Everolimus-eluting stents versus sirolimus-eluting stents in patients with cardiac allograft vasculopathy

Michał Hawranek¹, Łukasz Pyka¹, Bożena Szygula-Jurkiewicz², Piotr Desperak¹, Wioletta Szczurek¹, Andrzej Lekston¹, Michał Zembala², Szymon Pawlak², Mariusz Gąsior¹, Piotr Przybyłowski²,³

¹3rd Department of Cardiology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland
²Department of Cardiac, Vascular and Endovascular Surgery and Transplantology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Poland
³First Department of General Surgery, Jagiellonian University, Medical College, Krakow, Poland

Adv Interv Cardiol 2021; 17, 4 (66): 349–355
DOI: https://doi.org/10.5114/aic.2021.111891

Abstract

Introduction: Cardiac allograft vasculopathy remains one of the most important factors leading to chronic cardiac allograft rejection. When revascularization is needed percutaneous coronary interventions are the method of choice.

Aim: To compare the short- and long-term outcomes of cardiac allograft vasculopathy patients treated with everolimus- (EES) or sirolimus-eluting stents (SES).

Material and methods: Between December 2012 and December 2020, 319 patients after heart transplantation undergoing coronary angiography at our institution were analysed. Subsequently 39 patients underwent de novo angioplasty with second-generation EES. The primary study endpoint was angiographic restenosis as evaluated by quantitative coronary angiography. Secondary outcomes included binary restenosis, target lesion revascularization and cardiac death during the follow-up period (6 months).

Results: Twenty-four patients were treated with EES and 15 treated with SES. No significant differences were observed regarding the rate of risk factors of cardiovascular diseases and comorbidities. The patients treated with EES were younger (55.8 ± 11.8 vs. 60.1 ± 12.2) and less frequently male (79% vs. 93%). The majority of patients were diagnosed with single vessel disease with LAD involvement (62% and 86% in the EES group, and 47% and 56% in the SES group). In 6 months follow-up, late lumen loss was comparable in both groups, 0.19 ± 0.15 vs. 0.14 ± 0.15, and binary restenosis was 4% and 0% for EES and SES groups, respectively.

Conclusions: Second generation drug-eluting stents eluting rapamycin analogues are associated with high direct efficacy of procedures and low incidence of restenosis in a 6-month follow-up.

Key words: cardiac allograft vasculopathy, percutaneous coronary intervention, drug-eluting stents.

Summary

Cardiac allograft vasculopathy remains one of the most important factors leading to chronic cardiac allograft rejection. When revascularization is needed percutaneous coronary interventions with drug-eluting stents are the method of choice. Everolimus-eluting second generation stents are characterized by the lowest restenosis rate. Data regarding other rapamycin analogues are scarce. In the current analysis the 6 months restenosis rates were low and comparable for everolimus- and sirolimus-eluting stents, indicating safety and efficacy of both substances in the treatment of cardiac allograft vasculopathy.

Introduction

Cardiac allograft vasculopathy (CAV) remains one of the most important factors leading to chronic cardiac allograft rejection. According to the ISHLT report of 2017, CAV is responsible for 32.5% of deaths in the period between 5 and 10 years after heart transplantation. With time, CAV affects most patients after orthotopic heart transplantation (OHT). Its incidence is 29.3% and 47.4
at 5 and 10 years after the transplantation, respective-
ly [1]. The pathomechanism of CAV involves numer-
ous factors related to the immune system, the clinical
profile of the donor and recipient, and to the surgery
technique [2]. CAV differs from classic coronary atherosclerosis in
that the stenoses are diffuse and concentric in nature,
they do not break the internal lamina, and rarely include
calcifications. Importantly, patients after heart trans-
plantation may experience both forms of coronary artery dis-
ease at the same time [3].

The only effective method of CAV treatment is re-trans-
plantation of the heart, which involves, however, a much
higher risk of complications and death than the first heart
transplantation [4]. In view of the above, and due to low
organ availability, the basic treatment in clinical practice
is based on continuous modifications of risk factors, the
use of statins, and modifications of the immunosuppres-
sive therapy [3]. Nevertheless, these methods have limited
efficacy, and some patients require revascularization. Sur-
gical treatment is rarely used, since it is technically chal-
lenging and has poor prognosis [5]. Therefore, the majority
of patients with significant stenosis of coronary arteries
secondary to CAV are qualified for percutaneous coronary
intervention (PCI) [5]. With development of interventional
cardiology, subsequent generations of devices were used
in CAV patients, achieving a gradual improvement in long-
term outcomes of the interventions performed [6–9]. Ne-
evertheless, data on the efficacy of second generation stents
eluting rapamycin analogues are limited.

