Normal limits of ejection fraction and volumes determined by gated SPECT in clinically normal patients without cardiac events: A study based on the J-ACCESS database

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ABSTRACT

Purpose: Quantitative gated single-photon emission computed tomography (SPECT) is known to have high accuracy and precision for measurement of the principal cardiac functional parameters. We hypothesised that normal values for EF and LV volumes may differ among nationalities, and that optimal threshold values specific to the study population are required.

Methods: Among 4,670 consecutively registered patients for a J-ACCESS (Japanese investigation for prognosis based on gated SPECT) study from 117 hospitals, a total of 268 patients (149 women, 119 men) were selected from those with no baseline cardiac diseases and with no cardiac events for a three-year period. A gated SPECT study was performed with ^{99m}Tc tetrofosmin and analyzed with Cedars Sinai Medical Center's quantitative gated SPECT (QGS) software. The results of ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV) and stroke volume (SV), and EDV, ESV and SV normalized by body surface area (EDVI, ESVI and SVI) were calculated and summarized to obtain normal limits.

Results: EF for women and men was 74% ± 9 % and 63% ± 7% ($p<0.0001$). EDV, ESV and SV were significantly smaller in women than in men. Based on multiple regressions for linear models, the primary and secondary predictors of EF, EDVI, ESVI were gender and age. By stepwise multiple regression analysis, the statistically significant third predictor for EDV, ESV, SV and SVI was body weight. No colinearity was found between age and body weight. Important factors for the studied Japanese population included a high incidence of small hearts in women and the relatively advanced age of the population (the mean age ±SD was 64.1±10.0 years for women and 60.9±11.7 years for men).

Conclusion: EF and volumes by gated SPECT with QGS were significantly affected by gender and ages, with body weight as the third predictor for volumes. Moreover, the normal limits were so specific for the population studied that standards appropriate for the study

should be utilized.

Key Words:

Gated SPECT - ejection fraction - left ventricular volume - normal limits - quantification of cardiac function

Introduction

Left ventricular (LV) ejection fraction (EF) and ventricular volumes have been considered as one of the important factors for diagnosis and management of patients with cardiac diseases as well as prognostic values for future cardiac events [1-3]. Although echocardiography and gated blood-pool studies have been well-established methods for cardiology practice, gated myocardial perfusion SPECT has also been known to have high accuracy and precision for measuring principal cardiac functional parameters [1, 4, 5]. Some studies have reported the importance of generating normal limits for parameters of cardiac function using gated myocardial perfusion SPECT and their dependency on gender and, to some extent, age [6-8]. Determining normal values has also been considered important for the assessment of diastolic function with gated SPECT [9].

Nuclear studies with gated myocardial perfusion SPECT has become widely utilized in many countries because of its high accuracy and precision for LV EF and volumes [4, 10-13]. In daily clinical practice, however, we have sometimes felt that the same standards could not be used universally, and previous studies based on a US or European population could not be readily applicable to Japanese population.

We have been conducting a multi-center prognostic study (J-ACCESS; Japanese Assessment of Cardiac Event and Survival Study by Quantitative Gated SPECT) in 4670 patients, and 117 hospitals have been involved. The study design has been described elsewhere [14]. Since this study was performed in a series of consecutive patients, near-normal subjects without specific evidence of cardiac disease were included; for the purpose of the present study, this permitted the selection of patients with no baseline cardiac diseases and absence of cardiac events during the preceding 3-year period. In other words, it was possible to apply strict criteria for normality or low likelihood of cardiac disease.

Thus, we hypothesized that 1) a Japanese population has a different background and characteristics for LV EF and ventricular volumes, 2) The functional parameters may depend on gender and ages, but the mode of dependency may differ in this population. Finally, the normal limits obtained for the various ventricular functional parameters were compared with the results of previous US and European studies.

