Journal of Medicine in Scientific Research

Volume 3 | Issue 2 Article 8

Subject Area:

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Recommended Citation

Zayed, Ahmed; Algebaly, Ahmed; and El Banna, Tamer (2020) "Comparison of drug-eluting and bare-metal stents in patients with saphenous vein graft stenosis," *Journal of Medicine in Scientific Research*: Vol. 3: Iss. 2, Article 8.
DOI: https://doi.org/10.4103/JMISR.JMISR_10_20

Original Article

Comparison of drug-eluting and bare-metal stents in patients with saphenous vein graft stenosis

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Abstract

Background

The use of drug-eluting stents (DES) during the percutaneous coronary intervention of patients with degenerated saphenous vein graft (SVG) is uncertain. Although previous studies showed that DES might decrease the rate of re-intervention in patients with SVG stenosis, randomized controlled trials comparing bare-metal stents (BMS) and DES in SVG lesions have been inconclusive.

Objective

The purpose of this study was to compare the outcomes in patients undergoing SVG stent implantation treated with DES or BMS.

Patients and methods

This was a retrospective observational study that included 60 patients who underwent percutaneous coronary intervention for SVG lesions, comprising 30 patients who were treated with BMS and 30 patients who were treated with DES at National Heart Institute from March 2015 to March 2018. Three years of outcome and major adverse cardiac event (MACE) were recorded. MACE was defined as death, myocardial infarction (MI), target vessel revascularization, and stroke.

Results

After three years, there was no significant difference between the two groups in MACE. MACE was reported in five (16.6%) patients in the DES group vs eight (26.6%) patients in the BMS group (P>0.05). Death was reported in one (3.3%) patient in each group. MI was reported in two (6.6%) patients in the DES group vs three (10%) patients in the BMS group (P>0.05). One (3.3%) patient developed stroke in the DES group vs two (6.6%) patients in the BMS group (P>0.05). The need for repeat revascularization was reported in one (3.3%) patient in the DES group vs two (6.6%) patients in the BMS group (P>0.05). Stent thrombosis was reported in six (20%) patients in the DES group vs four (13.3%) patients in the BMS group (P>0.05)

Conclusion

Our results in this study showed that there was no significant difference between BMS and DES in patients undergoing percutaneous coronary intervention for SVG lesions for MACE, such as death, target vessel revascularization, and MI.

Keywords: Bare-metal stent, drug-eluting stent, saphenous vein graft

Background

Percutaneous revascularization procedures of saphenous vein graft (SVG) lesions are associated with a higher risk of complications [1]. The use of bare-metal stents (BMS) to treat SVG lesions has resulted in a significant reduction in major adverse events, including the need for repeat revascularization [2]. However, restenosis at the target lesion as well as the development of new lesions underlies the higher rates of long-term graft failure after the percutaneous coronary intervention (PCI) [3]. Although drug-eluting stents (DES) are effective in decreasing the rate of revascularization in native coronary arteries [4,5], they are associated with a higher risk of stent thrombosis [6].

Access this article online

Quick Response Code:

Website: www.jmsr.eg.net

DOI: 10.4103/JMISR.JMISR_10_20

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Submitted: 08-Jan-2020 **Revised:** 09-Jan-2020 **Accepted:** 05-Apr-20 **Published:** 24-Aug-2020

How to cite this article: Zayed A, BannaT El, Algebaly A. Comparison of drug-eluting and bare-metal stents in patients with saphenous vein graft stenosis. J Med Sci Res 2020;3:131-5.

Furthermore, the pathophysiology in SVG stenosis is different compared with atherosclerosis in coronary arteries [7,8]. So, the results of DES in native coronary artery disease cannot be applied to degenerated SVG [9]. Despite the fact that previous studies have shown that DES might decrease the rate of re-intervention in patients with SVG stenosis [10,11], there were conflicting results on mortality [12].

Objectives

The purpose of this study was to compare the outcomes in patients undergoing SVG stent implantation treated with DES or BMS.