### Material and methods

Between December 2012 and December 2020, we
analysed 369 post-heart transplantation patients subject
to coronary angiography at our facility. In the study pe-
riod, 67 patients underwent PCI. Patients with balloon
angioplasty of a restenotic lesion or a previously treated
vessel, those with implanted stents other than second
generation EES or SES, patients who underwent coronary
artery bypass graft (CABG) after heart transplantation
and patients with no angiography control were excluded
from further analysis. Finally, 39 patients were enrolled in
the study. The study design is shown in Figure 1.

The PCI procedures were conducted in accordance
with standard local practice. The patients routinely re-
ceived unfractionated heparin with target time of co-
agulation activation between 250 and 300 s. Intracor-
ony nitroglycerine (100 to 200 mg) was used during
coronary angiography and before angioplasty. Baseline
and follow-up angiography was performed using the
same views. Quantitative coronary angiography (QCA)
was performed by two independent specialists in all
the patients enrolled. QCA calibration was performed
with a guiding catheter. The following parameters were
assessed in the study: minimum lumen diameter, refer-
ence vessel diameter, percent diameter stenosis and
late lumen loss.

The primary endpoint of the study was the occurrence
of angiographically significant restenosis assessed with
QCA. Secondary endpoints included: binary restenosis,
target lesion revascularisation (TLR) and cardiac death
during a 6-month follow-up period. Standard definitions
of endpoints were used in the study. Binary restenosis
was defined as late lumen loss by at least 50%. TLR was
defined as planned or urgent PCI of a previously treated
lesion, covering the area of 5 mm after and before the
implanted stent. All deaths were considered cardiac un-
less a definitive non-cardiac cause could be established.
Clinical, angiographic, procedural, and mortality data
were obtained retrospectively using the online reporting
system. The patients were followed for 6 months after
the first procedure. Follow-up coronary angiography in
patients undergoing PCI was performed after 6 months
of the initial procedure, in accordance with the protocol
adopted at our site.

Additional information was obtained by telephone
contact or, if necessary, from medical records. The study
was approved by the Bioethics Committee of the Medical
University of Silesia and was conducted in accordance
with the principles set forth in the Declaration of Helsin-
ki. All the patients gave their informed consent.

| Study population | 39 patients | 46 lesions |
|-------------------|-------------|-----------|
| **Group 1**       | 24 patients | 30 lesions| Everolimus eluting stent |
| **Group 2**       | 15 patients | 16 lesions| Sirolimus eluting stent |

**Figure 1. Study flow chart**
Results

The final number of patients enrolled in the study was 39, including 24 patients treated with EES and 15 treated with SES. The clinical characteristics of the analysed groups are presented in Table I. No significant differences were observed regarding the rate of risk factors of cardiovascular diseases and comorbidities. In most patients, OHT was caused by ischaemic cardiomyopathy. The patients treated with EES were younger (55.8 ±11.8 vs. 60.1 ±12.2) and less frequently male (79% vs. 93%). The incidence of hypertension, hypercholesterolaemia and type 2 diabetes was high in both groups. The SES group showed a slightly higher blood pressure (123 ±10.6 vs. 132 ±39) and a slightly lower left ventricle ejection fraction (53.3 ±2 vs. 51.7 ±6.7). The patients treated with SES had a higher level of blood everolimus (6.9 ±2.8 vs. 12.3 ±2.0 ng/ml).

Angiographic and perioperative characteristics are illustrated in Table II. Most patients had ad hoc PCI (92% and 93%). In the EES group 30 stenoses were treated with 31 stents, and in the SES group 16 stenoses were treated using 25 stents. The majority of patients were diagnosed with single vessel disease with LAD involvement (62% and 86% in the EES group, and 47% and 56% in the SES group). Balloon predilation was more common in the patients treated with EES (57% vs. 12%). A higher number of stents was used in the group treated with SES (1.1 ±0.3 vs. 1.4 ±0.7). The frequency of perioperative complications was low in both groups.

