

# Validity of ejection fraction as a measure of myocardial functional state: impact of asynchrony

Felix A. Blyakhman<sup>1,2\*</sup>, Anna M. Naidich<sup>1,3</sup>, Svetlana G. Kolchanova<sup>2</sup>, Sergey Yu. Sokolov<sup>1,2</sup>, Yulia V. Kremleva<sup>4</sup>, and Vasily V. Chestukhin<sup>4</sup>

<sup>1</sup>Department of Biomedical Physics, Ural State Medical Academy, 3 Repin Str., Ekaterinburg 620219, Russia; <sup>2</sup>Department of Physics, Ural State University, 51 Lenin Ave., Ekaterinburg 620083, Russia; <sup>3</sup>Therapeutic Department, City Clinic 'Preobrazhenskaya', 28 Gagarin Str., Ekaterinburg 620078, Russia; and <sup>4</sup>Diagnostics Department, Institute of Transplantology and Artificial Organs, 1 Sthukinskaya Str., Moscow 123182, Russia

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## KEYWORDS

Left ventricle;  
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Regional wall motion;  
Mechanical asynchrony;  
Ultrasound examination;  
3D reconstruction

**Aims** The goal of this study was to test whether peculiarities of left ventricular (LV) regional function place limits on the validity of ejection fraction (EF) as a measure of the myocardial functional state.

**Methods and results** Transthoracic and transoesophageal data from patients with a variety of cardiac conditions were used for analysis of LV regional function. The focus was on the effects of mechanical asynchrony. Ejection fraction was calculated on the basis of LV end-diastolic volume and end-systolic volume obtained by two different ways: (i) end-systolic volume as a whole; and (ii) the sum of all regional end-systolic volumes (which may occur at different times). The relative difference, D-EF, between EFs obtained by (i) and (ii) was taken as the 'merit' of EF. A value of zero is the highest merit. Irrespective of the examination method, we found that D-EF was always higher than zero, and that its value depended on the extent of mechanical asynchrony.

**Conclusions** Ejection fraction is not the arithmetic average of regional EFs. An increase of asynchrony increases D-EF, i.e. it reduces the merit of EF as a measure of cardiac function.

## Introduction

Left ventricular ejection fraction (LVEF), which is a non-dimensional quantity that is defined as LV stroke-volume divided by the end-diastolic volume, multiplied by 100%, reflects the ability of the LV to eject blood. Since this mainly depends on myocardial function, EF serves as an indirect measure of LV contractile state as a whole.

At the same time, LVEF is the result of regional function. Theoretically, the contributions of all myocardial regions to the EF should be the same when there is LV functional (mechanical) homogeneity. In that case, LVEF is equal to any regional EF (r-EF) and, therefore, LVEF is 100% a reflection of the myocardial functional state. Meanwhile, even in the normal LV, regional myocardial function is non-uniform, depending on local peculiarities of LV wall structure.<sup>1–3</sup>

In pathological states, disease impairs myocardial structure and function dynamically and unequally, resulting in some degree of mechanical asynchrony.<sup>4–7</sup> In general, asynchrony implies differences in time course of contraction between

different LV wall regions. In the pathological state, asynchrony may be a reflection not only of abnormalities in the LV conduction system but also myocardial ischaemia or damage.<sup>8–11</sup>

The presence of mechanical asynchrony implies that the time course of local ejection during the cycle may differ in different regions. In that case, LVEF defined at the end of systole is not equal to the arithmetic average of all r-EFs. Therefore, LV asynchrony may influence the EF value as a measure of overall myocardial functional state.

In this paper, we present evidence that the merit of EF as a measure of the overall functional state depends on the extent of mechanical asynchrony. We present data from patients with a variety of cardiac conditions, obtained by transthoracic (TTE) and transoesophageal (TEE) ultrasound. Using regional LV wall-motion analysis of single long-axis sections and with LV 3D reconstruction, we show that LVEF merit as a reflection of myocardial functional state as a whole depends on the peculiarities of LV regional function.