Materials and Methods

J-ACCESS study

J-ACCESS aimed to establish a Japanese database for the diagnosis and treatment of ischemic heart disease, and patient registration was performed from October 1, 2001 to March 31, 2002. A total of 117 Japanese hospitals participated in this study. The patients were consecutively registered according to the following criteria: age $\geq$ 20 years old, only those scheduled to take part in stress-rest gated SPECT study due to definite or possible ischemic heart disease, and availability of a written informed consent. Exclusion criteria from the initial registration were patients with an onset of myocardial infarction or unstable angina pectoris within 3 months, valvular heart disease, idiopathic cardiomyopathy, severe arrhythmia, heart failure with class III or higher New York Heart Association (NYHA) classification, or severe liver or renal disorders. Among 4,670 registered patients, 41 patients were excluded because they did not fulfill the selection criteria, leaving 4,629 patients for follow-up investigations for three years. The gender and age distributions were 2,989 men (aged 21 to 90 years; average and SD, 64.9 ± 10.3) and 1,640 women (aged 20 to 93 years; 67.2 ± 9.7). Since this registration was performed consecutively, patients with low risks for cardiac diseases were included. Age, gender, height, weight, subjective symptoms, history of present illness, medical history, risk factors, obesity and treatment before SPECT examination including revascularization and medication were surveyed. The registered patients underwent stress and rest myocardial perfusion SPECT with ^{99m}Tc tetrofosmin.

Gated SPECT was performed at rest, and standard QGS analysis (Cedars Sinai Medical Center, CA, US) was performed in each institute. As there was variation in reconstruction among the participating institutes, the inter-institution reproducibility of QGS results was assessed, as reported previously [15] and found to be good. The following examinations were conducted within two months before or after SPECT imaging: ECG at rest in 94% of the patients, stress ECG in 40%, echocardiography in 63%, chest X rays in 74%, coronary arteriography in 48%, and contrast left ventriculography in 37%. The findings were abnormal in 2,604 (60%) of the 4,367 patients who underwent ECG at rest.

Patient selection

Based on the patients' backgrounds, results of the stress and resting perfusion study and the cardiac events over a three-year period, the following criteria were used for selecting the patients appropriate for this study.

1) No present or past history of cardiac disease was recorded.

2) Absence of any of the following abnormalities or electrocardiographic (ECG) findings suggestive of ischaemia: left ventricular strain pattern, complete or incomplete bundle branch block, pacemaker implantation, atrial fibrillation, Q waves, QS patterns, inverted T waves, myocardial hypertrophy, sinus bradycardia or tachycardia, atrial flutter and atrioventricular block in the resting condition. Based on stress ECG records, patients with positive or borderline ECG changes and patients who had chest symptoms at peak exercise were also excluded.

3) Based on the 20-segment segmentation and 5-point (0, normal; 4, absent uptake) scoring model, both the summed stress score and summed rest score were scored to be 3 or less [16, 17].

4) During the follow-up of three years, no cardiac events were observed including percutaneous coronary intervention, angina pectoris and non-severe heart failure as soft

events, and cardiac death, non-cardiac death, myocardial infarction and severe heart failure as hard events.

5) Regarding the underlying diseases, patients who had medications for hypertension or diabetes mellitus were excluded. However, patients with borderline hypertension or glucose intolerance, who were not indicated for medical therapy as a subclinical condition, were possibly included.

Gated SPECT

Gated SPECT acquisition varied depending on the preference of the institutes. Since a total of 120 SPECT systems were used in the 117 institutes, adequacy of the following data was confirmed for 120 SPECT and computer systems. All institutes used a multi-detector camera: dual-detector with rectangular configuration (n=44), dual-detector with parallel configuration (n=31) and triple-detector (n=45) systems. The collimator type was high-resolution parallel (n=70), general purpose parallel (n=40) and other types (n=10). The matrix size of a frame was 64x64 (n=116) and 128x128 (n=4). The frame division per cardiac beat was 16 (n=38), 12 (n=11), 10 (n=4), 8 (n=64) and others (n=3). Acquisition time per view had a median of 30 seconds, a range of 20 to 60 seconds. Bad beat rejection for arrhythmia was performed in 88 of 120 systems. The acceptance window for data acquisition ranged from 10 to 60% with a median of 40%. Filtered back projection was used in 115 institutes, and the remaining institutes used ordered subset expectation maximization algorithm. The reconstruction of SPECT slices was performed by a ramp filter (n=105), and the remaining institutes by a Shepp-Logan filter. A Butterworth filter was used in 116 institutes as a pre-processing filter. Gender, age and body stature and weight were not found to vary according to the above acquisition conditions, thereby excluding technical bias.

