A COMPARITIVE STUDY OF 16-FRAME AND 8-FRAME GATED SPECT IMAGING FOR DETERMINATION OF LEFT VENTRICULAR VOLUMES AND EJECTION FRACTION

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ABSTRACT:

Back Ground: *The aim of this study was to compare the effect of 8-Frame and 16-Frame gated Single photon emission computerized tomography (SPECT) on measurement of left ventricular (LV) volumes.*

Method: *A total of 20 patients underwent technetium-99m-MIBI SPECT myocardial perfusion imaging using 16-frame per cardiac cycle acquisition. Eight-frame gated SPECT images were generated by summation of contiguous frames. Left ventricular end-diastolic volume (EDV), end-systolic volume (ESV) and ejection fraction (EF) were calculated from the 16-frame and 8-frame data sets.*

Results: *Imaging was performed with the advised dose of 20mCi. Sixteen frame per cardiac cycle acquisition resulted larger EDV (82.6 34.3 ml vs 80.9 42.5ml, P=NS) smaller ESV (34.7 31.4ml vs 38.9 40.1ml, P=NS but significant) and higher LVEF (63 14.1ml vs 59.1 15ml, P<0.000) as compared to 8 frame SPECT imaging.*

Conclusion: *This study shows that EDV, ESV and left ventricular ejection fraction (LVEF) determine by 16-frame gated SPECT are not 100% significantly different from those determined by 8-frame gated SPECT. However, 16frame gated SPECT study is preferred due to higher temporal resolution.*

Keywords: SPECT, 8-Frame and 16-Frame gated SPECT, Technetium-99m-MIBI SPECT, and Left ventricular ejection fraction (LVEF).

INTRODUCTION

Electrocardiographic (ECG) gated single photon emission computerized tomography (SPECT) allow for simultaneous assessment left ventricular (LV) function and myocardial perfusion. Presently 8-frame per cardiac cycle ECG gating of SPECT images is standard. Single photon emission computerized tomography (SPECT) imaging is performed by obtaining planner images with the scintillation cameras from many angles around the patients [1, 2]. Images are acquired from 360° around the patient, except in myocardial perfusion studies, where 180-degree right anterior obliques to left posterior oblique images over the interior chest are reacquired. Images are acquired in 64 x 64 resolutions for most studies for single detector cameras are low count images from multiple detector systems. Images of 128x128 resolutions can be acquired on high-count studies. The planner projection SPECT images are first viewed cinematically to ensure no significant patient motion has occurred. Image data are then back projected to overlay areas of increased activity and create a transverse slice image. Back projection produces a streak or star artifact that results from data being late on to the slice image from various projections. A technique called filtered back projection reduces the streak artifact. In the reconstruction process a frequency space filter is used to modify the projection data in essence creating negative values on each side of areas of increase counts. These negative numbers when combined with positive valued cancel each other out eliminating steak artifact. Streaks are also produces by obtaining images from many angles, about 120 images in 360 degrees essentially viewing objects from more angles(3 - 5). Electrocardiographically gated myocardial SPECT (GSPECT) is a state of the art technique for the combined evaluation of myocardial perfusion and LV function within a single study. It is currently one of the most commonly performed cardiology procedures in a NM department [6]. NM technique is a logical extension of the results of a standard perfusion quantification technique and it allows integration of perfusion and functional information. Ventricular function information can help to differentiate an attenuation artifact from an infarct and is helpful in diagnosing 3- vessel coronary disease. Germano G et al have developed a completely automatic algorithm to quantitatively measure LVEF from gated to Tc-99m sestamibi myocardial perfusion SPECT images [7-12]. ECG gated SPET allows for simultaneous assessment if myocardial perfusion and LV function. The radiotracer dose and perfusion defects do not affect the estimation of LV parameters are same for 16-frame and 8-frame gated SPET [6, 13-17]. Nuclear pharmacy provides us with RPs needed to perform diagnostic and therapeutic procedures. Radioactive isotopes are used to label the pharmaceuticals. So they can be detected by gamma camera [11, 16, 18, 19]. Gated SPET has many advantages; it allows evaluation of myocardial wall motion, wall thickening and calculation of LVEF (20). The use of 8-frame per cardiac cycle by necessity resolution time and using 16-frame per cardiac cycle dose improve the time resolution, it leads to either fewer counts per frame or prolongation of acquisition [3].

