European Heart Journal (2000) **21,** 1387–1396
doi:10.1053/euhj.2000.2011, available online at http://www.idealibrary.com on IDEAL®

Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance

Are they interchangeable?

N. G. Bellenger[1], M. I. Burgess[2], S. G. Ray[2], A. Lahiri[3], A. J. S. Coats[1], J. G. F. Cleland[4] and D. J. Pennell[1]

CHRISTMAS Study Steering Committee and Investigators

[1]*Cardiovascular MR Unit, Royal Brompton Hospital, National Heart and Lung Institute, Imperial College, London, U.K.;* [2]*Northwest Regional Cardiac Centre, Wythenshawe Hospital, Manchester, U.K.;* [3]*Northwick Park Hospital, London, U.K.;* [4]*University of Hull, Hull, U.K.*

Aims To prospectively compare the agreement of left ventricular volumes and ejection fraction by M-mode echocardiography (echo), 2D echo, radionuclide ventriculography and cardiovascular magnetic resonance performed in patients with chronic stable heart failure. It is important to know whether the results of each technique are interchangable, and thereby how the results of large studies in heart failure utilizing one technique can be applied using another. Some studies have compared cardiovascular magnetic resonance with echo or radionuclude ventriculography but few contain patients with heart failure and none have compared these techniques with the current fast breath-hold acquisition cardiovascular magnetic resonance.

Methods and Results Fifty two patients with chronic stable heart failure taking part in the CHRISTMAS Study, underwent M-mode echo, 2D echo, radionuclude ventriculography and cardiovascular magnetic resonance within 4 weeks. The scans were analysed independently in blinded fashion by a single investigator at three core laboratories. Of the echocardiograms, 86% had sufficient image quality to obtain left ventricular ejection fraction by M-mode method, but only 69% by 2D Simpson's biplane analysis. All 52 patients tolerated the radionuclude ventriculography and cardiovascular magnetic resonance, and all these scans were analysable. The mean left ventricular ejection fraction by M-mode cube method was $39 \pm 16\%$ and $29 \pm 15\%$ by Teichholz M-mode method. The mean left ventricular ejection fraction by 2D echo Simpson's biplane was $31 \pm 10\%$, by radionuclude ventriculography was $24 \pm 9\%$ and by cardiovascular magnetic resonance was 30 ± 11. All the mean left ventricular ejection fractions by each technique were significantly different from all other techniques ($P<0{\cdot}001$), except for cardiovascular magnetic resonance ejection fraction and 2D echo ejection fraction by Simpson's rule ($P=0{\cdot}23$). The Bland–Altman limits of agreement encompassing four standard deviations was widest for both cardiovascular magnetic resonance vs cube M-mode echo and cardiovascular magnetic resonance vs Teichholz M-mode echo at 66% each, and was 58% for radionuclude ventriculography vs cube M-mode echo, 44% for cardiovascular magnetic resonance vs Simpson's 2D echo, 39% for radionuclide ventriculography vs Simpson's 2D echo, and smallest at 31% for cardiovascular magnetic resonance–radionuclide ventriculography. Similarly, the end-diastolic volume and end-systolic volume by 2D echo and cardiovascular magnetic resonance revealed wide limits of agreement (52 ml to 216 ml and 11 ml to 188 ml, respectively).

Conclusion These results suggest that ejection fraction measurements by various techniques are not interchangeable. The conclusions and recommendations of research studies in heart failure should therefore be interpreted in the context of locally available techniques. In addition, there are very wide variances in volumes and ejection fraction between techniques, which are most marked in comparisons using echocardiography. This suggests that cardiovascular magnetic resonance is the preferred technique for volume and ejection fraction estimation in heart failure patients, because of its 3D approach for non-symmetric ventricles and superior image quality.

(Eur Heart J 2000; 21, 1387–1396)

Key Words: Heart failure, echocardiography, radionuclide ventriculography, cardiovascular magnetic resonance.

See page 1295 for the Editorial comment on this article

Revision submitted 27 October 1999, and accepted 2 November 1999. Second revision submitted and accepted 28 March 2000.

Correspondence: Dr N. G. Bellenger, CMR Unit, Royal Brompton Hospital, Sydney Street, London, SW3 6NP, U.K.

0195-668X/00/211387+10 $35.00/0

Introduction

The assessment of cardiac volumes and ejection fraction has valuable diagnostic, prognostic and therapeutic implications for patients suffering from left ventricular dysfunction[1–7]. With the increased recognition of the process of cardiac remodelling, and the advent of therapeutic interventions to mediate this, single or multiple estimates of volumes and ejection fraction are frequently used to assess an individual's need for and response to treatment. Furthermore, many therapeutic trials use these parameters as a threshold for randomization or as a primary outcome measure. Currently, the three commonly used non-invasive methods are echocardiography (echo), radionuclide ventriculography and cardiovascular magnetic resonance.

Echocardiography has been widely used as it is readily available and non-invasive. It does, however, suffer a number of limitations. M-mode echo is acoustic window and operator dependent and relies on geometric assumptions that do not hold true in patients with dilated, remodelled ventricles[8]. The assumption that a single segment is representative of the entire left ventricular is particularly problematic in patients with wall motion abnormalities[9]. 2D echo overcomes some of these problems but still extrapolates data from a limited sampling of the left ventricle and is highly dependent on good endocardial border definition.

Radionuclide ventriculography has been established as a useful measure of left ventricular ejection fraction[10,11], but is usually based on projection imaging and hence is affected by varying attenuation between anterior and posterior walls, is subject to background subtraction errors and is less appealing for sequential studies due to the need for repeated use of gamma radiation.

Cardiovascular magnetic resonance provides an assessment of left ventricular volumes and ejection fraction that is free of geometric assumptions and ionizing radiation. Cardiovascular magnetic resonance is becoming more available and faster and breath-hold acquisition sequences now require significantly less time than radionuclide ventriculography[12]. This had led to the increasing use and publication of data and recommendations derived from cardiovascular magnetic resonance based studies.

