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KISSING STENTING OF AORTIC BIFURCATION FOR AORTO-ILIAC OBSTRUCTIVE DISEASE: A COMPARISON BETWEEN BARE METAL STENTS AND COVERED STENTS

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ABSTRACT

INTRODUCTION

Aorto-iliac occlusive disease (AIOD) is the aortic and iliac localization of peripheral artery disease (PAD), resulting in disabling claudication, rest pain and tissue loss. During the last decades, as a result of rapid improvement in materials and surgeon's expertise, endovascular revascularization of AIOD has become the first line approach in high-risk patients, also in case of TASC-C and D lesions. In particular, the kissing stent (KS) technique is one of the most widely accepted approaches for complex lesions involving distal aorta and/or the ostium of common iliac artery in patients with severe comorbidities; nevertheless, several issues of the endovascular treatment of these lesions as technique, materials, postoperative medical treatment, and factors influencing the long-term results are still a matter of debate. During the years, both bare metal stents (BMS) and covered stents (CS) have been widely used for the treatment of AIOD. The aim of our multicentric study was to compare the short- and mid-term results of BMS versus CS in the kissing stenting technique.

METHODS

Patients undertaking a kissing reconstruction of aortic bifurcation between January 2017 to August 2021 in the Department of Metropolitan Vascular Surgery Policlinico Sant'Orsola-Malpighi (University of Bologna) and Department of Vascular Surgery Infermi Hospital of Rimini (Italy) were included into this study. Morphological features of iliac plaques were studied and classified in two subgroups as per the extension of calcium involvement at CTA and as per thrombosis extension. Patients were treated with BMS or CS. The primary outcomes measured were: Technical Success, Procedural Success, Primary Patency, and Clinical Success. The secondary outcomes measured were: Assisted primary Patency, Secondary Patency, Survival rate, Thrombosis rate, Limb Salvage according to Rutherford Classification, procedure-related

complications and predictors of patency and mid- and long-term results. Every endpoint and outcome were compared in relation to BMS or CS treatment. All patients included received in the post-operative standard statin treatment and dual anti-platelets (DAPT) for at least one month followed by monotherapy, unless oral anticoagulation was indicated for other reasons.

RESULTS

Thirty-four patients were enrolled, 17 treated with BMS and 17 treated with CS in a kissing configuration. The average age was 66 years. The 80% of patients were part of TASC C-D categories, indicating that a large number of lesions were high complexity lesions. DAPT was administered to 82.4% (28/34) of patients with a mean duration of 4.4 ± 1.6 months. Mean follow-up was 32.1 ± 17.8 SD months. Technical Success was reached in 100% of cases. Immediate Clinical Success was reached in 29 cases (85.3%). Analysing in detail the differences between the groups, immediate and 30-day Clinical Success was statistically different between BMS and CS group (64.7% vs 100%, $p = .01$), in favour of CS group. Focusing on mid-term results, overall Clinical Success at 1-year follow-up was 91.2%, and resulted significantly higher in CS than in BMS group (in detail, BMS group 82.4% vs CS group 100%, p .04). Regarding results about patency, overall Primary Patency, Assisted Patency, and Secondary Patency at 30 days were 97.1%, 97.1%, and 100%, without differences between BMS and CS group (94.1% vs 100%, 94.1% vs 100%, and 100% vs 100%; $p = .7$), respectively. Two cases (5.9%) of thrombosis were registered, and both occurred within 3 months after the procedure and both in the BMS group, without statistical differences with the CS group (11.8% vs 0%, p .48). Both cases of thrombosis occurred in patients who were not treated with dual antiplatelet therapy (in detail, single antiplatelet therapy (SAPT) group 33.3% vs dual antiplatelet therapy (DAPT) group 0%, p .027). Overall Survival at 30 days, 12 months, and at the mean follow-up was 100%, 97.1%, and 85.3% respectively with a difference between the groups. Survival statistically differed only at the mean follow-up in favour of CS group (in detail, BMS group 70.6% and CS group 100%, p .04).

Reintervention rate at follow-up was 5.9% and no significant differences between the groups were found (in detail, BMS group 11.7% vs CS group 0% CS, *p* .25). Amputation rate was 8.9% at follow-up. No differences in terms of survival, patency, clinical success, reintervention, and complication rate were found in terms of TASC classification class and/or presence of calcified lesions or extensive thrombosis.

CONCLUSIONS

The endovascular approach is currently safe and effective in the treatment of aorto-iliac occlusive disease and kissing stenting offers excellent results in terms of technical success, procedural success and patency rates in the short- and medium-term. The use of CS seems to provide clinical better results than BMS; however, in our study no statistically significant differences emerged between the two types of stents in terms of patency, reintervention and complications. DAPT seems to warrant the best results in terms of patency, although there is still no consensus about the ideal duration of administration. Further studies are needed to better clarify the correlation between the nature of the lesions to be treated and the type of device able to guarantee the best results over time.

INTRODUCTION

Aorto-iliac occlusive disease (AIOD) is the aortic and iliac localization of peripheral artery disease (PAD), resulting in disabling claudication, rest pain and tissue loss. It usually affects relatively young (often aged less than 70 years), smoking, and dyslipidemic patients[1,2].

On the basis of Trans-Atlantic Inter-Society (TASC) II classification[2], aorto-iliac lesions can be categorized into 4 groups: TASC A (limited and short stenosis), B (diffused and long stenosis or focal occlusions and focal aortic stenosis), C (bilateral occlusions of common iliac arteries, diffused long stenosis of iliac axis not involving aorta and iliac stenosis associated with an occlusion), and D (complete aortoiliac obstruction and diffused stenosis involving aorta and/or bilateral occlusion of iliac axes). Following these guidelines, TASC A and B iliac lesions should be treated by endovascular therapy and TASC C-D lesions with surgery (e.g. aorto-bifemoral bypass)[3].

For what concerns open repair, it has a primary patency rate of 90% at 5 years not excepting from an increased risk of complications and mortality; it is undoubtedly considered a durable treatment for young and "fit for surgery" patients[4,5].

During the last decades, as a result of rapid improvement in materials and surgeon's expertise, endovascular revascularization of AIOD has become the first line approach in high-risk patients, also in case of TASC C and D lesions. Moreover, different techniques and several devices are promptly expanding the endovascular approach[2,6], with satisfying technical results[7-11].

