Wolters Kluwer Health | Lippincott Williams & Wilkins

Nuclear Medicine Communications

Journal Information

Lippincott Williams & Wilkins is a leading international publisher of professional health information for physicians, nurses, specialized clinicians and students. For a complete listing of titles currently published by Lippincott Williams & Wilkins and detailed information about print, online, and other offerings, please visit the LWW Online Store.

Nuclear Medicine Communications is a monthly rapid communications journal publishing research and clinical work in all areas of nuclear medicine for an international readership. In addition to refereed papers, the journal features frankly written editorials, topical reviews, book reviews, and incisive reporting of international conferences. Authors and readers benefit from the timeliness of the journal's six-month publication time and four week response following the receipt of a paper.

Official Journal of the British Nuclear Medicine Society

Publication & Editorial Staff Contacts

To inquire about this, or other titles, please visit the LWW Online Store and select the **Contact LWW** link located in the top right corner of the screen. This page will provide you with contact information for our different offices and departments.

JOURNAL RESOURCES

- Editorial Board
- Advertising Information
- Classified Ads
- Special Sales

SUBSCRIPTION SERVICES

- New Subscriptions
- Renewal Information
- Address Changes
- Trial Issue Request

JOURNAL PROFILE

- Category: Radiology, Nuclear Medicine & Medical Imaging
- Impact Factor: **1.097**
- Ranking and Category: **55th of 84 Radiology & Nuclear Medicine**

INDEXING SOURCES

- Biomedical Engineering Citation Index
- Cambridge Scientific Abstracts
- Chemical Abstracts
- Current Awareness in Biological Sciences
- Current Contents/Clinical Medicine
- EMBASE/Excerpta Medica

Publisher
Phil Daly
Phil.Daly@wolterskluwer.com

Production Editor
David Amy
David.Amy@wolterskluwer.com

Marketing Manager
Charlee Lindsey
Charlee.Lindsey@wolterskluwer.com

Advertising Representative
The Point of Difference
4 Chase Avenue
London SW20 8LU
Tel: +44 (0)20 8542 3200
Fax: +44 (0)20 8543 3810
pointofdifference@btinternet.com

LWW Business Offices
250 Waterloo Road
London SE1 8RD UK
Tel: +44 (0)20 7981 0600
Fax: +44 (0)20 7981 0601

Editorial Correspondence

For specific manuscript submission instructions please view the Editors' List in the **Author & Reviewer Info** section of this website.

Society Information
British Nuclear Medicine Society
Regent House, 291 Kirkdale
London SE26 4QD
Telephone 020 8676 7864
Facsimile 020 8676 8417

- Index Medicus/Medline
- Medical Documentation Service
- Research Alert
- Science Citation Index
- Scisearch

Original article

Nuclear Medicine Communications

A correlative study comparing current different methods of calculating left ventricular ejection fraction

Ali Gholamrezanezhad[a,b], Sahar Mirpour[a], Armaghan F. Esfehani[a], Mohsen Saghari[a], Koorosh Mirpour[d], Davood Beiki[a] and Maryam Soheilifar[c]

Background **Left ventricular ejection fraction (EF) is a major determinant of survival in patients with coronary artery disease (CAD). Comparative accuracy of numerous modalities in calculating EF is not well investigated.**

Method **We compared EF as calculated by rest and post-stress Cedars automated quantitative gated SPECT (AQGS), rest and post-stress semi-automatically processed gated SPECT (MQGS), echocardiography and contrast ventriculography (LVG) to those determined by rest and post-stress cavity-to-myocardium ratio (CMR) in 109 patients. Gated SPECT was performed based on a 2-day protocol using Tc-MIBI.**

Results **Mean EF in LVG, echo, post-stress CMR, rest CMR, post-stress AQGS, rest AQGS, post-stress MQGS and rest MQGS were 41.8%±12.1, 44.8%±11.8, 38.1%±10.7, 35.7%±12.1, 44.5%±15.1, 46.9%±14.7, 40.1%±14.3 and 43.5%±14.3 respectively. Although significant differences were observed between some of these methods, good and excellent linear correlations were present among values (all Pearson correlations >0.63). Considering LVG as the 'gold standard', we defined two groups: EF <35% (class 1) and >35% (class 2). Discriminant analysis showed that SPECT has the ability to predict patients' classes. In 4/18 of patients with normal SPECT (on both visual and quantitative analyses, SSS <4), EF on QGS showed a significant decrease on post-stress compared with rest.**

Conclusion **There is a good correlation in calculating EF by LVG, QGS and echocardiography, regardless of EF value. Whenever QGS is impossible, CMR is a reliable indirect indicator of EF. Gating of both phases (and when impossible, CMR of both phases) has an additional value in diagnosis of CAD.** *Nucl Med Commun* **28:41–48 © 2007 Lippincott Williams & Wilkins.**

Nuclear Medicine Communications 2007, **28**:41–48

Keywords: ejection fraction, gated SPECT, echocardiography, contrast ventriculography

[a]Research Institute for Nuclear Medicine, Tehran University of Medical Sciences, [b]Young Researchers Club, Azad University of Medical Sciences, Tehran, [c]Department of Cardiology, Iran University of Medical Sciences, Tehran, Iran and [d]School of Cognitire Sciences Institute for studies in Theoretical Physics and Mathematics, Tehran, Iran.

