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Contemporary coronary intervention in bifurcation lesions – two-year follow-up in an unselected cohort

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Optimization of coronary angioplasty in bifurcation lesions remains a major challenge for percutaneous revascularization techniques.

Material/Methods: We evaluated procedural success, major in-hospital complications, target vessel revascularization, and 2-year clinical outcomes in 45 patients who underwent PTCA of a bifurcation lesion using currently available techniques and rigorous criteria for optimal immediate result.

Results: Angiographic success occurred in 100% of the parent vessels and in 84.4% of both vessels. Within the first 24 hours, there were no deaths or Q-wave myocardial infarction. Three non-Q-wave myocardial infarctions occurred (6.6%) and one emergency PTCA was necessary (2.2%). Therefore, clinical success was achieved in 91.2% of these patients. At 2-year follow-up, 3 cardiac deaths had occurred, the target revascularization rate was 20%, and the total frequency of major adverse cardiac events (MACE) was 37.8%.

Conclusions: Optimization of coronary angioplasty in bifurcation lesions is possible and results in a high angiographic success rate, low risk of acute complications and acceptable long-term clinical outcomes. However, the fairly high incidence of MACE at 2 years suggests that bifurcation lesions remain a challenge in everyday practice despite contemporary intervention methods and the use of GPIIb/IIIa inhibitors.

key words: **angioplasty • stent • coronary • bifurcation • outcome • clinical**

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BACKGROUND

Optimization of coronary angioplasty in bifurcation lesions remains one of the unresolved problems in percutaneous revascularization [1]. Advances in coronary stenting have dramatically reduced the periprocedural complications of coronary angioplasty. The possibilities for safe treatment of patients with complex lesions and multivessel disease, who would previously have been considered candidates for surgical treatment only [2], have markedly expanded. On the average, the acute and long-term outcomes of percutaneous interventions have consistently improved with the widespread use of stents [3]. On the other hand, the cost of stent is still a concern, preventing more widespread use, particularly in countries where public funding limitations are an important factor in health care strategies.

Apart from the economic aspect, the nearly universal utilization of coronary stents has not eliminated all the complications involved in percutaneous revascularization. In-stent restenosis has emerged as a new clinical entity [4], and the occurrence of side branch compromise has not decreased with stent placement in comparison to balloon angioplasty [5]. Despite significant progress in technology, these two factors have stalled any major breakthrough in the treatment of bifurcation lesions [6].

Several stenting techniques have been proposed for the treatment of bifurcation stenoses: 'T-stenting' [7], 'V-stenting' [8], 'Y-stenting' [9], 'trouser-leg stenting' [10], and the 'culotte' technique [11]. More recently, it has been shown that those approaches which are based on stenting both the parent vessel and the side branch provide no advantage over stenting one vessel and performing balloon angioplasty alone in the other [12,13]. The purpose of the present study was to examine short- and long-term outcomes in an unselected cohort of patients treated for bifurcation coronary stenoses with currently available techniques and rigorous criteria for optimal immediate results.

MATERIAL AND METHODS

Forty-five patients who presented with symptomatic coronary bifurcation lesions and underwent angioplasty and/or stenting between January 1998 and June 1999 were included in our study. A minimum side branch diameter of 2 mm by visual estimate was a prerequisite for inclusion. Informed consent for coronary angiography and percutaneous intervention was obtained from all patients. Based on the angiographic picture, the lesions were qualified as types 1-4b as previously described [14] (Figure 1).

The baseline demographic and clinical data are presented in Table 1. Type 1 bifurcation lesions ('true' bifurcation lesions, with more than 50% stenosis of both the parent vessel and the ostium of the side branch) were found in 19 patients. Lesion types 2-4b were diagnosed in 26 patients.

Table 1. Baseline demographic and clinical characteristics of the study group.

