

Validity of Resting Strain/strain Rate in Prediction of Myocardial Viability

Amr Hanafy (✉ amrhanafy75@gmail.com)

Aswan University <https://orcid.org/0000-0002-7663-7505>

Soliman Ghareb Ibrahim

Cairo University

Hossam Eldein Mohamed Mohamed Mansour

Aswan University

Aml Mohamed Soliman

Aswan University <https://orcid.org/0000-0003-3715-3273>

Mohamed Kamal Salama

Kafr el-Sheikh University: Kafrelsheikh University

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Abstract

Purpose

To evaluate the validity of the resting strain/strain rate measurements in predicting myocardial viability taking delayed enhancement cardiac magnetic resonance imaging as the gold standard. Methods: A cohort of 60 patients at three months followed up after acute myocardial infarction were recruited for this study. Resting echocardiography with offline analysis of deformation indices and gadolinium contrast enhanced cardiac magnetic resonance imaging were applied for all patients.

Results

For the final assessment, 268 segments with significant resting wall motion abnormalities were presented. Resting longitudinal strain was significantly ($p < 0.05$) higher in viable, compared with non-viable segments in all the studied individual myocardial segments (apical inferior, mid antro-lateral, mid-inferolateral, mid infero-septum, and all other segments). Likewise, resting longitudinal strain rate was significantly ($p < 0.05$) higher in viable, compared with non-viable segments in almost all studied individual myocardial segments apart from apical inferior, mid inferolateral and basal antro-septum ($p = 0.245$, $p = 0.098$, $p = 0.097$ respectively).

Conclusion

Resting Strain and Resting Strain rate could be used as accurate predictors of myocardia viability following acute myocardial infarction.

Introduction

Patients with ischemic heart disease (IHD) and left ventricular dysfunction (LVD) carry poor prognosis [1]. In some patients, myocardial dysfunction improves significantly with revascularization and thus prognosis improves [2]. Several non-invasive modalities (such as single photon emission computed tomography (SPECT), dobutamine stress echocardiography (DSE), positron emission tomography (PET) and Cardiac Magnetic Resonance Imaging (CMR)) [3] have been approved to determine patients with viable myocardium, who will most benefit from revascularization [2].

Out of the newly validated methods for assessment of myocardial viability, DSE was the most widely available approach [4] with an overall similar sensitivity compared with other non-invasive imaging modalities and highest specificity [5]. However, its subjectivity limits its diagnostic value as its liable for inter-observer and intra-observer variability [6]. Some researchers explored the potentiality of adding deformation indices measurement to DSE protocol in the atrial function to overcome its subjectivity and the results were promising [7–9].

In general, deformation indices allow for more direct assessment of myocardial muscle shortening and lengthening throughout the cardiac cycle by assessing regional myocardial strain and strain rate. Strain

is defined as the change in length of a segment of myocardium relative to its resting length; strain rate is the rate of this deformation. Longitudinal and circumferential shortening results in negative strain values, whereas radial thickening results in a positive strain value [10–11].

Resting Longitudinal Strain (RLS) and Longitudinal Strain Rate (RLSR) imaging can be measured based on either tissue Doppler imaging or 2-dimensional speckle tracking (STE) [12]. Echocardiography and CMR can be used to quantify myocardial strain and strain rate [4, 13]. It was proposed that it is safer and easier for diagnosis if resting strain/strain rate could accurately predict myocardial viability [13].

The current study aimed to evaluate the validity criteria of resting strain/strain rate in predicting myocardial viability taking DE-CMR as gold standard.

Patients And Methods

A prospective follow-up design was adopted for this study. Sixty patients 3-months post-acute myocardial infarction (AMI) were recruited for the current study after fulfilling the inclusion/exclusion criteria from Aswan university hospitals and Aswan heart center (AHC). Patients were visiting the clinics for assessment of myocardial viability. The study period was from March 2019 to June 2020.

