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Comparison between the Outcomes of Using Biodegradable-Polymer Drug-Eluting Stents and Those of Using Durable-Polymer Drug-Eluting Stents in Acute Coronary Syndrome Patients Undergoing Percutaneous Coronary Intervention

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Keywords: Non-ST Segment Elevation; Acute Coronary Syndrome; Biodegradable-Polymer DES; Major Adverse Cardiac Events

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Abstract

BACKGROUND: Many randomised control studies showed that percutaneous coronary interventions using biodegradable-polymer drug-eluting stents (DES) offer a safe and effective alternative to durable-polymer DES. However, not many studies have discussed its use in the setting of acute coronary syndromes.

AIM: We aim to compare the biodegradable-polymer DES with durable-polymer DES when it comes to reducing the incidence of non-ST elevation acute coronary syndrome (NSTEACS) associated with adverse events.

METHODS: We enrolled 205 patients presenting with NSTEACS and a TIMI risk score ≥ 3 in this study and divided them into two groups, group A and group B. Biodegradable-polymer DESs were exclusively used in group A, while durable-polymer DESs were used in group B. Major adverse events were reported in both groups during the hospital stay and patients were followed-up for 1 year.

RESULTS: In our patients, we intervened on 390 diseased segments in a total of 360 vessels. After intervention, TIMI 0 was achieved in 0.97%, TIMI 1 in 1.46%, TIMI 2 in 2.45%, and TIMI 3 in 95.12% of the treated segments (P-value= 0.677). We implanted 121 biodegradable-polymer DESs and 146 durable-polymer DESs. Clinical success was achieved in 95.12% of our cases. We had 55 patients who needed repeated coronary angiography within 1 year (15 patients treated with biodegradable-polymer DES and 24 patients treated with durable-polymer DES). Eighteen patients experienced angina pains (8 patients treated with biodegradable-polymer DES and 10 patients treated with durable-polymer DES). Only 5 patients needed TLR (2 patients treated with biodegradable-polymer DES and 3 patients treated with durable -polymer DES) (P-value = 0.591), three of them had a myocardial infarction with documented angiographic evidence of significant in-stent restenosis (1 patient treated with biodegradable-polymer DES and 2 patients treated with durable-polymer DESs).

CONCLUSION: Biodegradable-polymer DES represents a comparable alternative to durable-polymer DES in the setting of acute coronary syndromes.

Introduction

Patients with non-ST segment elevation acute coronary syndromes (NSTEACS), including unstable angina (UA) and non-ST segment elevation myocardial infarction (NSTEMI), have a high risk for death and cardiac ischemic events [1].

Percutaneous coronary intervention (PCI) in these cases can result in three major complications; namely, acute vessel closure, subacute vessel closure and late vessel stenosis. Continuous improvements to the stenting technique and stent designs were made and resulted in a reduction in the incidence of these complications [2].

Although drug-eluting stents (DES) use has resulted in lesser revascularisations, when compared to bare metal stents, owing to their strong suppression of neointimal hyperplasia [3], [4], their implantation leaves the stent with a durable-polymer coating. This polymer has been implicated as a potential cause for a chronic inflammatory response that leads to stent thrombosis [5], [6].

Biodegradable polymer-based DES averts stent thrombosis by leaving a stent that will have the same bare metal lining as a bare metal stent. This may result in an improved long-term clinical outcome of coronary stenting. Biodegradable polymer-based DES has been established as a safe and effective alternative to durable polymer-based stent platforms as evidenced in several randomised clinical trials [7], [8]. Also, an optical coherence tomography study showed improved healing of the stented coronary artery after implanting a biodegradable-polymer DES in comparison to durable-polymer sirolimus-eluting stents (SES) at 9 months [9].

In our study, we aim to assess the role of biodegradable-polymer DES in decreasing the incidence of major adverse cardiac events (MACE) compared to durable-polymer DES in patients with NSTEACS.

Material and Methods

We enrolled 205 NSTEACS patients from amongst all patients admitted to the Cairo University Critical Care Medicine Department during the period from January 2015 to January 2017. We followed up those patients for 1 year clinically, via telephone calls, and directly in our outpatient clinics. The follow-up angiographies were done earlier in patients who experienced ischemic symptoms or signs before the end of their follow-up duration.

