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Outcomes of Endovascular Treatment in Patients with Superficial Femoral Artery In-Stent Restenosis

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ABSTRACT

Background: The femoropopliteal artery lesions classed as trans-Atlantic inter-society consensus (TASC) A-C lesions and some TASC D cases should be treated with endovascular therapy, according to current recommendations (Level C, Class I, recommendations based on expert opinion and retrospective studies)

Aim: This study aimed to evaluate the effectiveness and safety of endovascular balloon angioplasty in cases of superficial femoral artery stenosis.

Patients and Methods: This study was presented to the faculty of medicine's department of vascular surgery at Assiut University Hospital between October 2019 and October 2021. It is a prospective hospital-based study for patients with superficial femoral artery in-stent restenosis.

Results: The primary patency rate at 12 months was 82.6%, demonstrating that none of the 23 patients who received effective endovascular therapy experienced any loss of function or passed away during the observation period.

Conclusion: Endovascular treatment is a safe and effective way for treating chronic lower limb ischemia caused by SFA-ISR. Both DCB and traditional balloon angioplasty are associated with low post-procedural morbidity and death. It is an excellent surgical replacement with a high rate of technical success. Drug-coated balloon angioplasty is a helpful operation with a significant decrease in recurring stenosis and repeat angioplasty for up to a year because of the anti-proliferative effects of paclitaxel.

Keywords: Outcomes, Endovascular treatment, Patients, Superficial femoral artery, In-stent restenosis.

INTRODUCTION

Current recommendations (Level C, Class I, recommendations based on expert opinion and retrospective studies) advise endovascular therapy of the femoropopliteal artery as the first line of treatment, especially in trans-Atlantic inter-society consensus (TASC) A-C lesions and in some TASC D instances [(1)]. The femoropopliteal segment is one of the most difficult arterial regions to treat endovascularly because of its anatomical location and mechanical characteristics, as it has a significant risk of restenosis and vessel recoil. Actually, the two primary downsides of stenting in the femoropopliteal region are stent fracture and in-stent restenosis (ISR) [(2)].

Restenosis in stents refers to the decrease in luminal volume brought on by the encroachment of cells, extracellular matrix, and thrombi inside the cylinder of the stented artery and/or at the 5-mm margins proximal and distal to the stent (ISR) [(3)]. For an endovascular specialist, femoro-popliteal in-stent restenosis (ISR) continues to rank among the most bothersome issues. Within the first year following femoro-popliteal artery stenting, it happens in 18% to 40% of patients, making it a rather prevalent occurrence. After stenting of longer lesions, SFA-ISR is more frequent and may be related to stent breakage [(4)]. Initial procedural success rates for ISR treatment are high, but long-term, permanent patency is relatively uncommon. Recent studies have demonstrated that anti-proliferative drug-coated balloon angioplasty treatments had higher patency rates than those utilising plain balloons. A number of interventional centres gradually started using drug-coated balloons (DCBs) to treat femoro-popliteal blockages [(5)].

Drug-coated balloons (DCBs) have been a viable therapeutic alternative in the field of interventional therapy in recent years. By allowing antiproliferative medications to be temporarily given to the artery wall without the need for an implanted drug delivery system, this method may minimise the negative effects of polymer-based stent technology. Paclitaxel-coated balloons are safe and effective in decreasing restenosis in individuals with coronary ISR and de novo femoropopliteal lesions, according to small clinical randomised studies [(6)]. The purpose of the study was to evaluate the effectiveness and safety of endovascular balloon angioplasty in cases of superficial femoral artery stenosis.

PATIENTS AND METHODS

This study is a prospective hospital-based study for patients with superficial femoral artery in-stent restenosis that was presented to The Faculty of Medicine's Department of Vascular Surgery at Assiut University Hospital between October 2019 and October 2021.

Inclusion criteria: All patients with SFA-ISR-caused chronic lower limb ischemia who met one or more of the following criteria: Rutherford categories 4 to 6 patients, patients with a peak systolic velocity ratio (PSVR) of more than 2.4 by duplex at any point inside the stent, which indicates more than 50% stenosis, and patients with patent popliteal artery with at least one patent tibial vessel as backup.

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Exclusion criteria: We excluded all patients with untreated ipsilateral iliac or aortic lesions, non-salvageable limb, allergic or intolerant to contrast media, aspirin, clopidogrel, ticlopidine or paclitaxel, patients presented with Acute limb Ischemia, duplex showing < 50% ISR and absent at least one tibial vessel.

