



Normal limits of left ventricle functional parameters by gated SPECT myocardial perfusion imaging in a sample of the Egyptian population

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ABSTRACT

Background: Cardiovascular disease prevalence increases in developing countries. Gated single-photon emission computed tomography (SPECT) has taken over the myocardial perfusion imaging (MPI) studies. It is also known that in symptomatic patients, SPECT MPI has significant affinity in diagnosing cardio-vascular diseases (CVD). **Aim of the work:** establish a normal local reference for left ventricular functional dimensions (ejection fraction, end-diastolic volume, and end-systolic volume) at rest and post-stress conditions by gated SPECT myocardial perfusion scan and compare it with global references of different populations that may help the process of prevention, early intervention, and dispensing unnecessary invasive interventions based on gated SPECT MPI results. **Methods:** This was a Cross-sectional observational study that retrospectively analyzed 80 patients sent for rest/stress-gated SPECT with Tc-99 MIBI because of suspected coronary artery disease (CAD). **Results:** EF at rest was higher significantly than stress in the studied group, there was no significant difference between this study finding and international value, international European value as regards EF, but ESV and EDV were significantly higher among international value. Significant gender differences between parameters were recorded. **Conclusion:** cardiac volumes and function assessment by using gated SPECT should consider gender-matched normative values and to much extent influenced by ethnicity or geographical origin with normalization of other variables such as isotope used and number of frames per cycle should also be considered when interpreting results, since accuracy of measurements can be affected.

Keywords: gated SPECT; ESV; EDV; CAD; Tc-99 MIBI.

INTRODUCTION

Cardiovascular diseases are considered one of the most common causes of death globally with increased rates in developing

countries, latest statistics from WHO regional reports about cardiovascular disease (CVD) Deaths rank Egypt 18 in the world [1].

Assessment and evaluation of left ventricular function, using Left ventricular (LV) ejection fraction (EF) and ventricular volumes are the main cornerstone of cardiac diagnostics [2]. Multiple imaging techniques are in diagnostic practice bringing a primitive assumption for the non-expertise that these methods would provide the same results with the same accuracy [3]. Gated single-photon emission computed tomography (SPECT) has taken the myocardial perfusion imaging (MPI) studies, being non-operator dependent as other primary methods, echocardiography for example, quite affordable and noninvasive imaging method as well as providing a combined assessment of myocardial perfusion and left ventricular function with single radiotracer injection. The automatic quantification method gated SPECT performs has become a routine part of MPI acquisition and interpretation [4]. In symptomatic patients, SPECT MPI has high diagnostic accuracy for the detection of significant CVD [5].

METHODS

This was an observational retrospective study. The review of the data was carried out at radiology department in Zagazig University Hospital (ZUH). The current study retrospectively analyzed reports of 150 patients in the 6 months (September 2019 to May 2020) sent for rest/stress-gated SPECT with Tc-99 MIBI because of suspected coronary artery disease (CAD).

Written informed consent was obtained from all participants, the study was approved by the research ethical committee of the Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

There are 80 patients (36 females and 44 males) who met our inclusion criteria that were: Age <60 years, normal baseline ECG, achievement of at least 85% of maximum predicted heart rate during symptom-limited exercise testing, no angina or ECG changes (defined as ST depression of 1 mm or greater) and normal myocardial perfusion by visual and automated analyses.

The rest of the patients were excluded according to the exclusion criteria were: Elderly aged 60 years and above, patients with known CAD, uncontrolled diabetes and hypertension, LV hypertrophy by echocardiogram or ECG, cardiomyopathy of any cause, valve disease, rhythm disorders, or intra ventricular conduction alterations were excluded.

The main investigation started with patient preparations as they were asked to get all previous studies, companion as the test, which takes about 4-5 hours and to be away from children and pregnant women after the test to avoid radiation exposure, to keep themselves away from any stressful issues either mentally or physically the night and day of the stress test.

Some medications have to be stopped the day before the test as Nitromak, Monomak, Evox, and Isosorbide. Other medications have to be stopped 4 days before the test as Concor, indral, bisocard, and atenolol. Before the week of the test they should also stop taking lanoxin, cardioxane, and digoxin, and patients who were suffering from asthma, had internal pacemaker or any disc lesions should inform the doctor before the test.