Patients enrolled in this study were all 18 years of age or older. Also, they had coronary lesions that were narrowed by more than 60%. They were indicated for PCI using DES as per the ACC/AHA/SCAI and ESC/EACTS guidelines or the clinical judgment of the treating interventionists [10], [11]. All participants were randomly assigned to one of two treatment groups, group A and group B. Group A received PCI using biodegradable-polymer DES “BIOTRONIK-Orsiro® Hybrid drug-eluting Stent or Terumo Nobori®-Drug eluting stent”, while group B received PCI using durable-polymer DES “Medtronic Resolute Integrity® Drug-Eluting Coronary Stent or Boston scientific The PROMUS Element ®drug eluting stent”. In our study, we excluded NSTEACS patients with: low TIMI risk score (< 3) [12] who were subjected to conservative strategy, marked impairment of LV systolic function (LVEF < 30%), cardiogenic shock (Killip class IV) [13], contraindication to the use of antiplatelet and anticoagulation (aspirin, clopidogrel) or heparin therapy e.g. active peptic ulcer in addition to patients who co-presented with significant external or internal bleeding and those who had severe thrombocytopenia (platelet count < 50,000/cmm).

All of the enrolled patients were admitted to our ICU and subjected to full medical history taking, demographic characterization, thorough clinical examination (general and cardiac examinations), a serial twelve-lead ECG, echocardiographic examination in addition to routine laboratory investigations, including repeated sets of cardiac enzymes and troponin, serum creatinine, complete blood picture, coagulation profile, and viral hepatitis markers. Each patient was given a TIMI score [14].

Following PCI, all patients were re-evaluated clinically by re-analysing their symptoms, performing a careful cardiac examination, acquiring serial 12-lead ECGs to detect any dynamic changes or cardiac arrhythmias, and ordering follow-up cardiac enzymes and troponin whenever it was necessary.

After receiving the acute care in the ICU, patients were then discharged and followed up to detect the incidence of any of our primary endpoints which constituted the major adverse cardiac events (MACE); namely, 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.

Furthermore, patients who did not develop any of our primary endpoints during the1-year follow-up duration were subjected to a follow-up diagnostic coronary angiography at the end of that year if the patient consented.

The follow-up coronary angiography views were evaluated using quantitative coronary angiography (QCA) with edge detection method to evaluate the coronary lesions. Minimal luminal diameter (MLD), reference vessel diameter (RVD), per cent diameter stenosis (%DS), acute gain, late loss, and late loss index were estimated.

The study was approved by the ethical committee of the Critical Care Department, Cairo University. All the participants agreed to sign a written informed consent.

Results

A total number of 205 patients were enrolled in this study. It included 141 males (68.6%) and 64 females (31.4%) with a mean age of 57.4 ± 10.2 years. The average length of stay was 2.7 ± 0.8 days.

In this study, 100 patients received biodegradable polymer-based DES (48.7%), while 105 patients received durable polymer-based DES (51.30%).

There was no statistical significance between the biodegradable-polymer DES and durable-polymer DES groups concerning the risk (Figure 1).

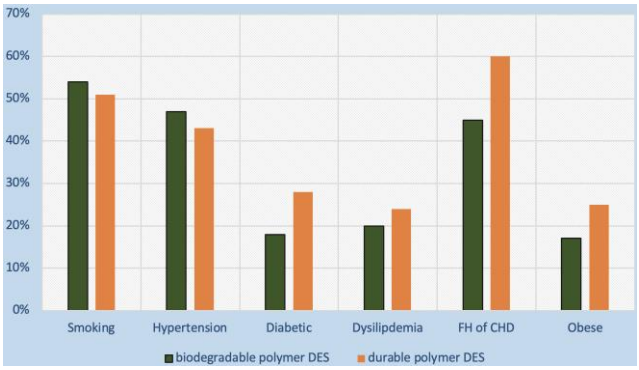

Figure 1: Risk factors for CAD, illustrated by the frequency

There were 390 targeted segments in 360 vessels in our patients with stenosis percentage of ≥ 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
	No	%	No	%	
Single vessel disease	72	72%	85	80.9%	0.599
Two vessel disease	28	28%	20	19.1%	

Long/calcific lesions

Prevalence of long lesions (≥ 20mm) was 66.1% in our study. There was no significant difference in the prevalence of long/calcific lesions between both groups (67.2% for biodegradable-polymer DES group versus 61.8% for durable-polymer DES group, P-value = 0.357).

Prevalence of calcific lesions was 7.0% in our study, (2.2% for biodegradable-polymer DES group versus 8.6% for durable-polymer DES group, P-value = 0.203).

TIMI flow classification

Reviewing TIMI flow classification for treated lesions before PCI, TIMI 0 was present in 7 patients (3.4%), TIMI 1 in 5 patients (2.4%), TIMI 2 in 92 patients (44.9%), and TIMI 3 in 101 patients (49.3 %) (Table 2).