All patients underwent the following:

Full history taking: Demographic data and risk factors were collected for all cases included in this series also history of previous PTA/stenting and onset and duration of symptoms.

Clinical evaluation: A physical examination should be included in the first assessment to look for any physical indicators of limb ischemia, with a focus on peripheral pulses, hair loss, skin tone changes, and trophic skin abnormalities. The ankle brachial index (ABI) is a frequently used measurement that compares the systolic pressure at the brachial artery to that at the dorsalis pedis or posterior tibial artery.

Investigations: Laboratory investigations: All routine investigations were done to all patients including complete blood count, prothrombin concentration, renal function tests and Electrocardiogram (ECG). **Radiological investigations:** Duplex ultrasound to assess site of stenosed segment, to classify stenosis/occlusion, to confirm > 50% stenosis by PSVR > 2.4 and to evaluate distal run-off vessels and computed tomographic angiography (CTA) to diagnose the location and degree of SFA in-stent restenosis when needed to confirm all data obtained by Duplex ultrasound.

Follow-up: At our outpatient clinic, patients were then booked for normal follow-up appointments that included clinical and Duplex ultrasound examinations after one month and then every three months thereafter until one year. Following surgery, at least one month of postoperative aspirin and clopidogrel (75 mg/day) treatment was given before starting lifelong aspirin. ABI measurement, Rutherford classification evaluation, and wound evaluation were all included in the clinical follow-up. Duplex revealed restenosis greater than 50% of the stent as PSVR > 2.4.

Ethical Approval: Assiut University Ethics Board approved the study, and the patients received all the information they required to comprehend the trial. Each study participant provided signed consent after receiving all necessary information. The Declaration of Helsinki, the guideline of ethics for the World Medical Association, was followed when conducting this study on humans.

Statistical analysis

SPSS 25.0 and MedCalc 16.8 (SPSS Inc., Chicago, IL, USA) were used for the statistical analysis (MedCalc Software, Ostend, Belgium). Continuous variables were expressed as mean ± SD, median, and/or IQR, whilst categorical variables were expressed as frequency and%. The log-rank test was used to evaluate intergroup differences after the patency rates were analysed using the Kaplan-Meier survival curve on an "intention to treat" basis. Multiple demographic, access, and lesion characteristics were examined in a multivariate study to determine their influence on primary patency. This analysis used a stepwise Cox proportional-hazards regression model. The results are shown as a hazard ratio (HR) and 95% confidence interval (CI). The level of 0.05 designated statistical significance.

RESULTS

From October 2019 to October 2021, 25 patients with chronic lower limb ischemia due to SFA-ISR were admitted to Vascular Surgery Department in Assiut university Hospital. All patients underwent endovascular angioplasty using either POBA or DCB. There were 19 (76%) men and 6 (24%) women (Figure 1), with a mean age of 63.88 ± 5.16 years (range; 53-71 years) as shown in table (1).

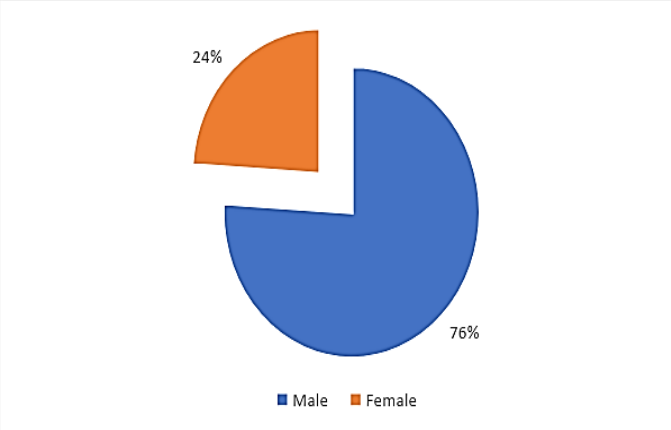

Figure (1): Sex distribution in the study.

Table (1): Demographics of patients in our study

No. of patients	25
Minimum age (years)	53
Maximum age (years)	71
Mean age (years) ± SD	63.88 ± 5.16

SD: Standard Deviation.

In this study, diabetes was encountered in 13 (52%) patients, smoking in 13 (52%) patients, hypertension in 18 (72%) patients, coronary artery disease in 8 (32%) patients, and hyperlipidemia in 3 (12%) patients as shown in table (2).