Blagosklonov O et al, 2003 performed Ti-201 myocardial SPECT using a single of dual-head gamma camera on patients after exercise stress, they have observed in some a sudden increase in the counting rate between the 16th and 17th images [21 -23] This increase provoked motion like artifacts, which increased the number of false-position findings. Mark W. Groch et al 2001 developed several prototype devices for SPECT over the years, but modern commercially available SPECT instrumentation is based on the rotating gamma camera either single headed or multiple headed [24, 25]. Where for high sensitivity NCO (non-circular orbits) allows the detector to remain close to the patient's body COR (center of rotation) is another SPECT quality parameter. Muphy R. J. *et al*, 1977 made first detector to rotate around the patient rotating 26 - 29]. In past patient rotated around the detector [30]. First practical system was construction in 1977 [31-33]. Investigations show that radioisotopes like Tc–99m MIBI and Ti-201 play an important role in cardiac imaging. The main aims and objectives of the study was to make a comparison between 8-frames GSPECT and 16-frames GSPECT by finding the value of ejection fraction (EF), end- diastolic volume (EDV) and end- systolic volume (ESV).

EXPERIMENTAL TECHNIQUE AND METHOD:

To study the LV volume and ejection fraction following materials are used: Tc-99m eluted from Amertec II Technetium-99m Sterile (Mo99-Tc99m) generator, Pharmaceutical MIBI (methoxyisobutylisonitrile) generic name sestamibi, Dose calibrator to measure the dose advised by nuclear medicine physician, Siemens gamma camera (E-CAM) linked to computerized image processing system, ECG machine with electrodes, Jogging track machine, Injection of percentine and aminophiline (anti-dote), 20 no. of patients.

A dose of 20 mCi of Tc-99m MIBI injected to the patient during exercise or after percentine and aminophiline for a stress test. For rest study only 20mCi dose of Tc-99m without MIBI is advised. Gamma camera (E. CAM) imaging procedure: Study Name was myocardial perfusion, Organ was Heart, Series name was Rest/Stressed Gated, Matrix Size was 64x64, Zoom was 1.78 and Framing was 8 and 16. Timing of scan was Tc-99m MIBI 2 hours after dose. Acquisitions of images were taken after Tc-99m MIBI 35 minutes. Positioning was supine, Patient Scanning Mode was Step and Shoot. Study of imaging was carried out by Gated Single photon emission computerized tomography (GSPECT). Instrumentation is as follows:

Rejected PVC Beats given 1, Windows given 1, Rotation Direction given CCW, Starting Angle given 45 , Degree of Rotation given 180 , No. of view given 64, Time per view given 25sec, Orbit was Non-Circular, Cut off given 0.5, Reconstruction Filter given butter worth and Pixel size given 5.3 x 5.3 mm.

RESULTS:

Clinical Observations

A total of 20 patients selected clinically referred from different cardiologists there were 6 females and 14 males with the average of 40. They were scanned at Bahawalpur institute of nuclear medicine and Oncology Bahawalpur (BINO). These patients had been studied with the advised dose of 20mCi Tc-99m MIBI. Gated SPECT with 8 frames and 16 frames results are in Table 1. Polar maps (Perfusion in arties) and time volume curve obtained with 8 frames and 16 frames, which shows the normal values of EF which should be 50% to 75% and curve should be valley shaped as soon in figure 1 .

The scatter plot, Figure 4 used shows a straight line satisfying nearly all the points. The Pearson correlation of ESV8 and ESV16 shows value r = 0.989, which shows that almost perfect relationship exists between these ESV variables. The Figure 4 (c) line chart also confirms the same increasing pattern. Figure 4(b) dot plot shows that 2 points of each ESV differ from the rest of the data. Figures 8 also suggest that shows a good confirmation that all the observations are very close to the regression line, but the plot shows that two observations looks aberrant or outlying from rest of data.

The regression analysis suggests that the observations 6 and 17 are the outlying observations expected to show large influence while the observation 4 is having large residual.

The regression equation is ESV16 = 4.56 + 0.774 ESV8 with R-Sq = 97.8%. The regression coefficient of EDV8 is 0.774 with positive sign and its t-value having shows that EDV16 significantly depends on the values of EDV8. The large value of R-Sq = 97.8 % shows a very good fit of regression as shown in table II.

R denotes an observation with a large standardized residual.

X denotes an observation whose X value gives it large influence.

Paired T-Test and Confidence Interval for ESV8 and ESV16 , Two-tailed paired student t-test shows that the results are significant difference between ESV8 and ESV16 as the t-value is 1.86 with p-value = 0.079 is significant at 7.9% but insignificant at 0.05. Thus the 95% confidence Interval (CI) for mean difference in ESV8 and ESV16 is (-0.53941, 9.03941). Correlation and Linear Regression Analysis of % EF\ **Statistical Techniques**

Left ventricular parameters (EDV, ESV and %EF) derived from 8-frame and 16- frame images are compared. Linear regression analyses along with Exploratory Data Analysis (EDA) techniques scatter plot, line- chart and dot-plot have been used. Hypothesis testing and confidence intervals for paired-comparison using Student t-distribution have been implemented. Lastly ,

Zonal study (a quality control technique) is preferred to study whether the data follows mean standard deviation criterion or not. Correlation and Linear Regression Analysis of EDV is given in figure 3.

