Stent Placement Compared with Balloon Angioplasty for Obstructed Coronary Artery Disease in Thai Elderly Patients : Initial Result and 6 Months Follow-up†

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Abstract

Percutaneous Old Balloon Angioplasty (POBA) is accepted worldwide for the treatment of obstructive coronary artery disease because this technique is safe, and quick and the patient may return to work earlier than with bypass surgery (particularly elderly patients). But the major problem with POBA is restenosis which occurs between 20-40 per cent. Stent placement has been reported to reduce the restenosis rate to 10-20 per cent.

Objective : The purpose of this study was to compare the effects of stent placement with those of balloon angioplasty on clinical and angiographic outcomes in elderly Thai patients with obstructive coronary artery disease.

Method : The study was a randomized controlled trial. The sample size was 45 lesions in 42 patients who were assigned into 2 groups; 23 in the balloon angioplasty group and 22 in the stent placement group (Crown Stent). Clinical information and coronary angiography were recorded and performed at the time of the index procedure and six months later.

Results : There was 100 per cent procedural success in 22 lesions treated in the stent group and 82.6 per cent in the 23 lesions treated in the balloon angioplasty group. Patients in the stent group had a lesser degree of stenosis immediately after the procedure (8.78 ± 8.63 *vs* $30.92 \pm 9.01\%$, $p < 0.001$) and a greater minimal luminal diameter (MLD) (3.04 ± 0.44 *vs* 2.15 ± 0.33 mm, $p < 0.001$). There were no major complications in either group during the procedure or during their hospital stay. These were not maintained at the six months follow-up. (26.88 ± 16.23 *vs* 33.82 ± 14.63 mm, $p = 0.19$, 2.28 ± 0.67 *vs* 2.01 ± 0.51 mm, $p = 0.17$) for the degree of stenosis and the MLD respectively. The restenosis rate, which was the primary endpoint of the study, was 4.5 per cent in the stent group and 21 per cent in the balloon angioplasty group ($p = 0.10$)

Conclusions : Stenting in Thai elderly ischemic patients has a higher procedural success rate when compared with balloon angioplasty. The restenosis rate of stenting is also lower than that of balloon angioplasty but did not reach statistical significance. However, both techniques had no major complications either during the procedure or in-hospital.

Key word : Coronary Artery Disease, Elderly, Stent

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Nowadays, the treatment of patients with obstructive coronary artery disease by percutaneous old balloon angioplasty (POBA), is one of the most convenient, safe and effective treatments in this group of patients. It also has less morbidity and mortality compared with coronary artery bypass graft particularly in elderly patients who have comorbid diseases. However, the problem of restenosis in POBA is still high 20-50 per cent[1-3]. Sigward et al[4] were the first group to use a stent in order to decrease the restenosis rate in 1987. Since then, there have been rapid developments of stent design, materials or adjunctive therapy. Surruys et al (1994)[5] reported the advantage of stent insertion in terms of reducing the restenosis rate in coronary artery stenosis from 38 per cent to 22 per cent when compared with POBA. Although elderly patients have a higher incidence of procedure-related death and late recurrence of angina after POBA, the recently reported complication rates for POBA seem to be lower. Thomson et al[6] (1996) reported the changing outcome of POBA in the elderly; the success rate in 1989-1990 was 88.1 per cent compared with a success rate of 93.5 per cent in 1990-1992. No trial has been reported comparing POBA and stent in elderly patients directly. Accordingly, the authors conducted a prospective, randomized trial to compare stent implantation with POBA for the treatment of obstructive coronary artery disease in elderly Thai patients.

METHOD

The study was done with co-operation between the Division of Cardiology, Department of Medicine and Her Majesty's Cardiac Center, Faculty of Medicine Siriraj Hospital, Mahidol University. The study protocol was approved by the institutional review board.

