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Does global longitudinal speckle-tracking strain predict left ventricular remodeling in patients with myocardial infarction? a systematic review

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ABSTRACT

Introduction: Left ventricular remodeling is a relatively prevalent complication of acute myocardial infarction (AMI), and it is associated with higher rates of medical issues and mortality. Left ventricle ejection fraction (LVEF) and wall motion score index (WMSI) are unable to detect accurately minor lesions following AMI. Global longitudinal strain (GLS), which is obtained through 2D-speckle tracking echocardiography (2D-STE), provides an angle-dependent measurement by which the infarcted area can be assessed as a means of identifying potential dysfunction. The main objective of this study was to evaluate whether GLS could adequately predict LV remodeling in AMI patients.
Methods: The MEDLINE database from database inception to May 6th, 2015, was searched for relevant keywords and the reference lists of systematic reviews and eligible studies were also screened. All studies involving patients with their first reported case of AMI were examined for GLS by 2D-STE and were evaluated for LV remodeling at a three-month follow-up point. Four English-language prospective cohort studies were eligible for inclusion in this study.
Result: A total of 291 AMI patients (mean age=57.92 years) were investigated across four different studies. The main finding of this study was that the most reliable and consistent measurement for the purposes of predicting LV remodeling in AMI patients is GLS obtained at the time of discharge, especially in STEMI patients.
Discussion: In addition to their poor reproducibility, inability to stratify risks, and inter-observer variability, compensatory hyperkinesis of intact myocytes and myocardial stunning after an AMI are among the main reasons why LVEF and WMSI may not be the most effective predictors of LV remodeling in AMI
Conclusion: GLS obtained by 2D-STE at the time of discharge could be used as a reliable predictor of LV remodeling in AMI patients.

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Introduction

Acute myocardial infarction (AMI) is a common disease that has serious and life-threatening complications. It is considered to represent a potentially major healthcare issue and, if it remains untreated, can lead to the development of severe medical conditions. Myocardial damages following an AMI lead to numerous mechanical and chemical changes in the left ventricular (LV) environment and these may result in transformations in chamber volume and shape that are commonly referred to as "LV re-

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modeling" (1). Although the LV remodeling mechanism is not well understood, it is assumed to be a complex process of myocyte hypertrophy, fibrosis, and apoptosis that is characterized by increased muscle mass without a change in wall thickness (2,3). The detection of LV remodeling is important in predicting morbidities and mortality in patients with AMI and/or congestive heart failure (CHF) (2). Even in the reperfusion era, and following the introduction of percutaneous coronary intervention (PCI) into routine practice, LV remodeling occurs in about 30-35% of patients following an AMI. It is particularly common in cases involving anterior wall ST-segment elevation myocardial infarction (STEMI) (2). Some authors report that infarct size, the coronary artery involved, and the enzymatic biomarkers of AMI all play a crucial role in LV remodeling following AMI (4-6).

In light of the above, careful initial and follow-up evaluation of myocardium function is an important clinical element of every treatment procedure. Assessment of the LV systolic function represents one of the well-known measures through which the prognosis of AMI patients can be determined (7-10). Several methods have been suggested as a means of assessing LV systolic function, including LV ejection fraction (LVEF) and wall motion score index (WMSI). Of these, LVEF is the most popular measure, and it is widely employed as the initial evaluation method for every AMI patient (11). However, there are numerous limitations associated with the existing measures; for example, poor reproducibility, limited capability of risk stratification, their time-consuming nature, limitations in LV hypertrophy, and inter-observer variability (12,13). Although LVEF appears normal in some patients, subtle lesions exist that can even lead to acute heart failure (14).

To address these problems, echocardiographic tools, including strain and strain-rate, provide promising technologies through which myocardial injuries and deformation processes can be detected. Of particular interest, is two-dimensional (2D) speckle-tracking echocardiography, which allows angle-independent quantification of myocardial deformities (15,16). Recently, an LV global longitudinal strain (GLS) has been reported in several conditions, including heart failure, valvular heart disease, cardiomyopathy, and ischemic heart disease, as a prognostic factor for short- or long-term complications (17-19). It is also utilized to evaluate LV remodeling, which may occur following an AMI (20-23). In this systematic review, we aimed to evaluate several factors that may predict LV remodeling after an AMI. In particular, we placed a specific focus on GLS, which is obtained by 2D speckle tracking echocardiography.

Methods

Data sources

Using a set of relevant keywords, we searched the records in the MEDLINE database from inception to May 6th, 2015. We also reviewed the reference lists of eligible studies suggested by experts to identify any additional articles that were of potential interest to the research objective. Our literature search keywords were [speckle AND "myocardial infarction" AND "global longitudinal strain"] and the search was limited to human studies.