Table (2): Distribution of risk factors in the study

Risk factors	**No.**	**%**
Diabetes	13	52%
Smoking	13	52%
Hypertension	18	72%
Coronary artery diseases	8	32%
Hyperlipidemia	3	12%

In our study the mean pre-procedure ABI was 0.528 ± 0.106. In addition, 9 (36%) patients presented with Rutherford category IV, 14 (56%) patients with Rutherford category V, and 2 (8%) patients with Rutherford category VI as shown in table (3).

Table (3): Clinical presentation of patients included in the study

Clinical presentation	No.	%
Rutherford IV	9	36%
Rutherford V	14	56%
Rutherford VI	2	8%

Figure (2) showed that 6 (24%) patients presented with Tosaka class I, 15 (60%) patients presented with Tosaka class II, and 4 (16%) patients presented with Tosaka class III.

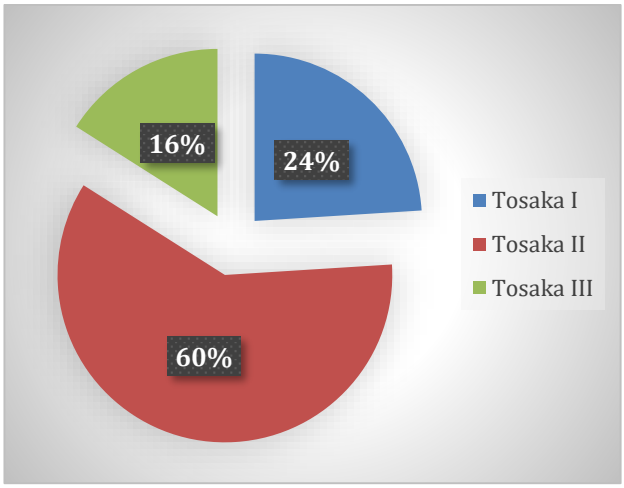

Figure (2): Angiographic classification of patients in our study.

In our study, angiographic study showed patent one run off vessel in 12 (48%) of patients, patent two run off vessels in 7 (28%) of patients, and patent three runoff vessels in 6 (24%) of patients. Table (4) demonstrated that the mean lesion length was 85.400 ± 35.44 mm, range (35 mm-150 mm).

Table 4: Lesion length in our patients

Minimum lesion length	35mm
Maximum lesion length	150mm
Mean lesion length	85.400 mm
Std. Deviation	35.44

In our study, 5 (21.7%) patients underwent plain old balloon angioplasty while 18 (78.2%) of patients underwent drug coated balloon angioplasty.
In the DCB group, 14 (77.7%) patients underwent PTA using only one drug coated balloon, while in 4 (22.2%) patients we used two drug coated balloons. Mean length was 133.2 ± 30.5 mm ranging from 80 mm to 150 mm. In all cases we used 6mm balloons. Bailout stenting was necessary in 3 (13%) patients due to flow limiting dissections at the treated stent edges or residual stenosis > 30%. Technical success was obtained in 92% of cases (23/25), we failed to cross the occluded stent in 2 patients even after usage of retrograde (Tibial) access. These 2 patients underwent thereafter femoro-popliteal bypass. Post-operatively, the mean ABI increased significantly from 0.528 ± 0.106 to 0.99 ± 0.073 (P < 0.0001). In this study, complications were encountered in 6 (26%) patients, in the form of: Flow limiting dissections at the treated stent edges in 3 patients and was managed in the same setting by bailout stent, CFA pseudoaneurysm in one patient and was managed by surgery. Access site minor hematoma in 2 patients were managed by conservative means as shown in table (5).

Table (5): Complications encountered in our study

Complications (n = 6)	NO.	%
Flow limiting dissection	3	13%
Pseudoaneurysm of CFA	1	4.4%
Access site hematoma	2	8.6%

CFA=Common femoral artery

Out of the 23 patients with successful endovascular treatment, the Primary Patency rate at 12 months was 82.6% (19) as shown in Figure (3), No patients lost or died during the follow up period.

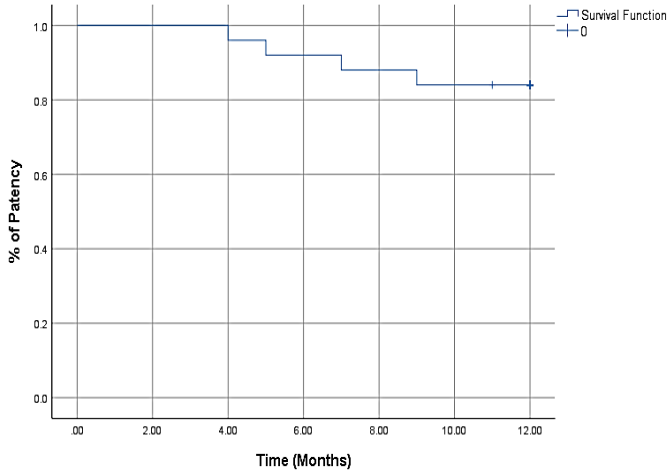

Figure (3): The cumulative primary patency of our patients were shown by the Kaplan-Meier curve.