The radionuclide was Tc-99m sestamibi (T_{1/2}: 6 hours, Energy: 140 KeV, Type: IT, g generator), adult dose range: 10-30 mCi administrated by IV injection with passive transport into myocardial mitochondrial in

proportion to blood flow.

Equipment was Gamma camera (Dual head GE discovery NM 630 camera large field of view, Static: Timed for 300 sec with a collimator of Low energy, high resolution, and single photon emission computed tomography (SPECT): 180 arcs, 64 projections at 20-40 sec/frame, gated 8 frame/cycle, matrix at 64x64 runs 25 minutes. The technique used a day split dose rest/stress protocol. Rest protocol was performed in the morning and patients were injected with 10 ml of Tc-99m sestamibi and then waited about 30-60 min before rest imaging was obtained. The patient was given a glass of cold water before imaging to clear the thyroid, liver, and bowel then was positioned supine with the heart in the center field of view and left arm up overhead if possible. If the arm is down at the side because of problems with the shoulder joint or recent surgery, both the rest and stress images should be taken the same way.

SPECT images were started with the camera right anterior oblique to left posterior oblique with computed analysis of the left ventricle showing the vertical axis, horizontal long axis, and short axis

Stress protocol obtained by exercise on the treadmill until heart rate between 85% and 100% of maximum reached under monitoring heart rate, blood pressure, and ECG changes (closely). Inject and flush on physician's order (when target heart rate is obtained or about 1 minute before patient gives out) then maintain exercise for 60–90 seconds after injection and wait 35-45 min to image.

For gated studies, we connected three lead ECGs for checking good R-R interval and the same imaging technique of the rest test was done with additional software ejection fraction information.

STATISTICAL ANALYSIS

Data collected throughout history, basic clinical examination, laboratory investigations, and outcome measures were coded, entered, and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative data is represented as number and percentage, and quantitative continues group is represented by mean \pm SD, the following tests were used to test differences for significance; Differences between quantitative independent groups by T-test and paired by paired T, correlation by Pearson's correlation,. P value was set at <0.05 for significant results & <0.001 for high significant results.

RESULTS

Regarding demographic data, age was distributed as 52.52 ± 4.99 with a minimum age of 40 and a maximum of 60 years, regarding sex males were 55% and females 45%.

Regarding Risk factors, 61.3% were controlled HTN 66.3% were controlled DM, 66.3% had FH, chest pain 60%, and smoker were 38.8%.

As regards EF, ESV, and EDV distribution between stress and rest in the same group, EF at rest was significantly higher than stress in our studied group as they were distributed as 64.97 ± 7.69 and 67.47 ± 4.66 respectively between stress and rest, ESV was significantly lower at rest than at stress as it was distributed as 21.82 ± 7.12 and 19.98 ± 6.25 respectively, regarding EDV there was no significant difference between stress and rest (table, 1. Figure 1).

Also, there was no significant difference between our study finding and international

value and international European value as regard EF, but regard ESV and EDV they were significantly higher among international values.

Regarding sex distribution, ESV at rest and stress were significantly lower infemales than males and EF was significantly lower among males at rest and stress and EDV was

significantly lower at stress only (table 2), (fig. 2,3).

Finally, there was no significant difference between cases with DM, HTN, smoking, FH and No FH, chest pain, and cases without neither rest or stress. However, there was a significant correlation regarding EDV as it was significantly positively correlated with age at rest and stress.

Table 1: EF, ESV, and EDV distribution between stress and rest in the same group (n=80).

