

Comparison between biodegradable polymer drug eluting stents and durable polymer drug eluting stents on the outcome of percutaneous coronary intervention in patients of Acute Coronary Syndrome

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ABSTRACT

Introduction: Patients with NSTEMACS have a wide spectrum of risk of death and cardiac ischemic events. Biodegradable polymer-based DES have been established as a safe and effective alternative to durable polymer-based stent platforms as evidenced in several randomized clinical trials.

Aim of the study: to assess of the role of biodegradable polymer DES in decreasing the incidence of major adverse cardiac events in comparison with durable polymer DES in patients with NSTEMACS.

Methods: 121 patients enrolled in the study divided into; group A: biodegradable polymer DES and group B: durable polymer DES. Patients presented with NSTEMACS having TIMI risk score ≥ 3 were subjected to early invasive strategy. One year views after the index procedure coronary angiography were evaluated by quantitative coronary angiography (QCA) with edge detection method used for evaluation of coronary lesion in index and follow up procedures. Minimal luminal diameter (MLD), reference vessel diameter (RVD), percent diameter stenosis (%DS), acute gain, late loss and late loss index were estimated.

Results: There were 155 targeted segments in 146 vessels in our patients with stenosis percentage $\geq 60\%$. TIMI 0 was achieved in 0.82% of treated segments, TIMI 1 was achieved in 1.7% of treated segments, TIMI 2 was achieved in 5.8% of treated segments, and TIMI 3 was achieved in 92.6% of treated segments (p-value NS). For biodegradable polymer DES group, 71 stents have been implanted. For durable polymer DES, 86 stents have been implanted. Restoring TIMI flow III after the PCI procedure was achieved in 92.6% of treated segments. Clinical success was achieved in 93.4% of cases. Thirty nine patients had repeated coronary angiography within 1 year (15 biodegradable DES and 24 durable DES). Eighteen patients experienced angina pains for which they were examined thoroughly (8 biodegradable DES and 10 durable DES). Only five patients needed TLR (2 biodegradable DES & 3 durable polymer DES). Three of them had a myocardial infarction with documented angiographic evidence of significant in-stent restenosis (1 biodegradable polymer DES & 2 durable polymer DES) (p-value NS).

Conclusion: Biodegradable polymer and durable polymer DES are associated with similar clinical outcomes at 1 year. Biodegradable polymer DES is a safe alternative to durable polymer DES.

Kew word: Non-ST segment elevation acute coronary syndrome, biodegradable polymer DES, major adverse cardiac events

INTRODUCTION

Patients with non-ST segment elevation acute coronary syndromes (NSTEMACS), including unstable angina (UA) and non-ST segment elevation myocardial infarction (NSTEMI), have a wide spectrum of risk of death and cardiac ischemic events.⁽¹⁾

Percutaneous coronary intervention (PCI) in these cases had three major shortcomings including; acute vessel closure, subacute vessel closure and late vessel stenosis. The continuous improvements in the stent technique and design have resulted in reduction in the complications.⁽²⁾ Although drug-eluting stents (DES) provide strong suppression of neo-intimal hyperplasia and reduce the risk of revascularization in comparison with bare metal stents,^(3, 4) the continuous presence of

durable polymer coatings after completing the drug release has been implicated as a potential cause for the chronic inflammatory response leading to stent thrombosis.^(5,6)

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Biodegradable polymer-based DES may improve long-term clinical outcomes after coronary stenting, by making the stent surface similar to a bare metal stent free of a chronic inflammatory stimulus. Biodegradable polymer-based DES have been established as a safe and effective alternative to durable polymer-based stent platforms as evidenced in several randomized clinical trials.^(7,8) Also an optical coherence tomography study has shown an improved healing of the stented coronary artery after implanting a biodegradable polymer DES in comparison with durable polymer sirolimus eluting stents (SES) at 9 months.⁽⁹⁾

In our study, we aimed to assess of the role of biodegradable polymer Drug eluting stents in decreasing the incidence of major adverse cardiac events (MACE) in comparison with durable polymer drug eluting stent (DES) in patients with non-ST segment elevation acute coronary syndromes (NSTEMI).