Four patients (16%) demonstrated substantial target lesion restenosis during the follow-up period, three patients due to focal stenoses (<50mm) and one patient due to diffuse recurrent stenosis. Two out of three patients with focal re-stenoses were managed with DCB and the remaining one underwent femoro-popliteal surgical bypass. The last patient underwent major amputation after failure of both endovascular and surgical means. In this study, limb salvage or amputation-free survival rate recorded at 30 days and 12 months was 100% and 96%, respectively. One major amputation was done in the ninth month. On the other hand, 30-days survival rate in our patients was 100% with no deaths during the follow up period.

CASE PRESENTATION
CASE 1

A male patient, 57 years old, diabetic, hypertensive, presented with chronic Rt lower limb ischemia Rutherford category V with gangrenous 2nd toe with ABI= 0.3. Duplex was done and revealed occluded SFA stent (Tosaka III). Angiography revealed occluded stent at mid SFA, with patent three distal run-off vessels. Balloon angioplasty was done using Paclitaxel eluting 6mm*80 mm IN. PACT™ Admiral™ Medtronic Balloon. Completion angiography showed successful balloon angioplasty of SFA with no residual stenosis or dissection flaps. Amputation of the gangrenous 2nd toe was done two days later with improved ABI to 0.9.

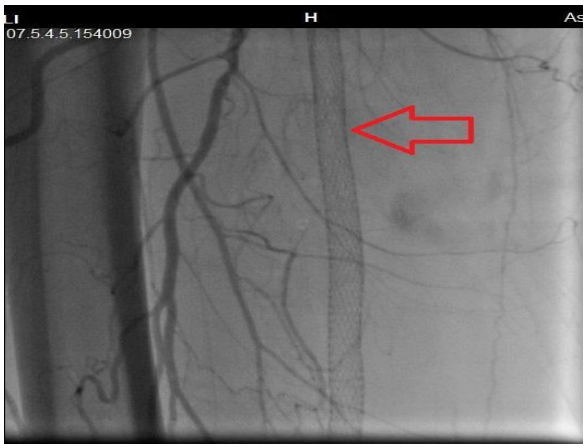

Fig (4) Diagnostic angiography showing occluded SFA stent (Tosaka III)

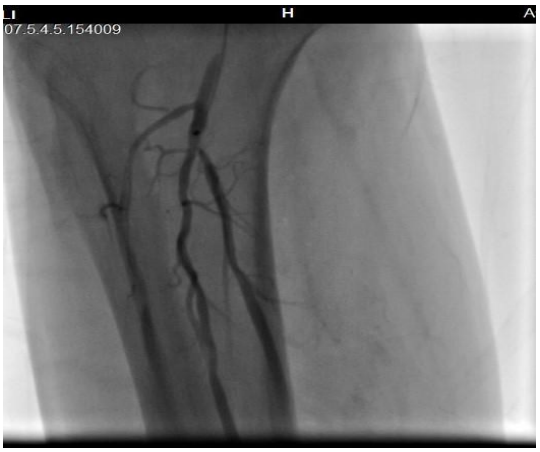

Fig (5) Diagnostic angiography showing patent three distal run-off vessels

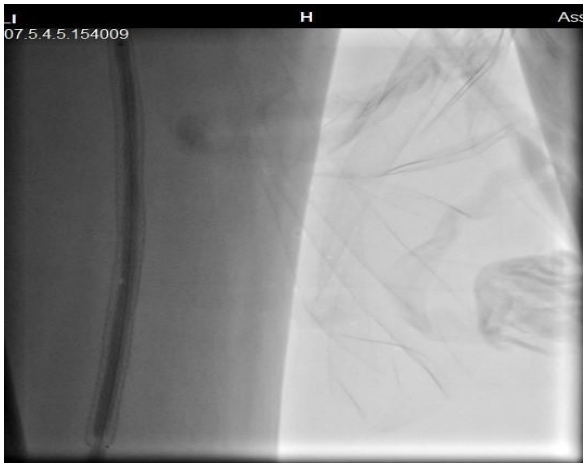

Fig (6) Fluoroscopy showing balloon angioplasty using Paclitaxel coated balloon 6mm*80mm in. PACT admiral