Selection of patients

Consective elderly patients (age $\geq$ 60 years) with single or two vessel disease who were scheduled to undergo percutaneous transluminal coronary angioplasty for one or two lesions in either the left or the right coronary artery were eligible for this study. The general exclusion criteria were bed-ridden cases with severe disability, severe hepatic or renal diseases, participation in another study within the past 30 days, factors making follow-up difficult, intended surgical interventions, factors making repeated angiography unlikely, patients with left bundle branch block or bifascicular block or patients with a pacemaker, patients unwilling to sign an informed consent form or patients who were not capable of understanding the consent form. The exclusion criteria related to the

procedure were:- previous angioplasty of the same vessel or branches, intended angioplasty of a coronary bypass, intended angioplasty of a lesion in a vessel supplied by a graft, intended angioplasty of a lesion less than 3.0 mm in diameter, or when a stent of less than 3.0 mm was implanted, intended angioplasty of a lesion longer than 15 mm, intended angioplasty of occluded vessels, intended angioplasty of a main stem left coronary or ostial lesion, intended angioplasty of a moderate to heavity calcified lesion, or intended angioplasty of an infarct-related artery. The exclusion criteria related to concomittant medication were patients with intolerance to acetyl salicylic acid, contraindications to acetyl salicylic acid therapy, cerebrovascular accident within the last six months, severe or uncontrolled hypertension (diastolic and/or systolic blood pressure over 130 and 220 mmHg respectively), patients with thrombocytopenia (< 100,000 per sq.mm), patients with renal impairment (serum creatinine > 3.0 mg/dl), patients using anticoagulants which could not be replaced by acetyl salicylic acid. After giving informed consent, patients were randomly assigned to either POBA or stent implantation.

Protocols

The stent used in this trial was a Crown Stent which is a bare stent (Johnson & Johnson Interventional Systems). Patients assigned to stent placement received aspirin 300 mg daily, beginning at least 24 hours before the procedure, ticlopidine (250 mg) twice a day beginning at least 48 hours before the procedure. During the procedure, 7,500 units of heparin were given and a dose of 2,500 units of heparin given every 45 minutes in order to maintain an activated clotting time (ACT) of more than 300 seconds. Patients assigned to POBA received aspirin 300 mg daily, beginning at least 24 hours before the procedure and the other drugs as given in the stent placement group except for ticlopidine. Both groups received aspirin indefinitely, but the stent placement group received ticlopidine (200 mg) twice a day for 1 month. Crossover to stent placement was permitted as a bailout procedure in the event of an abrupt or threatened vessel closure or unacceptable result (residual stenosis > 30%). Patients assigned to the angioplasty group who required stent placement as a bailout procedure received ticlopidine in addition to aspirin as in the stent group.

Follow-up

Patients were evaluated clinically one, three and six months after the procedure. Coronary angiography was repeated at six months. Angiography was performed earlier if there were recurrent symptoms before the 6 month's follow-up.

Angiographic analysis

Angiography was performed in orthogonal views as a base line investigation, after the procedure, and at six months. Quantitative coronary analysis was performed at on-line QCA of Philip System. The diameters of the "normal" segments proximal and distal to the lesion were averaged to determine the reference vessel diameter. The minimal luminal diameter, reference diameter and degree of stenosis as a percentage of the vessel diameter were calculated as mean values from orthogonal projections.

Endpoints

The primary angiographic endpoint was restenosis, defined as a stenosis of 50 per cent or more of the luminal diameter as follow-up. Secondary angiographic endpoints included procedural success and changes in reference diameter at the dilated or stented segments at six months relative to its baseline. Procedural success was defined as a reduction in the degree of stenosis to less than 30 per cent. The primary clinical endpoints were a composite outcome of cardiac death, acute myocardial infarction and recurrent symptoms of angina which required further intervention therapy of the target lesion.

Statistical analysis

The target sample size based on the assumption that the rate of restenosis of POBA in a de novo lesion would be 30 per cent and the rate of restenosis of stent placement would be less than 10 per cent, was 70 lesions. Data were recorded in case-record form and charts.