MATERIAL AND METHODS

Our study enrolled 121 patients presenting to Critical Care Medicine Department, Cairo University with NSTEMI between March 2015 and March 2016. Participants were followed up clinically after 1 year. We conducted this follow-up as telephone interviews or patient visits. An angiographic follow-up was done whenever possible at 1 year post-procedure or earlier should the patient experience ischemic symptoms or show non-invasive evidence of ischemia.

Prospective subjects were those with age ≥ 18 years presenting with acute coronary syndrome and coronary lesions $>60\%$, in whom PCI with DES implantation is indicated, based on the current recommendations of ACC/AHA/SCAI and ESC/EACTS guidelines or the clinical judgment of the interventional cardiologist.^(10,11) All participants were randomly assigned to either:

1. Group A: biodegradable polymer DES "BIOTRONIK Orsiro® Hybrid drug eluting Stent or Terumo Nobori® - Drug eluting stent".
2. Group B: durable polymer DES "Medtronic Resolute Integrity® Drug Eluting Coronary Stent or Boston scientific The PROMUS Element ®drug eluting stent".

We excluded from our study:

1. Patients with NSTEMI having low TIMI risk score (< 3)⁽¹²⁾ who are subjects to conservative strategy.
2. Patients with marked impairment of LV systolic function (LVEF $<30\%$).
3. Patients with cardiogenic shock (Killip class IV).⁽¹³⁾
4. Contraindication to antiplatelet and anticoagulation (aspirin, clopidogrel) or heparin therapy e.g. active peptic ulcer.
5. Significant external or internal bleeding.

6. Severe thrombocytopenia (Platelet count $< 50,000/\text{cmm}$).

All patients were subjected on ICU admission to: full medical history and demographic characteristics, full clinical examination: including general and cardiac assessment, serial twelve-lead ECG, echocardiographic examination, routine laboratory investigations: including repeated sets of cardiac enzymes and troponin, serum creatinine, complete blood picture, coagulation profile and hepatitis markers B,C and assessments using TIMI risk score.

Patients presented with NSTEMI having TIMI risk score ≥ 3 ,⁽¹³⁾ who meet the inclusion criteria, were subjected to early invasive strategy (early coronary angiography with PCI if feasible). PCI was done using biodegradable drug eluting stent for patients of group A and durable polymer DES for patients of group B.

Patients were followed up within 1 year duration.

A) Clinical and laboratory follow up:

- Patients were re-evaluated by complete analysis of chest pain, careful cardiac examination and serial 12-lead ECG to assess dynamic changes or cardiac arrhythmias, follow up cardiac enzymes and troponin (if indicated).
- The primary endpoint was major adverse cardiac events (MACE) defined as: recurrent angina pectoris, post-infarction angina, new or recurrent myocardial infarction, target lesion revascularization (TLR), target vessel revascularization (TVR), left ventricular dysfunction, cardiac arrhythmias and cardiac death.

B) Coronary angiographic follow up:

- Patients were subjected to follow up diagnostic coronary angiography 1 year after PCI (whenever possible).

One year views after the index procedure coronary angiography were evaluated by quantitative coronary angiography (QCA) with edge detection method used for evaluation of coronary lesion in index and follow up procedures. Minimal luminal diameter (MLD), reference vessel diameter (RVD), percent diameter stenosis (%DS), acute gain, late loss and late loss index were estimated.

The study was approved by the ethical committee of critical care department, Cairo University. All the participants agreed to sign a written informed consent.

