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Evaluation of three methods for quantifying valvular regurgitation using gated equilibrium radionuclide ventriculography

R. Sciagrà, E. Voth*, U. Tebbe, H. Schicha* and K.-L. Neuhaus

*Department of Cardiology and *Department of Nuclear Medicine, University of Göttingen, Göttingen, F.R.G.*

KEY WORDS: Aortic regurgitation, mitral regurgitation, gated equilibrium radionuclide ventriculography, stroke count ratio.

The non-invasive quantification of mitral and aortic regurgitation using the left-to-right stroke count ratio (SCR) calculated with gated equilibrium radionuclide ventriculography (RNV), is affected by the overlap of atria and ventricles and the consequent difficult definition of the ventricular regions of interest (ROI). Various solutions of the problem have been proposed. In this study we evaluated the results obtained with a technique based on visual inspection of the RNV images (variable ROI method — VRI) and those of two approaches which utilize functional images (stroke volume image method — SVI — and Fourier amplitude ratio — FAR), by comparing them with the invasive quantification of valvular regurgitation according to Sandler et al.[1] *(stroke volume ratio — SVR). Forty patients (15 controls and 25 valvular patients) were studied.*

In the control group the range of the SVR was 0·81 ± 1·11 (mean ± 1 SD = 1·01 ± 0·08). The SCR was 0·83–1·28 (1·03 ± 0·15) with VRI, 1·10–1·15 (1·30 ± 0·14) with SVI and 1·11–1·58 (1·35 ± 0·17) with FAR. The correlations between SVR and SCR were $r = 0{\cdot}47$ ($P < 0{\cdot}05$), $r = 0{\cdot}62$ ($P < 0{\cdot}001$) *and* $r = 0{\cdot}55$ ($P < 0{\cdot}01$) *respectively with VRI, SVI and FAR. The SCR of valvular patients fell in the range of controls in 11/25 using VRI, 6/25 using SVI and in 4/25 using FAR. This overlap was present in 2/25 with the invasive quantification. Irrespective of the method used, a reliable assessment of the valvular regurgitation was not possible in two patients with severely depressed left ventricular function. We conclude that the use of techniques based on functional images clearly improves the effectiveness of the non-invasive quantification of valvular regurgitation with the SCR even if this cannot be regarded as a substitute for invasive quantification and has a limited reliability in particular groups of patients.*

Introduction

The quantification of regurgitant volume certainly represents one of the most useful applications of radionuclide ventriculography (RNV) in the assessment of patients affected by mitral or aortic regurgitation[2]. This quantification can be obtained by the comparison of left and right ventricular stroke counts. Theoretically, the left-to-right stroke count ratio (SCR) should be unity in patients without valvular regurgitation or intracardiac shunts, and above unity in patients with mitral and/or aortic regurgitation[3,4].

Unfortunately, the determination of the SCR is affected by technical problems, particularly by the superimposition of atria and ventricles in the left anterior oblique projection (LAO), usually employed for the RNV. Because of this overlap, the definition of the boundaries of the two ventricles, especially of the right one, is made difficult[5–16]. Several modifications of the original method have therefore been introduced. Among them, the use of functional images (subtraction images, Fourier phase and amplitude images) for the definition of the ventricular regions of interest (ROI) is interesting and promising[8,13–15,17–22].

In this study, we evaluated for the first time in the

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Address for correspondence: Dr K.-L. Neuhaus, Abteilung Kardiologie und Pulmologie, Zentrum Innere Medizin, Universitätsklinikum, Robert-Koch-Strasse 40, D-3400 Göttingen, F.R.G.

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same patient population, the results obtained by a traditional ROI definition method and by two techniques based on functional images. The effectiveness of the three methods has been assessed by comparing the calculated SCRs with the invasive quantification of valvular regurgitation performed according to Sandler *et al.*[1]

Methods

SUBJECT SELECTION

Fifteen patients (mean age $52 \pm 8{\cdot}5$ years, range 42–63), who underwent diagnostic cardiac catheterization for the evaluation of ischaemic heart disease and had no evidence of valvular regurgitation or intracardiac shunts served as a control group. All these patients were in normal sinus rhythm and received either no treatment or were given oral nitrates, without any change in drug regimen between cardiac catheterization and RNV.

The second group consisted of twenty-nine consecutive patients (mean age $54{\cdot}8 \pm 11{\cdot}2$ years, range 34–75), who were referred to our catheterization laboratory for the evaluation of valvular disease. In these patients, mitral or aortic valve regurgitation was suspected on the basis of clinical data and Doppler echocardiography. According to the results of cardiac catheterization, four patients who had tricuspid regurgitation were excluded from further evaluation. Of the remaining twenty-five patients who had no evidence of intracardiac shunts and/or tricuspid or pulmonary regurgitation, eighteen showed aortic insufficiency (twelve isolated and 6 with associated mild stenosis of the valve), five presented with mitral regurgitation (four with associated mitral stenosis), and two showed both aortic and mitral regurgitation.

All valvular patients were in normal sinus rhythm (frequency range 54–96 beats min^{-1}), except for two patients with mitral valve disease with atrial fibrillation. Between catheterization and RNV no changes occurred in clinical status and cardiac medication (digitalis and/or diuretics administered in 8 cases).