Outcomes were analyzed according to the intention-to-treat principle. Categorical data were assessed by the chi-square test or Fisher's exact test. Two-tailed p-values were calculated with values below 0.05 considered to indicate statistical significance.

RESULTS

Between October 1998 and December 1999, 42 patients (45 lesions) were enrolled, 23 lesions were assigned to POBA and 22 lesions to stent placement. The base-line clinical and angiographic characteristics of both groups are shown in Table 1 and 2 respectively. Both groups were well matched with no statistical difference between them.

Table 1. Base-line clinical characteristics of the patients.

	POBA arm	Stenting arm	P-value
Number of lesions	23	22	
Age	71.31 ± 6.16	67.02 ± 6.41	0.476
Sex (male : female)	16 : 7	13 : 9	0.468
Degree of angina			
CCSC 1-2	20	15	0.134
CCSC 3-4	3	7	
Hypertension	14	12	0.671
Diabetes mellitus	7	6	0.817
Dyslipidemia	11	14	0.213
Ex-smoker	9	6	0.262
Prior history of MI	7	7	0.921

Table 2. Base-line anatomical characteristics of the patients.

	POBA arm	Stenting arm	P-value
Number of lesions	23	22	
Site of study vessels			
Left anterior descending artery	6	5	
Left circumflex artery	4	5	
Right coronary artery	13	12	
Type of study lesion			
Type A	1	2	
Type B_1	14	13	
Type B_2	5	6	
Type C	3	1	
Presence of thrombus	0	1	
Lesion morphology			
Concentric	12	8	
Eccentric	11	14	
Mean % diameter stenosis	68.65 ± 9.25	66.63 ± 13.40	0.558
Mean minimal luminal diameter	0.96 ± 0.37	1.03 ± 0.49	0.581
Mean reference diameter	3.05 ± 0.47	3.10 ± 0.54	0.737
Mean lesion length	10.97 ± 3.49	9.66 ± 3.24	0.201

Procedural outcomes

The rate of procedural success was 82.6 per cent (19/23) in the POBA group and 100 per cent (22/22) in the stent placement group. There were 4 lesions in the POBA group that crossed over to stent placement because of dissection in 3 and an unacceptable result (residual stenosis more than 30%) in 1 as shown in Diagram 1. No other significant procedural complications in either group were observed in this trial.

Angiographic results

Coronary angiography was repeated a mean of 185 ± 19 days after the initial procedural in POBA group and 184 ± 30 days in the stent placement group. The follow-up rate was 82.6 per cent (19/23) in the POBA group, 2 patients died before the follow-up period (1 from sudden cardiac death, 1 from cancer of the cervix), 2 patients who were free of symptoms refused repeated angiography. In the stent placement group, the follow-up rate was 100 per cent (22/22). The quantitative angiographic results are shown in Table 3. Immediately after the procedure, a large mean luminal diameter was achieved in the stent placement group (3.04 ± 0.44 *vs* 2.15 ± 0.33, $p < 0.001$) and a lesser degree of mean residual stenosis in the stent group (8.78 ± 8.63 *vs* 30.92 ± 9.01, $p < 0.001$). Although the late loss of luminal diameter was significantly higher after stenting (0.76 ± 0.55 *vs* 0.15 ± 0.61, p 0.004), there was a greater mean net gain in luminal diameter in 6 months with stenting but this