RESULTS

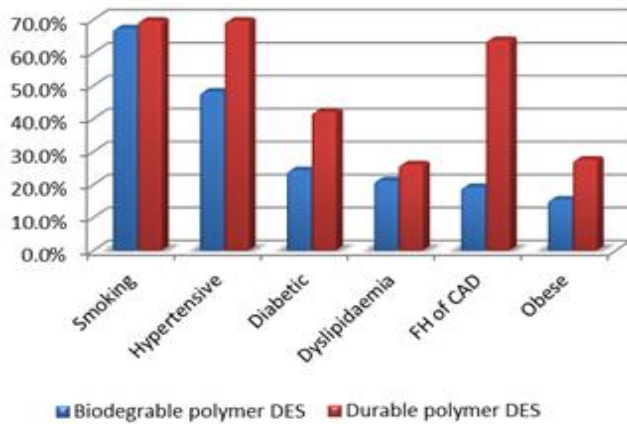
A total number of 121 patients were enrolled in our study. The study included 83 males (68.6%), 38 females (31.4%) with mean age 58.8 ± 9.2 years. Average length of stay was (2.2 ± 0.7 days).

In our study, 52 patients received biodegradable polymer based DES (43.0%) while 69 patients received durable polymer based DES (57.0%).

There was no statistical significance between biodegradable polymer DES and durable polymer DES groups, concerning their risk factors apart from prevalence of hypertension between both groups (48.1% in biodegradable polymer DES group versus

69.6% in durable polymer DES group, *P* value 0.014). (Fig-1).

Figure-1. Risk factors for CAD, illustrated by frequency



There were 155 targeted segments in 146 vessels in our patients with stenosis percentage $\geq 60\%$. (Table-1).

Table-1. Number of vessels, recorded in our registry, classified according to PCI procedure and outcome.

	Biodegradable polymer DES	Durable polymer DES	P value
Single vessel disease	40 (76.9%)	56 (81.2%)	0.60
Two vessel disease	12 (23.1%)	13 (18.8%)	2

Long/ calcific lesions

Prevalence of long ($\geq 20\text{mm}$) lesions was 66.1% in our study. There was no significant difference for prevalence of long/calcific lesions between both groups, (69.2% for biodegradable polymer versus 63.8% for durable polymer, *P* value 0.333).

Prevalence of calcific lesions was 5.0% in our study, (1.9% for biodegradable polymer versus 7.2% for durable polymer, *P* value 0.183).

TIMI flow classification

Reviewing TIMI flow classification for treated lesions before PCI, TIMI 0 was present in 4 patients (3.3%), TIMI 1 was present in 3 patients (2.47%), TIMI 2 was present in 54 patients (44.6%), and TIMI 3 was present in 60 patients (49.5 %). (Table-2)

Table-2. TIMI flow classification patterns among PCI procedures

TIMI flow	Biodegradable polymer DES	Durable polymer DES	P value
TIMI 0	1 (1.9%)	3 (4.3%)	0.554

TIMI 1	1 (1.9%)	2 (2.9%)
TIMI 2	23 (44.2%)	31 (44.9%)
TIMI 3	27 (51.9%)	33 (47.8%)

PCI procedure details

PCI procedure data

In our study, there were 155 segments reported. Ninety nine patients (81.8%) were subjected to complete revascularization, while twenty two patients (18.2%) had incomplete revascularization. There was no significant difference between both groups, (82.7% for biodegradable polymer vs. 81.2% for durable polymer, *P* value 0.512). (Table-3).

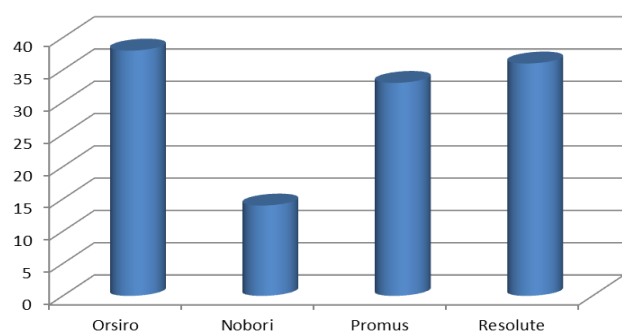
Table-3. Stent length, diameter and pressure.

	Biodegradable polymer DES	Durable polymer DES	P value
Stent length (mm)	25.8 \pm 8.2	26.2 \pm 8.0	0.758
Stent diameter (mm)	3.2 \pm 0.4	3.2 \pm 0.5	0.515
Pressure (atm)	13.7 \pm 1.8	14.2 \pm 2.3	0.145

TIMI 0 was achieved in 0.82% of treated segments, TIMI 1 was achieved in 1.7% of treated segments, TIMI 2 was achieved in 5.8% of treated segments, and TIMI 3 was achieved in 92.6% of treated segments. There was no significant difference between both groups.

