Annals of Nuclear Medicine Vol. 3, No. 2, 83–88, 1989

Factor analysis of multigated cardiac blood pool scintigram for the measurement of left ventricular ejection fraction

Norinari HONDA,* Kikuo MACHIDA,* Toshio MAMIYA,* Taku TAKAHASHI,* Teruo TAKISHIMA,* Tsuyoshi KAMANO,* Noriko HASEGAWA,* Masanori HASHIMOTO,* Ken OHNO* and Minoru HOSOBA**

*Division of Nuclear Medicine, Department of Radiology, Saitama Medical Center Saitama Medical School
**Shimadzu Corporation

Left ventricular ejection fraction (EF) was measured by factor analysis (FA) of multigated cardiac blood pool scintigram in 38 consecutive patients, and compared with that measured by the variable ROI method (EFVROI) with automated left ventricular contour detection. FA was automatically performed without operator intervention with a success rate of 100%. The correlation of EF with EFVROI was significant in the group of 22 patients with normal wall motion ($r=0.65$, $p<0.001$), and the entire group of patients ($r=0.70$, $p<0.001$), but not significant ($p=0.19$) in the group of 16 patients with abnormal wall motion. In conclusion, left ventricular ejection fraction can be estimated by factor analysis of MUGA in patients with normal wall motion.

Key Words: Factor analysis, Radionuclide ventriculography, Ejection fraction, Ventricular wall motion

INTRODUCTION

DETERMINATION of left ventricular ejection fraction (LVEF) is one of the most important indications in multigated cardiac blood pool scintigram (MUGA) since its introduction to clinical medicine.[1] MUGA has been used successfully for LVEF determination by somewhat different settings of the left ventricular region of interest (ROI) and background ROI.[2–7] However, inter- and intra-observer variance as well as reproducibility was the problem in these radionuclide methods.[3–11]

Because the development of fully automated left ventricular ROI setting[12–15] obviates the need for operator intervention, inter- and intra-observer variance seems to be less important. But, automated ROI setting takes a long time—about 20 minutes with our data processing system[14]—and in about 5–8% of patients this method fails.[13–15] Thus, a new method of LVEF determination that is less time-consuming and has a much higher success rate is desirable.

Factor analysis is the method used to isolate normalized time activity curves (called factor curves) from dynamic data composed of several compartments of different temporal changes in tracer activity. This analytical method is free from inter- and intra-observer variance, once identical analytical parameters are set for all patients, and processing time is less than required for automated left ventricular contour detection.

The purpose of this study is to test, first, whether factor analysis of MUGA can measure LVEF or not, and second, whether masking the right ventricle (RV) out of MUGA can improve the accuracy of LVEF measurement or not.

MATERIAL AND METHODS

Patients

The material was left anterior oblique (LAO) images

Received November 21, 1988; revision accepted January 30, 1989.

For reprint contact: Norinari Honda M.D., Division of Nuclear Medicine, Department of Radiology, Saitama Medical Center, Saitama Medical School, 1981 Tsujido, Kamoda, Kawagoe, Saitama 350

of MUGA obtained from patients who were also examined with both first-pass radionuclide ventriculography and gated cardiac blood pool single photon emission computed tomography (SPECT) on the same day as the MUGA from November, 1986 to December, 1987. Forty patients were studied in this period, but two were excluded from this study because automated LV contour detection (14) failed. The mean age ± SD of the 38 patients was 60.9±16.0 years of age with a female: male ratio of 14: 24.

The patients were divided into two groups: one group with normal left ventricular wall motion (22 patients, mean age±SD=64.2±12.0), and the other with abnormal wall motion (16 patients, mean age± SD=65.9±9.5). Left ventricular wall motion was judged by the authors by visually inspecting the cinematic displays of LAO images of MUGA, RAO 40 images of first-pass radionuclide ventriculogram, and gated cardiac blood pool SPECT.

