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Original Article

Comparison of Left Ventricular Ejection Fraction in Heart Failure Patients on Echocardiography, Cardiac Magnetic Resonance Imaging and Single Photon Emission Computed Tomography

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ABSTRACT

Objective: To compare the left ventricular ejection fraction on echocardiograph, cardiac magnetic resonance imaging and single-photon emission computed tomography scan in heart failure patients.

Study Design: Prospective cross-sectional study.

Place and Duration of Study: Tertiary Cardiac Care Center of Rawalpindi, Pakistan, from Nov 2021 to Apr 2022.

Methodology: Thirty (n=30) heart failure patients of either gender with reduced ejection fraction were selected by consecutive sampling technique and were analyzed to quantify their left ventricular ejection fraction (LVEF) using Echo, CMR and SPECT scan. All three modalities were used to measure LVEF in these patients and were compared accordingly.

Results: The LVEF measured by Cardiac Magnetic Resonance Imaging, Single Photon Emission Computed Tomography Scan and Echocardiography was in the range of 15% to 67%. The mean LVEF was 37.2±14.2 by CMR, 37.17±14.1 by SPECT and 38±12.3 by Echo. The mean LVEF determined by SPECT was slightly lower while that determined by Echocardiography was slightly higher. The measured *p*-value of LVEF by the three modalities, however, indicated statistically difference (*p*-value <0.05).

Conclusion: Although the literature shows diversity in results of these modalities, CMR is considered the standard reference for assessment of LVEF when interpreted by an expert observer. We in our study found that all three modalities are complimentary to each other and can be used interchangeably depending upon the availability of the equipment and reporting expertise of the observers.

Keywords: Cardiac magnetic resonance imaging, Echocardiography, Heart failure, Left ventricular ejection fraction, Single photon emission computed tomography scan.

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INTRODUCTION

Heart failure (HF) is a significant shareholder of major morbidities and mortalities ubiquitously. Globally, 64.3 million people are affected from HF each year.[1] Estimated prevalence of known cases of HF in developed countries ranges from 1% to 2% of adult populace.[2-3] In United States, 5.7 million people are suffering from this disease and it is anticipated that this number will increase to 8 million by 2030.[4] In Pakistan the estimated prevalence of HF is 2.8 million.[5] Hence, it is one of the most trending health conditions in the field of health science.

Current classification,[6] categorizes HF into three major categories, (1) HF with reduced ejection fraction (HFrEF) i.e symptomatic HF patients with left ventricular ejection fraction (LVEF) ≤40%, (2) HF with mildly reduced ejection fraction (HFmrEF) i.e., symptomatic HF patients with LVEF 41-49%, (3) HF with preserved ejection fraction (HFpEF) i.e., symptomatic HF patients with LVEF ≥50%. Management of HF is based on an individual patient's symptoms and accurate assessment of LVEF.[7]

An accurate measurement of LVEF is of paramount importance. A precise, definite and reproducible quantification of LVEF is therefore a cornerstone measure of non-invasive imaging modalities,[8] as it has marked diagnostic, therapeutic and prognostic implication in patients of heart failure, arrhythmias, valvular heart disease, coronary artery disease (CAD), and cardiomyopathy and for those who are potential candidates of Implantable cardioverter-defibrillator (ICD) therapy, cardiac resynchronization therapy (CRT) and recipients of chemotherapy.[7] This also has important prognostic outcomes in patients of coronary artery disease after revascularization.[9]

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Currently, various non-invasive imaging methods are being used to determine LVEF. Three most commonly used non-invasive imaging modalities in our country are echocardiography (Echo), cardiac magnetic resonance imaging (CMR) and 99 mTc-sestamibi methoxyisobuty lisonitrile single photon emission computed tomography (SPECT) scan. Echocardiographic examination is widely available and most commonly used non-invasive imaging methods but it has number of limitations including operator's expertise, issues of sub -optimal window in obese, emphy-sematous, lean and ill patients. SPECT scan is a useful alternative modality for determining LVEF but due to rather less common availability and an exposure to potentially hazardous ionizing radiation it is less appealing in sequential studies. CMR appears to be the reference standard imaging modality for the assessment of morphology and systolic function of LV due to lack of ionizing radiation, high image quality, reproducibility and lack of reliance on geometric assumptions. However, this is costly, less widely available and operator dependent.[10] We conducted this study to determine LVEF association between various non-invasive imaging modalities including Echo, CMR and SPECT scan in heart failure patients.

METHODOLOGY

This was a prospective cross-sectional study.

Sample Size: All the patients who underwent dignostic proceduers during study period contituted study sample n=30.

