

Assessment of hemodynamics of the hand arteries and skin microcirculation in Dupuytren's contracture stages 3 to 4 of before and after surgical treatment with the use of Ilizarov transosseous fixation

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Purpose Hemodynamics of the hand arteries and microcirculation of the skin in patients with Dupuytren's contracture in grades 3-4 at the stages of treatment with the use of transosseous fixation was analyzed. **Materials and methods** Skin microcirculation using laser Doppler flowmetry as well as the microhemodynamics of the arcus palmaris superficialis and the digital arteries using pulse Doppler sonography were studied in 12 patients before surgery and following two to 11 months after the surgery of selective fasciectomy, arthrolysis and transosseous fixation. The state of the arteries of the palmar aponeurosis was verified histologically using light microscopy of paraffin sections of the surgical material. **Results** Before surgery, seven out of 12 patients had vasoconstriction of the digital arteries on the ulnar side of the hand and the palmar arch. Histologically, the arteries of the palmar aponeurosis were of small caliber (four or less layers of smooth muscle cells in the media) with signs of muscle hyperplasia and remodeling of the elastic membrane; larger arteries featured damage to the internal elastic membrane and neointimal thickening. Eight to 10 days after the intervention, there were no hemodynamic signs of vasoconstriction; volumetric systolic velocity was increased three times. At long-term follow-up after the surgery, the index of peak blood flow was increased 1.5 times ($p < 0.05$) relative to the values of the immediate postoperative period. **Discussion** In the postoperative period, the reactivity of the vessels of the precapillary flow was reduced and the spastic-stasis type of microcirculation prevailed. However, the potential of the microvascular bed was not impaired. **Conclusion** The method applied for treatment of Dupuytren's contracture provides correction of the deformity of the hand and elimination of vasoconstriction which is the most important trigger in the pathogenesis of fascial fibromatosis.

Keywords: Dupuytren's contracture, microhemodynamics, histology

ВВЕДЕНИЕ

Dupuytren's disease (palmar fascial fibromatosis) is a progressive flexion contracture of the metacarpophalangeal and proximal interphalangeal joints of the fingers and the interfalangeal spaces of the hand [1]. The disease leads to a significant decrease in the activity and quality of patients' life, what determines its social significance [2], depending on the ethnic and age group [3]. The pathological process is tumor-like fibroproliferative growth of tissues of palmar and finger aponeurosis with the formation of knots and cords that infiltrate the dermis of the skin, causing it to become retracted, thicken and shorten longitudinal fascial structures. It limits the extension of the fingers and displaces vasculonervous bundles of fingers [4, 5].

The etiology of palmar fascial fibromatosis remains unknown. However, all generally accepted risk factors such as abnormal genes, chronic trauma to the hand during manual labor, alcoholism and smoking [6], as well as association with aging, diabetes and HIV [7] lead, in one way or another, to

narrowing of microvessels with subsequent tissue ischemia and formation of free radicals. Stimulated by hypoxia and lipid peroxidation products, proliferation of fibroblasts and myofibroblasts around narrowed microvessels is considered a key event in the pathogenesis [8].

Despite numerous studies of conservative methods of treatment [9], surgery is the only effective method to eliminate Dupuytren's contracture. The contracture of the metacarpophalangeal joint of more than 30 degrees, and the presence of contractures of the proximal interphalangeal joint of any degree are generally accepted indications for surgical treatment [10]. However, a significant number of patients start seeking surgical assistance when they have a more pronounced shortage of extension (over 90 degrees).

Among the numerous options of surgical treatment, partial fascioectomy is a method of choice, which, when carefully performed, provides a guaranteed removal of pathologically changed tissues and the fewest number of complications. In particular, a

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meta-analysis of 277 publications devoted to large cohorts of patients ($n > 100$) showed that the incidence of complications and recurrences was significantly less after open partial fascioectomy than after needle aponeuroectomy [11].