Correspondence to Dr Ali Gholamrezanezhad, Research Institute for Nuclear Medicine, Shariati Hospital, North Karegar Street, 14114 Tehran, Iran.
Tel: +0098 21 8633431; fax: +0098 21 8633039;
e-mail: gholamrezanejhad@razi.tums.ac.ir

Received 24 June 2006 **Accepted** 13 July 2006

Introduction

Left ventricular ejection fraction (EF) has been shown to be a major determinant of long-term survival in patients with coronary artery disease (CAD) [1]. Therefore, numerous modalities have been evolved to calculate this important determinant of cardiac performance. However, the comparative accuracy of and correlations across various types of measures in calculating ejection fraction are not well understood. On the other hand, each of these modalities has its own limitations and drawbacks and also sometimes discrepant results are obtained.

Gated myocardial perfusion single photon emission computed tomography (SPECT) has been used to calculate EF and has correlated well with other conventional methods. The main benefit of gated myocardial perfusion SPECT is the simultaneous assessment of myocardial perfusion and function with one injection and one imaging sequence. However, it is not clear whether ECG gating of the images for assessment of EF should be set at the post-stress phase or rest phase image acquisition. Additionally, it is not well known which results of what phase of the study are more correlated with other measures of EF. It seems that ECG gating of the images set at the post-stress phase are, in fact, a measure of resting EF (as the stress has finished at the time of acquisition) but it can be postulated that exercise-induced myocardial ischaemia may be associated with post-stress-reduced EF, probably due to prolonged stress-induced myocardial stunning; therefore, post-stress EF does not necessarily represent resting EF.

Another method for the calculation of EF, based on the scintigraphic images, has been evolved, and this uses the cavity-to-myocardium ratio (LVCMR). There are few previous reports to indicate that this parameter is well correlated with other methods of calculating EF. Furthermore, it has not been determined whether EF should be

calculated based on the post-stress phase images or rest phase views.

Echocardiography is one of the most accepted techniques for the assessment of left ventricular EF. Contrast left ventriculography (CLV) during routine angiographic analysis of coronary arteries is also another well known method of calculating EF, although generally it is done by a visual review of data, which is highly subjective.

The aim of our study was to assess the correlation of the results obtained by using these different routine methods of calculating EF–CLV, echocardiography, single photon emission tomography–which are currently the most widely used methods of calculating EF.

Patients and method

The study was performed between January and May 2005 and 109 (94 males and 15 females) with a mean age of 54.9 ± 10.1 years (range: 34–76 years) participated. All patients were selected from a population of patients who were referred to our nuclear medicine department by their primary cardiologists for scintigraphic assessment of myocardial perfusion. Nevertheless, verbal consent was obtained from all patients. Only those patients were entered in the study who had undergone coronary angiography and ventriculographic calculation of EF within the previous 3 months. All patients also underwent echocardiographic calculation of EF.

Following intravenous injection of 666–814 MBq ^{99m}Tc-MIBI at peak pharmacological stress with dipyridamole, all patients underwent standard stress ECG-gated SPECT. For the pharmacological stress $0.56\,mg{\cdot}kg^{-1}$ dipyridamole was infused intravenously over a 4 min period. Radiotracer was injected intravenously, 3–5 min after the completion of dipyridamole infusion. A rest-phase study (rest ECG-gated SPECT) was performed on another day with administration of the same dose, following administration of sublingual tri-nitroglycerine.

A commercial MIBI kit was used and the labeling and quality control procedures were performed according to the manufacturer's instructions. Image acquisition was performed with a rotating, single-head gamma camera (ADAC). Both rest and stress data acquisitions employed low energy, high resolution, parallel hole collimation with step and shoot mode, elliptical orbits, matrix size of $64 \times 64 \times 16$, and using a roving 38.0 cm^2 detector mask. A 20% window around the 140 keV energy peak of ^{99m}Tc-MIBI was used. Patients were in a supine position during acquisition. The projection data sets were pre-filtered with a two-dimensional Butterworth filter (cut-off 0.40, order 5.0), reconstructed with filtered back-projection and no attenuation correction. The resulting transaxial image sets were reoriented into short-axis sets vertical and horizontal long-axis images for qualitative analysis. The scan findings were interpreted by two expert nuclear medicine physicians blinded to other clinical data and angiographic results. Quantitative analysis of myocardial perfusion and EF was performed using the Cedars-Sinai program and according to a 20-segment model. The value of EF was determined based on both automatic (automatically processed post-stress gated SPECT (APGS), automatically processed rest gated SPECT (ARGS)) and semi-automatic process (semi-automatically processed post-stress gated SPECT (MPGS), semi-automatically processed rest gated SPECT (MRGS)) of the scintigraphic data. Also, subtraction of post-stress EF and rest EF was determined as ΔEF.

Finally, the short-axis tomogram from the mid-ventricle was used for calculation of the LVCMR on each of the stress and rest phase images. A 5×5 pixel rectangular region of interest (ROI) was drawn in the visually determined centre of the LV cavity and the mean counts per pixel was obtained. Then the ROI was dragged to the hottest area of the LV wall and the mean counts per pixel were again obtained. The ratio of counts in the LV cavity to that in the myocardium was calculated as the LVCMR. Therefore, two rest and stress LVCMRs were determined for analysis [2].