Data acquisition

MUGA images using 740 MBq(20 mCi) of *in vivo* labeled red blood cells were obtained from LAO 35–40 with a large-field-of-view gamma camera in the ×1.25 zoom mode. Oblique angulation of the camera was selected individually to separate right and left ventricles most clearly. Twenty 64×64-pixel-sized frames of 40 msec duration were collected for each heart beat and accumulated for 500 heart beats. Pixel size was 4.8 mm. A low energy, all purpose, parallel hole collimator was used and the pulse height analyzer was centered at a 140 keV energy peak with a window width of 20%.

Factor analysis (FA)

MUGA data were processed with a 3-point moving average with uniform weighting for temporal smoothing, and an eighth-order Butterworth-Wiener filter with cutoff of 0.125/pixel for spatial smoothing, followed by 2× zooming. FA was automatically performed without operator intervention in the following way on these zoomed images: First, LAO images of MUGA were compressed into 8×8-pixel images. Second, forty out of 64 dixels* were selected for FA according to their amplitude (=difference between maximum and minimum values). The number of factor was set to 3 for all the patients. Third, the method of DiPaola et al (16) was utilized to separate factor curves. The weight of each pixel for each of the isolated factor curves was then calculated on the smoothed and zoomed 64×64-pixel images and displayed as an image (called the "factor image"). These FA condition were the same throughout this study. In all of the patients, the 40 dixels selected covered the area of the heart and great vessels. Zooming of the MUGA images was used in framing out some of the background activities, liver, and spleen. The compression of 64×64 into 8×8-pixel images was necessary because of the limited computer ability.

FA was also performed on all of the patients after masking RV out of MUGA images. ROI over RV was set on an end-diastolic MUGA image with the aid of its phase image in order to separate the right atrium and ventricle.

Ejection fraction calculation

LVEF by FA was calculated from the factor curve, which corresponded to the left ventricle (Fig. 1), as follows:

$$\text{LVEF}=100\ (\text{Max}-\text{Min})/\text{Max}\ (\%),$$

where Max and Min are the maximum and the minimum values on the LV factor curve, respectively. In patients with abnormal wall motion, usually two factor curves were obtained in the left ventricle. When two factor curves had their nadirs in the systolic phase, the curve that occupied greater areas in LV was selected for LVEF calculation. When one curve had its nadir in the systolic phase and another in the diastolic phase, the curve with its nadir in the systolic phase was selected (Fig. 1).

LVEF was also measured from MUGA data by the variable ROI method (EFVROI) with fully automated left ventricular contour detection (14) applied to the 2×-zoomed images. LVEF measured by FA before and after RV masking was compared with EFVROI. Statistical significance was tested by paired-*t* test. A probability (P) value smaller than 5% was considered significant in this study.

RESULTS

Factor analysis was successfully performed automatically in all of the patients, and its processing time was about 3 minutes for each of the patients. Even in the two patients excluded from the study becuase of unsuccessful automated contour detection, factor analysis was successful. Figure 2 shows the correlation of the ejection fraction obtained by FA (EFFA) with EFVROI. The correlation was significant ($r=0.70$, $p<0.001$) in entire group of patients, and also significant in the group of patients with normal wall motion ($r=0.65$, $p=0.001$). It was not significant ($p=0.19$) in the group of patients with abnormal wall motion.

Figure 3 shows the correlation of ejection fraction

* The dixel (i, j) is defined as the temporal array of the values of the pixel (i, j). In this study, there were 64 dixels (8×8), and each of the dixels was composed of 20 pixel values (20 frames/heart beat)