CARDIAC CATHETERIZATION

In the fasting state, all patients (controls and subjects with valvular regurgitation) underwent left heart catheterization with left ventricular and coronary angiography through the brachial[23] or percutaneous transfemoral approaches[24]. Right heart catheterization was also performed via the same route. Heart rate was simultaneously registered during the whole procedure.

Effective forward cardiac output was measured in most of the patients by the thermodilution method with several injections of 10 ml of cold 0·9% sodium chloride solution in the right atrium and the thermistor placed within the pulmonary artery[25]. Several measurements were performed immediately before contrast angiography and the average of the values was considered. In few remaining patients effective forward cardiac output was calculated by the Fick oxygen method. Before contrast angiography, blood samples were obtained from the aorta and from the pulmonary artery and haemoglobin concentration and oxygen saturation were measured. Oxygen consumption was estimated on the basis of the patient's age, sex, body surface area and heart rate[26]. The right ventricular stroke volume was obtained by dividing the forward cardiac output by the simultaneously registered heart frequency.

A left ventricular angiogram and, if indicated, an aortic root angiogram were performed in biplane 30° right anterior and 60° left anterior oblique projections. A well opacified, normally conducted cycle, not preceded by an ectopic beat was analyzed. In patients with atrial fibrillation more cycles were evaluated in order to achieve a representative assessment. Left ventricular volumes were calculated by the area-length method, with a magnification correction by calibrated grid filming, and using the regression equation[27]:

$$\text{actual volume} = 0{\cdot}928 \times \text{calculated volume} - 3{\cdot}8$$

Valvular regurgitation was also graded by two experienced observers on the basis of the regurgitant jet visualized during contrast angiography, according to the qualitative grading score proposed by Grossman *et al.*[28] In two patients with concomitant aortic and mitral regurgitation the grading score was obtained by adding the scores of aortic and mitral assessment[29,30].

Left ventricular ejection fraction was measured as usual. The stroke volume ratio was calculated according to the formula by Todd Makler *et al.*[14]:

$$\frac{\text{left ventricular stroke volume}}{\text{right ventricular stroke volume}}$$

This value was used for the comparison with the stroke count ratio, instead of the usual regurgitant volume (left ventricular output − effective forward cardiac output).

RADIONUCLIDE VENTRICULOGRAPHY

The RNV was performed after *in vitro* labelling of red blood cells with 20 mCi (740 MBq) of ^{99m}Tc[31], using an Anger camera (LEM, Siemens) equipped with a low-energy all-purpose collimator. The acquisition time was 10 minutes. Images were acquired with a dedicated computer system (IMAC 7300, CGR, Koch and Sterzel), in frame mode with a rate of 16 frames per cardiac cycle, using a 64 × 64 matrix and a 1·5 zoom, in the best septal LAO view. Studies were performed with and without a 15° caudal tilt. Because no significant improvement was achieved by the introduction of the caudal tilt, only the data obtained with our routine approach, i.e. straight LAO projection, were considered for the analysis of the results.

Three methods of SCR calculation were employed.

Variable region of interest method (VRI)[7]

According to this method, two separate ROIs were constructed for each ventricle on the respective end-diastolic and end-systolic frames, which were separately identified at the peak and at the nadir respectively of each ventricular time-activity curve. The boundaries of the left ventricular ROI were defined by a semi-automatic programme. The operator performed manual corrections, if necessary, with the help of endless loop movie format images. The definition of the right ventricular ROI was completely manual based on the endless loop movie format images[5]. These usually allow a good recognition of the boundaries between right atrium and ventricle. Background correction was performed using a fixed left paracardiac ROI, generated automatically by the programme. The SCR was calculated according to the formula:

$$\frac{\text{left ventricular end-diastolic} - \text{end-systolic counts}}{\text{right ventricular end-diastolic} - \text{end-systolic counts}}$$

Stroke volume image method (SVI)[19]

Stroke volume images of both ventricles were obtained by subtracting end-systolic from end-diastolic images, selected separately according to the respective time–activity curve. ROIs were constructed manually on these images. The SCR was calculated directly from the stroke volume images by dividing left by right ventricular counts.

Fourier amplitude images (FAR)[13,14]

Using a first harmonic Fourier analysis program, amplitude and phase images together with phase histograms were generated. A ventricular amplitude image was constructed from these by displaying the amplitudes of all pixels having a phase difference less than 90° from the centre of the ventricular peak in the phase histogram. On this image, the two ventricles are clearly delineated as the only two areas having a significant amplitude. Left and right ventricular ROIs were defined manually on the ventricular amplitude image, additionally considering the configuration of the ventricles in the blood pool scan in cases with low amplitude values. The ventricular amplitude ratio was then calculated by dividing left by right ventricular amplitudes in the ventricular amplitude image. The ventricular amplitude ratio is called FAR in the following sections.

The RNV was performed within three days of cardiac catheterization. All studies were analysed independently by two experienced observers without any knowledge of the catheterization results.