	Stress	Rest	Paired t	P
EF (%)	64.97±7.69 (53-87)	67.47±4.66 (58-78)	-4.308	0.00**
ESV (ml)	21.82±7.12 (5-59)	19.98±6.25 (7-56)	2.728	0.008*
EDV (ml)	63.66±21.23 (14-59)	62.48±20.36 (23-100)	0.890	0.376

Table 2: EF, ESV, and EDV distribution between males and females at rest and stress

	Females	Males	P
EDV rest (ml)	61.58±21.09	63.41±20.58	0.285
ESV rest (ml)	18.25±6.85	22.77±8.13	0.035*
EF rest (%)	68.86±4.66	65.28±4.69	0.042*
EDV stress (ml)	60.81±21.52	66.91±19.85	0.011*
ESV stress (ml)	20.44±7.85	24.50±6.52	0.028*
EF stress (%)	66.54±6.73	63.41±7.73	0.018*

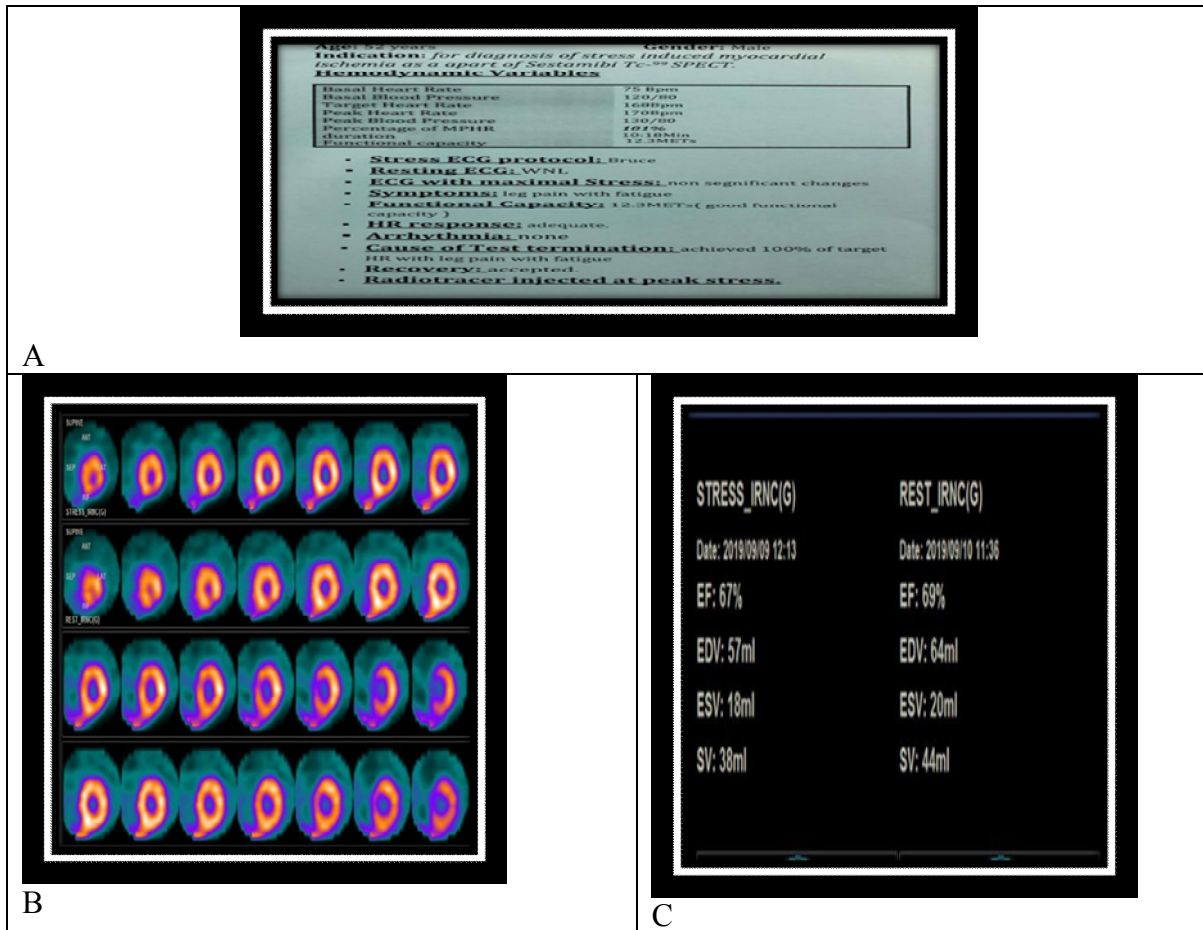


Figure 1: Male patient 52 y was complaining of fatigue and leg pain. A: Stress-induced ECG report shows non-significant ischemic changes. B: Normal perfusion at SPECT MPI short axis view at both rest and stress. C: Gated SPECT analysis of LV function at rest and stress.