Demography and risk factors			Clinical presentation		
Mean age	56±8	years	Stable angina	32	(71%)
Male sex	36	(80%)	Unstable angina	13	(29%)
Hypertension	19	(42%)	Previous MI	21	(47%)
Diabetes	4	(9%)	Previous PTCA	0	(0%)
Hyperlipidemia	22	(49%)	Previous CABG	0	(0%)
Smoking	34	(76%)			
Family history	28	(62%)			
Distribution of the lesions in the coronary tree					
LAD/Dg		56%	CX/OM		40%
RCA/RPD		2%	LMCA/LAD/IM		2%

MI – myocardial infarction; PTCA – percutaneous transluminal coronary angioplasty; CABG – coronary artery bypass grafting;
LAD – left anterior descending coronary artery; Dg – diagonal branch;
CX – circumflex coronary artery; OM – obtuse marginal branch;
RCA – right coronary artery, RPD – right posterior descending coronary artery;
LMCA – left main coronary artery; IM – intermediate branch (ramus)

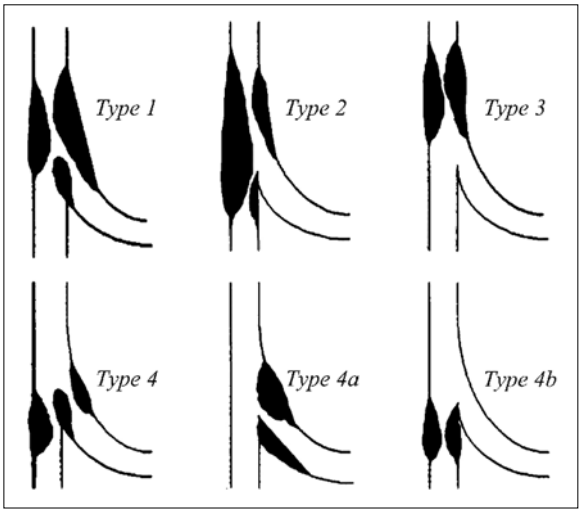

Figure 1. Classification of bifurcation lesions according to the distribution of the plaque material in the parent and branch vessels. Type 1, the 'true bifurcation lesion' is characterized by the presence of narrowing in the parent vessel both beyond and beneath the side branch, as well as by the disease of the side branch. In contrast, in types 2-4b, some portion of the parent vessel or the side branch is free of significant stenosis, but the localization of the plaques puts the side branch at risk.

All patients were treated with aspirin and ticlopidine at the moment of intervention. The transfemoral approach was used throughout and heparin was administered prior to the procedure (100 U/kg followed by additional doses to maintain the ACT above 300 s). Dual guide wiring was mandatory in Type 1 bifurcation lesions, while in other lesion types it was used at the operator's discretion. 'Kissing' balloons were also used at the operator's discretion, guided by the angiographic result. Stents were implanted in the parent vessel in the event of a suboptimal angiographic result of angioplasty (>30% residual diameter stenosis) or for abrupt or

threatened vessel closure. Stenting of the side branch along with the parent vessel was permitted only in the event of an abrupt or threatened vessel closure. Indications for the use of abciximab (bolus 0.25 mg/kg i.v. + infusion of 0.125 μg/kg/min. i.v. over 12 hours) included abrupt or threatened vessel closure with visible thrombus, suboptimal result after stenting (more than 30% residual stenosis), and the presence of slow flow post procedure – Thrombolysis in Myocardial Infarction (TIMI) grade 2 [15] – or the 'no reflow' phenomenon.

