

STUDY COMPARING CORONARY STENTING IN SMALLER VESSELS VERSUS LARGE VESSELS

Harish Oruganti, Indrani Garre, Bharathi Vanaparty, Sreekanth Yerram

ABSTRACT:

Background: *Smaller vessel PTCA account to approximately on third of all PTCA worldwide. With increasing incidence of diabetes mellitus and aging, this proportion can increase considerably. This is a region of interest for us because Indians, in particular, are known to have smaller coronaries. There are limited studies in coronary vessels < 2.5 are available. Most of the previous studies defined small vessel as < 3 or 2.75 mm.*

Methods and Results: *This is an observational single center study where we analyzed 650 patients, 52 in the small vessel group (< 2.5 mm) and 598 in large vessel group (≥ 2.5 mm) with similar mean age between the both the groups (57.5 ± 11.4 vs 57.9 ± 11.1 yrs). Hypertension and smoking are more in large vessel group (74.7% vs 61.9, $p=0.004$; 22.1% vs 13.4%, $p=0.007$), whereas no difference for presence of diabetes (54.2% vs 54.3%) or type of CAD (CSA – chronic stable angina – 70.3% vs 76.1%, $p=0.2$). Large vessel group patients had more LV dysfunction (40.3% vs 24.6%, $p=0.000$).*

Mean Pre reference diameter was 1.9 ± 0.5 mm in small vessel group versus 2.9 ± 0.5 mm in large vessel group. Mean minimum lesion diameter in small vessel group is 0.8 ± 0.3 mm versus 1.3 ± 1.9 mm in large vessel group. Mean pre-lesion length is 16.7 ± 3.5 mm in small vessel group versus 18.3 ± 8.3 mm in large vessel group. Mean stent size is 2.33 mm in small vessel group versus 3.04 mm in large vessel group. Mean stent length is 17.27 mm in small vessel group versus 21.8 mm in large vessel group. The success of PCI in small vessel group was 96% (not able to deliver stent in one patient and in one patient there was a non-flow limiting distal stent dissection) and 98% in large vessel group.

In one year follow-up, 5 (3.5%) patients from small vessel group and 34 (4.5%) patients from large vessel group had MACCE which is not statistically significant ($p=0.6$)

Conclusions: *Small vessel (really small means less than 2.5 mm) PCI, not only acute but also one-year results are good with MACCE rate of 3.5% and comparable to large vessel PCI.*

Keywords: *Small Coronaries, Percutaneous Coronary Interventions.*

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INTRODUCTION:

Percutaneous transluminal coronary angioplasty with stenting is an established treatment for patients with symptomatic coronary artery disease [1,2]. More than a third of coronary lesions treated with angioplasty are estimated to be in vessels smaller than 3.0 mm (in a few studies, it is almost about 50% [3,4]). With increasing aging population and with the increasing incidence of diabetes mellitus, this proportion is likely to increase further. The topic of small vessel stenting is of importance for us, as Indians are believed to have smaller coronary arteries and increasing diabetics. Most studies that have documented the benefit of elective stent implantation following angioplasty, including the BENESTENT¹ and STRESS² trials, had excluded lesions in vessels with a diameter of less than 3.0 mm. Therefore, stenting is generally recommended as a treatment option only for larger vessels.³ Analyses after PTCA have generally shown an inverse relationship between vessel size and severity of angiographic restenosis at follow-up [5,6]. (PCI) of small vessels has historically been associated with high rates of acute vessel closure, restenosis, target lesion revascularization (TLR), and stent thrombosis, particularly in diabetic patients [7,8,10]. The purpose of the present study is to analyze the outcomes and various factors associated with smaller vessel (<2.5 mm diameter) coronary stenting.

METHODS:

This is an observational single center study where we analyzed the PCI patient details over two-year period at Nizam's institute of medical sciences, Hyderabad, Telangana, India.

