Impact of Routine Stenting on Clinical Outcome in Diabetic Patients Undergoing Primary Angioplasty for ST-Segment Elevation Myocardial Infarction

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The benefits of coronary stenting in patients with ST-segment elevation myocardial infarction (STEMI) have been related to a significant reduction in restenosis and target vessel revascularization (TVR) (1–7). However, few data have been reported in patients suffering from diabetes that have been demonstrated to be associated with in-stent restenosis and worse outcome (8–11). The Zwolle-6 (12) randomized trial investigated the actual role of routine stenting, as compared with balloon angioplasty, in a large cohort of unselected patients with STEMI without exclusion criteria. In this study, we present data in diabetic patients.

Table 1—*Clinical and angiographic characteristics according to initial randomization*

	Stent	Balloon	*P* value
n	84	76	
Age (years)	65 ± 11	64 ± 10	NS
Female sex	41.7	27.6	NS
Hypertension	40.5	51.3	NS
Insulin-dependent diabetes	17.8	10.5	NS
Hypercholesterolemia	29.8	22.4	NS
Door-to-balloon time (min)	57 ± 38	54 ± 29	NS
Ischemia time (min)	341 ± 302	312 ± 292	NS
Killip class 1	90.5	89.5	NS
Anterior myocardial infarction	45.2	48.7	NS
Ejection fraction ($n = 125$)	42 ± 12	42 ± 12	NS
Complete ST-segment resolution ($n = 111$)	37.3	48.1	NS
Multivessel disease	54.8	61.8	NS
Thrombolysis in myocardial infarction pre-3	21.4	10.5	NS
Thrombolysis in myocardial infarction post-3	85.7	85.5	NS
Myocardial blush grade 2–3	82.1	81.6	NS
Distal embolization	18.9	11.9	NS
Cross-over	20.2	30.3	NS
Angiographic success	84.5	82.9	NS

Data are means ± SD or percent. NS, not significant.

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Abbreviations: STEMI, ST-segment elevation myocardial infarction; TVR, target vessel revascularization.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

— From April 1997 to October 2001, all patients with STEMI, who were admitted within the first 6 h or between 6 and 24 h if they had persistent symptoms with evidence of ongoing ischemia, were randomized to stenting or balloon angioplasty before the initial angiogram (12). Informed consent was obtained from each patient (or from their relatives in case of patient's inability) before the angiogram. No exclusion criteria was applied. Our study was approved by the institutional review board. After the intervention, all patients received oral aspirin daily, with additional ticlopidine (250 mg/day) or clopidogrel (after June 1999; 300-mg loading dose followed by 75 mg/day) for 4 weeks. Diabetes was considered present if patients were treated with oral hypoglycemic agents or insulin or if the patients had a history of diabetes that was controlled by diet.

Quantitative coronary angiography was analyzed by an independent core laboratory (Diagram, Zwolle, the Netherlands) blinded to all clinical data and outcome. Angiographic success was defined as postprocedural thrombolysis in myocardial infarction 3 flow and a residual stenosis <50%. Predischarge left ventricular ejection fraction and analysis of ST-segment resolution were performed as previously described (13). All patients were reviewed at outpatient clinic. No patient was lost to follow-up. Routine angiographic follow-up at 6 months was planned in patients enrolled from April 1997 to October 1999. Angiographic restenosis was defined as diameter stenosis of >50% at quantitative coronary angiography.

Statistical analysis was performed with the SPSS 10.0 statistical package. Continuous data were expressed as means ± SD and categorical data as percentage. The ANOVA and the χ^2 test were appropriately used for continuous and categorical variables, respectively. The difference in event rates between groups during the follow-up period was assessed by the Kaplan-Meier method using the log-rank test.

Table 2—*Clinical outcome at 1-year follow-up according initial randomization*

	Overall population				Patients without cross-over			
	Stent	Balloon	RR (95% CI)	*P* value	Stent	Balloon	RR (95% CI)	*P* value
n	84	76			67	53		
Death (%)	10.7	9.2	1.03 (0.64–1.64)	NS	7.5	7.5	0.97 (0.26–3.63)	NS
Death and/or repeat myocardial infarction (%)	14.3	11.8	1.29 (0.52–3.2)	NS	10.4	11.3	1.03 (0.28–3.82)	NS
TVR (%)	21.4	18.4	1.27 (0.62–2.62)	NS	23.9	20.8	1.21 (0.56–2.61)	NS
Major adverse cardiac events (%)	32.1	25.0	1.34 (0.73–2.46)	NS	31.3	24.5	1.34 (0.67–2.68)	NS

RR, relative risk.