Much work has centred on the accuracy and reproducibility of each technique[11,13–15], but few studies have compared the techniques directly. Ultimately the choice of technique for a clinician is based on local availability. It is, therefore, important to know how interchangeable the results of each technique are, and thereby how uniformly the results of large studies utilizing one technique can be applied. Previously published reports suggest that 2D echo and radionuclide ventriculography are equally acceptable methods of comparing left ventricular ejection fraction[16–18]. This, however, was based on correlation coefficients, but correlation can occur without agreement[19–21]. Subsequent work was published on the agreement (using Bland–Altman Analysis) between 2D echo and radionuclide ventriculography[22]. Some studies have compared cardiovascular magnetic resonance with echo[23,24], or radionuclide ventriculography[25,26], but few contain patients with heart failure and the only published study of ejection fraction by all three techniques did not use the currently accepted method of cardiovascular magnetic resonance volume analysis and did not perform Bland–Altman analysis[27].

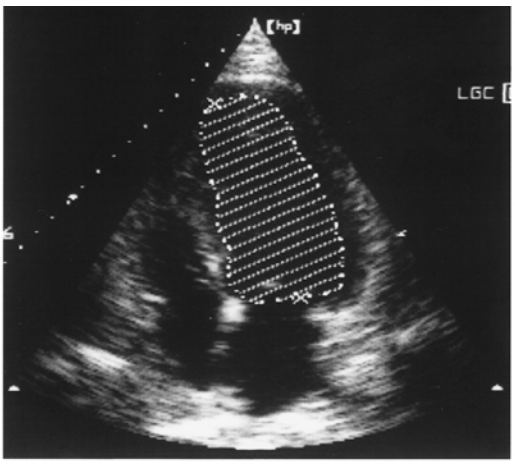
We therefore prospectively compared the agreement of M-mode echo, 2D echo, radionuclide ventriculography and cardiovascular magnetic resonance performed in patients with chronic, stable heart failure. We also analysed the available published data comparing these techniques.

Methods

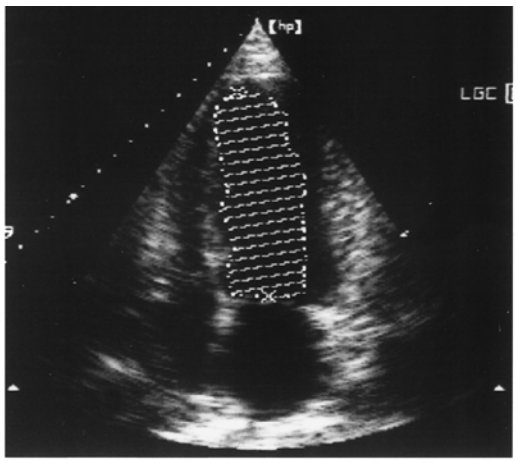
Patients

Fifty-two consecutive patients who were recruited for the cardiovascular magnetic resonance substudy of the CHRISTMAS (The Carvedilol Hibernation Reversible Ischaemia Trial; Marker of Success) trial were included in this study[28,29]. Patients came from two of the participating centres. Patients were included if they had chronic, stable heart failure (NYHA grade I–III) due to systolic dysfunction, were receiving optimized treatment (including an ACE inhibitor) and if their echo views were sufficient for the performance of wall motion analysis. Patients with atrial fibrillation or severe valvular disease were excluded from the trial. Patients underwent 2D echo, radionuclide ventriculography and cardiovascular magnetic resonance within the initial 4 week screening period (Fig. 1). There was no change in medication or clinical condition between each scan. The echo and nuclear imaging were performed at two centres, and all cardiovascular magnetic resonance scans at one centre. All analysis was performed by a single

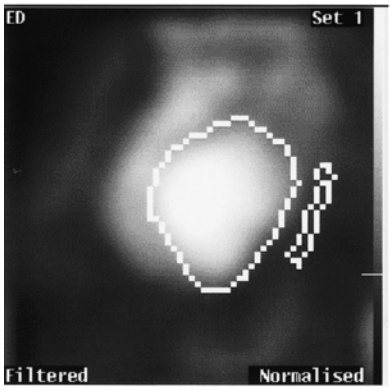
Figure 1 **Measurement of left ventricular function by echocardiography (a,b), radionuclide ventriculography (c,d,e), and cardiovascular magnetic resonance (f, g, h, i) in the same patient. (a) Apical four chamber view in diastole, and (b) systole with endocardial border and analysis by method of discs. (c) Radionuclide ventriculography diastolic and (d) systolic images with computerized analysis of ejection fraction (e). Vertical long axis (f) and horizontal axis (g) diastolic frames by cardiovascular magnetic resonance. A stack of short axis images (h) are acquired from the horizontal long axis view. (i) This represents the diastolic frame of one 16 frame short axis cine. The ejection fraction in this patient by 2D echo was 31%, radionuclide ventriculography was 18%, and cardiovascular magnetic resonance was 25%**