According to the power calculation via G*Power 3 software [14], a calculated minimum sample of 254 segments with significant resting wall motion abnormalities in patients with STEMI were needed to detect an effect size of 0.1 in the mean RLS/RLSR among viable vs. non-viable segments, with an error probability of 0.05 and 90% power on a two-tailed test.

Patients presented 3-months post-AMI, aged > 18 years with segmental wall motion abnormalities (WMA) as diagnosed by 2-D-Echocardiography were included. Exclusion criteria were, patients with early post-infarction unstable angina, severe hemodynamic instability, clinically evident congestive heart failure, mechanical complications of MI, significant valvular/congenital heart disease/any myocardial disease apart from ischemia, atrial fibrillation and bundle branch block and technically inadequate Echocardiographic imaging defined as more than two non-analyzable segments in the infarct zone.

Study tools

Baseline data including socio-demographics, history of chronic disease (hypertension and diabetes mellitus), family history of cardiac disease and smoking were obtained from the patients/or their caregivers.

All patients were subjected to:

- **2-D speckle tracking based strain and strain rate (Fig. 1):**

Echocardiographic images were obtained using Philips 4D (GE Healthcare, Horton, Norway) with a 3.5-MHz transducer. 2-D echocardiography was used for assessment LV dimensions, resting wall motion

abnormalities, LV function by Simpson's method. Apical 4-chamber, 3-chamber and 2-chamber views were recorded at baseline. Images were digitized in cine-loop format and saved for subsequent playback and analysis.

Using the 17-segment model of the Philips Q lab. -10 software, myocardial RLS/SR with STE were calculated offline individually for each segment. Of the 17 segments, only those segments that had baseline resting significant WMA (Akinesia, dyskinesia or marked hypokinesia) were included in this study. STE based S/SR were measured in 1 cardiac cycle per view. A machine-generated frame was applied to stored images in various views to generate results. The software then tracked speckles frame-by-frame throughout the entire cardiac cycle. Initially, automatic traces were applied by the machine and if traces were not corresponding with cardiac borders, they were manually corrected to match to get final observation. The automated software then generated traces depicting regional strain and strain rate, from which peak systolic strain and strain rate were recorded.

• **DE- CMR (Fig. 2):**

DE-CMR was performed at least three months after STEMI occurrence. Magnetic resonance (MR) images were acquired using a Siemens IRA 1.5 T system. For DE-CMR analysis, a 17-segment LV model was used. The protocol included scouts, short-axis, 4-chamber, 2-chamber, 3 chamber cine acquisitions, early gadolinium enhancement (within the first 1–3 minutes after contrast infusion) to look for a microvascular obstruction indicating a no reflow as well as LV thrombi, and late gadolinium enhancement using phase-sensitive inversion recovery sequences technique for the determination of trans-murality. In accordance with the clinical definition, viability is deemed as present when trans-murality is below 50% of the area of the affected segment, and absent when greater than 50% [15].

Statistical analysis:

Data were verified, coded by the researcher, and analysed using IBM-SPSS 24.0 [16]. Descriptive statistics: Means, standard deviations were calculated. Test of significances: Independent sample t-test was carried out to compare the means between groups. Validity statistics (sensitivity, specificity, positive and negative predictive value –PPV & NPV-) were calculated. Receiver operating characteristic (ROC) curve for the RLS/RLSR for every segment was calculated, analyzed as the area under the curve (AUC), standard error (SE) and 95% CI. A p-value < 0.05 was considered significant.

Statement of Ethics

The IRB of the Medical Faculty, Aswan University approved the study (IRB No. 222/3/18). The study was carried out in accordance with the guidelines of the Declaration of Helsinki [17]. Also, all participants completed a written consent form that indicate the aim and methods of the study, as well as the benefits and drawbacks of participation. Participants were given the freedom to withdraw at any time. Moreover, confidentiality and anonymity were assured. Neither incentives nor rewards were offered for the participants.

