Angiographic Predictors and Clinical Outcome of Acute Side Branch Occlusion after Coronary Artery Stent Implantation

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Abstract

Objective- The aim of this study was to identify the incidence, angiographic and procedural predictors, and clinical outcome of acute side branch occlusion (SBO) following coronary stent implantation.

Methods- In total, 138 patients who underwent coronary artery stenting were included. The stents had covered 185 side branches with a luminal diameter greater than 1 mm and less than 2 mm. All the procedures were performed according to the current standards. The data on the clinical events and angiographic characteristics were analyzed. The side branch size and the ostium involvement and its location within the stent were evaluated. SBO was defined as a (thrombolysis in myocardial infarction) TIMI flow ≤1.

Results- Acute SBO after stent implantation occurred in 24 (12.9%) side branches. A significant side branch ostial stenosis (≥50%) and side branch diameter at base line ≤1.5 mm were predictors of SBO. Non Q-wave myocardial infarction (MI) was observed in 16.6% of the patients with acute SBO and in 4% of the cases without SBO (P=0.001). However, during hospital stay and long-term follow-up, the incidence of major adverse cardiac events (MACE) comprising death, need for target vessel revascularization, and Q-wave MI was almost similar in the patients with and in those without acute SBO. No MACE related to SBO was seen in these patients.

Conclusion- The incidence of acute SBO after coronary stent implantation is relatively frequent. Major predictors of SBO are side branch diameter <1.5 mm and the presence of an ostial side branch stenosis (≥50%). These data yield support to the assumption that the occlusion of small and medium-sized branches during coronary artery stent implantation is not associated with an adverse clinical outcome and should not hinder an optimal interventional therapy of the target lesion ***(Iranian Heart Journal 2008; 9 (3):18 -24).***

Keywords: coronary artery disease ■ side branch occlusion ■ stent implantation

Side branches are seen within the vicinity of the angioplasty site in over 50% of cases; and although many are unaffected, acute side branch compromise or occlusion after native coronary stenting is a matter of concern.

Most studies performed on this topic have attempted to identify the predictors of acute side branch occlusion (SBO) after coronary interventions, but little data are available about the possible clinical impact of SBO after coronary balloon angioplasty and stent

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implantation in patients with coronary artery lesions.[1-3]

The purpose of this study was to define the incidence and predictors of SBO after target lesion stent implantation and also to assess the clinical impact of SBO after this procedure.

Methods

Study design and patient population

This observational, prospective, non-randomized study was conducted between 2002 and 2006 in 138 patients who underwent percutaneous transluminal coronary angioplasty (PTCA) and stent implantation.

These patients had side branches with a luminal diameter ≥ 1mm and less than 2 mm. In addition, their ostia were spanned by a stent and originated from the target lesion. Exclusion criteria were acute myocardial infarction (AMI) during the previous 2 weeks, terminal renal insufficiency, side branch dilatation or side branch protection by guide-wire during the angioplasty procedure, and side branches with a luminal diameter less than 1 mm and >2 mm. This is a reasonable threshold, since larger-sized vessels usually constitute targets for revascularization.[4]

Procedure

All the procedures were performed according to the current standards. The patients were admitted to the hospital on the same day or a day before intervention. All of them received either long-term aspirin therapy or a loading dose of 240-500mg ASA, continued with 160-250mg daily indefinitely.

A loading dose of 450-600mg clopidogrel (unless patients were already pretreated) was administered optimally 48 hours before the index procedure with a minimum of 4 hours, followed by 75mg daily for one month in bare metal stent implantation and 9-12 months in patients with drug-eluting stents.

Alternatively, treatment with ticlopidine at a dose of 250mg twice daily was begun 3 days before the procedure and continued for one month in patients with bare metal stents. Additionally, 7500 to 10,000µgr of intravenous unfractionated heparin was given during the procedure, followed by a continuous infusion of 700-1000µgr/hr for 12-18 hours. All the patients were monitored in the CCU for at least 18-24h after PTCA.

Electrocardiograms were obtained at baseline and also recorded immediately after PTCA, during chest discomfort, at the next morning, and during follow-up.

The levels of creatine kinase and its MB isoenzyme were measured in the first 12-18 h after intervention.