[hp]
LGC

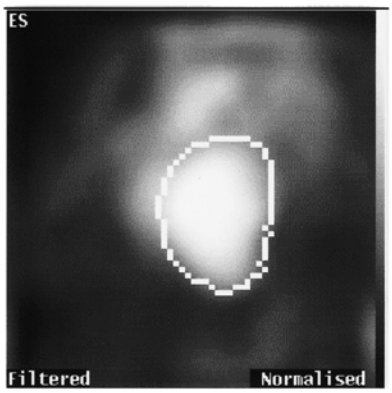
a


[hp]
LGC

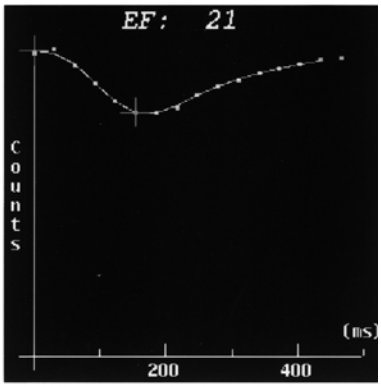
b


ED
Set 1
Filtered
Normalised

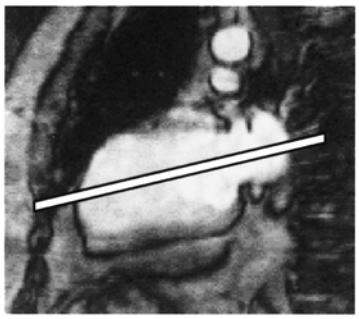
c


ES
Filtered
Normalised

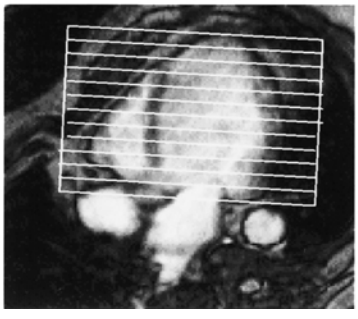
d


EF: 21
counts
(ms)
200
400

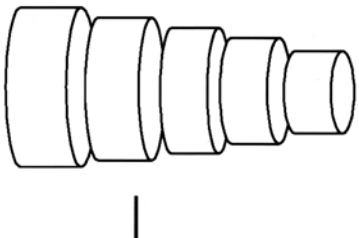
e



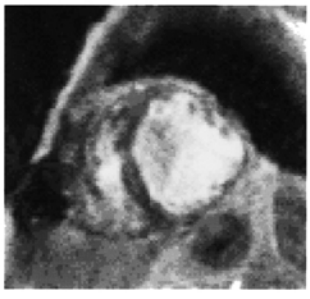
f



g



h



i

investigator in the respective echo, radionuclide ventriculography or cardiovascular magnetic resonance core-lab to maintain quality control and minimize variability. The study was approved by the ethics committee of both centres and written consent was obtained.

Echocardiography

M-mode and two dimensional echocardiography was performed by experienced operators. A standardized imaging protocol was adopted with cross-sectional imaging of the left ventricle immediately distal to the mitral valve tips and apical two-dimensional imaging based on orthogonal four- and two-chamber views. M-mode measurements applied the leading edge to leading edge principle as recommended by the American Society of Echocardiography[30]. M-mode left ventricular ejection fraction based on the cubed method was equal to (end-diastolic volume − end-systolic volume)/end-systolic volume where the end diastolic volume = EDD^3 and end-systolic volume = ESD^3. M-mode left ventricular ejection fraction was also calculated using the Teichholz correction[31], where end-diastolic volume = $7/(2{\cdot}4+EDD) \times EDD^3$ and end-systolic volume = $7/(2{\cdot}4+ESD) \times ESD^3$.

2D echo left ventricular ejection fraction was also evaluated by Simpson's biplane method of discs with manual planimetry of the endocardial border in end-diastolic (largest) and end-systolic (smallest) frames[32]. All measurements were made at the core laboratory from videotape recordings. Volumes were calculated from three cardiac cycles disregarding ectopic and post-ectopic beats with derivation of left ventricular ejection fraction.

Radionuclide ventriculography

In vivo labelling was performed using stannous pyrophosphate and 800 MBq pertechnetate and data were acquired in the left anterior oblique view with the patient in the supine position. Parameters included: ECG gating with a 10% window, photopeak 140 KeV, 20% window with no offset, 64 × 64 matrix, 3–4 mm pixel size, 32 frames and acquisition to 5 million counts. Left ventricular ejection fraction was calculated by dividing the background-corrected difference in end-systolic (minimum) and end-diastolic (maximum) counts by the end-diastolic counts.

Cardiovascular magnetic resonance

All subjects were imaged by one investigator at one centre using a Picker Edge 1·5 T scanner (Picker, Cleveland, OH, U.S.A.), a body coil and electrocardiogram (ECG) triggering. The cardiac short axis was determined from three scout images: transverse, vertical long axis and breath-hold diastolic horizontal long axis. The basal short axis slice was positioned just forward of the atrioventricular ring, and all subsequent breath-hold cines were acquired in 1 cm steps towards the apex. A breath-hold segmented gradient echo fast low-angle shot (FLASH) sequence was used for each of the contiguous short axis slices. Parameters were as follows: echo time (TE) 3·8 ms, repeat time (TR) = RR interval, slice thickness 10 mm, field of view 35 × 35 cm, read matrix 256, phase matrix 128, frames 16, flip angle 35°, phase encode group 6–10. An average of 10 short axis segments was needed to encompass the entire left ventricle. The average scanning time was 18 min.

Image analysis was performed on a personal computer using in-house developed software (CMR tools © Royal Brompton and Harefield NHS Trust, London, U.K.). End-diastolic and end-systolic images were chosen as the maximal and minimal mid-ventricular cross-sectional areas in a cinematic display. Short axis end-diastolic and end-systolic endocardial borders were traced manually for each slice. These areas were multiplied by the slice thickness (10 mm) and added together to obtain the end-diastolic volume and end-systolic volume, respectively. Ejection fraction (%) was calculated as left ventricular stroke volume (equal to end-diastolic volume − end-systolic volume) divided by the left ventricular end-diastolic volume. Papillary muscles were excluded from the volume measurements. Care was taken not to include atrial slices at end-systole secondary to apical movement of the base of the heart during left ventricular contraction.

To reduce variability, all the echo, radionuclide ventriculography and cardiovascular magnetic resonance images were analysed by one respective core lab investigator (M.B., D.J.P., N.G.B., respectively) who was blinded to the results of the other techniques.

Retrospective analysis of published data

A computer-assisted Medline search for published articles comparing ejection fractions by 2D echo ± radionuclude ventriculography ± cardiovascular magnetic resonance was performed. For inclusion the studies had to directly compare the mean ejection fraction or quote agreement by Bland–Altman or equivalent analysis. Studies that only quoted correlation coefficient were not included.