Results

The current study included 60 patients presented at least 3 months following AMI according to the assigned inclusion/exclusion criteria. The mean patient's age was 60.3 ± 9.9 years; 80% were males, 36.7% were diabetic, 46.7% were hypertensive, 51.7% were smokers and 26.7% had a family history of IHD. Regarding the type of infarction, about 60% of the studied cohort had anterior STEMI (n = 35), 37% had inferior STEMI (n = 22), whereas only 5% had posterior STEMI (n = 3) (Fig. 3).

The basic Echocardiographic results revealed that the mean EF% was about 46%, the mean LVEDD was 5.7cm, the mean LVESD was 3.1cm and 278 segments with significant WMA at rest were available for analysis. Seven segments could not be analyzed because of poor image quality. For basal anterolateral segments (3 segments), there were no corresponding non-viable segments, hence excluded from the final analysis. DE-CMR image analysis was feasible in all segments. So, a total of 268 segments were available for final analysis.

Table 1 showed the distribution of akinetic viable and non-viable segments (as assessed by DE-CMR) in the study group. For the total sample, the non-viable segments represented about 40% (n = 107). The most frequent segment with non-viability were apical proper (60.5%), mid-infero-lateral (50%), basal infero-lateral (43%), apical septum (42.5%) and mid-antero-septum (42%).

Table 1
Distribution of Viable and Non-viable Segments:

Segment	Viable (n = 161)	Non-Viable (n = 107)
• Apical Proper	15 (39.5%)	23 (60.5%)
• Apical Anterior	18 (60%)	12 (40%)
• Apical Lateral	11 (68.8%)	5 (31.2%)
• Apical Inferior	10 (62.5%)	6 (37.5%)
• Apical Septum	19 (57.6%)	14 (42.4%)
• Mid Anterior	12 (66.7%)	6 (33.3%)
• Mid Antro-Lateral	6 (75%)	2 (25%)
• Mid Infero-Lateral	4 (50%)	4 (50%)
• Mid Inferior	14 (73.7%)	5 (26.3%)
• Mid Infero-Septum	4 (66.7%)	2 (33.3%)
• Mid Antro-Septum	11 (57.9%)	8 (42.1%)
• Basal Anterior	7 (70%)	3 (30%)
• Basal Infero-Lateral	4 (57.1%)	3 (42.9%)
• Basal Inferior	12 (66.7%)	6 (33.3%)
• Basal Infero-Septum	5 (62.5%)	3 (37.5%)
• Basal Antro-Septum	9 (64.3%)	5 (35.7%)
TOTAL	161 (60.1%)	107 (39.9%)

RLS was significantly higher in viable than non-viable segments in all the studied individual myocardial segments ($p = 0.002$ for apical inferior, 0.010 for mid antro-lateral, 0.001 for mid inferolateral, 0.017 for mid infero-septum and < 0.001 for the other segments). The differences in the mean RLS% ranged between 5% in the mid antero-lateral segment to 8% in the basal inferior segment (Table 2). Likewise, RLSR was significantly higher in viable compared with non-viable segments in almost all studied individual myocardial segments apart from apical inferior, mid inferolateral and basal antro-septum ($p = 0.245$, $p = 0.098$, $p = 0.097$, respectively), p -value < 0.05 for all other segments. For the segments with significantly different results, the differences in the mean RLSR ranged between 0.17 s^{-1} in the apical lateral segment to 0.35 s^{-1} in the basal inferior segment (Table 3).