Table I. Baseline characteristics of the study population

| Parameter                                      | Everolimus n = 24 | Sirolimus n = 15 | P-value |
|------------------------------------------------|------------------|-----------------|----------|
| Time from heart transplant to PCI [years]     | 9.7 ±5.33        | 9 ±4.75         | NS       |
| Age [years] mean ± SD                         | 55.8 ±11.8       | 60.1 ±12.2      | NS       |
| Male sex, n/N (%)                             | 19/24 (79)       | 14/15 (93)      | NS       |
| BMI [kg/m²] mean ± SD                         | 27.5 ±5.6        | 26.8 ±4.6       | NS       |
| Weight [kg] mean ± SD                         | 81.3 ±16.6       | 83.2 ±17        | NS       |
| Height [m] mean ± SD                          | 1.72 ±9          | 1.76 ±6.3       | NS       |
| Cause of OHT, n/N (%)                         |                  |                 |          |
| Coronary artery disease                       | 15/24 (62)       | 10/15 (66)      | NS       |
| Dilated cardiomyopathy                        | 8/24 (33)        | 5/15 (33)       | NS       |
| Others                                         | 1/24 (4)         | 0/15 (0)        | NS       |
| Cardiovascular risk factors, n/N (%)          |                  |                 |          |
| Arterial hypertension                         | 19/24 (79)       | 13/15 (87)      | NS       |
| Hypercholesterolaemia                         | 17/24 (71)       | 13/15 (87)      | NS       |
| Diabetes mellitus                             | 20/24 (83)       | 12/15 (80)      | NS       |
| Obesity                                        | 8/24 (33)        | 2/15 (13)       | NS       |
| Previous PCI after OHT, n/N (%)               | 12/24 (50)       | 5/15 (33)       | NS       |
| Previous stroke, n/N (%)                      | 4/24 (17)        | 2/15 (13)       | NS       |
| Previous PAD, n/N (%)                         | 3/24 (12.5)      | 1/15 (7)        | NS       |
| Chronic kidney disease, n/N (%)               | 11/24 (46)       | 7/15 (47)       | NS       |
| Hyperthyroidism, n/N (%)                      | 2/24 (8)         | 0/15 (0)        | NS       |
| Hypothyroidism, n/N (%)                       | 5/24 (21)        | 1/15 (7)        | NS       |
| SBP [mm Hg] mean ± SD                         | 123 ±10.6        | 132 ±39         |          |
| DBP [mm Hg] mean ± SD                         | 78 ±7.5          | 78 ±7           |          |
| Creatinine [μmol/l] mean ± SD                 | 120 ±32          | 123 ±25         |          |
| Haemoglobin [mmol/l] mean ± SD                | 8.5 ±1.05        | 8.7 ±1.13       |          |
| Haematocrit (%) mean ± SD                     | 40.3 ±4.6        | 41.5 ±5.0       |          |
| Red blood cells [× 10⁹/ml] mean ± SD          | 4.7 ±0.62        | 4.9 ±0.54       |          |
| White blood cells [× 10⁹/ml] mean ± SD        | 6.4 ±1.8         | 6.9 ±1.8        |          |
| Platelets [× 10⁹/ml] mean ± SD                | 206 ±58          | 192 ±54         |          |
| Serum tacrolimus level [ng/ml] mean ± SD      | 6.3 ±2.5         | 7.4 ±3.0        |          |
| Serum mycophenolate mofetil level mean ± SD   | 1.6 ±0.3         | 1.8 ±0.8        |          |
| Serum everolimus level [ng/ml] mean ± SD      | 6.9 ±2.8         | 12.3 ±2.0       | 0.016    |
| LVEF (%) mean ± SD                            | 53.3 ±2          | 51.7 ±6.7       |          |

BMI – body mass index, CABG – coronary artery bypass grafting, DBP – diastolic blood pressure, LVEF – left ventricular ejection fraction, MI – myocardial infarction, OHT – orthotopic heart transplant, PAD – peripheral artery disease, PCI – percutaneous coronary intervention, SBP – systolic blood pressure.
The results of the QCA analysis are presented in Table III. Mean length of stenoses was 18.7 ±7.11 vs. 15 ±5.66 for EES and SES groups, respectively. Minimal lumen diameter (MLD) obtained after the surgery was comparable in both groups (2.44 ±0.47 vs. 2.47 ±0.37) although % stenosis of lumen area (%MLA) was slightly higher in the group treated with EES (12.2 ±8.6 vs. 1.57 ±0.78), as was the acute lumen gain (1.82 ±0.53 vs. 1.57 ±0.78). In 6 months follow-up, late lumen loss was comparable in both groups, 0.19 ±0.15 vs. 0.14 ±0.15, and binary restenosis was 4% and 0% for EES and SES groups, respectively.

