Two-Year Outcomes of Excimer Laser Ablation Combined with Drug-Coated Balloon for Treating De Novo Lesions and In-Stent Restenosis in Femoropopliteal Artery of Chronic Limb-Threatening Ischemia Patients

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Background: To evaluate the safety and efficacy of excimer laser ablation (ELA) combined with drug-coated balloon (DCB) in the treatment of chronic limb-threatening ischemia (CLTI) patients with de novo and in-stent restenosis (ISR) lesions in the femoropopliteal artery (FPA).
Methods: A retrospective, single-center analysis was performed on data collected between January 2017 and December 2021. The study included CLTI patients who underwent treatment with ELA combined with DCB for de novo and ISR lesions in the FPA. The primary endpoint was the 24-month primary patency rate. Secondary endpoints included technical success rate and the incidence of major adverse events (MAEs), defined as death, major limb amputation, or target vessel revascularization.
Results: A total of 44 patients were included in the study, comprising 24 cases in the de novo lesion group and 20 cases in the ISR group. The mean patient age was 73.4 ± 7.7 years, with approximately one-third presenting with concomitant chronic coronary artery disease (CAD) or cerebrovascular disease (CVD). Around one-third of the patients exhibited foot ulcers or gangrene, with a mean lesion length of 239.09 ± 120.09 mm. In the de novo lesion group, 79.2% of lesions were classified as chronic total occlusions (CTOs), whereas 75% of lesions in the ISR group were categorized as Tosaka III. For such complex lesions, the technical success rate was 100% in both groups. The primary patency rates for the de novo group were 86.9% at 12 months and 64.3% at 24 months, compared to 77.0% and 56.5% in the ISR group. Freedom from target lesion revascularization (TLR) rates in the de novo group were 95.8% and 85.4% at 12 and 24 months, respectively, while the ISR group achieved rates of 88.9% and 76.6%. Despite lower primary patency and freedom from TLR rates in the ISR group, the differences were not statistically significant ($P = 0.74$).MAE were observed in 12.5% of patients in the de novo group and 35% in the ISR group, with no statistically significant difference ($P = 0.27$).
Conclusion: For CLTI patients with complex lesions, including extensive occlusions and severe calcification, the combination of ELA and DCB demonstrates high technical success and favorable safety profiles for both de novo and ISR lesions. Mid-term outcomes indicate a potential trend toward better efficacy in treating de novo lesions compared to ISR lesions.

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Ethical Approval: All methods used in our study comply with the relevant guidelines and regulations, including Declaration of Helsinki. The study was approved by the ethics committee of Xuanwu Hospital, Capital Medical University. All participants provided written informed consent prior to their inclusion in the study.

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INTRODUCTION

With the aging population, the incidence of peripheral artery diseases (PAD) has been increasing annually, reaching approximately 19.8% in the elderly population, significantly impacting patients' quality of life and life expectancy.[1,2] CLTI is defined as PAD complicated by rest pain, ulceration, or gangrene lasting more than 2 weeks, representing the end stage of PAD. A meta-analysis involving 83,000 patients demonstrated a total CLTI prevalence of 0.74%.[3] The progression of PAD into CLTI significantly increases the cardiovascular and cerebrovascular morbidity. Without timely intervention, the prognosis for CLTI is poor, with amputation and mortality rates exceeding 20% within 1 year,[4] and a 5-year mortality rate of approximately 50%.[5] Effective revascularization remains a crucial therapeutic approach for symptom relief and wound healing in CLTI patients.

With advances in medical technology, various endovascular treatments and devices have gained prominence, complementing traditional arterial bypass surgery. Conventional balloon angioplasty (CBA) and stent implantation are well-established procedures for endovascular treatment.[6–8] However, vessel recoil and ISR remain major factors affecting their efficacy.[9,10] Due to its unique anatomical structure—subject to muscle tension, compression, and torsion—the FPA is more prone to ISR, with rates of 40%–50% at 1 year[11] and up to 60% at 2 years poststent implantation.[12] Long-term outcomes for these treatments are suboptimal and improving long-term vessel patency while reducing stent implantation rates remain key goals of endovascular interventions. For both de novo lesions and ISR, adequate lumen preparation is critical for improving vessel patency. ''Debulking'' techniques, which clear the luminal contents, not only improve immediate outcomes but also enhance long-term patency, making them a focus in current endovascular therapies. Numerous studies have demonstrated that ELA and DCB treatment, when used alone, yield satisfactory short-term results in complex lesions. However, long-term follow-up results are often less favorable.[13] ELA offers effective lumen preparation, creating optimal vascular conditions for DCB use and potentially improving long-term patency. ELA has primarily been indicated for ISR lesions; several studies have confirmed its excellent performance when combined with DCB in treating femoropopliteal ISR lesions.[14,15] This study aimed to evaluate the safety and efficacy of ELA combined with DCB in treating both de novo and ISR femoropopliteal complex lesions in CLTI patients at our center.

