Research Article

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Treatment of Patients with Thrombosis of the Arteries of the Lower Extremities and Coronavirus Infection

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ABSTRACT The course of severe coronavirus infection is accompanied by hypercoagulability with micro- and macroangiopathy, which may be the cause of arterial and venous thrombosis. In March, 2021 — May 2021, 14 patients with COVID-19 and acute ischemia of the lower extremities due to arterial thrombosis were operated in the Infectious Pavilion of the N.V. Sklifosovsky Research Institute for Emergency Medicine. Retrombosis in the immediate postoperative period developed in 4 patients (26.7%). The amputation at the level of the thigh was performed in 2 patients (13.3%) due to the development of ischemic gangrene. The mortality was 71.4%, 10 patients died. The main cause of death was the progression of multiple organ failure in the course of severe viral-bacterial pneumonia. The best results were obtained with a combination of open surgery and endovascular technique, performing hybrid operations.

Keywords: coronavirus infection, arterial thrombosis

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ALV – artificial lung ventilation
CAD – coronary artery disease
CT – computed tomography
COPD – chronic obstructive pulmonary disease
ECG – echocardiography
ECMO – extracorporeal membrane oxygenation
EF – ejection fraction
LV – left ventricle
MSCT – multislice computed tomography
MSCTA – multislice computed tomography - angiography
SPPA – systolic pressure in the pulmonary artery

There are many reports that the course of severe coronavirus infection is accompanied by hypercoagulability with micro- and macroangiopathy. This is confirmed by laboratory data: the levels of D-dimer, prothrombin and fibrinogen are significantly increased [1, 2]. In addition, the severe form of the course *of COVID*-19 is accompanied by significant anti-inflammatory reaction with an increase in interleukins and cytokines, which also contributes to the development of intravascular coagulopathy. Many cases of venous thrombosis have been described in patients with *COVID*-19, while there are only a few reports of arterial thrombosis.

MATERIALS AND METHODS

There were 14 patients with coronavirus infection caused by *COVID*-19 and acute ischemia associated with thrombosis of the arteries of the lower extremities, admitted and operated on in the infectious diseases building of the N.V. Sklifosovsky Research Institute for Emergency Medicine from March to May, 2021. There were 11 men (78.6%) and 3 women (21.4%). The age of the patients ranged from 47 to 77 years. The mean age was 66.4±6.7 years. All patients were transferred from other medical institutions where they were treated for viral pneumonia. The condition of all patients was regarded as "severe". According to computed tomography (CT), lung damage in 6 patients (42.9%) was 75% or more (CT-4), lung tissue damage was 50% (CT-3) in 4 patients (28.6%), 25% (CT-2) in 3 (21.4%) and only in one patient (7.1%) lung damage was less than 25% (CT-1). All patients had respiratory failure. Eight patients (57.1%) were admitted with oxygen support, 4 (28.6%) were put on a ventilator (ALV).

The mean time from the onset of *COVID-19* disease to the development of thrombosis and ischemia of the lower extremities was 13.2 days. In all patients, acute arterial thrombosis developed during the stay and treatment in the infectious diseases departments of other hospitals. After establishing the diagnosis and consulting an angio surgeon, the patients were transferred to the N.V. Sklifosovsky Institute. The median time between diagnosis and transfer was 12 hours. In the majority of patients (85.7%), acute limb ischemia developed suddenly without any vascular history. Only 2 patients (14.3%) had a history of disturbing intermittent claudication, and one patient had previously been operated on, he had aortofemoral bifurcation prosthesis for Leriche syndrome. All patients had acute ischemia of the extremities of 2 A-B degrees.

Damage level:

— iliac artery, 5 (31.2%);
— femoral artery, 3 (18.7%);
— popliteal artery, 7 (43.8%) (two patients had thrombosis of the popliteal arteries on both sides);
— branch of the aorto-femoral bifurcation prosthesis, 1 (6.3%).

Most patients were admitted with a distal lesion, thrombosis of the popliteal arteries (43.8%).

Accompanying illnesses:

— coronary artery disease (CAD), 9 (64.3%);
— hypertension, 12 (85.7%);
— diabetes mellitus, 6 (42.9%);
— chronic obstructive pulmonary disease (COPD), 7 (50.0%);
— chronic kidney disease, 3 (21.4%);
— obesity, 3 (21.4%);
— myocardial infarction, 1 (7.1%);
— mesenteric thrombosis, 1 (7.1%).

All patients underwent Doppler ultrasonography upon at admission, which confirmed arterial thrombosis. In all studies, there was no restoration of blood flow distal to the site of occlusion. In 5 cases (35.7%), multispiral computed tomography (MSCT) of the abdominal aorta, iliac and arteries of the lower extremities was performed. It should be noted that 4 out of 5 studies revealed a multilevel lesion: in addition to occlusion of the arteries below the inguinal ligament, stenosis of the abdominal aorta or iliac arteries from 50 to 90% was detected due to parietal thrombotic masses with preserved pulsation on the femoral artery (Fig. 1).