Patients and methods

Ethics committee approval was taken. This was a retrospective observational study that included 60 patients who underwent PCI for SVG lesions, comprising 30 patients who were treated with BMS and 30 patients who were treated with DES at National Heart Institute from March 2015 to March 2018.

Data collected included patient characteristics [age; prior myocardial infarction (MI), PCI, and coronary artery bypass grafting (CABG); hypertension; diabetes mellitus; hypercholesterolemia; New York Heart Association class; smoking status; chronic renal impairment; and left ventricular function] and procedure-related data [indications for PCI, target vessel, number of diseased vessels, and use of glycoprotein (GP) IIb/IIIa inhibitor]. The interventional strategy was at the discretion of the operator, including the use of direct stenting, predilatation/postdilatation. Angiographic success was defined as residual stenosis less than 30% with thrombolysis in myocardial infarction (TIMI) flow grade 3. All patients received aspirin 300 mg and either clopidogrel 300 or 600 mg before the procedure. All patients were prescribed 75 mg aspirin and 75 mg clopidogrel as maintenance therapy. Clopidogrel maintenance therapy was recommended for one month in the BMS group and 12 months in the DES group. Unfractionated heparin 10 000 µl was given during the procedure. GP IIb/IIIa inhibitors were used at the operator's discretion and according to local guidelines. Procedural complications and major adverse cardiac events (MACE) were recorded. MACE was defined as death, MI (new pathologic Q waves in the distribution of the treated coronary artery with an increase of creatine kinase MB to ≥2 times the reference value or significant rise in Troponin T values), target vessel revascularization (TVR), and stroke. Procedural complications recorded included MI, emergency CABG, arterial complications, aortic/coronary dissection, side branch occlusion, and arrhythmia. Stent thrombosis was defined according to the Academic Research Consortium definition as angiographic or pathologic confirmation of partial or total thrombotic occlusion within the peristent region plus at least one of acute ischemic symptoms, ischemic electrocardiogram changes, or elevated cardiac biomarkers [13].

Statistical analysis

Data are presented as mean ± SD for continuous data and as number (%) for categorical data. Between-group analysis was done using Student's *t*-test for continuous data and χ^2-test for qualitative data. The level of evidence was detected to be significant at *P* value less than 0.05.

Results

A total of 60 patients underwent PCI for SVG lesions, comprising 30 patients who underwent PCI with BMS and 30 patients who underwent PCI with DES.

Analysis of baseline clinical characteristics

Baseline characteristics for both groups were similar, with no statistically significant difference. All patients in both groups were male. The mean age was 56 ± 9.7 years in the DES group vs 60 ± 4.6 years in the BMS group ($P > 0.05$). Smoking was present in 20 (66.6%) patients in DES group vs 24 (80%) patients in BMS group ($P > 0.05$). Diabetes mellitus was present in 12 (40%) patients in the DES group vs 19 (63%) patients in the BMS group ($P > 0.05$). Hypertension was present in 15 (50%) patients in the DES group vs 18 (60%) patients in the BMS group ($P > 0.05$). Dyslipidemia was present in 16 (53.3%) patients is the DES group vs 13 (43.3%) patients in the BMS group ($P > 0.05$). The mean HR was 101 ± 7.5 beats/min in the DES group vs 97 ± 7.8beats/min in the BMS group ($P > 0.05$). Regarding the cardiac rhythm, normal sinus rhythm was found in all patients in both groups. Regarding the site of MI, anterior MI was present in 18 (60%) patients in the DES group vs 15 (50%) patients in the BMS group ($P > 0.05$). Inferior MI was presents in 12 (40%) patients in the DES group vs 15 (50%) patients in the BMS group ($P > 0.05$). Left ventricular ejection fraction was 50 ± 0.16 in the DES group vs 48 ± 0.19 in the BMS group ($P > 0.05$) (Table 1).

