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Cutting Balloons versus Stenting in Small Vessel Coronary Disease, Angiographic and Clinical Outcomes

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ABSTRACT:

Background&Aim: Vessel size is inversely correlated with the risk of restenosis and adverse outcome after percutaneous coronary interventions. There are no well defined recommendations regarding the intervention of choice in the setting of small coronary vessels. This is currently considered as a great challenge to all coronary artery interventionists. The purpose of this study was to determine the impact of cutting balloon angioplasty (CBA) compared with coronary stents on clinical and angiographic outcomes in small coronary vessels (< 3 mm in diameter)

Patients & Methods: 118 patients with symptomatic coronary artery disease were divided into 3 groups according to the treatment strategy: Drug eluting stent (DES); bare metal stent (BMS); cutting balloon angioplasty, Repeat angiography was done at 6-month follow up. The primary end-point of the study was the incidence of angiographic restenosis (>50% diameter stenosis) at follow up. Death, Myocardial infarction, stroke and target vessel revascularization were assessed as secondary end points.

Results Baseline clinical and angiographic characteristics were similar among the 3 groups. The DES group had the best immediate and late angiographic results. Surprisingly the CB group showed better late angiographic result when compared with the BMS group, in terms of better MLD, net gain, and percent restenosis rate with statistically significant values.

Conclusions DES in general is the treatment of choice so far for patients with small coronary artery disease CBA showed favourable immediate post-procedural results and better late clinical and angiographic results comparing with bare metal stent, hence cutting balloon could be a good tool in this subset of patients with considerably lesser cost comparing with BMS.

Key words: Cutting Balloons, Stenting, Coronary Disease, Angiographic.

INTRODUCTION

Vessel size is inversely correlated with the risk of restenosis and adverse outcome after percutaneous coronary interventions¹⁻³. This is because a smaller vessel is more limited in the ability to accommodate lumen restenosis, which invariably occurs to some degree in most vessels after balloon dilatation^{4, 5}. PTCA and stenting

are the two most frequently used interventions in patients with coronary artery disease⁶. Large coronary vessels represent an established indication for stenting because of its superiority compared with PTCA, as shown in several randomized clinical trials⁷⁻⁹. Stenting is associated with increased procedural costs,

however, the improved outcome, with a reduction in the need for reinterventions, has rendered this technique more cost-effective in the long term than PTCA¹⁰. A retrospective analysis has shown that stenting might be also superior to conventional balloon angioplasty in small coronary vessels¹¹. However still carries some risk of late instant restenosis or sub-acute thrombosis, and these are encountered more in patients with small coronary vessels. The cutting balloon is a new device for coronary angioplasty, which by the combination of incision and dilatation of the plaque, is believed to minimize arterial wall trauma, the neoproliferative response, and subsequent restenosis¹¹. Because of the absence of appropriately designed randomized studies, there are no well defined recommendations¹² regarding the intervention of choice in the setting of small coronary vessels. This is currently considered as a limitation in interventional cardiology and represents a great challenge to all coronary artery interventionists¹³.

AIM OF THE WORK

The aim of this study was to compare coronary stenting and cutting balloon angioplasty as regard the early and late clinical and angiographic outcomes in small coronary vessels (< 3 mm in diameter) in patients with symptomatic coronary artery disease.

PATIENTS AND METHODS

Patient population: 118 patients with significant lesions ($\geq 50\%$ diameter stenosis) in a native small sized coronary vessel were included in this study and were divided into three groups: DES, BMS, and CBA groups. All patients were admitted and followed in Tanta university hospital, Egypt, in the period between April 2004 and May 2006.

Exclusion criteria: Interventions in the sitting of acute myocardial infarction (within the last seventy two hours before the intervention), Contraindication to anti-thrombotic medications that will be used in this study, Severe hepatic or renal insufficiency, Factors that could make clinical or angiographic follow up uncertain, angiographic exclusion criteria (Lesions

produced by in-stent restenosis, Lesion containing extensive calcification, and previous angioplasty of the target lesion

Study Endpoints: The primary end-point of the study was the incidence of angiographic restenosis (>50% diameter stenosis) at follow up. Death, Myocardial infarction, stroke and target vessel revascularization were assessed as secondary end points.