Results

All 52 patients underwent 2D echo and were included according to the criteria that they had an adequate echo window to provide wall motion data. However, the echo core laboratory subsequently judged that only 45 (86%) had sufficient image quality to obtain left ventricular ejection fraction by the M-mode echo method, and 36 (69%) by 2D Simpson's biplane analysis. One patient

Table 1 Number of patients and mean ± SD data for left ventricular (LV) end-diastolic diameter, end-systolic diameter, end-diastolic volume, end-systolic volume and ejection fraction by echocardiography (M-mode and 2D echo), radionuclide ventriculography (RNV) and cardiovascular magnetic resonance (CMR)

Parameter	Number	Mean ± SD
M-mode echo		
LV end-diastolic diameter	45	59 ± 11 mm
LV end-systolic diameter	45	50 ± 16 mm
Fractional shortening	45	16 ± 13%
Ejection fraction by cube	45	39 ± 22%
Ejection fraction by Teichholz	45	29 ± 15%
2D echo		
LV end-diastolic volume	36	136 ± 51 ml
LV end-systolic volume	36	98 ± 37 ml
EF by Simpson's biplane	36	31 ± 5%
RNV		
Ejection fraction	51	24 ± 21%
CMR		
LV end-diastolic volume	52	267 ± 106 ml
LV end-systolic volume	52	192 ± 98 ml
LV ejection fraction	52	30 ± 9%

underwent echo and cardiovascular magnetic resonance but withdrew from the study prior to having their radionuclide ventriculography. All 52 patients studied tolerated the cardiovascular magnetic resonance, and all cardiovascular magnetic resonance scans were analysable.

Comparison of ejection fraction

The mean left ventricular ejection fraction by the M-mode cube method was 39 ± 16% and 29 ± 15% by the Teichholz M-mode method. The mean left ventricular ejection fraction by 2D echo Simpson's biplane was 31 ± 10%, by radionuclide ventriculography was 24 ± 9% and by cardiovascular magnetic resonance was 30 ± 11%. The mean data from all the techniques is shown in Table 1. All the mean left ventricular ejection fractions by each technique were significantly different from all other techniques ($P<0{\cdot}001$), except for cardiovascular magnetic resonance ejection fraction and 2D echo ejection fraction by Simpson's rule ($P=0{\cdot}23$) (Table 2).

The correlation, mean difference and Bland–Altman plots for the left ventricular ejection fraction by the three techniques are illustrated in Table 2. The Bland–Altman range encompassing 4 SD was widest for both cardiovascular magnetic resonance–cube M-mode echo and cardiovascular magnetic resonance–Teichholz M-mode echo at 66% each, and was 58% for radionuclide ventriculography–cube M-mode echo, 44% for cardiovascular magnetic resonance–Simpson's 2D echo, 39% for radionuclide ventriculography–Simpson's 2D echo, and narrowest at 31% for cardiovascular magnetic resonance–radionuclude ventriculography (Fig. 2).

Comparison of volumes

The end-diastolic volume and end-systolic volume by Simpson's biplane 2D echo and cardiovascular magnetic resonance revealed very wide limits of agreement (52 ml to 216 ml and 11 ml to 188 ml respectively) (Table 3), despite relatively good correlation.

Discussion

In view of the important prognostic and therapeutic implications of both cardiac volumes and ejection fraction, as well as the increasing availability and use of cardiovascular magnetic resonance, it is important to know how interchangeable are the results obtained from echo, radionuclide ventriculography and cardiovascular magnetic resonance. The mean ejection fraction by each technique was shown to differ significantly from the other techniques in all but the cardiovascular magnetic resonance–Simpson's biplane 2D echo comparison. Although there was no significant difference between the mean ejection fractions in this last group, the Bland–Altman plot reveals wide limits of agreement for this and all groups. These wide limits of agreement are consistent with previous studies (Table 4) but this represents the first comparison of 2D echo, radionuclide ventriculography and the current standard cardiovascular magnetic resonance analysis in patients with

Table 2 Mean difference, correlation coefficient, t-test, Bland–Altman (BA) limits and total range of agreement (equal to ± 4 SD) for the comparison of ejection fraction between echocardiography (both M-mode cube and 2D Simpson's method), radionuclide ventriculography (RNV) and cardiovascular magnetic resonance (CMR)

	M-mode echo–2D echo	RNV–M-mode echo	RNV–2D echo	CMR–RNV	CMR–M-mode echo	CMR–2D echo
Mean diff ± SD (%)	8·5 ± 11·8	− 15 ± 15	− 7 ± 10	6 ± 8	− 10 to 17	− 2 ± 11
Corr coef, r	0·72	0·44	0·46	0·67	0·22	0·41
P	<0·001	<0·0001	<0·0001	<0·0001	<0·001	0·23
BA limits (%)	− 15 to 32	− 45 to 13	− 27 to 12	− 9 to 22	− 43 to 23	− 24 to 20
BA range (%)	47	58	39	31	66	44