Inclusion Criteria: The study included (n=30) consecutive patients between the ages of 20 to 70 years with either gender fulfilling the inclusion criteria i.e., having an old history of myocardial infarction or any other documented left ventricular systolic dysfunction, after the approval of ethical committee.

Exclusion criteria: Patients with claustrophobia, metallic implants (non-compatible to 3 Tesla MRI scanner) and allergic to gadolinium-based contrast agents were excluded from the study. The patients underwent all the three scans i.e., echocardiography, SPECT and cardiac magnetic resonance imaging. Study was conducted at echo department, nuclear scan department and cardiac MRI department of a tertiary cardiac care center of Rawalpindi from November 2021 till April 2022 after approval from IERB (IERB letter # 24/12/R&D/2021/124). Patients with evidence of HF with reduced ejection fraction were evaluated by echocardiography for volumetric analyses and regional wall motion abnormalities and were further worked up with SPECT scan and CMR. All three modalities worked on the same formula for EF calculation i.e., $EF = \frac{EDV-ESV}{EDV} X\ 100$.

Echo was performed on Phillips Epiq,[7] GE vivid E95 and Phillips iE33 echo machines. Scans were performed on patients lying in left lateral decubitus position, and left parasternal (parasternal long axis and short axis) and apical four chamber echo views were obtained with M-mode measurements and Doppler studies. Images were taken from the apex to obtain maximum length of LV and evade foreshortening. Simpson's method was used by calculating end diastolic volume and end systolic volume by dividing LV into 20 cylindrical segments as shown in Figure-1. It was further checked by visual method & eye-balling of the experienced observers.

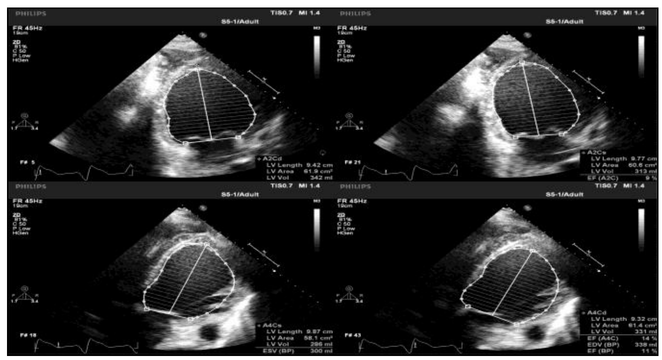

Figure-1: Simpson's method for EF quantification using two and four chamber Echo views

Single Photon Emission Computed Tomography Scan was performed on DDD gamma camera CorCam machine. Technetium 99m (99mTc) radio-labeled sestamibi was injected to the patient that is taken up by the myocardium. Scan was done with a patient lying in supine position and images were acquired from right anterior oblique to left posterior oblique view. ECG gated images were obtained after a sufficient amount of time for the tracer to be washed out from the blood pool. Three-dimensional data was then analyzed by Cedar Sinai Quantitative Gated and Perfusion SPECT and 4DM software. The ECG gating divides the cardiac cycle into a predetermined number of frames per cycle. LVEF and volumetric analysis was done automatically with above mentioned soft wares by automated edge detection as shown in Figure-2.

Cardiac MRI was performed on Siemens 3 Tesla Magnetom Skyra and then images were post-processed on syngo.via. Patient lies in a supine head first position with a flexible 18 channel or 32 channel coil on his chest. Steady state free precession (SsFP) cine images were obtained for the evaluation of ejection fraction.[9] short axis slices and 1 slice for each 3 long axis views were taken with 25 segments calculated by Simpson's method of EF calculation on syngo.via auto-mated software. Endocardial and epicardial contours were drawn on all short axes images with complete cardiac cycle from base to apex as shown in Figure-3. Base points were marked on all long axes views i.e., 2, 3 and 4 chamber views.

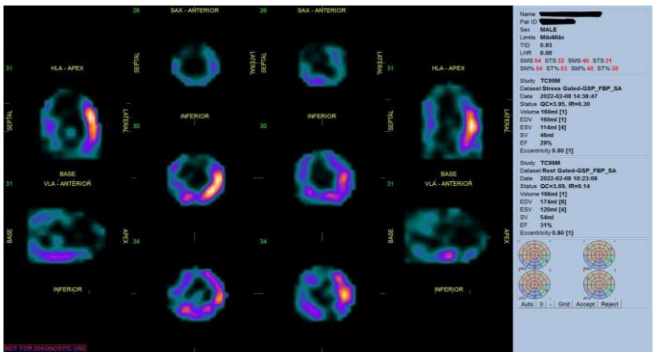

Figure-2: Quantification of LVEF and LV volumes of a Patient Using SPECT Software