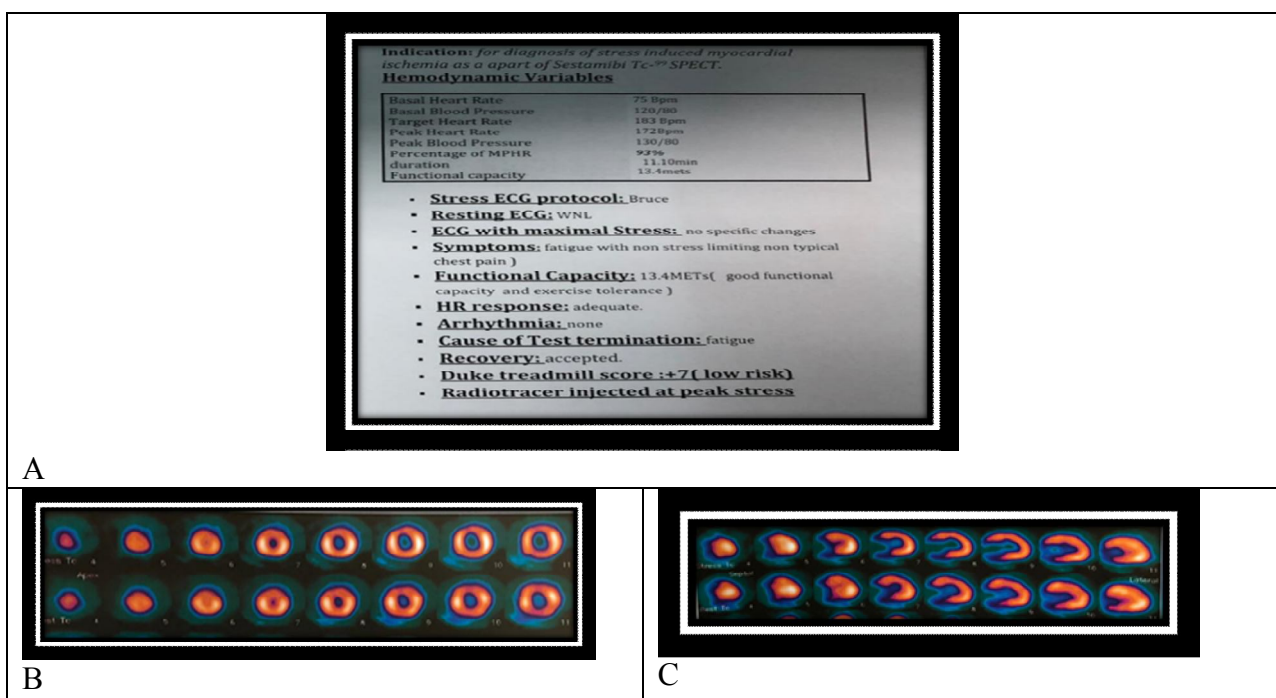


Figure 2: A female patient was complaining of fatigue with atypical chest pain. A: Stress-induced ECG shows no significant ischemic changes. B: normal perfusion of SPECT MPI short axis view at both stress and rest. C: Normal perfusion of SPECT MPI horizontal axis view at

both stress and rest.

