The Effect of Clinical Characteristics and Stent Parameters on Left Ventricular Mechanical Dyssynchrony

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Aim. To study short term effect of stent size and number on left ventricular mechanical dyssynchrony after elective percutaneous coronary intervention (PCI) to left anterior descending (LAD) artery.
Materials and methods. the study included 150 adult patients with LAD lesion treated with PCI using drug-eluting stent. Patients were evaluated pre PCI then 1 month and 3 months post PCI for evaluation of mechanical dyssynchrony using tissue synchronization image (TSI).
Results. Before revascularization mean left ventricular ejection fraction was 51.2±5.7 %, mean time to peak TSI was 213.6±10.9 ms; 1 month after PCI TSI improved significantly to 163.7±17.6 ms (p<0.001), 3 months after PCI showed more improvement to 120.7±26.9 ms (p<0.001). After 3m; 61 patients (40.7%) showed recovery to normal TSI value. The predictors of non-improvement of time to peak TSI after 3 months were diabetes mellitus (p=0.007), dyslipidemia (p=0.001) and stent length (p=0.001), number of stents (p=0.004). There were strong negative correlation between stent length and improvement of the time to peak TSI at 1 month (r=-0.352, p<0.001) and at 3 months (r=-0.509, p<0.001),and also with number of stent at 1 month (r= -0.173, p=0.034) and at 3 months (r=-0.499, p<0.001), but the correlation between stent diameter and improvement of the TSI wasn't significant neither at 1 month nor at 3 months (r=0.055, p=0.504 and r= -0.018, p=0.827) respectively.
Conclusion. Increased number and length of the implanted stents were predictors to non-improvement of mechanical dyssynchrony, while stent diameter didn't affects the recovery.

Key words: stent, coronary vessel, echocardiography

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Background

Left ventricular (LV) systolic function is a major predictor of long-term survival in patients with coronary artery disease. Evaluation of regional and global subclinical LV systolic dysfunction could be a good strategy to identify myocardial regions with impaired coronary artery flow and reduced myocardial perfusion [1].

Among the objectives of a successful percutaneous coronary intervention (PCI) is to improve the myocardial perfusion and LV systolic function. It is clear that the availability of coronary stents, and platelet glycoprotein (GP)IIb/IIIa receptor inhibitors has dramatically changed the early and late clinical outcomes associated with PCI [2].

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The management of long coronary lesions by PCI has become increasingly important because of the rising incidence of long or complex lesions in aging populations. For long lesions, the preferred strategy is long stent PCI. Long lesions were associated with adverse outcomes in PCI treated with bare metal stents. However, the exact impact of lesion length on the short and long-term clinical outcomes of drug-eluting stent (DES) implantations is not clear as yet [3].

Mechanical dyssynchrony is used to describe the mechanical effects of asynchronous ventricular contraction and relaxation, which may or may not be associated with electrical conduction delay. LV dyssynchrony was recognized as electrical conduction delay in systolic heart failure with widened QRS complexes but previous studies have reported that it also

exists in approximately 30-40% of patients with a normal QRS duration [4], it can also occur in those without HF with a preserved LV ejection fraction (LVEF) who have a narrow QRS complex [2]. The presence of LV mechanical dyssynchrony is associated with impairment of LV systolic and diastolic function and adverse clinical outcome and also exercise tolerance [2].

How do stent size and number affect recovery of left ventricular mechanical dyssynchrony after PCI using DES? There is no clear data up till now.

Aim of study: the aim of this study is to evaluate short term effect of stent size (length and diameter) and number on left ventricular mechanical dyssynchrony after elective left anterior descending artery (LAD) stenting with DES using tissue synchronization image (TSI).

Material and methods

Study design

It was a single center, prospective observational study that was conducted during the period from November 2018 till October 2019.

Inclusion criteria: adult patients with angiographically significant LAD lesion treated with PCI using DES were enrolled in the study. Patients were evaluated pre PCI and after 1m and 3m after PCI using TSI.

Exclusion criteria: patients with bundle branch block, previous PCI, previous coronary artery bypass graft (CABG), rhythm other than sinus, rheumatic heart disease, prosthetic valve, complicated or unsuccessful procedure, patients with significant degenerative changes, patients with previous ST-elevation myocardial infarction, and dropped patients from follow up were excluded from the study.