In particular, the kissing stent (KS) technique is one of the most widely accepted approaches for complex lesions involving distal aorta and/or the ostium of common iliac artery[12] in patients with severe comorbidities. Some authors suggest that this technique has early and late results comparable to open surgery, with a very low rate of major complications[12,13]; nevertheless, several issues of the endovascular treatment (EVT) of TASC C and D aortoiliac occlusive disease such as technique, materials, postoperative medical treatment, and factors influencing the long-term results are still a matter of debate[3,14,15]. During the last two decades, both bare metal stents (BMS) and covered stents

(CS) have been widely used for the treatment of AIOD. Concerning the available literature, even if several studies have compared CS versus BMS results in AIOD treatment, solid data relating to kissing configuration are still lacking[16-19].

The aim of our multicentric study was to compare the short- and mid-term results of BMS versus CS in the kissing stenting technique.

METHODS

Study design

This is a multi-centric, retrospective analysis of prospectively collected data, performed in line with the requirements of the local ethics committee and adhering to the declaration of Helsinki. The study design allowed an assessment of safety and efficacy of both BMS and CS in the treatment of symptomatic aorto-iliac occlusive disease. Patients undertaking a kissing reconstruction of aortic bifurcation between January 2017 to August 2021 in the Department of Metropolitan Vascular Surgery Policlinico Sant'Orsola-Malpighi (University of Bologna) and the Department of Vascular Surgery Infermi Hospital of Rimini (Italy) were included into this study, in an equal number, collected prospectively into a dedicated database and retrospectively evaluated.

Written consent from each patient was obtained before procedures.

Bilateral iliac stenting without kissing configuration, acute limb ischemia, graft stenosis and iliac aneurysm were considered as exclusion criteria.

Demographics, clinical status, cardiovascular risk factors, comorbidities, medical history, radiographic and procedural aspects were collected and compared between the BMS and CS group. Clinical status was assessed according to the Rutherford Classification[20]. Diagnosis was determined from physical examination, duplex ultrasound and computed tomography angiography (CTA) findings. All patients' preoperatory CTA were reviewed and scored according to the Trans-Atlantic Inter-Society Consensus (TASC) II criteria[2].

Morphological features of iliac plaques were studied and classified in two subgroups as per the extension of calcium involvement at CTA: severe iliac calcification (SIC) -calcified plaques involving >70% of the circumferential diameter of the common iliac arteries- versus not SICs (NSICs) -calcified plaques involving <70% of the circumferential diameter of the common iliac arteries and with predominance of thrombotic aspects-. The evaluation was made calculating the circumferential length of the calcifications in the most calcified iliac section and compared with the

total circumference of the artery in that point. Interruptions in calcifications were subtracted from the calcifications' length count. We choose 70% as cut-off because the last quartile in the statistical evaluation of the median value was 70% in line with Konijn et al[21].

Need of perioperative distal revascularization was also assessed, such as common femoral endarterectomy, femoro-popliteal or femoro-distal bypass, major or minor amputation.

Procedure

In Rimini, the procedures were performed in a surgical suite equipped with a Ziehm Vision RFD (Ziehm Imaging GmbH, Nuremberg, Germany), while in Bologna procedures were taken into a Philips hybrid operating room (www.philips.it/healthcare).

The procedure was conducted with the same approach in both institutions. A bilateral percutaneous femoral access under local anaesthesia was obtained in patients Rutherford <4, and femoral cutdown under locoregional anaesthesia was performed in patients Rutherford 4 or in those at high risk for distal embolization during recanalization -that is heavily calcified plaque or wide thrombotic involvement of the iliac artery-. In those patients, the procedure was performed with the common femoral artery clamped distally to the introducer and carefully declamped after removal of the introducer sheath and adequate irrigation of the arterial lumen. If an upward recanalization was necessary, a left surgical brachial access was performed under general anaesthesia. The bilateral retrograde femoral approach was obtained through a 6 or 8F 45 cm introducer sheath (Cordis, Milpitas, CA, USA; Flexor, Cook Medical, Bloomington, IN, USA). In case of left proximal brachial access, a 6 or 8F, 90 cm flexor sheath (Cook Medical, Bloomington, IN, USA) was used, placing the tip as close as possible to the aortic bifurcation.

Systemic heparinization was obtained with 0.5 pro kg of Heparin once the introducers inserted and modulated to maintain an activated clotting time > 200.

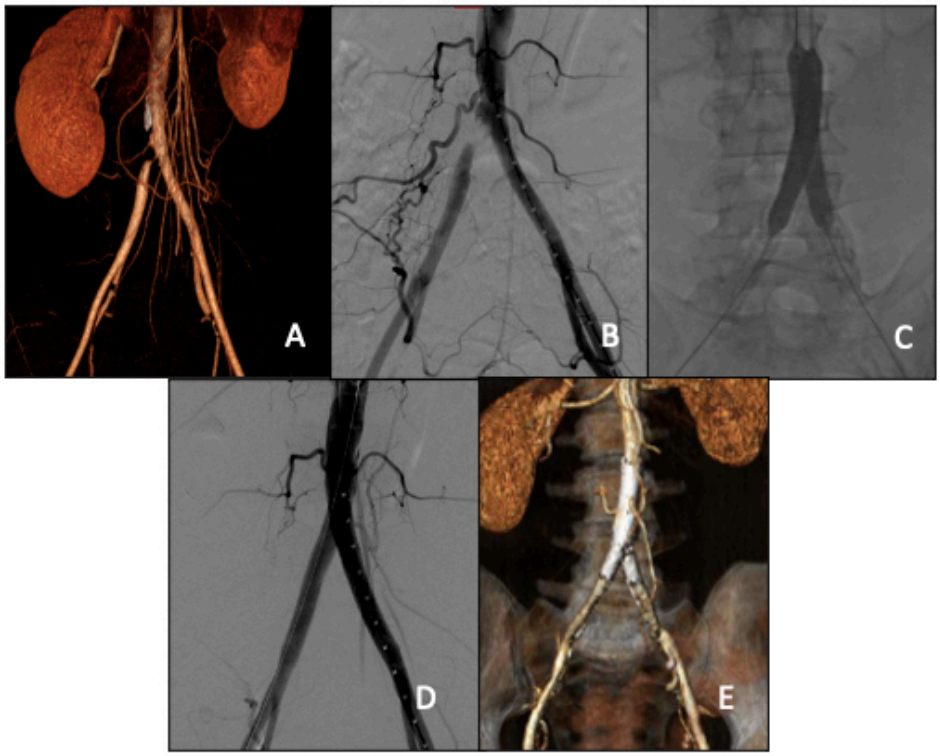
The common iliac artery lesions were crossed with a 0.014'' (Command ES, Abbott, Chicago, IL, USA), 0.018'' (V18, Boston Scientific, Marlborough, MA, USA), or a 0.035'' guidewire (Terumo