Quantitative data are expressed as mean $\pm$ SD. The ANOVA test was used to calculate the significance of the differences between the quantitative and the qualitative variables. We performed the Student's *t*-test to assess the differences between quantitative variables. Discriminant and regression analysis were used for calculating the prediction models and agreement between different modalities. $P < 0.05$ was considered to be statistically significant. SPSS for Windows (Release 12.0.0) was used for statistical analysis.

Results

Mean LVEF values in angiography and echocardiography were $41.8\% \pm 12.1$ and $44.8\% \pm 11.8$, respectively. Mean post-stress and rest LVCMR were $38.1\% \pm 10.7$ and $35.7\% \pm 12.1$, correspondingly. Mean EF values on APGS and ARGS were measured $44.5\% \pm 15.1$ and $46.9\% \pm 14.7$, respectively. Also calculated means of MPGS and MRGS resulted in $40.1\% \pm 14.3$ and $43.5\% \pm 14.3$, correspondingly.

The mean of EF calculated based on different methods (angiography, echocardiography and SPECT images) was significantly different when determined by the paired *t*-test, except for some pairs parameters (P values > 0.05). These pairs are shown in Table 1.

Correlation studies

Correlation studies showed that the predicted EF based on SPECT is highly correlated with angiographic and

echocardiographic EF values. The significance and *r* value of correlations are given in Table 2.

Multiple regression analysis

The results of multiple regression analysis showed that scintigraphic predicted EF by linear models is correlated with angiographic and echocardiographic EF of patients. The results of linear regressive models are shown in Table 3. The results revealed that EF on MPGS and LVCMR on rest images are the best parameters for prediction of angiographic EF. They can predict the EF on angiography significantly (*P* value of models < 0.0001). Our models divided as two groups: model 1 was based on EF on MPGS ($r = 0.709$) and model 2 was derived from two parameters including EF on MPGS and LVCMR on rest images ($r = 0.724$). The other parameters did not show good prediction values and were excluded from our models.

Table 1 Paired comparisons of different methods of calculating ejection fraction

Paired samples		*P* value
1	EF on CLV–EF on echocardiography	0.002
2	EF on CLV–EF on MPGS	0.075*
3	EF on CLV–EF on MRGS	0.117*
4	EF on CLV–EF on APGS	0.014
5	EF on CLV–EF on ARGS	0.000
6	EF on CLV–LVCMR on stress images	0.001
7	EF on CLV–LVCMR on rest images	0.000
8	EF on echocardiography–EF on MPGS	0.000
9	EF on echocardiography–EF on MRGS	0.165*
10	EF on echocardiography–EF on APGS	0.740*
11	EF on echocardiography–EF on ARGS	0.037
12	EF on echocardiography–LVCMR on stress images	0.000
13	EF on echocardiography–LVCMR on rest images	0.000
14	EF on MPGS–EF on MRGS	0.000
15	EF on MPGS–EF on APGS	0.000
16	EF on MPGS–EF on ARGS	0.000
17	EF on MPGS–LVCMR on stress images	0.058*
18	EF on MRGS–LVCMR on rest images	0.000
19	EF on MRGS–EF on APGS	0.142*
20	EF on MRGS–EF on ARGS	0.000
21	EF on MRGS–LVCMR on stress images	0.000
22	EF on MRGS–LVCMR on rest images	0.000
23	EF on APGS–EF on ARGS	0.001
24	EF on APGS–LVCMR on stress images	0.000
25	EF on APGS–LVCMR on rest images	0.000
26	EF on ARGS–LVCMR on stress images	0.000
27	EF on ARGS–LVCMR on rest images	0.000
28	LVCMR on stress images–LVCMR on rest images	0.000

*Insignificant differences. EF, ejection fraction; CLV, contrast left ventriculography; MPGS, semi-automatically processed rest gated SPECT; APGS, automatically processed post-stress gated SPECT; ARGS, automatically processed rest gated SPECT; LVCMR, cavity to myocardium ratio.

Categorization of patients according to echocardiographic ejection fraction values

It should be noted that the exact value of EF is not as important as the functional status of the heart and we should establish how much these different evaluation systems can correctly predict the functional status of the hearts. So, we categorized patients based on echocardiographic EF values derived from previous studies and then tried to assess how much our evaluation system is successful in guessing the functional groups based on SPECT method.

We defined two functional groups: class 1, with echocardiographic EF less that 25% (as severely decreased EF); and class 2, with EF greater than 25% [3]. Discriminant analysis showed that we could significantly predict the severe groups of patients by their properties of SPECT (*P* value of discriminant analysis was less than 0.0001). The discriminant model predicted patient class by using six variables extracted from SPECT. The best predictor in the model was EF on APGS due to the value of the structural matrix in discriminant analysis. The structural matrix values and the order of the other factors are given in Table 4.

The discriminant model classified the patients into class 1, 100% correctly and to class 2, 81.6% correctly (Fisher's exact test *P* value < 0.0001). Overall classification performance showed that 82.6% of originally grouped cases were correctly classified.