In pronounced contractures, excision of the pathologically altered palmar aponeurosis and arthrolysis is not enough to eliminate the extension deficit. The choice of additional means of treatment, splinting [12] or external transosseous dynamic fixation [13, 14], remains controversial, since both approaches may be associated with additional complications. The first option may result in necrosis of

mobilized skin flaps and development of finger flexion deficit, and the second one in infection around wires. Information about the conditions of hemodynamics of the hand arteries and skin microcirculation at the stages of treatment of Dupuytren's contracture is not available in the literature. However, such data are necessary not only to assess its quality and results, but also to develop additive therapy.

The **purpose** of the study is the analysis of hemodynamics of the arteries of the hand and skin microcirculation in patients with Dupuytren's contracture of grades 3-4 at the stages of treatment with the use of transosseous fixation.

MATERIAL AND METHODS

The study involved 12 patients with bilateral palmar fascial fibromatosis who had surgical treatment at the RISC for RTO in 2017–2018. The age of patients ranged from 45 to 68 years. The contracture in the affected hand corresponded to the third stage in seven patients, and in five patients the grade was 3 to 4 according to the classification of R. Tubiana [15]. The surgical technique included the excision of the affected areas of the palmar aponeurosis, arthrolysis of the finger joints and transosseous fixation of the hand with the Ilizarov mini-apparatus. For this purpose, the mounting of basic supports was performed separately on each phalanx of the finger. If a single-moment maximum extension of the finger did not cause ischemic disorders of the integumentary tissues, the supports of the apparatus were interconnected in the position of the maximum extension achieved. Within two weeks (the period of wound healing), the apparatus served for fixation of extension. If acute extension was impossible or unsuitable, the contracture was eliminated according to the principle of gradual distraction. To do this, the apparatus assembly included traction rods and hinges. In flexion contracture of the joints of several rays, the apparatus allowed the elimination of the contracture of each joint separately, without limiting the range of movements of the other fingers. The direction of distraction was regulated so as not to cause compressive or distracting efforts along the joint lines. The extension rate was set individually, on average 0.5 mm four times a day (180°, half a turn of the nut around the traction rod). When pain in the hand and/or signs of significant tension of the skin and scars developed, the extension of the finger was temporarily suspended (usually, 7–10 days after surgery). Once full extension was achieved,

the dynamic fixation was initiated which consisted in fixation of the joints at night and their training with exercises in the daytime. On average, dosed extension and dynamic fixation continued three weeks, after which the device was dismantled, the wires were removed and a course of physiotherapy, physical therapy, and massage was indicated.

For the pathomorphological study, the areas of palmar aponeurosis and subcutaneous tissue excised during the operation were fixed in 10 % neutral formalin, fixed for 5 days in a mixture of 20 g/L solutions of glutamic and paraformaldehyde on phosphate buffer (pH 7.4) with the addition of 1 g/L picric acid, and then according to standard methods, enclosed in paraffin blocks. Longitudinal and transverse sections, 5–7 μm thick, were produced on a Reichert microtome (Austria), and then stained with hematoxylin and eosin. For the differentiated detection of elastic and collagen fibers, some sections were stained according to Weigert-Van Gieson or by Masson's three-color method. Light microscopy of sections and their digital microphotography were performed on a hardware-software complex, consisting of a Carl Zeiss Primo Star USB microscope, a trinocular digital camera, a UCMOS 3.1 megapixel video camera, and a MicroCapture Ver 6.6 image capture and processing program.

Evaluation of skin microcirculation was carried out using laser Doppler flowmetry (LDF) on a BLF21 installation (Transonic Systems Inc., USA). The laser with a wavelength of 780 nm and a measurement depth of 0.5–1.0 mm was used. The probe was mounted on the palmar surface of the hand at two sites of pronounced fibromatosis and was attached using a double-sided adhesive membrane. The LDF

measurements were expressed in arbitrary perfusion units (PU). To study the mechanisms of endothelium-dependent dilatation, a local 3-minute arterial ischemic test was used with an occlusive cuff on the forearm (**Fig. 1, a**). After recording the data at rest (Kkrest, PU) and 3-minute ischemia (Kkpeak, PU), the peak blood flow index was calculated ($IPK, \% = Kkpeak / Kkrest \times 100 \%$); $\Delta t \text{ sec}$ – latency of vasodilator response; half-recovery period of capillary blood flow ($T1/2, s$); the duration of the hyperemic response; intensity (area) of the hyperemic response [16].