Table 2: TIMI flow classification patterns among PCI procedures

TIMI flow	Biodegradable polymer DES		Durable polymer DES		P value
	No	%	No	%	
TIMI 0	3	(2.3%)	4	(4.3%)	0.677
TIMI 1	3	(2.3%)	2	(3.4%)	
TIMI 2	43	(44.3%)	49	(44.4%)	
TIMI 3	51	(51.1%)	50	(47.9%)	

PCI procedure details

A. PCI procedure data

In our study, there were 390 segments reported. One hundred and sixty-eight patients (82%) had complete revascularisation, while 37 patients (18%) had incomplete revascularisation. There was no significant difference between both groups (81.9% for biodegradable-polymer DES group vs 82.4% for durable-polymer DES group, P-value = 0.589). Stent length, diameter and inflating pressures are shown in Table 3.

Table 3: Stent length, diameter and pressure

	Biodegradable polymer DES	Durable polymer DES	P value
Stent length (mm)	26.6 ± 7.4	26.2 ± 8.0	0.699
Stent diameter (mm)	3.4 ± 0.4	3.4 ± 0.5	0.542
Pressure (atm)	14.2 ± 1.7	14.7 ± 2.6	0.237

TIMI 0, TIMI 1, TIMI 2, and TIMI 3 were achieved in 0.97%, 1.46%, 2.45%, and 95.12% of the treated segments, respectively. There was no significant difference between both groups.

For the biodegradable-polymer DES group, 121 stents were implanted, while for the durable polymer DES group, 146 stents were implanted (Figure 2).

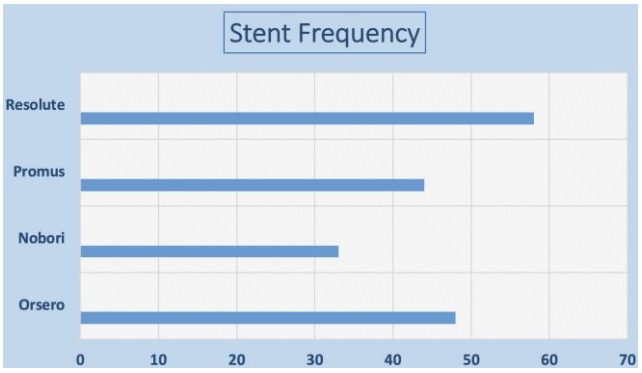

Figure 2: Stent frequency

B. Procedural complications:

The angiographic success of PCI procedure:

Restoring TIMI flow III after the PCI procedure was achieved in 95.12% of the treated segments in our study.

Angiographic complications, irrelevant to post-PCI TIMI flow pattern, occurred in 10 patients (4.9%). These complications were acute in-stent thrombosis, no-reflow phenomenon, and coronary dissection. Three of the patients who suffered from coronary dissection were complicated by the no-reflow phenomenon (Table 4).

Table 4: Detailed procedural complications, according to PCI procedures

	Biodegradable polymer DES		Durable polymer DES		P value
	N	%	N	%	
Acute stent closure	0	0.0	1	0.9	0.561
No reflow	1	1	2	1.9	0.598
Coronary dissection	2	2	3	2.85	0.770

C. Clinical Success of PCI procedure and IN-Hospital MACE:

It was defined as accomplishing PCI procedure with no in-hospital MACE (death, target lesion revascularisation, myocardial infarction, LV dysfunction, major bleeding, new or worsening renal impairment). Clinical success was achieved in 95.12% of the cases (Table 5).

Table 5: MACE In-hospital details

In-hospital MACE	Biodegradable polymer DES		Durable polymer DES		P value
	N	%	N	%	
Mortality	0	0.0	1	0.9	0.711
TLR	2	2	1	0.9	0.577
Myocardial infarction	1	1	1	0.9	0.680
LV dysfunction	3	3	4	3.8	0.549

Follow-Up data and 1-year MACE:

Fifty-five patients consented to have repeated coronary angiography within 1 year of their initial coronary angiography (23 patients treated with biodegradable-polymer DES and 32 patients treated with durable-polymer DES). Eighteen of these patients experienced angina pains for which they were examined thoroughly (8 patients treated with biodegradable-polymer DES and 10 patients treated with durable-polymer DES). Only five patients needed TLR (2 patients with biodegradable-polymer DES and 3 patients treated with durable-polymer DES). Three of them had a myocardial infarction with documented angiographic evidence of significant in-stent restenosis (1 patient treated with biodegradable-polymer DES and 2 patients treated with durable polymer DES) (Table 6).

