Comparison of Stent Graft, Sirolimus Stent, and Bare Metal Stent Implanted in Patients with Acute Coronary Syndrome: Clinical and Angiographic Follow-up

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Aim To compare polytetrafluoroethylene stent graft (PTFE) with sirolimus and bare metal stents in reducing in-stent restenosis in native coronary vessels in patients with acute coronary syndrome.

Methods The study included patients who underwent stent implantation in acute coronary syndrome from January 2003 to May 2004. The patients (n = 119) were randomized either to stent graft group (n = 40), sirolimus eluting stent group (n = 39), or bare metal stent group (n = 40). The main outcome measure of the study was the incidence restenosis at 6-month. The secondary outcome was 6-month major adverse coronary event rate.

Results The incidence of 6-month major adverse coronary events was similar in all three groups (8 events in stent graft, 9 in sirolimus eluting stent, and 16 in bare metal stent group events). The target lesion revascularization was higher in the bare metal stent group ($P = 0.044$). Restenosis rate, at six-month follow-up was higher in the bare metal stent group compared with the stent graft and sirolimus eluting stent groups. The percent diameter stenosis in the follow-up was significantly higher in the bare metal stent group ($P = 0.005$). The late loss was significantly lower in the sirolimus eluting stent group (mean ± standard deviation, 0.2 ± 0.5 mm), compared with the bare metal stent group (0.7 ± 0.7 mm, $P = 0.034$). There was a trend of lower late loss in the stent graft group than in the bare metal stent group.

Conclusion Three groups of stents implanted in patients with acute coronary syndrome did not differ in the incidence of major adverse cardiac events. Sirolimus-eluting stents had a lower incidence of in-stent restenosis than bare metal stent group. Stent graft implanted in native coronary arteries appears to be safe and efficient in patients with acute coronary syndrome, but a significant reduction in in-stent restenosis was not achieved.

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Percutaneous coronary intervention with stent implantation has become a standard procedure in patients with coronary disease in acute coronary syndrome (1). The long-term outcomes are good (2), but the problem of in-stent restenosis has not yet been solved (3). Drug eluting stents, which have recently appeared, seem to be an answer to this challenge, but there has still been no evidence-based data about their long-term outcome in the acute coronary syndrome. Stent grafts (polytetrafluoroethylene covered stent) could also reduce the incidence of acute complications and restenosis during follow-up by reduction in active plaque protrusion through stent struts and distal embolization (4), and on the other hand by reduction in interaction of tissue and blood growth factors in the early postinterventional period (5), reducing in that way the incidence of in-stent restenosis.

This was a single-center randomized trial with an aim to compare polytetrafluoroethylene grafts with sirolimus and bare metal stents stent in patients with acute coronary syndrome. The primary endpoint was angiographic restenosis on quantitative coronary angiography analysis during 6-month follow-up. The secondary endpoint was 6-month major adverse coronary event rate.

Patients and methods

The study included patients who underwent stent implantation in acute coronary syndrome from January 2003 to May 2004. A diagnosis of acute coronary syndrome included acute myocardial infarction with ST elevation, prolonged angina for more than 20 minutes, or recurrent episodes at rest with indicators of cardiac ischemia or injury (cardiac enzyme elevation and ST segment denivelation).

Patients with previous percutaneous coronary intervention or coronary artery bypass graft surgery, multivessel, diffuse disease, tortuous vessel, arteries less than 3 mm in diameter, distal stenosis location, and left main and bifurcation lesions were excluded from the study. A total number of 119 patients were randomized to stent-graft, sirolimus, or bare-metal stent group. Treatment assignment was determined by computer-generated randomization codes. Demographic, angiographic, and procedural characteristics were similar for all three groups (Table 1). The study protocol was approved by the Ethics Committee of the Zagreb University Hospital, and written informed consent was obtained from all patients.

Table 1. Demographic, clinical, and angiographic data of patients with acute coronary syndrome who underwent stent graft, sirolimus stent, or bare metal stent implantation*

Parameters	Findings (mean±SD) in group with			
	stent graft	sirolimus	bare metal	*P*
No:	40	39	40	
Age (years)	57.8 ± 9.9	58.5 ± 9.8	57.1 ± 10.4	0.828
Male (%)	82.5	74.4	82.5	0.586
Hypercholesterolemia (%)	55	59	70	0.367
Hypertension (%)	50	64.1	52.5	0.411
Diabetes (%)	30	33.3	30	0.935
Smoking (%)	15	15.4	15	0.419
Acute myocardial infarction (%)	47.5	20.5	45	0.243
Target vessel (%)				
LAD	35	48.7	42.5	
CX	10	7.7	15	
RCA	50	30.8	32.5	
LMCA	5	7.7	5	
OM1	0	5.1	5	0.577
Lesions' length (mm)	11.5 ± 2.4	13.5 ± 4.6	13.1 ± 4	0.052

*Abbreviations: SD – standard deviation; LAD – left anterior descending coronary artery; CX – circumflex coronary artery; RCA – right coronary artery; LMCA – left main coronary artery; OM1 – first obtuse marginal branch of circumflex coronary artery.

