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Identification of Candidates for Implantable Cardioverter Defibrillator Insertion as Primary Prevention: Global Longitudinal Strain Helps

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ABSTRACT

Background: Heart failure is a life-threatening event that could lead to sudden cardiac death. It is primarily prevented by the use of implantable cardioverter defibrillators. Applying this therapy is mainly determined by left ventricular ejection fraction. However, this criterion results in considerable pitfalls. Improving the discrimination strategies in order to select eligible patients can help avoid unnecessary insertions.
Objectives: This study aimed to compare global longitudinal myocardial strain and left ventricular ejection fraction in predicting sustained ventricular tachyarrhythmia in heart failure patients.
Methods: This study was performed on 70 ischemic or dilated cardiomyopathic patients randomly selected from Imam Reza clinic. Patients with left ventricular ejection fraction ≤ 40% who had undergone implantable cardioverter defibrillator implantation were recruited into the research. Left ventricular ejection fraction and global longitudinal strain were measured by 3D echocardiography. Independent sample t-test was used for analysis and statistical significance was set at < 0.05.
Results: The data were expressed as mean ± SD. The study subjects in the ischemic and dilated cardiomyopathic groups were categorized according to the occurrence of ventricular tachyarrhythmia. The results showed a significant difference between arrhythmic and non-arrhythmic cases only in the ischemic group regarding the amount of left ventricular ejection fraction. Meanwhile, a significant difference was observed between arrhythmic subjects and their counterparts in both ischemic and dilated cardiomyopathic groups concerning global longitudinal strain parameters.
Conclusion: Global longitudinal strain could be considered as a valuable predictor of ventricular tachyarrhythmia occurrence beside left ventricular ejection fraction. This helps selection of appropriate patients for implantable cardioverter defibrillator therapy.

1. Background

Sudden cardiac death due to Heart Failure (HF) has become the leading cause of death pertinent to cardiovascular areas (1). HF is a pathophysiological state in which the heart, due to an abnormality of cardiac function, fails to pump the blood at a rate commensurate with the requirements of the metabolizing tissues or is able to work only with an elevated diastolic filling pressure (2). Ischemic or non-ischemic reasons could result in HF. Specifically, coronary heart disease and non-ischemic cardiomyopathies solely account for approximately 95% of cardiac arrests. Indeed, according to Kandala et al., the rate of survival following out-of-hospital cardiac arrest is only 10% (1). In this regard, as shown in several studies, primary prevention by means of Implantable Cardioverter Defibrillator (ICD) has been significantly associated with an increase in the survival rate (3-6). In fact, ICD implantation is the therapy of choice for Ventricular Tachyarrhythmia (VT) in ischemic heart diseases with reduced Left Ventricular Ejection Fraction (LVEF) and non-ischemic dilated cardiomyopathies (7).

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Decision for ICD insertion relies mainly on LVEF. In other words, ICD therapy is indicated for the following groups: ischemic cardiomyopathy with LVEF < 35% or 30% depending on New York Heart Association (NYHA) functional class and non-ischemic cardiomyopathy with LVEF < 35% and NYHA functional class II or III (8). However, its use comes along with some considerations. ICD therapy is a matter of cost-effectiveness. Utilization and maintenance of this device through an individual's life span imposes financial burdens on the healthcare system as well as on the patient him/herself. On the other hand, useless implantation of ICD in MADIT-II has been shown to be correlated to an increased number of hospitalizations (9). Furthermore, a considerable number of patients who had implanted ICD as the primary prevention never received therapeutic shocks (3). Moreover, it was demonstrated in a group of patients that despite low LVEF, they remained at low risk of Sudden Cardiac Death (SCD) (4, 10). Therefore, it seems that the current predictive assessment for ICD utilization is not valid enough and needs more effective risk stratification.

Speckle Tracking Echocardiography (STE) is a method for non-Doppler-based and angle-independent measurement of the left ventricular function. In this method, any change in the length of myocardial segments is measured based on a semi-automated algorithm that tracks the displacement of acoustic "speckles" in the myocardium (11). Compared to LVEF, STE is affected to a much lesser degree by changes in ventricular loading conditions, myocardial compliance, and afterload properties because it measures myocardial deformation directly (12). The most common unit of measurement in STE is strain, defined as the change in the length of myocardial fiber at end-systole compared to its original length at end-diastole, expressed as percentage. Strain can be measured in the longitudinal, radial, and circumferential directions. Assessing Global Longitudinal Strain (GLS) using automated STE is an emerging technique for detecting and quantifying subtle disturbances in Left Ventricular (LV) systolic function (13).

2. Objectives

This study was designed to assess the value of GLS beside LVEF as a benchmark for ICD implantation. In this regard, the rate of VTs was assessed in patients with ischemic heart disease or dilated cardiomyopathy who received ICDs. GLS was measured in these patients, as well. The correlation between the probability of VTs incidence as a marker for the efficiency of implanted ICDs and GLS value was also investigated.