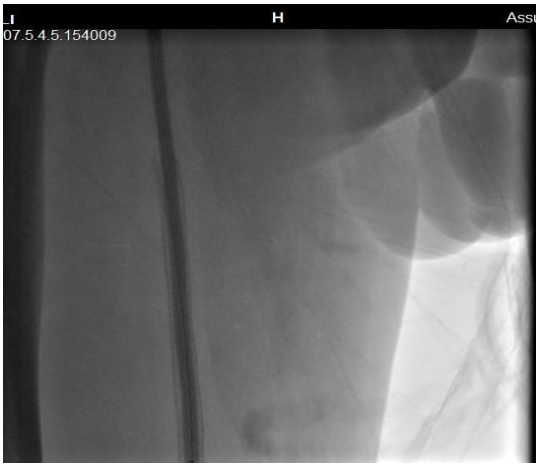

Fig (7) completion angiography showing patent SFA stent without residual stenosis

CASE 2

A male patient, 65 years old, diabetic, hypertensive and smoker, presented with chronic Rt lower limb ischemia Rutherford category IV (rest pain) with ABI= 0.2. Preoperative duplex revealed SFA-ISR at proximal part of SFA >50%. Angiography revealed occluded SFA from origin with multiple in-stent stenoses (Tosaka II), with patent one distal run-off vessel. Balloon angioplasty was done using Paclitaxel eluting 6mm*80 mm IN. PACT™ Admiral™ Medtronic Balloon. Post angioplasty completion angiography revealed flow limiting dissection flaps proximal to the occluded stent, bailout stent at the proximal part was done using ELUMINEXX, BARD 6mm*80 mm self-expandable stent. Then another completion angiography was done revealed no residual stenoses or dissection flaps with patent SFA stent.

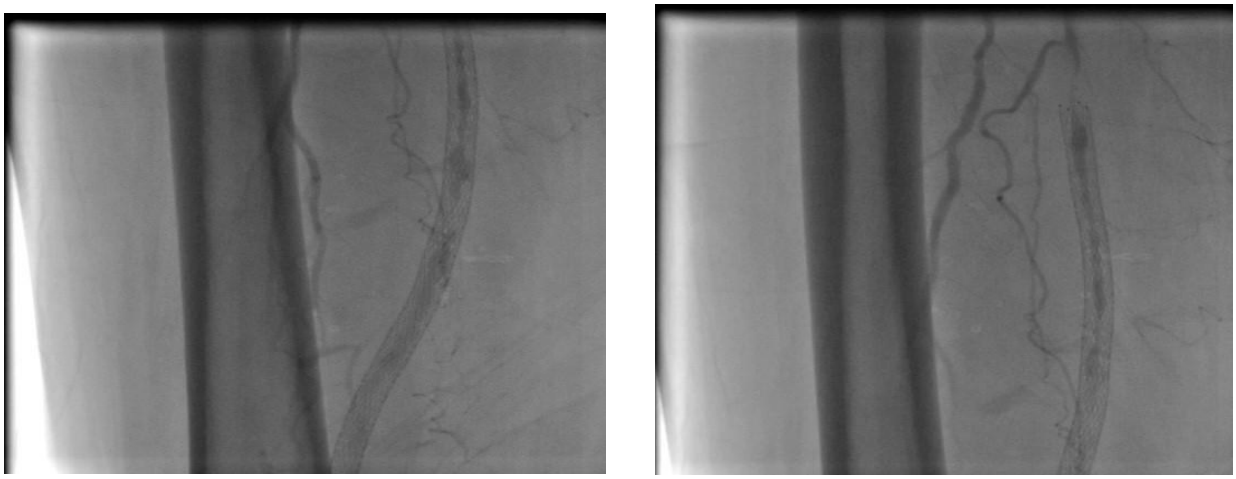

Fig (8) Diagnostic angiogram showing occluded SFA from origin with multiple in stent stenoses.