No significant differences in the administered pharmacotherapy were found with regard to both cardiologic and immunosuppressive pharmacotherapy (Table IV). During the 6-month follow-up period, no death, including cardiovascular death, was registered. 1 TLF was observed in the EES group.

**Table II. Procedural characteristics of study population**

| Parameter                           | Everolimus n = 24 | Sirolimus n = 15 | P-value |
|-------------------------------------|-------------------|------------------|---------|
| PCI ad hoc, n/N (%)                 | 22/24 (92)        | 14/15 (93)       | NS      |
| Vascular access during PCI, n/N (%):|                   |                  |         |
| Radial                             | 13/24 (54)        | 9/15 (60)        | NS      |
| Femoral                            | 12/24 (46)        | 6/15 (40)        |         |
| Vascular access conversion, n/N (%)| 2/24 (8)          | 2/15 (13)        | NS      |
| No. of affected major vessels, n/N (%): |                 |                  |         |
| 1                                  | 15/24 (62)        | 13/15 (86)       | NS      |
| 2                                  | 8/24 (33)         | 1/15 (7)         |         |
| 3                                  | 1/24 (4)          | 1/15 (7)         |         |
| Total number of treated lesions, n:| 30                | 16               |         |
| Lesions per patient, number, mean ± SD | 1.2 ±0.56        | 1.25 ±0.67       | NS      |
| Percent diameter stenosis (%) mean ± SD | 75.8 ±12.4       | 84.9 ±9.45       | NS      |
| Bifurcation, n/N (%)                | 9/30 (30)         | 4/16 (25)        | NS      |
| Predilatation, n/N (%)              | 17/30 (57)        | 2/16 (12)        | 0.03    |
| Postdilatation, n/N (%)             | 10/30 (33)        | 7/16 (44)        | NS      |
| Treated vessels, n/N (%):           |                   |                  |         |
| LAD                                | 14/30 (47)        | 9/16 (56)        | NS      |
| LCx                                | 9/30 (30)         | 3/16 (19)        |         |
| RCA                                | 7/30 (23)         | 4/16 (25)        |         |
| TIMI flow 3 after intervention, n/N (%): | 30/30 (100)     | 16/16 (100)      |         |
| Total number of stents, n:          | 31                | 25               |         |
| Device per patient, number, mean ± SD | 1.1 ±0.3          | 1.4 ±0.7         | 0.01    |
| Device length [mm] mean ± SD       | 20.8 ±6.8         | 17.3 ±7.3        | NS      |
| Device diameter [mm] mean ± SD     | 2.89 ±0.59        | 2.79 ±0.47       | NS      |
| Deployment pressure [atm] mean ± SD | 14.2 ±2.7         | 14.5 ±2          | NS      |
| Complications during PCI, n/N (%):  |                   |                  |         |
| Acute occlusions                    | 0/24 (0)          | 0/15 (0)         |         |
| Dissection                          | 0/24 (0)          | 1/15 (7)         |         |
| Slow/No-reflow                      | 0/24 (0)          | 0/15 (0)         |         |
| GP IIb/IIIa inhibitor               | 1/24 (4)          | 0/15 (0)         |         |

**Discussion**

The analysis showed that the use of second generation DES eluting rapamycin analogues is associated with high direct efficacy of surgery and low incidence of restenosis, late lumen loss and serious cardiac events in long-term follow-up. No differences were observed in relation to the type of antimitotic substance eluted (everolimus vs. sirolimus).

