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Prediction of Post-revascularization Ejection Fraction in Patients with Coronory Artery Disease Using Cavity-to-Myocardial Ratio of Thallium Reinjection Image (Multicenter Trial)

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Abstract

Background: We reported the high correlation between cavity-to-myocardial (C/M) count ratio at stress and rest thallium SPECT, and stress-rest EF calculated by MUGA test, this was confirmed by others. This correlation was explained partially by the functional mass. On the other hand, two important prognostic parameters should be considered before any revascularization technique:

(1) Identification of viable myocardium and its amount,

(2) Prediction of EF improvement post revascularization.

Aim of the study: Correlating EF (C/M) on RD and RI image (EF_{RD} & EF_{RI}) image to actual EF (prevascularization EF_1) and 1 year post revascularization EF_2.

Patients and methods: 78 patients with CAD (68 males and 10 females with mean age of 54.2+9 years) had been subjected to: (1) St-RD-RI thallium SPECT with assessment of reversible or fixed perfusion defects and calculation of C/M and consequently the EFC/M at the three settings. (2) Assessment of EF by MUGA at rest pre and 1 year post revascularization EF_1 & EF_2 respectively. These patients had been subjected to revascularization either by PTCA and stent (23/78 i.e., 29.5%) or by CABG (55/78, i.e., 70.5%).

Results: Out of the 1560 myocardial segments (20 segments × 78 patients), 780 (50%) segments had abnormal resting wall motion. 441/780 (56.5%) of these segments were either of normal thallium uptake or with reversible perfusion defects while the rest (43.5%) showed fixed defects. 233/441 (52.8%) of those normal uptake or reversible segments showed recovery of wall motion post revascularization (PRV) while only 29/339 (15.1%) showed similar improvements. EF_{RI} was found higher than EF_{RD} in 44/78 of patients, no change in 23/78 patients and worsened in 11/78 patients with total agreements of 63/78 (80.8%) with EF_2. On the other hand, EF_{RD} was matched with EF_1 in 64/78 of patients. 30/64 (46.9%) showed higher EF_2, 23/64 (35.9%) showed similar EF_2 while 11/64 (17.2%) showed lower EF_2. The rest of cases 14/78 showed mismatch between EF_{RD} and EF_1 with higher values of EF_{RD}. These patients still had higher values of EF_{RI} and EF_2 than EF_{RD}.

Conclusion: (1) Mismatch between EF_{RD} and EF_1 is an indication of presence of stunning myocardium and of good prognosis. (2) EF_{RI} can be used to predict EF_2 and so helps on selecting patients who can benefit from revascularization.

Keywords: Cavity to myocardial ratio (C/M); Left ventricular ejection fraction (EF); Postrevascularization

Introduction

In patients with coronary artery disease (CAD), chronically dysfunctional left ventricular myocardium which recovers contractile function after revascularization has been defined as "hibernating" [1].

Presumably, the beneficial effects of revascularization result from restoring blood supply to dysfunctional but viable myocardial regions, with subsequent improvement in regional and global left ventricular function [2]. The proportion of viable myocardium is a critical factor in determining the likelihood of functional recovery after successful revascularization [3]. This fact is a reflection to the previously reported strong correlation between cavity-to- myocardial count ratio (C/M) of stress and redistribution thallium SPECT and stress and rest E.F. as measured by MUGA study [4]. This was explained by the facts that: It represents the actual functional mass [1], and the attenuating power of blood in the cardiac cavity to the cavity radioactivity [2,4-5].

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Accordingly, the aim of the current study is to correlate ejection fraction (EF) as predicted by C/M on redistribution (EF_{RD}) and reinjection (EF_{RI}) at rest by MUGA prevascularization (EF_1) and postrevascularization (EF_2).