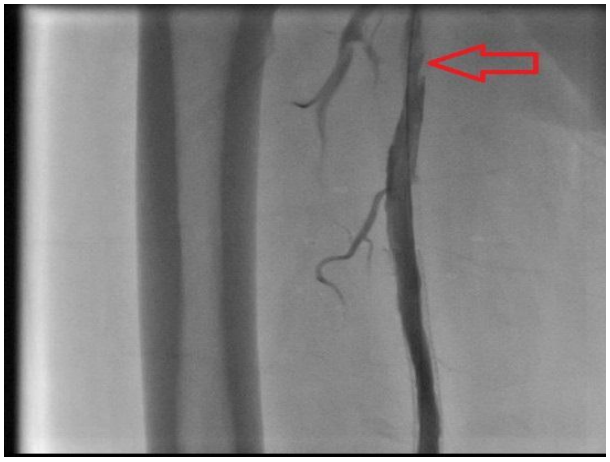

Fig (9): Angiogram showing patent posterior tibial artery as a distal run-off vessel

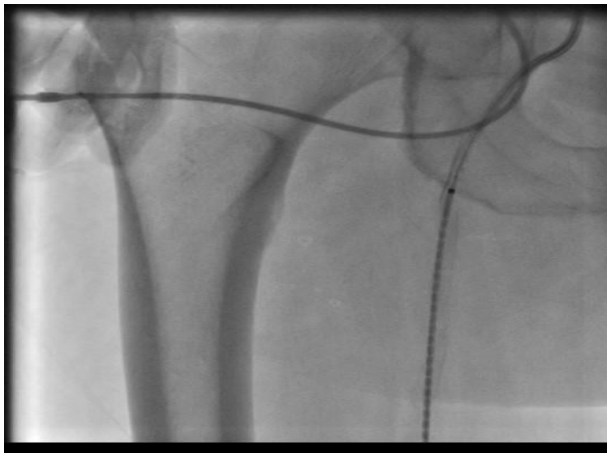

Fig (10): Balloon angioplasty using Paclitaxel coated balloon 6mm*80mm IN. PACT Admiral

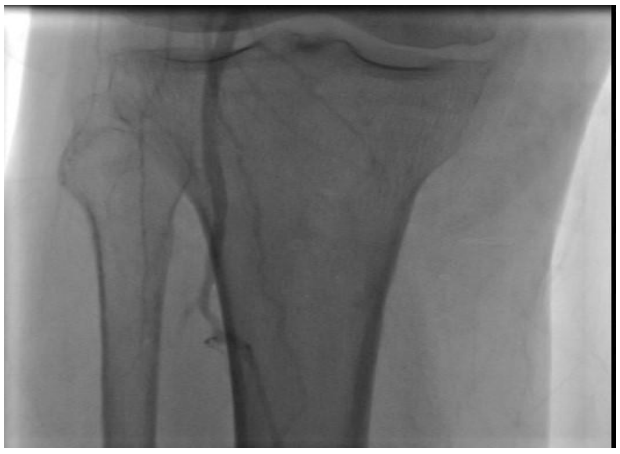

Fig (11): post angioplasty completion angiography revealing dissection flaps proximal to the stent

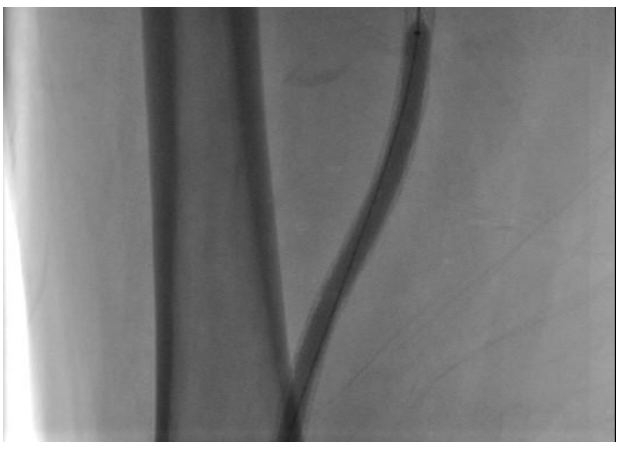

Fig (12): Bailout stent at proximal SFA segment using mm self-expandable stent.