The study was approved by the local ethical committee and all patients signed informed consent

Methods

History taking: with emphases on age, sex and risk factors (diabetes mellitus, hypertension, family history of premature coronary artery disease).

Laboratory: lipid profile, fasting and 2h post prandial blood glucose.

Transthoracic Echocardiography: Echocardiography was performed by (Vivid 7, GE USA) machine with multi-frequency transducer. Off-line quantitative analysis of recorded images with assessment of inter-laboratory reproducibility of measurements.

By conventional echocardiography: two-dimensional echocardiograms were obtained in accordance with the American Society of Echocardiography guidelines. Global LV function was assessed by measuring LV end-diastolic and end systolic volumes from two-dimensional apical views by measuring LV ejection fraction by means of the modified biplane Simpson's method [6].

TSI Portrays regional dyssynchrony on 2D images by transforming the timing of regional peak positive velocity of TDI data into color codes, the normal myocardium, which achieved Vp (peak velocity) at an early stage of contraction, was coded green, which meant no delay in motion (Tp "time to peak velocity" 20-150 ms). The myocardium showing delayed contraction was coded yellow or red according to the degree of delayed time in Vp. The myocardium that achieved Vp at an advanced stage of contraction or diastolic phase was coded yellow, for a mild to moderate delay (Tp, 150-300 ms) or red for a severe delay (Tp, 300-500 ms) [6].

Coronary angiography: coronary angiography was done for all the patients according to the Judkins technique, significant coronary artery disease was defined as >70% luminar diameter stenosis. The following data was obtained:

- Site of stent implantation within LAD.
- Length, diameter and number of stents.
- TIMI flow after stent deployment.

Statistical methods

Data management and statistical analysis were done using SPSS v.25. (IBM, USA). Numerical data was summarized as means and standard deviations. Categorical data was summarized as numbers and percentages. Speckle tracking echocardiography and TSI of different segments were compared at different timepoints using repeated measures ANOVA. Post hoc analysis was done and all post hoc were Bonferroni adjusted for multiple comparisons. Correlation analysis was done between stent length, stent diameter and percent change TSI at 1 month and 3 months using Pearson's correlation. "r" is the correlation coefficient. It ranges from -1 to +1. -1 indicates

strong negative correlation. +1 indicates strong positive correlation while 0 indicates no correlation. Multivariate linear regression analyses were done for prediction of TSI at 3 months. Regression coefficient (β) with 95% confidence intervals were calculated for predictors. All P values were two sided. P values less than 0.05 were considered significant.

Results

This is a single center, prospective study that was conducted during the period from October 2018 till June 2019. Of the 265 patients included in the study, only 150 patients fulfilled the inclusion criteria (11 patients had diseased vessels other than LAD, 23 patients had previous revascularization, 44 patients needed revascularization in right coronary artery or left circumflex artery, 15 patients had rhythm other than sinus rhythm, and 22 dropped patients during follow up visits).

Of the 150 patients of the study 100 patients (66.7%) were males, with mean age 53±9; 65 patients (43.3%) were diabetics, 76 patients (50.7%) were hypertensive, 80 patients (53.3%) were smokers, while 15 patients (10%) were ex-smokers, 89 patients (59.3%) had dyslipidemia and 53 patients (35.3%) had family history of premature coronary artery disease.

Before revascularization the mean left ventricular end systolic volume was 43.2±12.8 ml, the mean left ventricular end diastolic volume was 88.3±21.6 ml, and mean LVEF was 51.2±5.7%, WMSI (wall motion score index) 1.10±0.38, mean duration of QRS was 110±8 ms, mean TSI was 213.6±10.98 ms.

All patients had drug eluting stents, 132 patients (88%) had single stent while 18 patients (12%) had two stents. As regard site of stent 15 patients (10%) had distal LAD stenting, 100 patients (66.7%) had mid LAD stenting while 35 patients (23.3%) had proximal LAD stenting, and mean stent length (mm) was 29.9±10 with mean stent diameter (mm) 3.16±0.4 (table 1).