J-tip, Terumo Medical Corporation, Shibuya-Tokyo, Japan), supported by a Vertebral 135 catheter (Cordis, Milpitas, CA, USA) after angiographic setup. In case of sub-obstructive or obstructive common iliac artery lesions, an intraluminal recanalization and a balloon pre-dilatation was performed. After these maneuvers, two stents were deployed in a kissing configuration at the aortic bifurcation with a proximal landing zone of at least 2 centimetres upstream of the aortic bifurcation. The same type of stent was used in both sides. Both in case of BMS and CS, all the stents used for kissing stenting were balloon-expandable stents. The patients treated in Bologna were all given BMS, in particular with Visi-Pro stents (Medtronic, Minneapolis, MN, USA), while the patients treated in Rimini were given CS, in particular with Gore Viabahn VBX stentgrafts (W. L. Gore & Associates, Inc., Newark, DE, USA). Length and diameter stent sizes were chosen on the basis of preoperative CTA evaluation. If an external iliac artery stenosis >50% was present, that lesion was treated immediately with a self-expandable stent, landing proximally in the common iliac artery with an overlap of at least 2 cm. Technical Success was verified by a 3-projections (anteroposterior and right and left oblique) completion angiography.

In figure 1, the procedural steps of kissing stenting are reported.

Figure 1

A: preoperative CTA 3D-reconstruction of the case treated showing a steno-obstructive lesion of the ostium of right common iliac artery; B: pre-procedural angiography which shows a steno-obstructive lesion of the ostium of right common iliac artery; C: kissing stenting with two covered balloon-expandable stents; D: completion angiography; E: postoperative CTA 3D-reconstruction.



Endpoints and definitions

The primary outcomes measured were: Overall Technical Success, Procedural Success, Primary Patency, and Clinical Success.

The secondary outcomes measured were: Assisted primary Patency, Secondary Patency, Survival rate, Thrombosis rate, Limb Salvage according to Rutherford Classification, procedure-related complications and predictors of patency and mid- and long-term results.

Classifications were used according to the reporting standards[20,22].

Technical Success (TS) is defined as the presence of antegrade flow in both iliac axis with <30% residual stenosis through the treated segment at completion angiography.

Procedural Success[22] (PS) is defined as technical success and completion of the procedure without complications (e.g. arterial rupture, dissection, and access bleeding).

Primary Patency[20] (PP) is defined as stent patency with the presence of uninterrupted flow through the treated segment in absence of re-stenosis or occlusion, without need of further procedures after the initial intervention, measured by angio-CT scan at follow-up.

Clinical Success (ClS) is defined as clinical improvement of Rutherford categories ≥2 and/or pain resolution.

Assisted primary Patency[20] (AP) characterized the presence of patent iliac requiring endovascular intervention to treat recurrent stenosis. Restenosis is identified as a lesion with a peak systolic value (PSV) ratio >2.5 as a measured intrastent or inside the endograft or an angiographic diameter reduction of >50%.

Secondary Patency[20] (SP) clarifies any successful procedure that restores patency after the initial treatment episode (occlusion treatment).

Criteria for re-intervention included clinical deterioration based on occlusion or stenosis, or stent collapse.

Limb Salvage (LS) is defined as all patients without above ankle amputations previously presenting Rutherford classification category 4 to 6.

Post-Operative Medical Therapy

All patients included received in the post-operative standard statin treatment and dual anti-platelets (acetylsalicylic acid 100 mg/day associated with clopidogrel 75 mg/day) for at least one month followed by monotherapy, unless oral anticoagulation was indicated for other reasons.

Follow-up

Clinical examination, DUS evaluation of aortoiliac and infra-inguinal arteries, and CTA of abdominal arteries were performed routinely before the discharge. Follow-up included physical examination and DUS of the aorta and iliac arteries at 3 and 12 months after treatment and yearly thereafter. In case of a clinical/DUS suspicion of iliac restenosis, a CTA was performed.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) in case of normal distribution, or median plus interquartile range (IQR) and were compared by Mann-Whitney's test for other distributions. A value of P 0.05 (two-tailed) was considered significant.

Clinical Success, primary, assisted, and secondary patency, limb salvage, and survival rate were determined by Kaplan-Meier life-table analysis. Cox regression was used to define the impact of iliac disease and stent type on TS, the impact of clinical and morphological iliac factors and stent type on PP and CS and on the other outcomes, and the impact of clinical factors on S. Statistics were performed with an SPSS 26.0 software (SPSS Inc, Chicago, IL, USA).

RESULTS

Between January 2017 and August 2021, 34 patients affected by AIOD who underwent endovascular therapy with kissing stenting of aortic bifurcation in the two Vascular Surgery centers were recruited. Seventeen (50%) received a BMS treatment and the other half a CS treatment, representing two different populations.

The average age was 66 ± 1.37 years (range 44-87), with a majority of men (22/12, 64.7%). Demographics, patients' characteristics and type of stent used with specifics analysed by type of stent are reported in Table 1.

Table 1.
Demographics, patients' characteristics and type of stent used, with specifics analysed by type of stent (BMS: bare metal stent; CS: covered stent).