The scatter plot Figure 3(a) used here serves as a graphical tool to checking the relationship between two variables, whether the variables shows dependency (regression relation) or interdependency (correlation). The Pearson correlation of EDV8 and EDV16 shows value r = 0.972, which confirms a very strong (nearly perfect) relationship. It means that both the variables EDV8 and EDV16 show increase in positive directions. The Figure 3 (b)-dot chart and Figure 3(c) line plot also confirm the same phenomenon. The Figure 3(a) shows that all the observations are near to the regression line (some time called straight line) but the plot shows that two observations looks to be far away from rest of the observation. The regression analysis suggests that the observations 6 and 17 are the outlying observations expected to show large influence while the observation 4 is having large residual. The regression equation is EDV16 = 20.5 + 0.772 EDV8 with R-Sq = 94.4%. The regression coefficient (slope of the regression line) of EDV8 is 0.77 with positive sign and its t-value having shown that EDV16 significantly depends on the values of EDV8 as shown in table II. The large value of R-Sq = 94.4% shows very good fit of regression

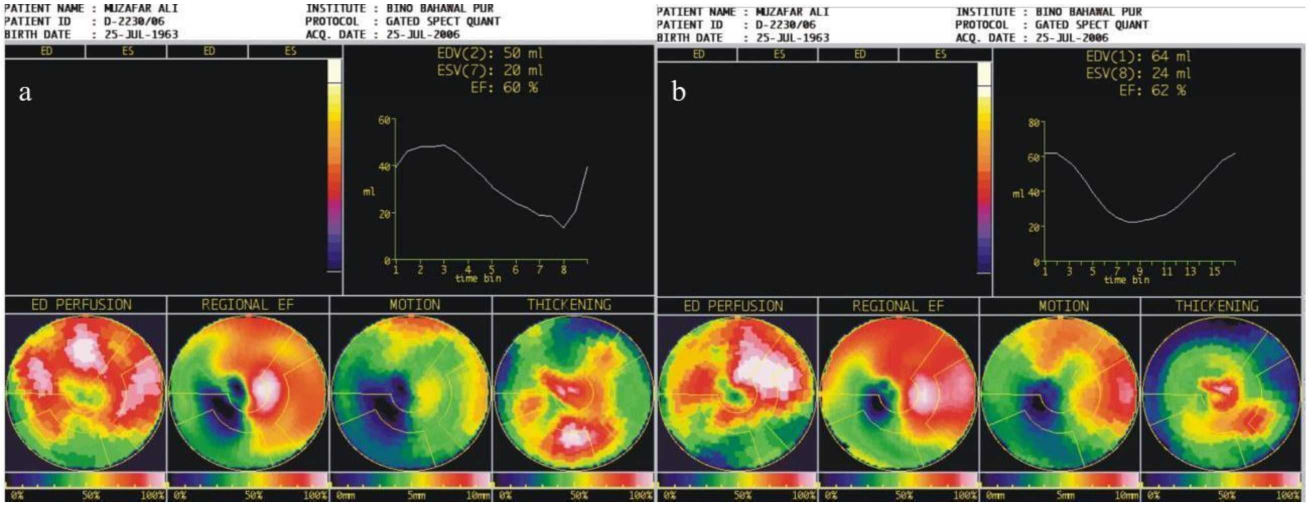

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Figure: 1 (a) shows that the EF of above patient lie in normal range and its curve is not valley shaped with 8frames (b) Shows that the EF of above patient lie in normal range and its curve is valley shaped with 16 frames

Polar maps (Perfusion in arties) and time volume curve obtained with 8 frames and 16 frames which shows the abnormal values of EF which is out of range as soon in figure 2.