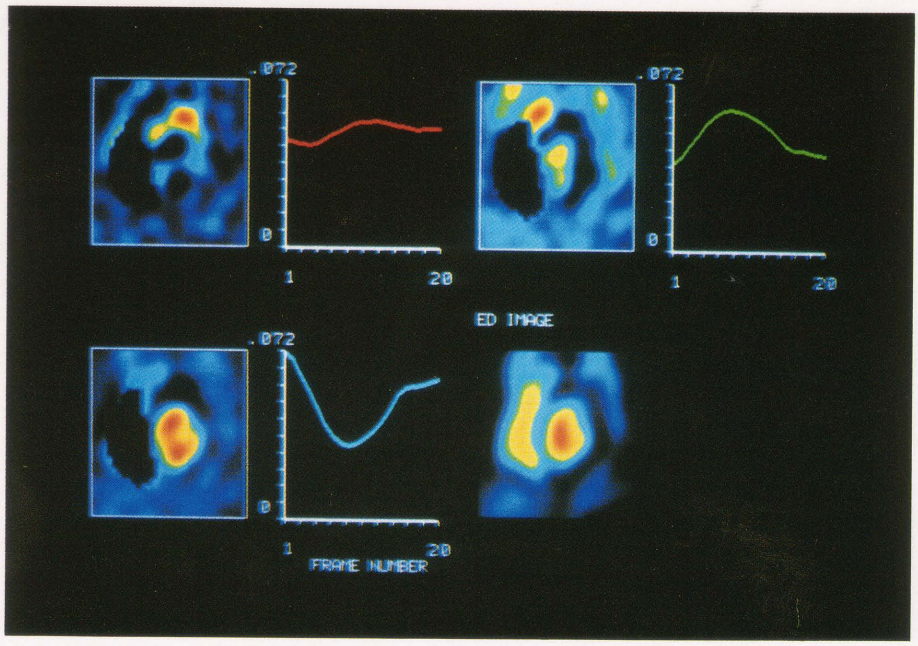


Fig. 1 Result of RV masked factor analysis in a patient with old inferior myocardial infarction (75 years of age, male). Left upper image and curve: the factor image and curve for the left atrium and background activity; right upper image and curve: aorta and pulmonary artery factor image and curve; lower image and curve: left ventricular factor image and factor curve. The left upper image shows a blue area in the left ventricle that indicates background activity in addition to the red areas (left atrium). Abnormal wall motion is shown in the right upper factor image as a yellow portion in the left ventricle. Right lower image is an end-diastolic image. Measured ejection fraction was 47% by the variable ROI method, 43% by factor analysis, and 53% by RV masked factor analysis.

obtained by FA after RV masking [EFFA (RVM)] with EFVROI. The correlation was significant in all groups: $r=0.66$, $p<0.001$ in the entire group of patients; $r=0.46$, $p=0.03$ in the normal wall motion group; and $r=0.55$ $p=0.03$ in the abnormal wall motion group. These results indicate that RV masking did not improve the accuracy of LVEF estimation by FA except in patients with abnormal left ventricular wall motion.

Table 1 Statistics of left ventricular ejection fraction by various methods

Group	Method	n	Mean	SD
All patients	EFVROI	38	53.2	18.3
	EFFA	38	45.8	11.4
	EFFA (RVM)	38	46.8	13.3
Patients with normal WM*	EFVROI	22	64.2	12.0
	EFFA	22	51.1	9.7
	EFFA (RVM)	22	51.5	9.5
Patients with abnormal WM*	EFVROI	16	37.9	13.8
	EFFA	16	38.4	9.2
	EFFA (RVM)	16	40.4	10.3

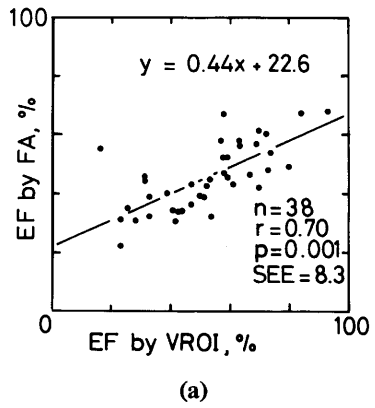
* WM=left ventricular wall motion
EFVROI=Ejection fraction measured by variable ROI method,
EFFA=Ejection fraction measured by factor analysis,
EFFA (RVM)=Ejection fraction measured by factor analysis after masking right ventricle.

Mean values, and standard deviations of EFVROI, EFFA, and EFFA (RVM) are summarized in Table 1. The difference in the ejection fraction was significant ($p<0.05$) between EFVROI and both EFFA and EFFA (RVM) in all groups. But it was not significant between EFFA and EFFA (RVM) in any patient group. This indicates that FA underestimated LVEF compared to the variable ROI method.