Variable	**Value**		
Patients (n)	34		
Type of stent, no. (%)	- BMS : 17 (50%) - CS : 17 (50%)	**BMS**	**CS**
Mean Age (years)	66 ± 1.37	65.9 ± 8.6	66.2 ± 11.5
Gender, M/F no. (%)	22/12 (64.7% vs 35.3%)	10/7 (58.8% vs 41.2%)	12/5 (70.% vs 29.4%)
Hypertension, no. (%)	30 (88.2%)	12 (70.6%)	15 (88.2%)
Smoking, no. (%)	27 (79.4%)	15 (88.2%)	12 (70.6%)
Dyslipidemia, no. (%)	23 (67.6%)	12 (70.6%)	11 (64.7%)
Diabetes, no. (%)	14 (41.2%)	10 (58.8%)	4 (23.5%)
Ischemic coronary dis., no. (%)	11 (32.4%)	8 (47.1%)	3 (17.6%)
Rutherford classification, no. (%)	- 3 : 21 (61.8%) - 4 : 8 (23.5%) - 5 : 3 (8.8%) - 6 : 2 (5.9%)	- 3 : 8 (47.1%) - 4 : 4 (23.5%) - 5 : 3 (17.6%) - 6 : 2 (11.8%)	- 3 : 13 (76.5%) - 4 : 4 (23.5%) - 5 : 0 (0%) - 6 : 0 (0%)

Population characteristics and clinical presentation are comparable in the two groups, without significant differences. There was a prevalence of some comorbidities in the BMS group, although not in a significant way: in particular, ischemic coronary disease was present in 47.1% of BMS patients vs 17.6% of CS patients (*p* .14), and diabetes was present in 58.8% of BMS patients vs 23.5% of CS patients (*p* .07). No differences between Rutherford category and type of treatment were found (for Rutherford cat. 3, 47.1% BMS and 76.5% CS, *p* .1; for Rutherford cat. 4, 23.5% BMS and 23.5% CS, *p* =1; for Rutherford cat. 5, 17.6% BMS and 0% CS, *p* .22; for Rutherford cat. 6, 11.8% BMS and 0% CS, *p* .48).

The morphological features of the iliac arteries' lesions are reported in Table 2.

Table 2.
Lesion type according to TASC-II classification, occlusive/stenotic lesions reported by TASC class and quality of plaque of the study population.

Variable	Value
Lesion type	
• TASC B, no (%)	7 (20.6%)
• TASC C, no (%)	8 (23.5%)
• TASC D, no (%)	19 (55.9%)
Occlusive lesions	18 (52.9%)
• TASC B, no (%)	3 (16.7%)
• TASC C, no (%)	2 (11.1%)
• TASC D, no (%)	13 (72.2%)
Stenotic lesions	16 (47.1%)
• TASC B, no (%)	4 (25%)
• TASC C, no (%)	6 (37.5%)
• TASC D, no (%)	6 (37.5%)
Quality of plaque	
• SIC, no (%)	17 (50%)
• NSIC, no (%)	17 (50%)
• Extensive thrombosis, no (%)	16 (47.1%)
• No/mild thrombosis, no (%)	18 (52.9%)

An interesting and important data is that 80% of patients enrolled in this study were part of TASC C-D categories, indicating that a large number of lesions were high complexity lesions.
Reporting data about TASC classification, no significant difference in terms of TASC category was found between the groups (in detail, for TASC-B, 11.8%, BMS and B 29.4% CS, p .38; for TASC-C, 35.3% BMS and 11.8% CS, p .22; for TASC-D, 52.9% BMS and 58.8% CS, p .49).
As for the TASC classification, no differences between grade of calcification and type of treatment were found (in detail, for SIC, 47.1% BMS and 52.9% CS, $p = 1$; for NSIC, 52.9% BMS and 47.1% CS, $p = 1$), such as for grade of thrombosis (in detail, for extensive thrombosis 41.2% BMS and 52.9% CS, p .7; for no/mild thrombosis 58.8% BMS and 47.1% CS, p .8).

The arterial access was obtained most often through a bilateral surgical cutdown (47.1%), then with a bilateral percutaneous access (17.6%), surgical in one groin and percutaneous contralateral (17.6%), and with an associated brachial access (17.6%).

None of the patients received a combined downstream revascularization, although in 14 (41.2%) cases a common femoral artery endarterectomy was performed (6 in BMS group and 8 in CS group), without significant differences between the groups (p .7).

Median hospitalization was 4 days (3-6.25 Q1-Q3; range 1-53).

Dual antiplatelet therapy (DAPT) was administered to 82.4% (28/34) of patients with a mean duration of 4.4 ± 1.6 months (range 1-6).

Mean follow-up was 32.1 ± 17.8 SD months (range 5-66). No patient was lost at follow-up.

Technical Success was reached in 100% of cases, and in both groups. No intra-operative complications occurred, and no intra-operative surgical conversions were needed, underlying that also Procedural Success was obtained in 100% of patients.

Focusing on ClS, immediate Clinical Success was reached in 29 cases (85.3%). Analysing in detail the differences between the groups, immediate ClS was statistically different between BMS and CS group (64.7% vs 100%, p .01), in favour of CS group. No patient died during the hospitalization.

Focusing on peri-operative (within 30 days) results, complications occurred in 6 (17.6%) cases, equally divided between the groups. In particular, 3 were complications which did not require any surgical intervention and included one gluteal embolization with trophic lesion (subsequent to the treatment of a highly thrombotic iliac lesion that led to a right hypogastric embolization with the appearance of a gluteal lesion on the third post-operative day), one inguinal hematoma, and one post-procedural angina with negative coronarography; the other 3 cases required a surgical intervention and included two inguinal dehiscences, and one femoral bleeding.

Regarding results about patency, overall PP, AP, and SP at 30 days were 97.1%, 97.1%, and 100%, without differences between BMS and CS group (94.1% vs 100%, 94.1% vs 100%, and 100% vs 100%; *p* .7), respectively.

Overall 30-day ClS was 82.4%, with statistically significant difference between the groups in favour of CS patients (64.7% BMS vs 100% CS, *p* .01).

Amputation rate at 30 days was 0%, and Survival rate was 100%.

In tables 3 and 4 are reported the endpoints at 30 days, 12 months and at the mean follow-up, divided into primary and secondary outcomes.

Table 3.
Primary endpoints described for BMS group, CS group and overall at 30 days, 12 months, and at follow-up.

Primary Endpoints	**30 days**	**12 months**	**follow-up**
Technical Success		-	-
• BMS	100%		
• CS	100%		
• overall	100%		
Procedural Success		-	-
• BMS	100%		
• CS	100%		
• overall	100%		
Primary Patency			
• BMS	94.1%	94.1%	88.2%
• CS	100%	100%	100%
• overall	97.1%	97.1%	94.1%
Clinical Success			
• BMS	64.7%	82.4%	88.2%
• CS	100%	100%	100%
• overall	82.4%	91.2%	94.1%

Table 4.
Secondary endpoints described for BMS group, CS group and overall at 30 days, 12 months, and at follow-up.