We also used cross-validation measures for the analysis. In this method, each case is classified by the functions derived from all cases other than that case. We found that

Table 3 Model summary

Model*	*R*	R^2	*P* value
1	0.709(a)	0.503	0.0001
2	0.724(b)	0.524	0.0001

*Predictive models calculated by multiple regression analysis. Model 1 predictor is ejection fraction on MPGS. Model 2 predictors consisted of ejection fraction on MPGS, and LVCMR on rest images. EF can be predicted by the following linear formulae:
Model 1, predicted EF = 17.8 + (0.60 × EF on MPGS).
Model 2, predicted EF = 15.5 + (0.46 × EF on MPGS) + (0.22 × LVCMR on rest images).
Abbreviations as in the footnote to Table 1.

Table 2 Correlation studies that predicted ejection fraction (Pearson correlation)

		EF on MRGS	EF on MPGS	EF on ARGS	LVCMR on rest	LVCMR on stress	EF on echo	EF on APGS
EF on CLV	Pearson correlation	0.687	0.709	0.669	0.632	0.544	0.683	0.690
	P value	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001

Abbreviations as in the footnote to Table 1.

Table 4 Structural matrix values obtained when patients were categorized according to echocardiographic values for ejection fraction

Predictor variable	Structural matrix value
EF on APGS	0.859
EF on MRGS	0.841
EF on ARGS	0.821
EF on MPGS	0.692
LVCMR on stress images	0.580
LVCMR on rest images	0.506

These values show within-group correlations of each predictor variable with the canonical function. Abbreviations as in the footnote to Table 1.

80.7% of cross-validated grouped cases were correctly classified.

For classifying a new patient based on the discriminant model, we can make a linear Fisher discriminant model for each patient class. Then we can test the predictors of the patient in each model. The patient belongs to the class which shows greater model score. The Fisher discriminant model for group 1 is:

Class 1 score = 0.1(EF on MPGSM – EF on APGS) + 0.2(EF on ARGS – EF on MRGS) + (LVCMR on stress images × 0.3) – (LVCMR on rest images × 0.02) – 4.2.

The Fisher discriminant model for group 2 is:

Class 2 score = – (EF on MPGS × 0.02) + 0.3 × (EF on MRGS – LVCMR on stress images + EF on ARGS) + (EF on APGS × 0.04) – (LVCMR on rest images × 0.1) – 8.9.

Categorization of patients based on angiographic ejection fraction values

The same analysis was performed based on angiographic EF. We defined two functional groups: group 1, with angiographic EF less that 35% as severely decreased EF (class 1) and group 2, with EF greater than 35% (class 2) [4].

Discriminant analysis again showed that we could significantly predict the class 1 patients by their SPECT findings (P value of discriminant analysis was less than 0.0001). The best predictor in the model was EF on MPGS due to the value of structural matrix in discriminant analysis. The structural matrix values and the order of the other factors are given in Table 5. The discriminant model determined class 1 patients 90% correctly and the class 2 patients, 82.6% properly (Fisher's exact test P value < 0.0001). Overall classification performance showed that 85.3% of original grouped cases were correctly classified.

For classifying a new patient based on the discriminant model, we can make a linear Fisher discriminant model for each patient class. Then we can test the predictors of the patient in each model. The patient belongs to the class which shows the greater model score. The Fisher discriminant model for group 1 is:

Class 1 score = (EF on MPGS × 0.05) – (EF on MPGS × 0.08) – (EF on APGS × 0.1) + (EF on ARGS × 0.2) + (LVCMR on stress images × 0.3) – (LVCMR on stress images × 0.06) – 7.

For group 2 the score is:

Class 2 score = (EF on MPGS × 0.2) – (EF on MPGS × 0.2) + (EF on APGS × 0.03) + (EF on ARGS × 0.3) + (LVCMR on stress images × 0.2) + (LVCMR on stress images × 0.08) – 13.6.

Regression analysis showed that prediction of angiographic EF based on post-stress gated SPECT by semi-automatic or automatic process in patients with SSS ≥ 13 was low ($r = 0.23$ and $r = 0.29$, respectively with $P = 0.001$), but the results of such analysis in the patients with SSS < 13 demonstrated good prediction of angiographic EF by semi-automatic and automatic post-stress gated SPECT ($r = 0.68$ and $r = 70$ with $P = 0.001$, respectively).

Discriminant analysis showed that we could significantly predict the class 1 patients of angiographic classification by SSS, SDS and SRS indices (P value of discriminant analysis was less than 0.0001). The best predictor was the SRS index due to the value of the structural matrix in discriminant analysis. The structural matrix values and the order of the other factors are given in Table 6.

Out of 109 patients, 11 showed normal coronary angiography and 98 revealed abnormal angiographic results (CAD with at least one coronary lesion of more than 50% stenosis). We assessed the diagnostic accuracy

Table 5 Structural matrix values obtained when patients were categorized according to angiographic values for ejection fraction

Predictor variable	Structural matrix value
EF on MPGS	0.865
EF on APGS	0.860
EF on ARGS	0.814
EF on MRGS	0.781
CMR on rest images	0.758
CMR on stress images	0.541

Abbreviations as in the footnote to Table 1.

Table 6 Structural matrix values obtained when patients were categorized according to discriminant analysis

Predictor variable	Structural matrix value
Summed rest score (SRS)	0.807
Summed stress score (SSS)	0.709
Summed difference score (SDS)	0.199

of ΔEF in predicting the presence or absence of CAD. The best results of ROC analysis was a cut-off point of 5.5, which showed that considering the ΔEF as the only predictor of CAD the sensitivity and specificity of test is 71.4% and 18.9%, respectively.