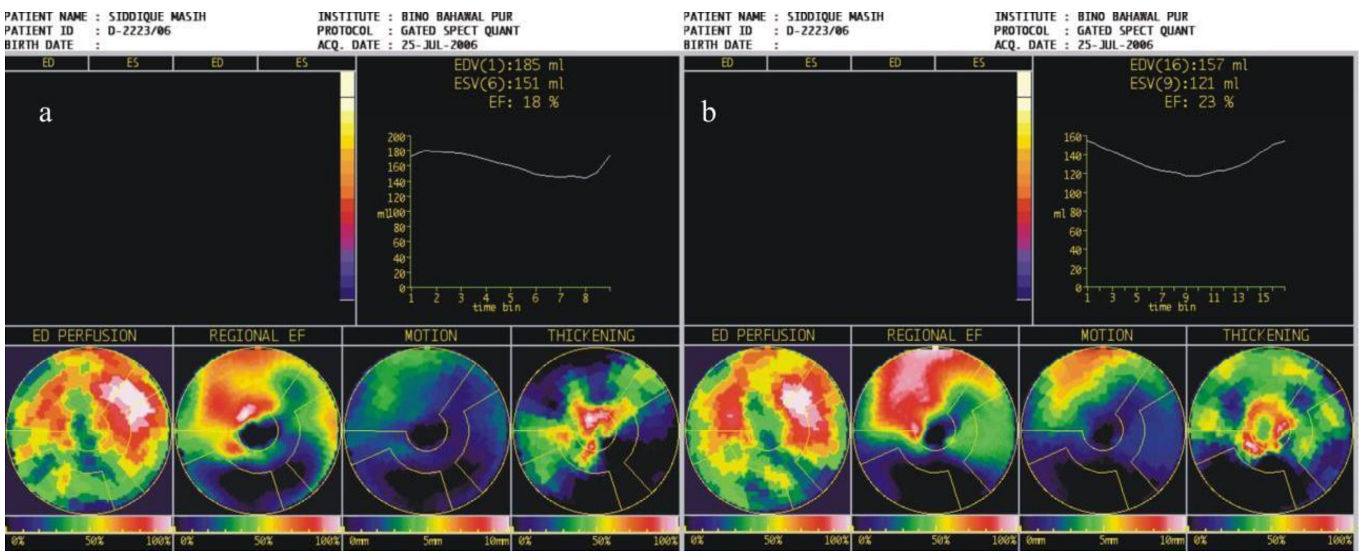


Figure: 2 (a) Shows that the EF of above patient lie out of normal range and its curve is not valley shaped with 8 frames (b)(Shows that the EF of above patient lie out of normal range and its curve is little bit valley shaped with 16 frames

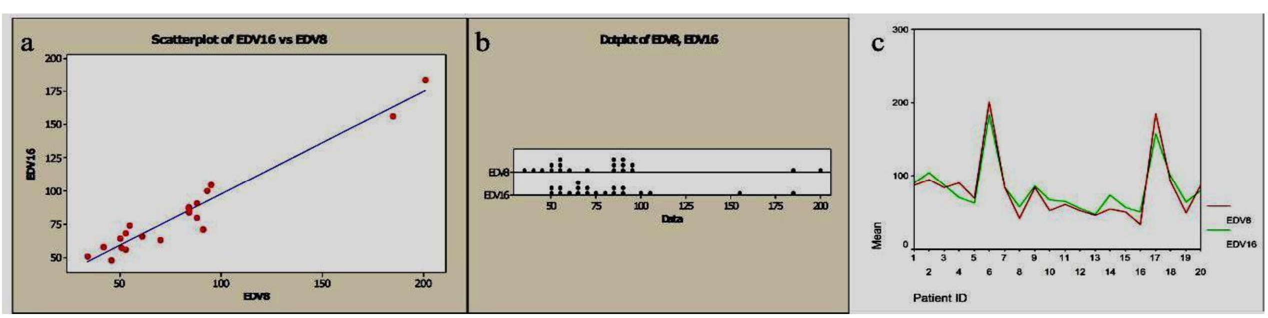


Figure 3: (a) Scatter plot of EDV16 versus EDV8 (b) Dot plot of EDV8 and EDV16 (c) Line chart of EDV8 and EDV16

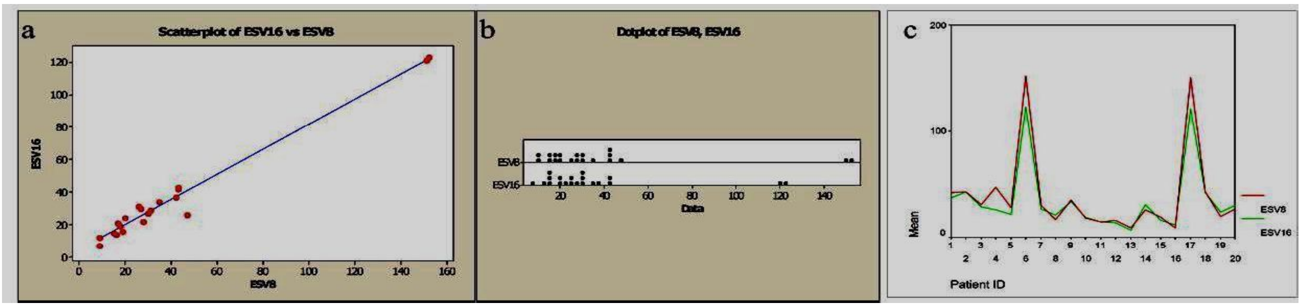


Fig 4 (a) Scatter plot of ESV16 versus ESV8 (b) Dot plot of ESV8 and ESV16 (c) Line chart of ESV8 and ESV16

Table 1: Shows the observed values of EDV, ESV and EF with 8 frames and 16 frames.