Data analysis and statistics

The parameters of EF (%), EDV (ml), ESV (ml) and SV (ml) were calculated in each institute by QGS software [4] and sent to the J-ACCESS office. Normalization by body surface area (BSA) was used to calculate EDV, ESV and SV indices (EDVI, ESVI and SVI: unit ml/m^2). Statistics of the average, standard deviation (SD), median and percentile of distribution were calculated in each group. An analysis of variance for the mean was performed based on groups with gender, age and body weight. A multiple regression analysis with a linear model was performed with the standard and stepwise methods. Colinearity among parameters was also examined. A p value less than 0.05 was considered as significant.

Results

Based on the criteria for normal patients or low possibility of cardiac diseases, 268 patients (5.8%) were selected out of 4,629 patients. Table 1 summarizes the gender-based patients demographics and parameters. The average and SD of the ages were 64.1 ± 10.0 years for women and 60.9 ± 11.7 years for men ($p=0.0172$). The patients selected for this study were younger than the average age of J-ACCESS study (67.2 ± 9.7 for women and 64.9 ± 10.3 for men). The patient's height, weight and body surface area were smaller in women than in men. The average blood pressure at rest was 145/82 mmHg and 143/83 mmHg for women and men, showing high-normal or borderline hypertension reflecting the high-aged population. The heart rate and blood pressure at peak exercise did not differ significantly between genders. The changes in heart rate and blood pressure at pharmacological stress showed no gender differences.

The value of EF was 74% ± 9% and 63 ± 7 % for women and men ($p<0.0001$). The EDV and ESV were smaller in women than in men. The EDVI was 39 ± 11 ml/m^2 and 51 ± 12 ml/m^2, and ESVI was 11 ± 6 ml/m^2 and 19 ± 7 ml/m^2, respectively ($p<0.0001$ for both). Gated SPECT after stress showed similar gender differences. The resting SV was 43 ± 9 ml vs. 55 ± 13 ml for women and men ($p<0.0001$), and the SVI was 28 ± 6 vs. 32 ± 7 ml/m^2 for women and men ($p<0.0001$), respectively. When the resting SVI (y) was plotted versus the resting EDVI (x), the regression lines were $y=0.483\ x + 9.43$ for women and $y=0.489\ x + 7.08$ for men, both showing similar slopes and a slightly higher intercept in women than in men. When the small heart was defined as ESV<20, the percentage of the small heart was 74% and 13% for women and men, respectively ($p<0.0001$).

Differences in age were summarized for three age groups of less than 60, 60 to 69 and 70 or more (Table 2). In women, EF did not differ significantly among the three age groups. EDV, ESV, SV, EDVI, ESVI and SVI also did not differ significantly, although the percentage of patients with a small heart was higher in older female age groups (63% for <60 year group, 77% for 60-69 year group, 81% for ≥ 70% group; p=0.0227). In men, EF did not differ significantly among the three age groups, although the average value was slightly higher in older groups. EDV, ESV and SV decreased with age (p=0.0034, 0.0085 and 0.0211, respectively). ESVI showed smaller values in the higher age group (p= 0.0278), but EDVI and SVI did not show a significant difference. The percentage of patients with a small heart did not differ among male age groups, although it was slightly higher (28%) in the ≥70 group. The patients' height, weight and body weight were smaller in higher age groups.

Multiple regression analysis was performed for EF, EDV, ESV, SV, EDVI, ESVI and SVI regarding the differences in gender, age and body weight as variables (Table 3). Significant variables for EF were gender and age based on a forward stepwise regression model. Gender, age and body weight were all significant variables for EDV, ESV and SV. When the possibility of colinearity was examined for variables of age and body weight, they were judged as independent indices for estimating volumes. When the ventricular volumes were normalized by body surface area, EDVI and ESVI showed gender and age as significant variables for multiple regression analysis. For all these models, gender was the primary predictor and age was the second predictor for LV volumes and volume indices. The variable of body weight was the third weak predictor for LV volumes. When stepwise fit by all possible models was performed for EF, EDVI, ESVI and SVI, use of the 3 variables including body weight increased R^2 only slightly and was not considered a significant additive value.