Before PCI 112 patients (75%) had mechanical dyssynchrony, 1 month after PCI mean TSI improved significantly from 213.6±10.9 ms to 163.7±17.6 ms (p<0.001), 3 months after PCI showed more improvement to become 120.7±26.9 ms (p<0.001); after 3 months 61 patients (40.7%) showed recovery to normal TSI values in all segments (table 2).

Table 1. Stent characteristics in the whole study population

Parameter	value	
Stent Type	DES, n (%)	150 (100.0)
Site	Distal, n (%)	15 (10.0)
	Mid, n (%)	100 (66.7)
	Proximal, n (%)	35 (23.3)
Number	1 stent, n (%)	132 (88)
	2 stents, n (%)	18 (12)
Length, mm		29.9±10
Diameter, mm		3.16±0.4

DES – drug-eluting stent

Data are presented as M±SD, unless otherwise indicated

Table 2. Value of TSI prePCI, 1 month and 3 months post PCI

TSI	Mean	p value
Pre	213,6±10,9	<0.001
1 month	163,7±17,6	
3 months	120,7±26,9	

Data presented as M±SD

Repeated measures ANOVA was used. Post hoc analysis was done and different letters indicate significant pair. All post hoc were adjusted for multiple comparisons.

TSI – tissue synchronization imaging, PCI – percutaneous coronary intervention

By multivariate linear regression analysis the predictors of non improvement of TSI after 3 months were diabetes mellitus (p=0.007), hypertension (p=0.015), smoking (p=0.011), dyslipidemia (p=0.001), baseline LVEF% (p<0.001), and stent length(p=0.001), number of stents (p=0.004) (table 3).

There was strong negative correlation between stent length and improvement of the time to peak TSI at 1 month (r=-0.352, p<0.001) and at 3 months (r=-0.509, p<0.001). also there was strong negative correlation between number of stents and improvement at 1 month (r= -0.173, p=0.034) and at 3 months (r=-0.499, p<0.001), but the correlation between stent diameter and improvement of the TSI wasn't significant neither at 1 month nor at 3 months (r=0.055, p=0.504 and r=-0.018, p=0.827) respectively (table 4).

Table 3. Multivariate linear regression analysis for prediction of TSI at 3 months

Parameter	β	95% CI for β	p value
Age	0.273	-0.099-0.645	0.15
Gender	-4.254	-13.186-4.678	0.348
DM	8.547	2.036-15.059	0.01
Hypertension	8.797	1.729-15.866	0.015
Smoking	11.446	2.653-20.238	0.011
Dyslipidemia	11.539	4.617-18.46	0.001
LVESV	0.044	-0.242-0.331	0.761
LVEF	-1.315	-1.965 - -0.664	<0.001
Stent length	1.609	1.287-1.931	<0.001
Stent diameter	-0.422	-8.439-7.595	0.917
Stent number	10.956	3.637-18.275	0.004

β – regression coefficient, 95% CI – 95% confidence interval,

TSI – tissue synchronization imaging, DM – diabetes mellitus, LVESV – left ventricular end systolic volume, LVEF – left ventricular ejection fraction

Discussion

TSI is an imaging modality that allows regional myocardial velocity measurements. Precise determination of the amplitude, timing of onset and peak systolic and diastolic velocities can be obtained in relation to the electrocardiogram signal [7].

LV dyssynchrony has for several years been the target of cardiac resynchronization therapy, indicating that decreasing LV dyssynchrony provides functional benefits with improved systolic and diastolic function as a results. LV dyssynchrony measured as the time difference between peak anteroseptal and peak posterior radial strain is a strong prognosticator of adverse outcomes in HF with reduced ejection fraction even in the absence of electrical dyssynchrony. Also, LV mechanical dyssynchrony (LVMD) has been shown to be an independent predictor of ventricular arrhythmias in patients with non-ischemic dilated cardiomyopathy and in patients following anterior myocardial infarction. LV dyssynchrony, has also been shown to be a sensitive marker of the degree of subclinical atherosclerotic burden in coronary and carotid arteries in the multiethnic study of atherosclerosis [8].

In a recent study LVMD may be a potential candidate for prediction of sudden cardiac death in the general population. These considerations point to LVMD being a sensitive integrated marker of both ischemic and nonischemic cardiovascular mortalities [9].