Evaluation of data on stenting in this subgroup of patients is complicated by the fact that studies have used different criteria to define "small" coronary artery. The upper cut-off for reference vessel diameter has varied from 2.5 to 3.0 mm. Earlier studies had mostly defined vessels <3 mm as small vessels which may not be true in Indians scenario. We have taken a cut off value of 2.5 mm. Patients with a lesion with core laboratory-

measured RVD ≤ 2.25 mm was defined as the small vessel group, while those with an RVD > 2.5 mm were defined as the large vessel group. Patients with multiple lesions treated during the procedure were categorized accordingly. Target lesion failure (TLF) was defined as cardiac death, target vessel myocardial infarction, and clinically driven TLR. Major adverse cardiac events (MACE) were defined as all-cause death, myocardial infarction, emergent coronary artery bypass surgery, or repeat clinically indicated target lesion percutaneous or surgical revascularization. Target vessel failure (TVF) was defined as cardiac death, myocardial infarction, or clinically driven TVR by percutaneous or surgical methods. Clinically driven TLR (and TVR) was defined as revascularization at the target lesion (and target vessel) associated with positive functional ischemia study or ischemic symptoms and an angiographic minimal lumen diameter stenosis $\geq 50\%$ by quantitative coronary angiography, or revascularization of a target lesion with diameter stenosis $\geq 70\%$ by quantitative coronary angiography without either angina or a positive functional study. Stent thrombosis was defined as Academic Research Consortium (ARC) definite or probable stent thrombosis [9].

Institutional ethics committee approval was taken and we collected clinical, demographic and PCI details of all these patients. All these patients were followed for one year either clinically or telephonically.

The study population comprised all 650 patients, 52 in the small vessel group (< 2.5 mm) and 598 in large vessel group (≥ 2.5 mm) from Nizam's institute of medical sciences, with successful stent placement (stent at the desired position, residual stenosis $< 30\%$) during the period from May 2013 through may 2015. Excluded from the study were patients with cardiogenic shock or mechanical ventilation before PTCA.

All patients received 5000 U of heparin and 325 mg of aspirin with 300mg of clopidogrel or other antiplatelet according to Mehran bleeding risk score before PTCA.

Adequacy of the result was based solely on visual assessment of the stent site in the angiogram; Standardized image acquisition was used, consisting of multiple projections for each lesion, accurately reproduced in each angiographic session. Quantitative analysis was performed on the baseline angiogram, on that containing the maximally inflated balloon, and on final post stenting angiogram.

Statistical Analyses:

Statistical analysis was performed with SPSS statistical software. The study population was subdivided into 2 groups according to RD; the ranges were < 2.5 mm for the first group, > 2.5 mm for the second. Continuous parameters are presented as mean \pm standard deviation and compared using the t-test or Wilcoxon rank-sum test as appropriate. Nominal parameters are presented as percentages and compared using Fisher's exact test. Multivariate logistic regression was used to assess the independent role of vessel size in restenosis after adjustment for other covariates. Differences were statistically significant when the respective P values were < 0.05 .

RESULTS:

Of 650 patients, 52 were in the small vessel group (< 2.5 mm) and 598 were in large vessel group (≥ 2.5 mm).

Mean age was similar between both the groups (57.5 ± 11.4 vs 57.9 ± 11.1 yrs.). Percentage of females was significantly higher in the small vessel group (31(59.6%) compared to large vessel group 197(32.9%), $p=0.001$.

Table 1 shows that hypertension and smoking were found to be more common in large vessel group (74.7% vs 61.9%, $p=0.004$; 22.1% vs 13.4%, $p=0.007$), but there was no difference for presence of diabetes (54.2% vs 54.3%) or type of CAD (CSA -chronic stable angina - 70.3% vs 76.1%, $p=0.2$) between the two groups. Large vessel group patients had more LV dysfunction. (40.3% vs 24.6%, $p=0.000$). There was no difference in anthropometric parameters like height weight or BMI between the two groups as shown in table 2.