For biodegradable polymer DES group, 71 stents have been implanted. For durable polymer DES, 86 stents have been implanted. (Fig-2)

Figure-2. Stent frequency



Procedural complications:

Angiographic success of PCI procedure:

Restoring TIMI flow III after the PCI procedure was achieved in 92.6% of treated segments in our study. Angiographic complications, irrelevant to post-PCI TIMI flow pattern, occurred in 6 patients (5.0%).

These complications were acute in-stent thrombosis, no reflow phenomenon and coronary dissection. Two of the patients who suffered from

coronary dissection were complicated by no-reflow phenomenon. (Table-3)

Table-3. Detailed procedural complications, according to PCI procedures.

	Biodegradable polymer DES	Durable polymer DES	<i>P</i> value
Acute stent closure	0 (0.0%)	1 (1.4%)	0.570
No reflow	1 (1.9%)	1 (1.4%)	0.677
Coronary dissection	2 (3.8%)	3 (4.3%)	0.632

Clinical Success of PCI procedure and IN-Hospital MACE:

It was defined as accomplishing PCI procedure with no in-hospital MACE (death, target lesion revascularization and myocardial infarction, LV dysfunction, major bleeding, new or worsening renal impairment). Clinical success was achieved in 93.4% of cases. (Table-4).

Table-4. MACE In-hospital details

In-hospital MACE	Biodegradable polymer DES	Durable polymer DES	<i>P</i> value
Mortality	0 (0.0%)	1 (1.4%)	0.570
TLR	1 (1.9%)	1 (1.4%)	0.677
Myocardial infarction	1 (1.9%)	1 (1.4%)	0.677
LV dysfunction	2 (3.8%)	4 (5.8%)	0.482

Follow Up data and 1 year MACE:

Thirty nine patients consented to have repeated coronary angiography within 1 year of their initial coronary angiography (15 biodegradable DES and 24 durable DES). Eighteen of these patients have experienced angina pains for which they were examined thoroughly (8 biodegradable DES and 10 durable DES). Only five patients needed TLR (2 biodegradable DES & 3 durable polymer DES). Three of them had a myocardial infarction with documented angiographic evidence of significant in-stent restenosis (1 biodegradable polymer DES & 2 durable polymer DES). (Table-5).

Table-5. Mortality, TLR and MI in different groups

F/U MACE	Biodegradable polymer DES	Durable polymer DES	<i>P</i> value
Mortality	1 (1.9%)	1 (1.4%)	0.677

TLR	2 (3.8%)	3 (4.3%)	0.632
Myocardial infarction	1 (1.9%)	2 (2.9%)	0.606
LV dysfunction	1 (1.9%)	3 (4.3%)	0.422

DISCUSSION

In our study a total of 121 participants with ACS have been enrolled into our trial, of whom 52 patients with 69 lesions were allocated to treatment with BP DES and 69 patients with 86 lesions to treatment with DP DES. There were no significant differences in terms of baseline characteristics or angiographic features between the two treatment arms.

Our study clearly shows that the 1 year clinical outcomes after BP DES implantation are comparable to those of DP DES, which is considered the DES standard. Both types of stents showed a low incidence of TLF and MACE, which suggests the safety and efficacy of these two stent types.

For overall incidence of in-hospital complications, comprising acute myocardial infarction, need for target lesion revascularization, urgent deferral to CABG and death were very limited and did not show statistical significance between different types of stents, (P 0.725).