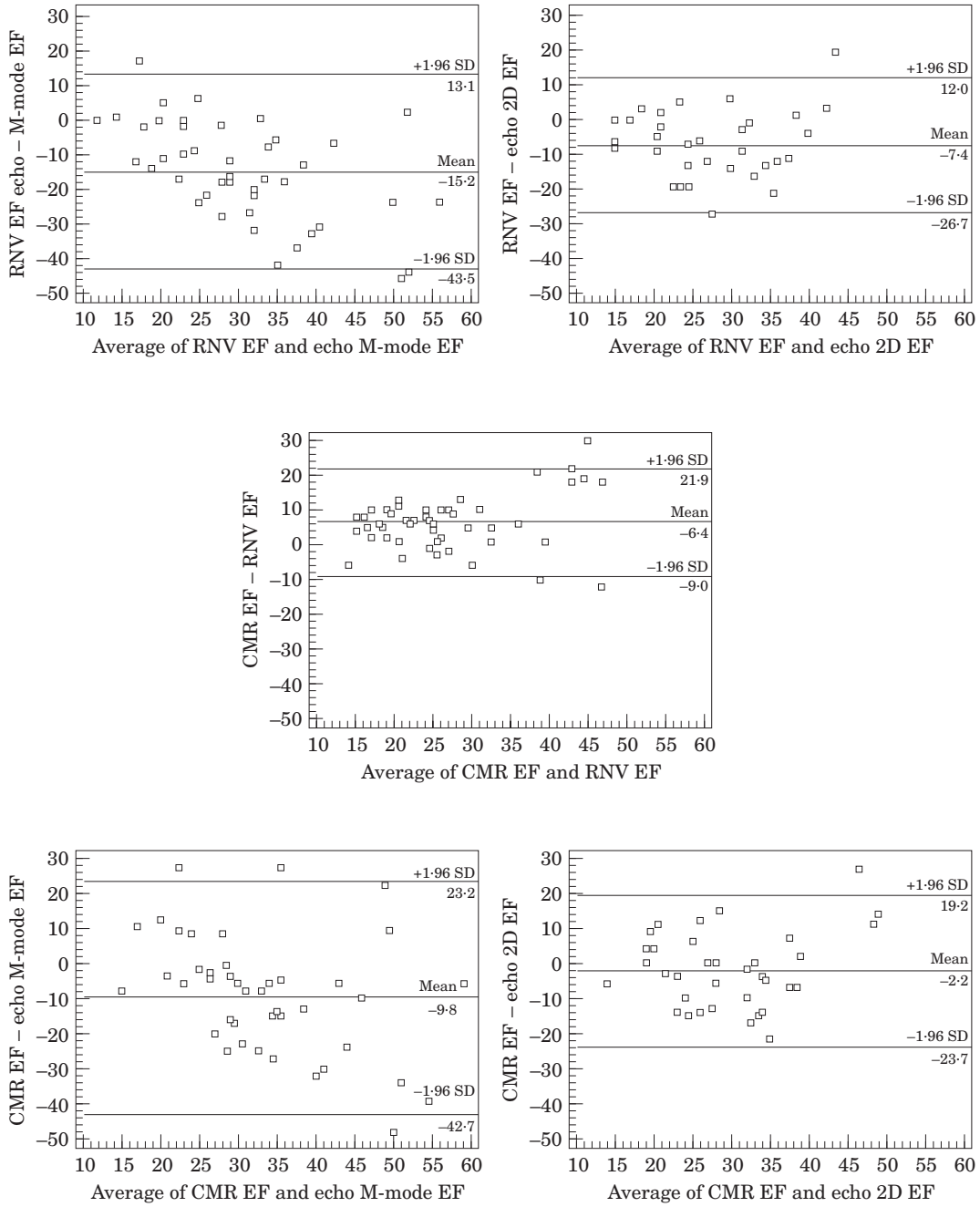


Figure 2 **Bland–Altman plots for the relationship between echo M-mode, 2D echo, radionuclide ventriculography (RNV) and cardiovascular magnetic resonance (CMR) assessment of ejection fraction (EF).**

chronic, stable heart failure. The results suggest that an assessment of ejection fraction by one method cannot be assumed to be universal. Although some discrepancy exists, most of the published data on comparison of these techniques would suggest that, irrespective of the patient population studied, cardiovascular magnetic resonance tends to give a higher ejection fraction than radionuclide ventriculography and echo gives a higher ejection fraction than either cardiovascular magnetic resonance or radionuclide ventriculography (Table 4).

Echo is widely used in large trials within the heart failure population but is considerably disadvantaged by the reliance on geometric assumptions. These do not hold true as the left ventricle undergoes progressive dilatation in heart failure. As the left ventricular volume increases the left ventricle becomes more spherical and the relationship between length and diameter is altered[31]. As a result, as the left ventricle diameter increases, the 95% confidence interval of prediction of left ventricular volume from the diameter rapidly

Table 3 Mean difference, correlation coefficient, t-test, Bland–Altman (BA) limits and total range of agreement (equal to ± 4 SD) for the comparison between the end-diastolic volume (EDV) and end-systolic volume (ESV) by echocardiography (2D-echo using Simpson's rule) and cardiovascular magnetic resonance (CMR)

	EDV CMR–2D echo	ESV CMR–2D echo
Mean diff ± SD (ml)	133 ± 42	99 ± 45
Corr coef, r	0·83	0·8
P	<0·0001	<0·0001
BA limits (ml)	52 to 216	11 to 188
BA range (ml)	268	199

increases[33]. Echo is also unreliable in the presence of regional asynergy, as it assumes that the area where the echo measurements are taken is representative of the entire left ventricle[9,34]. The Simpson's biplane 2D echo method is regarded as more accurate than M-mode methods[35], but it still extrapolates data from a limited sampling of the left ventricle. In clinical practice the biplane method is often not used as it is time consuming and even more dependent on good endocardial border definition. Our study is consistent with this, in that 86% of patients had images of sufficient quality to be analysed by M-mode echo, compared to 69% for the 2D Simpson's biplane method. Echo also suffers from errors introduced by gain-dependent edge identification and transducer position during imaging. These sources of error may contribute to the difference between echo and

Table 4 Published data that quotes direct comparison between echo ± radionuclide ventriculography (RNV) ± cardiovascular magnetic resonance (CMR) ejection fractions, with Bland–Altman limits (and range) of agreement where calculated. The number of patients (n), diagnosis (post MI, mixed group or ischaemic heart disease), technique used, comparison of mean ejection fraction (< or >), standard deviation of the difference (SD), correlation coefficient (r) and Bland–Altman limits are shown

