

Endovascular therapy for steno-occlusive subclavian artery disease early and long-term outcomes in a multicentric Tunisian study



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Imtinene Ben Mrad*, Rim Miri**, Daniela Mazzaccaro***, Melek Ben Mrad**, Sobhi Mleyhi**, Ihsen Zairi*, Rania Hammami****, Giovanni Nano***/*, Sondos Kraiem*, Raouf Denguir**

*Cardiology Department, Habib Thameur Hospital Tunis, Tunisia

**Cardiovascular Surgery Department, La Rabta Hospital, Tunis, Tunisia

***Operative Unit of Vascular Surgery, IRCCS, Policlinico San Donato, San Donato Milanese, Milan, Italy

****Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

*****Cardiology Department, Hedi Chaker Hospital, Sfax, Tunisia

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AIM: To evaluate the outcomes of endovascular therapy in patients with subclavian steno-occlusive disease over the short and long term in a Tunisian population.

MATERIALS AND METHODS: Patients who underwent endovascular treatment of subclavian artery (SCA) steno-occlusive disease between 2013 and 2019 in three Tunisian centers were evaluated retrospectively. After treatment, patients were follow-up was scheduled at 1, 3, 6, 12 months postoperatively and annually afterwards by Doppler ultrasound and clinical findings. Primary outcomes included technical, clinical procedural success rates and limb salvage rate. Secondary outcomes included the occurrence of periprocedural complications and primary patency rates.

RESULTS: 56 patients (33 males, 58.9%) were evaluated. Patients' mean age was 61.5 + years. Technical success rate was 94.6 %, being 100% in case of stenosis and 78.5% in case of occlusion. The technical success rate was 94.6%. The clinical success rate was 100% and the upper limb salvage rate was 100%. Minor amputations were performed on 5 patients. Perioperative mortality and morbidity rates were 0% and 8.9% respectively. Mean follow-up was 26.7±16.4 months (range 12-86 months). Two in-stent restenosis occurred (at 12 and 15 months) and one case of thrombosis at the 16th month. The primary patency rates were 88.7%+4.3% at the end of the first year and 78.7%+6.1% at 3 years.

CONCLUSION: Endovascular treatment can be considered as a safe and effective treatment of SCA steno-occlusive disease, with low perioperative complication rates and a good patency rates over long term.

KEY WORDS: Subclavian artery stenosis, Subclavian artery occlusion, endovascular, subclavian revascularization.

Introduction

Steno-occlusive lesions of the subclavian artery (SCA) are rare. The prevalence varies greatly across different groups

of patients. It was estimated at 0.8% to 1.9% in the general population and up to 8.5% in patients with coronary artery disease¹⁻³. Atherosclerosis is the most common etiology³, but there are other causes such as inflammation (Takayasu and other forms of arteritis), congenital malformations, fibro muscular dysplasia, neurofibromatosis, radiation exposure and mechanical causes (trauma or compression syndrome)⁴.

SCA stenosis or occlusion are often asymptomatic¹, but when symptoms occur, patients may require endovascular or surgical revascularization. Open surgical repair has

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Correspondence to: Imtinene Ben Mrad, Cardiology Department, Habib Thameur Hospital, Tunis, Tunisia (e-mail: imtinenebenmrad12@gmail.com)

been the gold standard for long time, but thanks to the availability of new materials and technical improvement endovascular treatment has become the first-line option, if lesions are suitable⁴. Reports of early and long-term outcomes of the endovascular treatment of SCA steno-occlusive disease are mainly limited to patients treated before 2013⁵.

We aimed to evaluate the results of treatment for SCA steno-occlusive lesions over the short and long term in a cohort of patients submitted to endovascular procedures after 2013.

Materials and Methods

We conduct a retrospective study including consecutive patients who underwent angioplasty for steno-occlusive lesions of the SCA in three Tunisian centers: the cardiovascular surgery department of Rabta Hospital of Tunis, the cardiology department of Sfax Hospital and the cardiology department of Habib Thameur Hospital of Tunis, and this for the period between 2013 and 2019.

We included patients who had at least 12 months of follow-up. Patients who were lost to follow-up before 12 months were excluded.