Also there was no significant differences among different stents in their 1 year follow up; seven patients were reported in "follow-up MACE". Mortality was 1.7% (1 biodegradable polymer DES & 1 durable polymer DES). (P 0.654) Five patients needed TLR (2 biodegradable DES & 3 durable DES). (P 0.632)

Our result agree with Windecker, S., et al. where they compared the ultrathin strut drug-eluting stent releasing sirolimus from a biodegradable polymer (Orsiro, O-SES) with the durable polymer Xience Prime everolimus-eluting stent (X-EES). They studied A total of 452 patients were randomly assigned 2:1 to treatment with O-SES (298 patients, 332 lesions) or X-EES (154 patients, 173 lesions) in a multicenter, noninferiority trial. The primary end point was in-stent late loss at 9 months. O-SES was noninferior to X-EES for the primary end. Clinical outcome showed similar rates of target-lesion failure at 1 year (O-SES 6.5% versus X-EES 8.0%; hazard ratio=0.82; 95% confidence interval, 0.40-1.68; log-rank test: P=0.58) without cases of stent thrombosis. They concluded that the biodegradable polymer-based O-SES was found noninferior for the primary end point in-stent late lumen loss at 9 months. Clinical event rates were comparable without cases of stent thrombosis throughout 1 year of follow-up. (14)

Also our results concur with Jinnouchi, H., et al. they studied total of 1,132 patients treated only with Biolimus-eluting stents BES (612 patients) or cobalt chromium everolimus-eluting stents EES (520 patients) in small vessel disease (stent size 2.5-mm) by retrospective analysis. they assessed the cumulative 2-year incidence of major adverse cardiovascular events (MACE), defined as a composite of cardiac death, myocardial infarction (MI), definite stent thrombosis (ST), and clinically driven target lesion revascularization (CD-TLR). The

cumulative 2-year incidence of MACE was similar between the two groups (12.1% vs. 11.8%, $P = 0.77$). The cumulative incidence of cardiac death, CD-TLR, and definite ST were also not significantly different between both groups (3.2% vs. 3.6%, $P = 0.78$; 8.3% vs. 8.4%, $P = 1.00$; 0.33% vs. 0.21%, $P = 0.66$, respectively). And they concluded that the Two-year clinical outcomes of BES are similar to those of CoCr-EES in patients with small vessel disease. The use of BES is acceptable for small coronary artery disease.⁽¹⁵⁾

Our results did not agree with Stefanini, G.G., et al., they sought to compare long-term outcomes in patients treated with biodegradable polymer DES vs. durable polymer sirolimus-eluting stents (SES). They pooled individual patient data from large-scale multicentre randomized clinical trials comparing biodegradable polymer DES with durable polymer SES and assessed clinical outcomes during follow-up through 4 years.⁽¹⁶⁾

The efficacy endpoint of interest was target lesion revascularization and the safety endpoint of interest was definite stent thrombosis. Out of 4062 patients included in the present analysis, 2358 were randomly assigned to treatment with biodegradable polymer DES (sirolimus-eluting, $n = 1501$; biolimus-eluting, $n = 857$) and 1704 patients to durable polymer SES. No heterogeneity across the trials was observed in analyses of the primary and secondary endpoints. At 4 years, the risk of target lesion revascularization was significantly lower among patients treated with biodegradable polymer DES vs. durable polymer SES (hazard ratio 0.82, 95% CI 0.68-0.98, $P = 0.029$). In addition, the risk of stent thrombosis was significantly reduced with biodegradable polymer DES vs. durable polymer SES (hazard ratio 0.56, 95% CI 0.35-0.90, $P = 0.015$), in landmark analysis between 1 and 4 years, the incidence of myocardial infarction was lower for patients treated with biodegradable polymer DES vs. durable polymer SES (hazard ratio 0.59, 95% CI 0.73-0.95, $P = 0.031$). and they concluded that Biodegradable polymer DES improve safety and efficacy compared with durable polymer SES during long-term follow-up to 4 years.⁽¹⁸⁾ The difference in our results may be attributed to the larger number of patients the studies also they only studied the BP DES against only one type of DP DES (sirolimus-eluting stents)⁽¹⁶⁾

CONCLUSION

Biodegradable polymer and durable polymer DES are associated with similar clinical outcomes at 1 year. Biodegradable polymer DES is a safe alternative to durable polymer DES. More studies with more number of patients are needed to prove superiority of Biodegradable polymer over durable polymer DES.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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