Furthermore, of the total of 109 patients, in 25 cases the SSS index was less than 4. Of these, seven showed normal and 18 abnormal angiographic results. Therefore, considering the SSS as the only determinant of abnormal coronary artery, only 80/98 of patients will be correctly diagnosed. Four of these 18 patients with abnormal coronary angiography and SSS < 4 showed a significant drop ($\Delta EF > -5.5\%$) in the post-stress phase as compared to the rest images; however, none of the patients with SSS < 4 and normal angiography revealed a significant drop between two stages (all ΔEF values were less than -5.5%).

Discussion

Does good correlation exist between different methods for assessment of ejection fraction?

A large amount of research has been carried out in order to find the correlation that exists between different methods for the calculation of EF. In 1999 Ruiz-Salmeron *et al.* [5] found that gated tomography was significantly correlated to contrast ventriculography in the calculation of EF, both with acquisition at rest and throughout dobutamine infusion. Yoshioka *et al.* [6] showed there was also a good correlation between EDV, ESV and LVEF by quantitative gated SPECT (QGS) and LVG. Kondo *et al.* [7] concluded that in patients with ECG gating set at eight intervals, QGS systematically underestimates LV volumes and EF compared with both LVG and MRI. Bacher-Stier *et al.* [8] obtained a good correlation between echo LVEF and ^{201}Tl-gated SPECT LVEF both post-stress and at rest but closer correlation was observed with gated SPECT LVEF at rest. In 2001, researchers discovered that LVCMR easily calculated from ^{99m}Tc-tetrofosmin as well as ^{201}T1 or ^{99m}Tc-MIBI myocardial SPECT images can be useful in directly identifying patients with abnormal LVEF [9,10]. Additionally, in 2004, Kakhki *et al.* [11] observed a significant correlation between EF and LVCMR. Pontillo *et al.* [12] showed that the evaluation of global LV function by means of myocardial perfusion imaging may represent a valuable and affordable alternative to expensive and time-consuming methods, especially in the presence of difficult technical settings such as two-dimensional Doppler echocardiography.

Nahar *et al.* [13] compared the EF measurements between four methods of echocardiography (fundamental alone, fundamental with contrast, harmonic alone and harmonic with contrast) and radionuclide angiography. A total of 50 patients who underwent radionuclide EF measurement underwent echocardiography by four methods. Three echocardiologists measured echocardiographic LVEF independently and were blinded to radionuclide angiography. The correlation of echocardiographic EF with radionuclide EF improved incrementally with each method. However, contrast with harmonic imaging provided the closest correlation. At the same time, Bellenger *et al.* [14] endeavoured to compare the agreement of left ventricular volumes and ejection fraction by M-mode echocardiography, two-dimensional echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance in patients with chronic stable heart failure. They suggested that EF measurements by various techniques were not interchangeable and wide variances in volumes and EF between techniques exist, which are most marked in comparisons using echocardiography. They stated that cardiovascular magnetic resonance is the preferred technique for volume and EF estimation in heart failure patients, because of its three-dimensional approach for non-symmetric ventricles and superior image quality. In 2004, researchers examined the concordance between LVEF, wall motion and wall thickening scores derived from gated SPECT, echocardiography and equilibrium radionuclide ventriculography, in a group of 16 patients with suspected ischaemic heart disease. They concluded that estimation of EF by all the three studied modalities agreed to a degree sufficient for routine clinical practice. However, estimates of wall thickening from echocardiography cannot be used interchangeably with those derived from gated myocardial perfusion SPECT [15].

On the whole, most researchers have evinced good linear correlation among different methods such as contrast ventriculography, echocardiography, radionuclide ventriculography and gated SPECT in estimation of EF. Our study also verified previous reports, and a striking result which has been obtained from this study is that the raw numbers of EF are not identical in different techniques and they are not comparable. In fact, the values obtained by each of these methods cannot be used interchangeably with those derived from other methods. A fine linear correlation in the wide range of values exists among EF values that have been attained from different methods but such correlation does not imply equality and similarity of the raw values of divergent methods. In other words, the increase in EF values in the gated SPECT is proportional to the increase in the echocardiography and angiography methods in spite of the fact that their raw values are not the same or equal [16].

Due to this reason specialists should be aware of such a limitation when they want to interpret and compare the EF values. For example if physicians intend to compare EF values before and after treatment, they must certainly measure EFs with the same method in these two stages.

Also, they should take into consideration the fact that the raw values of EF are not of the same value in two different methods. For instance, if calculated EF is equal to 35% by gated SPECT, it does not imply that the same value obtains with regard to equal EF number echocardiography. The existence of technical differences, such as low resolution in the radionuclide imaging, can make such variations. Due to such a reason, the normal ranges of EF vary among the different methods and the limits which may indicate normal value for one method can be abnormal for the other.

Kakhki *et al.* [11] revealed that LVEF can be reliably predicted from the combination of rest LVCMR and SRS. Our study also showed that angiographic and echocardiographic LVEF in severely decreased cardiac performance can be reliably predicted from the SPECT properties. The best-fit models were mentioned in the result section.

Is there any benefit in performing a gated procedure in both phases of the study?