For each patient we collected from medical records: pre-operative comorbidities, the etiology of the subclavian lesion, the indication for revascularization and data about the angioplasty procedure (vessel access, type of anesthesia, applied procedure, type and size of the stent). The localization of the lesion at the SCA, the degree of the obstruction, the degree of calcification and the length of the lesion were recorded from per operative procedure, as well from preoperative imaging.

A stenosis of more than 70% was classified as severe. The proximal and distal SCA segments were defined with respect to the origin of the vertebral artery.

Primary outcomes included technical, clinical procedural success rates and limb salvage rate. Technical success in particular was defined as the restoration of a patent subclavian artery without residual stenosis greater than 30%. The clinical success was defined by the combination of the both technical success and symptoms resolution. Limb salvage was defined by absence of major amputation of the upper limb during follow-up.

Secondary outcomes included the occurrence of perioperative complications and primary patency rates. Perioperative complications were defined as the occurrence of any general or local complication during the first 30 days following the procedure. Primary patency was defined as the interval of time during which the patency of the SCA segment was maintained without restenosis or need for a repeat intervention. Restenosis was defined as recurrence of at least 50% reduction of the arterial lumen diameter within the stent.

All collected data were inserted in a database and ana-

lyzed as appropriate using the software STATA-IC®. Continuous variables were reported as mean±2 standard deviation for normally distributed variables, or median and inter-quartile range (IQR) for non-Gaussian values; categorical variables are presented as number (percentage). A P value <0.05 was considered statistically significant. Kaplan-Meier analysis was used to estimate the rates of limb salvage and primary patency.

Results

BASELINE CLINICAL CHARACTERISTICS

Fifty-six patients were included. Patients' mean age was 61.5±12.5 years, and 58.9% of them were males. As described in Table I, patients were mainly affected by hypertension (64.3%) and were current smokers (60.7%). About a half (46.4%) were diabetics and 25% had dyslipidemia. Previous percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) were reported in 10.7 % and 14.3% of cases, respectively.

As described in (Table I), the main indications for the treatment were critical upper limb ischemia in 23 cases (41.1%), upper limb claudication in 13 cases (23.2%), vertebral subclavian steal syndrome in 12 cases (21.4%) and coronary steal syndrome in 7 cases (12.5%). In the remaining patient (1.8%), the SCA revascularization was performed prior to an aorto-coronary bypass without any symptoms. The etiology was atherosclerotic in all cases.

TABLE I - Clinical characteristics of the study population and indications for revascularization

Age (years), mean±SD (range)	61.55 ±12.54 (29-89)
Male, n (%)	33 (58.9%)
<i>Risk Factors</i>	
Diabetes mellitus, n (%)	26 (46.4%)
Hypertension, n (%)	36 (64.3%)
Dyslipidemia, n (%)	14 (25%)
Current Smoking, n (%)	34 (60.7%)
<i>Previous coronary revascularization</i>	
PCI, n (%)	6 (10.7%)
CABG, n (%)	8 (14.3%)
Peripheral artery disease, n (%)	7 (12.5%)
Chronic kidney disease, n (%)	2 (3.6%)
<i>Indications for procedure</i>	
Upper limb critical ischemia, n (%)	23 (41.1%)
Upper limb claudication, n (%)	13 (23.2%)
Vertebral subclavian steal syndrome, n (%)	12 (21.4%)
Coronary steal syndrome, n (%)	7 (12.5%)
Planned CABG, n (%)*	1 (1.8%)

* Left internal mammary artery to left anterior descending coronary branch.

Preoperative evaluation included physical assessment with pulse examination and blood pressure measurements in both arms. At clinical evaluation, the mean difference of systolic blood pressure between both arms was 28 ± 18 mm Hg.

Radiologic Lesions characteristics

The diagnosis was confirmed by ultrasound duplex in all patients, followed by an Angio-CT scan in 54 cases and Angio-MRI in the remaining two cases. Left SCA was involved in 49 cases (87.5%) and right SCA in the remaining cases. Three quarter of the lesions were classified as severe stenosis, while the SCA was occluded in the remaining 25% of cases (Table II).

PROCEDURES DESCRIPTION AND FINDINGS

Endovascular treatment was chosen over surgical revascularization for stenosis shorter than 10 cm or short occlusions (<4 cm), otherwise open surgical approach was preferred.