3. Patients and Methods

All authors certify that this study is in agreement with the Helsinki declaration and Iranian national guidelines for ethics in research. Also, the research protocol was approved by the research Ethics Committee of Shiraz University of Medical Sciences (reference number: IR.SUMS.REC.700/112). Indeed, all participants were asked to sign written informed consent forms approved by the research Ethics Committee for enrollment in the study.

The sample size was determined by considering power of 80%, type one error of 5%, and effect size of about 50% and using a formula for two means difference. Accordingly, 70 patients with HF (ischemic or dilated cardiomyopathy) who had undergone ICD implantation were enrolled in this study. Ischemic cardiomyopathy was defined as stenosis of more than one coronary artery (left anterior descending artery, left circumflex artery, or right coronary artery) detected by coronary angiography or history of old Myocardial Infarction (MI). Dilated cardiomyopathy was documented by echocardiography. The inclusion criteria for HF patients were set as EF ≤ 40% and having undergone ICD implantation. It should be noted that the implanted ICD recorded any sustained VT. Patients with the following characteristics were excluded from the study: absence of normal sinus rhythm, less than 1-year duration of ICD implantation, history of MI within the last three months, coronary artery bypass graft surgery within three months, and existence of congenital heart disease, vulvular disease, or severe liver or kidney dysfunction.

Biplane Simpson method and longitudinal strain analysis were performed using AFI software by GE vivid E9 color Doppler echocardiography. Global two-dimensional left ventricular longitudinal strain was automatically predicted by the AFI software and was calculated as the weighted average of the segmental peak longitudinal strain amount in three apical 4-chamber, apical 2-chamber, and apical 3-chamber views. Additionally, the patients' demographic information was collected via a questionnaire.

Data analysis was based on the per protocol method. Normal distribution of the continuous variables was checked using Shapiro-Wilks test. The data were expressed as mean ± Standard Deviation (SD). Differences between the study groups regarding continuous variables were evaluated using independent sample t-test or Mann-Whitney test, where appropriated. At this stage, SPSS statistical software, version 21 was used and P ≤ 0.05 was considered to be significant.

4. Results

This study was performed on 70 HF patients aged 40 - 65 years. Among the participants, 63% were male. Besides, 37 and 33 cases were categorized in ischemic and Dilated Cardiomyopathic (DCM) groups, respectively. Follow-up duration after ICD insertion was 1 to 3 years.

The means of LVEF and GLS were lower in the ischemic and DCM patients than in their counterparts. However, neither LVEF nor GLS showed a significant correlation with the type of HF (Table 1). It is noticeable that hereafter, the absolute number of the amounts was considered for comparison.

The prevalence of VTs in two different HF groups was evaluated. The results indicated a slightly larger number of ischemic patients who had undergone ATP/DC shock therapy for their VTs (43.2%) compared to DCM patients (42.4%). However, no significant correlation was observed between the types of HF and VT occurrence.

The study subjects were categorized based on VT occurrence (Table 2). VT was detected only in 30 patients. In fact, when VT occurred, ICD acted as a defibrillator and the patient received ATP/DC shocks. The relationship between

Table 1. The Relationship between LVEF and GLS in Ischemic and DCM Patients

	LVEF		GLS	
	Ischemic	**DCM**	**Ischemic**	**DCM**
Number	37	33	37	33
Mean ± SD	28.64 ± 7.33	29.87 ± 7.46	-9.84 ± 5.45	-9.63 ± 3.11
P value	0.489		0.846	

Abbreviations: LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; DCM, dilated cardiomyopathy

Table 2. The Relationship between LVEF and GLS in Patients with and without VT

	LVEF		GLS	
	VT	**No VT**	**VT**	**No VT**
Number	30	40	30	40
Mean ± SD	26.56 ± 6.62	31.22 ± 7.33	-6.97 ± 3.06	-11.82 ± 4.25
P-value	0.008		< 0.001	

Abbreviations: LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; VT, ventricular tachyarrhythmia

Table 3. The Relationship between GLS amount and VT Incidence in Ischemic and DCM Patients

	Ischemic		DCM	
	VT	**No VT**	**VT**	**No VT**
Number	16	21	14	19
GLS (Mean ± SD)	-6.13 ± 3.46	-12.66 ± 5.02	-7.92 ± 2.29	-10.88 ± 3.7
P-value	< 0.001		0.005	

Abbreviations: GLS, global longitudinal strain; DCM, dilated cardiomyopathy; VT, ventricular tachyarrhythmia

Table 4. The Relationship between LVEF and VT Incidence in Ischemic and DCM Patients

	Ischemic		DCM	
	VT	**No VT**	**VT**	**No VT**
Number	16	21	14	19
LVEF (Mean ± SD)	25.93 ± 6.37	30.71 ± 7.47	27.28 ± 7.07	31.78 ± 7.33
P-value	0.048		0.087	