Study	n	Diagnosis	Technique*	Echo:RNV	SD	r	Upper	Lower	range
Echo vs RNV									
Current study	52	Heart failure	2,4	>	15	0·44	13	−45	58
			1,4	>	10	0·46	12	−27	39
Folland *et al.*[18]	35		1		9·2	0·75	20·2	−17·4	37·6
Quinones *et al.*[17]	55	Mixed	1	>	7·0	0·93	15·5	−12·2	27·7
Starling *et al.*[46]	59		1		10·3	0·81	26·2	−15·4	41·6
Naik *et al.*[22]	25	Mixed	1		5·6	0·93	11·6	−11·5	23·2
Ray *et al.*[44]	99	Post MI	1	>	11·0		8	−35	43
Senior *et al.*[47]	49	Post MI	1	<	5·9		12·2	−11·4	33·6
Bellenger *et al.*[12]	16	IHD	2	>	14·7	0·2	19·1	−38·6	57·7
Study	n	Diagnosis	Technique	Echo:CMR	SD	r	Upper	Lower	range
Echo vs CMR									
Current study	52	Heart failure	2,4	>	17	0·22	23	−43	66
			1,4	>	11	0·41	20	−24	44
Mogelvang *et al.*[48]	22	IHD	1,3	<		0·9			
Bellenger *et al.*[12]	22	IHD	2,4	>	12·1	0·6	17·6	−29·9	47·5
Bloomgarden[48]		N, mixed	1,4	<					
Study	n	Diagnosis	Technique	RNV:CMR	SD	r	Upper	Lower	range
Radionuclide ventriculography vs cardiovascular magnetic resonance									
Current study	52	Heart failure	4	<	8	0·67	22	−9	31
Gaudio *et al.*[50]	32	DCM	5	>		0·91	7	−4	11
Mogelvang *et al.*[48]	22	IHD	1	<		0·87			
Underwood *et al.*[26]			5	<					
Bellenger *et al.*[12]	26	IHD	4	<	7·5	0·7	18·9	−10·5	29·4
Bloomgarden[49]			4	<					

*1=2D echocardiography using Simpson's biplane method.
2=M-mode echo using American Society of Echocardiography recommendations.
3=Cardiovascular magnetic resonance using either transverse slices or four short axis slices with four SA slices in subsequent extrapolation to fit the entire left ventricle.
4=Cardiovascular magnetic resonance using contiguous breath-hold short axis slices that encompass the entire left ventricle.
5=Cardiovascular magnetic resonance using spin echo short axis slices.

both radionuclide ventriculography and cardiovascular magnetic resonance. Furthermore, they may explain why the Bland–Altman limits of agreement between the cube M-mode echo and Simpson's 2D echo method were −14·6 to 31·7% in this study. Radionuclide ventriculography suffers from poor resolution, the need for background correction and errors from overlapping structures. radionuclide ventriculography analysis is also centre dependent, with the lower limit of the normal range of ejection fraction ranging from 35% to 75%[36]. Cardiovascular magnetic resonance, by comparison, acquires high resolution tomographic images that are free of geometric assumptions, without the need for ionizing radiation. Cardiovascular magnetic resonance has been shown to be both accurate and reproducible in both normal and dilated hearts[13,15,37,38]. This, together with the limitations of echo and radionuclide ventriculography, would suggest that cardiovascular magnetic resonance is the method of choice for the evaluation of left ventricular volumes and function, especially in dilated hearts. Gated SPECT can also be used to measure volumes and ejection fraction in the heart either with a manual analysis[39], or with an automated analysis programme[40]. One study using automated analysis showed a reasonable correlation of volumes and ejection fraction derived from gated SPECT compared to cardiovascular magnetic resonance, although the limits of agreement were wide, with non-zero differences between the techniques (systematic bias)[41]. Comparisons with other techniques, such as first pass radionuclide ventriculography similarly show wide agreement limits and systematic bias in volume estimation[42]. The inter-study reproducibility of ejection fraction measurements with gated SPECT is good[43]. More experience is required with this technique before its clinical application compared with cardiovascular magnetic resonance can be defined.

While these problems of each technique may explain the difference, the choice of technique used is often governed more by the availability of local resources and the important practical issue may not be which method is better, but that the techniques do not provide comparable results[44]. If a cut-off figure for ejection fraction is used for risk stratification or as a guide to treatment, the differing techniques will have considerable impact on who is treated, with both clinical and financial consequences. Naik *et al.*[22] argued that because a patient with an ejection fraction of 40% could have an ejection fraction of between 20 and 60% by radionuclide ventriculography, a second method could be used to provide more confidence in the estimate. Alternatively, if cardiovascular magnetic resonance offers greater accuracy and reproducibility[12,15], in one examination, albeit at greater initial cost, then there may be arguments to suggest that one cardiovascular magnetic resonance scan would provide a more cost effective assessment. The important difference between the reproducibility of cardiovascular magnetic resonance and other techniques is highlighted by the number of patients required to detect a clinical change. For example, Bottini *et al.*[45] found that to detect a 10 g difference in mass with a power of 90% and an α error of 0·05 would require 505 patients by echo and 14 by cardiovascular magnetic resonance.

Study limitations

Variability can occur in both the acquisition and the analysis of data. Errors in acquisition were minimized by following standard guidelines and by ensuring that the same investigator performed all the data acquisition for one technique for each site. As both the echo and radionuclide ventriculography data were acquired by two centres, the potential exists for greater variability of acquisition than for the cardiovascular magnetic resonance that was acquired at only one site; however, both centres had considerable experience with both imaging techniques. Variability in analysis was minimized by the use of core laboratories. Despite this, the use of taped echo data rather than on-line or digital analysis may have had a detrimental effect on echo quality, compared to the digital MR data.

The patient population was selected by the fact that the CHRISTMAS study required adequate echo views for wall motion analysis. In studies not requiring wall motion analysis, worse image quality may be accepted, which may result in even greater difference between echocardiography and the other imaging modalities.

Conclusion

These results suggest that ejection fraction measurements by various techniques are not interchangeable. The conclusions and recommendations of research studies in heart failure should therefore be interpreted in the context of locally available techniques. In addition, there are very wide variances in volumes and ejection fraction between techniques, which are most marked in comparisons using echocardiography. This suggests that cardiovascular magnetic resonance is the preferred technique for volume and ejection fraction estimation in heart failure patients.