Study selection

We included all English-language studies that involved an assessment of patients who had reported their first case of AMI. At a minimum, the articles needed to describe studies in which a 2D speckle tracking echocardiography was performed for all AMI patients to assess GLS and to divide patients into two groups based on the presence of LV remodeling at the time of follow-up visit (mean follow-up ranges between 3 to 6 months). All included articles were also required to describe the use of conventional echocardiography by experienced physicians or sonographers to assess patients using commercially available ultrasound systems to measure LVEF at an early stage following AMI and during the follow-up.

LV remodeling was defined as an LVEDV increase of at least 20% compared with the echocardiographic results at discharge. As LV remodeling might have a confounding rule in our results, and reperfusion effectively inhibits LV remodeling, we only included studies that employed PCI as the sole reperfusion therapy method.

Studies that included patients with cardiomyopathies, previous myocardial infarction, atrial fibrillation, and severe valvular diseases, and patients who underwent coronary artery bypass surgery were excluded from this systematic review. In addition, studies that described patients with poor echocardiographic window and/or low quality of images were excluded.

In all studies, patients received standard treatment and, at time of discharge, were evaluated by conventional and speckle echocardiography. We excluded case reports that included less than ten patients and articles that did not present personal findings and/or communications.

Results

A total of 43 articles were identified in the MEDLINE electronic database that met the initial inclusion criteria. Initial screening of the titles and abstracts of all 43 of these articles revealed that 17 of them did not fulfill our inclusion criteria, and one was not written in the English language. We further evaluated the full text of the remaining articles and 21 additional articles were omitted due to insufficient outcome data and/or unsuitable methodology. Although we reviewed the reference lists of the eligible studies and forward and backward searches, we couldn't find any other eligible studies to include in this study. Finally, four articles (23-26) that fulfilled our inclusion criteria with adequate outcome and appropriate method were reviewed as part of the present systematic review (Figure 1).

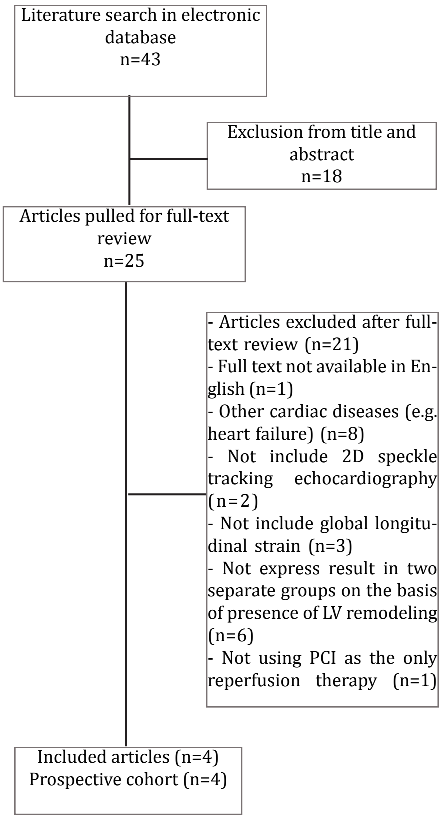

Figure 1. Summary of evidence search and selection

Study characteristics

Our systematic review included the cases of 357 patients with their first reported case of AMI. All included studies were designed as prospective cohorts and involved follow-up with the patients at least three months after the discharge. Among the four studies that were included in our study, two studies evaluated only STEMI patients, one study assessed Non-STEMI (NSTEMI) patients, and the remaining study included both STEMI and NSTEMI patients. The findings revealed that the symptom to balloon time and time interval between echocardiographic examination and AMI in patients who participated in a study by D'Andrea et al. (23) were dramatically different from the other three studies. With the exception of the Lacalzada et al. (26) study, most of the patients involved in the research studies were male and, in all studies, the mean age was above 55 years old (overall mean age = 57.92 years). Other demographic characteristics, including cardiac diseases' risk factors, coronary angiography results, cardiac enzymes, and echocardiographic results, are summarized in Table 1.

Discussion

Despite the introduction of PCI, adverse LV remodeling remains an issue and occurs in -30 %35 of AMI patients (1,4). In various studies, LV remodeling is considered to represent a predisposing factor for arrhythmias (27) and heart failure (2), and it is also accompanied by higher rates of mortality (8). In our systematic review, the overall rate of LV remodeling at follow-up visit was %34.17 (ranged between %30.95 and %45.7), which is in agreement with the findings of previous studies. The highest rate of LV remodeling was seen in the D'Andrea et al. (23) study, which included NSTEMI patients only. Lacalzada et al. (26) claimed that the relatively higher rate of LV remodeling in their study might be related to the prevalence of anterior AMI in the study participants. Although higher rates of left anterior descending (LAD) artery involvement in studies included mostly STEMI patients (i.e., Zaliaduonyte –Peksiene et al. (24) and Bonios et al. (25) studies, their LV remodeling rates were less than the Lacalzada et al. (26) study (%34.1 and %30.95 vs. %39.17 respectively).