Finally the effect of the number of frames per cardiac cycle was examined to check the dependency of the frame division on the gated SPECT results. A 16-frame division was used in 85 patients (32%) and an 8-frame division in 157 patients (59%). In women, EFs were 75%±9% (n=48) and 74±9% (n=89) for the 16-frame and 8-frame studies, respectively (p=n. s.). In men, EF with the 16-frame study was significantly higher than that with the 8-frame study: 66±7% (n=37) vs. 62±7% (n=68) (p=0.006). As for ESV, the 16-frame and 8-frame studies showed 17±8 ml vs. 16±10 ml in women (p=n. s.) and 32±14 ml vs. 33±14 ml in men (p=n. s.). The distribution of the different frame groups did not differ significantly among the subgroups in terms of age, body weight, body surface area and genders based on contingency table analyses.

Discussion

Normal limits for gated SPECT and QGS software were determined based on the J-ACCESS database that has been compiled since 2001 [14]. The major conclusion of this study was that normal values for EF and LV volumes were significantly influenced by gender, and subsequently by age and body weight. The normal values for female patients showed a higher EF and a lower volumes in comparison to non-Japanese studies, and body weight was an important factor when LV volumes were not corrected by body surface area. The results suggested the importance of standards specific for each population.

Characteristics of Japanese population

This study was performed from consecutive SPECT studies, and thus it reflects the daily nuclear medicine practice in Japan. When considering the average age of the subjects selected for the normal limits, the mean age indicated for nuclear cardiology seemed to be 5 to 9 years higher in our study compared with those of previous studies conducted in the US and Europe. The subgroups of <60 years, 60-69 years and ≥70 years were used because the mode of age distribution was in the sixties in our study. According to the report from the Ministry and of Health and Welfare of Japan, the life expectancy of a newborn in Japan in 2004 was 78.36 and 85.33 years old for males and females, respectively. In 65 year olds, cardiac disease was the cause of 14.83% of deaths among men and 19.67% among women, while in 80 year olds it was the cause of 15.79% of deaths among men and 20.63% among women. The cause of death from cardiac disease was the second highest following the malignant neoplasm, and the importance of cardiac studies should be emphasized. Another characteristic of this population was the frequency of patients with a small heart. Akincioglu et al. has excluded patients with a small heart defined as ESV <20 ml, because the main purpose was the evaluation of diastolic phase in their study [9]. It has been known that the values determined by QGS were less accurate for calculating small left ventricular volumes [11, 18-20]. At first we intended to exclude the small-heart patients, but we decided to include all of them because the percentage of subjects with a small heart was unexpectedly high in our study population, as high as ~80% for normal female patients particularly in patients in older age groups. Thus this study reflected the actual situation when we performed gated SPECT in Japan, and a similar situation might be applicable for other population in the East Asia.

Dependency on gender

Gender-specific differences have been described in previous studies with gated SPECT [6-9] as well as a larger scale MRI study in a probability-based Dallas heart study

[21]. Even after normalization of EF and volumes by body surface area, the difference between men and women was significantly different, implying dependency on an intrinsic physiologic difference between genders. Women had relatively small EDV, ESV and higher EF than men. Since heart rate was not different between genders, SVI should be similar for given EDVI to maintain comparable cardiac index (output per body surface area). The present study showed lower mean SV and SVI in women than in men, but the SVI for a given EDVI was found to be similar or rather slightly higher in women than in men. This EDV-SV relationship was also noted by an MRI study [21], and gated SPECT data also seemed to support the observation. In addition, the mean BSA for men in our study was approximately the same as the mean BSA for women in the European study [8]. However, EF was still higher in European women than in Japanese men. This finding appears to add further evidence that the higher EF is related to a female gender and not just the small body and heart size.

Dependency of age

Age-related differences were found in men but not in women in the three age groups in this study. De Bondt et al. found differences in EF or volumetric parameters between the different age groups only in women of the >65 year age group who had significantly higher EF and significantly lower volumes [8]. Rozanski et al. found that the age correlated only weakly with LVEF and did not correlate with LV volume [6]. The age-related characteristics differed among studies, although the statistical significance was only weak in each study. The age-related differences might have been related to patient populations. Multiple regression analysis in the present study showed age to be an important contributing factor for EF, EDV, ESV and SV for both genders, but it was a significant variable only in men; this indicates age to be a secondary factor.