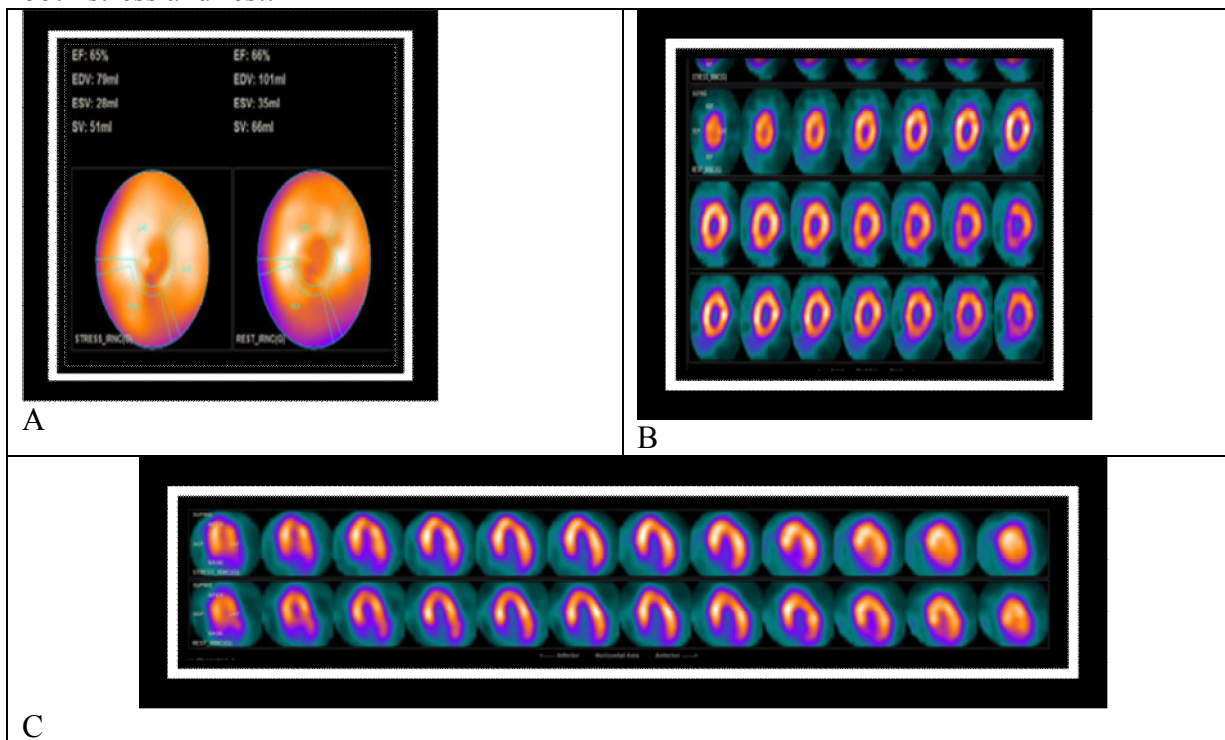


Figure 3: A male patient was complaining of atypical epigastric pain. A: SPECT polar map shows LV functional parameters. B: Normal perfusion of SPECT MPI short axis view at both stress and rest. C: Normal perfusion of SPECT MPI vertical axis view at both stress and rest

DISCUSSION

This study clarifies the importance of establishing normal values for specific nationalities or races, or put more strictly, the need to use standards specific to each study. Since the backgrounds of patients referred to nuclear cardiology studies may vary between races, caution should be observed when applying results from other countries.

Eighty patients were included in this study, the total group LVEF upper limit was 78 and 87 ml and the lower limit was 58 and 53 ml at rest and stress respectively. Also, ESV was 56 and 59ml as an upper limit, 7ml and 5 ml as a lower limit at rest and stress respectively. Another parameter is EDV the upper limit was 100 and 59 while the lower limit was 23 and 14 ml at rest and stress respectively.

The current study revealed that EF at rest was significantly higher than stress in studied group as they were distributed as 64.97 ± 7.69

and 67.47 ± 4.66 ($P=0.00$) respectively between stress and rest. ESV was significantly lower at rest than at stress as it was distributed as 21.82 ± 7.12 and 19.98 ± 6.25 ($P=0.008$) respectively, Regarding EDV there was no significant difference between stress and rest.

Lang et al [6] showed as an update from the American Society of Cardiology for the American standards that EF was 67.47 ± 4.66 at rest and 64.23 ± 8.52 at stress. The ESV was 30.57 ± 8.25 , 32.55 ± 8.12 and the EDV was 73.02 ± 15.26 , 77.78 ± 18.56 both are at rest and stress respectively. We found that ESV and EDV were significantly higher than our study both at rest and stress while there was no significant difference regards the EF.