The effect of revascularization on improvement of mechanical dyssynchrony is studied in patients with acute coronary syndrome [10, 11], but not well studied in patients with elective PCI.

To the level of our knowledge this is the first study to evaluate the effect of stent size and number on recovery of left ventricular mechanical dyssynchrony in patients with normal LVEF and QRS duration.

Successful PCI should be evaluated at different levels not only angiographic success but also clinical success. Some patients in spite of successful angiographic results of PCI and good systolic function as evaluated by LVEF, still complains of dyspnea and decreased exercise capacity which may be explained by mechanical dyssynchrony.

The present study included one hundred and fifty patients of both genders during the period from November 2018 till October 2019. Patients were evaluated pre-PCI, 1 month and 3 months after PCI by conventional echo and TSI.

In the current study there was significant improvement of TSI which was observed at 1 month and at 3 months (p<0.001), 40.7% of the included patients recovered to normal value. There was significant negative correlation between stent length and number and improvement of mechanical dyssynchrony, but there wasn't significant correlation regarding stent diameter.

Table 4. Correlation between stent length, diameter and number and % decrease of TSI at 1 and 3 months

TSI	Stent length		Stent diameter		Stent number	
	r	p	r	p	r	p
1 month	-0,352	<0,001	0,055	0,504	-0,173	0,034
3 months	-0,509	<0,001	-0,018	0,827	-0,499	<0,001

TSI – tissue synchronization imaging, r – correlation coefficient

This was comparable to S. Mostafa et al., who evaluated the impact of elective PCI on left intraventricular mechanical dyssynchrony in patients with chronic stable angina. They showed that the latest activated segment improved by 21.02% from baseline values. One month after PCI, it improved by 41.69% from baseline values. The Ts values of all segments were significantly decreased in post-PCI measurements ($p<0.001$) [12, 13].

Also S. Inci et al. studied the effect of percutaneous coronary intervention on left ventricular dyssynchrony. They found that the tissue synchronization values of the basal anteroseptal, basal anterior and mid anterior segments were significantly decreased 1 week after PCI (p value <0.01) [14].

Why size matter? Asked B. Edoardo et al. [15], they found what stent size (length and diameter) ensures the best immediate result and the lowest possible long-term complication rate. It is known that larger stents induce more trauma to vessels and therefore more intimal hyperplasia, more edge dissections and more coronary ruptures and so more incidence of complications.

Stent length was an important predictive factor of LV recovery to normal value after elective PCI, it was associated also with increase in major adverse cardiac events [16]. Sandeep et al. [16] studied the effect of stent length on clinical outcome in patients with coronary artery disease founded that overall major adverse cardiac events was significantly high in patients with stent length more than 32 mm compared to 29 to 32 mm and 24 to 28 mm ($p=0.045$). Stent length has been major predictor of adverse events after PCI.

This was disconcordant with M. Agirbasli et al. [17] who found that the mean stent length was 17.4±6mm and the stent length did not correlate with the LVEF change ($p = 0.369$), this can be explained that the stents were relatively short. While, patients who received LAD stent diameter >3 mm had significantly higher LVEF change after PCI compared to those who received a stent with ⩽3 mm in diameter P value =0.041

Most of the studies that included DES patients, focused on long term outcome to study the effect of limited neoinitimal hyperplasia on outcome, other studied its value in different groups of patients as diabetics. Limited data about short term outcome using speckle tracking echocardiography which was our aim in the present study.

Limitations

The main limitations of the present study are single centre, short term follow up, all cases had focal LAD lesions and non of the cases had complex PCI or complicated procedure, all patients had pre PCI normal ejection fraction by conventional echo and non had impaired systolic function so our focus on recovery by deformation image in patients with normal ejection fraction.

Conclusion

After elective PCI of LAD artery using DES number of stents implanted and length of stents were predictors to improvement of mechanical dyssynchrony as you go shorter in stent length and fewer in number of stent implanted, left ventricle has better chance to improve while stent diameter doesn't affect LV recovery.

Study registered to: clinicaltrials.gov (NCT04228874).

Relationships and Activities: none.

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