## Methods

This investigation conforms to the principles outlined in the Declaration of Helsinki. Transoesophageal echocardiographic data from 10

\* Corresponding author. Tel: +7 343 375 6548; fax: +7 343 261 6778.  
E-mail address: user-214@usu2.usu.ru

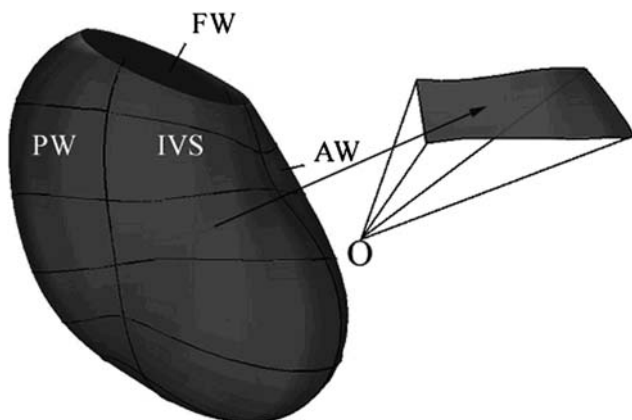
patients were obtained in the Diagnostics Department of the Transplantology Institute (Moscow) and were used for 3D reconstruction and subsequent analysis. Similar data from TTE studies in 40 patients from the City Clinic 'Preobrazhenskaya' (Ekaterinburg) were used for LV regional wall-motion analysis. In the TEE group, five patients had ischaemic heart disease (NYHA III–IV) and five had terminal renal failure (NYHA II–III). In the TTE group, four patients had ischaemic heart disease (NYHA II–III), 17 patients had mitral valve prolapse (NYHA I–II), and 19 had essential arterial hypertension (NYHA I–III).

Left ventricular 3D reconstruction on the basis of TEE was described in detail in our earlier paper.<sup>12</sup> Briefly, 2D LV long-axis sections were obtained with a TEE machine (Powervision-380, Toshiba, Japan). Subsequently, the transducer was rotated by 15° steps until a complete volume scan was obtained. Typically, the complete volume scan took ~1 min, and contained 12 scanning planes.

Frame-by-frame (with 40 ms interval) LV endocardial borders were outlined by hand with DICOR<sup>®</sup> software.<sup>13</sup> This was done for all sections. Left ventricular 3D reconstruction was carried out by rotation of the plane of each cross-section by the angle corresponding to the transducer plane. Since the number of LV 2D cross-sections was rather limited, LV surface approximation was carried out with fitted spherical functions.

To estimate the contribution of individual LV regions to global EF, LV EDV was divided into 24 pyramids. *Figure 1* illustrates the principle of division, based on a spherical co-ordinate system. The apex of each pyramid was set at the LV centre of mass, and the LV surface region coincided with the bottom of each pyramid. Regional ejection fractions (r-EFs) were calculated by two ways: (i) on the basis of regional end-diastolic volume (*ed-V*) and this region's volume at LV end-systole; and (ii) at different times (frames) during the cardiac cycle in accordance with regional *ed-V* and regional end-systolic volume (*es-V*). Global ventricular EF (LVEF) was estimated on the basis of LV EDV and ESV (standard method, *st-EF*), and according to LV EDV and the sum of all regional *es-Vs* (anticipated value, *an-EF*). Left ventricular EF 'merit,' D-EF, was taken as the relative difference between values of EF calculated using those two methods. Thus,  $D-EF = (an-EF - st-EF) / st-EF$ , multiplied by 100%. An increase of this parameter signifies a decrease of EF merit as a measure of the myocardial functional state.

Mechanical asynchrony was assessed as a space–time phenomenon: the extent of asynchrony was estimated in space (*As*) and in time (*At*). *As* was defined as the coefficient of variation of r-EF obtained at end-systole. This coefficient was calculated as the RMS deviation of the parameter used, divided by its average value, multiplied by 100%. *At* was determined from RMS variations of times at which regional ESVs were attained.



**Figure 1** Example of 3D reconstructed left ventricle. IVS, interventricular septum; AW, anterior wall; FW, free wall; PW, posterior wall. 'O', centre of mass (see text for explanation).