The study of the arcus palmaris superficialis and digital arteries was performed by pulse Doppler sonography (USDG) using a Minimax-Doppler K ultrasound diagnostic device (SP Minimax, St. Petersburg, Russia) with a high-frequency sensor operating at frequency of 20 MHz, and area of working surface of 3.14 mm² (**Fig. 1, b**). Post-computer signal processing was estimated

with standard automatic conclusion: systolic blood flow velocity (Vs, cm/sec); mean linear blood flow velocity (Vm, cm/sec); Vad – maximum diastolic velocity along the mean velocity curve (cm/sec); Qas (ml/sec), Qam (ml/sec) – volume systolic and average velocities along the curve of average velocity; RI – resistance index (Purcello); PI – pulsatility index (Gosling). The indicated indices are relative values that do not have units.

Statistical data processing was performed using the Microsoft Excel-2000 Excel and AtteStat data analysis package using non-parametric statistics methods and a significance level of $p \leq 0.05$. The quantitative characteristics of the samples are presented in the table as a median with a level of 25÷75 % percentiles; the number of observations (n) is equal to the number of studies. The statistical significance of the differences was determined using the Wilcoxon test.

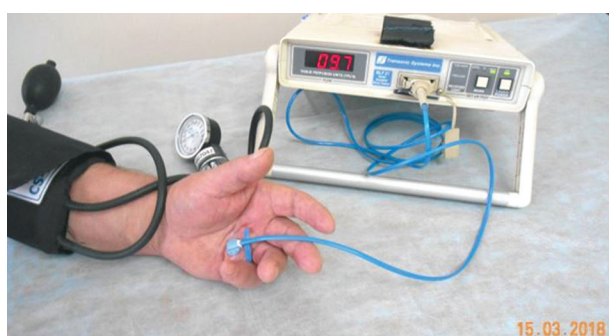


Fig. 1 Recording: a – LDF, b – USDG

RESULTS

Complete elimination of contracture was achieved in 10 patients and two patients had partial correction. At follow-up examinations after the period from two to 11 months, a partial loss of the correction achieved was detected in two patients.

Histological examination of the arteries of the palmar aponeurosis in surgical material samples showed that small-caliber arteries (four or less layers of smooth muscle cells in the middle sheath) mostly had passable lumen (**Fig. 2**), but were partially and completely obliterated. Most of the arteries had hyperplastic muscular sheath (**Fig. 2, a, b**), periadventicular edema and fibrosis (**Fig. 2, a-c**), some with signs of elastolysis and remodeling of the elastic membrane (**Fig. 2, c**), the areas of its lysis are determined and duplications of the internal elastic membrane).

Smooth muscle cells in the state of overcontraction were often encountered in the

media of large arteries (**Fig. 3, a**). The border between media and intima was not clear; the inner elastic membrane was fragmented, and neointimal cells were present in the luminal lining. In some arteries, they were cord-like, overlapping the lumen (**Fig. 3, b**). In other arteries, despite significant polymorphocellular myointimal thickening and luminal deformation, a new luminal lining was formed around the lumen, represented mainly by endotheliocytes (**Fig. 3, c**).

After surgery, following 8-10 days, the indices of a three-minute arterial ischemic test (Table 1) did not have significant differences from the preoperative ones; but there was a tendency to an increase in the half-recovery period and a decrease in the intensity of the hyperemic response. At long-term follow-up, a statistically significant increase in the peak blood flow index relative to the immediate postoperative period was documented.