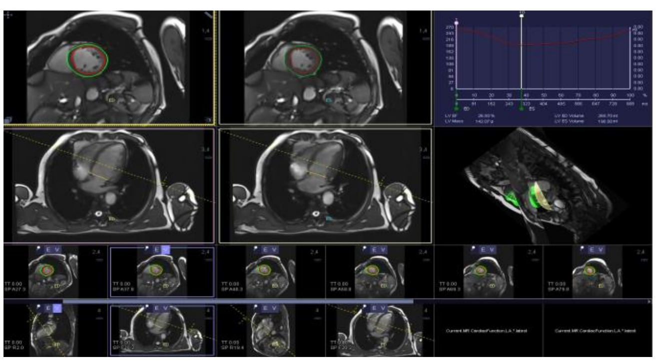

Figure-3: Calculating EF Simpson's Method Using Syngo.via Siemens Software

RESULTS

Thirty patients (n=30) were included in this study. Twenty five (n=25) of them were male and (n=5) were female. Average age was 52.4±13.7 years. All patients were diagnosed cases of heart failure with reduced ejection fraction. The baseline demographics characteristics of this study population are depicted in Table-I. (n=15) patients had Triple vessel CAD (TVCAD), (n=6) had double vessel CAD (DVCAD), (n=4) had single vessel CAD (CAD) and (n=5) had unobstructed coronary arteries. The LVEF measured by CMR, SPECT scan and Echo was in range of 15% to 67%. The mean LVEF was 37.2 + 14.2 by CMR, 37.17 + 14.4 by SPECT scan and 38 + 12.3 by 2D-Echo.

Table-II is depicting the number of patients and mean & standard deviation with respect to LVEF estimated by ECHO, SPECT scan and CMR.

ANOVA test findings presented in Table-III are depicting statistically significant difference in the variance of LVEF associated with coronary artery disease on ECHO, SPECT scan and CMR (*p*-value <0.05).

Table-I: Demographic, Clinical Findings and Procedural Details of Study Partciicpants

Variables (n=30)		(Mean±SD); n(%)
Age (Years)		52.4±13.7
Gender	Male	25(83.3%)
	Female	5(16.7%)
Comorbids and Procedural Details		
Risk Factors	HTN	19(63.3%)
	DM	13(43.3%)
Previous MI	AWMI	17(56.6%)
	IWMI	9(30%)
CT Angiography	SVCAD	4(13.3%)
	DVCAD	6(20%)
	TVCAD	15(50%)
LVEF (Mean+SD)	CMR	37.2±14.2
	SPECT scan	37.17±14.8
	ECHO	38±12.3

Table-II:LVEF value at Echo, SPECT scan and CMR

		n(%)	Mean	SD
LVEF by ECHO	>55	6(20)	59.17	2.041
	45-54	3(10)	48.67	3.215
	30-44	15(50)	34.33	4.577
	<30	6(20)	24.17	2.041
	Total	30(100)	38.70	12.758
LVEF by SPECT	>55	6(25)	51.50	13.428
	45-54	2(8.3)	41.00	28.284
	30-44	11(45.8)	33.27	11.774
	<30	5(20.8)	27.00	4.243
	Total	24(100)	37.17	14.899
LVEF by CMR	>55	6(20)	55.83	13.197
	45-54	3(10)	35.00	13.115
	30-44	15(50)	34.93	10.030
	<30	6(20)	25.33	6.919
	Total	30(100)	37.20	14.242

Table-III: Association of LVEF on Echo, SPECT scan and CMR

		Sum of Squares	Mean Square	*p*-value
ECHO	Between Groups	4364.633	1454.878	<0.001
	Within Groups	355.667	13.679	
SPECT	Between Groups	1945.652	648.551	0.020
	Within Groups	3159.682	157.984	
CMR	Between Groups	3019.700	1006.567	<0.001
	Within Groups	2862.480	110.095	