Johnson *et al.* [17] claimed that the post-stress LVEF calculated using volume programs from the gated SPECT data cannot be considered to represent the basal LVEF value in all patients. However, based on our study results, a considerable depression in the EF value ($\Delta EF > -5.5\%$) in the post-stress stage relative to the rest period can be an index of ischaemic heart diseases. This situation, which has been investigated repeatedly and has been attributed mainly to the stunning phenomenon, can be the only index of ischaemic heart diseases in a low percentage of patients. Such conditions were confirmed in our patients. For the patients in whom our research was conducted, there were 25 with SSS less than 4. Of these, 18 had abnormal coronary angiography and seven showed normal results in angiography. If an SSS of less than 4 was considered as negative, MPI for significant CAD, a false negative rate of 18/98 (18.7%) would be present; however, in 4/18 of patients with abnormal angiogram and SSS < 4 there was a significant drop in EF of post-stress images as compared to the rest phase images.

In contrast, none of the patients with normal coronary artery angiogram and SSS < 4 showed a significant decrease in EF of post-stress images in comparison to the rest-phase gated SPECT. Therefore, if instead of SSS only, the combination of SSS and considerable depression ($\Delta EF > -5.5\%$) in EF of the post-stress images were considered as an index for detection of CAD, the false negative ratio in the identification of CAD by scintigraphy would decline from 20/103 to 16/103. As we expressed in the results section, if detection of CAD is determined only by ΔEF, the diagnostic accuracy will be very low and ΔEF alone is not a reliable index for screening CAD patients. Meanwhile, adding this index to the other ischaemic indices in scintigraphy (SSS, SDS and SRS) can increase the diagnostic accuracy. Performing both rest EF and stress EF on patients may allow identification of post-stress stunning that may aid in the diagnosis of CAD, particularly in multi-vessel disease [18]. The presence of a post-ischaemic reduction in LVEF is probably another marker of disease severity and probably a marker of reduced event-free survival.

Which is the best index as a predictor of ejection fraction?

Many studies have demonstrated that the LVEF and the SSS provide important prognostic information [19,20]. Sciagra *et al.* [21] recently demonstrated that there is a significant correlation between LVEF and the infarct size. In the study by Kakhki *et al.* [11] there was significant correlation between LVEF and SSS or SRS also.

Achtert *et al.* [22] and Manrique *et al.* [23] found that the QGS program underestimated LVEF in patients with large myocardial perfusion defects. In contrast, Gayed *et al.* [24] showed that myocardial perfusion defects did not seem to affect the accuracy of LVEF calculation using the QGS algorithm.

Our study has indicated that a reverse correlation exists between perfusion indices (SSS, SDS and SRS) and EF values in that as the amount of one increases, that of the other decreases. To the extent that the ischaemic cardiac injuries (ischaemia and infarction) increase dramatically, the decline in the EF values will also be more pronounced. In discriminant analysis the SRS index was a most important factor among the others (SSS, SRS and SDS). Perhaps the cause of such a fact was that our acquisitions were performed on the post-stress phase. If the acquisitions were carried out in the stress phase it would be possible that SSS or SDS were determined as the best indices in the detection of CAD.

Which process is better: the semi-automatic or the automatic?

So far, much research has been performed on the gated information in order to establish whether the semi-automatic or automatic process is the more reliable. Nichols *et al.* [25] showed that the results of automated gated SPECT LVEF correlated well with those of semi-automatic gated SPECT and gated first-pass and equilibrium blood pool values and were highly reproducible. These authors also demonstrated excellent intra-observer reproducibility for ejection fractions and volumes and the results showed good agreement with values for ejection fractions and volumes derived from an expert's semi-automatic drawings [26]. Our study showed that post-stress gated SPECT by a semi-automatic or automatic process could not predict angiographic EF in patients with SSS > 13 as accurately as in patients with SSS < 13. Also, the prediction of EF in patients with SSS ≥ 13

based on the semi-automatic process was minimally better than the automatic one. There was no difference between these two processes in patients with SSS < 13. Based on our findings both methods have good correlation in the determination of EF. However, it could be recommended that in patients with large defects (SSS ≥ 13), the semi-automatic processing of the SPECT data is preferable.

Recent advances

The same findings might occur with important new technologies such as cardiac CT and cardiac MRI [27–33]. In fact, these techniques have shown acceptable correlations for the results of ejection fraction with those of the previously mentioned methods. In the study by Coche *et al.* it was found that in comparison with equilibrium radionuclide ventriculography, ECG-gated 16-slice CT demonstrates a good correlation for ventricular ejection fraction [28]. Schaefer *et al.* also noted that LVEF as determined by gated ^{99m}Tc-MIBI SPECT agrees over a wide range of clinically relevant values with MRI [29].

Conclusion

We conclude that:

1. Good correlation exists among different routine methods such as contrast ventriculography, echocardiography and gated SPECT for the estimation of EF, but the raw values of EF are not identical and solely comparable in different techniques and they cannot be used interchangeably.
2. Adding ΔEF to the other ischaemic indices in scintigraphy (SSS, SDS and SRS) can increase the CAD diagnostic accuracy. Thus performing gated procedure on both phases of the study and therefore calculating both rest EF and stress EF of patients may allow identification of post-stress stunning, which may aid the diagnosis of CAD, particularly in multi-vessel disease.
3. In the patients with SSS ≥ 13, post-stress gated SPECT by the semi-automatic or automatic process could not predict angiographic EF as accurately as for patients with SSS < 13.
4. Whenever gating of the images is impossible, calculation of LVCMR can be a reliable indicator of LVEF.