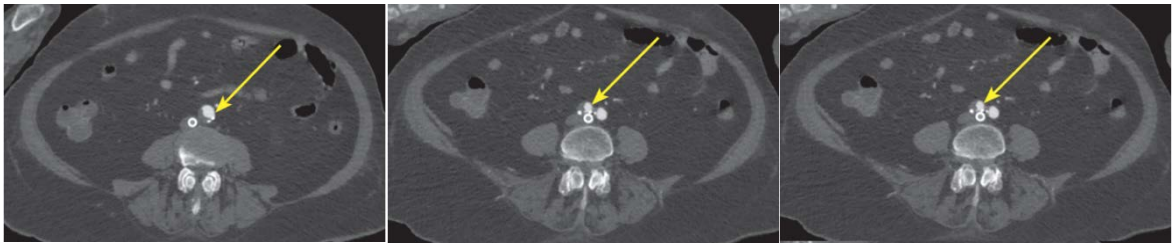

Fig. 1. Multislice computed tomography and angiography. Non-occlusive parietal thrombus of the abdominal aorta, passing to the initial section of the right common iliac artery (the patient has a cannula for extracorporeal membrane oxygenation)

RESULTS

The average time from admission to surgery was 43±8.5 hours. Two patients (14.3%) were operated on immidiately (within 2 hours), 9 patients (64.3%) were operated urgently (24–48 hours), 3 patients (21.4%) were operated later (2–7 days). This spread in time is explained by the fact that all patients with limb ischemia 2A were treated with conservative rheological anticoagulant therapy, and despite that, the ischemia progressed, which was the reason for the operation.

In this work, we analyzed the results of only operated patients (table).

Table

Operations performed and results

Operation	*n*	%	Repeated trombosis		Amputation		Mortality	
			n	%	*n*	%	*n*	%
Thrombectomy	9	60.0	2	22.2	2	22.2	8	88.9
Thrombendarterectomy with patch plasty	2	13.3	1	50.0	–	–	1	50.0
Endovascular thrombectomy with plasty and stenting	1	6.7	1	100	–	–	–	–
Endovascular mechanical aspiration thrombectomy	1	6.7	–	–	–	–	1	100
Hybrid operation	2	13.3	–	–	–	–	–	–
TOTAL	15	100	4	26.7	2	13.3	10	71.4

In all cases of thrombectomy, the access, depending on the level of thrombosis, was either in the femoral triangle to the common femoral artery or to the popliteal artery by tibiomedial access. The arteries were minimally atherosclerotically changed, so thrombectomy was performed from a transverse arteriotomy followed by a twisting suture. In 2 patients, where the arteries were markedly atherosclerotically altered, thromboendarterectomy was performed with synthetic patch plasty. In case of thrombosis of the distal popliteal artery and leg arteries, one patient underwent mechanical and aspiration thrombectomy, and one patient underwent endovascular thrombectomy with balloon angioplasty and stenting. In 2 patients admitted with a multilevel lesion, stenosis of the iliac artery or aorta was diagnosed due to parietal thrombotic masses and thrombosis of the arteries below the inguinal ligament. They underwent hybrid operations from access to the femoral arteries. Using a double-lumen Fogarty catheter, clots were maximally removed from the proximal and distal sections, the distal part was washed with saline solution with heparin, then, after comparative intraoperative angiography, selective thrombectomy was performed from the lower leg arteries and, if required, stenting was performed.

The repeated thrombosis in the immediate postoperative period developed in 4 patients (26.7%). The amputation at the level of the thigh was performed in 2 patients (13.3%) due to the development of ischemic gangrene. The mortality was 71.4%, 10 patients died. The main cause of death was the progression of multiple organ failure in the course of severe viral-bacterial pneumonia.

We report is a clinical case of successful treatment of a patient with *COVID-19* infection and thrombosis of the arteries of the right lower limb and acute ischemia 2A-B stage.

A 47-year-old male patient A. was admitted with complaints of pain in the right foot at rest, a feeling of numbness, coldness in it.

He fell ill with coronavirus infection 2 weeks before hospitalization, when chills appeared, body temperature increased to 39-40°C. Outpatient CT showed a clear picture of viral pneumonia CT-2. He was admitted to one of the temporary hospitals in Moscow via ambulance. After 2 weeks from the moment of inpatient treatment, there were acute complaints of pain and numbness in the right foot, so he was transferred for further treatment to the infectious diseases building of the Research Institute for Emergency Medicine.