Dependency on body weight

Body weight was considered as the third factor for determining the LV volume as shown by the multiple regression analysis. However, after normalization by body surface area, weight was not selected as the significant determinant except for SV and SVI. Since women had lower body weight and the aged groups had lower body weight in our study, we suspected colinearity of gender and ages to body weight. But statistical analysis showed that colinearity was not significant between body weight and other variables. Thus use of volume index in the unit of ml/m^2 is recommended rather than volume itself. When the parameters of EDV and ESV are directly used in a study, the effect of body weight should be kept in mind and its distribution should be confirmed among groups.

Importance of population-specific standards

This study demonstrated the importance of normal values for specific nationalities or races, or more strictly speaking, standards specific to each individual study should be used. Since the backgrounds of patients referred to nuclear cardiology studies may vary between races, caution should be observed when results from other countries are applied. Table 4 shows the variability of normal EF, EDV and ESV, etc. from several studies we have mentioned in this discussion. The average age for gated SPECT was the highest in Japan, showing 64 ± 10 years and more than 10 years higher than the US studies [6-8]. When mean-2SD was used for normal lower limits, borderline EFs by Rozanski [6], Ababneh [7], De Bondt [8] and our data were 49%, 51%, 48% and 56% for women, and 41%, 48%, 47% and 49% for men, respectively. The higher borderlines (average +2SD) of EDV were 106, 91, 121 and 93 ml for women, and 157, 118, 156 and 132 ml for men, respectively. Similarly, the upper borderlines of ESV were 47, 41, 55 and 37 ml for women, and 78, 55, 72 and 59 ml for men. Hence, the Japanese population showed the highest EF and the lower EDV and ESV as threshold values for abnormality.

The differences in EF and volumes for various nationalities are probably dependent on combinations of body weight, age and patient background rather than being specific to ethnicity per se. Taking these factors into account, however, the present study demonstrated the requirement for population-specific standards.

Effect of technical issues

When gated SPECT was analyzed with QGS software, one of the most important issues was underestimation of LV volumes in small heart patients. Our previous mathematical model showed non-linear underestimation of small volumes and pediatric studies, and was affected by acquisition conditions and processing parameters [4, 18]. This underestimation could not be readily corrected by a simple correction formula.

Another factor was inconsistency of the acquisition protocol in 117 hospitals: including 8-16 frames per cardiac cycle, 360 or 180-degree rotations, heart-rate acceptance windows for data acquisition, etc. This study demonstrated that a 16-frame gated study resulted in approximately a 4% higher EF only in men compared with an 8-frame study. However, even if several possible combinations had been existed for acquisition and processing, we decided to disregard this if there was no bias for specific gender, age and body weight. Ababneh et al. compared EF, EDV and ESV obtained using ^{201}Tl and ^{99m}Tc-sestamibi in patients with normal exercise tolerance and no wall motion abnormalities, and found no significant difference between the tracers. They also found no differences between 180-degree and 360-degree rotations. Relatively low variability or acceptable precision by this J-ACCESS study was demonstrated by the study of the inter-institution preference based variability, which showed <3.6% (SD) for EF and <10% (CV) for EDV and ESV [15].

Conclusion

The normal limits were examined based on the J-ACCESS database with 268 of 4670 patients registered for the multicenter study. The parameters of gender and age were important determinants for EF and LV volumes. Body weight was the third predictor when the volume was not normalized by body surface area. Higher ages and frequency of small heart were characteristics of our study group, and the importance of population-specific standards should be emphasized.