Patients and Methods

Study population

Seventy eight patients with CAD liable to revascularization were subjected to the current study in Cairo university hospital, together with the National Heart Institute (Egypt) and Alhada Armed Force hospital, (Taif, Saudia Arabia). They were 68 males and 10 females (6.8:1) and had 54.2+9.1 years old (Table 1). Patients were eligible for inclusion: If they had severe regional dysfunction in the anatomic distribution of a significantly narrowed or occluded epicardial artery as determined by contrast left ventriculography and if the coronary arteries supplying the area of dysfunction were suitable for coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) [1,2]. Exclusions criteria included: Unstable angina, or myocardial infarction between revascularization and the scintigraphic studies or after intervention, patients with 3-4+ (moderate to severe) mitral regurgitation [1,2]. Each patient gave informed consent to the study protocol, which was approved by the ethical committees of the participating hospitals.

Age (years)	54.2+9.1
Sex (Male/female)	68/10 (6.8:1)
Left ventricular EF	36.8+15.3%
Coronary artery disease	
One-vessel disease	10 (12.8%)
Two-vessel disease	25 (32.1%)
Three-vessel disease	43 (55.1%)
Revascularization	
PTCA	23 (29.5%)
CABG	55 (69.5%)

Table 1: Demographic data and clinical characteristics in 78 patients. EF: Ejection Fraction; PTCA: Percutaneous Transluminal Coronary Angioplasty; CABG: Coronary Artery Bypass Grafting.

Methods

All patients underwent exercise-redistribution-reinjection thallium scintigraphy, resting multigated study (MUGA) pre and post revascularization and coronary angiography. Subsequently, 23 patients underwent PTCA while 55 patients underwent CABG. The decision concerning the choice of treatment was left to the referring cardiologists and was not based on the results of the viability studies.

Coronary angiography

Selective coronary angiography and contrast left ventriculography were performed from the femoral approach. Significant coronary artery disease was defined as >70% luminal diameter stenosis in any major coronary branch. Accordingly, 10 patients had one vessel disease, 25 patients had two vessel diseases and 43 patients had three vessel disease.

Thallium SPECT protocol

All patients underwent symptom-limited treadmill exercise testing with a standardized multistage protocol with continuous monitoring of heart rate and rhythm, blood pressure and electrocardiography. Criteria for interrupting the exercise test, included age-predicted maximal heart rate, severe angina, development of marked ST-segment depression, appearance of frequent or complex ventricular arrhythmia, hypotension and exercise-limited dypsnea. Three millicurie (mCi) of thallium was injected IV at peak exercise and continuation of exercise for one minute was done after that. Acquisition of tomographic images was performed within 5 minutes after thallium injection as reported previously [6]. Four hours later redistribution images (RD) were obtained. This was followed by reinjection (RI) of 1.5 mCi of thallium then 1 hour later another SPECT set was done.

SPECT was performed as described by Cuocolo et al. [7] with large field of view gamma camera (G.E. XC/L interfaced with 4000I Star Cam Computer) equipped with a low-energy, all-purpose, parallel-hole collimator. Thirty-two projections (40 sec/projection) were obtained over a semicircular 180-degree arc, which extended from the 45-degree RAO to the LPO. Dual energy windows had been applied: one for a 15% centered on the 70 KeV to 80 KeV, and 25% on the 169 KeV. Filtered back projection was then performed with a low-resolution. Butterworth filter with a cut-off frequency of 0.5 cycles/pixel, order 5.0. No attenuation or scatter correction was applied.