METHOD

Study Design

We conducted a retrospective analysis of CLTI patients undergoing endovascular treatment for FPA lesions using ELA combined with DCB at Xuanwu Hospital, Capital Medical University. The objective was to evaluate the safety and efficacy of this treatment approach. The study was approved by the institutional review board of Xuanwu Hospital, Capital Medical University, and all enrolled patients provided written informed consent. Patients or the public were not involved in the design, conduct, reporting, or dissemination of this research.

Inclusion and Exclusion Criteria

The inclusion criteria are as follows: (1) age $\geq$35 years old; (2) CLTI patients with Rutherford classification grade 4 or above; (3) diagnosis of lower extremity atherosclerotic occlusive disease; (4) presence of de novo lesions and ISR lesions of the FPA, confirmed by digital subtraction angiography (DSA) or computed tomography angiography (CTA), with stenosis>50%; and (5) informed consent provided by the patient.

The exclusion criteria are as follows: (1) life expectancy <1 year; (2) allergy to contrast agents, heparin, or antiplatelet drugs; (3) severe cardiovascular, hepatic, or renal dysfunction precluding surgery; (4) severe coagulation disorders; (5) lesions with an impassable true lumen; (6) acute or subacute lower limb ischemia due to thrombosis at the target lesion; (7) no optimal inflow or at least one runoff vessel that cannot be successfully revascularized; (8) pregnant or lactating women; and (9) patients unable to comply with regular follow-up.

TREATMENT AND MEDICAL THERAPY

Preoperative Preparation

Preinterventional assessment included dual ultrasound examination and CTA to localize the lesions. Dual antiplatelet therapy consisting of 100 mg of aspirin and 75 mg of clopidogrel daily was initiated at least 3 days prior to the endovascular intervention.

Endovascular Interventions

Based on the lesion characteristics, either antegrade puncture of the femoral artery or retrograde puncture via the cross-over or distal retrograde approach was chosen. DSA was performed to assess calcification using the peripheral artery calcium scoring

system (PACSS).[16] Contrast imaging was then utilized to clarify the lesion's location, characteristics, length, and status of the runoff vessels. A 0.018- or 0.035-inch guidewire, along with a supporting catheter, was used to navigate the true lumen. Once the guidewire passed through the target lesion, a Turbo-Elite laser catheter (1.7−2.5 mm, Spectranetics, USA) was advanced along the guidewire from the proximal end of the occluded lesion in the superficial femoral artery (SFA) at a rate of 1 mm/s, ablating toward the distal arterial lumen. Before DCB dilation, at least 1 conventional balloon was used for vessel preparation, with the balloon diameter matched to the reference vessel diameter in a 1:1 ratio. Following this, Orchid DCB (Acotec Scientific, China) was deployed, with the balloon diameter equal to or 0.5 mm larger than the conventional balloon. The length of the DCBs used was sufficient to cover the entire lesion. The use of distal embolic protection devices was determined by the operator. In cases of post-treatment, flow-limiting dissections or residual stenosis exceeding 30% of the vessel diameter, bailout-stent placement was performed. Bare metal stents (Medtronic, USA; Bard, USA; Biotronik, Germany) with diameters ranging from 4 to 6 mm were selected. Conventional balloons or bare metal stents were also permitted for treating relevant iliac or infrapopliteal lesions to ensure optimal inflow or runoff vessel. After the procedure, the operator decided whether to use closure devices to suture the femoral artery puncture site.

Postoperative Medical Advice

Following the endovascular intervention, patients were instructed to orally administer 100 mg of aspirin and 75 mg of clopidogrel daily for at least 3 months postoperatively. After this period, patients were advised to continue taking 100 mg of aspirin daily for life. Intraoperative anticoagulants were managed by the operator to maintain appropriate activated clotting time.

FOLLOW-UP

Patients were evaluated prior to discharge and at 1, 3, 6, 12, 18, and 24 months post endovascular intervention. Follow-up assessments include clinical manifestations (claudication distance, relief of rest pain, and ulcer healing), physical examination, Rutherford classification, and ankle-brachial index (ABI). Duplex ultrasound evaluations were conducted prior to discharge and at 30 days post procedure, followed by assessments at 6, 12, 18, and 24 months postoperatively. If duplex ultrasound detects arterial restenosis >50%, CTA or DSA was performed.

