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Review

Present Status of Coronary Bifurcation Stenting

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Summary

Percutaneous coronary intervention (PCI) for bifurcation lesions is technically limited by the risk of side branch occlusion. In comparison with nonbifurcation interventions, bifurcation interventions have a lower rate of procedural success, higher procedural costs and a higher rate of clinical and angiographic restenosis. The recent introduction of drug-eluting stents (DES) has resulted in reduced incidence of main vessel restenosis compared with historical controls. However, side-branch ostial residual stenosis and long-term restenosis still remain problematic. In the era of DES, techniques employing two stents have emerged that allow stenting of the large side branch in addition to the main artery. Stenting of the main vessel with provisional side branch stenting seems to be the prevailing approach. This paper reviews outcome data with different treatment modalities for this complex lesion with particular emphasis on the use of DES as well as potential new therapeutic approaches.

Key words: coronary bifurcation, stenting, drug-eluting stents, bare metal stents, percutaneous coronary intervention

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Introduction

Bifurcation stenosis is one of the most complex coronary lesions for endovascular treatment because lumen of both the main vessel and the side branch needs to be restored. Balloon angioplasty alone to treat bifurcation lesions has resulted in relatively low angiographic success and high restenosis rates. Although the introduction of bare metal stents (BMS) resulted in more predictable results and higher success rates, angiographic restenosis rates still remained high. Introduction of drug-eluting stents (DES) in clinical practice has changed treatment perspective in dealing with this type of lesion.

Atherosclerosis in Coronary Bifurcation

Regardless of the cause of endothelial dysfunction, atherosclerosis occurs often at branch points and curvatures, perhaps as a result of hemodynamic turbulence.[1] Excess stress on the vessel wall causes expression on the endothelium of adhesion molecules, which allow rolling and subsequent subendothelial migration of monocytes. These adhesion molecules are also present on smooth muscle cells and fibroblasts. Nonetheless, as the disease process progresses, sudden change in shear stress may result in rupture of the vulnerable plaque, adhesion and aggregation of platelets, and formation of an occlusive thrombus.

Because of limitation of blood flow in a narrowed artery, catheter based interventions are frequently employed to open narrowed coronary arteries. However, these interventions per se can cause endothelial injury resulting in acute thrombosis and subsequently smooth muscle cell hypertrophy as response to injury resulting in delayed restenosis.

Clinical Outcome Data

Coronary bifurcation lesion account for 15–18% of all coronary lesions that require percutaneous coronary intervention (PCI).[2] The axial plaque redistribution after

PCI of lesions located next to a coronary bifurcation almost inevitably causes plaque shifting in the side branches and that makes coronary bifurcation lesions particularly challenging.

In earlier studies with balloon dilatation, there was usually less than satisfactory immediate lumen restoration, a high complication rate, and an unacceptable restenosis rate.[3,4] The "kissing balloon technique" resulted in improved, though suboptimal, lumen restoration.[3] Several other approaches such as rotative or directional atherectomy were also attempted, but these techniques did not translate into significantly better results.[5] With the advent of second generation stents in 1996, coronary bifurcation stenting techniques (novel strategies) became available. Currently two approaches are generally accepted for treatment of bifurcation lesions:

1. *Stenting the main branch and dilating the side branch through the stent struts*: A simple way to treat a bifurcation lesion is to stent the main branch covering the ostium of the side branch. In cases of significant impairment of flow in the side branch that may occur because of plaque shift during deployment of main branch stent or preexistent severe ostial side branch stenosis, treatment of the side branch is performed. This is imperative if there are features of acute ischemia such as chest pain or electrocardiographic changes, despite achieving an adequate result in the main vessel.
2. *Stenting both the main branch and side branch utilizing two stents*: There are various techniques to accomplish deployment of two stents at the bifurcation. The various techniques are V or simultaneous kissing stents, crush, T, culottes, Y and skirt to allow stenting in the side branch when needed. Each technique has its own limitations and advantages.[6]