TABLE II - Lesions and procedural characteristics

<i>Side</i>	
Left	49 (87.5%)
Right	7 (12.5%)
<i>Localization of the lesion</i>	
Prevertebral	53 (94.6 %)
Postvertebral	3 (5.4%)
<i>Type of lesion</i>	
Stenosis	42 (75%)
Occlusion	14 (25%)
<i>Degree of lesions' calcification</i>	
- Low	8 (14.28%)
Pts treated for Stenosis	6/42
Pts treated for Occlusion	2/14
- Moderate	4 (7.14%)
Pts treated for Stenosis	3/42
Pts treated for Occlusion	1/14
- High	6 (10.71%)
Pts treated for Stenosis	4/42
Pts treated for Occlusion	2/14
<i>Lesion's length (median, IQR)</i>	
In stenosis	18 (5-38)
In total occlusions	17 (8-38)
In total occlusions	21 (5-30)
<i>Stent</i>	
Primary stenting	53 (94.6%)
Predilatation*	46 (82.2%)
Balloon-expandable stent	10 (17.8%)
Balloon-expandable stent	53 (100%)
Stent length (mm; median, IQR)	30 (20-37)
Stent Diameter (mm; median, IQR)	(7-8)

*with a 6 mm balloon

All procedures were performed under local anaesthesia via a retrograde approach, mainly through a brachial surgical access (6-7 Fr) in 27 patients (48.2%) or a percutaneous radial access (6 Fr) (24 patients, 42.8%). A percutaneous brachial access (6-7 Fr) was used in the remaining 5 patients. Systemic heparin was administered intraoperatively to achieve an activated clotting time of 250 sec.

On angiographic findings, SCA lesions were located in the proximal segment in 53 cases (94.6 %) while in the remaining 3 cases it was distal to the origin of the vertebral artery. In particular, the lesions were located at the ostium of the SCA in 8 cases of stenosis and 6 cases of occlusion. The mean length of the lesion was 18.14 ± 7.82 mm, ranging from 5 to 38 mm.

Calcifications were found upon angiogram in 18 lesions (32.14%).

A balloon-expandable stent was deployed in 53 (94.6%) cases. In 10 cases, predilatation with simple balloon was used. In 46 cases primary stenting was performed. In 7 cases, a secondary stenting was indicated for recoil of arterial dissection. We used stents of 7 or 8 mm in diameter, while mean stent length was 32.2 ± 13.57 mm (ranging from 17 to 75 mm). In particular, the following stent types were used: Express (Boston Scientific) in 21 patients (39.6%), Visi-Pro (Medtronic) in 13 patients (24.5%), Scuba (Invatec) in 9 patients (17%), Assurant (Medtronic) in 6 patients (11.3%), Palmaz (Cordis) in 3 patients (5.7%), and Omnilink (Abbott Vascular) in the remaining patient (1.9%). No embolic protection device was used.

PER PROCEDURAL OUTCOMES

Endovascular procedure was successful in 53/56 cases, resulting in an overall technical success rate of 94.6%. According to the lesion type, the success rate was 100% (42/ 42 patients) for stenotic lesions and 78.57 % (11/14) patients) for occlusive lesions (Table III). The

TABLE III - Periprocedural Outcomes

<i>Technical success rate</i>	
Overall, n	53/56 (94.6%)
Stenosis, n	42/42
Occlusion, n	11/14
Symptoms resolution (%)	100%
Upper Limb salvage (%)	100%
<i>Periprocedural complications</i>	
Mortality, n	0/56 (0%)
Neurologic Events, n	0/56 (0%)
Hematoma at access sites, n	2/56 (3.6%)
Acute upper limb ischemia, n	3/56 (5.3%)
Brachial artery thrombosis, n	1/56 (1.8%)
Distal embolism, n	2/56 (3.6%)

recanalization failure occurred in three cases (5.4%) because of an inability to cross the lesion with the wire despite multiple attempts. These cases were managed surgically by a carotid-axillary bypass. The clinical success rate was 100% and the upper limb salvage rate was 100%. Minor amputations were performed on 5 patients who had initially presented trophic disorders on one or more fingers.

There were 5 periprocedural complications, including 3 cases of limb ischemia (one of which was caused by brachial access site thrombosis and two by distal embolization managed by embolectomy with a Fogarty catheter) and two hematomas at the brachial access, that required surgical evacuation with arterial repair. No cerebrovascular events were observed during the periprocedural period.