Procedure

All procedures were performed using standard transfemoral approach (6) with seven-French guiding catheters (6). All patients received aspirin (300 mg), heparin (10 000 IU or more in longer procedures), and eptifibatide (Integrilin, Glaxo Group, Greenford, United Kingdom) 180 μg/kg bolus in angiographic evidence of thrombus, followed by 6-12 hours infusion (2 $\mu g\ kg^{-1}\ min^{-1}$). Standard percutaneous coronary intervention was performed with balloon predilation, stent placement, and post-dilation if needed (6).

Procedural success was defined as residual stenosis <20% of the reference diameter (7). Major adverse cardiac events included death, myocar-

dial infarction, coronary artery bypass graft surgery, or repeated percutaneous coronary intervention (8). Myocardial infarction was defined as chest pain, development of electrocardiographic changes, and rise in serum creatine kinase-MB concentration (8).

Post procedural medications included aspirin 100 mg/d and ticlopidine 500 mg/d (clopidogrel was not available). Ticlopidine was stopped 6 weeks after the procedure. All patients were asked to return to our center for evaluation 6 months after discharge.

Quantitative coronary arteriography analysis

Digital angiograms were analyzed with an automated edge-detector (Advantx GE – GEMNET, General Electric Company, Fairfield, CT, USA). Quantitative data included reference diameter, minimal luminal diameter, lesion length, percentage diameter stenosis, acute gain, and late lumen loss (the difference between the minimal luminal diameter after the procedure and the minimal luminal diameter at follow-up).

Statistical analysis

Categorical variables were expressed as percentages. Continuous variables were presented as mean ± standard deviation (SD). Categorical variables were compared with χ^2 test or Fisher test when appropriate. Continuous variables were compared with *t* test or ANOVA. A two-tailed probability value of 0.05 or less was considered significant. Analyses were performed with MedCalc Software (MedCalc Inc., Mariakerke, Belgium).

Results

Quantitative angiographic measurements are presented in Table 2. Baseline lesion characteristics were similar in all three groups. After treatment, an average minimal luminal diameter ± SD in stent graft group was 3.5 ± 0.3 mm, in sirolimus group 3.0 ± 0.3 mm, and in bare metal stent group 3.0 ± 0.5 mm ($P = 0.010$). Stenosis of luminal diameter in stent graft group was 9.3 ± 7.6%, in sirolimus group 9.4 ± 6.7%, and in bare metal stent group 16.1 ± 11.4% ($P = 0.004$).

Table 2. Quantitative angiographic measurements of patients with acute coronary syndrome who underwent stent graft, sirolimus stent, or bare metal stent implantation*

Parameters	Findings (mean±SD) in group with			*P*
	stent graft	sirolimus	bare metal	
No.	40	39	40	
Before treatment:				
RD (mm)	3.5 ± 0.4	3.4 ± 0.3	3.4 ± 0.5	0.337
MLD (mm)	1.2 ± 0.8	1.2 ± 0.6	1.1 ± 0.7	0.815
stenosis of LD (%)	84.5 ± 14.1	82.0 ± 15.9	86.0 ± 11.6	0.441
After treatment:				
MLD (mm)	3.5 ± 0.3	3.0 ± 0.3	3.0 ± 0.5	0.010
stenosis of LD (%)	9.3 ± 7.6	9.4 ± 6.7	16.1 ± 11.4	0.004
Follow-up:				
MLD (mm)	3.0 ± 1.0	2.7 ± 0.6	2.4 ± 0.9	0.006
stenosis (%) of LD	21.4 ± 27.4	16.4 ± 20.6	39.6 ± 27.7	0.005
Changes in MLD:				
acute gain (mm)	2.3 ± 0.7	1.8 ± 0.5	1.9 ± 0.7	0.012
late loss (mm)	0.4 ± 0.8	0.2 ± 0.5	0.7 ± 0.7	0.034

*Abbreviations: SD – standard deviation; RD – reference diameter; MLD – minimal luminal diameter; LD – luminal diameter.