ENDPOINTS AND DEFINITIONS

The primary endpoint is the primary patency rate at 24 months. Primary patency rate is defined as the absence of significant restenosis or occlusion, as assessed by duplex ultrasound or CTA evaluation, without the need for reintervention. Secondary endpoints include the technical success rate and MAEs, with MAEs further defined to include clinically driven target lesion revascularization (CD-TLR), major amputation, and all-cause mortality. Significant restenosis is indicated by a peak systolic velocity ratio >2.0, calculated as the peak systolic flow velocity at the lesion divided by the peak systolic flow velocity 1 cm distal to the lesion. Technical success is defined as residual stenosis <30% at the completion of angiography, with no flow-limiting dissection. CD-TLR is defined as any reintervention or surgical vascular reconstruction in the target lesion, with diameter stenosis ≥70% and an Rutherford Classification (RCC) deterioration of at least 2 grades or an ABI decrease >0.15 compared to baseline. The Rutherford Classification is a clinical system used to categorize the severity of PAD and CLTI based on symptoms and hemodynamic impairment. It ranges from category 0 (asymptomatic) to category 6 (major tissue loss and gangrene). The stages of the Rutherford Classification are as follows: category 0: asymptomatic, category 1: mild claudication, category 2: moderate claudication, category 3: severe claudication, category 4: rest pain, category 5: minor tissue loss (nonhealing ulcer, focal gangrene without infection), category 6: major tissue loss (extensive gangrene or necrosis requiring amputation). The TASC II Classification (TransAtlantic Inter-Society Consensus II) is a system used to categorize the severity of PAD in the iliac and femoropopliteal arteries. It divides lesions into 4 categories based on their location, length, and complexity: category A: simple lesions, suitable for standard interventions; category B: moderate complexity lesions, requiring more advanced techniques; category C: complex lesions, often involving multiple segments or significant calcification, requiring advanced interventions; category D: extensive lesions with severe calcification, typically necessitating surgical procedures. The Peripheral Arterial Calcium Scoring Scale were used to quantify the vessel wall calcification, In the PACSS scale, grade 0 represents the absence of visible calcium at

Table I. Baseline demographics and clinical variables

Variable	Overall ($N = 44$)	De novo ($N = 24$)	ISR ($N = 20$)	P
Age, years				0.28
Mean ± standard deviation	73.4 ± 7.7	74.5 ± 6.5	71.9 ± 8.9	
Range (Min, Max)	(52, 87)	(61, 87)	(52, 86)	
Gender (male) (%)	24 (54.5)	10 (41.7)	14 (70.0)	0.06
Risk factors				
Smoking (%)	17 (38.6)	9 (37.5)	8 (40.0)	0.86
Diabetes (%)	24 (54.5)	12 (50.0)	12 (60.0)	0.51
Hypertension (%)	32 (72.7)	15 (62.5)	17 (85.0)	0.09
Hyperlipidemia (%)	19 (43.2)	12 (50.0)	7 (35.0)	0.32
Renal dysfunction (%)	4 (9.1)	3 (12.5)	1 (5.0)	0.39
History of CAD (%)	16 (36.4)	9 (37.5)	7 (35.0)	0.86
History of CVD (%)	12 (27.3)	5 (20.8)	7 (35.0)	0.29

Values are mean ± SD or n (%).
ISR, in-stent restenosis; CAD, Coronary Artery Disease; CVD, cerebrovascular disease.

the target lesion, grade 1 refers to unilateral calcification <5 cm, grade 2 to unilateral wall calcification >5 cm, grade 3 indicates bilateral wall calcification <5 cm, and grade 4 represents bilateral wall calcification with calcium extension >5 cm. Severe calcification is defined as grade 4 on the PACSS scale. Lesion characteristics were analyzed by CTA or angiography.

STATISTICAL ANALYSIS

Categorical data are presented as counts or proportions (%). Continuous data are presented as mean ± standard deviation. Between-group differences are assessed using t-tests for continuous variables or chi-square tests for categorical variables (or Fisher's exact test when expected cell values are<5). Time-to-event outcomes are analyzed with 2-sided P values, with statistical significance set at 0.05 and 95% confidence interval. Survival analysis is performed using Kaplan–Meier curves and log-rank tests to compare primary patency rates and freedom from TLR between groups. All data are statistically analyzed using SPSS software (SPSS 20.0, Chicago, Illinois). A core laboratory evaluates and analyzes the data, with analysts blinded to the type of procedure performed to avoid bias.