Image processing

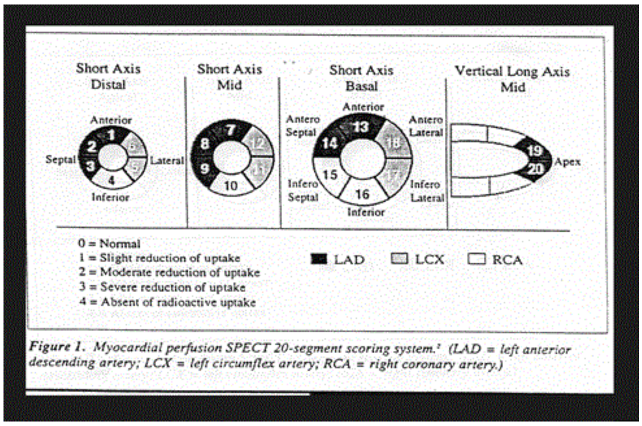

Figure 1: Myocardial segmentation model. Myocardial segments: distal anterior (1), medial (7), basal (13); distal anteroseptal (2), medial (8), basal (14); distal inferoseptal (3), medial (9), basal (15); distalinferior (4), medial (10), basal (16); inferolateral (5), medial (11), basal (17); anterolateral (6), medial (12), basal (18); distal antero-apical (19), distal infero-apical (20) [8].

Comprehensive semiquantitative perfusion defect analysis using 20-segment visual analysis has been used. The 20-segment scoring system is based on three-short axis slices (distal, mid, and basal) to represent the entire left ventricle, with the apex represented by two segments visualized in a mid-vertical long axis image. Each of the 20 segments has a distinct name (number) (Figure 1) [8]. Each segment is visually scored as follows: 0 = normal, 1 = slight reduction of uptake (equivocal); 2 = moderate reduction of uptake (usually implies a significant abnormality); 3 = severe reduction of uptake; 4 = absence of radioactive uptake. Then the summed stress score (SSS) is defined as the sum of the stress scores, the summed rest score (SRS) is the sum of the rest or redistribution scores. The summed difference score (SDS), measuring the degree of reversibility, is defined as the difference between the SSS and the SRS.

For C/M ratio a short axis at the mid-left ventricle (LV) level was used in both initial and delayed images. Two regions of interest had been drawn: one delineating the inner border to represent the cavity©, and the other delineating the outer border to represent myocardium (M). Then, the C/M count ratio will be calculated and E.F. will be derived from the previously mentioned regression equation [5]:

E.F. = - 4.89 + (C/M×77.4), + 6.9 [5]

Multigated study (MUGA)

Gated blood pool cardiac scintigraphy was performed 1 week later after myocardial perfusion study to assess left ventricular ejection fraction at rest using red blood cells labeled in vivo with 20-25 mCi 99mTc. Imaging was accomplished using a high sensitivity, parallel hole collimator. Patients were imaged supine in best left anterior oblique view.

The camera was set at 140 KeV photopeak +20%, with 64×64 and 24 frames. Edge detection of left ventricle had been done depending on the phase image. Left ventricular ejection fraction was derived by computer analysis of the scintigraphic data with the lower normal limit of resting EF is 50%.

Statistical analysis

Data were analyzed using SPSS (version 15.0. SPSS Inc., Chicago, IL). Data are presented as mean +standard deviation (SD). Differences in the mean of the different groups were performed using unpaired t-test.

Differences in the frequency of patients of the different groups had been performed using X_2 analysis. Linear regression analysis was done to see if EF_{RD} and EF_{RI} were correlated strongly with EF_1 and EF_2 $P < 0.05$ was considered significant statistically [9].

Results

*Distribution of patients according to the actual post-revascularization (EF_2)

Number of vessels affected	Improved	Same	Worsen
3 vessel disease	23 (43.4%)	13 (30.2%)	7 (16.3%)
2 vessel disease	15 (60%)	7 (28%)	3 (12%)
1 vessel disease	6 (60%)	4 (40%)	0 (0%)
Total	44 (56.4%)	24 (30.7%)	10 (12.8%)

Table 2: Distribution of patients according to actual post-revascularization ejection fraction (EF_2).

Table 2 revealed 44 patients (56.4%) with improved E.F. 23/44 with 3 vessel disease (3 VD), 15 with 2 VD, and 6 with 1 VD. 24 patients (30.7%) with similar pre and post revascularization E.F: 13/24 with 3 VD, 7/24 with 2 VD and 4/24 with 1 VD. On the other hand, 10 patients (12.8%) showed worsening of E.F. post-revascularization, 7/10 with 3 VD and 3/10 with 2 VD. None with 1 VD.