Patient No.	Patient Name	Patient ID	EDV8 Ml	EDV16 ml	ESV8 ml	ESV16 ml	EF8 %	EF16 %
1	Abdul Hameed	1155/15	88	91	42	37	53	59
2	Syed Mushtaq	1145/16	95	105	43	43	54	59
3	Abdul Karim	002/16	84	88	31	29	63	67
4	Sultan Mehmood	1917/16	91	71	47	26	49	64
5	Shah Nawaz	692/16	70	63	28	22	61	65
6	Gulzar	1672/16	201	184	152	123	24	33
7	Mubashir Tariq	1996/16	84	84	30	27	64	68
8	Shabbir Ahmed	2000/16	42	58	17	21	59	64
9	Tahir Laghari	19/13	84	87	35	34	59	61
10	Ghulam Hussain	2144/16	53	68	18	19	65	72
11	Zubaida Bibi	1495/16	61	66	15	15	75	77
12	Zakia Begum	775/16	53	56	16	14	70	74
13	Suryia Bibi	1364/16	46	48	9	7	81	85
14	Sughran Bibi	1501/16	55	74	26	31	53	58
15	Sadia khan	522/16	51	57	19	16	63	73
16	Suryia Ghauri	454/16	34	51	9	12	74	76
17	Sadiq Massih	2223/16	185	157	151	121	18	23
18	M. Akram	2232/16	93	100	43	42	57	58
19	Muzaffar Ali	2230/16	50	64	20	24	60	62
20	Fahad Bashir	1499/16	88	80	27	30	69	62

Table II: Regression analysis of EDV8 VS EDV16

Predictor	Coefficients	P-value
Constant	20.492	0.000
EDV8	0.77249	0.000 (Significant)

Observations	EDV8	Residual	Standardized Residual
4	91	-19.79	-2.45 **R**
6	201	8.24	1.35 X
17	185	-6.40	-0.96 X

Note: R denotes an observation with a large standardized residual.

X denotes an observation whose X value gives it large influence.

Paired T-Test and Confidence Interval for EDV8 and EDV16

Two-tailed paired student t-test shows insignificant or non-significant difference between EDV8 and EDV16 as the t-value is -0.77 with P-value = 0.449 >0.05 (NS). The more reliable method is the interval estimation. Thus 95% confidence Interval (CI) for mean difference in EDV8 and EDV16 is (-8.15220, 3.75220). Correlation and Linear Regression Analysis of ESV

Table III: Regression analysis of ESV8 VS ESV16

Predictor	Coefficients	SE Coef	t-value	P-value
Constant	4.558	1.525	2.99	0.008
ESV8	0.77357	0.02764	27.99	0.000 (Significant)

Unusual Observations

Observations	ESV8	ESV16	Residual	Standardized
				Residual
4	47	26.00	-14.92	-3.17R
6	152	123.00	0.86	0.24 X
17	151	121.00	-0.37	-0.10 X

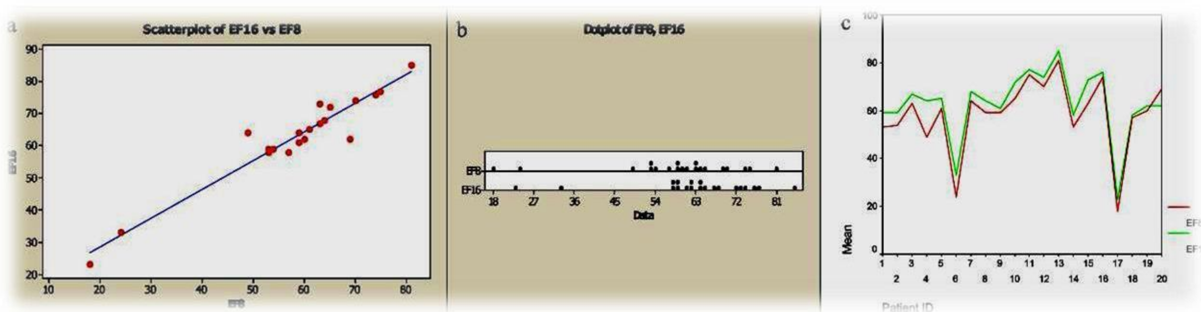


Fig 5 (a) Scatter plot of EF16 versus EF8 (b) Dot plot of EF8 and EF16 (c) Line chart of EF8 and EF16

The scatter plot, Figure 5 used shows a straight line, but some points are little far from the regression lines. The Pearson correlation of EF8 and EF16 shows value r = 0.961, which indicate very high correlation between these EF variables. The Figure 5(c) -line chart indicates that some observation is getting very low in a process and shows the increasing or decreeing pattern for both variables EF8 and EF16. Figure 5 (b) dot plot shows that more than 2 points of each EF differ from the bulk of data. Figures 5 also suggest that shows a good confirmation that all the observations are very close to regression line, but some are aberrant or outlying from rest of the data.