Clinical Outcome with Bare Metal Stent

There are no large prospective randomized trials addressing long-term clinical outcome after placement of BMS versus balloon dilatation or surgery and of different stenting techniques. The majority of the information is based on reports from registries and retrospective data. The data on outcome after stenting with BMS is summarized in Table 1.[7–12] In these reports, the technical success rate in opening of the main as well as the side branch, was over 87% in the majority of cases, but the clinical outcome data remained variable. The restenosis rate was 25–62% in the two stents group versus 12.5–48% in single stent group, and the target lesion revascularization rate (TLR) was 24–43% in the two stents group versus 8–36% in the single stent group.

Brunel et al.[13] conducted a study with a strategy of provisional t-stenting with a tubular stent and final kissing balloon angioplasty for the treatment of coronary bifurcation lesions. The side branch was stented in 34% of patients. This technique was associated with a low TLR rate at 7 months. Recent data has, however, challenged this concept of final kissing balloon to avoid distortion of the main vessel stent. In the BISCOR registery,[14] a total of 421 consecutive patients, who had bifurcation stenting with a high-end BMS (Coroflex, BBraun, Berlin, Germany), allowing side branch coronary angioplasty through the stent struts without distraction of the main vessel stent from the vessel wall or other distortions, were prospectively followed. This approach obviated the 2-wire technique and kissing balloons, and was associated with a high technical success (90% success rate in two vessels and 99% in the main vessel) and low TLR of 17%. Stenting of side branch in this registry was associated with a significantly higher TLR (33% versus 16%, $p < 0.004$) at 6 months follow up.

Overall, the data on the use of BMS suggest a tendency toward increased restenosis after dual stenting of the main vessel and side branch, compared to single vessel stenting.[7–12,15]

Clinical Outcome with Drug-eluting Stent

Recently, an intense interest in the use of DES in treating bifurcation lesions has evolved. The results of several studies in this area are summarized in Table 2.[16–25] Overall success rate had been 94–100%. The restenosis rate varied from 5.1–28% in two stent group versus 5.3–18.7% in single stent group and TLR was 1.0–31.1% in two stent group versus 1.9–5.4% in single stent group. This was also associated with late stent thrombosis from 0.5–4.3%.

Recently published Nordic Bifurcation Study[25] compared the strategy of stenting both the main vessel and the side branch with stenting of the main vessel only, with optional stenting of the side branch, with sirolimus-eluting stents. At 6 months, there were no significant differences in Major Adverse Cardiac Events (MACE) between the two groups. But stenting of the main vessel and side branch was associated with significantly longer procedure and fluoroscopy times, higher contrast volumes, and higher rates of procedure-related increases in biomarkers of myocardial injury.

Overall, the data on the use of DES suggest a tendency toward less restenosis rates at long-term follow-up in comparison with BMS. Stenting both main vessel and side branch offers a better visual satisfaction but a slightly increased propensity towards subacute stent thrombosis in early follow-up period. Single stent technique has advantage over stenting of both main vessel and side branch with regard to procedural success, fluoroscopic time, and contrast volume with overall decrease in TLR.

TABLE 1 A comparison of restenosis rate and target lesion revascularization with Bare Metal Stent in bifurcation lesions with single main vessel stent versus both main vessel and side-branch stent

	Randomization	Technique	Patients (*n*)	Follow-up (months)	Restenosis rate (%)	Target lesion revascularization (%)
Suwaidi et al.[7]	No	S+S*$	77	12	–	19.4
		S+P	54	–	–	20.5
Chevalier et al.[8]	No	S+S¥	50	6	28	24
Yamashita et al.[9]	No	S+S¥*!$	53	6	62	38
		S+P	39	–	48	36
Pan et al.[10]	No	S+S*!$	23	18	43	39
		S+P	47	–	19	17
Anzumi et al.[11]	No	S+S*	45	12	25	35.5
		S+P	45	–	12.5	15.5
Brunel et al.[12]	No	S+S	50	6	57	43
		S+P	56	–	21	8
Brunel et al.[13]	No	Provisional t-stenting	186	7	–	15.9
Rux et al.[14]	No	Coroflex stent	421	6	–	17

S+S: stenting both main vessel and side branch; S+P: main vessel stent and side branch angioplasty; *: t-stenting technique; $: y-stenting; ¥: culotte technique; !: v-stenting.