Table 2
Resting Strain Values in Individual Myocardial Segments

Segment	Viable	Non-Viable	P-value*
• Apical Proper	-14.40 ± 1.5	-7.61 ± 1.9	< 0.001
• Apical Anterior	-13.61 ± 1.6	-8.58 ± 1.4	< 0.001
• Apical Lateral	-14.27 ± 1.4	-8.20 ± 1.1	< 0.001
• Apical Inferior	-12.80 ± 2.8	-7.83 ± 1.9	= 0.002
• Apical Septum	-14.26 ± 1.4	-7.43 ± 1.3	< 0.001
• Mid Anterior	-13.91 ± 1.8	-8.00 ± 1.2	< 0.001
• Mid Antro-Lateral	-14.00 ± 1.8	-9.00 ± 0.1	= 0.010
• Mid Infero-Lateral	-13.25 ± 1.5	-6.75 ± 1.7	= 0.001
• Mid Inferior	-13.50 ± 1.1	-7.20 ± 1.3	< 0.001
• Mid Infero-Septum	-13.25 ± 1.5	-7.50 ± 1.1	= 0.017
• Mid Antro-Septum	-14.45 ± 1.3	-8.50 ± 1.9	< 0.001
• Basal Anterior	-13.86 ± 1.6	-6.67 ± 2.1	< 0.001
• Basal Infero-Lateral	-12.75 ± 1.0	-6.33 ± 0.6	< 0.001
• Basal Inferior	-13.17 ± 1.4	-5.67 ± 0.8	< 0.001
• Basal Infero-Septum	-12.20 ± 0.8	-6.67 ± 0.6	< 0.001
• Basal Antro-Septum	-13.22 ± 1.8	-7.00 ± 0.7	< 0.001
*Independent t-test was used to compare difference in mean between groups			

Table 3
Resting Strain Rate in Individual Myocardial Segments

Segment	Viable	Non-Viable	P-value*
• Apical Proper	-0.79 ± 0.1	-0.48 ± 0.1	< 0.001
• Apical Anterior	-0.77 ± 0.1	-0.59 ± 0.1	< 0.001
• Apical Lateral	-0.72 ± 0.1	-0.55 ± 0.1	= 0.003
• Apical Inferior	-0.71 ± 0.1	-0.64 ± 0.1	= 0.245
• Apical Septum	-0.77 ± 0.1	-0.51 ± 0.1	< 0.001
• Mid Anterior	-0.77 ± 0.1	-0.59 ± 0.1	= 0.002
• Mid Antro-Lateral	-0.81 ± 0.03	-0.62 ± 0.04	= 0.001
• Mid Infero-Lateral	-0.74 ± 0.04	-0.57 ± 0.1	= 0.098
• Mid Inferior	-0.78 ± 0.04	-0.51 ± 0.07	= 0.001
• Mid Infero-Septum	-0.76 ± 0.03	-0.47 ± 0.1	= 0.007
• Mid Antro-Septum	-0.80 ± 0.05	-0.61 ± 0.1	< 0.001
• Basal Anterior	-0.80 ± 0.09	-0.52 ± 0.1	= 0.011
• Basal Infero-Lateral	-0.74 ± 0.02	-0.48 ± 0.1	= 0.023
• Basal Inferior	-0.76 ± 0.03	-0.41 ± 0.08	< 0.001
• Basal Infero-Septum	-0.74 ± 0.02	-0.48 ± 0.08	= 0.027
• Basal Antro-Septum	-0.69 ± 0.1	-0.60 ± 0.07	= 0.097
*Independent t-test was used to compare difference in mean between groups			

Taking DE-CMR as the gold standard for diagnosis of viability, a cutoff value ranging from - 10.5 to - 13.5% (with a sensitivity ranging from 92–100% and specificity ranging from 70–100%) for the RLS% identified viability in apical and mid segments, whereas a cutoff value ranging from - 9.5 to - 12.5% (with sensitivity and specificity ranging from 71–100%) for the RLS% identified viability in basal segments (Table 4). In the same way, a cutoff value ranging from - 0.68 to - 0.70 s⁻¹ (with a sensitivity ranging from 90–100% and specificity ranging from 82–94%) for the RLSR identified viability in apical segments, from - 0.70 to - 0.73 s⁻¹ (with 100% sensitivity and specificity ranging from 91–96%) in mid- segments, whereas a cutoff value ranging from - 0.70 to - 0.71 s⁻¹ (with 100% sensitivity and specificity ranging from 86–97%) for the RLSR identified viability in basal segments (Table 5).