We would like to acknowledge the work of all those involved in the CHRISTMAS study who supported this work at Royal Brompton and Northwick Park Hospitals, particularly Jane Webster, Glyn Davies, Michael Henein, Usha Raval and Prem Soman. Nick Bellenger was supported by an unrestricted research grant from SmithKline Beecham. The CHRISTMAS study is supported by Roche, Du Pont and Nuclear Diagnostics. The CHRISTMAS study steering committee is: J. G. F. Cleland (Chairman), D. J. Pennell, G. Murray, A. J. S. Coats, A. Cowley, S. Ray, A. Lahiri, P. MacFarlane, J. Dalle Mule, Z. Vered, The CHRISTMAS study principal site investigators are: **UK:** J. G. F. Cleland, A. J. S. Coats, A. Lahiri, A. Cowley, M. Joy, J. McGowan, M. Davies, A. Marshall, S. Holmberg, K. Channer, A. Tweddel, G. Lip, D. de Bono, M. Millar-Craig, C. Ward, J. Adgey, D. Sugrue, C. Bucknall, D. O'Gorman; **USA:** J. Lindenfeld; **Italy:** A. Cuocolo, J. Dalle Mule, R. Giubbini, P. Zanco, R. Buchberger; **Hungary:** I. Edes, M. Csanady, G. Polak, K. Karlocai, M. Karman; **Israel:** A. Caspi, Z. Vered, R. Zimlichman, A. Marmor, E. Klainman, M. Omary, D. David.

References

[1] McKee PA, Castell WP, Mcnamara PM, Kannel WP. The natural history of congestive heart failure: The Framingham study. N Engl J Med 1971; 285: 1441–5.

[2] St John Sutton M, Pfeffer MA, Moye L *et al*. Cardiovascular death and left ventricular remodeling two years after myocardial infarction: baseline predictors and impact of long-term use of captopril: information from the Survival and Ventricular Enlargement (SAVE) trial. Circulation 1997; 96: 3294–9.

[3] White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. Circulation 1987; 76: 44–51.

[4] Cintron G, Johnson G, Francis G, Cobb F, Cohn JN. Prognostic significance of serial changes in left ventricular ejection fraction in patients with congestive heart failure. Circulation 1993; 87 (Suppl VI): 7–23.

[5] Ghali JK, Liao Y, Cooper RS. Influence of left ventricular geometric patterns on prognosis in patients with or without coronary artery disease. J Am Coll Cardiol 1998; 31: 1635–40.

[6] Konstam MA, Rousseau MF, Kronenberg MW *et al*. Effects of the angiotensin converting enzyme inhibitor enalapril on the long-term progression of ventricular dysfunction in patients with heart failure. Circulation 1992; 86: 431–8.

[7] St John Sutton M, Pfeffer MA. Prevention of post-infarction left ventricular remodeling by ACE-inhibitors. Cardiologia 1994; 39 (12 Suppl 1): 27–30.

[8] Kronik G, Slany J, Mosslacher H. Comparative value of eight M-mode echocardiographic formulas for determining left ventricular stroke volume. Circulation 1979; 60: 1308–16.

[9] Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: Echocardiographic-angiographic correlations in the presence or absence of asynergy. Am J Cardiol 1976; 37: 7–11.

[10] Hains AD, Khawaja IA, Hinge DA, Lahiri A, Raftery EB. Radionuclide left ventricular ejection fraction: a comparison of three methods. Br Heart J 1987; 57: 232–6.

[11] Wackers FJT, Berger HJ, Johnstone DE *et al*. Multiple gated cardiac blood pool imaging for left ventricular ejection fraction: validation of the technique and assessment of variability. Am J Cardiol 1979; 43: 1159–66.

[12] Bellenger NG, Francis JM, Davies LC, Coats AJS, Pennell DJ. Establishment and performance of a magnetic resonance cardiac function clinic. J Cardiovasc Magn Reson 1999; 1 (4): 323–30.

[13] Semelka RC, Tomei E, Wagner S *et al*. Interstudy reproducibility of dimensional and functional measurements between cine magnetic resonance imaging studies in the morphologically abnormal left ventricle. Am Heart J 1990; 119: 1367–73.

[14] Bogaert JG, Bosmans HT, Rademakers FE *et al*. Left ventricular quantification with breath hold MR imaging: comparison with echocardiography. MAGMA 1995; 3: 5–12.

[15] Bellenger NG, Francis JM, Davies LC, Pennell DJ. Reproducibility of fast acquisition CMR sequences for left ventricular function in patients. (Abstract). J Cardiovasc Magn Reson 1999; 1: 81.

[16] Schiller NB, Acquatella H, Ports TA *et al*. Left ventricular volume from biplane two-dimensional echocardiography. Circulation 1979; 60: 547–55.

[17] Quinones MA, Waggoner AD, Reduto LA *et al*. A new simplified and accurate method for determining ejection fraction with 2D echocardiography. Circulation 1981; 744–53.

[18] Folland ED, Parisi AF, Moynihan PF, Jones DR, Feldman CL, Tow DE. Assessment of left ventricular ejection fraction and volumes by real time two-dimensional echocardiography. Circulation 1979; 60: 760–6.

[19] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurements. Lancet 1986; 1: 307–10.

[20] Bookbinder MJ, Panosian KJMJ. Using correlation of coefficient in method comparison studies. Clin Chem 1987; 33: 1170–6.

[21] Porter AMW. Misuse of correlation and regression in three medical journals. J R Soc Med 1999; 92: 123–8.

[22] Naik MM, Diamond GA, Soffer A, Siegel RJ. Correspondence of left ventricular ejection fraction determinations from two-dimensional echocardiography, radionuclide ventriculography and contrast cineangiography. J Am Coll Cardiol 1995; 25: 937–42.

[23] Germain P, Roul G, Kastler B, Mossard JM, Bareiss P, Sacrez A. Inter-study variability in left ventricular mass measurement. Comparison between M-mode echo and MRI. Eur Heart J 1991; 13: 1011–9.