RESULTS — Diabetes was present in 160 of 1,548 patients (10.3%), 84 randomized to stent and 76 to balloon angioplasty. Baseline characteristics were comparable between the groups, without any difference in terms of distal embolization and/or myocardial perfusion (Table 1). A total of 17 patients (20.2%) randomized to stent underwent cross-over to balloon angioplasty mostly because of unsuitable anatomy, whereas 23 patients (30.3%) initially randomized to balloon angioplasty were finally treated with coronary stenting because of unsatisfactory result or residual dissection after balloon angioplasty (Table 1). As shown in Table 2, no difference in clinical outcome was observed between balloon and stenting at 1 year of follow-up, even after the exclusion of patients who underwent cross-over.

A total of 65 (40.5%) patients underwent scheduled angiographic follow-up. As shown in Table 3, stenting, despite better postprocedural minimal lumen diameter, was not associated with a reduction in restenosis.

CONCLUSIONS — Previous randomized trials (1–7) have shown that stenting is superior to balloon angioplasty in terms of restenosis and TVR. However, despite their high-risk features and worse outcome after coronary stenting (8–11), very few data have been reported in diabetic patients undergoing primary angioplasty for STEMI. Data from the STENT PAMI (Primary Angioplasty in Myocardial Infarction) trial (14) showed that among 135 diabetic patients coronary stenting did not reduce restenosis or improve outcomes compared with balloon angioplasty.

A subanalysis of the CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) trial (15) analyzed the impact of stenting and abciximab in 346 diabetic patients. Stenting was associated with a reduction in TVR, without any benefits in terms of death and reinfarction, whereas abciximab did not improve clinical outcome. However, no data were reported on myocardial perfusion. In fact, diabetes has been shown to be associated with impaired reperfusion (16).

The Zwolle-6 randomized trial (12) addressed the actual role of routine stenting in a large cohort of unselected patients undergoing primary angioplasty, without any exclusion criteria. Furthermore, routine follow-up angiography was scheduled in only a part of patients. Therefore, the results may provide a better insight into daily clinical practice.

In this subanalysis in diabetic patients, we found a similar outcome between stent and balloon in terms of thrombolysis in myocardial infarction flow, distal embolization, ST-segment resolution, and myocardial blush, all major determinants of mortality (13,17). Differently from the CADILLAC trial (15), but in accordance with the STENT PAMI trial (14), stenting did not improve outcome in terms of restenosis and TVR.

Recent studies in elective patients have shown significant benefits from drug-eluting stents in terms of restenosis and TVR (18–19), particularly in diabetic patients (20–21). In the DIABETES (Diabetes and Sirolimus-Eluting Stent) trial (20), the sirolimus-eluting stent significantly reduced target lesion revascularization from 31.3 to 7.3%. Similar findings were observed in the subanalysis of the TAXUS-IV trial (21), which showed among diabetic patients a significant reduction in TVR (from 24.0 to 11.3%). Even though the reduction in restenosis will not be expected to reduce the incidence of acute coronary events (18–22), drug-eluting stents might determine a further reduction in costs due to reduction in TVR, particularly in patients that have high chances of restenosis, such as those suffering from diabetes (8–9). Although the initial results showed the feasibility of drug-eluting stents for STEMI (23), its safety issue for STEMI remains to be established. Therefore, future randomized studies, without strict inclusion cri-

Table 3—*Quantitative angiography in 65 patients undergoing angiographic follow-up*

	Overall population			Patients without cross-over		
	Stent	Balloon	*P* value	Stent	Balloon	*P* value
n	31	34		27	28	
Reference diameter (mm)	2.89 ± 0.56	2.86 ± 0.62	NS	3.08 ± 0.51	2.94 ± 0.5	0.004
Minimal lumen diameter (post) (mm)	2.38 ± 0.48	2.05 ± 0.6	0.016	2.56 ± 0.42	2.03 ± 0.50	<0.001
Minimal lumen diameter (follow-up) (mm)	1.4 ± 0.77	1.44 ± 0.73	NS	1.68 ± 0.80	1.52 ± 0.73	NS
Restenosis >50% (%)	48.4	44.1	NS	44.4	50.0	NS
Restenosis >70% (%)	12.9	11.8	NS	11.1	14.3	NS

Data are means ± SD, unless otherwise indicated.

teria, should be conducted to provide safety and cost-benefit analysis of an unrestricted use of drug-eluting stents in diabetic patients undergoing primary angioplasty for STEMI.

Limitations

Since the benefits of adjunctive glycoprotein IIb-IIIa inhibitors have only been shown recently (21), only 5% of our patients received this additional drug. Our results may have been affected by the relatively high cross-over rate observed in our trial, as a consequence of the absence of exclusion criteria and the early randomization strategy in comparison with previous randomized trials (25). However, our results were confirmed even in the analysis performed excluding patients who underwent cross-over (Table 2). Finally, this was a subanalysis of a large randomized trial and was thus potentially underpowered to detect any difference among the two groups.

Summary

As compared with balloon angioplasty, routine coronary stenting does not seem to improve clinical outcome in diabetic patients undergoing primary angioplasty for STEMI.

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