Also, Muraru et al [7] regarding the European standards stated that among the European population, the EF was 66.17 ± 13.11 at rest

and 63.54 ± 12.58 at stress. The ESV was 21.85 ± 7.25 , 23.85 ± 7.25 and the EDV was 57.47 ± 14.59 , 58.36 ± 17.58 both are at rest and stress respectively. According to that the EDV was significantly lower than current study group at both rest and stress while there was no significant difference regards the EF and ESV.

Differences related to gender have been described in previous studies with gated SPECT, we can rely on an intrinsic physiological difference between the genders. Women had lower EDV and ESV and higher EF than men as they have small hearts which may simply be the result of lower volumes and higher EF found in women.

In the present study group there were 44 were males and 36 were females. We found that LVEF was $66.54 \pm 6.73\%$ post-stress and $68.86 \pm 4.66\%$ at rest in women and $63.41 \pm 7.73\%$ and $65.28 \pm 4.69\%$ in men. EDV was $60.81 \pm 21.52\%$ post-stress and $61.58 \pm 21.09\%$ at rest in women and $66.91 \pm 19.85\%$ and $63.41 \pm 20.58\%$ in men. ESV was $20.44 \pm 7.85\%$ post-stress and $18.25 \pm 6.85\%$ at rest in women and $24.50 \pm 6.52\%$ and $22.77 \pm 8.13\%$ in men.

ESV at rest and stress were significantly lower at female than male and EF was significantly lower among male at rest and stress and EDV was significantly lower at stress only. The study of Kapitan et al [8] reported in a study of the Latin American population that there was a significant difference between men and women as LV volumes were larger in men than women. LVEF was $67 \pm 7\%$ post-stress and $70 \pm 7\%$ at rest in women, and $62 \pm 7\%$ and $63 \pm 7\%$ in men. Upper limits for LVEF post stress and rest were 81% and 84% in women, and 75% and 76% in men.

Also, Kakhki et al [9] reported significant differences in LVVs and LVEF between men and women as in women, resting EDV and ESV were significantly smaller, and resting LVEF was significantly higher than in men.

The study of Nakajima et al [10] found in a study of the Japanese population that the EF was $74\% \pm 9\%$ and $63 \pm 7\%$ for women and men, respectively. The EDV and ESV were smaller in women than in men. Gated SPECT after stress showed similar gender differences. The difference between men and women was significant ($p < 0.0001$).

Also, Yamada et al [11] report data from Brazil using QGS software, but they only gated the post-stress portion of the study using eight frames per cardiac cycle, and they did not include information on the standard deviation of their measurements, so statistical comparison with our data was not possible. Post-stress LVEF was 65% in women and 59% in men, values slightly lower than our means of 64% and 65%, respectively; this difference could be partially explained by the use of eight instead of 16 frames per cardiac cycle, potentially resulting in some underestimation of the true EF.

Strict comparison with values from the literature obtained in other populations was difficult because published data varies in terms of study conditions (stress or rest), isotope used, number of frames per cardiac cycle, information on BSA for indexing purposes, and other variables.

Consistently, volumetric measures are significantly larger in men worldwide (even after adjustment for BSA), and LVEF is generally higher in women.

CONCLUSION

The current study aimed to construct a “normal” local database that could be helpful for the interpretation of gated SPECT MPI

data in Egypt using identical protocol as used in this study. Findings indicate that the evaluation of cardiac function and volumes by gated SPECT should consider gender-matched normative values and to much extent influenced by ethnicity or geographical origin with normalization of other variables such as isotope used and number of frames per cycle should also be considered when interpreting results, since accuracy of measurements can be affected.

The relatively small sample size and including only low-risk participants for CAD were the main limitations of our study also we did not compare our results to other modalities as cardiac functional parameters

RECOMMENDATIONS

This is the first study on the Egyptian population to establish a local reference for the normal value of left ventricular functions using a gated SPECT myocardial perfusion scan. We should do more studies in other different institutes in Egypt and include multiple other variants to build a strong local reference for our population that will help in the assessment and prevention of cardiac diseases.

CONFLICT OF INTEREST

The authors declared no conflict of interest

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