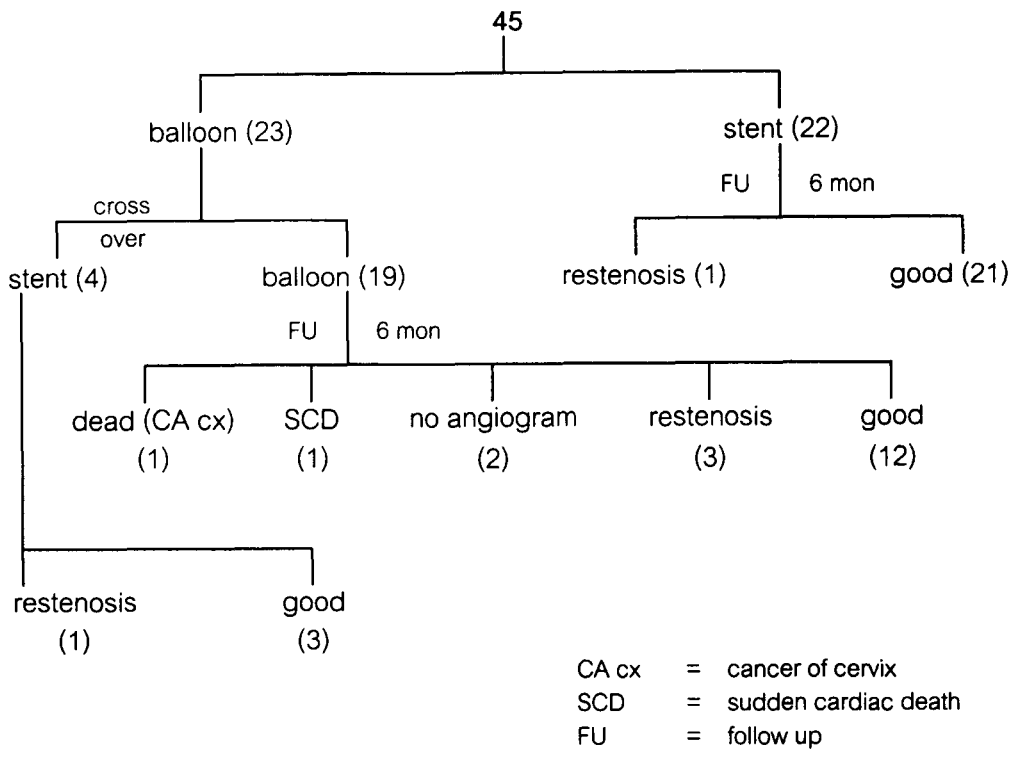

Diagram 1. Summary of the procedure, angiographic and clinical outcome of all 45 lesions.

was not statistically significant (1.28 ± 0.83 *vs* 1.04 ± 0.63, p = 0.33). The minimal luminal diameter at six-months was 2.28 ± 0.67 in the stent group and 2.01 ± 0.51 in the POBA group (p = 0.17). The angiographic restenosis was found in 4 lesions in the POBA group (3 in POBA alone, 1 in the crossover to stent placement) and 1 lesion in the stent placement group (as shown in Diagram 1).

When the results were analyzed according to intention-to-treat principles and using the best scenario (1 death from CA cervix and 2 of free of symptoms without repeated angiogram were considered as showing no restenosis in the POBA group), the restenosis or death were found in 21.7 per cent (5/23) in the POBA group and 4.5 per cent (1/22) in the stent placement group (p = 0.10) and the power of the study was 50 per cent.

Clinical follow-up

There were 2 patients who experienced angina before the 6 month follow-up, one in each group, but angiogram revealed no significant obstructive lesion of the target vessel. One patient in the POBA group died suddenly from a suspected cardiac cause. The remainder had no serious cardiac events in the 6 month follow-up period.

DISCUSSION

Ischemic heart disease has now become one of the major problems in Thai Public Health. Percutaneous old balloon angioplasty (POBA) is widely accepted as one mode of treatment, if the coronary lesion is suitable. But restenosis remains the main limitation of POBA for revascularization. It is observed in 20 to over 50 per cent[1] of cases depending on the prevailing risk factors (particularly in elderly patients) and the techniques used. There are 2 strategies to solve this problem: mechanical and pharmacological strategies. Stenting is one of the mechanical methods shown to be effective as in the Benestent trial (1994)[5], the STRESS trial (1994)[7], and the START trial (1999)[8] which demonstrated that stenting reduced the rate of restenosis from 32 per cent to 22 per cent, 42 per cent to 31 per cent and 37 per cent to 22 per cent respectively. But all of these trials studied the general population, not elderly patients

Table 3. Characteristics of lesions at base-line and angiographic results immediately after the procedure and at six months.

