Investigation of ultrasonic chronic total occlusion system on a rabbit model

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Abstract

Background/Aim: Advanced treatment options are needed in chronic total occlusion (CTO), which is a special subgroup of peripheral artery disease. Endothelial damage remains a problem in the endovascular treatment of peripheral artery CTO. In our study, this subgroup was examined with an ultrasonic total occlusion system for vascular endothelial damage on an animal model.

Methods: We used twenty-four rabbits divided equally into three groups, created chronic total occlusion in the common iliac artery by applying a bioabsorbable polymer sponge, and waited four weeks for CTO formation. After four weeks, the samples obtained from the groups were examined histologically.

Results: Significantly less endothelial damage was detected in the ultrasonic total occlusion system group compared to the directional atherectomy group (P<0.05).

Conclusion: Ultrasonic atherectomy minimizes thrombus load and causes minimal endothelial damage. These findings show that the ultrasonic atherectomy method can be successfully used in CTO treatment.

Keywords: Peripheral artery, Ultrasonic chronic total occlusion system, Animal model, Endothelial injury
Introduction

Treatment of chronic total occlusion in patients with infrainguinal peripheral artery disease is particularly challenging for vascular surgery specialists. Surgical revascularization is the gold standard for CTO therapy; however, endovascular treatments have become the first choice, primarily due to the patients’ advanced age and increased comorbidities. In addition, many patients prefer endovascular treatment due to its low cost, shorter hospital stay, and low procedural morbidity [1].

Treatment procedures in segmental subtotal occlusions are relatively more precise and promising, while in CTOs, they are more ambiguous. CTOs reduce both the quality of life and daily activities of the patients and cause economic and social dependence with increased amputation rates [2].

The patients with CTO are negatively affected by many variables, from the anesthesia management to the factors included in surgical procedures. For this reason, minimally invasive methods, which have become more promising, are being used more frequently in this patient group. In our study, we compared the ultrasonic induced system with directional atherectomy in terms of endothelial damage for CTO treatment on an animal model.

Materials and methods

The ethics committee approval for our study was obtained with the decision numbered 65202830-050.04.04-331 from Sivas Cumhuriyet University Animal Experiments Local Ethics Committee. The study was conducted on three groups of eight rabbits each (New Zealand white rabbit, 6-8 months old, males weighing 3.2-3.5kg, females weighing 2.75-3kg). The rabbits were housed in equally sized cages and at a constant temperature of twenty degrees, in a laboratory environment capable of receiving twelve hours of night and twelve hours of daylight. Standard rabbit food was used in all rabbits and their water was changed every other day. Ninety milligrams per kilogram (mg/kg) subcutaneous ketamine and 3 mg/kg intraperitoneal xylazine were administered to the animals for anesthesia before surgical procedures.

Group 1 (Control group): The animals in this group did not undergo any procedures. After four weeks, samples were obtained from the iliac artery after sacrifice.

Group 2: CTO was created in the iliac artery and a directional atherectomy was performed. After four weeks, samples were obtained from the iliac artery after sacrifice.

Group 3: CTO was created in the iliac artery and atherectomy was performed with ultrasonic chronic total occlusion system. After four weeks, samples were obtained from the iliac artery after sacrifice.

The CTO model was created in Groups 2 and 3, as previously described by Suzuki et al. [3, 4]: A Bioabsorbable polymer sponge was surgically placed in the right common iliac artery to create total occlusion. At the end of four weeks, the right common iliac arteries of the rabbits were explored distal to the lesion under sterile conditions and general anesthesia. The ultrasonic atherectomy system (Metrical Medical Devices, Turkey) and directional atherectomy system (HawkOne Directional Atherectomy System, Medtronic, USA) were used in the relevant groups. Surgical procedures were performed under general anesthesia and following ethical rules. The iliac arteries of the animals were explored and an atherectomy was performed so that both the atherectomy catheters were visible and manually felt. The samples obtained after sacrifice of the animals were evaluated histopathologically and the results were compared among the three groups.

Histopathological method

After the animals were sacrificed, common iliac artery tissues were fixed in 10% neutral formalin solution. Tissues were embedded in paraffin blocks after a routine alcohol-xylol procedure. The 5 µ-thick sections placed on poly L-lysine coated slides were stained with hematoxylin-eosin. The size of the thrombotic mass was evaluated under a light microscope, and the damage to the endothelium was assessed as shown in Table 1.