Abbreviations: LVEF, left ventricular ejection fraction; DCM, dilated cardiomyopathy; VT, ventricular tachyarrhythmia

the amount of GLS and LVEF was also investigated in cases with and without VT. Based on the results, the mean of LVEF was lower in patients with VT than in non-arrhythmic ones. Additionally, the subjects with VT had lower amounts of GLS compared to those without VT. Moreover, VT incidence was significantly associated with both LVEF and GLS amount. Furthermore, more than 88.8% of the patients with GLS amounts less than 10.0 (0 < GLS absolute amount < 10) had received ATP/DC shocks for defibrillator therapy due to the incidence of VTs. GLS amount was measured in ischemic and DCM patients and its relationship with VT incidence was evaluated (Table 3). The results showed that the GLS amount was significantly lower in both ischemic and DCM patients who had received appropriate ATP/DC shocks as defibrillator therapy following VT occurrence in comparison to those who did not show VTs. Remarkably, GLS amount in the ischemic group with VT was about half of those without VT.

LVEF was measured in different HF groups and arrhythmic and non-arrhythmic subjects were compared. Although LVEF was lower in arrhythmic cases in both HF types, this difference was statistically significant only in ischemic patients (Table 4).

5. Discussion

This study aimed to investigate the potential of GLS amount as an indicator for ICD implantation for primary prevention in patients with HF. In so doing, GLS was measured in ICD-implanted HF patients and the incidence rate of VTs was evaluated. According to the results, ICD implantation was found to be an appropriate therapy for individuals with tachyarrhythmia.

The results showed that GLS in combination with LVEF acted more precisely than LVEF alone in identification of patients who would face VTs in future due to ischemic heart disease or dilated cardiomyopathy. Moreover, GLS amount was significantly lower in arrhythmic patients of both ischemic and DCM groups, while LVEF was different only in the ischemic group, but not in the DCM group. It should be noted that the inclusion criterion was LVEF < 40%, while the routine assignment of LVEF for ICD therapy is < 35% (8). This means that the healthier patients with a smaller risk of VTs occurrence had a chance of being entered into the study. Yet, the percentage of patients who were faced with VTs and had GLS amounts less than 10 was as high as 88.8%. It seems that GLS in this range could add a reliable criterion to LVEF for preventing ineffectual insertion and elevating the proportion of recognizing eligible patients for ICD therapy. Nowadays, candidates of ICD therapy, as the primary prevention, are selected based on LVEF. However, it seems that this strategy is not sensitive enough to truly differentiate the patients in need from the others. For instance, a sudden cardiac death study showed that only one fifth of the subjects had LVEF < 35%. This implies that 80% of the patients who had faced SCD were ruled out from ICD therapy (14). On the other hand, there are people with low LVEF (< 35%) who are simultaneously at a low risk of SCD occurrence (10). Therefore, it seems that making decision based solely on LVEF should be revised or improved by utilizing other approaches. GLS reflects the longitudinal contraction of the myocardium and its accuracy has been validated against tagged Magnetic Resonance Imaging (MRI). This method is operator-independent, more reproducible than EF, easily measured, and integrated to standard echocardiogram method in the general population and patients with HF (15). This technique was shown to be a superior predictor of cardiac events and all-cause mortality compared to EF. More recently, GLS was found to be a robust prognostic marker following MI, cardiac surgery, cardiomyopathy, and aortic stenosis. Moreover, GLS has been reported in several conditions, including HF, vulvular heart disease, cardiomyopathy, and ischemic heart disease, as an indicator for short- and long-term complications. It has also been utilized to evaluate LV remodeling, which may occur following an acute MI (16). Some other studies have also highlighted the value of longitudinal strain in predicting arrhythmic events in MI patients (17, 18). Meanwhile, LVEF suffers from low sensitivity in detecting the risk of Ventricular Arrhythmia (VA) (6, 19). The present study results revealed that GLS was a reliable predictor of VT in both ischemic and DCM subjects, whereas LVEF had a significant relationship with VT only in the ischemic group. Moreover, GLS range was defined quantitatively, so that the boundary between qualified patients for ICD therapy and others could be determined.

Overall, the current study findings showed that using GLS beside LVEF led to higher accuracy in prediction of VTs compared to LVEF alone in both DCM and ischemic HF patients with ICD implantation. The results also indicated that more than 88.8% of the patients who had GLS amounts less than -10.0 received ATP/DC shocks for defibrillator therapy. Furthermore, LVEF was significantly correlated to VA in just ischemic patients, while VT was significantly associated with GLS in both ischemic and DCM patients.

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Authors' Contribution

Study concept and design: MHN, RN, and AM. Acquisition of data: MHN, RN, and AM. Analysis and interpretation of data: RN, MS, and IRJ. Drafting of the manuscript: IRJ. Critical revision of the manuscript for important intellectual content: MHN, RN, AM, MS, and IRJ. Statistical analysis: RN and MS. Administrative, technical, and material support: MHN. Study supervision: MHN.

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The authors have no financial interests related to the material in the manuscript.

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