

## Dynamics of Instrumental and Morphological Parameters of Stimulation of Regional Blood Flow in Patients with Critical Ischemia of the Lower Extremities

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### Abstract

**Objective:** To study the dynamics of instrumental and morphological parameters of stimulation of regional blood flow in patients with critical lower limb ischemia against the background of distal steno-occlusions of the arteries.

**Materials and Methods:** The studies were conducted in 79 patients with CILE. In 48 patients, conventional conservative and surgical treatment was carried out without reconstruction and indirect stimulation (control group) In 31 patients, stimulation of regional blood flow was carried out by revascularizing osteotriphalangectomy with intramedullary laser irradiation, in which intravenous laser irradiation and cytokine therapy with Ronoleukin (main group) were used in the perioperative period. The following parameters of regional arterial and venous blood flow were studied: These parameters were compared with those of 48 healthy individuals (reference group). In the main group, 18 patients studied the dynamics of morphological and immunohistochemical parameters of some parameters of angiogenesis in the soft tissues of the limb (the density of CD34-positive microvessels, the density of VEGF-positive microvessels, the density of microvessels with a free lumen and a diameter of 4.1 mkm ).The "conditionally control" group consisted of soft tissues of 21 practically healthy individuals.

**Results:** In patients of the control group during inpatient treatment and after 3-4 months. There was only a tendency to improve regional arterial and venous bleeding (except for regional systolic pressure. In patients of the main group during inpatient treatment, a thorough improvement in the arterial and venous links of regional blood flow was observed. 3-4 months after discharge from the clinic, continued stimulation of regional blood circulation was revealed. Morphological and immunochemical studies revealed an increase in the density of CD34+-positive, VEGF-positive microvessels and density of microvessels with an open lumen in the soft tissues of the ischemic limb.

**Conclusion:** If it is impossible to perform direct revascularization, the proposed method of revascularizing osteotriphalangectomy with intramedullary laser irradiation using intravenous laser irradiation and cytokine therapy with Ronoleukin in the perioperative period significantly improves the instrumental parameters of regional blood flow, stimulates neoangiogenesis and increases the density of microvessels with a free lumen in soft tissues in patients with critical ischemia of the lower extremities.

**Keywords:** Dynamics; Blood Flow; Microvessels

## Introduction

In the surgical treatment of critical ischemia, the leading role is played by open, endovascular and hybrid operations. However, with distal lesions of the arteries, it is not always possible to perform direct revascularization or thrombotic complications are common. accompanied by an aggravation of the previous critical ischemia. In such cases, preference is given to indirect revascularization operations to stimulate regional arterial and venous blood flow [1-4]. Studies on the stimulation of angiogenesis in ischemic soft tissues in critical lower limb ischemia are isolated and the data obtained are often contradictory [5,6]. For objective assessment of angiogenesis, the density of CD34 and VEGF-positive microvessels, the density of microvessels with a free lumen and a diameter of 4.1 mkm are studied [8-11].

## Objective

To study the dynamics of instrumental and morphological parameters of stimulation of regional blood flow in patients with critical lower limb ischemia (CILE) against the background of distal steno-occlusions of the arteries.

## Materials and Methods

The studies were conducted in 79 patients with CILE. In 48 patients, conventional conservative and surgical treatment was carried out without reconstruction and indirect stimulation (control group) In 31 patients, stimulation of regional blood flow was carried out by revascularizing osteotrepation with intramedullary laser irradiation (ROT with IMLI), in which intravenous laser irradiation and cytokine therapy with Ronoleukin (main group) were used in the perioperative period. The following parameters of regional arterial and venous blood flow were studied: regional systolic pressure (RSP) standing and lying down, regional systolic pressure gradient (GRSP), postocclusive venous pressure (POVP) standing and lying down, postocclusive venous pressure gradient (GPOVD), venous arterial index (VAI) standing and lying down. These parameters were compared with those of 48 healthy individuals (reference group). In the main group, 18 patients studied the dynamics of morphological and immunohistochemical parameters of some parameters of angiogenesis in the soft tissues of the limb. The following parameters were studied: the density of CD34-positive microvessels in 1.0 mm<sup>2</sup>, the density of VEGF-positive microvessels in 1.0 mm<sup>2</sup>; The density of microvessels with a free