History of life: colds, childhood infections. No allergies. Upon admission:

Height/body length: 172 cm; body weight: 84 kg; temperature: 37.6°C. General condition: severe. Skin color: normal color. Skin moisture: normal. Peripheral edema: absent.

The state of the respiratory system.

Inhalations: no. SPO_2: 95 %;

The state of the cardiovascular system.

Systolic pressure: 140 mm Hg; diastolic pressure: 85 mm Hg; heart rate (HR): 105 beats/min; rhythmic.

Condition of the gastrointestinal tract.

Abdomen on palpation: soft. No tenderness.

The state of the genitourinary system.

Urination: independent. Urine color: yellow (normal). Diuresis: normal.

Local status: blood circulation in the left lower limb is fully compensated, the pulse is distinct at all levels. The right foot and lower leg are cyanotic, cool to the touch. Active movements in the foot are limited, there is no sensitivity in the fingers. The calf muscles are soft, moderately painful on compression. The pulse is determined to the level of the popliteal artery, distally is not determined.

Upon examination:

Chest CT scan: ground glass changes; consolidation; reticular changes on the ground glass background.

The percentage of involvement of the lung parenchyma: the right lung, 50-75%; left lung, 50-75%.

Background changes: axillary and mediastinal lymph nodes are not enlarged.

Bone-traumatic and bone-destructive changes were not revealed.

The mediastinum is not displaced, not expanded.

The structures of the mediastinum are differentiated.

The heart and large vessels are usually located, not dilated.

No contents were found in the pericardial cavity.

No contents were found in the pleural cavities.

Conclusion: CT-signs of infiltrative-inflammatory changes in both lungs, severe severity (CT-3, right lung — 50–75%, left lung — 50–75%), with a high probability of viral etiology.

Doppler ultrasound: Echo-signs of minimal atherosclerosis of the arteries of the lower extremities, on the right: occlusion of the popliteal artery with thrombotic masses without restoring blood flow in the distal third.

ECG (echocardiography): signs of impaired contractility of the myocardium of the left ventricle (LV) were not detected, ejection fraction (EF) 66%. SPPA (systolic pressure in the pulmonary artery) 21 mm Hg.

MSCTA (angiography): CT-signs: stenosis of the common iliac artery on the right, more than 90%; stenosis of the internal iliac artery on the right up to 50%; occlusion of the deep femoral artery on the right from the level of the upper third; occlusion of the popliteal artery on the right without further restoration of blood flow (Fig. 2).

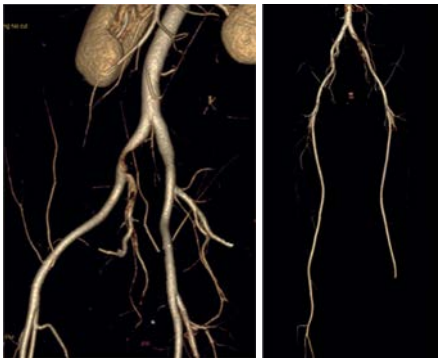

Fig. 2. Computed angiography. Parietal thrombus in the common iliac artery on the right, passing to the initial sections of the internal and external iliac arteries, occlusion of the right popliteal artery

Due to the deterioration of blood circulation in the right lower limb, ischemia progressed, active movements in the foot disappeared, the patient was urgently operated on 48 hours after admission.

A hybrid intervention was performed in the X-ray endovascular operating room. Under local anesthesia with novocaine 0.5%, 100 ml, the femoral arteries were isolated in the right femoral triangle. The latter are soft, pulsating. Transverse arteriotomy of the common femoral artery. The Fogarty probe passed in the proximal direction for 20 cm, then an obstacle was noted. The probe passed 20 cm into the deep artery of the thigh, and a small amount of thrombotic masses was removed. A good retrograde blood flow was obtained. The Fogarty catheter passed 65 cm into the superficial femoral artery, and a dense old clot was removed in the form of a cast. Good retrograde blood flow was noted. Further, given the impossibility of passing the probe in the proximal direction, an introducer was installed in the right mobilized common femoral artery, and angiography was performed. Angiography: thrombosis of the right common iliac artery with narrowing of the lumen up to 95%, occlusion of the popliteal artery in the distal segment (Fig. 3).

Fig. 3. Angiograms. Critical stenosis of the right common iliac artery and occlusion of the popliteal artery

The diagnostic guidewire through the stenosis in the common iliac artery was passed to the terminal aorta. Mechanical recanalization of the common iliac artery on the right was performed using the AngioJet system. Dilatation of the common iliac artery was performed using an *Advance* 9.0–40 mm balloon catheter. Next, a Protege 10–60 mm stent was implanted. The stent was fully extended, there was no dissection at the intervention site. Next, the *AQUATRACK* guidewire, supported by a diagnostic catheter, was inserted behind the site of occlusion of the anterior tibial artery. Multiple direct catheter aspiration from the anterior tibial artery was performed using a *JR 6F* guide catheter, and a small amount of thrombotic masses was obtained; however, no blood flow was obtained.