Table 1 Catheterization findings in patients with valvular regurgitation

Patient	Diagnosis	Grading score	SVR	LVEF
1	AR	IV	3·23	0·64
2	AR	III	2·09	0·76
3	AR	III	1·96	0·70
4	AR	II	1·23	0·48
5	AR	III	1·88	0·53
6	AR	III	3·13	0·74
7	AR	II	1·54	0·90
8	AR	III	3·58	0·54
9	MR	IV	2·17	0·59
10	MR+AR	I+I	1·42	0·50
11	AR	III	1·63	0·62
12	MR	IV	1·73	0·51
13	AR	IV	3·40	0·63
14	MR	III	1·58	0·72
15	MR	I	1·05	0·65
16	AR	II	2·31	0·72
17	MR	IV	2·86	0·33
18	AR	II	1·71	0·67
19	AR	III	1·09	0·53
20	AR	III	2·14	0·60
21	AR	III	1·19	0·47
22	MR+AR	I+I	2·84	0·30
23	AR	II	1·20	0·60
24	AR	III	1·38	0·48
25	AR	II	1·76	0·60

AR = Aortic regurgitation; MR = Mitral regurgitation
LVEF = Left ventricular ejection fraction.

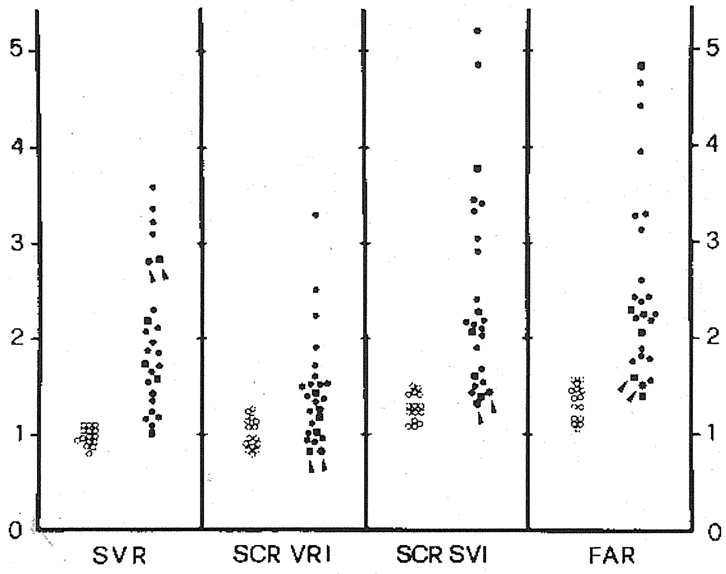

Figure 1 Values of the stroke volume ratio (SVR) and of the stroke count ratio (SCR) calculated with three different methods (variable region of interest — VRI —, stroke volume image — SVI — and Fourier amplitude ratio — FAR —) in normal subjects (open circles) and in patients affected by aortic regurgitation (black dots), by mitral regurgitation (black squares) or by both (black stars). Arrowheads identify patients with left ventricular ejection fraction <0·35.

STATISTICAL ANALYSIS

Data are presented as the range of the observed values and as their mean ± standard deviation after performing the Kolmogorov Smirnov normality test.

The Pearson's coefficient of correlation test and the Spearman's nonparametric technique were used for a comparison of the values calculated by the various methods.

Results

CARDIAC CATHETERIZATION

The SVR in the control group was 1·01 ± 0·08, (range 0·81 1·11). Individual data of the patients affected by valvular regurgitation are summarized in Table 1.

The correlation coefficient between SVR and the cineangiographic grading score was $r = 0{\cdot}45$ ($P < 0{\cdot}05$).

Only 2 patients out of 25 (8%) affected by valvular regurgitation had a SVR which fell in the range of controls (Fig. 1).

RNV

In the control group the SCR values calculated by VRI, SVI and FAR respectively were: 1·03 ± 0·15, (Range 0·83 1·28); 1·30 ± 0·14, (range 1·10 – 1·51); 1·35 ± 0·17, (range 1·11 1·58).

The SCR calculated in the patients affected by valvular regurgitation using the three different methods are listed in Table 2.

Low correlation coefficients between cineangiographic grading score and the SCR were found: they were respectively $r = 0{\cdot}34$ ($P < 0{\cdot}05$) with VRI, $r = 0{\cdot}47$ ($P < 0{\cdot}01$) with SVI and $r = 0{\cdot}54$ ($P < 0{\cdot}01$) with FAR.

The correlation coefficients found by comparing the SVR and the SCR and by taking into account the whole group of patients affected by valvular regurgitation were $r = 0{\cdot}47$ ($P < 0{\cdot}05$); $r = 0{\cdot}62$ ($P < 0{\cdot}001$) and $r = 0{\cdot}55$ ($P < 0{\cdot}01$) respectively with VRI, SVI and FAR. An improvement in the correlation coefficients between SVR and SCR could be found by considering the data of the patients with aortic regurgitation only: $r = 0{\cdot}62$ ($P < 0{\cdot}01$) with VRI; $r = 0{\cdot}81$ ($P < 0{\cdot}001$) with SVI and $r = 0{\cdot}77$

($P<0{\cdot}001$) with FAR. The exclusion from the comparison of two patients with severely depressed left ventricular function (left ventricular ejection fraction $<0{\cdot}35$) also allowed an increase in the correlation coefficients between SVR and SCR. The values obtained were $r=0{\cdot}65$ ($P<0{\cdot}001$); $r=0{\cdot}81$ ($P<0{\cdot}001$) and $r=0{\cdot}72$ ($P<0{\cdot}001$), respectively, with VRI, SVI and FAR (Figs 2, 3 and 4).