Agreement between $E.F._{RI}$ and EF_2

Table 3 revealed 63/78 patients agreement, i.e., 80.8% agreement with 37 patients predicted to show this actual improvement, 17 patients expected to show no change in E.F. post-revascularization (EF_2) and 9 patients expected to show worsening in E.F. These findings were furtherly analyzed in Table 3 where patients with 1 VD showed the highest agreement 9/10 (90%), patients with 2 VD showed 21/25 (84%) agreement while patients with 3 VD showed lowest agreement 33/44 (75%).

EF_2	EF_{RI}			Total
	Improved	Similar	Worsened	
One vessel disease				
Improved Similar Worsened	5 0 0	0 4 0	1 0 0	6 4 0
Total	5	4	1	10
Total agreement = 9/10 (90%), P < 0.001				
Two vessel disease				
Improved Similar Worsened	13 2 0	2 5 0	0 0 3	15 7 3
Total	15	7	3	25
Total agreement = 21/25 (84%), P < 0.01				
Three vessel disease				
Improved Similar Worsened	19 4 1	4 8 0	0 1 6	23 13 7
Total	24	12	7	44
Total agreement = 33/44 (75%), P < 0.05				
All 78 cases				
Improved Similar Worsened	37 6 1	6 17 0	1 1 9	44 24 10
Total	44	23	11	78
Total agreement = 63/78 (80.8%), P < 0.01				

Table 3: Degree of agreement between the EF_{RI} and EF_2. EF_{RI}: Ejection fraction as predicted by calculated by cavity-to-myocardial count ratio in reinjection image; EF_2: Actual ejection fraction post-revascularization.

*Comparison between EF as predicted from $_{RD}$ and $_{RI}$ (EF_{RD}& EF_{RI}) versus postrevascularization EF_2

Figure 2 revealed the mean +SD of patients with improved EF_2 compared to that predicted from EF_{RD} & EF_{RI}. It is significantly higher than that predicted from EF_{RD} (45+10 vs. 34.9+8.6 with $P < 0.01$) but insignificantly different from that predicted by EF_{RI} (45+10 vs. 47.1+12.1with $P > 0.05$). Similarly, patients with no change in E.F. where the mean value of EF was the same as predicted from EF_{RD} (36.7+11.8) compared to that predicted from EF_{RI} (36.8+14.5) and the actual postrevascularization EF_2 (37.9+12.3). On the other hand, patients with predicted worsening EF showed significantly higher EF_{RD} (34.7+10.2) than EF_{RI} (30.1+ 8.3) which is marginally higher than that actual postrevascularization EF_2 (28.4+7.4).

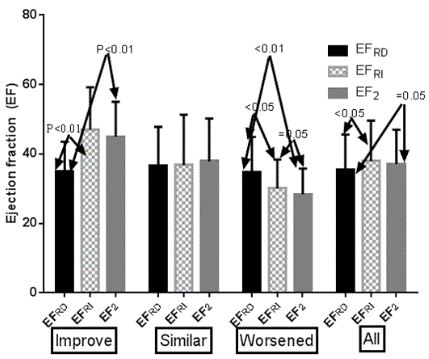

Figure 2: Mean and SD of preoperative predictable ejection fraction (EF_{RD} and EF_{RI}) postoperative actual EF (EF_2).

Relation between pre vascularization EF_1 and EF_{RD}

Figure 3a and 3b revealed strong correlation between EF_1 and EF_{RD} and between EF_2 and EF_{RI}. Patients had been divided according to the agreement between EF_1 and EF_{RD} into matched group (M) 64/78 (82.1%) patients (37.6+8.9 vs. 38+7.4, $P > 0.05$) and mismatched group (N) with lower EF_1 than EF_{RD} (31.4+10 vs. 36.4+8.3, $P < 0.05$).

This group included 14/78 (17.9%) of the studied patients.