Variable	POBA arm	Stenting arm	P-value
Number of lesions	23	22	
Days of follow-up	185.53 ± 19.80	184.29 ± 30.11	0.88
At base-line			
Diameter of reference vessel (mm)	3.02 ± 0.48	3.09 ± 0.55	0.69
Minimal luminal diameter (mm)	0.97 ± 0.35	1.00 ± 0.48	0.79
Degree of stenosis (% of diameter)	68.17 ± 8.51	67.42 ± 13.21	0.84
After procedure			
Diameter of reference vessel (mm)	3.14 ± 0.48	3.27 ± 0.57	0.46
Minimal luminal diameter (mm)	2.15 ± 0.33	3.04 ± 0.44	< 0.001
Degree of stenosis (% of diameter)	30.92 ± 9.01	8.78 ± 8.63	< 0.001
At 6 months			
Number of lesions	15	22	
Diameter of reference vessel (mm)	3.06 ± 0.50	3.09 ± 0.47	0.86
Minimal luminal diameter (mm)	2.01 ± 0.51	2.28 ± 0.67	0.17
Degree of stenosis (% of diameter)	33.82 ± 14.63	26.88 ± 16.23	0.19
Change in minimal luminal diameter (mm)			
Immediate gain (mm)	1.19 ± 0.43	2.04 ± 0.59	< 0.001
Late loss (mm)	0.15 ± 0.61	0.76 ± 0.55	0.004
Net gain (mm)	1.04 ± 0.63	1.28 ± 0.83	0.33

who are expected to have a lower success rate with more complications. A recent study by Thompson[9] showed an increasing success rate of POBA in elderly patients from a success rate of 88.1 per cent in 1980-1989 to 93.5 per cent in 1990-1992 ($p < 0.001$). This finding is the same as that of Peterson et al in 1994 [10]. But the rate of restenosis in this group of patients is still high at 25-43 per cent[11]. There is no study comparing the success rate and long-term follow-up of POBA and stent placement in elderly patients.

The results of the present randomized trial demonstrate that stent placement has a higher success rate than POBA (100% *vs* 82.6%, $p = 0.059$). The success rate in the POBA group was lower than Shaper et al[12] who reported a success rate of 91 per cent. Stenting was associated with superior initial angiographic results; less residual stenosis, and a larger minimal luminal diameter. But the late loss in the stenting group was higher than the POBA group as in a previous trial[5,13], so the net gain in luminal diameter favors the stent group but was not statistically significant in the present trial.

The combined primary endpoints of angiographic and clinical results in the present trial favor the stent placement group rather than the POBA group, in terms of restenosis rate, but this did not reach statistical significance (4.5% *vs* 21.7%, $p = 0.10$). The use of the intention-to-treat principle in a prospective, randomized trial may yield results that are less favorable than expected because of the cross over to the stenting arm of the trial in 4 cases (17.4%). However, the absolute reduction in the restenosis rate of the stent placement group was high (17.2%) and the power of study was 50 per cent which clearly demonstrates that the sample size was too small to show a statistically significant difference between the two groups.

The secondary angiographic endpoint; change in reference diameter at the dilated or stented segment at six months relative to its base line (net gain), was not different in either group. Even though the initial minimal luminal diameter (MLD) was larger in the stenting group than the POBA group (2.04 ± 0.59 *vs* 1.19 ± 0.43 mm, $p < 0.001$), the late loss was greater in the stenting group than the POBA group. (0.76 ± 0.55 *vs* 0.15 ± 0.61 mm, $p = 0.004$).

