

Left Ventricular Angiography Post Primary Percutaneous Intervention-does it Predict Subsequent Left Ventricular Dysfunction?

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Abstract

Objectives: We aimed to assess whether LV dysfunction assessed by LV angiography (LVA) during PPCI for STEMI predicts subsequent LV dysfunction at follow up. Left ventricular (LV) function as assessed by echocardiography has been demonstrated to improve in the first 6 months following primary percutaneous coronary intervention (PPCI). Data regarding the predictive value of LV angiography (LVA) performed immediately following PPCI are limited.

Methods: A retrospective analysis of our tertiary centre angiographic database was performed (2011-2013). Patients were divided into two groups based on LVA. Group 1: normal or mild LV dysfunction and group 2: moderate or severe LV dysfunction.

Results: Complete dataset was available for 89 patients (of a total of 194). 28.1% (16 patients) in group 1 compared to 46.9% (15 patients) in group 2 failed to improve LV function from baseline as assessed by follow-up echocardiography. LV function on LVA correlated significantly with subsequent LV function at follow up (Spearman's rho $p=0.007$). Binary regression analysis demonstrated that Symptom to Balloon Time (STB) was a significant predictor (OR 1.003, 95% CI 1.001-1.005, $p=0.008$) of lack of LV function recovery at a median follow up of 10 months. Patients in whom the thrombectomy catheter was used were less likely to have abnormal LV function at follow up (OR 0.214, 95% CI 0.063-0.730, $p=0.014$).

Conclusions: Baseline abnormal LV function on LVA predicted LV dysfunction at follow up. Increased STB time and lack of thrombectomy catheter use are significant predictors of abnormal LV function at follow up.

Condensed abstract: We aimed to assess whether LV dysfunction assessed by LV angiography (LVA) during PPCI for STEMI predicts subsequent LV dysfunction at follow up. A retrospective analysis of our tertiary centre angiographic database was performed (2011-2013). Patients were divided into two groups based on LVA - group 1: normal or mild LV dysfunction and group 2: moderate or severe LV dysfunction. Binary regression analysis demonstrated that Symptom to Balloon Time (STB) was a significant predictor (OR 1.003, 95% CI 1.001-1.005, $p=0.008$) of lack of LV function recovery at a median follow up of 10 months. Patients in whom the thrombectomy catheter was used were less likely to have abnormal LV function at follow up (OR 0.214, 95% CI 0.063-0.730, $p=0.014$). Baseline abnormal LV function on LVA predicted LV dysfunction at follow up. Increased STB time and lack of thrombectomy catheter use are significant predictors of abnormal LV function at follow up.

Keywords: Left ventricular function; STEMI; Echocardiography

Background

Left ventricular (LV) function following primary percutaneous coronary intervention (PPCI) as assessed by echocardiography has been demonstrated to improve in the first 6 months following PPCI [1]. Multiple predictors of LV function recovery assessed by baseline and follow up echocardiography have been demonstrated in previous studies including gender, cardiac biomarkers, symptom to balloon time (STB) and sum of ST segment elevation [1-3].

Data regarding the predictive value of LV angiography (LVA) performed at the end of the PPCI procedures are lacking. A recent survey of interventional cardiologists has shown that 66% of operators perform an LV angiogram (LVA) at the end of the PPCI procedure,

while 9% perform LVA before PPCI [4]. The purpose of this study was to determine correlation between LV angiography performed post PPCI for STEMI and subsequent LV dysfunction on echocardiography at follow up.

Methods

We performed a retrospective observational analysis of the PPCI database from 2011 to 2013 at our tertiary cardiac centre. All patients with STEMI presenting for PPCI were included irrespective of age or presence of cardiogenic shock. Patients who did not fulfil criteria for STEMI or did not undergo PPCI were excluded. Patients were brought to our tertiary PPCI centre directly by Emergency Medical Services (EMS). Angiograms were analysed using the HeartLab[®] analysis system by two independent observers. Coronary angiograms were

analysed for infarct related artery (IRA) location, initial and final Thrombolysis in Myocardial Infarction (TIMI) flow [5,6], presence and grade of thrombus, use of stent, post dilatation, distal embolization, myocardial blush grade (MBG) and LV ejection fraction (LVEF) on LVA (by measurement [7] and visual assessment in the right anterior oblique plane). We ensured that the LVEF was calculated in the initial phase and did not include cine loops with premature ventricular contractions. Patients were divided into two groups based on the estimation of LV function on LVA performed at the time of PPCI (normal or mild LV = group 1, moderate or severe LV = group 2). Follow up echocardiography assessed the LV function by Simson's biplane method. Definitions are in Appendix 1.