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Table 1. Parameters of gated SPECT with respect to gender difference

	Gender		p value
	Women	Men	
	Mean±SD	Mean±SD	
Number of patients	149	119	
Age	64.1±10.0	60.9±11.7	0.017
Range	30-85	21-82	
Stature			
BSA (m^2)	1.49±0.13	1.72±0.15	<0.0001
Height (cm)	152.3±5.8	165.8±7.2	<0.0001
Weight (kg)	53.9±8.8	65.1±10.2	<0.0001
HR and BP at rest			
HR (/min)	73.7±11.3	71.8±13.3	n. s.
SP (mmHg)	145±21.6	142.8±21.4	n. s.
DP (mmHg)	82.3±14.5	82.5±13.2	n. s.
HR and BP at peak exercise			
Number	110	93	
HR (/min)	133.2±20.8	133.6±19.7	n. s.
SP (mmHg)	197.6±28.6	204.2±28.9	n. s.
DP (mmHg)	97.1±19.4	97.7±19.7	n. s.
HR and BP at pharmacological stress			
Number	39	26	
HR (/min)	87.8±16.4	85.6±19.2	n. s.
SP (mmHg)	134.2±18.9	137.5±23.8	n. s.
DP (mmHg)	71.0±14.7	73.3±17.0	n. s.
Resting condition			
EF (%)	73.7±9.3	63.1±7.2	<0.0001
EDV (ml)	59.0±16.8	87.9±22.8	<0.0001
ESV (ml)	16.5±9.9	32.9±13.4	<0.0001
SV (ml)	42.5±9.4	54.9±12.6	<0.0001
EDVI (ml/m^2)	39.3±10.7	51.1±11.8	<0.0001
ESVI (ml/m^2)	10.9±6.4	19.0±7.1	<0.0001
SVI (ml/m^2)	28.4±6.1	32.1±6.9	<0.0001

Post-stress condition			
Number	101	75	
EF (%)	72.4±9.2	63.3±6.6	<0.0001
EDV (ml)	57.6±17.9	83.9±22.5	<0.0001
ESV (ml)	16.8±10.6	31.1±12.0	<0.0001
SV (ml)	40.8±9.7	52.9±13.2	<0.0001
EDVI (ml/m^2)	38.6±11.6	48.3±11.4	<0.0001
ESVI (ml/m^2)	11.2±7.1	17.8±5.8	<0.0001
SVI (ml/m^2)	27.3±6.2	30.5±7.3	0.002
Small heart (ESV<20 ml)	74%	13%	<0.0001

BSA, body surface area; HR, heart rate;

BP, blood pressure; SP, systolic pressure; DP, diastolic pressure;

EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume;

EDVI, end-diastolic volume index; ESVI, end-systolic volume index; SVI, stroke volume index

Table 2. Age-related difference of EF, volumes, volume indices

Parameters	Age groups (years old)			
	<60	60-69	>=70	ANOVA p
Women				
Number	41	60	48	
HR (/min)	76±12	75±12	71±10	n. s.
SP (mmHg)	141±21	146±21	148±23	n. s.
DP (mmHg)	83±13	85±13	79±16	n. s.
EF (%)	73.0±10.2	74.6±9.5	73.0±8.3	n. s.
EDV (ml)	63.1±19.3	58.0±13.8	56.8±17.6	n. s.
ESV (ml)	18.4±11.4	15.4±8.4	16.2±10.0	n. s.
SV (ml)	44.7±9.9	42.6±8.8	40.6±9.4	n. s.
EDVI (ml/m^2)	41.4±11.5	38.1±8.3	39.0±12.3	n. s.
ESVI (ml/m^2)	12.0±7.1	10.0±5.3	11.1±6.9	n. s.
SVI (ml/m^2)	29.4±5.9	28.1±5.7	27.8±6.7	n. s.
Small heart (%) *	63%	77%	81%	0.023
Height (cm)	156.4±5.8	152.2±4.6	148.9±4.9	<0.0001
Weight (kg)	53.8±8.3	55.1±9.3	52.6±8.5	n. s.
BSA (m^2)	1.52±0.12	1.50±0.12	1.45±0.12	0.021
Men				
Number	49	41	29	
HR (/min)	76±14	68±12	70±12	0.012
SP (mmHg)	140±19	140±18	151±27	0.046
DP (mmHg)	85±13	80±14	81±12	n. s.
EF (%)	62.1±7.7	63.0±6.2	65.0±7.8	n. s.
EDV (ml)	95.4±23.6	85.9±22.3	78.1±17.5	0.003
ESV (ml)	36.9±15.0	32.0±12.6	27.5±9.2	0.009
SV (ml)	58.4±12.3	53.9±12.9	50.5±11.5	0.021
EDVI (ml/m^2)	53.9±11.3	50.4±13.1	47.3±9.6	n. s.
ESVI (ml/m^2)	20.8±7.5	18.8±7.2	16.2±5.2	0.028
SVI (ml/m^2)	33.1±6.4	31.6±7.6	31.0±6.3	n. s.
Small heart (%) *	10%	7%	28%	n. s.
Height (cm)	168.6±7.8	165.0±6.3	162.1±5.6	0.0005
Weight (kg)	67.9±10.6	64.5±9.9	61.1±8.8	0.018
BSA (m^2)	1.77±0.16	1.70±0.14	1.64±0.13	0.002