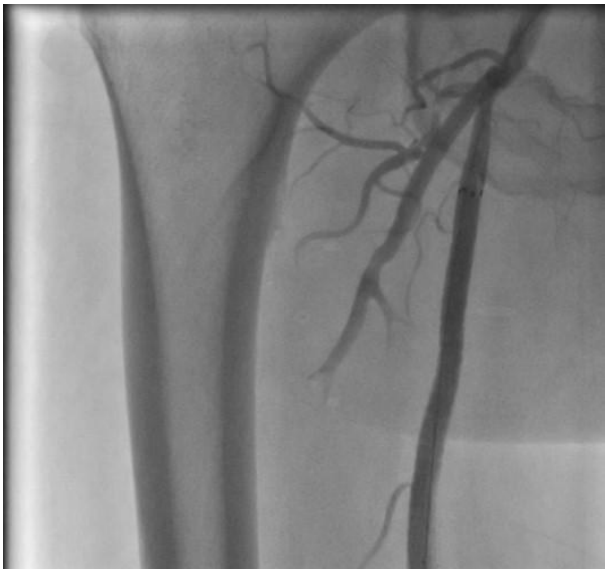

Fig (13): Post stenting angiography revealing no residual stenoses or dissection flaps with Patent SFA flow.

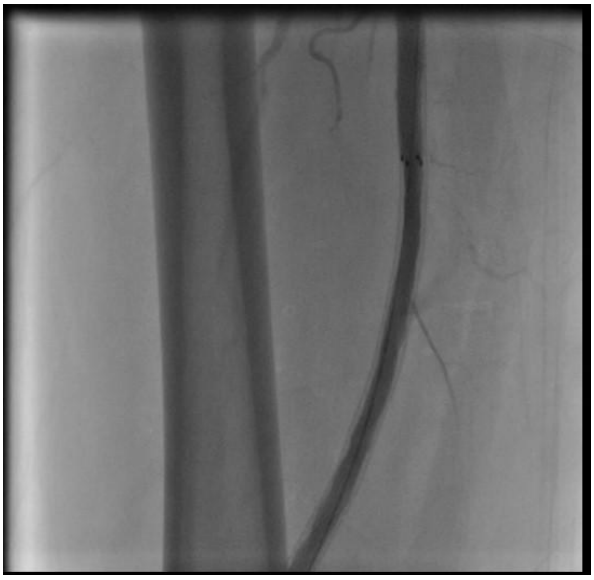

Fig (14): Final angiogram showing patent stent-in-stent of SFA

DISCUSSION

Anti-proliferative medications might be delivered to the ISR region using the newly created drug coated balloon (DCB), leaving no extra strut layer behind. DCB has been linked to excellent clinical and angiographic effectiveness in the treatment of femoropopliteal artery de novo lesions. The best course of action for patients with femoropopliteal ISR is still up for debate [(7)].

Different endovascular therapy modalities are used to manage in-stent restenosis (ISR) in SFA lesions. This study's objective is to evaluate their safety and efficacy. 25 people participated in our study, with a mean age of 63.88 ± 5.2 years; 76% of them were men. More than half of our patients smoked cigarettes, and most of them were suffering DM and HTN.

The clinical picture of patients at presentation showed that the largest proportion of patients are Rutherford stage five (56%), followed by patients with Rutherford stage four (36%) and only 2 patients had Rutherford stage 6 (8%). The technical success rate was 92% (23/25). We failed to cross the lesion in two patients with total occlusion of the stent (Tosaka III), both of them underwent femoral-popliteal bypass surgery with accepted clinical outcome. Other investigations, in contrast to our findings, revealed a marginally greater procedure success rate. In a trial with 39 patients who had SFA-ISR, **Stabile *et al.*** [(8)] demonstrated a slightly greater success rate of 100%. Additionally, the **Bague *et al.*** [(9)] with 55 limbs included, the research revealed a 98% technical success rate, 48 (87%) claudication cases, and 7 (13%) critical limb ischemia cases. Additionally, in the **Ott *et al.*** [(10)] study (Paclitaxel eluting balloon vs standard balloon angioplasty for In-Stent restenosis of superficial femoral artery), which included 70 patients, the technical success rate was 100%, which was somewhat higher than in our experiment.

19 out of 23 trial participants who made it through the 1-year follow-up met the main patency rate. Throughout the observation period, there were four patients who developed restenosis; two underwent balloon angioplasty with drug-coated balloons, another underwent femoral-popliteal bypass surgery, and the final patient underwent severe amputation after endovascular and surgical treatments proved ineffective. This is supported by the findings of **Stabile *et al.*** [(8)], who reported a high primary patency rate of 92.1% after one year. The primary patency rate at 1 year, as reported by **Bague *et al.*** [(9)], was 83.7%, which is comparable with our data. In five cases, target lesion revascularization was necessary.

At 6 and 7 months, two patients got FP bypasses; at 6 and 12 months, two patients underwent conventional angioplasty with bailout stenting and at 9 months, one patient underwent a typical balloon angioplasty. According to reports, the SFA-angiographic ISR's classification has a considerable impact in forecasting future outcomes [(11)].