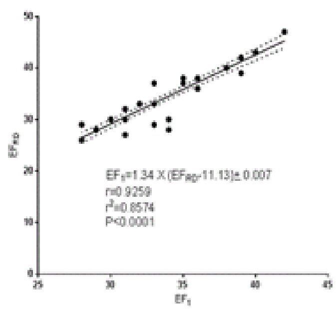

Figure 3a: Linear regression between pre-revascularization ejection fraction (EF_1) and redistribution EF (EF_{RD}).

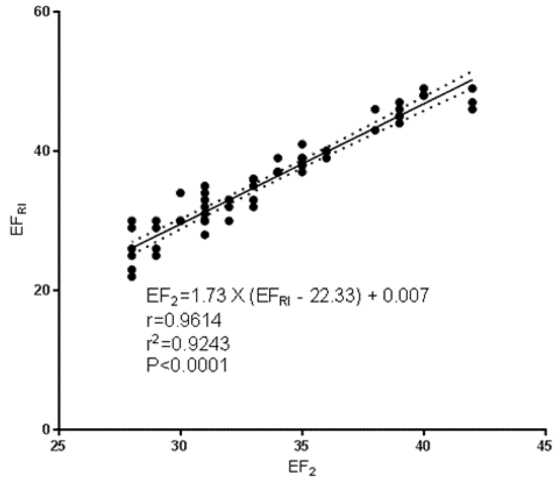

Figure 3b: Linear regression between pre-revascularization ejection fraction (EF_2) and reinjection EF (EF_{RI}).

On the other hand, Figure 4 showed flow chart including both matched (M) and mismatched (N) groups and the role of EF_{RI} in prediction of EF_2: where improved EF_2 as predicted by EF_{RI} in 30/64 (46.9%), no change in EF_2 as predicted by EF_{RI} 23/64 (35.9%) and worsening in EF_2 as predicted in 11/64 (17.2%). On the other hand, in group (N) showed improved EF_2 in all the cases 14/14 (100%). These patients still had higher values of EF_{RI} and EF_2 than EF_{RD}.

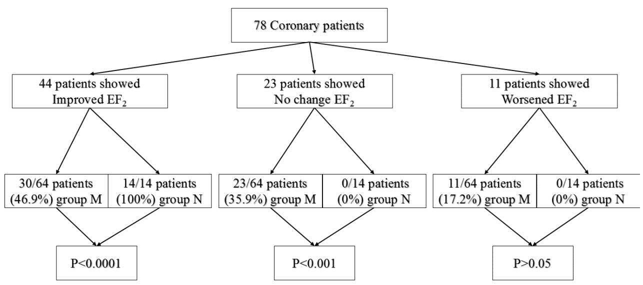

Figure 4: Prediction of post-revascularization EF_2 by calculated EF from reinjection C/M ratio in both M and N groups. EF_2 = Post-revascularization ejection fraction; C/M = Cavity to myocardial count ratio.

Reversibility and post revascularization outcome

Table 4 revealed the summed stress score (SSS) in each group of patients where patients with post-revascularization improved showed SSS = 2.59+0.77, summed rest score (SRS) = 0.53+0.09 with statistically significant difference, $P < 0.01$ and SDS = 2.06+0.68. For patients showing no change in EF_2 the SSS was 2.11+0.81, SRS = 1.47+0.63 and summed difference score (SDS) = 0.37+0.31. On the other hand, patients with worsened EF_2 the pre-vascularization of SSS = 3.24+1.7, SRS = 2.92+1.3 and SDS = 0.32+0.26.