Using the VRI, 11 (44%) of the 25 valvular patients had a SCR within the range of the control group values. This overlap between controls and valvular patients was also observed in 6 cases (24%) using the SVI and in 4 subjects (16%) using the FAR (Fig. 1).

The correlation coefficients of the SCR calculated by two different observers, were $r=0{\cdot}96$, $r=0{\cdot}99$ and $r=0{\cdot}99$ (all $P<0{\cdot}001$) with VRI, SVI and FAR, respectively.

Discussion

The selection of the appropriate timing of valvular replacement in patients affected by mitral or aortic regurgitation is a difficult problem for the cardiologist. In these patients, symptoms begin frequently in a late phase of the valvular disease history. At that moment, considerable impairment of the left ventricular function can be already present and the prognosis after valve replacement significantly worsens. The haemodynamic parameters of asymptomatic or mildly symptomatic patients need, therefore, to be checked frequently[16,32–35].

The reference method for this measurement and for the assessment of valvular patients would be the performance of right and left cardiac catheterization. The grade of valvular regurgitation is usually evaluated according to the regurgitant jet which is visualized during left ventricular or aortic root angiography. This qualitative assessment is frequently the only one performed and it has also been employed for the evaluation of the effectiveness of SCR by several authors[6,9,15,18,19,36–38]. However, as shown by our results, and as demonstrated by others in much larger patient populations[39,40], this is an inaccurate system for assessing valvular

Table 2 *Stroke count ratio in patients with valvular regurgitation*

Patient	VRI	SVI	FAR
1	1·73	3·45	3·15
2	1·26	2·41	2·25
3	1·53	2·18	2·19
4	1·42	1·55	1·75
5	1·52	3·05	3·31
6	3·31	3·48	3·95
7	1·01	1·50	1·79
8	1·91	4·85	4·43
9	1·45	3·79	4·83
10	1·27	2·29	2·27
11	0·95	1·67	1·78
12	1·21	2·08	2·03
13	2·24	5·19	4·65
14	1·36	1·59	2·31
15	1·02	1·40	1·41
16	1·52	2·20	2·40
17	0·83	1·35	1·59
18	0·91	1·91	2·27
19	1·15	2·03	1·86
20	2·51	2·91	2·46
21	1·60	2·12	2·46
22	0·83	1·45	1·51
23	1·50	2·19	2·60
24	1·37	3·34	3·32
25	0·93	1·43	1·53

VRI = variable region of interest method; SVI = stroke volume image method; FAR = Fourier amplitude ratio.

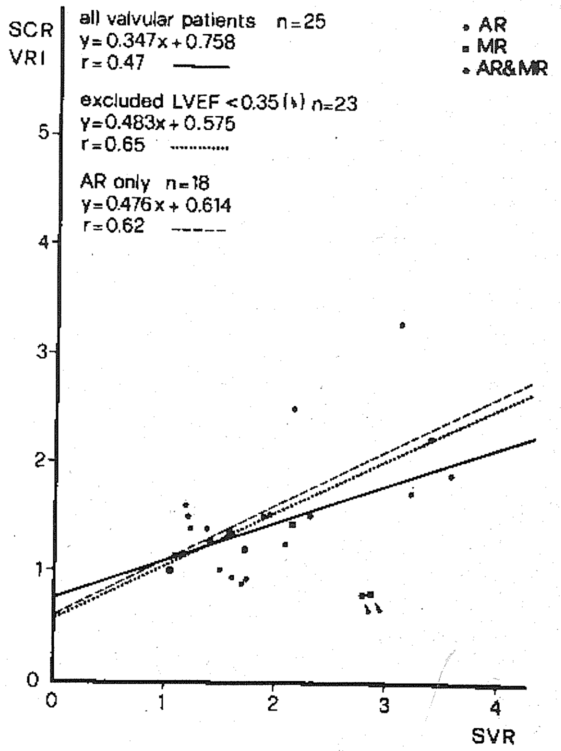

Figure 2 Comparison of SVR and SCR VRI in the whole valvular patients group, in patients with aortic regurgitation only and after exclusion of patients with left ventricular ejection fraction (LVEF) $<0{\cdot}35$.

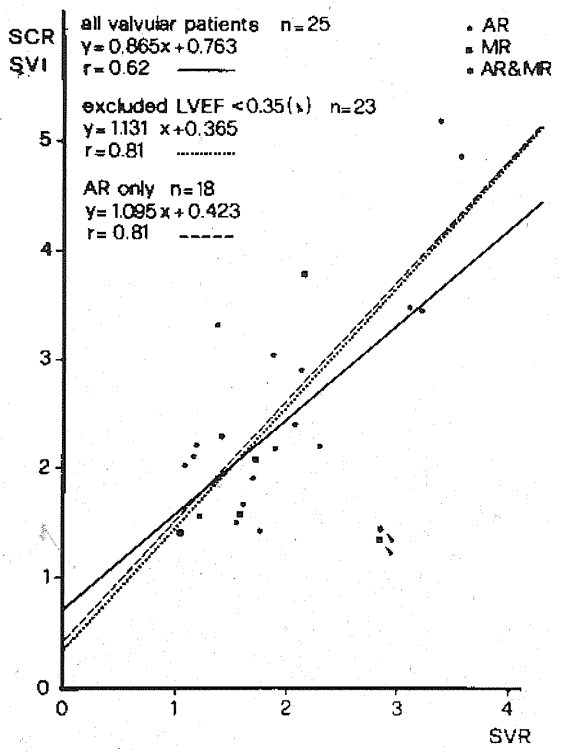

Figure 3 Comparison of SVR and SCR SVI in the whole valvular patients group, in patients with aortic regurgitation only and after exclusion of patients with left ventricular ejection fraction (LVEF) <0·35.