Secondary Endpoints	30 days	12 months	follow-up
Assisted Patency			
• BMS	94.1%	94.1%	88.2%
• CS	100%	100%	100%
• overall	97.1%	97.1%	94.1%
Secondary Patency			
• BMS	100%	94.1%	94.1%
• CS	100%	100%	100%
• overall	100%	97.1%	97.1%
Survival			
• BMS	100%	94.1%	70.6%
• CS	100%	100%	100%
• overall	100%	97.1%	85.3%
Thrombosis rate			
• BMS	5.9%	11.8%	11.8%
• CS	0%	0%	0%
• overall	2.9%	5.9%	5.9%
Limb Salvage			
• BMS	100%	94.1%	94.1%
• CS	100%	100%	100%
• overall	100%	100%	97.1%

Two cases (5.9%) of thrombosis were registered, and both occurred within 3 months after the procedure and both in the BMS group, without statistical differences with the CS group (11.8% vs 0%, *p* .48). One patient underwent a hybrid intervention, with thrombectomy and endovascular relining, while the other patient was given an axillo-bifemoral bypass. Both cases of thrombosis occurred in patients who were not treated with dual antiplatelet therapy (in detail, single antiplatelet therapy (SAPT) group 33.3% vs dual antiplatelet therapy (DAPT) group 0%, *p* .027).

Overall Clinical Success at 1-year follow-up was 91.2%, and resulted significantly higher in CS than in BMS group at, such as it was at 30 days (in detail, BMS group 82.4% vs CS group 100%, *p* .04).

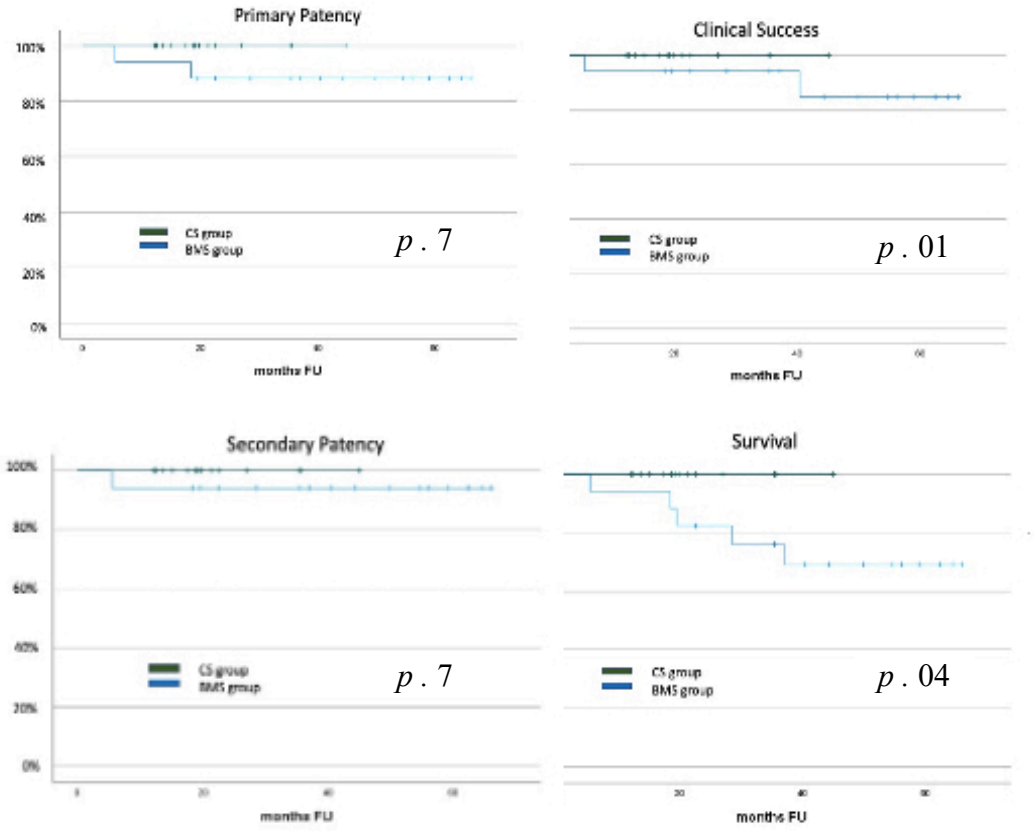
Overall Survival at 30 days, 12 months, and at the mean follow-up was 100%, 97.1%, and 85.3% respectively. Regarding the differences between the groups, Survival statistically differed only at follow-up in favour of CS group (in detail, BMS group 70.6% and CS group 100%, *p* .04).

Reintervention rate at follow-up was 5.9% and no significant differences between the groups were found (in detail, BMS group 11.7% vs CS group 0% CS, *p* .25).

Amputation rate was 8.9% at follow-up (one patient underwent thigh amputation for worsening of distal vessels arteriopathy 31 months after the kissing stenting with BMS).

No differences in terms of survival, patency, clinical success, reintervention, and complication rate were found in terms of TASC classification class and/or presence of SIC or extensive thrombosis.

In table 5 are reported the Kaplan-Meier curves of PP, ClS, SP, and Survival.



DISCUSSION

Over the last few decades, with the development and the spread of new devices and the refinement of recanalization techniques, endovascular approach progressively replaced surgical treatment for AIOD[2]. Surgical revascularization by aorto-bifemoral bypass remains an effective and durable option, mainly in young patients, with excellent patency rates and medium- and long-term survival rates[5]. Initially reserved for high-risk patients, the kissing stenting technique is now the first choice of treatment even in case of complex atherosclerotic lesions[1,23,24]. The multicentric study conducted by Dorigo et al. showed that short- and long-term results are comparable between kissing stent and surgical therapy, also in TASC II C and D lesions' treatment[13].