Analysis of procedural data

The femoral approach was done in all patients. Predilatation was done in 17 (56.6%) patients in the DES group vs 20 (66.6%) patients in the BMS group ($P > 0.05$). Aspiration devices were used in nine (30%) patients in the DES group vs 12 (40%) patients in the BMS group ($P > 0.05$). GP inhibitors were used in 12 (40%) patients in the DES group vs 15 (50%) patients in the BMS group ($P > 0.05$). In the DES group, the number of stents used was one stent in 18 (60%) patients and two stents in 12 (40%) patients. In the BMS group, the number of stents used was one stent in 22 (73.3%) patients and two stents in eight (26.6%) patients. The mean stent length was 25.85 + 4.9 mm in the DES group vs 20.6 + 5.8 mm in the BMS group ($P < 0.05$). The mean stent diameter was 2.8 + 0.37 mm is the DES group vs 3.5 + 0.6 mm in the BMS group ($P < 0.05$). TIMI flow after PCI was III in 27 (90%) patients in the DES group vs 25 (83.4%) patients in the BMS group. The TIMI flow was II in three (10%) patients is the DES group vs five (16.6%) patients in the BMS group.

Analysis of outcomes

After three years, there was no significant difference between the two groups in MACE. MACE was reported in five (16.6%) patients in the DES group vs eight (26.6%) patients in the BMS group ($P > 0.05$). Death was reported in one (3.3%) patient in each group. MI was reported in two (6.6%) patients in the DES group vs three (10%) patients in the BMS group ($P > 0.05$). One patient developed stroke in the DES group (3.3%) vs two (6.6%) patients in the BMS group ($P > 0.05$). The need for repeat revascularization was reported in one (3.3%) patient in the DES group vs two (6.6%) patients in the BMS group ($P > 0.05$). Stent thrombosis was reported in six (20%) patients in the DES group vs four (13.3%) patients in the BMS group ($P > 0.05$) (Table 2).

Discussion

PCI has emerged as a preferred choice for the treatment of SVG failure because repeat CABG increases the risk of morbidity and mortality relative to the initial surgery [14]. Owing to different pathophysiology of SVG, increased incidence of distal embolization of friable material, and increased risk of restenosis, PCI of the SVG is associated with increased risk [15]. Initially, BMS was evaluated for use in SVG-PCI, but they were associated with a high rate of restenosis and also increased risk of MACE [16]. Later, DES were studied owing to their proven benefit in reducing intimal hyperplasia and restenosis in native vessels [17,18], but similar results could not be translated in SVG-PCI [19]. In our study, DES did not have the benefit of BMS for overall mortality. This was in line with most of the randomized clinical trials (RCT), except DELAYED-RRISC, which had shown the use of DES increased mortality risk [20]. However, this trial was underpowered to assess mortality and also dual antiplatelet therapy was terminated prematurely. Our results are in contrast to a previous meta-analysis by Wiisanen *et al.*[21] who had shown that DES was associated with improved mortality compared with BMS. However, this analysis included only four small RCTs and also observational studies. There was no statistically significant difference between DES and BMS for MACE in the present study. This was consistent with most of the RCTs except for BASKET and BASKET-SAVAGE, which reported lower MACE with DES [22]. Both the studies had small sample sizes, and BASKET-SAVAGE was terminated prematurely because of poor enrollment. The lower rate of MACE was driven by lower TVR events reported with DES in these two studies. We observed no statistically significant difference between DES and BMS for stent thrombosis and MI. This was also comparable to previous meta-analyses [21,23]. The earlier first-generation DES were associated with increased risk of late stent thrombosis because of polymer-triggered hypersensitivity reactions and late acquired malapposition [6,24]. We observed no difference in the risk of TVR between DES and BMS. In contrast, BASKET and BASKET-SAVAGE showed a lower risk of TVR associated with DES [22]. This is probably related to the proven efficacy of DES in reducing neointimal hyperplasia [25]. Venous grafts are more vulnerable to rapidly progressive atherosclerotic disease, and there is a high risk of failure once a graft begins to degenerate [26]. The DES antiproliferative effect may prevent stented segment stenosis, but it may have no long-term effect on the remaining unstented vessel prone to atherosclerotic blockage. This was evident in the contemporary real-world experience using evidence from medical reports where a lower risk of TVR was found during a short period after DES implantation was lost during long-term follow-up [27,28]. Recently, the long-term results of the ISAR-CABG trial also showed that beneficial effects of DES over BMS observed during the early period were lost during the long-term follow-up at 5 years [29]. The primary outcome of the DIVA trial was target vessel failure, a composite of cardiac death, target vessel MI, and TVR, which was similar in both DES and BMS groups. This is comparable to our findings, where we did not find any significant difference between DES and BMS for MACE (composite of death, MI, and TVR). The trial investigators attributed the lack of benefit with DES to the higher rate of diabetes in the DIVA trial compared with prior trials and to the use of thin-strut BMS that were associated with a lower risk of restenosis compared with the earlier thick-strut BMS used in previous SVG-PCI studies [30]. In contrast to our results, Joyal *et al.*[31] found a reduction in MACE, death, and TVR with the use of DES. Lee *et al.*[32] found a decreased rate of MI and TVR in patients treated with DES but with no significant difference in death. The rationale in these analyses for the reported lower risk of death and MI in patients with DES is uncertain and raises concerns about