RESULTS

Baseline Characteristics

Between January 2017 and December 2021, a total of 44 patients were enrolled in the study. Four patients were lost to follow-up, resulting in a follow-up rate of 90.9%. The remaining patients successfully completed 24 months of follow-up and were included in the analysis, with demographic data presented in Table I. Of the 44 patients, 24 cases were in the de novo lesion group and 20 cases in the ISR group. The mean age of the patients was 73.4 ± 7.7 years. The proportion of male patients in the ISR group was higher at 70.0%, but no statistically significant difference was observed between the 2 groups ($P = 0.06$). Approximately, one-third of the patients had concomitant chronic coronary artery disease (CAD) and cerebrovascular disease (CVD).

Regarding lesion characteristics (Table II), approximately one-third of the patients presented with foot ulcers or gangrene. The mean lesion length was 239.09 ± 120.09 mm, with 31.8% of the patients having severely calcified lesions. Among the de novo lesions, 79.2% were chronic total occlusions (CTOs) lesions, while 75% of ISR lesions were classified as Tosaka III. The mean baseline ABI was 0.32 ± 0.29. Isolated popliteal artery lesions were less common, with most lesions being isolated SFA lesions or tandem lesions involving both the SFA and popliteal artery. In the ISR group, 20.0% of lesions were complicated by stent fracture.

Endovascular Intervention Procedure and Postoperative Outcomes

As shown in Table III. The technical success rate reached 100%. Patients with Rutherford grade 5 and 6 underwent below-the-knee artery revascularization following the angiosome principle. In both

Table II. Baseline angiographic and lesion characteristics

Variable	Overall ($N = 44$)	De novo ($N = 24$)	ISR ($N = 20$)	*P*
Rutherford category				0.43
4	27 (61.3)	14 (58.3)	13 (65.0)	
5	16 (36.4)	10 (41.7)	6 (30.0)	
6	1 (2.3)	0 (0)	1 (5.0)	
Glass FPA grade				0.78
1	4 (9.1)	3 (12.5)	1 (5.0)	
2	14 (31.8)	8 (33.3)	6 (30.0)	
3	9 (20.5)	5 (20.9)	4 (20.0)	
4	17 (38.6)	8 (33.3)	9 (45.0)	
Lesion location				0.13
Superficial femoral	18 (40.9)	8 (33.3)	10 (50.0)	
Popliteal	4 (9.1)	4 (16.7)	0 (0)	
Femoropopliteal	22 (50.0)	12 (50.0)	10 (50.0)	
Average lesion length	239.09 ± 120.09	225.13 ± 188.98	256.32 ± 122.28	0.40
Severe calcification	12 (27.3)	8 (33.3)	4 (20.0)	0.49
CTO lesion	34 (77.3)	19 (79.2)	15 (75.0)	0.74
ISR				-
Tosaka II	5 (11.4)	-	5 (25.0)	
Tosaka III	15 (34.1)	-	15 (75.0)	
Stent fracture	4 (9.1)	-	4 (20.0)	-
Run-off				0.94
0	11 (25.0)	6 (25.0)	5 (25.0)	
1	18 (40.9)	9 (37.5)	9 (45.0)	
2	13 (29.5)	8 (33.3)	5 (25.0)	
3	2 (4.5)	1 (4.2)	1 (5.0)	

Values are mean ± SD or *n* (%).
ISR, in-stent restenosis; FPA, femoropopliteal artery; CTO, chronic total occlusions.

Table III. Procedural characteristics

Variable	Overall ($N = 44$)	De Novo ($N = 24$)	ISR ($N = 20$)	*P*
Technical success rate	100%	100%	100%	1
Embolic protection device usage	19 (43.2%)	8 (33.3%)	11 (55.0%)	0.15
Embolus capture rate	11 (57.9%)	5 (62.5%)	6 (54.5%)	0.48
Complications	6 (13.6%)	4 (16.7%)	2 (10.0%)	0.67
Distal embolization	3 (6.8%)	2 (8.3%)	1 (5.0%)	
Thrombosis	1 (2.3%)	0 (0%)	1 (5.0%)	
Arterial rupture	1 (2.3%)	1 (4.2%)	0 (0%)	
Puncture site hematoma	1 (2.3%)	1 (4.2%)	0 (0%)	
Flow-limited dissection	14 (31.8%)	8 (33.3%)	6 (30.0%)	0.81
Bailout stenting	17 (38.6%)	9 (37.5%)	8 (40.0%)	0.86
Simultaneous below-knee intervention	21 (47.7%)	12 (50.0%)	9 (45.0%)	0.74
Preoperative ABI	0.32 ± 0.29	0.36 ± 0.32	0.27 ± 0.24	0.48
Postoperative ABI	0.75 ± 0.20	0.76 ± 0.22	0.73 ± 0.19	0.51