The AQUATRACK guidewire, supported by an Admiral 2.5/3.0-210 mm balloon catheter, was inserted behind the site of occlusion of the posterior tibial artery. Multiple direct catheter aspiration from the anterior tibial artery was performed using a *JR 6F* guide catheter, and a large number of thrombotic masses were obtained. The blood flow through the artery was restored up to the arteries of the foot (Fig. 4).

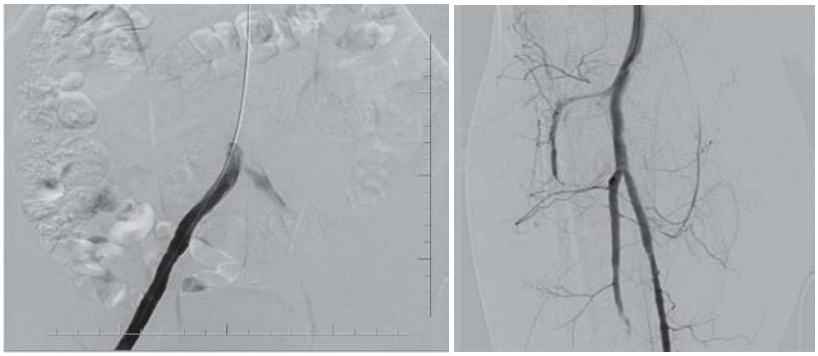

Fig. 4. Angiograms after stent installation in the right common iliac artery and thrombus extraction from the arteries of the leg

The postoperative period was uneventful. The wound healed by primary healing. The sutures were removed on the 8th day. The circulation in the right lower limb was completely compensated, the pulse was on the posterior tibial artery. The patient was discharged home in satisfactory condition after completing treatment for coronavirus infection.

DISCUSSION

Arterial thrombosis can also be a complication of severe *COVID*-19 coronavirus infection, in addition to the well-known and described ones, such as acute respiratory failure, septic shock, multiple organ failure, venous thrombosis. According to various authors, arterial thrombosis develops in approximately 4.4% of severe patients with *COVID*-19 [1]. The mechanisms of arterial thrombosis in these patients have not yet been elucidated. There is evidence suggesting that diffuse endothelial injury and infiltration by inflammatory cells occur in *COVID-19 [2]. COVID*-19 is also accompanied by hypercoagulability and is characterized by an increase in the level of *D* - dimers, prothrombin and fibrinogen and, consequently, the time of clot formation is reduced [3, 4]. These two factors, endothelial damage and hypercoagulability, together with prolonged immobilization of seriously ill patients, just constitute the Virchow triad, which provides a plausible explanation for the development of arterial thrombosis. It is noteworthy that in our observation, arterial thrombosis developed in 85.7% of patients without obvious signs of atherosclerosis and without a vascular history, which is also confirmed by other authors [5]. Also, according to our data, the majority of patients were elderly (mean age 66.4 years), which can also be explained by an increase in plasma concentrations of fibrinogen, coagulation factors V, VII, VIII, and X with age [6, 7]. The prevailing majority in our study were men (78.6%). Arterial thrombosis in the general population is generally more common in men than in women, due to differences in hormonal and genetic patterns, and it has also been found that men are more likely to get *COVID*-19 [8]. All patients had comorbidities, which is supported by the available data that chronic diseases increase the risk of infection and the severity of *COVID*-19 [9].

In our observation, the proportion of amputations was 13.3% and the mortality rate was 71.4% compared with 18% loss of limb and 50% of deaths reported in other studies in hospitalized patients with *COVID*-19 and acute lower limb ischemia [10]. At the same time, mortality in patients with arterial thrombosis of the arteries of the lower extremities in the population without *COVID*-19 is only 5–9% [11].

CONCLUSION

Arterial thrombosis occurs in approximately 4% of critically ill patients with *COVID*-19. Hypercoagulability in patients with *COVID*-19 is a predictor of arterial thrombosis and significantly worsens the prognosis for saving the limb and life of patients. Most of the patients are men, elderly people with comorbidities. Arterial thrombosis in coronavirus infection is characterized by simultaneous localtion in different arterial pools or there is a multilevel lesion. Considering such a clinical picture, the severity of the condition, the presence of concomitant pathology, it is advisable for patients with *COVID*-19 and arterial thrombosis to perform hybrid operations in order to minimize the volume of surgical intervention: maximally perform a thrombectomy using an open method, and restore blood flow through the arteries of the lower leg endovascularly.

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