	SSS	SRS (RI)	SDS	Number of segments
Improved	2.59+0.77	0.53+0.09	2.06+0.68	192
Same	2.11+0.81	1.47+0.63	0.37+0.31	258
Worsen	3.24+1.7	2.92+1.3	0.32+0.26	104

Table 4: Myocardial perfusion score in the studied patients. SSS: Summed Stress Score, SRS: Summed Rest Score; SDS: Summed Difference Score

Discussion

The presents study demonstrates that EF_{RI} is a useful parameter to stratify patients that will be subjected to revascularization and could be used to predict the degree of functional recovery postrevascularization. In addition, the current study revealed that mismatching between EF_1 and EF_{RD} is an indication of presence of dysfunction viable myocardium i.e., stunning myocardium. While the mismatch between the EF_{RD} and EF_{RI} is an indication of hibernating myocardium.

Pre vascularization EF_1 and predicting EF from C/M ratio

Several reports published a strong correlation between C/M count ratio and actual EF even in poor EF [4,5,10-15] depending on the following rational: The amount of myocardial mass prependicular to the crystal surface of the gamma camera [1] regional thallium accumulation [2], and the effect of tissue attenuation of radiation from the distant myocardial wall by the ventricular blood pool which is decreased in cases of good left ventricular ejection fraction (LVEF) in such way that attenuation is reduced and more radiation is found in the cavity [3]. This was supported by Hachamovich et al. (1998) [16] who stated that SSS is the perfusion analogue of the peak EF and similarly SRS for resting EF. Similarly, Bax et al. (2001) [17] reported strong correlation between the number of viable segments on SPECT and improvement in LVEF after revascularization. Thus, EF_{RD} represents the sum of the actually and potentially functioning mass. This explains the presence of the mismatched group (N group) which included 14 patients where actual EF_1 was 31.4+10 while the predictable EF_{RD} was 36.4+8.3 with $P < 0.05$. This means that there is potential functioning tissue (stunned) post revascularization.

In patients undergoing biopsy during surgical revascularization, it has been demonstrated that the level of thallium uptake after reinjection closely correlates to the amount of interstitial fibrosis [18]. On the other hand, several authors reported using quantitative analysis of thallium uptake a cutoff uptake value to separate reversibly dysfunctional from irreversibly dysfunctional myocardium with linear correlation between the functional recovery in a dysfunctional segment and thallium uptake. The shape of this correlation is such that it is possible to identify a cutoff point (usually below 30% to 40% of maximal uptake) under which recovery of function almost never occurs, but above which chances of recovery increase in parallel with the amount of tracer uptake [19]. All these lead to the other area of mismatch found between the EF_{RD} and EF_{RI} which could be attributed by the more viable segments that had been detected by RI technique and so more regional thallium accumulation scattering their radioactivity into the cavity to reduce the difference between the count in the cavity and myocardium. This is more apparent by Table 4, which showed that SRS in patients who showed postrevascularization improvement was 0.53+0.09 and also supported by work of Qureshi et al. (1997) who reported high thallium uptake in segments that exhibited ultimate recovery of function (68+12% to 81+11%, $n = 42$, $P < 0.01$) than in those that did not (52+19% vs. postrevascularization resting uptake of 55+21%, $n = 106$; $P > 0.05$) [20]. This goes on line with Bax et al. [17] report at 2001, they found that a substantial amount of viable myocardium (31% of the left ventricle) needs to be present to result in improvement in LVEF. They again reported division of their patients into three groups according to the amount of viable segments with linear increase in EF with more viable segments.

Degree of agreement between EF_2 and EF_{RI}

The current study could predict the functional outcome post-revascularization accurately in 63/78 patients, i.e., in ~81% of cases. This agreement is more in one and two vessel disease cases but less in three vessel disease cases which could be attributed to the technical problems that would be met during CABG and unpredictable myocardial loss during operations.

Conclusions

Mismatch between EF_{RD} and EF_1 is an indication of presence of stunning myocardium and of good prognosis.

EF_{RI} can be used to predict EF_2 and also helps on selecting patients who can benefit from revascularization.

Study limitations

The current study included small number of patients (78) which on further subdivisions decreases the number for further statistical analysis. In addition, the small number could not separate impact of PTCA versus CABG on post-revascularization ejection fraction (EF_2). Further research work with larger number is needed.

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