According to the Doppler ultrasound, $V_{ad} < 1$, $V_m / V_s < 50 \%$, $PI > 1.4$ were recorded in seven out of 12 patients in the preoperative period. The largest decrease in V_{ad} и V_m/V_s was recorded in the affected area (aa. Digitales palmares propriae of fingers 4 and 5; arcus palmaris superficialis).

After 8–10 postoperative days and at long term, all patients showed positive V_{ad} values (see example, Fig. 4). In addition, following 8 to 10 days after surgery, a threefold significant increase in Q_{as} was revealed as compared with the preoperative value.

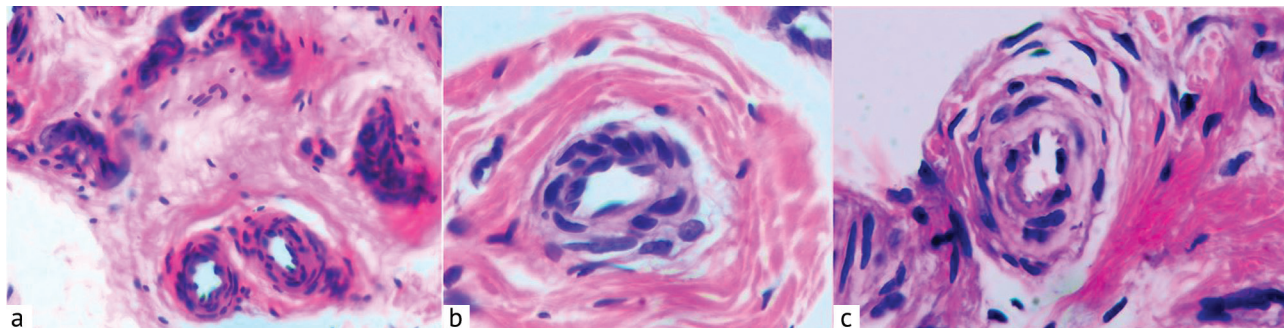


Fig. 2 Small caliber arteries in the sections of palmar aponeurosis of patients with Dupuytren's contracture. Hematoxylin-eosin staining. Magnification: a – 500 ×; b, c – 1250 × (oil immersion)

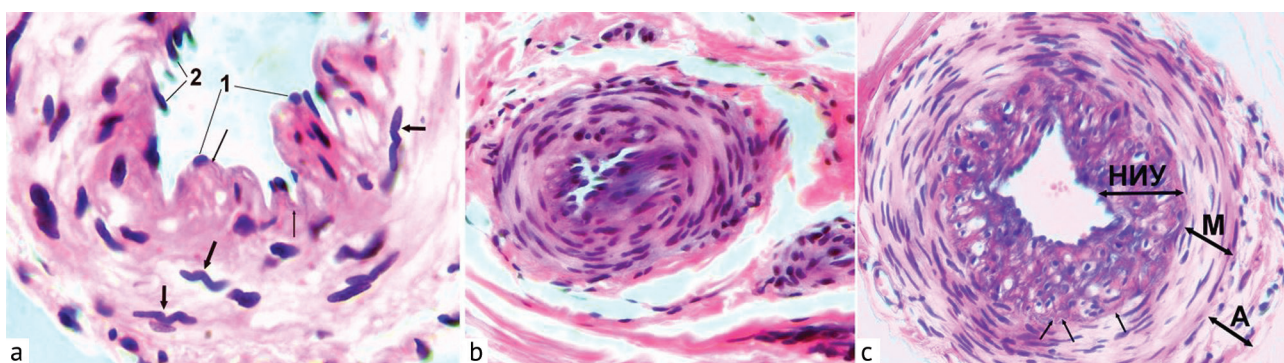


Fig. 3 Perforated arteries of palmar aponeurosis in patients with Dupuytren's contracture; staining with hematoxylin-eosin. Magnification: a – 1250 × (oil immersion); b, c – 500 ×. 1 – endotheliocytes; 2 – neointimal cells. Thin arrows show residual fragments of the lysing internal elastic membrane; thick arrows show nuclei of the re-contracted smooth muscle cells. A – adventitia; M – media, NIT – neointimal thickening

