Comparison of long-term results of drug-eluting stent and bare metal stent implantation in heart transplant recipients with coronary artery disease

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Abstract

Background: Transplanted heart coronary artery disease (TxCAD) may occur in a significant proportion of patients following cardiac transplantation. Drug-eluting stents (DES) have been successfully used in patients with CAD, but their efficacy in TxCAD patients has not been well established.

Aim: To compare long-term results of intracoronary implantation of DES and BMS in patients suffering from TxCAD.

Methods: We performed a retrospective analysis of all intracoronary stent implantations for TxCAD with at least one control coronary angiography performed during follow-up. We identified 28 DES (all sirolimus-eluting stents, SES) and 28 BMS implantations in 23 patients. The mean follow-up time was 410 ± 58 days after DES, and 572 ± 434 days after BMS implantation ($p = 0.004$). We compared the occurrence of in-stent restenosis (ISR) in DES and BMS, and survival of patients in the context of risk factors that were identified for each stent implantation separately.

Results: There were 2 (7%) ISR revealed in DES patients (mean time from PCI to restenosis 492 ± 58 days) vs. 17 (61%) ISR in BMS patients (mean time from PCI to restenosis 475 ± 345 days) ($p < 0.001$). There were 3 (18%) deaths in patients with DES, 4 (31%) in patients with BMS, and 1 (14%) in a patient with DES and BMS (NS). The risk factor profile was comparable, except for higher age at the time of transplantation (46 ± 7 vs. 41 ± 6 years, $p = 0.011$) and stent implantation (54 ± 7 vs. 49 ± 6 years, $p < 0.001$) for DES.

Conclusion: Favourable long-term results of DES compared with BMS implantation for TxCAD suggest the preferential use of DES in heart transplant recipients.

Key words: percutaneous coronary intervention, heart transplant, cardiac allograft vasculopathy

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Introduction

Patients after heart transplantation are at risk of transplanted heart coronary artery disease (TxCAD), also known as cardiac transplant vasculopathy. This condition is diagnosed in up to 42% of patients within 3 years after transplantation and it constitutes a major cause of death in this patient population. TxCAD differs from traditional atherosclerosis as it appears to be a diffuse process involving entire coronary arteries [1].

Coronary artery bypass graft surgery in the transplanted heart is associated with a high risk of complications and with about 35% risk of perioperative death [2]. Therefore, percutaneous coronary intervention (PCI) with stent implantation seems to be an appropriate management of TxCAD. However, the risk of restenosis in transplanted patients undergoing PCI is higher in comparison to non-transplanted patients with CAD [3]. Drug-eluting stent (DES) implantation improves the long-term results of PCI and reduces the risk of restenosis in CAD patients [4, 5]. Considering the different characteristics of TxCAD pathology it should be established whether use of DES in this patient group can improve the results of angioplasty.

The aim of this study was to compare retrospectively long-term results of TxCAD management with PCI using bare metal stents (BMS) vs. sirolimus-eluting stents (SES).

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Table I. Patient characteristics

	DES	BMS	p
Number of implanted stents	28	24	NS
Male gender [%]	100	100	NS
Age at transplantation [years]	46 ± 7	41 ± 6	0.011
Age at stent implantation [years]	54 ± 7	49 ± 6	0.0002
Ischaemic aetiology of heart failure [%]	75	75	NS
Arterial hypertension [%]	89	92	NS
Hyperlipidaemia [%]	100	100	NS
Diabetes mellitus [%]	54	38	NS
Overweight [%]	86	83	NS
Oral sirolimus use [%]	25	33	NS

Methods

Patient group

All patients with a history of heart transplantation undergoing PCI in our centre between April 2000 and September 2006 were analysed. Within this period 28 SES and 24 BMS were implanted in 23 patients. In 7 cases both BMS and SES were implanted, while SES or BMS alone were used in 10 and 6 patients, respectively. Follow-up angiogram was performed in all cases. Mean time to follow-up angiogram in patients with SES and BMS implanted was 410 ± 58 days and 572 ± 434 days respectively (p = 0.004).

Long-term follow-up

Long-term results (death, restenosis) of coronary angioplasty with the use of SES vs. BMS in TxCAD were compared. In all patients restenosis was assessed independently by two experienced interventional cardiologists. Restenosis of > 50% at the site of a previously implanted stent was considered significant.