Quantitative coronary angiographic (QCA) evaluation

In each patient, s quantitative coronary angiography evaluation (lesion length, vessel diameter, and percentage of artery stenosis) was performed with Hicor's own vessel analysis system (Siemens AG, Germany). All the pre- and post-procedural angiographic images were analyzed using the edge detection technique. For the estimation of absolute coronary dimensions, the tip of the guiding catheter before the injection of the contrast medium was used as the scaling device. Visual assessments included thrombolysis in myocardial infarction (TIMI) flow, lesion calcification, and type of lesion.

Angiograms were reviewed before intervention, after balloon pre-dilation, and before and after stent implantation. The following angiographic parameters were computed at each procedural step with the use of multiple projections:

Lumen diameter, percent diameter stenosis, lesion calcification, type of lesion, TIMI flows, lesion length, and number of side branches. Side branches were also characterized on each frame by the ostial and reference diameter, percentage of ostial stenosis, origin of side branch within the target lesion, and TIMI flow.

Follow-up

Clinical follow-up was scheduled at 2 weeks, and 2, 4, 6, 9, and 12 months.

In the clinical follow-up, the patients were asked about the interim development of angina, according to the Canadian Cardiovascular Society classification of stable angina and the Braunwald classification of unstable angina. The patients were also monitored for major cardiac events (death, Q-wave MI, and target vessel revascularization) in relation with SBO on hospital stay and during follow-up. An electrocardiogram was obtained at each visit. We were not able to retrieve complete follow-up information on 19 patients.

End-points and definitions

The primary end-points of this study were MACE during the procedure, hospitalization, and on follow-up. MACE was defined as a composite of death, non-fatal ST-elevation myocardial infarction, or target vessel revascularization in relation to SBO.

Non Q-wave MI was defined by an increase in creatine kinase and its isoenzyme MB level to more than three times the upper limit of normal according to the American Heart Association/ American College of Cardiology guidelines, in the absence of new Q-wave on the surface electrocardiogram. Coronary perfusion was graded according to the classification system of the TIMI trial.[5] SBO was defined as a persistent TIMI flow ≤1.

Statistical analysis

This is an observational, prospective, non-randomized study. The continuous data are expressed as mean ± standard deviation (SD), and the categorical variables as number and percentage. The differences between the groups were assessed using the non-parametric χ^2 test as Fisher's exact test for the categorical data and Student's *t*-test for comparing the continuous data. A P-value <0.05 was considered statistically significant.

Side branch and lesion characteristics as well as procedural data and their correlation with SBO were analyzed using the statistical software package SPSS for Windows (version 11.5).

Results

The baseline demographic, clinical, and procedural characteristics of the patients are presented in Table I.

Table I. Matching comparison of demographic, clinical and procedural data of patients with and without SBO

Data	Patients with SBO (N= 22)	Patients without SBO (N= 116)	P value
Age	57±10.3	56±10.4	0.681
Cigarette smoking	8 (35%)	38 (33%)	0.831
Hypertension	9 (40.9%)	45 (39%)	0.856
Diabetes mellitus	5 (22.9%)	28 (24.1%)	0.792
Dyslipidemia	16 (72%)	82 (70.7%)	0.905
Male sex	92 (66.7%)	46 (68.8%)	0.53
Stable angina	9 (40.9%)	50 (43.1%)	0.849
Unstable angina	7(31.8%)	31 (26.7%)	0.624
LVEF	56.4±12.3	56.2±12.8	0.89
Prior MI	7(31.8%)	34 (29.3%)	0.813
Median lesion length (mm)(range)	28(8-41)	33 (10-47)	0.403
Calcification	4(18.2%)	19 (i6.4%)	0.835
Prior revascularization	3(13.6%)	13 (11.2%)	0.744
Type A lesion %	32%	34%	0.882
Type B lesion %	47%	45%	0.951
Type C lesion %	22%	21%	0.962
Mean balloon pressure (atm)	13.2± 3.8	13± 3.7	0.763
Stent size (mm)	3.0± 0.4	2.9± 0.5	0.816
Stent length (mm)	20.97± 10.7	19.40± 8.2	0.315

Table II. Location of side branches in patients with and without SBO

Side branch location	With occlusion No. (%)	Without occlusion No. (%)
Diagonal	16 (66.7%)	88 (54.7%)
Septal	4 (16.7%)	32 (19.9%)
RVB	3 (12.5%)	19 (11.9%)
PDA	0 (0.0%)	5 (3.1%)
PLV	0 (0.0%)	1 (1.9%)
OM	1 (4.1%)	16 (9.9%)
Fisher's exact test P value = 0.726 df= 5 value = 3.30		

These findings were well matched between the 2 groups, with no important differences in their frequency.