Values are mean ± SD or *n* (%).
ISR, in-stent restenosis; ABI, ankle-brachial index.

groups, approximately 50.0% and 45.0% of patients, respectively, underwent concurrent treatment for below-the-knee lesions to ensure at least 1 runoff vessel. Among patients with de novo lesions and ISR lesions, 33.3% and 55.0%, respectively, used embolic protection devices, with emboli captured in 62.5% and 54.5% of cases. In the absence of embolic protection devices, distal

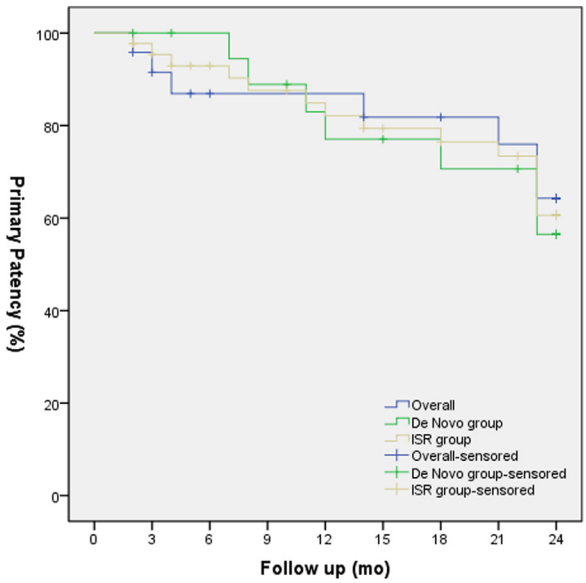

Fig. 1. 24-month primary patency rate. Kaplan–Meier curves of patients assigned to overall (*blue line*), de novo (*green line*) and ISR (*yellow line*). ISR, in-stent restenosis.

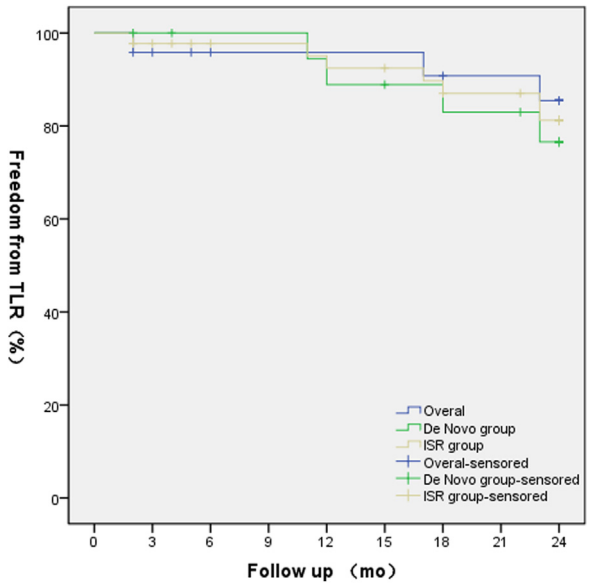

Fig. 2. 24-month rate of freedom from target lesion revascularization (TLR). Kaplan–Meier curves of patients assigned to overall (*blue line*), de novo (*green line*), and ISR (*yellow line*). ISR, in-stent restenosis.

embolization occurred in approximately 8.3% and 5.0% of cases, respectively, and was successfully managed with catheter-directed thrombolysis (CDT) combined with mechanical thrombectomy, resulting in restored distal arterial patency. One patient in the de novo lesion group experienced an intraprocedural vessel perforation, which was successfully managed with covered stent placement. In the ISR group, 1 patient developed intraprocedural thrombus formation, which was managed with urokinase thrombolysis, restoring blood flow. Flow-limiting dissections were observed in approximately 33.3% and 30.0% of patients in the de novo and ISR groups, respectively, and were successfully treated with bail-out stent placement, resulting in restored luminal patency. Postoperative ABI improved significantly in both groups, with values of 0.76 ± 0.22 and 0.73 ± 0.19, respectively, compared to preoperative values ($P < 0.05$).

In the de novo lesion group, the primary patency rates at 12 and 24 months were 86.9% and 64.3%, respectively, while in the ISR group, they were 77.0% and 56.5%, respectively (Figure 1). The rates of freedom from TLR at 12 and 24 months in the de novo lesion group were 95.8% and 85.4%, respectively, while in the ISR group, they were 88.9% and 76.6%, respectively. Although the ISR group exhibited slightly lower primary patency rates and freedom from TLR compared to the de novo lesion group, these differences were not statistically significant ($P = 0.74$), as shown in Figure 2.