regurgitation. Better results can be achieved by comparing the total left ventricular and the effective forward stroke volumes, as proposed by Sandler *et al.*[1]. Even this approach presents considerable limitations because the pitfalls of both the angiographic estimate of ventricular volumes and of the effective forward output measurement may affect the results. In spite of these problems, it still remains the only possible reference method[16], particularly for the evaluation of the accuracy of SCR. Naturally, invasive procedures must be reserved for preoperative evaluation and are not suitable for repeated examinations. On the contrary, RNV is a safe, repeatable, non-invasive method for the evaluation of cardiac function. Therefore, the possibility of a quantification of the regurgitant volume by means of the SCR would make the RNV an almost ideal approach for the assessment of patients affected by valvular regurgitation. Furthermore, both interventional studies (exercise stress testing, pharmacological stimulation) or serial evaluations of therapeutic effects become possible[7,15,41–44].

As already mentioned, however, the accuracy of the SCR measurement is affected by the overlap of atria and ventricles in the LAO projection. To overcome this difficulty first pass studies have been employed, or to calculate directly the stroke counts of both ventricles[45] or to measure with an indicator dilution method the effective forward stroke volume, which is then compared with the total left ventricular stroke volume obtained from the equilibrium RNV[46–50]. The first of the two techniques requires a very good separation of right and left ventricular phases and is therefore dependent on an optimal bolus injection and could be influenced by prolonged pulmonary transit times, not infrequent in valvular patients. The second approach is affected by the inaccuracy of using blood volume values derived from tables and a geometric method for the measurement of ventricular volumes. On the other hand, the measurement of effective blood volume and the use of the superior count-based technique for the left ventricular volume assessment[51] would

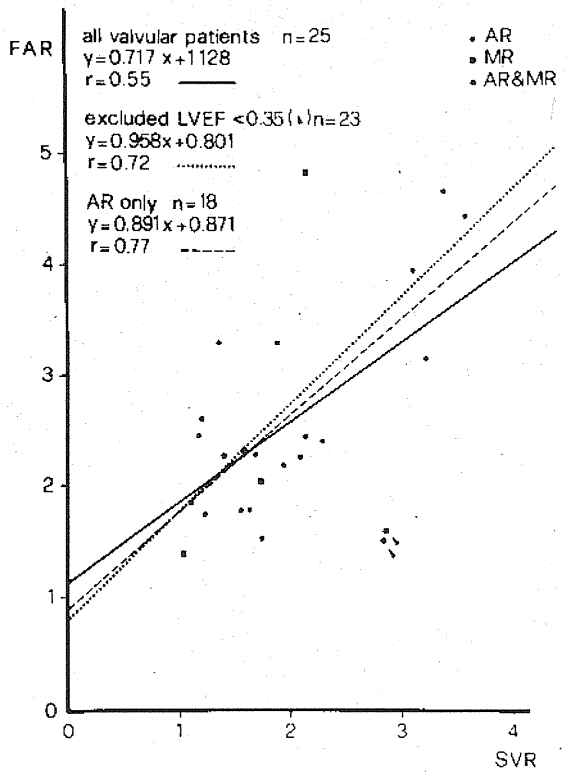

Figure 4 Comparison of SVR and FAR in the whole valvular patients group, in patients with aortic regurgitation only and after exclusion of patients with left ventricular ejection fraction (LVEF) <0·35.

make the procedure too complicated for clinical practice. Furthermore, first pass RNV performed with ^{99m}TC-labelled red blood cells, is not suited for interventional studies.

Equilibrium RNV remains, therefore, the simplest approach for the quantification of valvular regurgitation and several modifications of the original method have been proposed to overcome its limitations. Considerable improvements of the results are reported by obtaining higher count rates, which can be achieved through the use of in-vitro labelling of the red blood cells[52] and/or through the prolongation of the acquisition time[44,53].

In an attempt to obtain a better separation of atria and ventricles by modifying the straight LAO view, a caudal tilt of the gamma camera head has been introduced[9,11,12,19,20,42 44]. The influence of this approach has not been systematically evaluated until recently, but our results in a preliminary study do not confirm significant improvement[53]. On the contrary, the use of a 30° slant hole collimator seems to allow significantly better results[8,18], but this has not been unanimously confirmed[19].

The most important proposed improvements, however, regard the ROI definition method. In the original procedure, a single end-diastolic region was defined for each ventricle and the end-systolic counts in this region were calculated using the time activity curve of the single ventricle, since the nadir of the two curves is frequently not simultaneous[6]. To overcome this problem and to achieve a better exclusion of the atrial contribution to the ventricular counts, which mainly affects the right ventricular stroke counts, the use of two ROIs (end-diastolic and end-systolic) for each ventricle was proposed[7]. The method was reported to improve the accuracy of the results, even if the definition of background ROI was necessary[6,7].