The treatment of CAV remains highly challenging, since there are no standards regarding the management of the disease. The only effective method, heart re-transplantation, is virtually unavailable, and surgical treatment is associated with high risk of complications, including death [1]. Percutaneous coronary interventions remain an attractive option due to low invasiveness and high direct efficacy of the procedures [5]. However, they must be treated as palliative treatment, since the interventions do not involve a reduced risk of
As in the case of PCI due to native atherosclerosis, the treatment of CAV initially involved balloon angioplasty, followed by metal stents, 1st generation DES, and second generation DES. The use of balloon angioplasty and BMS was associated with a high incidence of restenosis, 72% and 39%, respectively, in an 8-month follow-up [13]. The data comparing BMS with DES are ambiguous. A study analysing 45 patients with CAV subject to PCI with BMS or DES showed no significant differences in the rate of restenosis or clinical events [14]. Similar results were ob-

progressive organ insufficiency and death [10, 11]. We do not have prospective studies in this area, and most data come from observational, retrospective studies. In a non-randomised study comparing CAV patients who were treated with PCI and patients in whom PCI was not possible, a lower mortality rate was observed in the PCI group, i.e. 20% vs. 43.5%, respectively, \( p = 0.03 \). Nevertheless, mean survival time after intervention was 4 years, and 32% of patients required a repeated intervention [12].

### Table III. Quantitative coronary analysis

| Parameter                     | Everolimus \( n = 24 \) | Sirolimus \( n = 15 \) | \( P \)-value |
|-------------------------------|--------------------------|------------------------|---------------|
| Index hospitalization:        |                          |                        |               |
| Lesion length [mm] mean ± SD  | 18.7 ±7.11               | 15 ±6.66               | NS            |
| MLD pre [mm] mean ± SD        | 0.62 ±0.46               | 0.67±0.51              | NS            |
| %MLD pre (%) mean ± SD        | 70.6±11.8                | 69.4±18.9              | NS            |
| RVD proximal [mm] mean ± SD   | 2.79 ±0.58               | 2.74 ±0.57             | NS            |
| RVD distal [mm] mean ± SD     | 2.58 ±0.48               | 2.49 ±0.48             | NS            |
| MLD post [mm] mean ± SD       | 2.44 ±0.47               | 2.47 ±0.37             | NS            |
| %MLD post (%) mean ± SD       | 6.7 ±4.9                 | 7.6 ±4.7               | NS            |
| %MLA post (%) mean ± SD       | 12.2 ±8.6                | 11.8 ±4.9              | 0.03          |
| Acute gain [mm] mean ± SD     | 1.82 ±0.53               | 1.57 ±0.78             | 0.07          |

Follow-up:

| Parameter                     | Everolimus \( n = 24 \) | Sirolimus \( n = 15 \) | \( P \)-value |
|-------------------------------|--------------------------|------------------------|---------------|
| MLD (mm) mean ± SD            | 2.2 ±0.67                | 2.3 ±0.39              | NS            |
| %MLD (%) mean ± SD            | 14.0 ±13.3               | 14.2 ±5.4              | NS            |
| %MLA (%) mean ± SD            | 23.2 ±19.7               | 26 ±9.2                | NS            |
| Late lumen loss, mean ± SD    | 0.19 ±0.15               | 0.14 ±0.15             | NS            |
| Binary restenosis, n/N (%)    | 1/24 (4)                 | 0/15 (0)               | NS            |

### Table IV. Pharmacotherapy on discharge

| Parameter                        | Everolimus \( n = 24 \) | Sirolimus \( n = 15 \) | \( P \)-value |
|----------------------------------|--------------------------|------------------------|---------------|
| Tacrolimus, n/N (%)              | 19/24 (79)               | 10/15 (67)             | NS            |
| Cyclosporine, n/N (%)            | 3/24 (12)                | 3/15 (20)              | NS            |
| Mycophenolate mofetil, n/N (%)   | 9/24 (37)                | 8/15 (53)              | NS            |
| Sirolimus, n/N (%)               | 3/24 (12)                | 1/15 (6.67)            | NS            |
| Everolimus, n/N (%)              | 8/24 (33)                | 4/15 (27)              | NS            |
| Acetylsalicylic acid, n/N (%)    | 24/24 (100)              | 14/15 (93)             | NS            |
| P2Y12 receptor inhibitor, n/N (%)| 22/24 (92)               | 14/15 (93)             | NS            |
| Beta-blocker, n/N (%)            | 5/24 (21)                | 6/15 (40)              | NS            |
| Alfa-blocker, n/N (%)            | 4/24 (17)                | 0/15 (0)               | NS            |
| ACE inhibitor/ARB, n/N (%)       | 16/24 (67)               | 11/15 (73)             | NS            |
| Calcium antagonist, n/N (%)      | 13/24 (54)               | 7/15 (47)              | NS            |
| Statin, n/N (%):                 |                          |                        |               |
| Atorvastatin                     | 13/24 (54)               | 8/15 (53)              | NS            |
| Rosuvastatin                     | 7/24 (29)                | 3/15 (20)              | NS            |
| Allopurinol, n/N (%)             | 8/24 (33)                | 2/15 (13)              | NS            |
| Metformin, n/N (%)               | 6/24 (25)                | 3/15 (20)              | NS            |
| Insulin, n/N (%)                 | 3/24 (12)                | 4/15 (27)              | NS            |

**MLD** – minimal lumen diameter, **MLA** – minimal lumen area, **PCI** – percutaneous coronary intervention, **RVD** – reference vessel diameter.