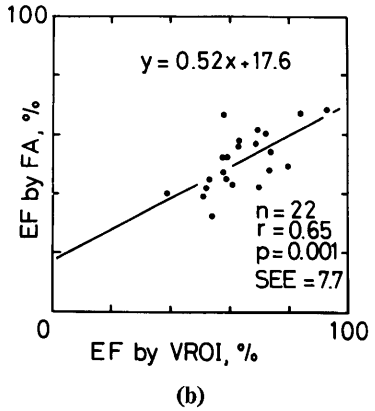
In 12 of the patients, contrast ventriculography was performed. The correlation of EFFA, EFFA (RVM), and EFVROI with the ejection fraction obtained in contrast ventriculography with area-length method (EFLVG) is significant in EFFA (RVM) ($r=0.75$, $p=0.005$), and not significant in EFVROI ($p=0.27$) and EFFA ($p=0.24$).

DISCUSSION

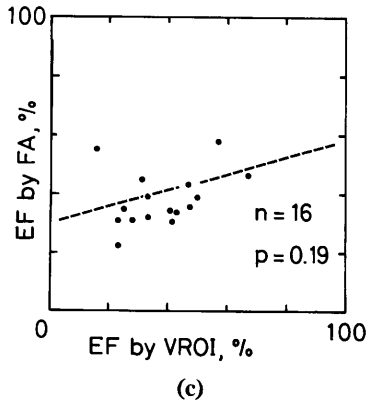
FA is reported to be useful in determining LVEF by first-pass radionuclide ventriculography,[17] cardiac shunt,[18] or regurgitant fraction.[19] To our knowledge,



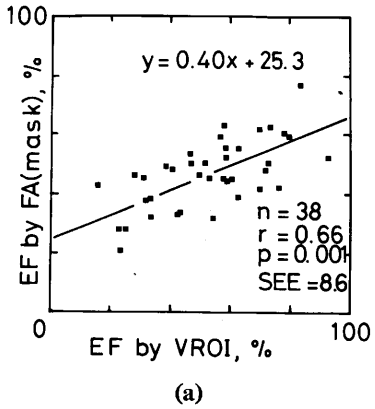
(a)



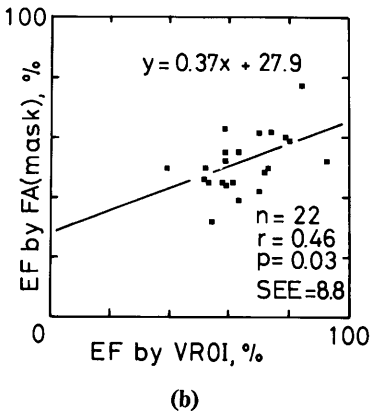
(b)



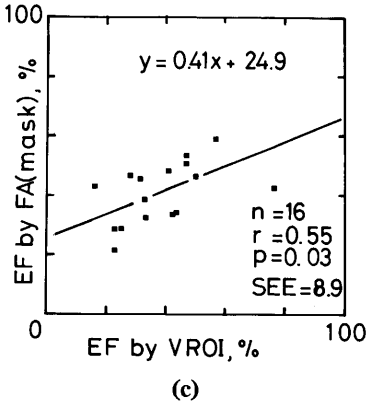
(c)



(a)



(b)



(c)

Fig. 2 Correlation of left ventricular ejection fraction measured by factor analysis with that measured by the variable ROI method in the entire group of patients (a), in the normal wall motion group (b), and in the abnormal wall motion group (c).

Fig. 3 Correlation of left ventricular ejection fraction measured by RV masked factor analysis with that measured by the variable ROI method in the entire group of patients (a), in the normal wall motion group (b), and in the abnormal wall motion group (c).

this is the first report on FA used for the determination of LVEF from MUGA.