Table 1: Histological scoring system

| Histopathological Score | Endothelial Damage |
|-------------------------|--------------------|
| Thrombus in the entire lumen (3) | Damage to the entire endothelium (3) |
| Thrombus in half of the lumen (2) | Damage to half of the endothelium (2) |
| Thrombus in a quarter of the lumen (1) | Damage to the quarter of the endothelium (1) |
| No thrombus (0) | No damage (0) |

Statistical analysis

The data were analyzed with the SPSS 20.00 program (StataCorp LP, College Station, TX, USA). The significance of the difference between the groups was assessed by the Kruskal Wallis test. The group that created the difference was further examined with the Mann-Whitney U test. P-values <0.05 were considered statistically significant.

Results

Common iliac artery samples significantly differed between the groups in terms of thrombosis and endothelial damage (P=0.03) (Table 2). The difference between the groups was analyzed by a post-hoc test. There was a mild thrombotic mass in the lumen of the vessels in the ultrasonic atherectomy group (P=0.03). In the directional atherectomy group, there were severe degenerative changes in the vascular endothelium. There was no thrombotic mass in the control group. Endothelial damage was severe in the directional atherectomy group compared to the other groups (Figure 1).

Table 2: Histopathological evaluation results

| Groups | Thrombosis | Endothelial Damage |
|--------|------------|--------------------|
| Group 1 (Control group), mean (SD) | 0.160±0.40^a | 1.33±0.51^a |
| Group 2 (directional atherectomy group) mean (SD) | 1.160±0.40^b | 2.160±0.40^b |
| Group 3 (Ultrasonic atherectomy group) mean (SD) | 0.330±0.51^c | 1.96±0.40^c |

 Statistical Significance

| P=0.03 | P=0.03 |

^a: Significant difference between Groups 1 and 2, ^b: Significant difference between Groups 1 and 3, ^c: Significant difference between Groups 2 and 3, p<0.05 for all.

Figure 1: A and B: Mild thrombotic mass (□, *). (x10, x40. Common iliac artery. H-E). C and D: Slightly degenerated vascular endothelium (□, arrowhead) (directional atherectomy group). E and F: Severe degenerated vascular endothelium (□, arrowhead) (Control group).
Discussion

The main purpose of treatment in CTOs is to provide blood supply to the distal part of the occluded segment. Therefore, the gold standard treatment method today is surgical revascularization. However, the current patient population is usually made up of the elderly and the added disease burden is high [5].

Treatment of CTO in patients with infrainguinal peripheral artery disease remains particularly challenging for vascular surgery specialists. Although surgical revascularization continues as the gold standard in CTO treatment, endovascular treatment methods have often become a priority due to the advanced age of the patients and increased comorbidities [6]. In addition, low cost, shorter hospital stays, and less procedural morbidity puts endovascular treatment in the foreground [1].

Balloon angioplasty alone has been shown to have a 5-year patency rate in the treatment of coronary artery CTO [7]. In the endovascular treatment of peripheral artery CTO, the chance of passing the lesion can often be low. Most of the time, this rate is between 40-60%, but various studies report over 90% success [8, 9].

While the treatment procedures in segmental subtotal occlusions are relatively more precise and promising, they are more ambiguous in CTOs. CTOs hinder the quality of life and daily activities of the patients, also causing economic and social dependence with increased amputation rates [2].

The elderly patient group with increased comorbidities is adversely affected by many factors, both related to anesthesia and surgical procedures. For this reason, minimally invasive methods are currently used more frequently in this patient group with satisfactory results. The atherectomy methods involved in the treatment of CTO due to peripheral artery disease include directional atherectomy, radiofrequency atherectomy, and intravascular ultrasound-guided atherectomy [10-12]. Each of these methods is applicable with different techniques [13-17]. As it is possible to pass through the atherosclerotic plaque that causes CTO directly, some devices allow recanalization with reentry by subintimal advancement [6, 13-19]. In our study, we observed that ultrasonic atherectomy was superior to directional atherectomy, resulting in less endothelial damage and thrombotic burden. Minimum endothelial damage helps prevent a recurrence, and the smallest thrombus burden is an indicator of positive response in the acute phase. The difficulty of long-term follow-up in animal experiments and the inability to create one-to-one human models necessitate long-term clinical studies. No studies have compared various atherectomy methods in terms of vascular endothelial damage in the literature. The absence of endothelial damage is essential for the effectiveness of treatment, long-term preservation of patency, and prevention of recurrence. With this study, important findings were obtained in comparing the endothelial damage between directional atherectomy and ultrasonic CTO systems. The minimum endothelial damage and thrombus load in ultrasonic atherectomy devices stand out as an advantage.

Limitations

There are several limitations to our study. First, only two of the atherectomy methods were compared. Second, conducting an animal experiment limited the chance of a long-term follow-up.

Conclusion

We observed that ultrasonic atherectomy minimizes thrombus load and endothelial damage. These findings show that the ultrasonic atherectomy method can be successfully used in CTO treatment.

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