Table 1

Estimated arterial three-minute ischemic test in patients with Dupuytren's contracture

Parameters	Before surgery (n = 28)	8-10 days post-surgery (n = 13)	Follow-up after 2 to 11 months (n = 11)
Capillary flow, baseline (KKrest, PU)	6.65 (4.35÷8.8)	7.3 (5.85÷7.4)	5.3 (4.0÷5.5)
Capillary flow, peak (KKpeak, PU)	21.9 (17.1÷29.9)	20.0 (11.5÷20.2)	18.3 (14.0÷24.4)
Index of peak flow (IPF, %)	302 (211÷514)	221 (192÷222)	388 (301÷528) $P^1=0.002$
Latency of hyperemic response, sec	20 (15÷90)	20 (17÷20)	20 (20÷20)
Half-recovery period (T1/2, сек.)	52.5 (30÷105)	105 (32.5÷127.5)	70 (40÷120)
Duration of hyperemic response, sec	475 (210÷617)	480 (207÷600)	430 (210÷607)
Intensity (area) of the hyperemic response, units	3225 (1216÷5407)	1470 (862÷2082)	2257 (1717÷3256)

Note: 1 – significance of difference $p < 0.05$ relative to the values before surgery

Table 2

Indicators of Doppler sonograms of the hand arteries, normal and at the treatment stages of Dupuytren's contracture

Parameters	Norm (n = 15)	Before surgery (n = 78)	8-10 days post-surgery (n = 42)	Follow-up after 2 to 11 months (n = 54)
V_s	16.98 (13.5÷20.2)	13.29 (11.0÷19.5)	15.46 (12.9÷18.52)	15.36 (12.75÷21.71)
V_m	9.37 (7.8 ÷ 10.2)	7.39 (6.39 ÷ 8.52)	7.84 (7.04 ÷ 10.08)	8.28 (6.79 ÷ 11.21)
V_{ad}	0.517 (0.130÷0.951)	0.00 (-0.345÷0.345)	0.172 (0.000÷0.775)	0.215 (0.000÷0.689)
Q_{as}	2.43 (1.46÷3.08)	2.00 (1.09÷3.97)	6.27 (4.02÷9.18) $P^1=0.00002$	5.03 (1.98÷7.22)
Q_{am}	1.05 (0.62÷1.16)	0.525 (0.266÷0.898)	0.747 (0.531÷1.19)	0.799 (0.508÷1.61)
PI	1.2 (0.97÷1.37)	1.48 (1.23÷1.87)	1.32 (1.01÷1.58)	1.43 (1.09÷1.8)
RI	0.76 (0.63÷0.91)	0.76 (0.71÷0.84)	0.72 (0.65÷0.80)	0.75 (0.67÷0.82)

Note: 1 – significance of difference $p < 0.05$ relative to the values before surgery

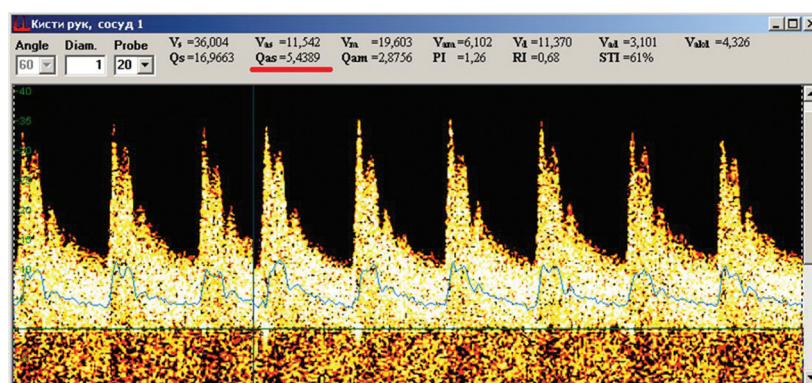


Fig. 4 Doppler sonogram of Arcus palmaris superficialis of patient K., 68 years old; postoperative day 8