[24] Bloomgarden DC, Fayad ZA, Ferrari VA, Chin B, St John Sutton M, Axel L. Global cardiac function using fast breathhold MRI: Validation of new acquisition and analysis techniques. Magn Reson Med 1997; 37: 683–92.

[25] Gaudio C, Tanzilli G, Mazzarotto P *et al*. Comparison of left ventricular ejection fraction by MRI and radionuclude ventriculography in idiopathic dilated cardiomyopathy. Am J Cardiol 1991; 67: 411–5.

[26] Underwood SR, Klipstein RH, Firmin DN, Fox KM, Poole-Wilson PA, Rees RS, Longmore DB. Magnetic resonance assessment of aortic and mitral regurgitation. Br Heart J 1986; 56: 455–62.

[27] Mogelvang J, Saunamaki K *et al*. Assessment of left ventricular volumes by magnetic resonance in comparison with radionuclide angiography, contrast angiography and echocardiography. Eur Heart J 1992; 13: 1677–83.

[28] Cleland JGF, Pennell DJ, Ray S *et al*. The Carvedilol Hibernation Reversible Ischaemia Trial: Marker of Success (CHRISTMAS) study. Eur J Heart Failure 1999; 1: 191–6.

[29] Pennell DJ, Ray SG, Davies G *et al*. The Carvedilol Hibernation Reversible Ischaemia Trial; Marker of Success (CHRISTMAS) study: Methodology of a randomised, placebo controlled, multicentre study of Carvedilol in hibernation and heart failure. Int J Cardiol 2000; 72: 265–74.

[30] Committee on M-mode Standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072–83.

[31] Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: Echocardiographic-angiographic correlations in the presence or absence of asynergy. Am J Cardiol 1976; 37: 7–11.

[32] Schiller NB, Shah PN, Crawford M. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989; 2: 258–67.

[33] Boudoulas H, Ruff PD, Fulkerson PK, Lewis RP. Relationship of angiographic and echocardiographic dimensions in chronic left ventricular dilatation. Am Heart J 1986; 106: 356–62.

[34] Morrison CA, Bodenheimer MM, Felman MS, Bnaka VS, Helfant RH. Ventriculographic-echocardiographic correlation in patients with asynergy. JAMA 1978; 39: 1855.

[35] Pluim BM, Beyerbacht HP, Chin JC *et al*. Comparison of echocardiography with magnetic resonance in the assessment of the athlete's heart. Eur Heart J 1997; 18: 1505–13.

[36] Underwood SR, Gibson C, Tweddel AC, Flint J. A survey of nuclear cardiological practice in Great Britain. Br Heart J 1992; 67: 273–7.

[37] Katz J, Milliken MC, Stray-Gundersen J *et al*. Estimation of human myocardial mass with MR imaging. Radiology 1988; 169: 495–8.

[38] Herrogods M, De Paep G, Bijnens B *et al*. Determination of left ventricular volume by two-dimensional echocardiography: comparison with magnetic resonance imaging. Eur Heart J 1994; 15: 1070–3.

[39] Mochizuki T, Murase K, Tanaka H, Kondoh T, Hamamoto K, Tauxe WN. Assessment of left ventricular volume using ECG-gated SPECT with technetium-99m-MIBI and technetium-99m-tetrofosmin. J Nucl Med 1997; 38: 53–7.
[40] Germano G, Kiat H, Kavanagh PB *et al*. Automaticquantification of ejection fraction from gated myocardial perfusion SPECT. J Nucl Med 1995; 36: 2138–47.
[41] Vaduganathan P, He ZX, Vick GW, Mahmarian JJ, Verani MS. Evaluation of left ventricular wall motion, volumes, and ejection fraction by gated myocardial tomography with technetium 99m-labeled tetrofosmin: a comparison with cine magnetic resonance imaging. J Nucl Cardiol 1999; 6: 3–10.
[42] Iskandrian AE, Germano G, van Decker W *et al*. Validation of left ventricular volume measurements by gated SPECT 99mTc-labeled sestamibi imaging. J Nucl Cardiol 1998; 5: 574–8.
[43] Johnson LL, Verdesca SA, Aude WY *et al*. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi. J Am Coll Cardiol 1997; 30: 1641–8.
[44] Ray SG, Metcalfe MJ, Oldroyd KG *et al*. Do radionuclide and echocardiographic techniques give a universal cut off value for left ventricular ejection fraction that can be used to select patients for treatment with ACE inhibitors after myocardial infarction? Br Heart J 1995; 73: 466–9.
[45] Bottini PB, Carr AA, Prisant M, Flickinger FW, Allison JD, Gottdiener JS. Magnetic resonance imaging compared to echocardiography to assess left ventricular mass in the hypertensive patient. Am J Hypertens 1995; 8: 221–8.
[46] Starling MR, Crawford MH, Sorenson SG, Levi B, Richards KL, O'Rourke RA. Comparative accuracy of apical bi-plane cross-sectional echocardiography and gated equilibrium radionuclide angiography for estimating left ventricular size and performance. Circulation 1981; 61: 1075–84.
[47] Senior R, Sridhara BS, Basu S *et al*. Comparison of radionuclide ventriculography and 2D echocardiography for the measurement of left ventricular ejection fraction following acute myocardial infarction. Eur Heart J 1994; 15: 1235–9.
[48] Mogelvang J, Stokholm KH, Saunamaki K *et al*. Assessment of left ventricular volumes by magnetic resonance in comparison with radionuclide angiography, contrast angiography and echocardiography. Eur Heart J 1992; 13: 1677–83.
[49] Bloomgarden DC, Fayad ZA, Ferrari VA, Chin B, St John Sutton M, Axel L. Global cardiac function using fast breathhold MRI: Validation of new acquisition and analysis techniques. Magn Reson Med 1997; 37: 683–92.
[50] Gaudio C, Tanzilli G, Mazzarotto P *et al*. Comparison of left ventricular ejection fraction by MRI and RNV in idiopathic dilated cardiomyopathy. Am J Cardiol 1991; 67: 411–5.