The overall 30 days mortality was 0%.

After endovascular procedures, all patients were discharged under dual antiplatelet therapy (Acetyl-Salicylic acid 100 mg/daily and Clopidogrel 75 mg/daily) for 3 months, and a single antiplatelet therapy was continued thereafter (Acetyl-Salicylic acid 100 mg/daily).

LONG-TERM OUTCOMES

After operation, a duplex ultrasound and a clinical outpatient visit were performed for all patients at 1, 6 and 12 months for the first year and annually thereafter. When restenosis or reocclusion of the SCA was detected at duplex ultrasound, the patients underwent an Angio-CT scan to confirm the diagnosis and plan any possible reintervention, if needed.

The mean follow-up was 26.7±16.4 months (range 12-86 months). During the follow-up period, reintervention for the target vessel was performed in 3 patients. A case of late stent thrombosis occurred in the 16th month in a patient who had initially been treated for left ostial SCA occlusion with severe calcification and required a surgical revascularization by carotid-axillary bypass. Two cases of in stent restenosis at the distal stent edge were observed respectively at 12th and 15th month and were treated by re-stenting with favourable outcomes. Two deaths happened at the 14th and 28th month respectively, respectively due to myocardial infarction and malignant tumor.

The primary patency rates were 88.7%±4.3% at the end of the first year and 78.7%±6.1% at 3 years (Fig. 1).

Discussion

Endovascular procedures have progressively emerged as an appealing option for the treatment of SCA steno-occlusive disease, given their less invasiveness and the ease of intervention, especially in patients with significant comorbidities ⁶.

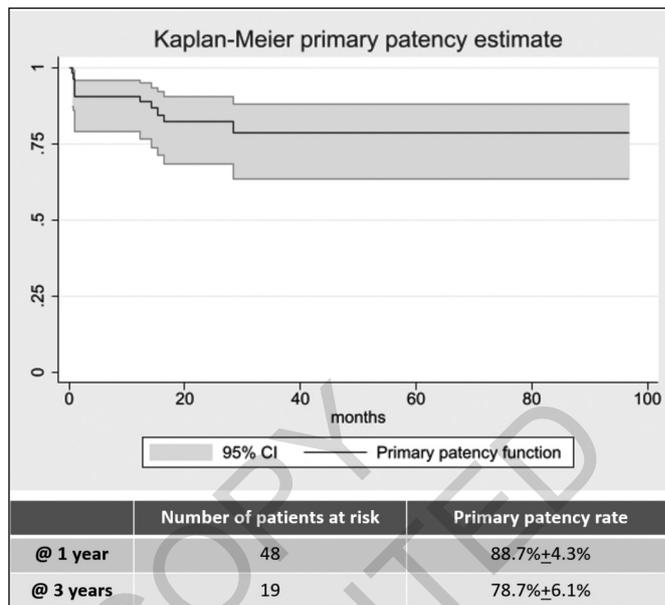


Fig. 1: Kaplan-Meier estimates for primary patency.

Furthermore, the evolution of materials and techniques have made over time endovascular approach a safe and effective alternative to surgical bypass.

Also in our experience, endovascular treatment of steno-occlusive SCA disease was safe and effective, being associated with good technical success and limb salvage rates, low periprocedural complication rates and good long-term patency rates.

These satisfying results are probably due to a series of strategies that are part of our current clinical practice. First, the choice of the vascular approach. In our experience, the radial access was the first approach whenever possible, given the shorter distance with the lesion if compared to a femoral approach, with the possibility of having greater strength to overcome stenotic and above all obstructive lesions. When radial artery was not accessible, we switched to the brachial approach. In this case, however, the occurrence of hematomas and upper limb ischemia following a percutaneous approach have convinced us to adopt the brachial surgical approach with a small incision.

As a second point of discussion, the choice for a primary stenting whenever possible, using in all cases balloon-expandable stents. This type of stent was preferred due to its better delivery profile, more precise deployment, and better radial force compared to self-expandable stents ^{4,7}.