lumen and a diameter of 4.1 mkm in 1.0 mm<sup>2</sup>. The “conditionally control” group consisted of soft tissues of 21 practically healthy individuals. Parametric and nonparametric statistical analyses were carried out to determine the parameters t, p,  $\chi^2$ , p, r.

## Results

Upon admission to the clinic, in comparison with the reference group, a sharp violation of regional arterial and venous blood flow was revealed. In the control group at the end of inpatient treatment there was a tendency to stimulani. min 3-4 months after discharge from the hospital stimulation of blood flow was also unreliable (except RSP : t = 1.98; p < 0.05). In the study group, there was a significant increase RSP in standing and lying down (t = 2.20; p < 0.05 and t = 3.52; p < 0.01), POVP lying high air flow (t = 2.03; p < 0.05), a significant decrease in standing and lying VAI, standing POVP (respectively t = 3.76; p < 0.001; t = 2.28; p < 0.05 and t = 2.56; p < 0.05). 3-4 months after discharge from the hospital, the stimulation of regional blood flow continued significantly. A significant dependence (p < 0.05-0.01-0.001; r = 0.4-0.5-0.7) of blood flow stimulation from ROT with IMLI was also revealed.

In the “conditionally control” group, the density of CD34-positive microvessels in 1.0 mm<sup>2</sup> was 36.2 ± 3.2. Upon admission to the clinic in the main group, the density of CD34-positive microvessels of 1.0 mm<sup>2</sup> decreased by 30.4% (25.2 ± 2.0; t = 2.83; p < 0.001), and after treatment increased by 27.0% (32.0.0 ± 2.5; (t = 2,12; p < 0,05). In the “conditionally control” group, the density of VEGF-positive microvessels in 1.0 mm<sup>2</sup> was 35.0 ± 3.0. Upon admission to the clinic in the main group, the density of VEGF-positive microvessels in 1.0 mm<sup>2</sup> decreased by 30.0% (24.5 ± 2.1; (t = 2.87; p < 0.01), and after treatment increased by 34.7% (33.0.0 ± 2.9; t = 2.37; p < 0.05). In the “conditionally control” group, the density of microvessels with a free lumen and a diameter of 4.1  $\mu$ m in 1.0 mm<sup>2</sup> was 25.0 ± 2.2. Upon admission to the clinic in the main group, the density of microvessels with a free lumen and a diameter of 4.1 mkm of 1.0 mm<sup>2</sup> decreased by 48.9% (12.9 ± 1.0; (t = 5,1; p < 0,001); and after treatment increased by 49.6% (19.3 ± 1.5; t = 3.55; p < 0.01).

## Discussion

The use of ROT with IMLI with the use of intravenous laser irradiation and cytokine therapy with Roncoleukin in the

perioperative period stimulates regional blood flow in patients with CILE against the background of distal steno-occlusion, which is evidenced by the positive dynamics of the results of instrumental studies [1,3,4]. Improvement in instrumental studies occurs as a result of an increase in the density of CD34 and VEGF-positive microvessels in 1.0 mm<sup>2</sup>, the density of microvessels with a free lumen and a diameter of 4.1 μm in 1.0 mm<sup>2</sup> [10,11].

### Conclusion

If it is impossible to perform direct revascularization, the proposed method of ROT with IMLI using intravenous laser irradiation and cytokine therapy with Roncoleukin in the perioperative period significantly improves the instrumental parameters of regional blood flow, stimulates neoangiogenesis and increases the density of microvessels with a free lumen and a diameter of 4.1 μm in 1.0 mm<sup>2</sup> in soft tissues in patients with critical ischemia of the lower extremities.

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