**ACE** – angiotensin converting enzyme, **ARB** – angiotensin receptor blocker.
tained in a study by Reddy et al., in which 42 patients treated with BMS or first generation DES were compared. The rate of restenosis was 22.6% and 22.7%, respectively. No differences in the incidence of adverse events were observed, either [15]. Nevertheless, an analysis of 6 studies including 312 patients with CAV, in which BMS were compared with 1st generation DES eluting sirolimus or paclitaxel, showed a significant reduction in restenosis when DES were used. As in the above-mentioned studies, this was not associated with a reduced incidence of serious cardiac events [16].

Available data on second generation DES indicate further improvement in PCI outcomes in patients with CAV. An analysis of 48 patients who underwent PCI regarding 113 stenoses showed that the incidence of binary restenosis increased by 3% in a 1-year follow-up [17]. In an analysis of 21 patients with CAV treated with EES, the rate of restenosis and TLR was 5.9% [18]. These results are similar to those achieved in the treatment of native coronary arteries [8, 9]. It is emphasised that everolimus may show additional benefits in the population of CAV patients in that it stops migration and proliferation of smooth muscle cells, and inhibits endothelial progenitor cells [19]. Moreover, systemic use of everolimus may be associated with inhibition of CAV progression [20].

In the present study, we found high direct efficacy of PCI procedures using EES and SES. QCA showed similar results in both groups, both directly after the procedure and in a long-term follow-up. The incidence of binary restenosis was low and comparable with the incidence observed in the above quoted studies. Of note is a higher number of stents used in the SES group; however, it did not affect the results of long-term angiographic follow-up. The obtained results show similar efficacy of both the rapamycin analogues in preventing restenosis in patients with CAV. Also, good results achieved with second generation stents may be associated not only with the type of the antimitotic substance released, but also with the construction of the stent platform. Nevertheless, small group sizes in the presented analysis prevent the formulation of final conclusions.

Advances in interventional cardiology, first of all the introduction of stents eluting antimitotic substances, are associated with improvement in direct efficacy of PCI procedures and with significant reduction in the restenosis rate. The efficacy of DES may result from the nature of CAV, which is characterised by excessive proliferation of the internal lamina. By reducing neointimal proliferation, DES reduces the incidence of restenosis [21]. On the other hand, DES do not reduce an increased lymphoproliferative response in the tunica intima, media and externa, and the mechanism is responsible for the progressive and diffuse nature of CAV beyond the stented lesion. This phenomenon may partially explain the lack of benefits from using DES in the reduction of adverse cardiac events in the published studies [10].

The presented analysis is a single-centre, observational, retrospective study, limited to CAV patients requiring revascularisation. In addition, the analysed groups are small, which affects the reliability of the analysis and the possibility of forming conclusions. Angiographic assessment was performed using QCA, and the sensitivity of angiography is known to be lower than that of intracoronary imaging using IVUS or OCT. Intracoronary imaging was not used in this study, so it was not possible to perform a detailed assessment of the mechanisms of late lumen loss, except for tunica intima hyperplasia. Since there are no standards of CAV management, a comparison of the conducted analysis with the results of other studies may involve a high number of confounding factors resulting from differences in the treatment administered, including immunosuppression, and modification of risk factors.

Conclusions

Second generation DESs eluting rapamycin analogues are associated with high direct efficacy of procedures and low incidence of restenosis in a 6-month follow-up. No differences were observed in relation to the type of the eluted substance – everolimus or sirolimus.

Conflict of interest

The authors declare no conflict of interest.