Our choice for a primary stenting instead of a simple balloon angioplasty is supported by the results reported in the literature. Ahmed et al. published a meta-analysis in 2016 ⁵, including 35 studies and a total of 1726 patients in which they compared the results of simple angioplasty versus stenting in the treatment of steno-occlusive SCA lesions. They showed that technical suc-

cess rate was significantly higher in the stenting group (92.8% vs. 86.8%, $P=0.007$). Nevertheless, long-term primary patency rates were similar (76.9% vs 79.6%, $P=0.73$) as well as symptoms resolution rates (82.2% vs 73.0%, $P=0.32$). The technical success rate in our consecutive cases was 94.6 % for all procedures being higher in case of stenosis rather than in occlusions, with total symptom resolution in all cases.

It has been reported that the technical success rate of endovascular therapy for occlusion has been improving over the years. Aziz et al.⁸ reported a mean technical success rate of 64% for occluded lesions from 26 studies dating from 1985 until 2008. In recent largest studies performed at high-volume centers with considerable experience the mean technical success rate ranges between 86 and 90%^{9,10}. Again, this could be explained by the improvement in materials and re-entry techniques.

Interestingly, no stroke occurred perioperatively in our study despite our choice of not to use embolic protection devices (EPDs). Periprocedural stroke may occur as a consequence of embolization in posterior cerebral circulation through the vertebral artery and the risk is around 1–5%¹¹.

There is currently no level one evidence for reduction of stroke incidence when using EPDs. The clear potential benefit of these devices needs to be balanced with increased procedure time and complexity as well as their complication risk, mainly vessel dissection and ischemia¹². However, it should be considered in high-risk lesions¹¹.

During the follow-up, the overall rate of restenosis was low (3.7%) and the primary patency rates were comparable with those reported in previous studies, which ranged between 70% and 90% after 2 years^{7,9,13,14}. Ben Hammamia and al. reported a 7-years primary patency rate of 100% for stenosis, and 62.5% for occlusions¹⁵. The use of covered stent seems to improve long-term patency¹⁶.

These patency rates underline that endovascular treatment can be an effective and durable therapeutic alternative to surgery. Restenosis remains the major limitation of the endovascular treatment, but long-term patency may be improved with repeat procedure leading to a high secondary patency^{4,9-11}.

Our study has some limitations, given its retrospective nature and the small size of population. Nevertheless, our results represent contemporary real-world practice in an all-comer symptomatic population in a tertiary referral centre.

Conclusion

Endovascular treatment can be considered as a safe and effective treatment of SCA steno-occlusive disease, with low perioperative complication rates and a good patency rates over long term.

Riassunto

Scopo dello studio è stato valutare i risultati del trattamento endovascolare a breve e lungo termine nei pazienti con malattia steno-occlusiva dell'arteria succlavia. Sono stati valutati retrospettivamente i dati dei pazienti sottoposti a trattamento endovascolare della malattia steno-occlusiva dell'arteria succlavia (SCA) tra il 2013 e il 2019. Dopo il trattamento, il follow-up dei pazienti è stato programmato a 1, 3, 6, 12 mesi dopo l'intervento e successivamente annualmente mediante ecocolore-Doppler e valutazione clinica. Gli outcomes primari includevano il tasso di successo tecnico procedurale e clinico e i tassi di salvataggio dell'arto. Come outcomes secondari sono stati valutati il verificarsi di complicanze peri-procedurali e tassi di pervietà primaria.

Sono stati valutati un totale di 56 pazienti (33 maschi, 58,9%). L'età media dei pazienti era di 61,5 anni. Il tasso di successo tecnico è stato del 94,6%, pari al 100% in caso di stenosi e al 78,5% in caso di occlusione. Il tasso di successo clinico è stato del 100% e il tasso di salvataggio dell'arto superiore è stato del 100%. Sono state eseguite amputazioni minori su 5 pazienti. I tassi di mortalità e morbilità perioperatoria sono stati rispettivamente dello 0% e dell'8,9%. Il follow-up medio è stato di $26,7 \pm 16,4$ mesi (intervallo 12-86 mesi). Si sono verificate due restenosi intra-stent (a 12 e 15 mesi) e un caso di trombosi al 16° mese. I tassi di pervietà primaria sono stati dell'88,7%+4,3% alla fine del primo anno e del 78,7%+6,1% a 3 anni.

Il trattamento endovascolare può essere considerato un trattamento sicuro ed efficace per la malattia steno-occlusiva della SCA, con bassi tassi di complicanze perioperatorie e buoni tassi di pervietà a lungo termine.

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