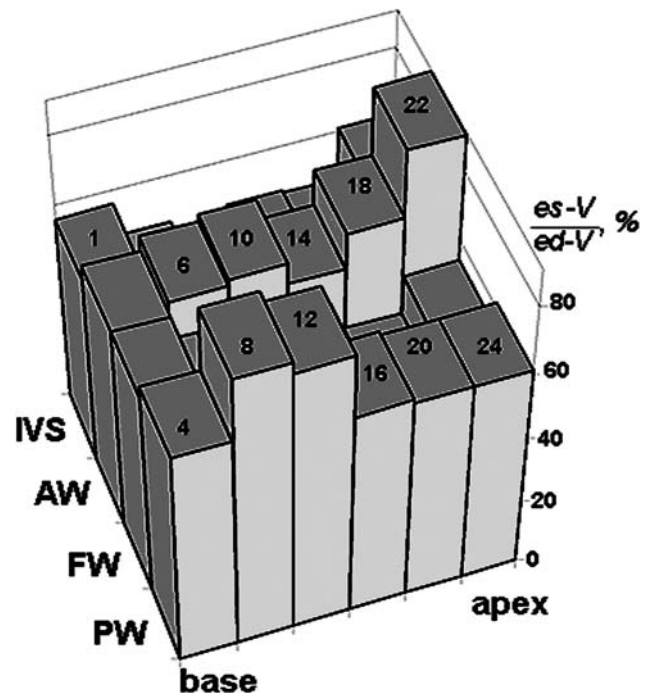
The same analysis was performed on TTE data obtained with a different echocardiography machine (Sonoline G60S, Siemens, USA). Frame-by-frame data processing was carried out for LV long-axis sections over the course of two to three cardiac cycles. Endocardial LV contours were outlined by hand. Left ventricular volume was calculated for each frame using an ellipsoidal model. Reproducibility of LV contouring was evaluated by comparing the curves of the temporal volume change over several cardiac cycles.

To analyse LV regional function over the whole cardiac cycle, the area within the LV contour for each frame was divided into 12 sectors using radii connecting to the centre of mass of the respective LV section. By doing so, 12 r-EFs could be determined.

## Results

*Figure 2* shows an example of r-EF distribution at end-systole in a patient with cardiac abnormalities due to the terminal renal failure (NYHA III). The data were obtained by TEE and subsequent 3D reconstruction. As is seen in *Figure 2*, the contribution of r-EF to the LVEF is fairly non-uniform ( $As = 32\%$ ). Meanwhile, the arithmetic average of r-EF (41.3%) is almost identical to the global EF (41.0%). Dynamic changes in LV regional volumes during the cardiac cycle for this patient are presented in *Figure 3*. The number of regions corresponds to the numeration are marked on the tops of columns in *Figure 2*.

The data show that the relative volume changes in different LV regions are not the same. Some regions contribute to LV ejection sooner and/or by a greater amount than others, so that at any given moment during the cardiac cycle, changes in any of the 24 regions are different. In other words, LV regional volume dynamics are asynchronous. Besides, as is seen in *Figure 3*, minimal (end-systolic) volumes for some regions appear at different times so that



**Figure 2** Example of regional ejection fraction distribution at left ventricular end-systole. Ordinate corresponds to regional end-systolic volume normalized to end-diastolic volume. IVS, interventricular septum; AW, anterior wall; FW, free wall; PW, posterior wall.

r-EF of these regions differs from r-EF at end-systole of LV as a whole.

Figure 4 illustrates these variables for a representative patient. Regional EFs measured at regional end-systole and at LV end-systole are plotted. The numbers of frames where individual r-EF were obtained are marked on the top of every column. One can see the variations of time points with RMS value of 48.4 ms ( $A_t$ ). Furthermore, r-EFs defined on the basis of regional ESV are greater than r-EFs calculated at LV end-systole. As a consequence, the  $st$ -EF