Table 1: Baseline characteristics in both groups

	DES group ($n=30$) [n (%)]	BMS group ($n=30$) [n (%)]	P
Age (years)	56±9.7	60±4.6	>0.05
Smoking	20 (66.6)	24 (80)	>0.05
Diabetes mellitus	12 (40)	19 (63)	>0.05
Hypertension	15 (50)	18 (60)	>0.05
Dyslipidemia	16 (53.3)	13 (43.3)	> 0.05
Heart rate (beats/min)	101±7.5	97±7.8	> 0.05
Anterior MI	18 (60)	15 (50)	> 0.05
Inferior MI	12 (40)	15 (50)	> 0.05

BMS, bare-metal stents; DES, drug-eluting stents; MI, myocardial infarction.

Table 2: 3 years of outcome in both groups

	DES group [n (%)]	BMS group [n (%)]	P
MACE	5 (16.6)	8 (26.6)	>0.05
Death	1 (3.3)	1 (3.3)	>0.05
Recurrent MI	2 (6.6)	3 (10)	>0.05
Stroke	1 (3.3)	2 (6.6)	>0.05
Repeat revascularization	1(3.3)	2 (6.6)	>0.05

BMS, bare-metal stents; DES, drug-eluting stents; MACE, major adverse cardiac event; MI, myocardial infarction.

the capacity of the meta-analysis to properly account for the specific and functional variations between patients with BMS and those with DES. The 2 DES vs BMS randomized controlled trials in SVG disease were small, and the findings were not definitive. The RRISC randomized 75 patients to DES vs BMS, and at 6 months, there was a decrease in TVR, but no difference in death and MI. However, there was no difference in TVR at 32 months with an increased risk of death and MI in the DES-treated patients [33]. In the SOS trial, 80 patients undergoing SVG intervention were randomized to DES vs BMS, and at 18 months, the DES-treated patients had no significant difference in TVR, MI, or death [10]. Eventually, in PCI procedures like SVG treatments, DES was increasingly preferred over BMS, whereas BMS was slowly excluded from many catheterization laboratories. Because atherosclerosis pathophysiology is unique in venous grafts compared with native coronary arteries, new strategies should be explored continuously. Further randomized trials with long-term follow-up are still required to determine if the outcome in SVG-PCI could be improved by the new DES generation.

Conclusion

In patients undergoing PCI for SVG lesions, the results of our study demonstrated that there was a statistically insignificant difference between DES and BMS stents in patients with SVG stenosis regarding MACE, such as mortality, MI, TVR, or stent thrombosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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