % of total | 63.5%   | 36.5%       | 100.0% |

( $n=18$ ) of subjects having been initially identified with normal RV function (Table 5, Figure 4). There was also no statistically significant association between the two classifications ( $\chi^2$  (1,  $n=63$ ) = 1.643,  $p=0.2$ ). Agreement analysis also did not yield significant results [ $k=0.076$ , CI (-0.2355, 0.3875)].

When comparing FAC and 3D RVEF classification, there was discordance in 28.5% ( $n=18$ ) of cases, with 20.6% ( $n=10$ ) of them having been initially identified with normal RV function (Table 6, Figure 5). However, there was significant association between the two methods ( $\chi^2$  (1,  $n=63$ ) = 7.725,  $p=0.005$ ) and also significant agreement [ $k=0.3345$ , CI (-0.0747, 0.5943)]. □



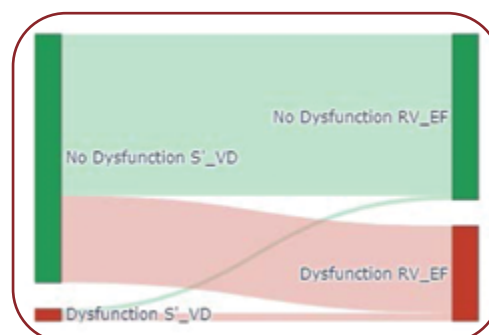
**FIGURE 3.** Q-Q plots showing the distribution of TAPSE,  $S'_T$ , FAC and 3D RVEF  
TAPSE=tricuspid annular plane systolic excursion;  $S'_T$ =right ventricular systolic wave velocity;  
FAC=fractional area change; 3D RVEF=three-dimensional right ventricular ejection fraction



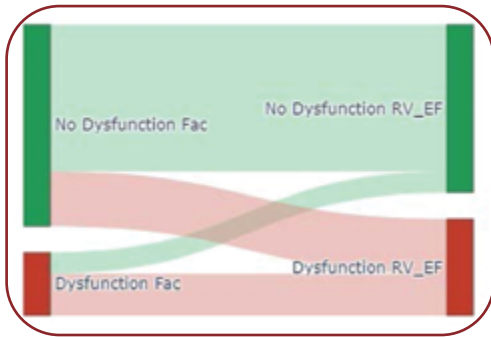
**FIGURE 4.** Scatter plots representing correlations between 3D-RVEF and  $S'_T$ , 3D-RVEF and TAPSE, and 3D-RVEF and FAC  
TAPSE=tricuspid annular plane systolic excursion;  $S'_T$ =right ventricular systolic wave velocity; FAC=fractional area change;  
3D RVEF=three-dimensional right ventricular ejection fraction



**FIGURE 5.** Sankey diagram representing the reclassification of patients when comparing TAPSE and 3D RVEF  
TAPSE=tricuspid annular plane systolic excursion; 3D RVEF=three-dimensional right ventricular ejection fraction



**FIGURE 6.** Sankey diagram representing the reclassification of patients when comparing  $S'_T$  and 3D RVEF  
 $S'_T$ =right ventricular systolic wave velocity;  
3D RVEF=three-dimensional right ventricular ejection fraction



**FIGURE 7.** Sankey diagram representing the reclassification of patients when comparing FAC and 3D RVEF

FAC=fractional area change;  
3D RVEF=three-dimensional  
right ventricular ejection fraction

## DISCUSSIONS

Routine echocardiographic assessment after AMI has level I class of recommendation in current clinical practice guidelines (10, 11). Focus is given to LV systolic function quantification through 2DE LVEF and assessment of possible complications arising after AMI. However, RV dysfunction has been shown to be associated with worse outcomes in various cardiac diseases, including AMI (2, 4, 5).

Routine 2DE RV assessment is done through quantification of TAPSE,  $S'_T$  and FAC, while 3DE RVEF is a more time consuming and operator dependent method which is currently less widely available.

In our study, when assessing RV function with 2DE, the proportion of patients identified with RV dysfunction by TAPSE,  $S'_T$  and FAC was 17.5%, 14.3% and 23.8%, respectively, which was in accordance with previous reports of echocardiographic findings in this clinical situation (12-14). Right ventricular dysfunction was identified in 36.5% of patients when considering 3D RVEF results. However, our findings show that there was no or low to moderate correlation between 2DE parameters and 3D RVEF in our patient sample.

One possible explanation for our study results resides in the complex anatomy of the RV – its crescent shape envelops the LV and contains only two layers of fibres that elicit a peristalsis-like longitudinal contraction (15, 16). Moreover, the LV is an important contributor to RV function considering that septal contraction ac-

counts for 20 to 40% of the RV stroke volume (15). Thus, parameters like TAPSE and  $S'_T$ , which are markers of lateral wall longitudinal function, may have limited value in assessing RV function in the setting of AMI, which often results in regional motion abnormalities. Fractional area change, although derived through measurements made in a one-cut plane of the RV, may be more suited to assess global RV function.

A significant proportion of patients were erroneously classified as having normal RV function as per the current 2DE cut-off values while being proven to have RV dysfunction when 3D RVEF was used. This finding is consistent with previous results reported by Tolvaj *et al*, who found a modest correlation between current cut-off values for 2DE parameters and 3D RVEF <45% (7). This finding has significant implications for two reasons: the presence of RV dysfunction assessed by 3DRVEF is associated with a higher risk of mortality that is independent of LVEF (5) and patients with normal standard parameters reclassified as having RV dysfunction based on RVEF showed a four-fold increase in mortality risk (7).

## Limitations of the study

Some limitations to the present study must be acknowledged. First of all, our patient sample was relatively small, mainly due to limitations regarding the good-quality image acquisition for a rigorous three-dimensional right ventricular assessment. Although the statistical tests used by us were appropriate for our patient sample size, our findings should be taken at hypothesis-generating value. Additionally, the present study did not include a protocol of CMR evaluation, which is currently the golden standard for RV assessment. □

## CONCLUSIONS

Our study has shown that in a population with acute myocardial infarction, right ventricular assessment limited to only classical two-dimensional parameters may not be sufficient to correctly identify patients with right ventricular dysfunction. Three-dimensional right ventricular function evaluation by 3D RVEF, although time consuming and expertise dependent, may be a useful tool for better risk stratification in these patients. □

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