During the 24-month follow-up period (Table IV), the incidence of MAEs in the 2 groups was 12.5% and 35.0%, respectively. Although the ISR group exhibited a higher rate of adverse events compared to the de novo lesion group, this difference did not reach statistical significance ($P = 0.27$). In the de novo lesion group, 10 patients and in the ISR group, 5 patients with foot ulcers and gangrene achieved wound healing within 3 months after wound debridement and dressing changes, with ulcer healing rates of 100% and 71. 4%, respectively. Only 1 patient in the ISR group underwent below-the-knee amputation 4 months after the endovascular intervention procedure due to nonhealing wounds. Additionally, 2 patients in the ISR group died from acute myocardial infarction 3 and 4 months after the procedure, respectively. There were no incidents of major bleeding during the follow-up period.

DISCUSSION

Although only 5% to 10% of PAD patients progress to CLTI, the incidence of CLTI is steadily increasing due to the aging population of PAD patients.[17] The primary objectives in the treatment of CLTI are to promote ulcer healing, prevent amputation, improve patients' quality of life, and prolong survival. Along with managing atherosclerosis-related risk factors, wound care, infection control, and

Table IV. Clinical outcomes in follow-up of 24 months

Variable	Overall ($N = 44$)	De novo ($N = 24$)	ISR ($N = 20$)	*P*
Primary patency rate (%)				0.74
12 months	82.1	86.9	77.0	
24 months	60.6	64.3	56.5	
FF-TLR(%)				0.82
12 months	92.4	95.8	88.9	
24 months	81.2	85.4	76.6	
MAEs	10 (22.7)	3 (12.5)	7 (35.0)	0.27
CD-TLR	7 (15.9)	3 (12.5)	4 (20.0)	
Major amputation	1 (2.3)	0 (0)	1 (5.0)	
All-cause death	2 (4.5)	0 (0)	2 (10.0)	

Values are mean ± SD or *n* (% Kaplan–Meier estimates).
ISR, in-stent restenosis; FF-TLR, Freedom from target lesion revascularization; MAEs, Major adverse events; CD-TLR, Clinically driven target lesion revascularization.

other supportive treatment, revascularization of target lesions plays a crucial role in restoring blood supply, which is essential for limb salvage.

For many years, surgical bypass has been the standard treatment for CLTI patients. Autogenous vein bypass offers high long-term patency rates but also carries higher surgical risks. In CLTI patients, using venous bypass with great saphenous vein as the first-line revascularization strategy has shown better outcomes in terms of composite major adverse limb events or death compared to endovascular-first revascularization strategies. However, in patients lacking suitable great saphenous vein for grafting or those unable to tolerate open surgery due to overall health conditions, outcomes between the 2 strategies are similar.[18] With the rapid development of endovascular techniques, endovascular treatment has gradually become the preferred option for CLTI.[19,20] Moreover, an increasing number of patients with TASC II C and D lesions are undergoing endovascular treatment, though restenosis remains the most important factor affecting long-term outcomes. For long-segment CTOs lesions, high failure rate of CBA alone is attributed to dissection after subintimal wire passage, severe calcified plaque compression, and elastic recoil of the vessel wall. Even after stent implantation to ensure patency, literature reports have shown an ISR rate of over 50% after 2 years after femoral artery stenting.[9,10,21] For ISR lesions, both CBA and self-expandable bare-metal stents have yielded unsatisfactory outcomes, with patency rates reported at only 28%–37% 1 year post-procedure.[22,23]

With the widespread clinical application of debulking therapy and its ''leave nothing behind'' strategy, these methods offer a promising alternative for achieving long-lasting vascular patency and reducing the need for reinterventions. Endovascular debulking devices are categorized into 4 types, as follows, based on the mechanism used to remove the atheroma: excimer laser, rotational, directional, and orbital. Directional atherectomy offers better directionality and is more suitable for eccentric stenotic lesions. It requires true lumen passage, providing immediate plaque removal effects. However, when treating complex lesions, there is a high risk of subintimal recanalization, and excessive atherectomy may result in arterial perforation. The Rotarex device is not recommended for severe calcified lesions. In the treatment of ISR lesions, there are risks of stent cutting and device entrapment.