The regression analysis suggests that the observations 6 and 17 are the outlying observations expected to show large influence while the observation 4 and 20 are having large residual. The regression equation is EF16 = 10.7 + 0.893 EF8 with R-Sq = 92.3%. The regression coefficient of EF8 is 0.89265 with positive sign and its t-value having shown that EF16 significantly depends on the values of EDV8. The high value of R-Sq = 92.3% shows a very good fit of regression as shown in table IV.

Table IV: Regression analysis of EF8 VS EF16

Predictor	Coefficients	SE Coef	t-value	P-value
Constant	10.735	3.662	2.93	0.009
EF8	0.89265	0.06064	14.72	0.000 (Significant)

Unusual Observations

EF8	EF16	Residual	St Resid	
4	49.0	64.000	9.525	2.46R
6	24.0	33.000	0.841	0.25 X
17	18.0	23.000	-3.803	-1.25 X
4	69.0	62.000	-10.328	-2.67R

R denotes an observation with a large standardized residual. X denotes an observation whose X value gives it large influence.

Table V: Mean SD analysis of EDV, ESV and EF

	16-frame ml	8-frame ml	
			Observation assessment from Zonal charts
EDV	82.60	80.40	Observation 6, 16 &17 are outside the Zone 1 in 8-
	34.29	43.14	frame Observation 6, 13, & 16 are outside the Zone
			1 in 16-frame
ESV	34.65 31.40	38.90	Observation 6 & 16 are outside the Zone 1 in 8-
		40.14	frame
			Observation 6 & 16 are outside the Zone 1 in 16-
			frame
EF	63.00	58.55	Observation 6, 11,13,16 &17 are outside the Zone I
	14.12	15.19	in 8-frame
			Observation 6, 163&17 are outside the Zone I in
			16-frame

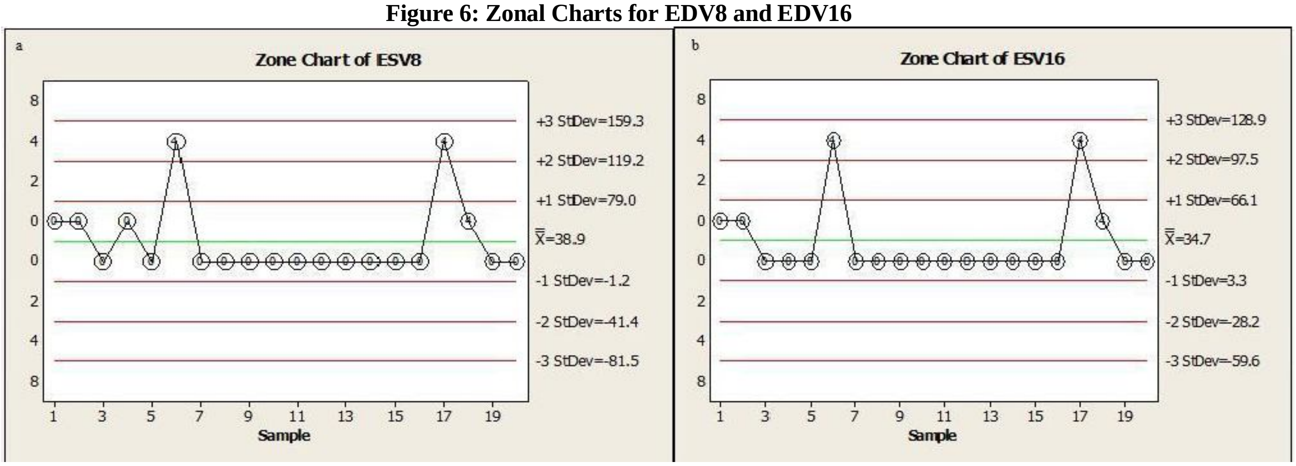
Paired T-Test and Confidence Interval for EF8 and EF16 , Two-tailed paired student t-test shows that te results are significant difference between EF8 and EF16 since the t-value is -4.70 with p-value = 0.000 <0.05 and the 95% confidence Interval (CI) for mean difference in EF8 and EF16 is (-6.43257, -2.46743).