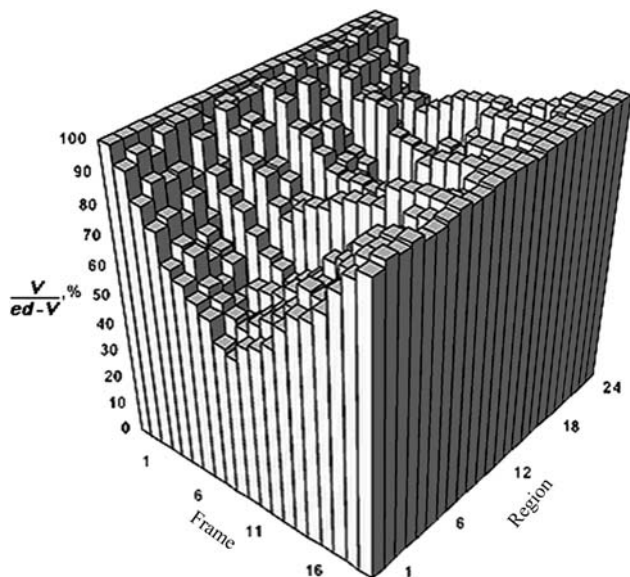


Figure 3 Left ventricular regional volume changes during a cardiac cycle assessed by 3D reconstruction. One hundred per cent on the ordinate corresponds to regional end-diastolic volume.

is less than the  $an$ -EF (41 and 45%, respectively). The D-EF for this case is equal to 9%.

Qualitatively similar results were obtained with TTE studies of LV regional function analysis of LV long-axis views. The area dynamics of 12 LV sectors during the cardiac cycle in a patient with IHD (HYHA III) is presented in Figure 5. Figure 6 shows the r-EF distribution in the same way as presented in Figure 4. In this case,  $A_s = 34%$ ,  $A_t = 56$  ms,  $st$ -EF = 37%,  $an$ -EF = 43%, and the D-EF was 11%.

Table 1 lists the mean values of asynchrony parameters, LVEF, and D-EF, obtained both by TEE and by TTE. In general, both methods showed large variations in all parameters. At the same time, mean values of  $st$ -EF for both TEE and TTE were less than those for  $an$ -EF (for TEE  $P > 0.05$ , for TTE  $P < 0.05$ ).

A close correlation was found between the asynchrony parameters and the EF relative difference. For TEE, the correlation coefficients between D-EF and  $A_s$  and D-EF and  $A_t$  were: 0.59 ( $n = 10$ ,  $P = 0.052$ ) and 0.73 ( $n = 10$ ,  $P < 0.05$ ); for TTE, they were 0.67 ( $n = 40$ ,  $P < 0.001$ ) and 0.69 ( $n = 40$ ,  $P < 0.001$ ), respectively.

Figures 7 and 8 show the graphical presentation of the relationships between D-EF and  $A_s$  for TEE data, and D-EF and  $A_t$  for TTE data, respectively. The data show that increases of spatial asynchrony resulted in increases of EF relative difference, i.e. in a diminution of EF merit. Time asynchrony influenced ID-EF in the same way as spatial asynchrony.

Close negative correlation between the EF relative difference and the  $st$ -EF was seen as well. The correlation coefficients for TEE and TTE were:  $-0.69$  ( $n = 10$ ,  $P < 0.05$ ) and  $-0.78$  ( $n = 40$ ,  $P < 0.001$ ), respectively. Negative correlation implies the lower the LVEF, the higher the D-EF. In