Acknowledgements

This study was carried out with the sponsorship of Tehran University of Medical Sciences, Research Institute for Nuclear Medicine. We are indebted to Dr. Mohammad Eftekhari, Dr. Babak Fallahi Sichani, Dr. Abbas Takavar for their consultations throughout the investigation. The authors would like to thank the staff and technologists of our department (Mr. N. Ahmadin, Ms. M. Darvishha, Mr. M. Sohrabi, Ms. F. Samimi and Mr. Sh. Yaraee) for their help and technical assistance.

References

1 De Sutter J, Kazmierczak J, Fonteyne W, Tavernier R, Jordaens LJ. Factors determining long-term outcomes and survival in patients with coronary artery disease and ventricular tachyarrhythmias: a single center experience. *Pacing Clin Electrophysiol* 2000; **23**:1947–1952.

2 Altun GD, Akdemir O, Ustun F, Altun A, Sarikaya A, Berkarda S. Technetium-99m sestamibi cavity/myocardium count ratio in the detection of left ventricular hypertrophy. *Clin Cardiol* 2003; **26**:143–146.

3 Bitran D, Merin O, Klutstein MW, Od-Allah S, Shapira N, Silberman S. Mitral valve repair in severe ischemic cardiomyopathy. *J Card Surg* 2001; **16**:79–82.

4 Hoffmann R, von Bardeleben S, ten Cate F, Borges AC, Kasprzak J, Firschke C, *et al.* Assessment of systolic left ventricular function: a multi-centre comparison of cineventriculography, cardiac magnetic resonance imaging, unenhanced and contrast-enhanced echocardiography. *Eur Heart J* 2005; **26**:607–616.

5 Ruiz-Salmeron R, Ponce de Leon E, Lopez A, Guitian R, Romeo D, del Campo V, *et al.* Validation of the three-dimensional method of sestamibi gated-SPECT in the calculation of the left ventricular ejection fraction in patients with ischemic heart disease. Comparison with contrast ventriculography. *Rev Esp Cardiol* 1999; **52**:671–680.

6 Yoshioka J, Hasegawa S, Yamaguchi H, Tokita N, Paul AK, Xiuli M, *et al.* Left ventricular volumes and ejection fraction calculated from quantitative electrocardiographic-gated ^{99m}Tc-tetrofosmin myocardial SPECT. *J Nucl Med* 1999; **40**:1693–1698.

7 Kondo C, Fukushima K, Kusakabe K. Measurement of left ventricular volumes and ejection fraction by quantitative gated SPET, contrast ventriculography and magnetic resonance imaging: a meta-analysis. *Eur J Nucl Med Mol Imaging* 2003; **30**:851–858.

8 Bacher-Stier C, Muller S, Pachinger O, Strolz S, Erler H, Moncayo R, *et al.* Thallium-201 gated single-photon emission tomography for the assessment of left ventricular ejection fraction and regional wall motion abnormalities in comparison with two-dimensional echocardiography. *Eur J Nucl Med* 1999; **26**:1533–1540.

9 Sciagra R, Bisi G, Buonamici P, Zerauschek F, Santoro GM, Meldolesi U, *et al.* Left ventricular cavity-to-myocardium count ratio in technetium-99m-sestamibi SPECT in the detection of resting left ventricular dysfunction. *J Nucl Med* 1997; **38**:766–770.

10 Roberti RR, Van Tosh A, Baruchin MA, Gallagher R, Friedman P, Ventura B, *et al.* Left ventricular cavity-to-myocardial count ratio: a new parameter for detecting resting left ventricular dysfunction directly from tomographic thallium perfusion scintigraphy. *J Nucl Med* 1993; **34**:193–198.

11 Kakhki VD, Zakavi SR, Jabari H. Prediction of the left ventricular ejection fraction using cavity-to-myocardium count ratio and perfusion scores in myocardial perfusion SPECT. *Hellenike Pyrenike Iatr* 2004; **7**: 127–130.

12 Pontillo D, Patruno N, Capezzuto A, Serra F, Sassara M, Scabbia EV. Comparison of two different methods for the evaluation of left ventricular ejection fraction in patients with coronary artery disease. *Angiology* 2002; **53**:693–698.

13 Nahar T, Croft L, Shapiro R, Fruchtman S, Diamond J, Henzlova M, *et al.* Comparison of four echocardiographic techniques for measuring left ventricular ejection fraction. *Am J Cardiol* 2000; **86**:1358–1362.

14 Bellenger NG, Burgess MI, Ray SG, Lahiri A, Coats AJ, Cleland JG, *et al.* Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance; are they interchangeable? *Eur Heart J* 2000; **21**:1387–1396.

15 Mohan HK, Livieratos L, Gallagher S, Bailey DL, Chambers J, Fogelman I. Comparison of myocardial gated single photon emission computerised tomography, planar radionuclide ventriculography and echocardiography in evaluating left ventricular ejection fraction, wall thickening and wall motion. *Int J Clin Pract* 2004; **58**:1120–1126.