Procedure:

- All patient continued their standard antianginal therapy before the procedure.
- An initial loading dose of clopidogril 300 mg followed by 75 mg once daily was generally administered before the revascularization procedure.
- During the procedure patients generally received a weight - adjusted bolus of Heparin (100 IU/Kg) and additional bolus of heparin 2500 U might be given during the procedure to maintain the activated clotting time (ACT) greater than 250 seconds.
- Bolus of abciximab (0.25 mg/kg) followed by continuous infusion (0.125 mg/kg per min for 12 hours) was given to some patients whenever indicated.
- Clopidogril (75 mg once daily) was continued at least for 12 months in DES group and 1 month in BMS group while aspirin was continued indefinitely in both groups.
- Intracoronary nitroglycerin (100-200 μ g) was given before the initial and final angiographic assessment.

Coronary angiography:

- Coronary angiograms were done in the following manner:
 - baseline angiography just before the intervention procedure.
 - Immediately after revascularization procedure.
 - At six months follow up.
- The severity of the coronary artery disease was assessed visually generally by two observers, with the use of orthogonal views.
- Angiograms were analysed using the offline automated edge detection system (Quantitative coronary angiography, QCA system). Matching views that show the most severe degree of

stenosis were selected before , immediate after the intervention and at the follow-up. QCA system was used to obtain more precise measurements pre and post the intervention procedure and at follow up angiography.

- Lesions were characterized according to the modified AHA/ACC (American Heart Association/American College of Cardiology) classification.

- Percutaneous coronary intervention (PCI) was performed using femoral approach.

Angiographic measurements:

Pre-intervention angiographic measurements included:

- Proximal and distal reference diameter: (RD1)
- Minimal lumen diameter: (MLD1). Percent diameter stenosis: $[DS\% = (RD1 - MLD1) / RD1]$.
- - RD1 = preintervention Reference diameter.
- MLD1 = preintervention minimal lumen diameter.
- Lesion length: was measured from the proximal to the distal lesion shoulder.

Immediate Post-intervention angiographic measurements include d:

- Post-procedure minimal lumen diameter (MLD2).
- Acute gain was calculated as the difference between the final and original MLD. $[AG = MLD2 - MLD1]$
- AG= acute gain
- MLD2 = immediate postintervention minimal lumen diameter.
- Relative gain represents the improvement in minimal lumen diameter as a result of the intervention. $[RG = (MLD2 - MLD1) / RD1]$.

Six month follow up Angiographic measurements include d:

- Proximal and distal reference diameter (RD2): defined as the reference diameter at six months follow up angiography.
- Minimal lumen diameter at six month follows up (MLD3).
- Late loss : shows change in MLD from immediate post-procedure to the follow up and calculated as follow $[LL = MLD2 - MLD3]$
- LL = late loss.

- Relative loss: defined as change in minimal lumen diameter from postprocedure to the follow up normalized to vessel size

$$[RL = (MLD2 - MLD3) / RD]$$

- RL= relative loss.

- Loss index which reflects the percentage of acute gain that is lost at follow up and is calculated as follow

$$[LI = (MLD2 - MLD3) / AG]$$

- LI= loss index

Patients follow up:

ECG was done in-hospital immediately post-procedure, before discharge and at 6 month follow up.

- Complications and clinical events were noted.
- All patients were asked to return for 6-month follow up regardless the presence or absence of symptoms. Angiography was performed earlier if there were any clinical indication
- At the time of follow up angiography, the following information was obtained and recorded: episodes of angina need for re-hospitalization, and cardiac events such as myocardial infarction, coronary bypass surgery, or death.

Statistical analysis: Statistical analysis was performed using the SPSS windows statistical package (version 11).

Continuous variables were presented as mean \pm standard deviation. Differences between groups were assessed by chi-square for categorical variables and unpaired student *t*-test for continuous variables. Within group comparisons of continuous variables were obtained using student's paired *t* test and one-way factorial analysis of variance (ANOVA). Probability value less than 0.05 was considered significant

RESULTS

- 49% of the stents used were SES stent while 51% of the remaining stents were bare metal stents.

- As regard the demographic and clinical characteristics there were no statistically significant differences between patients of the three groups.

Immediate and follow up clinical results:

- As regard the early in-hospital cardiac events , non fatal STEMI occurred in one patient of the DES group, One patient of the BMS group, and in the cutting balloon group one patient developed nonSTEMI.