ELA preserves branch arteries and minimizes stent implantation. This makes it particularly advantageous for complex lesions and nonstented areas, especially in the hip joint region. It also helps preserve potential anastomosis sites for future bypass procedures. ELA utilizes a xenon–chloride excimer laser that emits pulses at a wavelength of 308 nm. This wavelength induces a photochemical effect that disrupts molecular bonds within plaque tissue, resulting in tissue fragments smaller than 25 μm in diameter. These fragments are subsequently absorbed by the reticuloendothelial system, reducing the risk of microembolization. This mechanism facilitates effective plaque debulking and the removal of proliferative tissue. The 308 nm wavelength excimer laser has a penetration depth of less than 50 μm, and its emission from the circular tip of the laser catheter allows for gradual advancement through wire guidance,

thereby ensuring minimal trauma and high procedural safety.

Based on the characteristics of laser catheter mentioned above, Wissgott et al.[24] used the ''step-by-step'' crossing technique of laser catheter to recanalize the lumen in 40 cases of TASC II C and D lesions after initial unsuccessful CBA, followed by CBA treatment. The technical success rate reached 90%, and the 12-month follow-up results showed that the primary patency rate, assisted primary patency rate, and secondary patency rate were 58.9%, 67.8%, and 83.2%, respectively.[24] Numerous studies have confirmed the superiority of DCB over conventional balloon in preventing restenosis in both de novo lesions and ISR lesions of the femoral artery.[25,26] However, the use of DCB alone still carries risks of complications, such as arterial dissection and residual stenosis, akin to conventional balloon. Debulking therapy by removing plaque tissue from the vessel, reduces lesion burden, increases effective lumen area, and improves vessel compliance. Furthermore, debulking disrupts the vascular wall calcium barrier, improves drug penetration into the vessel wall, and provides optimal luminal preparation for subsequent DCB treatment. Consequently, the combination of ELA with DCB represents a promising therapeutic strategy that warrants further investigation.[27]

The potential benefits of combining ELA with DCB therapy may be attributed to several key factors. ELA can effectively loosen neointimal tissue within occluded stents, preventing recoil of neointimal tissue after balloon angioplasty. Furthermore, ELA has the capacity to vaporize thrombi commonly found in restenotic lesions, which are often characterized by heterogeneous.[28,29] By reshaping the plaque and creating endothelial micropores, ELA facilitates enhanced penetration of the drug carried by DCB into the neointimal tissue at these sites. Additionally, the kinetic energy generated by each pulse, along with the pressure waves induced by the laser, contributes to plaque reshaping, thereby minimizing potential limitations to stent expansion during subsequent DCB angioplasty. Thus, the synergistic mechanism underlying the combination of ELA with DCB therapy offers unique advantages in the treatment of femoropopliteal in-stent restenosis lesions.

A retrospective study involving 112 cases of femoral artery ISR categorized patients into 2 groups as follows: the ELA+DCB group ($n = 62$) and the ELA+CBA group ($n = 50$) based on treatment methods. The overall technical success rate reached 98%. Follow-up results at 12 months revealed that the ELA+DCB group demonstrated significant superiority over the ELA+CBA group in terms of TLR avoidance rate (31.7% vs. 58%, $P = 0.006$) and restenosis avoidance rate (72.5% vs. 50.5%, $P = 0.043$).[27] Additionally, a prospective randomized controlled study involving 48 cases of SFA ISR[29] showed that the ELA+DCB group had significantly higher patency rates at 6 and 12 months compared to the DCB group (91.7% vs. 66.7% and 58.3% vs. 37.5%, respectively, $P = 0.01$). The ELA+DCB group also exhibited a significantly lower TLR rate at 12 months compared to the DCB group (16.7% vs. 50.0%, $P = 0.01$). Moreover, the rate of major amputation events in the ELA+DCB group was significantly lower than that in the DCB group (8.0% vs. 46.0%, $P = 0.003$).[29] In this study, although limited by the relatively small sample size, no significant statistical differences were observed in baseline data and major endpoint events between the 2 groups. However, compared to the de novo lesion group, patients in the ISR group showed a decreasing trend in primary patency rate and a higher incidence of MEAs, including amputation and death. Although not statistically significant, the ISR group exhibited a trend toward poorer prognosis compared to the primary lesion group.

In this study, ELA+DCB demonstrated favorable safety profiles for both de novo and ISR lesions. The main complications associated with debulking devices include dissection formation, arterial rupture, and distal embolism. The incidence rates of flow-limiting dissections requiring bailout stent placement were 33.3% and 30.0% in the 2 groups, respectively. To minimize the occurrence of flow-limiting dissections, it is recommended to maintain the forward speed of the laser catheter at no more than 1 mm/s. If the catheter encounters resistance during ablation, it should be held in place at the site of difficulty to continue ablation, ultimately achieving plaque removal. Furthermore, adjusting energy and frequency is crucial for different types of lesions. For severely calcified lesions, increasing the frequency and appropriately reducing the energy can minimize debris shedding, reduce the incidence of flow-limiting dissections, and improve procedural success rates. During the procedure, selecting laser catheters with larger diameters within the allowable range can enhance ablation efficiency.