Statistical analysis

Statistical analysis was performed using Statistica 6.0 software (StatSoft Inc.). The results are presented as frequencies or means ± standard deviations (SD). Survival and lack of restenosis are shown as Kaplan-Meier curves. Differences between groups were compared by means of the log-rank test. Nominal and parametric variables were compared using chi square test and Mann-Whitney test respectively. The p value of < 0.05 was considered significant.

Results

The age of patients at the time of heart transplantation and at the time of coronary stent implantation was significantly higher in the SES group as compared to the BMS group (p = 0.011 and p < 0.0002, respectively). There was no significant difference between the groups with regards to aetiology of heart failure being an indication for heart transplantation or prevalence of co-existing hypertension, diabetes or overweight (Table I). Also there was no significant difference in the stent implantation site. There were 2 SES and 1 BMS implanted in the left main coronary artery, 18 SES and 10 BMS in the left anterior descending artery and its diagonal branch, 3 SES and 7 BMS in the circumflex artery, 5 SES and 7 BMS in the right coronary artery. Standard dual antiplatelet therapy of aspirin in a dose of 75 mg a day and ticlopidine in a dose of

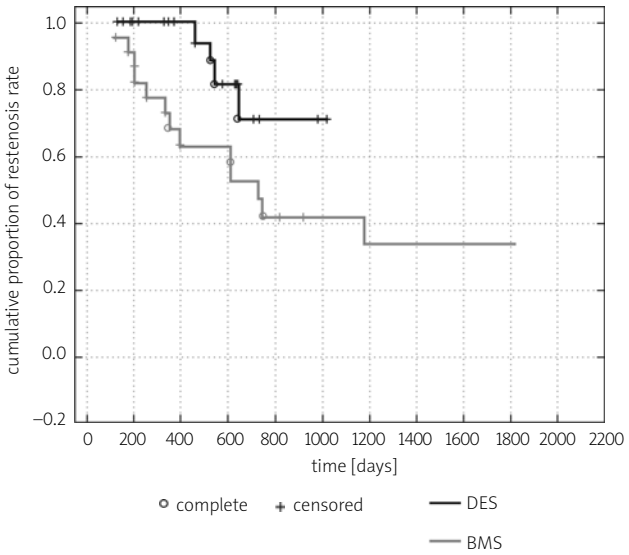

Figure 1. Comparison of the incidence of restenosis in patients with TxCAD after coronary angioplasty (DES vs. BMS)

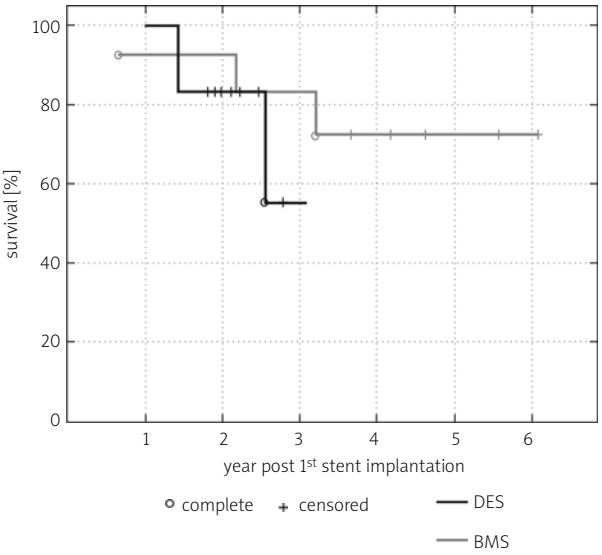

Figure 2. The Kaplan-Meier survival curves

250 mg twice a day was prescribed after coronary angioplasty (ticlopidine has been replaced by clopidogrel in a dose of 75 mg a day since 2005).

During long-term follow-up restenosis was found at the site of previously implanted SES in 2 (7%) cases, 15 and 18 months after angioplasty, whereas in the BMS group 14 (58%) patients suffered from in-stent restenosis 15 ± 11 months from PCI ($p < 0.0002$) (Figure 1). Mortality in the SES group was 18% (3 subjects) versus 31% (4 subjects) in the BMS group (NS). There was one patient with both SES and BMS implanted who died during follow-up. Survival curves are shown in Figure 2.