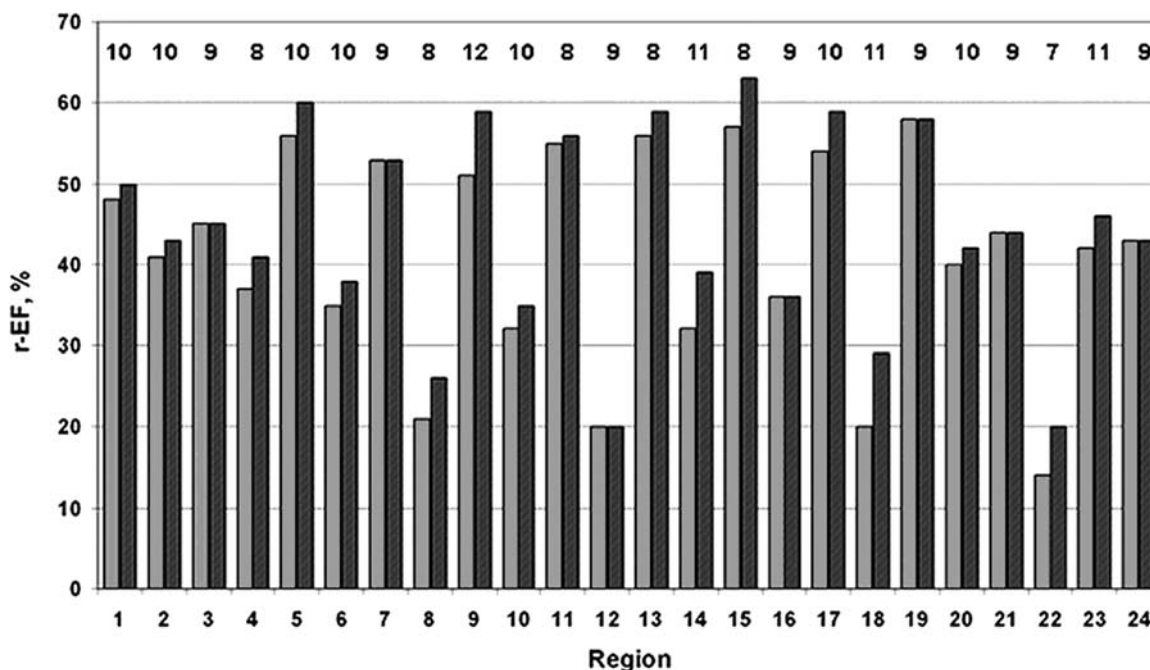
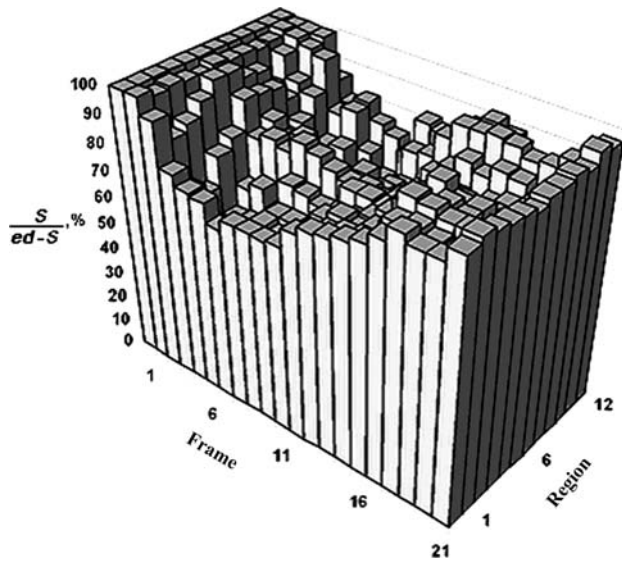
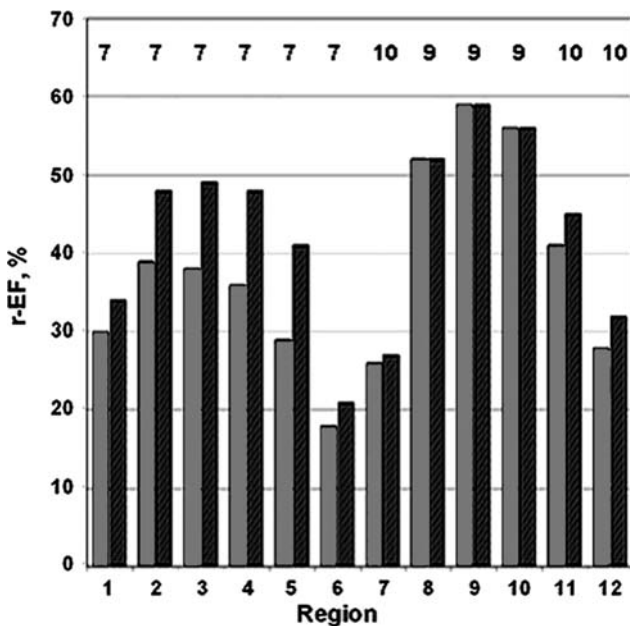


Figure 4 Regional ejection fraction (r-EF) distribution assessed by 3D reconstruction at end-systole of each region and end-systole of the left ventricle. Lighter columns correspond to r-EFs obtained at end-systole of the left ventricle. Number of frame where regional end-systolic volume was calculated is marked on the top of each column. (See text for further explanation.)