- As regard the Late (six month) clinical follow-up only two patients in the DES groups developed late non fatal STEMI, while non of the other two groups had such an event

Immediate and follow up angiographic results

- Immediately after the intervention procedure, the DES group and BMS group had a significantly greater minimal lumen diameter, acute gain and relative gain, than the CB group with statistically significant value (p=0.005)

- At the six month follow up angiogram , the MLD in the DES group was better than the BMS and CB groups with statistically significant values (0.005, 0.001 respectively) while it was

surprisingly noticed that CB group has a relatively better MLD than BMS but with statistically significant value. (DES, 2.21 ± 0.76 ; CBA, 1.79 ± 0.65 ; BMS 1.78 ± 0.55)

- Late loss, relative loss and loss index were the least in the DES group and were found to be less in CB group in comparison with BMS group with statistically significant value

- One cases of the DES group showed critical in-stent restenosis 5 months after the intervention (treated afterward with cutting balloon intrastent) and two cases showed intrastent thrombosis and total occlusion of the stent.

- The Binary restenosis rate was the least among patients in the DES group , and it was found to be less in CB group than in BMS group with statistically significant value(DES, 6.7% , CBA , 31.7% ; BMS, 39.7% ; p=0.04)

Table 1: Lesion and procedural characteristics

| | Stent | | CB | | p value | sign |
|------------------------|--------------|--------------|--------------|--|---------|------|
| | DES | BMS | Lesion n=60 | | | |
| Target vessel % | | | | | | |
| LAD | 13 | 11 | 27 | | 0.235 | NS |
| RCA | 8 | 7 | 12 | | .235 | NS |
| LCx | 8 | 7 | 10 | | .235 | NS |
| Diagonal | 2 | 2 | 3 | | .450 | NS |
| Marginal | 3 | 2 | 4 | | .204 | NS |
| Ramus | 1 | 1 | 4 | | .212 | NS |
| Lesion length | | | | | | |
| | 16.94 ± 7.44 | 15.87 ± 6.24 | 12.22 ± 3.53 | | 0.001 | S |
| Inflation | | | | | | |
| | 12.14 ± 2.17 | 13.24 ± 1.67 | 7.77 ± 0.59 | | 0.001 | S |

Table 2 Clinical and angiographic immediate and 6 month follow up results.

| Clinical events | Stent | | CB | p value | Sign |
|----------------------------------|--------------|-------------|-------------|---------|------|
| | DES(n=32) | BMS(n=33) | CB(n=60) | | |
| Inhospital events | | | | | |
| MI | 1(3.1%) | 1(3%) | 1(1.7%) | 0.453 | NS |
| Repeated intervention | 1(3.1%) | 1(3%) | 1(1.7%) | 0.243 | NS |
| Total MACE | 2(6.2%) | 2(6.0%) | 2(3.3%) | 0.350 | NS |
| Follow-up events | | | | | |
| MI | 2(6.2%) | 0 | 0 | 0.354 | NS |
| Angina | 1(3.1%) | 7(21%) | 5(8.3%) | 0.422 | NS |
| Repeated intervention | 2(6.2%) | 7(21%) | 5(8.3%) | 0.156 | NS |
| Total MACE | 4(12.5%) | 7(21%) | 5(8.3%) | 0.123 | NS |
| Angiographic measurements | | | | | |
| Before the procedure | | | | | |
| Reference diameter | 2,7 ± 2,25 | 2,74 ± 2,26 | 2,67 ± 2,40 | 0.234 | NS |
| MLD1 | 0,56 ± 0,10 | 0,58 ± 0,30 | 0,59 ± 0,40 | 0.207 | NS |
| %DS | 83,45 ± 70 | 81,80 ± 69 | 79,51 ± 72 | 0.064 | NS |
| Lesion length | 21,11 ± 9 | 18,07 ± 8 | 13,13 ± 7 | 0.001 | S |
| After procedure | | | | | |
| MLD2 | 2,72 ± 2,10 | 2,67 ± 2,25 | 2,61 ± 1,80 | 0.072 | NS |
| %DS | 2,16 ± ,00 | 3,23 ± 0,33 | 4,24 ± 0,30 | 0.084 | NS |
| Acute gain mm | 2,23 ± 1,67 | 2,15 ± 1,55 | 2,04 ± 1,40 | 0.005 | S |
| Relative gain | 0,82 ± 0,70 | 0,79 ± 0,70 | ,76 ± 0,60 | 0.005 | S |
| At 6 month follow-up | | | | | |
| Follow up ratio | 32(100%) | 31(93%) | 59(98.3%) | 0.215 | NS |
| MLD3 | 2,49 ± 0,00 | 2,05 ± 0,30 | 1,93 ± 0,50 | 0.002 | S |
| %DS | 28,08 ± 2,4 | 42,17 ± 2,4 | 37,54 ± 4,2 | 0.002 | S |
| Late loss | 0,67 ± 0,04 | 1,06 ± 0,13 | 0,89 ± 0,12 | 0.002 | S |
| Relative loss | 0,26 ± 0,01 | 0,39 ± 0,06 | 0,34 ± 0,04 | 0.002 | S |
| Loss index | 0,35 ± 0,02 | 0,52 ± 0,00 | 0,45 ± 0,04 | 0.002 | S |
| Net gain | 1,71 ± -0,80 | 1,25 ± 0,35 | 1,29 ± 0,22 | 0.002 | S |
| Restenosis Rate | 67% | 397% | 31.8% | 0.002 | S |