Table 4
Cut-off values for RLS% for Viability Prediction

Segment	Cut-off	Sensitivity	Specificity	PPV	NPV
• Apical Proper	-13.5	100%	74%	79%	100%
• Apical Anterior	-10.5	92%	100%	100%	93%
• Apical Lateral	-12.0	100%	91%	92%	100%
• Apical Inferior	-11.5	100%	70%	77%	100%
• Apical Septum	-12.5	100%	90%	91%	100%
• Mid Anterior	-11.5	100%	91%	92%	100%
• Mid Antro-Lateral	-12.0	100%	84%	86%	100%
• Mid Antro-Septum	-13.5	100%	73%	85.5%	100%
• Basal Anterior	-12.5	100%	71%	84%	100%
• Basal Antro-Septum	-11.0	100%	89%	90%	100%
• Mid Infero-Lateral	-10.5	100%	98%	98%	100%
• Mid Inferior	-10.5	100%	96%	96%	100%
• Mid Infero-Septum	-10.5	100%	97%	97%	100%
• Basal Infero-Lateral	-9.5	100%	95%	95%	100%
• Basal Inferior	-11.5	100%	80%	83%	100%
• Basal Infero-Septum	-11.5	100%	100%	100%	100%

Table 5
Cut-off values for RLSR for Viability Prediction

Segment	Cut-off	Sensitivity	Specificity	PPV	NPV
• Apical Proper	-0.70	100%	94%	94%	100%
• Apical Anterior	-0.70	90%	94%	94%	92%
• Apical Lateral	-0.68	100%	82%	85%	100%
• Apical Inferior	-0.73	84%	50%	63%	76%
• Apical Septum	-0.70	100%	84%	86%	100%
• Mid Anterior	-0.73	100%	91%	92%	100%
• Mid Antro-Lateral	-0.70	100%	96%	96%	100%
• Mid Antro-Septum	-0.73	100%	91%	92%	100%
• Basal Anterior	-0.70	100%	86%	88%	100%
• Basal Antro-Septum	-0.70	100%	78%	82%	100%
• Mid Infero-Lateral	-0.71	100%	75%	80%	100%
• Mid Inferior	-0.71	100%	93%	93.5%	100%
• Mid Infero-Septum	-0.70	100%	96%	96%	100%
• Basal Infero-Lateral	-0.70	100%	97%	97%	100%
• Basal Inferior	-0.71	100%	92%	92.5%	100%
• Basal Infero-Septum	-0.71	100%	96%	96%	100%

Discussion And Conclusion

Nowadays, myocardial strain is used mainly for quantification of left ventricular (LV) function. It can even detect sub-clinical myocardial dysfunction [18]. Some studies explored the usefulness of dobutamine induced strain and strain rate in predicting myocardial viability and there was almost agreement that strain and strain rate at low dose dobutamine stress echocardiography could be an accurate predictor of myocardial viability [19–20]. Searching for more simplicity, fewer studies explored the usefulness of resting strain and strain rate in predicting myocardial viability but unfortunately the findings were inconsistent [21–24].

The current study found that there was significant reduction in all segments regarding RLS% and the majority of segments for RLSR in non-viable compared with viable segments. This was inconsistent with Chan et al. [21] who found that there was significant reduction in circumferential S and SR in transmural infarct segments (non-viable) compared with subendocardial infarcts (viable) and normal myocardium,

but not in radial or longitudinal S and SR, in contrary. Zhang et al. [22] found that the peak longitudinal myocardial deformation by strain rate imaging (SRI) can differentiate transmural (non-viable) from non-transmural (viable) myocardial infarction (MI), and it allows non-invasive determination of transmural extent of the scar after MI and thereby the extent of non-viable myocardium.

In current study, we assessed resting LS and LSR at each individual myocardial segment and findings were stunning. We found that RLS were consistently significantly higher in viable compared with non-viable segments. We also found that RLSR were significantly higher in viable compared with non-viable segments in almost all individual myocardial segment apart from apical inferior, mid inferolateral and basal antero-septum.