The results of the present randomized trial demonstrate that elective stent placement procedure have a better angiographic outcome than balloon angioplasty in the treatment of de novo lesions in coronary arteries of elderly patients. Stenting was associated with superior initial angiographic results, higher rates of procedural success and lower complication rates. Although the rates of restenosis were not significantly different between the two treatment

strategies at six months, they favored the stenting group rather than the POBA group.

The restenosis rates of both groups in the present study were lower than in previous trials[3,7]. This could be explained by the differences in patient characteristics. Most of the presented patients had type A, or B[14] lesions which have a lower rate of restenosis compared with type C lesions.

Limitation of this trial

The sample size in this trial is too small. At the onset of the design of the trial the authors calculated that we needed a sample size of at least 70 lesions would be needed. During the trial the authors found that it was very difficult to enroll suitable patients to meet the trial targets. The authors have learnt that to perform a randomized controlled trial in interventional cardiology, a multicenter trial should be conducted in order to recruit a sample and complete the trial in the scheduled time.

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การเปรียบเทียบผลการรักษาเส้นเลือดหัวใจตีบในผู้ป่วยสูงอายุไทย ด้วยการถ่างขยายบอลลูนกับการใช้ท่อโลหะค้ำยัน : ผลการรักษาเบื้องต้นและระยะ 6 เดือนหลังการรักษา

ประดิษฐ์ ปัญจวีณิน, พบ, ดำรัส ตรีสุโกศล, พบ*, เรวัตร พันธุ์กิ่งทองคำ, พบ*, อดทน ศรียุทธศักดิ์, พบ*, ยงยุทธ สหัสสกุล, พบ*, รำไพพรรณ ทองสวัสดิ์, พยบ**

ได้ศึกษาเปรียบเทียบผลการรักษาภาวะเส้นเลือดหัวใจตีบชนิดที่ไม่ซับซ้อน ด้วยการถ่างขยายหลอดเลือดในผู้ป่วยสูงอายุไทยจำนวน 45 ตำแหน่ง จากจำนวนผู้ป่วย 42 คน โดยแบ่งเป็นกลุ่มที่ขยายด้วยบอลลูน จำนวน 23 ตำแหน่งและกลุ่มที่ใช้ท่อโลหะค้ำยัน จำนวน 22 ตำแหน่ง พบว่าผลการรักษาในเบื้องต้น ได้ผล 100% (22/22) ในกลุ่มที่ใช้ท่อโลหะค้ำยันเทียบกับ 82.6% (19/23) ในกลุ่มที่ใช้บอลลูน โดยไม่พบผลแทรกซ้อนที่สำคัญเลยในทั้ง 2 กลุ่มของการรักษา และผลหลังการรักษา 6 เดือน พบว่ามีอัตราการตีบซ้ำ 4.5% (1/22) ในกลุ่มที่ใช้ท่อโลหะค้ำยันเทียบกับ 21% (5/23) ในกลุ่มที่ใช้บอลลูน ($p = 0.10$)

จากการศึกษาสรุปว่าการรักษาภาวะเส้นเลือดหัวใจตีบชนิดไม่ซับซ้อนในผู้ป่วยสูงอายุไทย ด้วยวิธีการถ่างขยายสามารถทำได้ด้วยความปลอดภัยและได้ผลดี ทั้งการถ่างขยายด้วยบอลลูนและการใช้ท่อโลหะค้ำยัน โดยพบว่าการใช้ท่อโลหะค้ำยันจะได้ผลสำเร็จสูงกว่าและมีอัตราการตีบซ้ำต่ำกว่า (แม้จะไม่มีนัยสำคัญทางสถิติ) ซึ่งแนวโน้มน่าจะมีนัยสำคัญทางสถิติ ถ้าใช้จำนวนประชากรศึกษามากกว่านี้

คำสำคัญ : โรคหลอดเลือดหัวใจตีบ, ท่อโลหะค้ำยัน, ผู้สูงวัย

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