Mean SD Analysis

In normal distribution and Student t-distribution (which is approximately normal) mean SD contains 68.26%, mean 2 SD contains 695.446% and mean 3 SD contains 99.73% of data. Data showing mean standard deviation (mean SD) for Zone1 are presented in the table V. Also the Zonal charts for variables EDV, ESV and EF for 8-frame and 16-frame are given in Figures 6, figure 7 and figure 8. The interpretation of mean SD rule for the whole data is also given in the last column of the table V.

It is quite interesting that all the three variables (EDV, ESV and EF) have shown significant results with high correlation coefficients (r =0.972, 0.989 and 0.961 with p-value=0.0000< 0.05) such as for 16-frame and 8-frame method. This indicates that frame-16 observation which are actually simulated or produced from frame-8 have a strong positive relationship that is also observed in the line charts. Whether the 16-frame variables depend on 8-frame variables in case of EDV, ESV and %EF, we have found that in all cases the R-square value confirms the good fit ofregression. It is very surprising that in all the three regressions, some observations are outlying or highly influential, which require the use of regression diagnostics for further study. All the necessary calculation and graphs have been developed through SPSS v.10 and Minitab v 14. We have also tried to study the data using Mean SD methodology and the statistical quality control technique from control charts i.e. Zonal study was implemented but found that some observation in each variable for 8-frame as well as 16-frame fall outside the limit of mean SD, so they can never show p-value 0.000. It will be better to consider the case for mean 2 SD or mean 3SD. It is expected that the criteria mean 3SD will surely give a p-value of 0.0000.