*ESV<20 ml

Table 3.
Multiple regression analysis for EF, volumes and volume indices

Parameters	Variables and regression by Forward Stepwise Method*	Estimate of coefficient	Significant probability	R^2	Number of significant variables
EF	R^2=0.31, adjusted R^2=0.30				2
	Gender(women-men)	-4.69	<0.0001	0.28	
	Age	0.13	0.004	0.30	
	Body weight	-0.070	n. s.	0.31	
EDV	R^2=0.47, adjusted R^2=0.46				3
	Gender(women-men)	-11.35	<0.0001	0.36	
	Age	-0.55	<0.0001	0.44	
	Body weight	0.45	0.0002	0.47	
ESV	R^2=0.44, adjusted R^2=0.43				3
	Gender(women-men)	-6.60	<0.0001	0.34	
	Age	-0.32	<0.0001	0.42	
	Body weight	0.22	0.003	0.44	
SV	R^2=0.34, adjusted R^2=0.33				3
	Gender(women-men)	-4.75	<0.0001	0.26	
	Age	-0.23	<0.0001	0.31	
	Body weight	0.23	0.001	0.34	
EDVI	R^2=0.27, adjusted R^2=0.26				2
	Gender(women-men)	-6.05	<0.0001	0.22	
	Age	-0.27	0.0001	0.26	
	Body weight	-0.11	n. s.	0.27	
ESVI	R^2=0.32, adjusted R^2=0.31				2
	Gender(women-men)	-3.78	<0.0001	0.27	

	Age	-0.16	0.017	0.32	
	Body weight	0.0032	n. s.	0.32	
SVI	R^2=0.12, adjusted R^2=0.11				3
	Gender(women-men)	-2.27	<0.0001	0.075	
	Age	-0.11	0.017	0.095	
	Body weight	-0.11	0.010	0.12	

R^2 and adjusted R^2 are given by three variables with gender, age and body weight

Table 4. Mean values for LVEF and volumes compared with other studies

Author	Rozanski [6]	Ababneh [7]	de Bondt [8]	Akincioglu [9]	Nakajima [this study]
Women					
n	100	124	59	19	149
Age (years old)	52±13*	60±12**	59±12	52±12	64±10
LVEF (%)	67±9	67±8	66±9	67±6	74±9
LVEDV (ml)	62±22	57±17	75±23	91±17	59±17
LVESV	21±13	19±11	27±14	31±11	17±10
Mean EDV-Mean ESV (ml)	41	38	48	60	42
LVEDVI (ml/m^2)	35±11	32±8	43±11		39±11
LVESVI	12±7	10±5	16±7		11±6
Mean EDVI-Mean ESVI (ml/m^2)	23	22	27		28
BSA (m^2)	1.75±0.20		1.7±0.2		1.49±0.13
Men					
n	78	116	43	71	119
Age (years old)	52±13*	60±12**	56±13	53±11	61±12
LVEF (%)	59±9	62±7	59±6	63±5	63±7
LVEDV (ml)	95±31	74±22	106±25	110±20	88±22
LVESV	40±19	29±13	44±14	41±11	33±13
Mean EDV-Mean ESV (ml)	55	45	62	69	55
LVEDVI (ml/m^2)	48±14	38±9	54±14		51±12
LVESVI	20±9	15±6	23±8		19±7
Mean EDVI-Mean ESVI (ml/m^2)	28	23	31		32

BSA (m^2)	1.97±0.21		2.0±0.2		1.72±0.15
Methods					
	modified Simpson	QGS (both Tl-201 and Tc-99m)	QGS	QGS (ESV <20 not included)	QGS
Comments	* including men and women (n=214)	** including men and women (n=1513)			