To the best of our knowledge, Khaled et al. [23] was the first to assess usefulness of resting LS and LSR in predict myocardial viability at individual myocardial segments but unfortunately the results were disappointing. They found that RLS was significantly higher in viable as compared with non-viable segments in the basal inferior, basal anteroseptal, basal posterior, as well as apical inferior positions. Otherwise, no significant difference was found between the S of viable and non-viable segments in the rest of positions. Similarly, RLSR was significantly higher in viable as compared with non-viable segments in the mid-lateral, mid- and apical anterior, apical inferior, as well as basal anteroseptal positions. Otherwise, no significant difference was found between the SR of viable and non-viable segments in the rest of positions [23].

They utilized tissue doppler based RLS and RLSR in their study which is angle dependent, and this may have contributed to the inconsistency of their results. In the current study, 2D speckle tracking based RLS and RLSR was applied to overcome this shortcoming. In discordance with the current study, Khaled et al., took ^{99m}Tc-sestamibi scintigraphy as the gold standard for viability diagnosis, while CMR was assigned as gold standard for viability diagnosis in this study because of its availability in our institution.

Another point of disagreement, Kaled et al., performed RLS and RLSR at least one month following AMI, and this study was carried out at least three months following AMI. The benefit of the current study time selection was to give an adequate time for myocardial edema to resolve. This was reported by Løgstrup BB et al., who claimed that longitudinal systolic strain was significantly correlated with myocardial edema [24]. Finally, in the current study, the cutoff values for RLSR that best discriminate viable from non-viable myocardium were higher than that of Khaled et al. while our cutoff value for RLS were more or less like that of Khaled et al. [23].

In conclusion, the findings of this work suggested that both RLS and RLSR can be easily added to routine echocardiographic protocol for quantification of myocardial function and accurate prediction of myocardial viability. In the future, its simplicity, availability, safety, and cheap cost will make it the gold standard modality for prediction of myocardial viability.

Declarations

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Code availability: Custom code

Author Contributions: **Amr H. Mahmoud (AHM)**; concept, design, literature search, clinical studies, manuscript preparation, editing and review. **Soliman G. Ibrahim (SGI)**; design, literature search, manuscript preparation and review. **Hosam-Eldein M Mohammed (HMM)**; literature search, clinical studies, manuscript editing and final draft. **Aml M. Soliman (AMS)**; data analysis, clinical studies, manuscript preparation, editing and review. **Mohammed K. Salama (MKS)**; statistical analysis, manuscript editing and final revision.