A total of 185 stent-covered coronary artery side branches were found in 138 (151 coronary arteries) patients. In these cases, 159 stents were used. All the side branches had a diameter between 1 and 2 mm. The anatomical locations are depicted in Table II. The treated vessel distributions were similar between the two groups.

After the intervention was completed, 24 (12.9%) functionally occluded side branches were seen among a total of 185. Side branch ostial stenosis (≥ 50%) was detected in 21.8% of the patients with acute SBO, compared with 3.5% in the patients without significant side branch stenosis (P=0.011, Table III).

Table III. Ostial side branch stenosis in patient with and without SBO

Without side branch occlusion	With side branch occlusion	Ostial side branch stenosis
79 (78.2%)	21 (21.8%)	> 50%
82 (96.5%)	3 (3.5%)	< 50%
Fisher's exact test P value=0.011	df= 1	value=1.87

Furthermore, 92.3% of the side branches with a diameter ≥ 1.5 mm showed normal antegrade perfusion after the intervention. On the other hand, only 81.9% of the side branches with a diameter <1.5 mm showed complete perfusion (P=0.048, Table IV).

Table IV. Primary diameter of side branch in patients with and without SBO

Without side branch occlusion	With side branch occlusion	Diameter of side branch
77 (81.9%)	77 (18.1%)	1-1.5mm
84 (92.3%)	7 (7.7%)	≥ 1.5mm
X^2=1.13	df= 7	P= 0.048

The incidence of acute SBO for the side branches with a diameter ≥1.5 mm was 7.7% compared with 18.1% for the side branches <1.5 mm in diameter (P=0.048).

Direct stenting (DS) was performed in 78 (92 side branches) coronary artery lesions, whereas conventional stenting (CS) with balloon pre-dilation was done in 81 (93 side branches) lesions. The incidence of acute SBO in the CS group was 13.8% in comparison with 12% in the DS group, without reaching statistical significance (P=0.227). No significant correlation was found between the occurrence of SBO and variables such as stable angina, unstable angina, prior MI and revascularization, maximal balloon pressure, coronary calcification, or length and type of lesion.

Drug-eluting stents were used in 107 (67%) and bare metal stents implanted in 52 (33%) lesions. Acute SBO occurred in 17 (16%) of the side branches covered by drug-eluting stents vs. 7 (13.5%) in the side branches spanned by bare metal stents (P=0.243), but the difference was not significant. Shift of plaque after stent implantation and increase in the severity of side branch ostial stenosis without SBO occurred in 56 (30.3%) side branches. However, acute SBO was significantly associated with a pathological increase in the serum levels of CK and CK-MB compared with the cases without SBO (P=0.001).

The incidence of uncomplicated non Q-wave MI (non-STEMI) was 16.6% in the patients with acute SBO and 4% in the cases without SBO (P=0.001). The length of hospital stay in the patients with acute SBO was 48 ± 12 hours and 48 ± 5 hours in the patients without acute SBO (P=0.18). Apart from the patients with documented post-procedural non Q-wave MI, there was no MACE (death, need for revascularization, and Q-wave MI) during both the in-hospital period and at long-term follow-up in relation with acute SBO. However, no MACE related to SBO was observed during hospital stay and at long-term follow-up. Nineteen patients refused further follow-up.

Discussion

Interventional catheter-based therapy has been revolutionized by the wide spread use of coronary stents. Since the beginning of the stent era, stent implantation in coronary lesions involving side branches has been recognized as a potential source of acute complications.[6-10] We herein report our two-center experience with the natural course and clinical implications of SBO after the implantation of coronary stents.

In the present study, a total of 24 (12.9%) of all the side branches showed a compromised perfusion (SBO) after stent placement. Concerning elective stent implantation, other authors have found an SBO rate within a range of 7% to 21.2%.[1-3,6,7,9,11,12] The overall incidence of SBO in the present study was in agreement with that reported by other authors.[2,6,9] Our data suggest that a strong association exists between significant side branch ostial stenosis and prevalence of SBO. Significant ostial involvement of the side branches has been identified in most previous studies as a reliable predictor of SBO.[1,2,3,6,7]

In one of the most extensive studies regarding SBO, a preexisting ostial side branch stenosis in association with the origin of the side branch from the parent vessel lesion was found to be strongly predictive of SBO.[2]

Also, the present study revealed that the smaller coronary artery branches showed compromised antegrade flow after intervention more frequently than did the larger ones. (P=0.048). This finding is comparable with a previously published report showing that the vessel with a small diameter is an important predictor of SBO after coronary stent insertion.[3]