Table 1: Baseline demographic patient characteristics in small vessel and large vessel groups

Variable	Small Vessel	Large Vessel	p value
Number of patients	52	598	
Age (Mean \pm SD)	57.5 \pm 11.4	57.9 \pm 11.1	0.72
Sex (Females)	31(59.6%)	197(32.9%)	0.000
Hypertension (%)	61.97%	74.7%	0.004
Diabetes (%)	54.2%	54.3%	0.98
Smoker (%)	13.4%	21.1%	0.007
LV dysfunction (%)	24.7%	40.3%	0.000
Multi Vessel Disease (%)	20.4%	37.8%	0.000

Table 2: Comparison of clinical parameters between two groups

Variable	Small Vessel		Large Vessel		p value
	Mean± SD	Median	Mean± SD	Median	
SBP (mm Hg)	152.16±70	150	149.28±75	150	0.37
DBP (mm Hg)	75.14±40	80	76.01±40	70	0.83
Height (cm)	160.68±140	161	159.61±118	160	0.30
Weight (kg)	64.8±36	64	63.66±35	62	0.39
BMI (kg/m ²)	24.50±18.37	24.387	24.71±19.78	24.242	0.30

SBP: systolic blood pressure, DBP: diastolic blood pressure, BMI: body mass index Pre-ref: pre-reference vessel diameter, Pre-MLD: pre-minimal lumen diameter, Post-MLD: post minimal lumen diameter.

Table 3 shows that mean Pre-reference diameter was 1.9±0.89 mm in small vessel group versus 2.42±0.33 mm in large vessel group. Mean minimum lumen diameter in small vessel group is 0.8±0.36 mm versus 1.3±1.9 mm in large vessel group. Smaller vessel group has shorter length and fewer multivessel involvements compared to larger vessel group. Mean pre-lesion length is 16.7±3.5 mm in small vessel group versus 18.3±8.3 mm in large

vessel group. Mean stent size is 2.23 mm in small vessel group versus 3.04 mm in large vessel group. Mean stent length is 17.27 mm in small vessel group versus 21.8 mm in large vessel group. Success of PCI in small vessel group was 96% (not able to deliver stent in one patient and in one patient there was a no flow limiting distal stent dissection) and 98% in large vessel group.

Table 3: Comparison of angiographic characteristics of the two groups

Angiographic parameters	Small Vessel		Large Vessel		p value
	Mean± St Dev	Median	Mean± St Dev	Median	
Pre-ref	1.97 ±0.89	1.89	2.42±0.33	2.395	0.000
Pre-MLD	0.85±0.36	0.79	1.32±0.08	1.05	0.56
Pre-lesion length	16.77±0.78	5.58	18.33±0.85	7.555	0.004
Pre-stenosis (%)	57.62±32	56.5	58.67±13	57	0.55
Post-ref	2.42±1.46	2.2	2.79±1.65	2.69	0.99
Post MLD	1.91±1.03	1.91	2.35±0.48	2.29	0.56
Post stenosis (%)	17.38±6	15	15.20±1	14	0.069
stent size	2.230±2	2.25	3.04±2.5	3	0.000
stent length	17.28±10	16	21.81±6	19	0.001
Multi Vessel Disease (%)	20.4%		37.8%		0.000

DISCUSSION:

The relationships among stenosis severity, lesion length, and trans-lesional flow in an idealized system are governed by Poiseuille's law, which dictates that

flow varies directly as a function of luminal diameter and inversely as a function of lesion length:

$$\text{Flow} = \frac{\Delta P (r^4)}{8 \eta l}$$

in which ΔP is the pressure difference across the stenosis, r is the minimal lumen radius of the stenotic segment, η is blood viscosity, and l is the length of the lesion [11]. Because flow across the lesion varies in proportion to the fourth power of radius but only as the first power of length, lesion length would be expected to exert a relatively little impact on trans-lesional flow for discrete (e.g., <5 mm long) stenosis.

It is essential that physicians performing coronary angiography or angioplasty understand this basic concept [12].

