Endovascular Denervation Improves Limb Ischemia in Patients with Peripheral Artery Disease

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Study purpose

To evaluate the safety and preliminary efficacy of endovascular denervation (EDN) for the treatment of patients with peripheral artery disease (PAD).

Study design

This study was a prospective, single-center, open-labeled, randomized controlled trial designed to evaluate the safety and efficacy of ER combined with EDN for treating lower limb PAD. Patients who meet the following criteria were randomly assigned to the group of ER alone or ER combined with EDN. Subjects in the control group were treated with ER including PTA, DCB, and/or stenting, and patients in the ER+EDN group were treated with EDN from distal iliac artery to proximal superficial femoral artery before ER.

Sample size

1 site, 20 subjects.

The inclusion criteria:

(a) eligible subjects aged 18-75 years;

(b) clinically confirmed PAD in the lower extremities;

(c) Rutherford category II-VI.

The exclusion criteria:

(a) thrombolytic therapy performed within 30 days;

(b) patients who had undergone vascular bypass surgery before this study;

(c) allergy or contraindication of antiplatelet drugs, anticoagulants, thrombolytic drugs and contrast agents,;

(d) patients with obvious bleeding tendency, coagulation dysfunction, hypercoagulability and blood system diseases;

(e) serious liver and kidney diseases;

(f) history of hemorrhagic stroke within last month or ischemic stroke or transient ischemic attack within 2 weeks;

(g) pacemaker implants;

(h) patients who are pregnant, breast-feeding or planning pregnancy;

(i) expected survival < 24 months.

The primary endpoint was the improvement of ABI at 6-month post-procedure.

The secondary endpoints included transcutaneous oxygen pressure ($TcPO_2$), Rutherford category, numerical rating scale (NRS) score and safety.

Safety endpoints was the occurrence of trial-related adverse events that occurred during this trial. Possible adverse or serious adverse events during surgery: femoral artery stenosis, femoral artery dissection, thromboembolism (stroke or TIA), pus, hematoma at the puncture site, arteriovenous fistula requiring blood transfusion and/or surgical treatment, and other "serious" adverse events during the trial.

Statistics and Analysis

All continuous data are presented as mean ± standard deviation (SD) or median with interquartile range. Categorical data are reported as numbers and percentages. Paired *t*-test and Wilcoxon signed-rank test were used to compare parameters at baseline and the 6-month follow-up. Student's *t*-test and Mann-Whitney *U* test were used to compare parameters between the two groups. When multiple follow-ups were analyzed, one-way repeated-measures ANOVA along with Bonferroni correction were used. Differences in categorical data between the two groups were analyzed using the chi-square test. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS (version 22.0, SPSS, Chicago, USA) and GraphPad Prism 8 (GraphPad Software, San Diego, California).

Study process

Visit 1 (Subject Screening):

During this visit, cases are selected. Collect demographic data of patients, record patients' past medical history and medication, record vital signs, and collect patients' general physical examination. Blood pressure assessment, Rutherford scale, Wagner scale of diabetic foot ulcer, pain NRS score, painless walking distance PFWD examination, electrocardiogram examination, anklebrachial index (ABI), transcutaneous partial pressure of oxygen (TcPO2), foot sensory threshold measurement, thromboelastography (TEG), VUS microcirculation detection, and target vessels were performed Color Doppler ultrasound and computed tomography angiography (CTA) were used to sign informed consent for patients who met the initial criteria. Blood biochemical tests were performed, including blood routine, liver function, kidney function, urine routine, blood lipids, coagulation function, blood electrolytes, catecholamines, glycosylated hemoglobin, angiotensin II, aldosterone, insulin, glucagon, homocysteine, blood glucose.

Visit 2 (0 day, Baseline):

The visit was considered to determine the patient's admission/procedure date. For patients meeting the requirements, balloon catheter pre-dilation after DSA of the artery at the affected site, femoral popliteal artery stent implantation, balloon catheter post-dilation, and then arterial and nerve radiofrequency ablation were performed.

Visit 3 (7±2 days):

The visit was considered 7±2 days after surgery. Blood routine examination, renal function, liver function, blood electrolyte, catecholamine, glycated hemoglobin, angiotensin II, aldosterone, insulin, glucagon, homocysteine, blood pressure assessment, blood glucose, ankle-brachial index (ABI), transcutaneous partial pressure of oxygen (TcPO2), foot sensory threshold measurement, VUS microcirculation detection, pain NRS score were performed. Drug use and complications.

Visit 4 (1month±7 days):

The visit was considered 1 month ±7 days after surgery. Blood routine examination, renal function, liver function, coagulation function, blood lipid, catecholamine, glycated hemoglobin, angiotensin II, aldosterone, insulin, glucagon, homocysteine, blood pressure assessment, blood glucose, ankle-brachial index (ABI), transcutaneous partial pressure of oxygen (TcPO2), foot sensory threshold measurement, VUS microcirculation detection, Ruthe were performed rford scale, Wagner scale of diabetic foot ulcer, pain NRS score, painless walking distance PFWD examination, drug use and complications.

Visit 5 (3 months±7 days):

The visit was considered 3 months ±7 days after surgery. Blood routine examination, renal function, liver function, coagulation function, blood lipid, blood electrolyte, catecholamine, glycosylated hemoglobin, angiotensin II, aldosterone, insulin, glucagon,

homocysteine, blood pressure assessment, blood glucose, ankle-brachial index (ABI), transcutaneous partial pressure of oxygen (TcPO2), foot sensory threshold measurement, VUS microcirculation detection, blood pressure assessment, blood pressure assessment, blood pressure assessment. Rutherford scale, Wagner scale of diabetic foot ulcer, pain NRS score, painless walking distance PFWD examination, drug use and complications.

Visit 6 (6 months±7 days):

The visit was considered 6 months ±7 days after surgery. Blood routine examination, renal function, liver function, coagulation function, blood lipid, blood electrolyte, catecholamine, glycosylated hemoglobin, angiotensin II, aldosterone, insulin, glucagon, homocysteine, blood pressure assessment, blood glucose, ankle-brachial index (ABI), transcutaneous partial pressure of oxygen (TcPO2), foot sensory threshold measurement, VUS microcirculation detection, blood pressure assessment, blood pressure assessment, blood pressure assessment. Rutherford scale, Wagner scale of diabetic foot ulcer, pain NRS score, painless walking distance PFWD examination, color Doppler ultrasound, computed tomography angiography (CTA), drug use and complications.

Adverse event observation

All adverse events were observed, and detailed description of symptoms, date of occurrence, date of termination, relationship between degree and device, course of

treatment, and outcome were recorded. If fatal, disabling, teratogenic and other serious adverse events occur, regardless of whether they are related to the trial, emergency measures should be taken immediately to protect the interests of patients, and the main research unit, the ethics committee, the sponsor and the State Food and Drug Administration should be reported within 24 hours after being informed.