DISCUSSION

On account of its diagnostic, therapeutic and prognostic value, assessment of an accurate LV systolic function is vital. CMR is an emerging non-invasive imagining modality in the field of cardiology due to its high accuracy, high temporal and spatial resolution, reproducibility, and lack of exposure to biohazard ionizing radiations.[11] It is important to determine how much the results of CMR, echo and SPECT scan are interchangeable with each other in HF patients. Echo is most commonly used non-invasive imaging modality due to its easy accessibility in hospitals and time effective performance on bedside for the assessment of global and regional LV function. Conversely, it is operator and position dependent as well as difficult to perform in obese persons, COPD patients and in persons with chest deformities. Also due to dependence of echo on geometrical assumptions and the changes of LV shape with passage of time in HF and its lesser reproducibility makes it less reliable tool for precise study especially in the hands of in-experienced operators.[10] However, lack of radiations and portability are the plus points of echo.[12] Considering the better availability of SPECT scan in institutes for a longer period of time, it gives good results but presence of ionizing radiations does not make it ideal method for subsequent studies of LVEF measurements. It is usually used for measurement of LVEF when simultaneous assessment of myocardial perfusion is required. Many aspects should be kept in mind when deciding which modality is most suitable for an individual patient. A wide diversity is found in literature regarding LVEF measurements comparing echo, CMR and SPECT scan. Our results showed that there is a good association in results of echo in comparison with CMR and SPECT scan.

A wide diversity is found in literature regarding LVEF measurements comparing echo and CMR. Zhao *et al*.[10] reported that echo overestimates LVEF when compared to CMR. This in turn relied on the value of LVEF itself. Echo provided similar results to CMR when LVEF was greater than 50%. Accordingly, it over estimated LVEF remarkably whenever the value was below 50% and especially when it was less than 35%. On the contrary, Simpson *et al.*[13] reported that echo underestimates LVEF in comparison to CMR. Moreover, Wood *et al*.[14] reported that there is no significant difference in LVEF quantification between echo and CMR while a huge difference is found in LV volume measurements. Similarly, Schiau *et al*.[15] found that there is a little difference in LVEF measurement between 2D echo and CMR. This variability between these two modalities was perhaps due to geometrical remodeling of LV. However, 3D echo results correlate with CMR because of absence of geometric assumptions.[16]

The literature showed similar heterogeneity in the results of echo and SPECT scan. Rawala *et al*.[17] reported significant discordance (r=0.43) in LVEF between SPECT scan and echo in patients who had LVEF between 25% and 50% with a mean±SD LVEF of 46%± 11.3% and 42%±10.3%, respectively. Conversely, Garg *et al*.[18] reported a strong positive correlation between SPECT scan and echo (r=0.69, p<0.001). Shojaeifard *et al*.[19] similarly reported good correlation between these two modalities in forty one patients of HF (r=0.67, p-value<0.001). Sani *et al*.[20] reported significant difference between SPECT scan and echo in small hearts with end-systolic volume (ESV) less than 25 ml and in patients without prior history of MI whereas no difference between two modalities is found in large ventricles with ESV equal to or less than 25 ml as well as in patients with prior MI.

In accordance to us other studies showed overall good association between CMR and SPECT scan in quantification of LVEF. Beitner *et al.*[21] reported a very good association between CMR and SPECT scan with an intra-class correlation coefficient (ICC) of 0.89. Fathala *et al.*[22] reported moderate correlation for LVEF measurements between these two techniques in ninety one known CAD patients (r=0.5 and p-value <0.007). Likewise, Bavelaar-Croon *et al.*[23] reported good correlation (r=0.85) between these two methods in twenty one patients.

Meta-analysis conducted in 2014 showed closest limits of agreement between SPECT scan and CMR while echo showed statistically significant weaker correlation with CMR.[24] Demir *et al.*[25] reported very good correlation for echo, SPECT scan, and CMR (r=0.92, r=0.91, r=0.97, p <0.01) in twenty one patients. Pellikka *et al.*[8] reported a substantial variability between these three modalities in 2030 patients.

LIMITATIONS OF STUDY

This study had few limitations. First, it was a single center study. Second, the sample size was very small to make any statistical difference. Therefore, a large prospective, randomized trial is required in our population cohort to define outcomes and prognostic value of using these modalities for LVEF quantification.

CONCLUSION

Quantification of an accurate LVEF is extremely important in various cardiac diseases as many important future decisions are based on it. Different noninvasive modalities are used for this purpose including Echo, CMR and SPECT scan. Literature shows heterogeneity in results and CMR is considered the gold standard in the literature. We, however, found that there is good association between all these modalities which are interchangeable and complimentary to each other when reported by expert observers.

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Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

IA: Manuscript writing, drafting and editing

AN: Intellectual contribution, concept and final approval

NS: Manuscript writing, drafting and proof reading

SAS: Review of article, formatting and critical review

ZH: Study design, concept and critical review

MNT: Data management, data collection and manuscript writing

JK: Analysis, manuscript writing and proof reading

AM: Review of article, formatting and concept

NA: Analysis, manuscript writing and proof reading

SKS: Proof reading, Intellectual contribution, final approval

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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