Historically, LVEF and WMSI indices that were obtained by 2D echocardiography have been used to determine LV systolic function and the prognosis of AMI patients after AMI (11,28). Although there is evidence to suggest that high WMSI could represent an independent factor that can predict LV remodeling (29), these modalities have their own limitations, especially in the case of minor lesions and risk stratification (7,30). One reason for the diminishing value of LVEF in post-AMI patients is the hyperkinesis of the normal regions, which compensate for the decreased focal wall motion in the infarcted zone and, thus, LVEF may be inappropriately considered to be normal. On the other hand, the viability of myocardial fibers could not be assessed thoroughly by LVEF early after an AMI due to myocardial stunning phenomenon (12,31).

The findings indicate that, despite complete revascularization of the infarcted area, LV remodeling may escalate over time due to lack of microcirculation and tissue perfusion. Disturbances in the infarcted area could not be measured accurately by modalities of imaging assessed as part of this review (9,32). Initially, GLS was measured through a Doppler-based approach,

Table 1. Demographics, clinical profile, and echocardiographic reports of patients

Author Year Reference	LVr	n (%Male)	STEMI (%)	Age (mean±Sd)	Smoking (%)	DM (%)	HLP (%)	HTN (%)	MVD (%)	Peak TnI (mean±Sd)	Symptom to balloon (mean±Sd)	Coronary angiogram (%) (LAD, LCx, RCA)	Medical therapy (%) (Antiplatelets - ACEI/ ARBs - B-blocker - Statins)	GLS (%)	LVEF (%)	WMSI
D'Andrea 2011 (23)	No	38 (65.8)	0	61.4±7.3	46.7	24.8	54.6	27.7	40.7	-	7.1±7.6 days	42.4-33.6-24.5	98.2-78.2-74.7-90.3	-17.6±6.7(base), -19.8±6.7(post PCI)	48.7±5.5(base) 53.6±5.7(6m)	1.55±0.28
	Yes	32 (65.6)	0	62.4±9.1	44.6	42.5	56.7	25.5	59.8	-	7.6±7.3 days	45.5-32.7-22.2	97.9-77.6-72.5-89.3	-10.6±6.1(base), -10.8±5.1(post PCI)	44.8±6.9(base) 44.9±7.6(6m)	1.58±0.22
Zaliaduonyte –Peksiene 2012 (24)	No	54 (78.8)	85.2	57.1±12.0	59.3	13	92.5	70.4	42.6	8.3	318±228 min	44.4-20.4-29.6	100-96.2-100-92.6	-15.4±4.2	54.1±7.6(base) 55.3±9.7(4m)	1.5±0.3(base), 1.3±0.3(4m)
	Yes	28 (81.2)	96.4	57.9±9.4	67.9	7.1	89.3	75	28.6	11.3	438±348 min	75-3.6-28.6	98.2-89.3-96.4-100	-13.8±4.4	50.4±7.4(base) 47.8±11.6(4m)	1.7±0.3(base), 1.5±0.5(4m)
Bonios 2014 (25)	No	29 (-)	100	56±13	-	25	40	39	-	-	231±133 min	100-15-20	100-86-97-100	-9.7±1.9(4d) -9.7±1.6(3m)	42±7(4d) 35±7(3m)	-
	Yes	13 (-)	100	57±14	-	9	27	36	-	-	325±208 min	100-15-20	100-30-100-100	-12.9±2.9(4d) -16.0±3.4(3m)	48.9±6.3(4d) 52.8±7.5(3m)	-
Lacalzada 2015 (26)	No	59 (49)	100	55.5±11.7	56	37	61	44	43	17.6±9.7	215.2±69.3 min	43-13-44	100-43-76-89	-14.5±2.1	56.7±10.9(2d) 60.8±9.1(*)	1.43±0.28(2d), 1.4±0.36(*)
	Yes	38 (27)	100	57.4±11.2	57	89	46	45	54	59.8±35.6	235.9±71.7 min	54-5-39	100-50-82-82	-11.1±3.1	53.2±8.6(2d) 51.7±11.1(*)	1.44±0.28(2d), 1.5±0.56(*)