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Figures

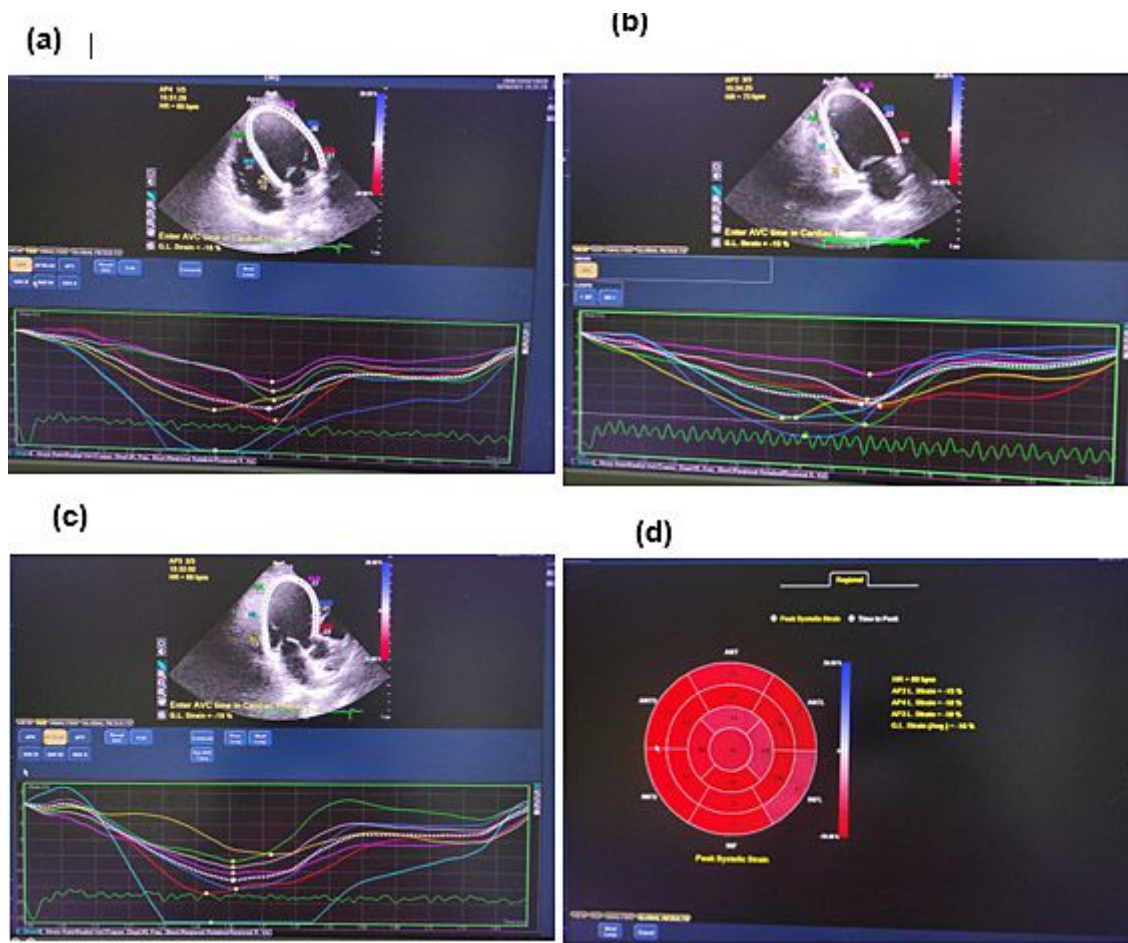


Figure 1

Diagram showing Measurement of Longitudinal Myocardial Strain using Speckle-tracking Echocardiography in patient with LAD cut-off: (A) Apical four chamber. (B) Apical two chamber. (C) Apical three chamber. (D) 17-segment bull's eye map for longitudinal strain.