Clinical and angiographic follow-up was possible for all patients. Mean±SD duration of follow-up was 187.7 ± 53.6 days. There was a significant statistical difference in quantitative angiographic measurements between the three groups 6 months after the procedure. An average minimal luminal diameter in stent graft group was 3.0 ± 1.0 mm, in sirolimus group 2.7 ± 0.6 mm, and in bare metal stent group 2.4 ± 0.9 mm ($P = 0.006$). Stenosis of luminal diameter in stent graft group was 21.4 ± 27.4%, in sirolimus group 16.4 ± 20.6%, and in bare metal stent group 39.6 ± 27.7% ($P = 0.005$). Acute gain in stent graft group was 2.3 ± 0.7 mm, in sirolimus group 1.8 ± 0.6 mm, and in bare metal stent group 1.9 ± 0.7 mm ($P = 0.012$). Late loss in stent graft group was 0.4 ± 0.8 mm, in sirolimus group 0.2 ± 0.5 mm, and in bare metal stent group 0.7 ± 0.7 mm ($P = 0.034$).

Clinical events that occurred at 6 months are listed in Table 3. There was no difference between the three groups except in the incidence of target lesion revascularization, which was significantly higher in bare metal stent group ($P = 0.044$).

Table 3. Clinical outcome in follow-up of patients with acute coronary syndrome who underwent stent graft, sirolimus stent, or bare metal stent implantation*

Parameters	Findings in group with			*P*
	stent graft	sirolimus	bare metal	
No.	40	39	40	
Death (%)	2.5	0	0	0.375
Myocardial infarction (%)	5	5.1	7.5	0.868
CABG (%)	0	7.7	5	0.232
PCI-nTLR (%)	7.7	5.1	5	0.868
TLR (%)	5	5.1	22.5	0.044
Total major adverse cardiac events (%)	20	23.1	40	0.187

*Abbreviations: CABG – coronary artery bypass graft surgery; PCI – percutaneous coronary intervention; TLR – target lesion revascularization; PCI-nTLR – percutaneous coronary intervention-no target lesion revascularization.

Discussion

We decided to use balloon-expandable covered stents in acute coronary syndrome for similar reason as in saphenous vein graft intervention, ie thrombus containing lesions, reduction of distal embolization, and possible reduction of restenosis. There were some proposals to use covered stents (self-expandable) in unstable lesions of carotid arteries, where a significant reduction of ipsilateral microembolization was achieved, but the study was stopped because of high restenosis rate (9).

At the time of this study, there was some evidence of restenosis reduction after percutaneous coronary intervention in acute coronary syndrome with sirolimus eluting stent (2,10), so we decided to randomize the patients in 3 groups. The reduction in restenosis in acute myocardial infarction with sirolimus eluting stent was proved in a randomized trial (3).

In our study, there was a significant reduction in restenosis after implantation of sirolimus stent, in comparison with bare metal stent. However, we failed to support the hypothesis that restenosis was reduced after stent-graft implantation, although there was a trend of lower late loss in this group. It is possible that this is a result of achieving higher minimal luminal diameter after stent-graft implantation (bigger stents available and the need for higher inflation pressure). There was no difference in the incidence of major adverse coronary events in the three groups, although one patient in the stent-graft group died. He died in the fifth month of the follow-up, possibly from late stent thrombosis. There was evidence of a higher incidence of stent thrombosis when covered stents were implanted. The mechanism might be delayed re-endothelialization (11). Ticlopidin therapy was administrated for three months in all 3 groups of patients.

The incidence of target lesion revascularization was higher in the bare metal stent group than in stent graft and sirolimus group ($P=0.044$). The only studies reporting in-stent restenosis of covered stents in native coronary arteries included various clinical settings in a small number of patients (12,13).

Since its first appearance in clinical practice, balloon-expandable covered stent was used in bailout situations (14). It was also used in percutaneous coronary intervention of old saphenous vein graft to reduce distal embolization of degenerated tissue and thrombus (4,15,16). Although there are some doubts about this indication (17), in saphenous vein graft interventions stent-grafts are still often used. The use of grafts is rare in native coronary arteries, except for closing perforation, coronary aneurysms, or fistulas (5,18-21). Only two studies (one involving 50 and the other 12 patients) described the use of stent graft in native coronary arteries without the above mentioned reasons. The primary results were acceptable, and after six-month of the follow-up the incidence of any major adverse coronary events including target lesion revascularization was 24% and 30% (22,23). Compared with in-stent restenosis rate after bare metal stent implantation, it was considered a good result. No further investigations were performed in this field.

The primary role of covered stents is management of complications (24), but we proved that early and late results of stent graft implantation in native coronary arteries in acute coronary syndrome were comparable with bare metal stents, with less need for target vessel revascularization, but higher restenosis rate in comparison with si-

rolimus stent. Maybe the results would be better if the only commercially available JOMED stent graft (Jomed International AB, Helsingborg, Sweden) would improve after almost 10 years on the market (25).

The study did not demonstrate a difference in cumulative major adverse coronary events among patients after implantation of stent grafts, sirolimus stents, and standard metal stents in acute coronary syndrome. There was a significant difference in restenosis rate between sirolimus stents and bare metal stents, and a trend of lower restenosis rate in stent graft than in bare metal stent in this group of patients.

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