16 Rozanski A, Nichols K, Yao SS, Malholtra S, Cohen R, DePuey EG. Development and application of normal limits for left ventricular ejection fraction and volume measurements from ^{99m}Tc-sestamibi myocardial perfusion gates SPECT. *J Nucl Med* 2000; **41**:1445–1450.

17 Johnson LL, Verdesca SA, Aude WY, Xavier RC, Nott LT, Campanella MW, *et al.* Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. *J Am Coll Cardiol* 1997; **30**:1641–1648.

18 Wheat JM, Currie GM. Rest versus stress ejection fraction on gated myocardial perfusion SPECT. *J Nucl Med Technol* 2005; **33**:218–223.

19 Murphy PB, Port SC. Radionuclide evaluation of left ventricular function. In: Sandler MP, Coleman RE, Patton JA, *et al.* (editors): *Diagnostic nuclear medicine*. Philadelphia: Lippincott Williams & Wilkins; 2003, pp. 239–271.

20 Sharir T, Germano G, Kang X, Lewin HC, Miranda R, Cohen I, *et al.* Prediction of myocardial infarction versus cardiac death by gated myocardial perfusion SPECT: risk stratification by the amount of stress-induced ischemia and the post stress ejection fraction. *J Nucl Med* 2001; **42**:831–837.

21 Sciagra R, Imperiale A, Antoniucci D, Migliorini A, Parodi G, Comis G, *et al.* Relationship of infarct size and severity versus left ventricular ejection fraction and volumes obtained from ^{99m}Tc-sestamibi gated single-photon emission computed tomography in patients treated with primary percutaneous coronary intervention. *Eur J Nucl Med Mol Imaging* 2004; **31**:969–974.

22 Achtert AD, King MA, Dahlberg ST, Pretorius PH, LaCroix KJ, Tsui BM. An investigation of the estimation of ejection fractions and cardiac volumes by a quantitative gated SPECT software package in simulated gated SPECT images. *J Nucl Cardiol* 1998; **5**:144–152.

23 Manrique A, Faraggi M, Vera P, Vilain D, Lebtahi R, Cribier A, *et al.* ^{201}Tl and ^{99m}Tc-MIBI gated SPECT in patients with large perfusion defects and left ventricular dysfunction: comparison with equilibrium radionuclide angiography. *J Nucl Med* 1999; **40**:805–809.

24 Gayed I, Cid E, Boccalandero F, Podoloff D. Factors affecting left ventricular ejection fraction using automated quantitative gated SPECT. *Clin Nucl Med* 2003; **28**:290–295.

25 Nichols K, DePuey EG, Rozanski A. Automation of gated tomographic left ventricular ejection fraction. *J Nucl Cardiol* 1996; **3(6 Pt 1**:475–482.

26 Nichols K, DePuey EG, Rozanski A, Salensky H, Friedman MI. Image enhancement of severely hypoperfused myocardia for computation of tomographic ejection fraction. *J Nucl Med* 1997; **38**:1411–1417.

27 Manghat NE, Morgan-Hughes GJ, Roobottom CA. Use of a semi-automated left ventricular 'rapid ejection fraction' algorithm with 16-detector row CT and comparison with two-dimensional echocardiography: initial experience in a UK centre. *Clin Radiol* 2006; **61**:206–208.

28 Coche E, Vlassenbroek A, Roelants V, D'Hoore W, Verschuren F, Goncette L, *et al.* Evaluation of biventricular ejection fraction with ECG-gated 16-slice CT: preliminary findings in acute pulmonary embolism in comparison with radionuclide ventriculography. *Eur Radiol* 2005; **15**:1432–1440.

29 Schaefer WM, Lipke CS, Standke D, Kuhl HP, Nowak B, Kaiser HJ, *et al.* Quantification of left ventricular volumes and ejection fraction from gated ^{99m}Tc-MIBI SPECT: MRI validation and comparison of the Emory Cardiac Tool Box with QGS and 4D-MSPECT. *J Nucl Med* 2005; **46**:1256–1263.

30 Schaefer WM, Lipke CS, Nowak B, Kaiser HJ, Reinartz P, Buecker A, *et al.* Validation of QGS and 4D-MSPECT for quantification of left ventricular volumes and ejection fraction from gated ^{18}F-FDG PET: comparison with cardiac MRI. *J Nucl Med* 2004; **45**:74–79.

31 Sierra-Galan LM, Ingkanisorn WP, Rhoads KL, Agyeman KO, Arai AE. Qualitative assessment of regional left ventricular function can predict MRI or radionuclide ejection fraction: an objective alternative to eyeball estimates. *J Cardiovasc Magn Reson* 2003; **5**:451–463.

32 Le Page R, Crandall CR, Hood CH, Enerson RD, Schrepel J, Sweatman TW, *et al.* A brief evaluation of cardiac gated MRI in left ventricular ejection fraction determinations: a comparison with standard left ventriculography DSA and nuclear medicine. *Ann Radiol* (Paris) 1986; **29**:87–90.

33 Vallejo E, Dione DP, Bruni WL, Constable RT, Borek PP, Soares JP, *et al.* Reproducibility and accuracy of gated SPECT for determination of left ventricular volumes and ejection fraction: experimental validation using MRI. *J Nucl Med* 2000; **41**:874–882.