In our study, 79.4% of patients had lesions classified as TASC C-D, confirming that complex lesions are being increasingly treated effectively by endovascular approach, in line with the literature[16,17]. Despite the prevalence of TASC-D lesions (55.9%), the BMS and CS groups in our population were homogeneous for what concerns TASC classification. After the analysis between BMS and CS, no statistical differences were found in terms of type of treatment and of the outcomes compared to TASC category. In detail, despite the large number of TASC-D lesions, the technical success rate in our population was 100%. In case of unsuccessful retrograde recanalization, a second combined femoral and brachial approach has allowed effective treatment of even the most difficult obstructions.

The main aim of our study was to compare the results of treatment with kissing stenting using BMS and CS and to analyse the outcomes.

No differences were found in terms of TASC lesion, grade of calcification and thrombosis compared to the type of stent used, underlying that the type of plaque did not affect technical success results and/or procedural success.

Regarding the two different platforms used, as reported in the Methods section, we exclusively used balloon-expandable stents. These two options have different characteristics: BMS have

generally lower-profile devices and are more adaptable to tortuous anatomies[6]; on the other hand, CS could avoid immediate protrusion of plaque through the cells and reduces the risk of intimal hyperplasia, also preventing rupture, and being made of PTFE and metal, they require a higher profile delivery system, exposing the patient to possibly increased access complications.

The COBEST trial was the first prospective, multicentric, randomized study to compare the results of BMS and CS in the treatment of aorto-iliac occlusions, showing that freedom from restenosis and thrombosis in the two groups was comparable in TASC B lesions. In contrast, CS provided higher patency rates and better clinical outcomes in patients with TASC-C and D lesions. The study, however, compared the outcomes of balloon and self-expandable BMS with only one type of balloon-expandable CS[18,19]. In our population, results were different: in fact, there were no statistical differences between BMS and CS in terms of patency, although CS group did better in terms of clinical success. In particular, the primary, assisted, and secondary patency rates in our population were 97.1%, 97.1% and 97.1% at 12 months, 94.1%, 94.1% and 97.1% at the mean follow-up, respectively, higher than those reported in the literature. In the meta-analysis by Groot Jebbink et al. made of 604 kissing stent patients, the reported rates were 86.1% (range 82.9-88.8%) at 12 months and 81.2% (range 77.4- 84.4%) at 24 months for primary patency, 94.8% (range 92.4-96.5%) at 12 months and 93% (range 90.2-95%) at 24 months for secondary patency[23]. Our results failed to confirm the COBEST study's hypothesis because covered stents did not lead to a better patency than bare metal stents. By summarizing the available literature[14,26], predictors of patency in kissing stent procedures have not been defined yet and further studies are needed to define how to prevent stent occlusion. SP is also satisfactory, being greater than 97% at medium follow-up of almost 3 years. These data show how an endovascular reintervention after stent occlusion is feasible and effective in most cases and continues to be a valid option during the follow-up also in case of TASC-D lesions.

In our series, results about ClS showed that overall 30-day ClS was 82.4%, with statistically significant difference between the groups in favour of CS patients (64.7% BMS vs 100% CS, p .01); this difference maintained at 1 year follow-up (overall ClS 91.2%, with 82.4% for BMS group and

100% for CS group, p .04), although resolved at the mean follow-up. Similarly to our data, Piazza et al.[16] demonstrated equal results between CS and BMS but considering only the treatment of TASC-C and D lesions. We think that this result in our small population could have been affected by the presence of a higher number of patients with trophic lesions (Rutherford 5-6) in the BMS group, even if not in a statistically significant number (for Rutherford cat. 3, 47.1% BMS and 76.5% CS, *p* .1; for Rutherford cat. 4, 23.5% BMS and 23.5% CS, *p* =1; for Rutherford cat. 5, 17.6% BMS and 0% CS, *p* .22; for Rutherford cat. 6, 11.8% BMS and 0% CS, *p* .48), and this data could have been responsible of the difficult increase in Rutherford category of this group of patients. Similarly, the anamnestic and comorbidity status of the population could have also affected the Survival rate: although it revealed to be very satisfying generally speaking (overall Survival at 30 days, 12 months, and at follow-up was 100%, 97.1%, and 85.3% respectively), Survival statistically differed at follow-up in favour of CS group (in detail, BMS group 70.6% and CS group 100%, p .04). This is symptomatic of the fact that BMS patients had more comorbidities than CS patients although the data was not statistically significant (ischemic coronary disease was present in 47% of BMS patients vs 17.6% of CS patients, *p* .14; diabetes was present in 58.8% of BMS patients vs 23.5% of CS patients, *p* .07), and this translated into a poorer survival during the follow-up.

In our population, complication rate was 17.6%, but only half of cases required a surgical intervention. The overall risk of 30-day complications is approximately 10% in the literature[11]. The worst not surgical complication we registered regarded a patient treated for a TASC-D, NSIC-lesion with extensive thrombosis with a BMS kissing stenting. He developed a right gluteal trophic lesion probably due to hypogastric embolization. Hypogastric embolization is a dreadful complication which cannot be prevented by operative maneuvers. The use of covered stents for the treatment of thrombotic lesions is a possible solution but remains one of the main open issues in this setting. Another possible technical trick is to clamp the common femoral artery and remove the embolic material at the end of the procedure to avoid embolization, although it cannot obviously prevent hypogastric complications.

Interestingly, all stent thrombosis in our series occurred within the first 3 months after the procedure. The mechanism of early occlusion may be related to the endothelial injury caused by the stent, with subsequent parietal thrombosis and smooth muscle cells proliferation and migration, leading to a neointima formation[15]. The platelets' activity subsequent to the endothelial lesion could also favour early in-stent thrombosis[15]. If this theory holds true, a dual antiplatelet therapy administered for 1 month should be sufficient; nevertheless, Schwartz et al.[14] observed a considerable neointimal hyperplasia with fresh mural thrombus formation in a coronary artery of a woman who died 10 months after angioplasty. The authors concluded that the new endothelium is indefinitely compromised, thus a dual antiplatelet therapy may be needed for a long time. Consistent with this theory, all cases of PP loss occurred in patients with no DAPT in our series. The most recent European Society of Cardiology guidelines[3] recommend DAPT administration for at least 4 weeks after the procedure, but a consensus on this topic has not been reached yet. As a matter of fact, a Cochrane review[27] failed to demonstrate an advantage of DAPT over monotherapy in preventing loss of patency at 6 months after an endovascular procedure. Interestingly, there is high variability among surgeons in prescribing patterns of antiplatelet agents after lower extremity endovascular procedures[28]. After iliac bare-metal stenting, 52% of them would prescribe DAPT, with different patterns: 20% for 1 month, 22% for 3 months, 6% for 6 months, and 4% for 12 months. Strobl et al.[29] showed how DAPT delivered for 6 months increased patency rate with no further advantage after its cessation; in this sense, cases at high risk for restenosis/occlusion may benefit from a prolonged DAPT. In our study, dual antiplatelet therapy was administered to 82.4% (28/34) of patients with a mean duration of 4.4 ± 1.6 months. Two cases (5.9%) of thrombosis were registered, both in the BMS group, without statistical differences with the CS group (11.8% vs 0%, p .48). Both cases of thrombosis occurred in patients who were not treated with dual antiplatelet therapy (in detail, single antiplatelet therapy (SAPT) group 33.3% vs dual antiplatelet therapy (DAPT) group 0%, p .027), so DAPT showed a significantly better patency than SAPT.