Discussion

This is an observational study aiming to compare the efficacy of PCI using SES vs. BMS in patients with TxCAD. Data in literature comparing DES and BMS in TxCAD have been conflicting [2, 5-8], probably because of the unique study group characteristics and relatively small patient population. Reddy et al. in their study observed comparable incidence of restenosis and mortality during one-year follow-up in patients after heart transplantation having DES or BMS implanted. Probably the failure to show expected superiority of DES over BMS was related to the use of systemic immunosuppression [9]. In our study the superiority of SES over BMS was demonstrated, however, all DES used in this analysis released an active substance called sirolimus; therefore the observed effect of reduction in restenosis may not be applicable to other DES. Despite a reduction in the number of restenosis with DES implantation, no impact on the long-term prognosis was noted as compared with the BMS group. We acknowledge that the study population was relatively small and heterogeneous with regards to the site of lesions causing ischaemia. The pathophysiological mechanisms and the characteristics of coronary stenosis in TxCAD are different to those in patients with native CAD. Therefore, the results of studies on DES implantation to native coronaries showing their superiority over BMS in the long-term follow-up may not refer to TxCAD.

Study limitations

This is a retrospective study with all its limitations. The follow-up period in patients with BMS was longer than that in patients with SES which might have be responsible for a higher rate of restenosis.

Conclusion

Implantation of SES as compared to BMS reduces the frequency of restenosis in patients after heart transplantation undergoing coronary angioplasty. Thus, SES should be preferably used in heart transplant patients with TxCAD referred for percutaneous coronary intervention.

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Porównanie odległych wyników angioplastyki wieńcowej z użyciem stentów uwalniających substancję antymitotyczną i stentów metalowych u chorych po transplantacji serca

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Streszczenie

Wstęp: Osoby po transplantacji serca są zagrożone wystąpieniem choroby tętnic wieńcowych przeszczepionego serca, określanej mianem waskulopatii przeszczepionego serca (ang. *transplant coronary artery disease*, TxCAD). Z uwagi na odnerwienie przeszczepionego serca, rozpoznanie choroby wieńcowej i/lub restenozy na podstawie objawów klinicznych i badań nieinwazyjnych jest praktycznie niemożliwe. Zastosowanie stentów uwalniających substancję antymitotyczną poprawia wyniki odległe przezskórnej interwencji wieńcowej (PCI), zmniejszając ryzyko restenozy u osób z chorobą wieńcową. Z powodu odmiennego charakteru procesu waskulopatii przeszczepionego serca, należy zbadać, czy zastosowanie stentów uwalniających substancję antymitotyczną w tej grupie chorych może poprawić wyniki angioplastyki.

Cel: Przeprowadzenie retrospektywnej analizy porównawczej odległych wyników leczenia waskulopatii przeszczepionego serca metodą angioplastyki wieńcowej z użyciem stentów metalowych (BMS) i uwalniających substancję antymitotyczną – sirolimus (SES).

Metody: Analizą objęto chorych hospitalizowanych pomiędzy kwietniem 2000 r. i wrześniem 2006 r., po przebytej transplantacji serca, poddanych zabiegom angioplastyki wieńcowej z powodu TxCAD (28 SES i 24 BMS, łącznie u 23 chorych). Nie stwierdzono różnic statystycznych pomiędzy porównywanymi grupami pod względem etiologii niewydolności serca będącej przyczyną transplantacji, częstości współwystępowania nadciśnienia tętniczego, cukrzycy i nadwagi.

Wyniki: W badaniu porównano wyniki odległe (zgon, restenoza) angioplastyki wieńcowej TxCAD z użyciem SES w porównaniu z BMS. Restenozę w miejscu uprzednio implantowanego SES stwierdzono w 2 (7%) przypadkach – w 15. oraz 18. miesiącu po implantacji stentu, natomiast w miejscu implantowanego BMS w 14 (58%) przypadkach, średnio po 15 ± 11 miesiącach od PCI ($p < 0,0002$). Śmiertelność w grupie SES wyniosła 18% (3 chorych) *vs* 31% (4 chorych) w grupie BMS.

Wnioski: W badaniu wykazano przewagę SES nad BMS u chorych poddanych angioplastyce wieńcowej po transplantacji serca. Implantacja SES w porównaniu z BMS pozwala na redukcję częstości występowania restenozy i poprawia rokowanie u chorych po transplantacji serca poddanych angioplastyce tętnic wieńcowych. Stenty uwalniające substancję antymitotyczną – sirolimus, powinny być stosowane w przypadku waskulopatii przeszczepionego serca.

Słowa kluczowe: przezskórna interwencja wieńcowa, transplantacja serca, waskulopatia przeszczepionego serca

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