The ejection fraction measured by the variable ROI method has been reported to correlate well with that measured by contrast left ventriculography with correlation coefficients of 0.83–0.95.[3,5–8,13–15] We therefore compared ejection fraction measured by FA with that measured by the variable ROI method. Direct comparison of EFFA or EFFA (RVM) with EFLVG was not done in this study because of the small number of patients (12 patients), and the different condition of each patient in MUGA and contrast ventriculography. Poor correlation of EFVROI with EFLVG raises the possibility that EFVROI was incorrect. We inspected all the automatically detected contours, and compared EFVROI with EF measured by the fixed ROI method. All of the contours inspected were found to be correct, and the correlation was nearly perfect ($r=0.99$, $p<0.001$). We therefore believe that EFVROI by automated contour detection worked well in this study.

In every patient, FA isolated a factor curve which had a similar shape to the left ventricular time activity curve, and the corresponding factor image located this curve at the left ventricle. This shows, together with the correlation shown in Figure 2, that FA can estimate LVEF in patients with normal wall motion but not in patients with abnormal left ventricular wall motion. No correlation of EFFA in patients with abnormal wall motion is explainable. FA can isolate factor curves which correspond to a normally moving portion and an abnormally moving portion of the left ventricle. Thus determination of EF for global LV is rather difficult. However, factor analysis shows the presence of abnormal wall motion in these situations. Since diagnosis of abnormal wall motion by FA is not the aim of this study, it is not discussed further.

The accuracy of LVEF determination by FA may be improved even in patients with abnormal wall motion, if the weighted mean is calculated from the ejection fractions of all pixels within the left ventricle. The weighting factors and ejection fractions of each pixel for this calculation should be those obtained by factor analysis. However, this process needs a ROI setting over LV, and therefore becomes the same procedure as the ROI method. The process also is a reverse calculation of factor analysis. This calculation is therefore not tested.

MUGA data have two compartments of similar time activity curves, *i.e.* for the left and right ventricle. Although the two compartments have different ejection fractions, usually both ventricles are expressed as one factor in FA in our experience. This means that the ejection fractions of the right and left ventricles would always be the same if FA is used. We therefore thought RV masking might improve the accuracy of LVEF measurement. The results in Figure 3 contradict this assumption in patients with normal wall motion. The reason for this result may be that FA was performed on large pixel size images. The final pixel size for FA after image zooming and pixel size conversion was 19.2 mm. The large pixel resulted in a loss of spatial resolution, which makes it difficult to distinguish between the left and right ventricle. To test this possibility, computer hardware must be changed so that FA can be performed in a short time on images with a much larger number of pixels such as a 32×32 or 64×64-pixel image. Such hardware was not available for this study.

The measured EFFA was smaller than EFVROI (Table 1). One possible cause of this is the inadequate background subtraction by FA or incomplete factor isolation by FA. Another possible cause of the underestimation is that LVEF would become the mean of the right and left ventricular ejection fraction since FA does not separate the right and left ventricles. Because RV masking did not improve the correlation of LVEF with EFVROI, and measured EF was not significantly different whether RV was masked or not, this possibility seems to be low. This also implies that significant inter- and intra-observer variance due to the RV ROI setting will not exist.

We performed three factor analyses, since the MUGA data for a normal heart can be regarded as having three compartments: (1) ventricles, (2) atria and great arteries, and (3) background. Theoretically, factor analysis can separate these factors. However, the results showed that the separation of background or superimposition on the left ventricle was not complete. This also is probably due to large pixel size in the factor analysis in this study. Although more than four compartments can be assumed in MUGA of abnormally moving hearts, four or five factor analysis is rarely possible, or rarely adds new information to the results of three factor analysis in our experience. We therefore performed three factor analysis for all of the patients.

Factor analysis is free from inter- and intra-observer variance if the same analytical parameters are used. Because we noticed at the beginning of this study that changes in the number of factors and/or dixels caused changes in LVEF, we performed FA under the same analytical conditions ensuring no inter- and intra-observer variance.

In conclusion, LVEF can be estimated by FA in patients with normal left ventricular wall motion. RV masking before FA did not improve the accuracy of LVEF in patients with normal wall motion in this study. Although FA is a good method because of its freedom from inter- and intra-observer variance and for its relatively short processing time and high suc-

cess rate, its application to the measurement of LVEF should be avoided in patients with abnormal left ventricular wall motion.