Regarding the differences between highly calcified and not calcified lesions, in our series we did not find any statistically significant difference in terms of technical success, patency and in general in terms of outcomes, also comparing the BMS and CS groups. In a paper published by our group in 2020[25], NSIC plaques were associated with lower primary patency at 1 year than SIC plaques (73% vs. 96%). All patients in this study were treated with BMS. Still, we can only speculate about the reason for this finding: it is possible that NSIC plaque may have a more thrombogenic effect, and bare stent is not able to prevent this phenomenon. This finding has not been discussed yet in the available literature, so further analysis should be needed in this regard. In general, the literature lacks specific analysis on the role of plaque characteristics. On one hand, calcified plaques are more stable than soft ones[30]; on the other hand, they may determine worse technical success in aortoiliac endovascular treatment, as suggested by Kim et al[31]. Therefore, in very limited and specific cases, calcified lesions may be worthy of surgical treatment in extreme cases, such as of ‘‘coral reef’’ disease. If an endovascular approach is possible, covered stents may be a solution to avoid major bleeding in case of arterial rupture during the procedure.

Overall Survival at 30 days, 12 months, and at the mean follow-up was 100%, 97.1%, and 85.3% respectively. Regarding the differences between the groups, Survival statistically differed only at follow-up in favour of CS group (in detail, BMS group 70.6% and CS group 100%, p .04).

Reintervention rate at follow-up was 5.9% and no significant differences between the groups were found (in detail, BMS group 11.7% vs CS group 0% CS, *p* .25). Amputation rate was 8.9% at follow-up (one patient underwent thigh amputation for worsening of distal vessels arteriopathy 31 months after the kissing stenting with BMS). No differences in terms of survival, patency, clinical success, reintervention, and complication rate were found in terms of TASC classification class and/or presence of SIC or extensive thrombosis.

Some limitations of this study should be considered. First, the small population of only 34 patients is probably the cause of the large amount of not significant results. The patients treated with CS were more often patients with lower number of comorbidities and it could affect the results of

clinical success and survival. Being a non-randomized study, the choice between CS and BMS was left to the operator; as a multicentric study, an additional bias may be related to the different materials available in the participating centers. Finally, a further aspect that deserves to be analysed is the correlation between the characteristics of the lesion in terms of location, extension, nature of the plaque (percentage of calcific component, presence of thrombus) and the type of stent chosen[25]. Indeed, it would be interesting to establish which stent is best suited to certain classes of lesions, in order to guide the operator in the choice of the material that guarantees the best patency rate and limb salvage.

CONCLUSIONS

The endovascular approach in the treatment of aorto-iliac occlusive disease is currently safe and effective. In particular, the kissing stent technique offers excellent results in terms of technical success, procedural success and patency rates in the short- and medium-term.

The use of CS seems to provide clinical better results than BMS; however, in our study no statistically significant differences emerged between the two types of stents in terms of patency, reintervention and complications.

Thrombosis occurred only in patients who were not treated with dual antiplatelet therapy. This data underlines the importance of the post-operative medical therapy, in fact DAPT seems to warrant the best results in terms of patency, although there is still no consensus about the ideal duration of administration.

Further studies are needed to better clarify the correlation between the nature of the lesions to be treated and the type of device able to guarantee the best results over time.

REFERENCES

1. TASC Steering Committee, Jaff MR, White CJ, Hiatt WR, Fowkes GR, Dormandy J, Razavi M, Reekers J, Norgren L. An Update on Methods for Revascularization and Expansion of the TASC Lesion Classification to Include Below-the-Knee Arteries: A Supplement to the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Vasc Med. 2015 Oct;20:465-78.

2. De Donato G, Bosiers M, Setacci F, Deloose K, Galzerano G, Verbist J, et al. 24-Month data from the BRAVISSIMO: a Large Scale Prospective Registry on iliac stenting for TASC A & B and TASC C & D lesions. Ann Vasc Surg 2015;29:738-50.

3. Aboyans V, Ricco JB, Bartelink MLEL, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J. 2018 Mar 1;39:763–816.

4. Indes JE, Pfaff MJ, Farrokhyar F, Brown H, Hashim P, Cheung K, et al. Clinical outcomes of 5358 patients undergoing direct open bypass or endovascular treatment for aortoiliac occlusive disease: a systematic review and meta-analysis. J Endovasc Ther Off J Int Soc Endovasc Spec. 2013 Aug;20:443–55.

5. Premaratne S, Newman J, Hobbs S, Garnham A, Wall M. Meta-analysis of direct surgical versus endovascular revascularization for aortoiliac occlusive disease. J Vasc Surg. 2020 Aug;72:726–37.

6. Feldman DN, Armstrong EJ, Aronow HD, Banerjee S, Díaz-Sandoval LJ, Jaff MR, et al. SCAI guidelines on device selection in Aorto-Iliac arterial interventions. Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv. 2020 Oct 1;96:915–29.

7. Kasemi H, Marino M, Dionisi CP, Di Angelo CL, Fadda GF. Seven-year approach evolution of the aortoiliac occlusive disease endovascular treatment. Ann Vasc Surg 2016;30:277-85.

8. Aihara H, Soga Y, Iida O, Suzuki K, Tazaki J, Shintani Y, et al. Long-term outcomes of endovascular therapy for aortoiliac bifurcation lesions in the Real-AI Registry. J Endovasc Ther 2014;21:25-33.