Demographic and procedural variables are presented as percentage (categorical variable) or median (Inter Quartile Range). Differences in the variables between the two groups were analysed by the chi-square test or Fisher's exact test for categorical variables and student's t-test or Mann Whitney u test for continuous variables. Missing values were replaced with the mean of two neighbouring points. Variables with missing values $\geq 10\%$ were not included in any analysis.

This study was reviewed and approved by UHN research ethics committee (UHN REB # 14-8100-BE) and has been performed in accordance with the ethical standards in the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using SPSS version 22. A propensity score was derived using LVA as the dependant variable and the following baseline characteristics as covariates: age, gender, hypertension (HTN), diabetes mellitus (DM), history of smoking, hypercholesterolemia, history of prior cerebrovascular accident (CVA) and peripheral vascular disease (PVD).

The propensity score was included as a covariate in a multivariable binary regression analysis to assess predictors of LV function recovery on follow up. The binary regression model constructed included variables which ensured absence of outliers, lack of multicollinearity and adequate sample size, with the final model ensuring existence of relationship between the dependent and the independent variables (IDV). The IDVs included were the derived propensity score, LV function on LVA at the time of PPCI, symptom onset to balloon time (STB), presence of thrombus, use of a thrombectomy catheter, final TIMI flow and MBG.

In addition a cross-tabs analysis was performed to analyse any relationship between covariates and LV function on follow up.

Inter-observer variability was tested by Kendall's tau-b (<0.2 = very poor agreement, $0.2-0.40$ = slight agreement, $0.4-0.6$ = moderate agreement, $0.6-0.8$ = high agreement, >0.8 = excellent agreement). Inter-observer variability for MBG, TIMI flow and LV function by LVA were all excellent (all >0.8 , $p < 0.01$).

Results

A complete dataset was available for 89 patients (of a total of 194 patients) of whom 57 (64%) patients were in group 1 and 32 (36%) patients in group 2. Group 1 had a significantly greater proportion of female patients (Table 1). There were no differences in the other baseline characteristics between the two groups.

Variable	Group 1	Group 2	Significance value	p
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	LVA grade 1 or 2	LVA grade 3 or 4	
	n=57	n=32	
Age	61.0 (53-66)	62.5 (55.5-69.5)	p=ns
Female	33.3 (19)	12.5 (4)	p=0.04
HTN*	56.1 (32)	43.8 (14)	p=ns
DM**	7.0 (4)	18.8 (6)	p=ns
Hypercholesterolemia	47.4 (27)	53.1 (17)	p=ns
Smoker	61.4 (35)	50.0 (16)	p=ns
Prior CABG#	0	0	na
Prior Stroke	1.8 (1)	9.4 (3)	p=ns
PVD#	3.5 (2)	3.1 (1)	P=ns
Cardiogenic Shock on admission	7.0 (4)	12.5 (4)	p=ns
LV \neq function on follow-up echocardiography (abnormal)	28.1 (16)	46.8 (15)	p=0.06

HTN*: Hypertension; DM**: Diabetes Mellitus; CABG#: Coronary Artery Bypass Graft; PVD#: Peripheral Vascular Disease; LV \neq : Left Ventricular

Table 1: Baseline characteristics of patients.

The Left Anterior Descending Artery (LAD) was more likely to be the culprit Infarct Related Artery (IRA) in patients from group 2 compared to group 1 (Table 2). There was no difference in initial pre-wire TIMI 0/1 flow between the groups (67.9% group 1 versus 71.9% group 2, p=ns). There was no correlation between distal embolization and lack of LV function recovery at follow up (35.5% without distal embolization versus 30.8% with distal embolization with abnormal LV at follow up, p=ns). Of the 66 patients with thrombus grade ≥ 4 , those in whom GPI was used were more likely to normalize their LV function at follow up (69.2% versus 54.7%, p=ns).