The correction of the ventricular counts by subtracting the counts of atrial ROI, which should represent the atrial contribution due to the anatomic superimposition, has been proposed by others[12,54,55]. However, the definition of the atrial ROI introduces additional sources of error, as the relatively high inter- and intraobserver variability demonstrates[37], and the complicated procedure is probably not justified by the limited improvement reported[56].

The most interesting technical improvement of the ROI definition technique was represented by the introduction of functional images as an aid in the SCR calculation. In our study we have evaluated for the first time in the same patient population, the behaviour of both the stroke volume images method and of the Fourier amplitude ratio and that of a traditional SCR calculation approach, in our case the VRI method. Our results show a clear superiority of the two methods based on functional images over the traditional approach. This is demonstrated by significantly higher correlation coefficients in the comparison with the reference method, i.e. the SVR, and by a better separation between the ranges of values obtained in normal subjects and in those with valvular regurgitation. On the other hand, practically no differences between the two methods could be found in our experience, because the slight superiority of the correlation coefficients obtained using the SVI is compensated for by the higher number of valvular patients whose SCR falls in the range of the control group. We found surprisingly low correlation coefficients using the traditional approach, even if similar values are reported by others[14]. However, the method was correctly performed, as the mean and the reduced variability of the control group demonstrate[2], and therefore, the poor results observed should be attributed to the intrinsic limitations of a technique based mainly on visual inspection of the RNV images.

Even if quite good results were obtained with the SVI and the FAR in the whole valvular patients group as well, significant improvements of the correlation coefficients could be achieved by considering only the patients affected by aortic regurgitation or by excluding from the comparison the two patients with severely depressed left ventricular function. It must be mentioned that an improvement can also be observed in this regard with the VRI.

The bad results obtained with the SCR in patients with depressed left ventricular function have been observed by others[9,15,19,22]. Several factors could play a role in determining this behaviour, as subclinical pulmonary or tricuspid insufficiency, heart chambers dilatation with more marked atrioventricular overlap and increasing attenuation effects. Since the catheterization results in our two patients with depressed left ventricular function excluded right-sided valvular regurgitation, it is our opinion that geometric factors and atrioventricular overlap are the main reasons of the poor reliability of the SCR in these patients. We believe that the behaviour of the SCR in patients with depressed left ventricular function stresses the importance of evaluating the results of the SCR only in unison with the other RNV findings.

The more significant left atrial and right ventricular enlargement usually present in mitral regurgitation could explain the higher correlation between SVR and SCR obtained when only patients affected by aortic insufficiency were considered. Similar results are reported by others[42,57]. However, we are not able to draw any certain conclusions about the superior reliability of SCR in aortic as compared to mitral regurgitation, because only four patients with mitral incompetence and well-maintained left ventricular function were present in our study group.

Another considerable limitation of the quantification of valvular regurgitation by means of the SCR which has been reported is the difficult identification of mild degrees of valvular insufficiency[6,9,10,19,20,41,42,49]. We observed this behaviour mainly with the VRI. The clinical relevance of this limitation 'per se' is probably low, since the diagnosis of mild valvular regurgitation is most often easily obtained by heart auscultation or even more efficiently by Doppler-echocardiography[58].

On the other hand, the behaviour of the SCR in patients with mild valvular regurgitation should be kept in mind both in follow-up and in interventional studies, because it could mean that slight changes of the regurgitant volume are difficult to assess.

In conclusion, our study clearly demonstrates the superior results of the SCR calculation methods based on functional images over the traditional techniques based on visual inspection of the RNV images only, whereas in our experience no significant differences between SVI and FAR could be found. Even the use of functional images leaves the main problem which affects the SCR, i.e. the atrio-ventricular overlap partially unsolved, but they significantly improve the SCR accuracy, and make possible an effective utilization of this parameter in clinical practice. Keeping in mind its limitations and the fact that it cannot be regarded as a substitute for invasive quantification in pre-operative evaluation, the SCR is a valuable aid in the assessment of patients affected by valvular regurgitation.

References

[1] Sandler H, Dodge HT, Hay RE, Rackley CE. Quantitation of valvular insufficiency in man by angiocardiography. Am Heart J 1963; 65: 501–13.

[2] Alderson PO. Radionuclide quantification of valvular regurgitation. J Nucl Med 1982; 23: 851–5.

[3] Franklin DL, Van Citters RL, Rushmer RF. Balance between right and left ventricular output. Circ Res 1962; 10: 17 26.

[4] Carlsson E, Keene RJ, Lee P, Goerke RJ. Angiocardiographic stroke volume correlation of the two cardiac ventricles in man. Invest Radiol 1971; 6: 44–51.

[5] Maddahi J, Berman DS, Matsuoka DT *et al.* A new technique for assessing right ventricular ejection fraction using rapid multiple-gated equilibrium cardiac blood pool scintigraphy. Description validation and findings in chronic coronary artery disease. Circulation 1979; 60: 581–9.

[6] Rigo P, Alderson PO, Robertson RM, Becker LC, Wagner HN Jr. Measurement of aortic and mitral regurgitation by gated cardiac blood pool scans. Circulation 1979; 60: 306 12.

[7] Sorensen SG, O'Rourke RA, Chaudhuri TK. Noninvasive quantitation of valvular regurgitation by gated equilibrium radionuclide angiography. Circulation 1980; 62: 1089–98.

[8] Gandsmann EJ, North DL, Shulman RS, Bough EW. Measurement of the ventricular stroke volume ratio by gated radionuclide antiography. Radiology 1981; 138: 161–5.