On-line and post-hoc quantitative coronary angiography (QCA) was perfomed with an ACA DCI system integrated into Philips Integris HM3000 angiographic equipment. The reference lumen diameter and minimum lumen diameter (MLD) were measured before and after percutaneous transluminal coronary angioplasty (PTCA). In the parent vessel, the diameter proximal to the stenosis was used as the reference diameter. In the side branch, the diameter distal to the stenosis was used as the reference diameter. Angiographic success was defined as residual stenosis of less than 30% of the reference diameter in the presence of TIMI 3 flow, and was determined separately for the parent vessel and the side branch. Procedural success was defined as angiographic success in the absence of major adverse cardiac events (MACE), resulting in the relief of angina or reduction of ischemia in a stress test. The events considered as MACE were death, myocardial infarction, or target lesion revascularization (TLR) by means of PTCA or coronary artery bypass grafting (CABG). Electrocardiograms and creatine kinase isoform MB levels were obtained every 6 hours during the first 24 hours post-procedure, and every 24 hours afterwards, until discharge. A diagnosis of Q wave myocardial infarction (QWMI) was made in the presence of new pathological (>0.04 s) Q waves in the electrocardiogram accompanied by an elevation of creatine kinase isoform MB by more than 3 times the normal value. A diagnosis of non-Q wave myocardial infarction (NQWMI) was made in presence of an elevation of creatine kinase isoform MB by more than 3 times the normal value without new pathological Q waves in the electrocardiogram. Emergency revascularization was defined as CABG or repeat PTCA within the first 24 hours after the procedure.

Clinical follow-up was performed by means of patient interview and documentation review for the occurrence of MACE at 24 hours, 30 days, 7 months and 2 years after the procedure. TLR was defined as any CABG or repeat PTCA to either the parent vessel or side branch, or both. An exercise treadmill test was performed after 1, 3 and 6 months. Patients who had angina and/or recurrence of ischemia in exercise electrocardiogram were subjected to repeat coronary angiogram.

Statistical analysis

Continuous variables are expressed as means ± standard deviation and were compared by means of the t-test. Frequencies are expressed as percentages and were compared by means of the chi-squared test. $P<0.05$ was considered significant.

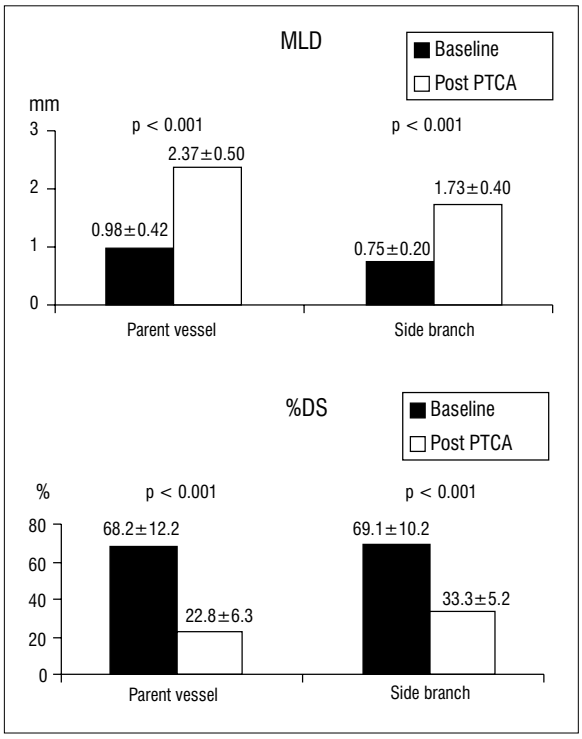

Figure 2. Improvement in lumen size of the parent vessel and the side branch from baseline (solid bars) to post-intervention (open bars) measured by quantitative coronary angiography (QCA). Upper panel: MLD – minimal luminal diameter (mm); lower panel: %DS – percent diameter stenosis (%).

Results

Two guidewires were used in 76% of the cases (95% in type 1 lesions, 54% in types 2-4b). 'Kissing' balloon inflations were performed in 24% of the cases (37% in type 1 lesions, 15% in types 2-4b). Stents were implanted in 24 bifurcations (53%): in 20 parent vessels, in 3 side branches and in both vessels in 1 patient. The stent types utilized were Crossflex (Cordis, n=9), Palmaz-Schatz (Cordis, n=7), Multilink Duet (Guidant, n=3), Crown (Cordis, n=3), Jostent (Jomed, n=2), NIR Primo (Boston Scientific, n=1).