LVr: left ventricle remodeling; n: number of patients; STEMI: ST-segment elevation myocardial infarction; DM: diabetes mellitus; HLP: hyperlipidemia; HTN: hypertension; MVD: multi-vessel disease; TnI: troponin I; Sd: Standard deviation; LAD: left anterior descending artery; LCx: left circumflex artery; RCA: right coronary artery; ACEI: angiotensin converting enzyme inhibitors; ARBs: angiotensin II receptor blockers; B-blocker: beta blocker; GLS: global longitudinal strain; LVEF: left ventricle ejection fraction; WMSI: wall motion score index; min: minute(s); base: baseline; (3,4,6)m: (3,4,6) months; (2,4) d: (2,4) days; PCI: percutaneous coronary intervention.
*: Follow-up echocardiography (19.8 ± 7.3 months)

which was rapidly replaced by the speckle tracking echocardiography method (12). In a systematic review and meta-analysis (33) of 4721 patients with various cardiac conditions, it was concluded that the prognostic value of GLS, especially in mild LV global impairment, is superior to LVEF. In our study, the highest GLS was found in the Bonios et al. (25) study, which involved non-remodeled patients, and the lowest GLS was found in the non-remodeled patients of D›Andrea et al. (23), especially after PCI. However, in all studies (-22 18), GLS was found to be an independent predictor that was more effective in predicting LV global impairment than LVEF and WMSI in either STEMI or NSTEMI patients. This finding was in agreement with those of previous research (19,22).

Along with GLS, some researchers have attempted to identify any possible relationship between other strain parameters (e.g., apical and/or global circumferential strain and global radial strain) and LV remodeling in AMI patients. Bonios et al. (25) claimed that apical circumferential strain significantly correlates with LV end-systolic volume change at three months post-AMI ($r=0.577$, $p=0.001$) and that this correlation is even stronger than that observed with GLS ($r=0.577$ vs. $r=0.319$). These findings were further confirmed in the VALIANT study (34), in which the prognosis was worse in patients that exhibited a lower circumferential strain of LV in first few days following an AMI. In a study using an experimental model of AMI in rats, stem cells were injected into an infarcted zone, and a significant improvement in LV apical circumferential strain, LVEF, and dyssynchrony was observed at one week and four weeks post-AMI (35).

Although LVEF is generally measured by radial as well as some longitudinal contractions of the wall, 2d-speckle tracking is potentially able to identify strain in almost all planes. As can be observed in the studies that measured strain parameters in AMI patients, in the current literature review, GLS and circumferential strain were found to be superior to radial strain in determining patients' prognosis. This could be explained by the complex longitudinal and circumferential orientation of heart muscle fibers. It is also worth mentioning that longitudinal sub-endocardial fibers are more sensitive to ischemia and may be injured prior to any other region of the heart (19,36). This mechanism may also explain, in part, why GLS could predict AMI patients' prognosis in patients with normal LVEF values.

To answer the question as to whether LVEF and WMSI could be sufficient predictors of LV remodeling following an AMI, we should consider the patients' circumstances. Only Bonios et al. (25) found LVEF to be a predictor of remodeling at the three-months follow-up stage, while others didn't find it entirely useless in this case. The role of WMSI in predicting LV remodeling in AMI patients was not approved in any of the studies involved in this review.

Among the other factors that were evaluated in this study, diabetes mellitus (DM) and maximum level of Troponin I were independent predicting factors. Lacalzada et al. (26) concluded that both DM and peak Troponin I levels are independent factors for predicting LV remodeling, while D'Andrea et al. (23) found only DM as an independent predicting factor. It has been hypothesized that inadequate compensatory mechanisms are responsible for the higher susceptibility of DM patients to LV remodeling following AMI (37). Also, peak troponin I level was observed as an independent factor in other studies (22,38).

A more thorough meta-analysis is required to confirm the findings of this review. Additionally, future studies should consider using other indices of LV strain (e.g., apical and/or global circumferential strain and radial strain) in 2D-speckle echocardiography and their ability to predict LV remodeling following AMI at longer follow-up periods. As is the case with many systematic reviews, including observational studies, this systematic review includes studies that involved non-uniform patient selection, assessment, and follow-up. However, we endeavored to diminish these problems by using strict inclusion and exclusion criteria in terms of both patient selection and measurement methods. Some risk factors (e.g., familial history of coronary artery diseases) and echocardiographic results (e.g., strain rate, LVED index, LV twist, and torsion) were not included in our systematic review because only few studies reported these variables.

Conclusion

The review of the studies that examine vitamin C intake and asthma did not conclusively find that vitamin C supplements can reduce the incidence of asthma. However, in light of the fact that vitamin C is a low-cost supplement that is safe for human consumption, it seems reasonable to recommend that it is prescribed to asthmatic children to alleviate the severity of asthma symptoms. Further research on the possible effects of vitamin C on asthma is required. Specifically, large multicenter randomized controlled trials are recommended.

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Conflict of Interest

The authors declare no conflict of interest.

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