[9] Lam W, Pavel D, Byron E, Sheikh A, Best D, Rosen K. Radionuclide regurgitant index: value and limitations. Am J Cardiol 1981; 47: 292–8.

[10] Kress P, Geffers H, Stauch M *et al.* Evaluation of aortic and mitral valve regurgitation by radionuclide ventriculography: comparison with the method of Sandler and Dodge. Clin Cardiol 1981; 4: 5–10.

[11] Manyari DE, Nolewajka AJ, Kostuk WJ. Quantitative assessment of aortic valvular insufficiency, by radionuclide angiography. Chest 1982; 81: 170–6.

[12] Henze E, Schelbert HR, Wisenberg G, Ratib O, Schön H. Assessment of regurgitant fraction and right and left ventricular function at rest and during exercise: a new technique for determination of right ventricular stroke counts from gated equilibrium blood pool studies. Am Heart J 1982; 104: 953–62.

[13] Todd Makler P Jr, McCarthy DM, Velchik MG, Goldstein HA, Alavi A. Fourier amplitude ratio: a new way to assess valvular regurgitation. J Nucl Med 1983; 24: 204–7.

[14] Todd Makler P Jr, McCarthy DM, Kleaveland JP, Doherty JU, Velchik MG. Validation of Fourier amplitude ratio to quantitate valvular regurgitation. J Am Coll Cardiol 1984; 3: 1482–7.

[15] Hurwitz RA, Treves S, Freed M, Girod DA, Caldwell RL. Quantitation of aortic and mitral regurgitation in the pediatric population: evaluation by radionuclide angiocardiography. Am J Cardiol 1983; 451 252–5.

[16] Iskandrian AS, Heo J. Radionuclide angiography evaluation of left ventricular performance at rest and during exercise in patients with aortic regurgitation. Am Heart J 1986; 111: 1143–9.

[17] Douglas KH, Links JM, Alderson PO, Wagner HN Jr. Temporal Fourier analysis in selection of right ventricular region of interest. In: Single photon emission computed tomography and other selected computer topics. New York: The Society of Nuclear Medicine, 1980: 187 93.

[18] Bough EW, Gandsman EJ, North DL, Shulman RS. Gated radionuclide angiographic evaluation of valve regurgitation. Am J Cardiol 1980; 46: 423–8.

[19] Nicod P, Corbett JR, Firth BG *et al.* Radionuclide techniques for valvular regurgitant index: comparison in patients with normal and depressed ventricular function. J Nucl Med 1982; 23: 763–9.

[20] Taylor DN, Tech B, Harris DNF, Condon B, Ogilvie B, Ackery DM, Fleming J, Goddard BA. Radionuclide evaluation of valvular regurgitation. Br J Radiol 1982; 55: 204–7.

[21] Rigo P, Chevigne M. Measurement of left-to-right shunts by gated radionuclide angiography: concise communication. J Nucl Med 1982; 23: 1070–5.

[22] Klepzig H Jr, Standke R, Nickelsen T, Maul FS, Hör G, Kaltenbach M. Grenzen der szintigraphisch bestimmten Links-, Rechts-Schlagvolumen Quotienten bei der Beurteilung der Schwere einer Aorteninsuffizienz. Z. Kardiol 1984; 73: 363–9.

[23] Sones FM, Shirey EK. Cine coronary arteriography. Mod Conc Cardiovasc Dis 1962; 31: 735–8.

[24] Judkins MP. Selective coronary arteriography: a percutaneous transfemoral technic. Radiology 1967; 89: 815–24.

[25] Ganz W, Swan HJC. Measurement of blood flow by thermodilution. Am J Cardiol 1972; 29: 241–6.

[26] La Farge CG, Miettinen OS. The estimation of oxygen consumption. Cardiovasc Res 1970; 4: 23–30.

[27] Dodge HT, Sandler H, Ballew DW, Lord JD Jr. The use of biplane angiocardiography for the measurement of left ventricular volume in man. Am Heart J 1960; 60: 762–76.

[28] Grossman W. Profiles in valvular heart disease. In: Grossman W. ed. Cardiac catheterization and angiography. Philadelphia: Lea & Febiger, 1986: 359–81.

[29] Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease. Technic indications and interpretations in 700 cases. Am J Cardiol 1964; 14: 437–47.

[30] Cohn LH, Mason DT, Ross J, Morrow AG, Braunwald E. Preoperative assessment of aortic regurgitation in patients with mitral valve disease. Am J Cardiol 1967; 19: 177–82.

[31] Bauer R, Bauer U, Sauer E, Langhammer H, Pabst HW. In-vivo/in-vitro Markierung von Erythrozyten mit ^{99m}Tc und ihre klinische Anwendung. Nuc Compact 1981; 12: 18–25.

[32] O'Rourke RA, Crawford MH. Timing of valve replacement in patient with chronic aortic regurgitation. (Editorial). Circulation 1980; 61: 493–5.

[33] Bonchek LI. Current status of cardiac valve replacement: selection of a prosthesis and indications for operation. Am Heart J 1981; 101: 96–106.

[34] Bonow RO, Rosing DR, Kent KM, Epstein SE. Timing of operation for chronic aortic regurgitation. Am J Cardiol 1982; 50: 325–36.