The source of blood flow to the fascial-dermal complex of the palm, the superficial palmar arch, supplies the worm-like muscles, tendons of the long muscles of the forearm and wrist, and also is the origin of the common digital arteries [17]. The Doppler study calculated parameters of vasoconstriction ($V_{ad} < 1$, $V_m / V_s < 50\%$, $PI > 1.4$) in 67 % of patients, recorded not only at the level of the finger arteries of the ulnar side of the hand, but also at the level of the palmar arch itself. In healthy volunteers, signs of retrograde blood flow and negative diastolic velocity values had been previously detected by us only in cold test conditions [18], and a decrease in all USDG parameters of the phalangeal arteries of the fingers in consequences of cold injury [19].

In this study, the hemodynamic signs of vasoconstriction of the palmar arch and digital arteries in patients with Dupuytren's contracture were consistent with the results of a pathological study of the arteries perforating the palmar aponeurosis and supplying the subcutaneous tissue of the palm, as well as the arterioles entering its layers [20]. Constrictive remodeling of these vessels was manifested not only by the overcontracted condition of the smooth muscle elements, but also by the hyperplasia of the media, by remodeling of its elastic components, including the inner elastic membrane, and by pronounced neointimal thickening in some of the larger arteries. Such changes inevitably lead to a decrease in vessel lumen and an increase in the ratio of intimal thickness to media thickness that are quantitative criteria for accelerated vascular aging, observed in arterial hypertension and insulin-dependent diabetes [21]. In patients with systemic lupus erythematosus, an increased intima / media ratio was detected even with normal blood pressure [22].

Our patients with Dupuytren's contracture, already following 8–10 days after surgery and at long term, had positive values of diastolic velocity in all cases and a threefold increase in volumetric systolic velocity. This is a diagnostic criterion of the compensatory adaptive response, reflecting a decrease in the reactivity of the microvasculature of the precapillary link (functional sympatholysis in arterioles perfusing tissues) and formation of a collateral network of arterio-venous anastomosis (AVA). The functional value of AVA is to adapt the blood circulation of tissues to the postoperative state, when capillary and filtration pressure increases, tissue overhydration occurs and the speed of nutritive blood flow in hyperhydrated tissues decreases due to increased venous and intrastitial pressure [23].

Microcirculation indicators according to LDF findings before and immediately after surgical treatment (KKrest and KKpeak) did not have significant differences; the vascular bed reserve capacity was not distorted and met the criteria for maintaining high microcirculation potential of the skin [24]. LDF values of the functional ischemic test fourteen days after the operation were not statistically different from the values before the operation; but there was a tendency to an increase in the half-recovery period of blood flow with a decrease in the intensity of the hyperemic response, which is also interpreted as a decrease in the reactivity of the precapillary microvessels. This dynamics of indicators corresponds to the predominance of the spastic-stasis hemodynamic microcirculation type [25]. The mechanisms of regulation of blood vessels in response to a surgical trauma are based on two ways: functional sympatholysis in the smallest arterioles and preservation of sympathetic

constriction in the above-located arterioles and first-order arteries. It enables to maintain a sufficient level of oxygen consumption in the tissues [26].

An increase in the reserve capacity of the vascular bed was observed at follow-ups two to 11 months

after the operation due to a decrease in the basic capillary blood flow. Diagnostic criteria of metabolic disorders or vascular endothelial dysfunction [27] were not revealed either in the immediate or long-term examination after the operation.

CONCLUSION

The study proves that surgical treatment of Dupuytren's contracture in stages 3 to 4 with the use of Ilizarov transosseous fixation provides both an effective

correction of the deformity of the hand and elimination of vasoconstriction, being the most important trigger in the pathogenesis of fascial fibromatosis.

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