9. Taeymans K, Groot Jebbink E, Holewijn S, Martens JM, Versluis M, Goverde PCJM, et al. Three-year outcome of the covered endovascular reconstruction of the aortic bifurcation technique for aortoiliac occlusive disease. J Vasc Surg 2018;67:1438-47.

10. Psacharopulo D, Ferrero E, Ferri M, Viazzo A, Singh Bahia S, Trucco A, et al. Increasing efficacy of endovascular recanalization with covered stent graft for TransAtlantic Inter-Society Consensus II D aortoiliac complex occlusion. J Vasc Surg 2015;62:1219-26.

11. Psacharopulo D, Ferrero E, Ferri M, Viazzo A, Singh Bahia S, Trucco A, et al. A systematic review of endovascular treatment of extensive aortoiliac occlusive disease. J Vasc Surg 2010;52:1376-83.

12. Groot Jebbink E, Holewijn S, Slump CH, Lardenoije JW, Reijnen MMPJ. Systematic review of results of kissing stents in the treatment of aortoiliac occlusive disease. Ann Vasc Surg 2017;42:328-36.

13. Dorigo W, Piffaretti G, Benedetto F, Tarallo A, Castelli P, Spinelli F, et al. A comparison between aortobifemoral bypass and aortoiliac kissing stents in patients with complex aortoiliac obstructive disease. J Vasc Surg. 2017 Jan;65:99–107.

14. Sharafuddin MJ, Hoballah JJ, Kresowik TF, Sharp WJ, Golzarian J, Sun S, et al. Long-term outcome following stent reconstruction of the aortic bifurcation and the role of geometric determinants. Ann Vasc Surg 2008;22:346-57.

15. Matas M, Dominguez Gonzalez JM, Montull E. Antiplatelet therapy in endovascular surgery: the RENDOVASC study. Ann Vasc Surg 2013;27:168-77.

16. Piazza M, Squizzato F, Spolverato G, Milan L, Bonvini S, Menegolo M, et al. Outcomes of polytetrafluoroethylene-covered stent versus bare-metal stent in the primary treatment of severe iliac artery obstructive lesions. J Vasc Surg. 2015 Nov;62:1210-1218-1.

17. Piazza M, Squizzato F, Dall'Antonia A, Lepidi S, Menegolo M, Grego F, et al. Editor's Choice - Outcomes of Self Expanding PTFE Covered Stent Versus Bare Metal Stent for Chronic Iliac Artery Occlusion in Matched Cohorts Using Propensity Score Modelling. Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg. 2017 Aug;54:177–85.

18. Mwipatayi BP, Thomas S, Wong J, Temple SEL, Vijayan V, Jackson M, et al. A comparison of covered vs bare expandable stents for the treatment of aortoiliac occlusive disease. J Vasc Surg. 2011 Dec;54:1561–70.

19. Mwipatayi BP, Sharma S, Daneshmand A, Thomas SD, Vijayan V, Altaf N, et al. Durability of the balloon-expandable covered versus bare-metal stents in the Covered versus Balloon Expandable Stent Trial (COBEST) for the treatment of aortoiliac occlusive disease. J Vasc Surg. 2016 Jul;64:83-94-1.

20. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg 1997;26:517-38.

21. Konijn LCD, van Overhagen H, Takx RAP, de Jong PA, Veger HTC, Mali WPTM. CT calcification patterns of peripheral arteries in patients without known peripheral arterial disease. Eur J Radiol 2020;128:108973.

22. Stoner MC, Calligaro KD, Chaer RA, Dietzek AM, Farber A, Guzman RJ, et al. Reporting standards of the Society for Vascular Surgery for endovascular treatment of chronic lower extremity peripheral artery disease: executive summary. J Vasc Surg 2016;64:227-8.

23. Groot Jebbink E, Holewijn S, Versluis M, Grimme F, Hinnen JW, Sixt S, et al. Metaanalysis of Individual Patient Data After Kissing Stent Treatment for Aortoiliac Occlusive Disease. J Endovasc Ther Off J Int Soc Endovasc Spec. 2019 Feb;26:31–40.

24. Bosiers M, Deloose K, Callaert J, Maene L, Beelen R, Keirse K, et al. BRAVISSIMO: 12-month results from a large scale prospective trial. J Cardiovasc Surg (Torino). 2013 Apr;54:235–53.

25. Sonetto A, Faggioli G, Pini R, Abualhin M, Goretti M, Fronterrè S, et al. Kissing Stent Technique for TASC C-D Lesions of Common Iliac Arteries: Clinical and Anatomical Predictors of Outcome. Ann Vasc Surg. 2021 Feb;71:288-297.

26. Vértes M, Juhász IZ, Nguyen TD, Veres DS, Hüttl A, Nemes B, et al. Stent protrusion >20 mm into the aorta: a new predictor for restenosis after kissing stent reconstruction of the aortoiliac bifurcation. J Endovasc Ther 2018;25:632-9.

27. Robertson L, Ghouri MA, Kovacs F. Antiplatelet and anticoagulant drugs for prevention of restenosis/reocclusion following peripheral endovascular treatment. Cochrane Database Syst Rev 2012;CD002071.

28. Allemang MT, Rajani RR, Nelson PR, Hingorani A, Kashyap VS. Prescribing patterns of antiplatelet agents are highly variable after lower extremity endovascular procedures. Ann Vasc Surg 2013;27:62-7.

29. Strobl FF, Brechtel K, Schmehl J, Zeller T, Reiser MF, Claussen CD, et al. Twelve-month results of a randomized trial comparing mono with dual antiplatelet therapy in endovascularly treated patients with peripheral artery disease. J Endovasc Ther 2013;20:699-706.

30. Vasuri F, Fittipaldi S, Pini R, Degiovanni A, Mauro R, D'Errico-Grigioni A, et al. Diffuse calcifications protect carotid plaques regardless of the amount of neoangiogenesis and related histological complications. Biomed Res Int 2015;2015:795672.

31. Kim TH, Ko YG, Kim U, Kim JS, Choi D, Hong MK, et al. Outcomes of endovascular treatment of chronic total occlusion of the infrarenal aorta. J Vasc Surg 2011;53:1542-9.