Discussion

In this study, we enrolled 205 ACS patients. One hundred of them, who had a total of 121 lesions, were treated with biodegradable-polymer drug-eluting stents (BP-DES). The other 105 patients, who had a total of 146 lesions, were treated with durable-polymer drug-eluting stents (DP-DES). The differences between the two groups were insignificant as regards angiographic findings and other characteristics. This study clearly shows that the 1-year clinical outcomes after BP-DES implantation are comparable to those of the standard DP-DES implantation. Both stent types were associated with a low incidence of target lesion failure (TLF) and MACE, indicating their safety and efficiency.

The incidence of in-hospital complications, including acute myocardial infarction, need for target lesion revascularisation, urgent referral to CABG and death, was very low in both groups. Moreover, the difference in the incidence of those complications was not statistically significant between the two different treatment arms (P = 0.725). Although the results of 1-year follow up for both patient groups were not significantly different, 7 patients were reported in “follow-up MACE”. Incident mortality was 1% in each group (1 patient treated with biodegradable-polymer DES and 1 patient treated with durable-polymer DES) (P = 0.627). In all of our patients, five patients needed TLR (2 patients treated with biodegradable-polymer DES and 3 patients treated with durable-polymer DES) (P = 0.591).

Our results agree with Windecker, S. et al., results [8]. In their study, they compared the biodegradable-polymer (with an ultrathin strut) sirolimus-eluting stent (Orsiro, O-SES) to the durable-polymer Xience Prime everolimus-eluting stent (X-EES). In their multicenter non-inferiority study which included a total of 452 patients who were randomly assigned to treatment with either O-SES (298 patients, 332 lesions) or X-EES (154 patients, 173 lesions), the patients’ ratio was 2:1, respectively. The primary endpoint was an in-stent late loss at 9 months. O-SES was found to be non-inferior to X-EES. Clinical outcomes of both patients’ groups were similar in 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) with no reported cases of stent thrombosis. They concluded that the biodegradable polymer-based O-SES was not inferior to the durable polymer-based X-EES at their specified endpoint. Clinical event rates were comparable with no cases of stent thrombosis reported till 1 year of follow-up [14].

Moreover, our results concur with Jinnouchi, H. et al., results [15]. In a retrospective analysis, they studied a total of 1,132 patients who were treated with either Biolimus-eluting stents BES (612 patients) or cobalt chromium everolimus-eluting stents EES (520 patients) for a small-vessel disease (stent size 2.5 mm). They assessed the 2-year cumulative 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 revascularisation (CD-TLR). The 2-year cumulative incidence of MACE was similar in both 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 the two 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). They concluded that the 2-year clinical outcomes of BES are similar to those of CoCr-EES when used in small vessel lesions. Thus, in their analysis, the use of BES was found to be acceptable

for small coronary artery lesions [15].

Our results did not agree with Stefanini, G.G. et al. results. They compared long-term outcomes in patients treated with biodegradable-polymer DES vs those treated with durable-polymer sirolimus-eluting stents (SES). They pooled individual patient data from large-scale multicentre randomised clinical trials comparing biodegradable-polymer DES with durable-polymer SES and assessed clinical outcomes during a follow-up period of 4 years [16]. The efficacy endpoint of interest was target lesion revascularisation, and the safety endpoint of interest was definite stent thrombosis. Out of 4062 patients included in the present analysis, 2358 patients were randomly assigned to treatment with biodegradable-polymer DES (sirolimus-eluting, n = 1501; biolimus-eluting, n= 857), while 1704 patients were assigned to treatment with durable-polymer SES. No heterogeneity across the trials was observed in analyses of the primary and secondary endpoints. During the 4 years of follow-up, the risk of target lesion revascularisation was significantly lower among patients treated with biodegradable-polymer DES than among those treated with durable polymer SES (hazard ratio 0.82, 95% CI 0.68-0.98, P = 0.029). Also, the risk of stent thrombosis was significantly reduced among patients treated with biodegradable-polymer DES vs those treated with durable-polymer SES (hazard ratio 0.56, 95% CI 0.35-0.90, P = 0.015). In a landmark analysis between 1 and 4 years, the incidence of myocardial infarction was lower for patients treated with biodegradable-polymer DES than for those treated with durable polymer SES (hazard ratio 0.59, 95% CI 0.73-0.95, P = 0.031). Thus, they concluded that the use of biodegradable-polymer DES had offered superior safety and efficacy compared to durable polymer SES throughout a 4-year follow up period [18]. The difference between our results and their results may be attributed to the larger number of patients enrolled in their study in addition to comparing the BP-DES with only one type of DP-DES (sirolimus-eluting stents) [16].

In conclusion, this study showed that biodegradable DES represents a comparable alternative to durable DES. We recommend carrying out larger studies to reinforce our conclusion.

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