References

1. Lund LH, Khush KK, Cherikh WS, et al.; International Society for Heart and Lung Transplantation. The registry of the international society for heart and lung transplantation: thirty-fourth adult heart transplantation report-2017; focus theme: allograft ischemic time. J Heart Lung Transplant 2017; 36: 1037-46.
2. Nikolova AR, Kobashigawa JA. Cardiac allograft vasculopathy: the enduring enemy of cardiac transplantation. Transplantation 2019; 103: 1338-48.
3. Mehra MR, Ventura HO, Smart FW, et al. New developments in the diagnosis and management of cardiac allograft vasculopathy. Tex Heart Inst J 1995; 22: 138-44.
4. Saito A, Novick RJ, Kiihl B, et al. Early and late outcomes after cardiac retransplantation. Can J Surg 2013; 56: 21-6.
5. Luc JG, Choi JH, Rizvi SA, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in heart transplant recipients with coronary allograft vasculopathy: a systematic review and meta-analysis of 1,520 patients. Ann Cardiothorac Surg 2018; 7: 19-30.
6. Simpson L, Lee EK, Hott BJ, et al. Long-term results of angioplasty vs stenting in cardiac transplant recipients with allograft vasculopathy. J Heart Lung Transplant 2005; 24: 1211-7.
7. Beggui F, Varnous S, Montalescot G, et al. Long-term outcome after bare-metal or drug eluting stenting for allograft coronary artery disease. J Heart Lung Transplant 2010; 29: 316-22.
8. Park KW, Chae IH, Lim DS, et al. Everolimus-eluting versus sirolimus-eluting stents in patients undergoing percutaneous coronary intervention: the EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) randomized trial. J Am Coll Cardiol 2011; 58: 1844-54.
9. Gada H, Kirtane AJ, Newman W, et al. 5-year results of a randomized comparison of XIENCE V everolimus-eluting and TAXUS paclitaxel-eluting stents: final results from the SPIRIT III trial (clinical evaluation of the XIENCE V everolimus eluting coronary stent system in the treatment of patients with de novo native coronary artery lesions). JACC Cardiovasc Interv 2013; 6: 1263-6.

10. Lee MS, Lluri G, Finch W, Woo Park K. Role of percutaneous coronary intervention in the treatment of cardiac allograft vasculopathy. Am J Cardiol 2018; 121: 1051-5.

11. Benatti RD, Taylor DO. Evolving concepts and treatment strategies for cardiac allograft vasculopathy. Curr Treat Options Cardiovasc Med 2014; 16: 278-94.

12. Agarwal S, Parashar A, Kapadia SR, et al. Long-term mortality after cardiac allograft vasculopathy: implications of percutaneous intervention. JACC Heart Fail 2014; 2: 281-8.

13. Benza RL, Zoghbi GJ, Tallaj J, et al. Palliation of allograft vasculopathy with transluminal angioplasty: a decade of experience. J Am Coll Cardiol 2004; 43: 1973-81.

14. Park KE, Huo T, Muller KE, et al. Drug-eluting stents may not reduce target lesion revascularization in cardiac allograft vasculopathy. J Interven Cardiol 2014; 27: 80-5.

15. Reddy PR, Gulati A, Steen L, et al. Outcomes of bare metal versus drug eluting stents in allograft vasculopathy. J Heart Lung Transplant 2008; 27: 1222-8.

16. Dasari TW, Hennebry TA, Hanna EB, Saucedo JF. Drug eluting versus bare metal stents in cardiac allograft vasculopathy: a systematic review of literature. Catheter Cardiovasc Interv 2011; 77: 962-9.

17. Cheng R, Vanichsarn C, Patel JK, et al. Long-term clinical and angiographic outcomes of percutaneous coronary intervention with everolimus-eluting stents for the treatment of cardiac allograft vasculopathy. Catheter Cardiovasc Interv 2017; 90: 48-55.

18. Azarbal B, Arbit B, Ramaraj R, et al. Clinical and angiographic outcomes with everolimus eluting stents for the treatment of cardiac allograft vasculopathy. J Interven Cardiol 2014; 27: 73-9.

19. Topilsky Y, Hasin T, Raichlin E, et al. Sirolimus as primary immunosuppression attenuates allograft vasculopathy with improved late survival and decreased cardiac events after cardiac transplantation. Circulation 2012; 125: 708-20.

20. Kobashigawa JA, Pauly DE, Starling RC, et al. Cardiac allograft vasculopathy by intravascular ultrasound in heart transplant patients: substudy from the everolimus versus mycophenolate mofetil randomized, multicenter trial. JACC Heart Failure 2013; 1: 389-99.

21. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002; 346: 1773-80.