TABLE 2 A comparison of restenosis rate and target lesion revascularization with drug-eluting stent in bifurcation lesions with single main vessel stent versus both main vessel and side-branch stent

	Randomization	Stent	Technique	Patients (*N*)	Follow-up (months)	Restenosis rate (%)	Target lesion revascularization (%)
Colombo et al.[16]	Yes	SES	S+S*	63	6	28	9.5
			S+P	22		18.7	4.5
Pan et al.[17]	Yes	SES	S+S*	47	11	20	5
			S+P	44		7	2
Ge et al.[18]	No	SES	S+S*†	117	9	24	8.9
			S+P	57		10	5.4
Ge et al.[19]	No	SES+PES	S+S†	181	9	11.5/21.6¶	14.9
Sharma et al.[20]	No	SES	S+S‡	200	9	–	4
Hoye et al.[21]	No	SES+PES	S+S¥	23	8	18.8/12.5¶	5.3
Hoye et al[22]	No	SES+PES	S+S†	231	9	9.1/25.3¶	9.7
Ge et al.[23]	No	SES+PES	S+S*	61	12	13	31.1
			S+S†	121		16.2	14
Moussa et al.[24]	No	SES	S+S†	120	6	11.3	11.3
Steigen et al.[25]	Yes	SES	S+S†¥*	206	8	5.1	1.0
			S+P	207		5.3	1.9

SES: sirolimus-eluting stent; S+S: stenting both main vessel and side branch; *: t-stenting; ‡: simultaneous kissing stent; ¶: main vessel/side branch restenosis; PES: paclitaxel-eluting stent; S+P: main vessel stent and side branch angioplasty; †: crush stenting; ¥: culotte stenting.

New Developments

Several types of dedicated stents have been designed since the mid 1990s with the notion that they will provide adequate coverage of main branch and the ostium of the side branch. The SLK-View stent (Advanced Stent Technologies, Inc., Pleasanton, Calif.) is a new scaffolding device incorporating a side aperture that allows access to the side branch of a bifurcation after deployment of the stent in main vessel. Ikeno et al.[26] studied 81 patients with 84 de novo coronary artery bifurcation lesions. Patients underwent SLK-view stent implantation with subsequent kissing balloon post dilatation. Procedural success rate was 97.6%. Binary restenosis rate at 6 month follow-up was 28.3% for main vessel and 37.7% side branch. The TLR rate at 6 months was 21% and coronary artery bypass grafting was needed in 6% of patients.

Conclusion

A clear management strategy dedicated to coronary bifurcation lesions remains to be defined in the era of DES. The general consensus is to try to keep the procedure quick, safe and simple. When the side branch is not severely diseased, implantation of a stent in the main vessel and provisional stenting in the side branch is the preferred strategy. Implantation of two stents as the initial approach is appropriate when both branches are significantly narrowed (diameter stenosis $>50\%$) and suitable for stenting. Final kissing balloon inflation should be performed in crush stent technique. Stent thrombosis when two DESs are used appears to be higher than that with a single stent use. Although dedicated stents are being developed, their clinical use in the format of DES is still very limited. However, these devices may have potentially important applications in proximal large bifurcations and in the left main trunk. Despite all the unanswered questions and persistent problems, two major achievements in bifurcational stenting have been achieved since the introduction of DES: first, the single-digit restenosis rates on the main branch, and second, focal restenosis in the side branch are often clinically silent.

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