Thus, the vessel radius has a greater impact on the vessel flow. Poiseuille's law relates to flow of fluids through cylindrical tubes in well-controlled experimental settings. It does not take into consideration complexities of human coronary artery disease (CAD) such as plaque irregularity and eccentricity, nonlaminar and pulsatile flow, vasoactive properties of the arterial wall, and the potential for compensatory dilation. There are certain procedural issues involving small vessel stenting that needs to be discussed.

These are:

(i) Difficulty in reaching the lesion site as small vessels tend to be peripheral and the stent may have to pass through several bends and curves before reaching the site. Therefore, the primary success rate of stenting such arteries may not be as high as that of larger vessels, especially if the stents used are not tracked able and flexible.

(ii) The chances of stent dislodgement are higher as stents may need to be placed in distal lesions after passing through a small and tortuous vessel. But with the availability of balloon-mounted stents, this is usually not a major problem.

(iii) The choice of stent itself may be an issue since routine stents deployed in small coronary vessels have a higher metal-to-artery ratio. This may increase the risk of subsequent problems such as subacute thrombosis and restenosis [13].

For small vessel treatment, stent implantation was not demonstrated to be superior to balloon angioplasty, therefore, small vessel stent implantation was a controversial issue in the bare metal stent (BMS) era [14,16] C-SIRUIS and E-SIRIUS evaluated the efficacy of sirolimus-eluting stent (SES) implantation for diffuse long and small vessel disease [17,18].

Procedural success rates in our study were 96% and 98% in small and large vessel groups respectively. This is in concordance with studies by Lau et al and Morice et al. According to Lau et al, early, and long-term results in 197 consecutive patients who underwent stent implantation in 207 vessels with a diameter <3.0 mm the procedural success rate was 97.3%, lesion severity reduced from 85±9% to 3±7%, with a subacute stent thrombosis rate of 0.5%. Survival without major target lesion-driven events was 77% and 74% at 1 and 2 years of follow-up, respectively. The 6-month angiographic restenosis rate was 30.1%. Diabetes mellitus, small vessel size and stent size <2.7 mm were found to be independent predictors of in-stent restenosis. In a similar study, Morice et al. 20 reported that among 190 patients stented with 2.5 mm stents, the procedural success rate was 98%, subacute thrombosis rate was 2.6% and repeat intervention rate on follow-up was 24.5%. Thus, several non-randomized trials of small vessel stenting have been reported. The initial procedural success rate ranged from 93% to 98%, subacute thrombosis rate from 0.5% to 3.8% and the restenosis rate from 21% to 36%. Adverse clinical events ranged from 11% to 26%.

The initial and long-term success rates of stenting in small coronary vessels were nearly the same as those for large vessel stenting in this era when mostly second generation DES is used [19,20,21]. These studies conclusively established the feasibility, safety, and efficacy of small vessel stenting, especially in situations where balloon angioplasty results were suboptimal (provisional stenting). Results from our study also reflect similar finding.

LIMITATIONS:

It is an observational single center study the results of which cannot be extrapolated to all the patient population. Operator skill and experience may have influenced the outcome of this study. Attempts were made to limit confounding using propensity matching in a multivariable analysis; however, this approach cannot entirely eliminate residual confounding of unmeasured factors. IVUS could not be performed in our study due to logistic concern. Various clinical and biological factors may theoretically modify the influence of vessel size on late angiographic outcome and deserve evaluation in

future studies. However, it is worth noting that although some clinical factors have been found to be independently correlated with luminal re-narrowing (e.g., diabetes and type and duration - angina before angioplasty, which was not analyzed in detail in this study.

CONCLUSION:

This study shows that demographic parameters may not significantly influence the outcome in small vessel stenting. Further studies need to evaluate these findings in Indian population. Small vessel (less than 2.5 mm) PCI has good immediate procedural and one year outcome and with a less MACE rate of 3.5% (2 TLR, 1 MI, 1 CABG, 0 TLF) i.e., comparable to large vessel PCI.

Conflicts of interest: None

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