60% of our patients in this study had Tosaka II, the most widely recognized type, trailed by Tosaka I (24%) and Tosaka III (16%). As indicated by **Armstrong *et al.*** [(11)] research, the angiographic FP-ISR characterization can anticipate restenosis and impediment following endovascular treatment. In spite of the fact that Class III ISR (stent impediment) had significantly more prominent paces of restenosis and re-impediment than different classes, all classes of ISR displayed high paces of restenosis and re-intervention. However, incongruous outcomes were seen by different

scientists. In **Bague *et al.*** [9] examination, there were no calculable contrasts between Tosaka class I (25 sores) and class II (29 injuries) sores concerning autonomy from TLR at 1 year after DCB treatment.

We didn't research the relationship between essential patency and sore length in our review with respect to the angiographic grouping of SFA-ISR as an indicator of later forecast and restenosis rate in light of the fact that to the little example size accessible. With respect to assessment of the paces of restenosis in various endovascular treatment modalities.

Research has shown that DCB is better than POBA. In the ISAR, **Ott *et al.*** [10] preliminary, double restenosis was altogether decreased with DCB contrasted with POBA (30% after DCB and 59% after POBA; P=0.03). Plain inflatable angioplasty (POBA) and DCB were looked at for the treatment of medium-length FP sores in a concentrate by **Krankenberg *et al.*** [12] from 2014 (82.3 mm). The DCB bunch got a sum of 62 patients, though the POBA bunch got 57 patients. TLR rates at 1 year were 90.8% contrasted with 52.6% (p =.001), and essential patency was 70.5% contrasted with 37.5% (p =.004), this study showed that DCB is better than POBA. Following percutaneous treatment with DCB rather than POBA, they found more powerful neointima expansion concealment at year angiography and a decrease in TLR at year follow-up. Three patients (13%) in this examination required bailout stenting due to stream restricting analyzation folds at the treated stent edges (two patients) or remaining stenosis more noteworthy than 30% (one patient). Furthermore, 11 patients in **Ott *et al.*** [10], who had angiographic proof of stream restricting analyzations following dilatation (6% versus 26%, DCB versus POBA, individually; p=0.02), had bailout stenting. Seven patients in the PACUBA concentrate on additionally required further stenting. One analyzation set two patients in the POBA bunch, while four analyzations put five patients in the DCB bunch. Thusly, having a bailout stent close by ought to be conceivable in these circumstances.

Post-interventional death rates detailed in our review were 0%. This goes in accordance with **Brodmann** [13]. Anyway different examinations detailed marginally higher death rates [10]. We can interpret this finding via cautious patient choice preceding the method and lower test size contrasted with different investigations.

Our safety outcomes are in accordance with the **Krankenberg *et al.*** [12] where no major amputation was required, 5 patients died, but none of the deaths were due to the operation in this study, which included 119 patients with SFA-ISR and were randomly assigned to DCB or POBA groups. The results in terms of primary patency, freedom from TLR, and improved clinical symptoms showed the safety and effectiveness of endovascular therapy for superficial femoral artery ISR. Last but not least, DCB need to be chosen over other percutaneous strategies like stents and plaque removal devices. In fact, stand-alone balloon angioplasty therapy (POPA&DCB), which employs debulking tools including laser atherectomy, has been associated with a range of midterm outcomes [14]. The gradual narrowing of the blood artery lumen brought on by several stent layers may compromise vascular compliance and increase the risk of recurrent ISR, similar to how drug-coated or covered stents have acceptable patency up to a year following insertion [15].

The following are some limitations of the study: with a small sample size, we lacked a comparison group because we did not compare patients treated with POBA to patients treated with DCB and because of the short follow-up period.

CONCLUSION

A safe and efficient method for treating persistent lower limb ischemia brought on by SFA-ISR is endovascular therapy. Low peri-procedural morbidity and mortality were associated with both DCB and plain old balloon angioplasty. It is a fantastic surgical substitute with a high technical success rate. Due to the anti-proliferative effects of paclitaxel, drug-coated balloon angioplasty is a beneficial procedure with a considerable reduction in recurring stenosis and repeat angioplasty up to one year.

DECLARATIONS

Consent for publication: I certify that all writers gave their consent to submit the work.
Availability of data and material: Available
Competing interests: None
Funding: No fund
Conflicts of interest: no conflicts of interest.

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