The incidence of SBO in the conventional stenting with balloon pre-dilation (CS) group was 13.8% compared to 12% in the direct stenting (DS) group (P=0.227). In other reports, there was no significant difference in the incidence of SBO among these sub-groups as well.[3-13] In contrast to the results of some previous studies[2,7,11,12] reporting that SBO was significantly correlated with high inflation pressures, the available data from more recent research[1,3,6] together with our results suggest that high pressure stenting does not influence SBO. The data from this study are in line with the observations in similar limited studies[6-13] inasmuch as the technical or procedural factors of stent implantation had no impact on the incidence of SBO. Furthermore, there was no correlation between the use of drug-eluting or bare metal stent and the occurrence of acute SBO in the current report.

Similarly, another group of researchers have found no significant difference in the incidence of the occlusion of side branches covered by drug-eluting stents versus bare metal stents.[14] Considering the above-mentioned observations, it seems unlikely that the implantation of drug-eluting stents in comparison with bare metal stents would notably change the fate of jailed side branches.[6-14]

The rate of plaque shift, which led to change in the severity of side branch stenosis without compromised side branch flow, occurred in 30.3% of the side branches. This result is similar to that reported by Bhargava et al., who found significant narrowing after PTCA in 26.7% of the side branches without total occlusion.[15]

It is generally accepted that SBO after coronary stent implantation is the most frequent cause of serum elevation of myocardial enzymes after coronary angioplasty.[10,16-18]

Pathological post-interventional elevations of CK and CK-MB showed a significant deviation among patients with SBO versus cases without this complication (P=0.001). Despite some data indicating that even a minimal CK elevation is associated with an increased incidence of cardiac events in the first year;[3,6,16-18] in the present study, the overall MACE-free survival in patients with and without elevations in these markers at one-year follow-up was similar.

The incidence of uncomplicated non Q-wave MI (N-STEMI) in the present study was fairly close to that reported by other authors.[3-6]

Most series have suggested that SBO after coronary artery stenting is a benign event.[1] Spontaneous re-canalization of the initially occluded side branch may explain, at least in part, the low rate of adverse events. In the present report, the patients with and without acute SBO presented no significant differences regarding the occurrence of MACE (death, Q- wave MI and need for repeat target vessel revascularization) during hospital stay and at follow-up. These data, comparable with most studies in this regard, suggest that the acute SBO of small and medium-sized side branches does not influence the incidence of MACE after PTCA and during follow-up.[2,3,6,12,18] Furthermore, as indicated by other research,[3] the occurrence of SBO did not significantly influence the overall hospital stay or the length of stay in the coronary care unit.

The precise mechanisms implicated in SBO after stent implantation are likely to be multifactorial and have not been sufficiently addressed yet. Speculated mechanisms include thrombus formation, dissection, plaque embolization, plaque shifting, ostial compromise by displaced stent struts, and spasm at the ostium.[1] On the other hand, the dynamic changes and a high rate of spontaneous reperfusion of initially-occluded side branches present an argument of the influence of coronary spasm or resolved thrombus on the pathogenesis of acute SBO.[3-6]

Study limitations

We may have underestimated the diameter narrowing due to the known limitations of angiography - QCA and the fact that the reference segment may have been diseased.

Several other limitations need to be mentioned. First, a major limitation is the observational, non-randomized character of our study, which may have potentially influenced the comparative analysis of small subsets of patients. Second, the use of semi-quantitative methods for the analysis of the recorded angiograms theoretically represents a source of errors. Third, the time of follow-up was not identical, although no significant difference was found between the patient groups.

Conclusion

Acute SBO is relatively frequent after coronary artery stenting, but this does not appear to have a major clinical relevance. The identification of threatened side branches is challenging, but significant ostial stenosis in the side branch and side branch size (<1.5 mm) constitute useful markers of vessels at risk.

The findings of this study support the view that the presence of small and medium-sized side branches should not preclude an optimal interventional therapy of the target lesion, including the implantation of a coronary stent. Nevertheless, certain particular situations such as the size of the myocardial territory that the branch supplies, branches supplying bridging collaterals to chronic occluded main vessels, left ventricular dysfunction, and separation of several side branches from the parent vessel that may benefit from revascularization, deserve an individualized approach. Therefore, it may be justifiable to

take special precautions in the management of side branches in these patients.

Conflict of Interest

No conflicts of interest have been claimed by the authors.

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