Variable	Group 1	Group 2	Significance p value
	LVA grade 1 or 2 n=57	LVA grade 3 or 4 n=32	
IRA ⁺ LAD**	33.3 (19)	56.3 (18)	p=0.04
Collaterals present	47.4 (27)	40.6 (13)	p=ns
MVD***	38.6 (22)	31.3 (10)	P=ns
TIMI# 3 flow final	96.5 (55)	87.5 (28)	p=ns
Thrombus grade ≥ 4	70.2 (40)	81.3 (26)	p=ns
Use of thrombectomy catheter	21.1 (12)	31.3 (10)	p=ns
Symptom to Balloon Time	181(129-352)	209 (137.5-311.8)	p=ns
Stent used	94.7 (54)	90.6 (29)	p=ns

DES[#]	14.8 (8/54)	6.9 (2/29)	p=ns
Post dilatation	71.9 (41/54)	68.8 (22/29)	p=ns
GPI[‡] use	21.1 (12)	15.6 (5)	p=ns
ACEI^{¶¶} at discharge	93.0 (53)	90.0 (29)	p=ns
Beta blocker at discharge	94.7 (54)	93.7 (30)	p=ns
ACEI at follow up	89.4 (42/47)	89.3 (25/28)	p=ns
Beta blocker at follow up	97.9 (46/47)	78.6 (22/28)	p=ns

IRA[‡]: Infarct Related Artery; LAD^{**}: Left Anterior Descending; MVD^{***}: Multi Vessel Disease; TIMI[†]: Thrombolysis In Myocardial Infarction; DES[#]: Drug Eluting Stent; GPI[‡]: Glycoprotein IIb/IIIa Inhibitor; ACEI^{¶¶}: Angiotensin Converting Enzyme Inhibitor.

Table 2: Procedural characteristics of patients.

Predictor	Significance	Odds Ratio	95% C.I.
Symptom to Balloon time	0.008	1.003	1.001 – 1.005
Thrombectomy catheter use	0.014	0.214	0.063 – 0.730

Table 3: Predictors of poor LV function recovery.

LV function on LVA at the time of PPCI was not a predictor of subsequent LV dysfunction by regression analysis but we demonstrated a significant correlation between LVA at the time of PPCI and subsequent follow up LV function (Spearman's rho p=0.007). 28.1% (16 patients) in group 1 compared to 46.9% (15 patients) in group 2 failed to recover their LV function back to normal on follow up echocardiography.

A significant relationship was also demonstrated between initial (pre-wire) thrombus grade ≥ 4 and lack of LV function recovery on follow up echocardiography (Cross tabs Fisher's p=0.012). There was no association between angiotensin converting enzyme inhibitor (ACEI) or beta-blocker use on discharge or follow up and LV function at follow up.

Discussion

In this retrospective observational study we have demonstrated that patients with reduced LV function on LVA at the time of index PPCI are less likely to recover their LV function back to normal at follow up. This is corroborated by the significant correlation between LV function by LVA and subsequent LV function on follow up echocardiography. In patients with STEMI undergoing PPCI, the adverse impact of LV dysfunction (assessed during index PPCI) is well known [8]. Data demonstrating the effect of index LV function (during PPCI) by LVA on subsequent LV function recovery are limited. Our study is one of the first to demonstrate the correlation between initial LV function on LVA and subsequent follow-up LV function on echocardiography. Physicians should be encouraged to perform an LVA at the end of the PPCI procedure as this practice is not widespread [4]. This would help to ensure implementation of optimal secondary prevention measures that aid in LV recovery.

Procedural characteristics were similar between the two groups. Patients in group 2 were less likely to be on beta blockers at a median follow up time of 10 months. Follow up echocardiography for assessment of LV function was performed at a median time interval of 10 months.

Symptom -To-Balloon-Time (STB) was a significant predictor of abnormal LV function on binary regression analysis (OR 1.003, 95% CI 1.001-1.005, p=0.0008, Table 3). The "Patient factor" component accounted for the majority of the STB (Figure 1). A numerical (but non-significant) increase in the overall STB was observed in group 2 compared to group 1 (Table 2). Regression analysis also demonstrated that patients in whom a thrombectomy catheter was used during the PPCI were less likely to have abnormal LV function on follow up echocardiography (OR 0.214, 95% CI 0.063-0.730, p=0.014, Table 3).