Figure 6: Zonal Charts for EDV8 and EDV16



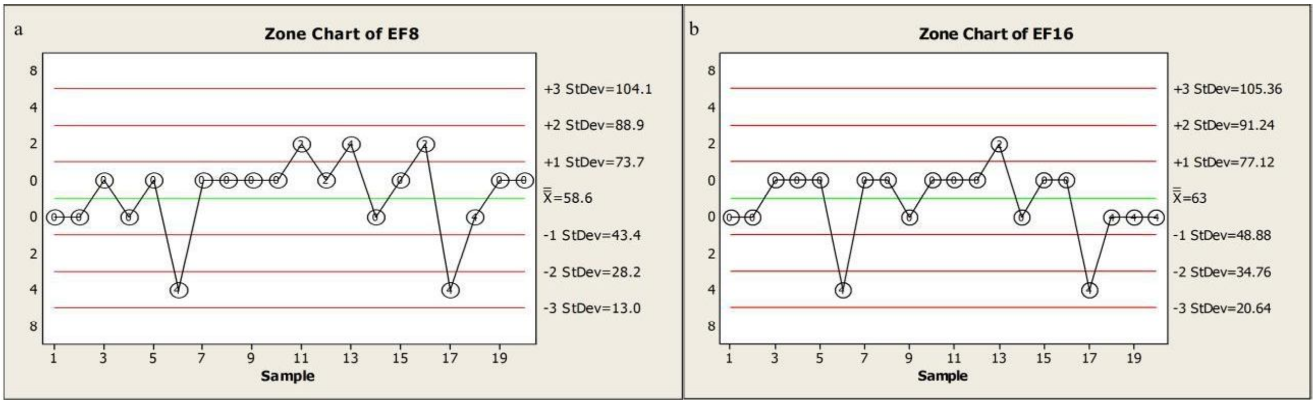


Figure 7: Zonal charts for ESV8 and ESV16

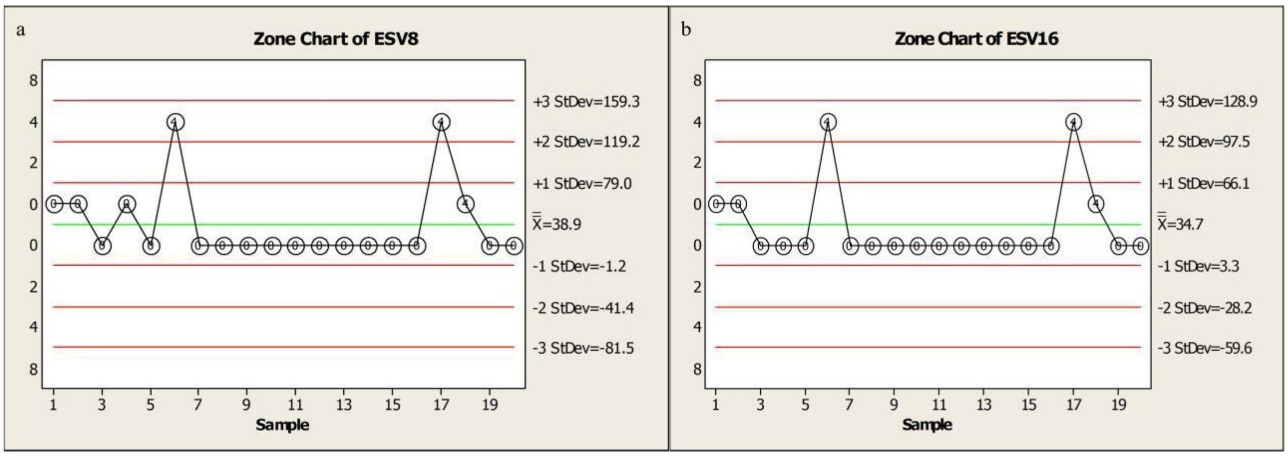


Figure 8: Zonal Charts for EF8 and EF16

DISCUSSION:

Clinical Aspects: State of the art single-photon emission computerized tomography (SPECT) imaging provides combined information about myocardial perfusion and function, from the same image data. This became feasible after the introduction of teachnitum-99m MIBI and acquisition with electrocardiographic (ECG) gating. The present study shows that the LV volumes calculated from 16-frame imaging data similar significantly from those calculated from 8-frame imaging data. Sixteen frame studies result in larger EDVs, smaller ESVs and higher LVEFs as compared to 8-frame studies. The difference in LV volumes mentioned can be explained by the superior temporal resolution of 16-frame studies as compared with 8-frame studies. The end-systolic frame in an 8-frame study contains residual volume from systole/diastole on either side and hence is larger than that in a 16-frame study. Higher temporal resolution of SPECT should result in more accurate determination of end-systolic and end-diastolic frames and hence more accurate assessment of ventricular volumes. We used stress/rest studies for our analysis, but mostly stress studies are routinely obtained by the 16-frame method in various institutions. Typically rest studies are obtained after a week if necessary.

Technical Aspects: The larger amount of computer storage space and longer acquisition and processing times required for 16-frame gated SPECT studies may result in an increase in costs as compared to 8-frame gated SPECT. The cost of storage media was a major concern 16-frame require 3 times larger data than 8 frames. The availability of faster and more sophisticated computers equipped with multiple processors and multi-tasking capability allows for fast and simultaneous acquisition and processing of multiple programs. This compensates for the longer acquisition and processing times necessary for 16-frame gated SPECT. The graph between frame and volume (time-volume curve) should be valley shape. But the curve obtained with 8-frame was not valley shaped properly. The study should be repeated if the results are same then it should not be reported. Curves obtained with 8-frames were not properly valley shaped. However, curves obtained with 16-frame were properly valley shaped. So, this study was reliable and should be reported.

Statistical Analysis: Left ventricular parameters derived from 8-frame and 16-frame images were first-compared in the entire study group, and then in patients with administered dose studies, and in patients with and without myocardial perfusion defects by using Minitab software. Data are presented as mean standard deviation and $P<0.05$ in the analysis was considered statically significant but our values was Larger EDV (82.6 34.3 ml vs 80.9 42.5ml, $P>0.05$) , Smaller ESV (34.7 31.4ml vs 38.9 40.1ml, $P>0.05$), Higher LVEF (63 14.1ml vs 59.1 15ml, P>0.05) and our P values are greater than our assumed values. Hence our values were not significant.

Study Limitations: A limitation of the present study is that LV volumes and ejection fractions, derived from 16-Frame and 8-Frame gated SPECT, were not compared with an independent gold standard. Hence there is no direct proof that the larger EDV, higher LVEF and lower ESV from 16-frame gated SPECT are indeed more accurate. However, prior studies with 8-Frame gating have shown that calculated LV EDV and LVEF are lower as compared to a "gold standard" such as angiography or cine MRI. Thus the change in LV volumes and ejection fraction with 16-frame gating is in the direction that makes them more comparable with established standards. Another limitation of our study was absence of high storage computer and multi detector camera. We used single detector camera and low storage computer.

CONCLUSION:

Measurement of LV volumes may have an important impact on the management of patients with variety of cardiac disorders, such as coronary artery disease and valvular heart disease. ESV has been shown to be a powerful predictor of mortality in patients after myocardial infraction and coronary artery bypass surgery. Our study shows that 16-frame gated SPECT provides volume measurements that are significantly same than those provided by 8-frame gated SPECT. Sixteen frame gating provides better temporal resolution than 8-frame gating in the estimation of LV volumes and ejection fraction. Curves are valley shaped will 16 frame thus the acquisition of 16-frame per cycle may be preferred mode for gated SPECT studies. It will be common within few years with multi detector cameras and high storage computers

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