In our study, the incidence of arterial perforation was 2.3%. No perforations were observed in ISR lesions, likely due to stent protection, while de novo lesions exhibited a lower risk of arterial perforation. When using ELA, prioritizing true lumen recanalization is essential, as subintimal recanalization

increases the risk of arterial perforation. The appropriate frequency and energy settings should be tailored to the nature of the lesion, and saline flushing should be employed to prevent vessel wall damage caused by contrast agent activation within the vessel.

In our study, distal protection devices were used in 33.0% and 55.0% of the 2 groups, respectively, with the distal embolism rates being 8.3% and 5.0%, respectively. However, the thrombus capture rates were relatively high at 62.5% and 54.5%, respectively. The routine use of distal vascular protection devices is not recommended when using ELA. However, for patients at high risk of distal embolization, such as those with severe calcification, poor distal runoff, long-segment CTOs, and ISR lesions, the use of distal protection devices is recommended. The distal embolic event protection using excimer laser ablation in peripheral vascular interventions study confirmed that, compared to CBA, ELA does not increase the risk of distal vascular embolization.[30] Nevertheless, Shammas et al. treated 20 cases of vascular occlusion caused by subacute and chronic thrombotic emboli with ELA, all utilizing distal vascular protection devices. The results showed that ELA significantly improved vascular lumen gain, but plaque fragments larger than 2 mm in maximum diameter were found in 85.7% of the protection devices.[31] Other studies have also confirmed that thrombus and long-segment CTOs are risk factors for distal vascular embolization, underscoring the necessity of distal vessel protection when using ELA of long-segment CTOs lesions.[32–36]

ELA+DCB therapy also has certain drawbacks, including limited effectiveness in addressing calcification compared to intravascular lithotripsy. It is recommended to combine it with an embolic protection device to minimize the risk of distal embolism, although this increases procedure time and costs. True lumen recanalization is preferred, as subintimal recanalization increases the risk of perforation. Furthermore, there is a learning curve associated with this technique, with key technical considerations, such as the need for saline flushing during the procedure, to prevent vessel wall injury from contrast agent activation. In tortuous vessels, patient immobilization is essential to minimize the risk of arterial perforation.

Strengths

This study investigates the safety and efficacy of excimer laser ablation (ELA) combined with drug-coated balloon (DCB) in treating de novo and in-stent restenosis (ISR) lesions in chronic limb-threatening ischemia (CLTI) patients. A single-center retrospective analysis was conducted to assess treatment outcomes from January 2017 to December 2021. The primary endpoint was the 24-month primary patency rate, with secondary endpoints, including technical success and major adverse event (MAEs). For CLTI patients with complex lesions, including extensive occlusions and severe calcification, ELA + DCB demonstrates high technical success and favorable safety profiles in both de novo and ISR lesions. The results demonstrated a 24-month primary patency rate of 64.3% in the de novo lesion group and 56.5% in the ISR group, with no significant difference between the groups. Mid-term outcomes indicate a potential trend toward better efficacy in treating de novo lesions compared to ISR lesions. ELA combined with DCB is safe and effective for treating complex femoropopliteal artery (FPA) lesions in CLTI patients.

Limitations

This study has several limitations. Firstly, as a single-center, observational real-world study, it is subject to biases and lacks randomization, which may impact the generalizability and internal validity of the findings. Second, the absence of a control group limits the ability to draw definitive causal conclusions. Additionally, the relatively small sample size, constrained by Chinese medical insurance policies, reduces the power of the study and its applicability to broader populations. Future research should involve larger, multicenter studies with control groups to improve validity and generalizability.

CONCLUSION

For CLTI patients with complex lesions, including extensive occlusions and severe calcification, the combination of ELA and DCB demonstrates high technical success and favorable safety profiles for both de novo and ISR lesions. Mid-term outcomes indicate a potential trend toward better efficacy in treating de novo lesions compared to ISR lesions. Larger-scale studies are warranted to assess long-term outcomes and further validate these findings.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Yang Li: Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing — original draft. **Zhu Tong:** Conceptualization, Data curation, Methodology, Software, Writing — original draft.

Jianming Guo: Formal analysis, Investigation, Methodology, Software. **Lianrui Guo:** Conceptualization, Formal analysis, Resources, Software. **Yongquan Gu:** Project administration, Supervision, Validation, Writing — review & editing.

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