ACKNOWLEDGMENTS

The authors thank Mr. Keiji Suzuki NMT and other technicians and nurses of our department for taking the images and caring for the patients.

Part of this investigation was orally presented at the annual meeting of the Japanese Society of Radiology in Tokyo on April, 1988.

REFERENCES

1. Strauss HW, Zaret BL, Hurley PJ, et al: A scintiphotographic method for measuring left ventricular ejection fraction in man without cardiac catheterization. *Am J Cardiol* 28: 575–580, 1976
2. Folland ED, Hamilton GW, Larson SM, et al: The radionuclide ejection fraction; A comparison of three radionuclide techniques with contrast angiography. *J Nucl Med* 18: 1159–1166, 1977
3. Burow RD, Strauss HW, Singleton R, et al. Analysis of left ventricular function from multiple gated acquisition cardiac blood pool imaging comparison to contrast angiography. *Circulation* 56: 1024–1028, 1977
4. Green MV, Brody WR, Douglous MA, et al. Ejection fraction by count rate from gated images. *J Nucl Med* 19: 880–883, 1978
5. Sorensen SG, Hamilton GW, Williams DL, et al: R-wave synchronized blood-pool imaging. *Radiology* 131: 473–478, 1979
6. Wackers FJT, Berger HJ, Jhonstone 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* 43: 1159–1166, 1979
7. Taylor DN, Garvie NW, Harris H, et al: The effect of various background protocols on the measurement of left ventricular ejection fraction in equilibrium radionuclide angiography. *Brit J Radiol* 53: 205–209, 1980
8. Slutsky, Karliner J, Battler A, et al: Reproducibility of ejection fraction and ventricular volume by gated radionuclide angiography after myocardial infarction. *Radiology* 132: 155–159, 1979
9. Pfisterer ME, Battler A, Swanson SM, et al: Reproducibility of ejection-fraction determination by equilibrium radionuclide angiography in response to supine bicycle exercise: concise communication. *J Nucl Med* 20: 491–495, 1979
10. Karsch KR, Schicha H, Rentrop P, et al: Validity of different gated equilibrium blood pool methods for determination of left ventricular ejection fraction *Eur J Nucl Med* 5: 439–445, 1980
11. Okada RD, Kirshenbaum HD, Kushner FG, et al. Observer variance in the qualitative evaluation of left ventricular wall motion and the quantitation of left ventricular ejection fraction using rest and exercise multigated blood pool imaging. *Circulation* 61: 128–136, 1980
12. Bourgignon MH, Douglass KH, Links JM, et al: Fully automated data acquisition, processing, and display in equilibrium radioventriculography. *Eur J Nucl Med* 6: 343–347, 1981
13. Reiber JHC, Lie SP, Simoons ML, et al. Clinical validation of fully automated computation of ejection fraction from gated equilibrium blood-pool scintigrams. *J Nucl Med* 24: 1099–1107, 1983
14. Hosoba M, Wani H, Hiroe M, et al: Clinical validation of fully-automated contour detection for gated radionuclide ventriculography with a slant hole collimator. *Eur J of Nucl Med* 12; 53–59, 1986
15. Kim B, Kimura K, Ishida Y, et al: Fully automated determination of the left ventricular contour in multigated radionuclide ventriculography. *Jpn J Nucl Med* 24: 27–34, 1987
16. Di Paola R, Bazin JP, Aubry F, et al. Handling of Dynamic sequences in nuclear medicine. *IEEE Trans Nucl Sci* NS-29: 1310–1319, 1982
17. Maublant JC, Mena I, Hanalin LG: Factor analysis in left ventricular first-pass radionuclide angiography: value of the ventricular factor to measure ejection fraction. *Int J Card Imaging* 1: 107–112, 1985
18. Villanueva-Meyer J, Philippe L, Cordero S, et al: Use of factor analysis in the evaluation of left to right cardiac shunts. *J Nucl Med* 27: 1442–1148, 1986
19. Philippe L, Mena I, Darcourt J, et al: Evaluation of valvular regurgitation fraction by factor analysis of first-pass angiography. *J Nucl Med* 29: 159–164, 1988