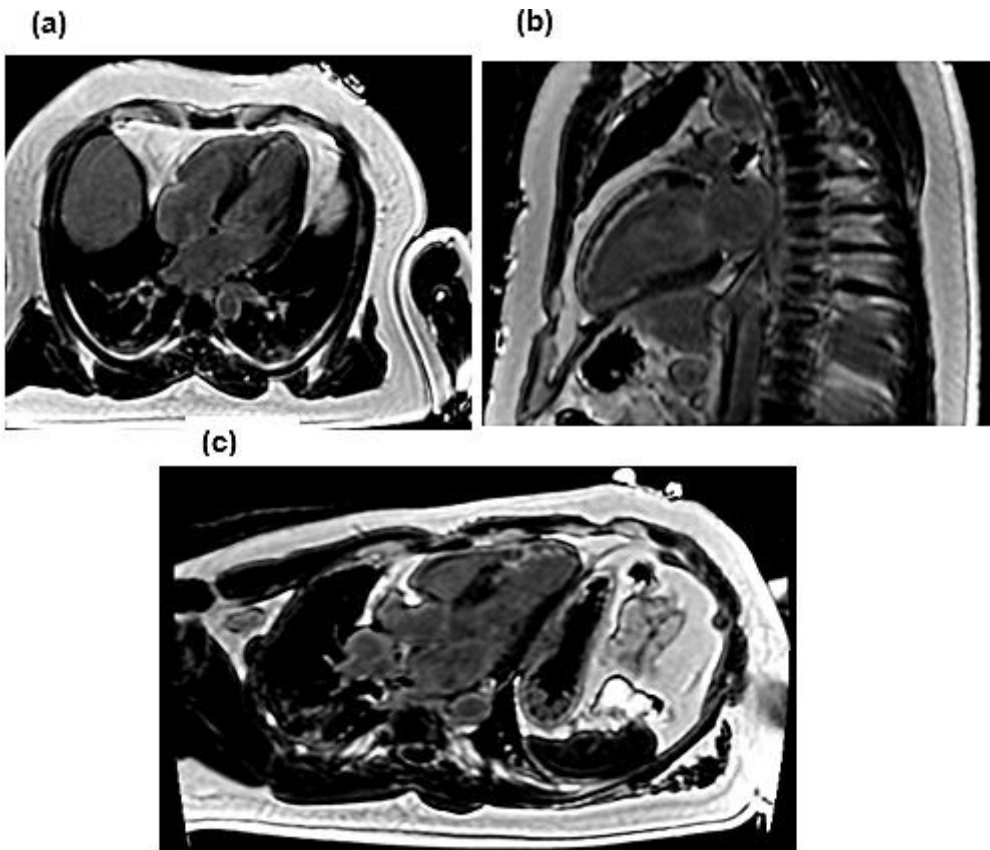


Figure 2

Diagram showing DE-CMR images in patient with LAD cut-off (same patient in figure 1): (A) PSIR four chamber. (B) PSIR two chamber. (C) PSIR three chamber.

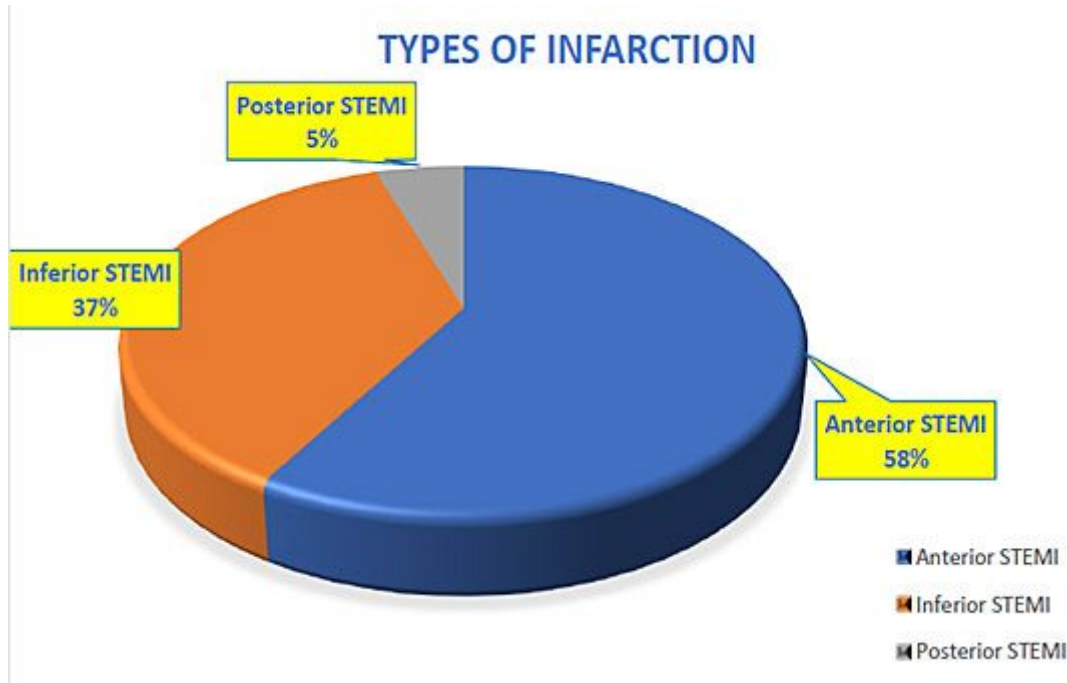


Figure 3

Types of Infarctions among the studied Cohort