Traditionally, the door to balloon (DTB) time has been considered a performance measure. Shorter DTB times are associated with better clinical outcomes [9-12]. It may however, be more relevant to focus on the STB. Our study demonstrated that increased STB time was a predictor of abnormal LV function at follow up. Rollando et al. have demonstrated that reduced STB time is associated with reduced mortality in patients with STEMI undergoing PPCI [13]. This benefit extends out to 7 years after the index STEMI event [13]. STB is the additive result of "patient factor" (time to FMC+ EMS response time + EMS to Cath. Lab. Notification time) + "transport factor" (EMS or transport to Cath. Lab time) + "procedural factor" (patient in the catheterization laboratory to balloon time). The "patient factor" component of STB, rather than transport or procedural factors, appeared to drive the delay in both groups in our study, (Figure 1). Increased time from first medical contact (FMC) to initiation of reperfusion has also been shown to be a predictor of mortality, the higher the FMC to reperfusion time, the greater the mortality rate [14]. European Society of Cardiology and American College of Cardiology Foundation /American Heart Association guidelines recommend that FMC to PPCI should be ≤ 90 minutes for patients with a STEMI undergoing PPCI and ≤ 60 minutes in patients with a large area of myocardium at risk [15,16]. The data we collected did not specify the time of FMC and only specified time of catheterisation laboratory notification. Better patient education regarding ischaemic symptoms and "calling for help" are essential to improving STB.

Patients in our study in whom manual thrombectomy catheter was used were less likely to have an abnormal LV at follow up. The TOTAL trial demonstrated no reduction in clinical event rates with the routine use of a thrombectomy catheter during PPCI for STEMI [17] but Overgaard et al. have shown that use of thrombectomy catheter is associated with reduced distal embolization in a STEMI setting [18]. Jo et al. [19] also demonstrated improved LV function on follow up echocardiography in STEMI patients who had undergone PPCI with

manual thrombectomy catheter compared to those who had PPCI alone. A plausible theory is that use of the thrombectomy catheter improves LV function recovery by improvement in microvascular perfusion. We demonstrated correlation between high thrombus grade (≥ 4) and lack of LV function recovery. Intracoronary thrombi impair LV microvascular perfusion and function [20] and thrombus size and composition are major predictors of distal embolization [20-22]. Use of the thrombectomy catheter may result in less distal embolization of large intra-coronary thrombi and reduce microvascular perfusion.

The majority of the patients were on beta-blockers and ACEI at discharge and on follow up although a complete dataset was not available for the follow up patients (Table 2). Trials and guidelines have demonstrated the benefit of these two classes of drugs for patients post MI [15,16,23,24]. We demonstrated no association between being on beta-blockers and ACEI (at discharge or follow-up) and LV function recovery, possibly because of the limited sample size.

Study Limitations

Firstly this is an observational study with a limited number of patients because of the lack of a complete dataset in a significant number of patients. Inclusion of a propensity score has circumvented some of the limitations of this observational study. Secondly time of FMC was not available. The “patient factor” component would include time to FMC, EMS response time and EMS to Cath. Lab. Notification time. It is highly unlikely that EMS response time or EMS to Cath. Lab. Notification time would have contributed significantly to any delay.

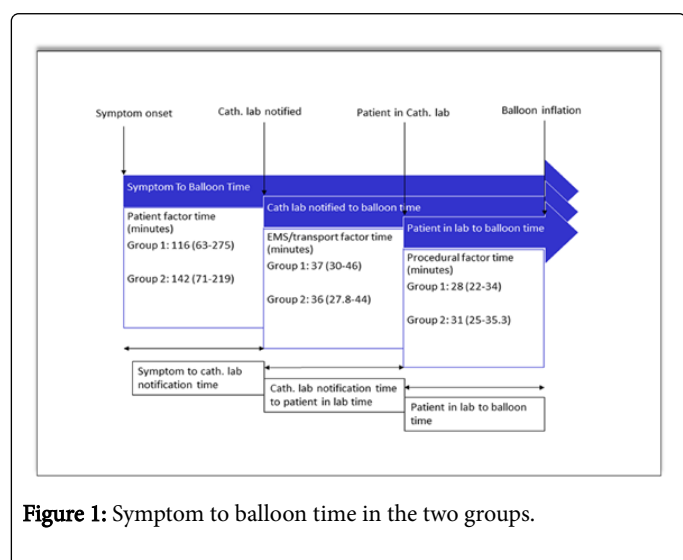


Figure 1: Symptom to balloon time in the two groups.

Conclusions

In conclusion, patients with abnormal LV function on LVA (at the time of PPCI for STEMI) are less likely to recover their LV function to normal on follow up. LV function on LVA significantly correlates with subsequent LV function at follow up. Predictors of reduced LV function at follow up include increased STB and lack of thrombectomy catheter use. Larger prospective studies are required to corroborate these findings.

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