Angiographic success occurred in 100% of the parent vessels (n=45) and in both vessels in 84.4% of the patients (n=38). The reasons for failure in the side branch were suboptimal dilatation (more than 30% residual stenosis, n=5, 11.1%) or side branch closure (n=2, 4.5%)

On the average, angioplasty resulted in a significant increase in MLD and a significant reduction in the percentage of stenosis in both parent vessels and side branches. QCA results are shown in Figure 2.

There were no deaths or QWMIs within the first 24 hours. Three patients suffered from NQWMI (6.6%), and one emergency PTCA was necessary (2.2%). Therefore, the overall incidence of MACE at 24 hours was 8.8%. Accordingly, clinical success was achieved in 91.2% of these patients.

After 30 days, there had been no other MACEs with the exception of one additional TLR. Thus the overall incidence of MACE at 30 days follow-up was 11.1%.

At 7 months of follow-up, two cardiac deaths had occurred. No autopsy was performed, but it is very likely that these deaths resulted from occlusions in lesions previously subjected to angioplasty. In both cases, after stenting of the parent vessels, re-dilation of side branches through the stent struts was performed without 'kissing' balloon inflations. No further myocardial infarctions were observed. Six additional patients had ischemia requiring repeat angiograms, which in all cases resulted in PTCA of the target lesion. Therefore, the TLR rate after 7 months reached 17.8%, while the total frequency of MACE was 28.9%. Accordingly, 71.1% patients remained free from MACE and free from angina at 7-month follow-up.

Between 7 months and 2 years, 1 more death occurred, 1 QWMI and 1 NQWMI were recorded, and 1 additional TLR was necessary. Thus the TLR rate at 2 years was 20%, and the total incidence of MACE was 37.8%.

The results achieved in the group of patients presenting initially with the so-called 'true bifurcation lesion', i.e. type 1, were initially similar to the results in patients with the other types of bifurcation lesions, i.e. types 2-4b. In fact, in the group with type 1 lesions, no MACEs were observed after 24 hours. All NQWMI occurred in the first 24 hours in patients with lesion types 2-4b, and there was 1 cardiac death in each of these two subgroups at 7 months follow-up (Table 2). However, between 7 months and 2 years relatively more events occurred in patients with type 1 lesions than in those with lesion types 2-4b.

Table 2. Incidence of major adverse cardiac events in subgroups according to the lesion type: type 1 lesion ("true bifurcation lesions", n=19) vs. lesion types 2–4b (n=26). Percentages are relative to the numbers of patients in each subgroup.

Lesion type 1 (n=19)	24 hours	30 days	7 months	2 years
Cardiac death	0	0	1 (5.3%)	1 (5.3%)
QMI	0	0	0	1 (5.3%)
NQWMI	0	0	0	1 (5.3%)
CABG	0	0	0	0
TLR	0	1 (5.3%)	3 (15.8%)	4 (21.1%)
Total MACE	**0**	**1 (5.3%)**	**4 (21.1%)**	**7 (36.8%)**
Lesion type 2–4b (n=26)	**24 hours**	**30 days**	**7 months**	**2 years**
Cardiac death	0	0	1 (3.8%)	2 (7.7%)
QMI	0	0	0	0
NQWMI	3 (11.5%)	3 (11.5%)	3 (11.5%)	3 (11.5%)
CABG	0	0	0	0
TLR	1 (3.8%)	1 (3.8%)	5 (19.2%)	5 (19.2%)
Total MACE	**4 (15.4%)**	**4 (15.4%)**	**9 (34.6%)**	**10 (38.5%)**

QWMI – Q wave myocardial infarction; NQWMI – non-Q wave myocardial infarction; CABG – coronary artery bypass grafting; TLR – target lesion revascularization, MACE – major adverse cardiac events

DISCUSSION

The treatment of coronary bifurcation stenoses continues to be a major challenge for percutaneous revascularization techniques. Early reports of balloon angioplasty identified shifting of the plaque material from the parent vessel to the side branch as a mechanism leading to stenosis or occlusion of the side branch [16,17]. To adequately protect the side branches, double wiring [18,19] and the kissing balloon technique [20] were introduced. However, reports from balloon angioplasty for bifurcation stenoses have continued to show high rates of procedural complications, as well as unfavorable long-term outcomes [21].