DISCUSSION

The cutting balloon is the first and only device to combine the features of conventional balloon angioplasty with advanced microsurgical capabilities. It is designed to minimize vessel wall trauma traditionally associated with

conventional balloon angioplasty and reduce the likelihood of restenosis.

In concordance with the results of our study, Raisuke L et al. ¹⁴, compared the CBA to either the conventional balloon angioplasty or the

stent implantation in 327 patients with vessels <2.5 mm in diameter, and the following two conclusions were reached:

Patients who underwent CBA for small vessel disease had a significantly lower restenosis rate and a better long-term clinical outcome than those who underwent balloon angioplasty or stent. (2) CBA had a significantly greater net gain than either the balloon angioplasty or stent group. Therefore they have stated that CBA provided superior angiographic and clinical outcomes to both stenting or balloon angioplasty and may be a cost-effective and reasonable approach for the treatment of lesions in small coronary vessels

S.Inoue et al ¹⁵ , conducted a similar study to compare cutting balloon alone versus coronary stenting in small coronary vessels, the study conducted over 97 patients, and the conclusion goes in agreement with our study, and showed that cutting balloon gives similar results to stenting but at dramatically reduced cost (about 50% cheaper). They found no significant difference between stent group and cutting balloon group in terms of acute gain (1.73 (0.86 mm vs 1.44 (0.34 ; respectively; p=0.43) and loss index (0.46 (2.6 vs 0.43 (1.01 ; p=0.94)

Chang-Min Chung et al ¹⁶ compared cutting balloon angioplasty and stenting alone in small branch ostial lesions of native coronary arteries, and the results go in agreement with the present study, the early post procedural results were in favour of stenting in terms of better minimal lumen diameter and less diameter stenosis. At 3 month follow up they found that MLD and diameter stenosis were almost identical in both groups however, late loss was lower in cutting balloon group.

STRESS I-II trial ¹¹ were in favor of small vessel stenting ; it showed that stent placement was associated with a 38% relative reduction in restenosis and a 33% reduction in clinical events compared with PTCA. This encouraging finding was questioned, since the stents used in the trial were primarily designed for large vessels.

The E-SIRIUS trial ¹⁷ is a multicenter European trial that randomly assigned 177 patients to receive the Bx Velocity stent (Cordis Corporation) and 175 patients to receive the SES

stent (cypher - Cordis Corporation). The stents were implanted in native coronary arteries of reference diameter between 2.5 mm and 3.0 mm by visual estimate. The 8-month follow-up angiogram showed that in-segment restenosis rate was dramatically less in the SES comparing with BMS (5.9% in the SES versus 42.3% in the BMS group; p<0.001). Stent thrombosis occurred to a similar extent in both treatment groups.

Limitations of the present study:

The number of patients are relatively small in each group.

IVUS was not in this study, that would have given more accurate data and precise measurements rather than those obtained by QCA alone, also using IVUS would have given a better understanding of the mechanism of CBA, and detecting some complications that could not be detected by visual assessment.

No other control group using conventional balloon was involved in this study.

CONCLUSION

(1) Drug eluting stent in general is the treatment of choice so far for patients with small coronary artery disease, however with incredible increase of the total procedural cost, other available tools like Bare metal stent or cutting balloon angioplasty still have a role in treating those patients.

(2) CBA showed favourable immediate post-procedural results and better late clinical and angiographic results comparing with bare metal stent, hence cutting balloon could be a good tool in these subset of patients with considerably lesser cost comparing with BMS.

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