[35] Hochreiter C, Niles N, Devereux RB, Kligfield P, Borer JS. Mitral regurgitation: reltionship of noninvasive descriptors of right and left ventricular performance to clinical and hemodynamic findings and to prognosis in medically and surgically treated patients. Circulation 1986; 73: 900–12.

[36] Geffers H, Stauch M. Assessment of regurgitation fractions by radionuclide ventriculography. Z Kardiol 1979; 68: 491–6.

[37] Reinders Folmer SCC, Koster RW, La Riviere AV, Dunning AJ. Radionuclide quantification of mitral and aortic regurgitation. Eur J Clin Invest 1983; 13: 325–30.

[38] Benjelloun H, El Haitem N, Itti R *et al.* Quantification radio-isotopique des insuffisances mitrales isolées. Arch Mal Coeur 1984; 77: 1494–501.

[39] Hunt D, Baxley WA, Kennedy JW, Judge TP, Williams JE, Dodge HT. Quantitative evaluation of cineaortography in the assessment of aortic regurgitation. Am J Cardiol 1973; 31: 696–700.

[40] Croft CM, Lipscomb K, Mathis K *et al.* Limitations of qualitative angiographic grading in aortic or mitral regurgitation. Am J Cardiol 1984; 53: 1593–8.

[41] Urquhart J, Patterson RE, Packer M *et al.* Quantification of valve regurgitation by radionuclide angiography before and after valve replacement surgery. Am J Cardiol 1981; 47: 287–91.

[42] Kress P, Miesner H, Sigel H, Wieshammer S, Stauch M, Adam WE. Die Radionuklidventrikulographie bei Aorten- und Mitralvitien. Untersuchung vor und nach Klappenersatzoperation. Z Kardiol 1984; 73: 1–14.

[43] Gerson MC, Engel PJ, Mantil JC, Bucher PD, Hertzberg VS, Adolph RJ. Effects of dynamic and isometric exercise on the radionuclide determined regurgitant fraction in aortic insufficiency. J Am Coll Cardiol 1984; 3: 98–106.

[44] Ormerod OJM, Barber RW, Stone DL, Wraight EP, Petch MC. A comparison of radionuclide methods of evaluating aortic regurgitation with observation on the effect of exercise and symptoms. Eur J Nucl Med 1986; 12: 72–6.

[45] Videll JS, Lumai FJ, Germon PA, Maranhao V, MacMillan RM, Gessman LJ. Radionuclide angiography in the quantitation of mitral regurgitation. Chest 1985; 87: 315–8.

[46] Weber PM, Dos Remidios LV, Jasko IA. Quantitative radioisotope angiocardiography. J Nucl Med 1972; 13: 815–22.

[47] Klepzig H Jr, Standke R, Kunkel B, Maul FD, Hör G, Kaltenbach M. Kombinierte First-Pass-Aequilibrium-Radionuklid-Ventrikulographie zur nichtinvasiven Beurteilung der Schwere einer Aorteninsuffizienz. Z Kardiol 1982; 71: 661–4.

[48] Nicoletti R, Brandt D, Fueger GF, Klein W. Quantitative Bestimmung der Regurgitation bei Herzklappeninsuffizienzen mit Hilfe der Radionuklid Ventrilulographie. Nuc Compact 1983; 14: 256–9.

[49] Klepzig H Jr, Standke R, Nickelsen T, Kunkel B, Maul FD, Hör G, Kaltenbach M. Volumetric evaluation of aortic regurgitation by combined first-pass/equilibrium radionuclide ventriculography. Eur Heart J 1984; 5: 317–25.

[50] Klepzig H Jr, Standke R, Nickelsen T *et al.* Combined first-pass and equilibrium radionuclide ventriculography and comparison with left ventricular/right ventricular stroke count ratio in mitral and aortic regurgitation. Am J Cardiol 1985; 55: 1048–53.

[51] Massie BM, Kramer BL, Gertz EW, Henderson SG. Radionuclide measurement of left ventricular volume: comparison of geometric and count-based methods. Circulation 1982; 65: 725–30.

[52] Neumann P, Schicha H, Schnürnbrand P, Bähre M, Emrich D. Visualizing cardiac blood pool. Comparison of three labelling methods. Eur J Nucl Med 1983; 8: 463–6.

[53] Sciagrà R, Voth E, Tebbe U *et al.* Influence of technical modifications on estimation of regurgitant fraction by radionuclide ventriculography. Z Kardiol 1986; 75 (Suppl 2): 48–9.

[54] Berthout P, Bassand JP, Faivre R *et al.* Methode de determination isotopique des regurgitations valvulaires aortiques. Arch Mal Coeur 1984; 77: 902–9.

[55] Berthout P, Cardot JC, Baud M *et al.* Factors influencing the quantification of valvular regurgitation by gated equilibrium radionuclide angiography. Eur J Nucl Med 1984; 9: 112 4.

[56] Fridrich L, Gassner A. Quantification of valvular regurgitation. Eur J Nucl Med 1984; 9: 566.

[57] Thompson R, Ross J, Elmes R. Quantification of valvular regurgitation by cardiac gated pool imaging. Br Heart J 1981; 46: 629 35.

[58] Pearlman AS, Scoblionko DP, Saal AK. Assessment of valvular heart disease by Doppler echocardiography. Clin Cardiol 1983; 6: 573–87.