The technique of implanting a stent across an ostium of a lateral branch continued to cause the 'snow-plow' effect as much as did balloon angioplasty [5]. Over the last few years, immediate and long-term clinical outcomes of bifurcation stenting have improved substantially [7,11,14]. Most recently, two studies from experienced institutions involving a total of more than 200 patients found that stenting of both branches provides no advantage over stent placement in the parent vessel with balloon angioplasty of the other branch [12,13].

The present study reports on an unselected series of patients, in whom the majority of recently proposed modifications have been utilized in approaching bifurcation stenoses. In all but one case, stenting was performed in only one of the two vessels. Angiographic success was defined as less than 30% residual stenosis, a criterion equally or more rigorous than those applied in some recent studies [12,13]. This strategy yielded good procedural outcomes, as well as intermediate-term (7-month) results comparable with recent studies [14], with a 17.8% target revascularization rate and 28.9% incidence of total MACE. However, between 7 months and 2 years the adverse events continued to accumulate and amounted up to 37.8%.

Obviously, numerous patients with bifurcation stenoses suffer from severe coronary disease, which means that many of the MACEs observed over the 2-year follow-up period may represent progression of this disease. For this reason, it is likely that this patient population may particularly benefit from post-intervention pharmacological adjuncts (e.g. statins) to slow the progression of atherosclerosis. Nevertheless, additional revascularization procedures underscore the high propensity for the restenosis characteristic of bifurcation disease, regardless of the disease progression. The overall target revascularization rate was 17.8% at 7 months and 20% at 2 years. Since there was no angiographic follow-up, the binary angiographic restenosis rate is unknown. It is well known, however, that many cases of bifurcation restenosis remain asymptomatic, and that the TLR rates are thus much lower than the binary restenosis rates [7].

In summary, despite technological and pharmacological advances, bifurcation lesions still present several factors for increased risk of MACE in the long run. In diabetic patients, a bifurcation lesion is an independent predic-

tor of restenosis [22]. Stent overlap, often occurring in the treatment of bifurcation lesions, has been associated with increased risk of MACE after 30 days [23]. Interventions in bifurcation stenoses create the potential for increased risk of restenosis by utilizing multiple stents [24,25]. Branch salvage has also been demonstrated to result in increased restenosis [19]. The preliminary data indicate that drug-eluting stents may reduce the incidence of restenosis, but their impact on the treatment of bifurcation lesions is virtually unknown at present. While technical advances have made it possible to tackle increasingly anatomically complex coronary problems, restenosis is the limiting factor for long-term success in bifurcation angioplasty. For this reason, it should be emphasized that CABG, with its current low complication rate, the increasing frequency of off-pump bypass and excellent long-term freedom from angina, remains a viable option for multivessel disease, including bifurcation stenoses not easily amenable to angioplasty and stenting [2].

CONCLUSIONS

The present study, along with those of other authors, emphasizes the continuous need to adhere to evidence-based recommendations (avoiding multiple stents and stenting of the side branch, attempting kissing balloon inflations as often as technically possible). Refinement of success criteria for immediate results is necessary in order to optimize the long-term outcomes in patients treated for coronary bifurcation stenoses. In addition, since many of these patients have advanced atherosclerosis, it is likely that they may particularly benefit from post-intervention pharmacological adjuncts (e.g. statins) to slow the progression of atherosclerosis.

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