**Figure 5** Left ventricular (LV) regional area changes during a cardiac cycle from transthoracic echocardiography LV long-axis view. One hundred per cent on the ordinate corresponds to regional end-diastolic area.



**Figure 6** Regional ejection fraction (r-EF) distribution from transthoracic echocardiography left ventricular (LV) long-axis view at end-systole of every region and end-systole of the left ventricle. Lighter columns correspond to r-EFs obtained at end-systole of the LV. (See text for further explanation.)

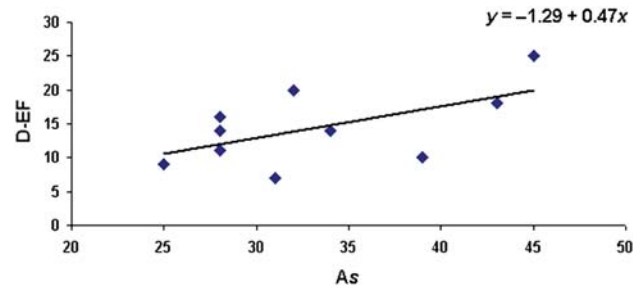
other words, a decrease of LVEF implies a decrease of LVEF merit as a measure of the myocardial functional state.

## Discussion

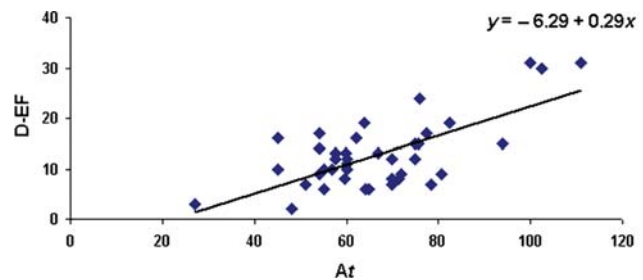
In routine clinical practice, EF is useful because of its simplicity. Its value can be obtained by using standard imaging techniques. However, numerous clinical studies have demonstrated

**Table 1** Main parameters of LV function

Parameter	TEE ( <i>n</i> = 10)		TTE ( <i>n</i> = 40)	
	Range	Mean	Range	Mean
As (%)	25–45	33.3 ± 2.2	12–99	34.9 ± 6.3
At (ms)	32–140	72.4 ± 10.5	45–111	66.1 ± 5.1
st-EF (%)	15–44	31.7 ± 3.5	32–76	55.6 ± 3.6
an-EF (%)	17–52	36.4 ± 3.7	40–79	66.1 ± 3.2
D-EF (%)	7–25	14.4 ± 1.8	2–31	12.9 ± 3.3



**Figure 7** Dependence of ejection fraction relative difference value (D-EF) on the extent of spatial asynchrony (As) for transoesophageal echocardiographic data. D-EF and As plotted in %.



**Figure 8** Dependence of ejection fraction relative difference value (D-EF) on the extent of time asynchrony (At) for transthoracic echocardiographic data. D-EF plotted in %, and At in ms.

low information content in the EF as a measure of the myocardial functional state. For example, EF does not reflect unambiguously the clinical result of myocardial revascularization: in spite of successful coronary bypass surgery or angioplasty, the EF value may either increase,<sup>14,15</sup> decrease, or remain unchanged despite changes in regional myocardial function.<sup>16–18</sup>

With standard cardiac ultrasound, the limitations of measured EF are largely related to the error in measuring LV end-diastolic and end-systolic volumes. At least three analytical algorithms have been used widely to calculate LV volume: ‘Teicholz’, ‘area-length’, and ‘Simpson’ algorithms. According to the comparative analysis between LV 3D reconstruction and standard ultrasound methods, the ‘Teicholz’ algorithm yields the highest error whereas the ‘Simpson’ method yields the minimum.<sup>19,20</sup> Thus, any analysis of the usefulness of LVEF as a measure of the myocardial functional state depends on the method used to measure it.

In this study, we turned our attention to the implications of using EF as a measure of myocardial function. Let us suppose that LVEF is a suitable measure of the myocardial functional state; if so, it would be best if it reflected the



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