**Research Article**

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# The Effectiveness of Compression Therapy in the Prevention of Venous Thromboembolic Complications in Patients With COVID-19

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**BACKGROUND** The main method for preventing thrombotic complications in patients with coronavirus infection is anticoagulant therapy (ACT). However, its use is not always possible, in particular in patients with bleeding. The only method of prevention in this case is elastic compression (EC) of the lower extremities.

**AIM OF STUDY** To evaluate the effectiveness of lower extremity EC for the prevention of venous thromboembolic complications (VTEC) in patients with a new coronavirus infection.

**MATERIAL AND METHODS** The study was approved by the local Ethics Committee of the Ryazan State Medical University of the Ministry of Health of Russian Federation and registered on the ClinicalTrials.gov platform (identifier NCT05143567). The study included 69 patients without prophylactic compression (Group 1) and 65 patients who used prophylactic compression stockings (Group 2). The patients were treated in the covid hospital from July to November 2021. All patients had verified coronavirus infection, they took ACT and underwent ultrasound duplex scanning of the veins of the lower extremities upon admission, in the intensive care unit and upon discharge. We assessed the frequency of venous thromboembolic complications (VTEC), hemorrhagic complications, and mortality. To assess the severity of bleeding, the classification of the Committee of the International Society on Thrombosis and Haemostasis (ISTH) was used.

**RESULTS** In patients without prophylactic compression (Group 1) there were 7 VTEC cases (10.14%); deep vein thrombosis (DVT) — 4 (5.8%), pulmonary embolism (PE) — 3 (4.3%). All 6 cases (8.7%) with PE were fatal. It was noted that 2 cases of PE (2.8%) were verified upon autopsy, and not clinically.

In patients of the 2nd group with the use of elastic compression, the overall incidence of VTEC was only one case (1.6%). When analyzing the frequency of bleeding in the 1st group, there was one pulmonary bleeding (1.4%), in the 2nd group there was also one case of intense intermuscular hematoma (1.6%). Significant bleeding was observed in one patient (1.4%) of the 1st group, and in 3 (4.8%) cases of the 2nd group. The minor bleeding was observed in 11 patients (15.9%) of the 1st group, and in 8 (12.7%) patients of the 2nd group. The mortality during hospitalization was 11 (15.9%) cases in patients of the 1st group (without EC) and 7 (11.1%) in patients of the 2nd group (with EC) (p=0.419).

**CONCLUSIONS** The mortality in patients with coronavirus infection without compression therapy is higher than in patients with compression stockings (p=0.419). Patients wearing compression stockings in the hospital had a low incidence of VTEC (1.6% of cases in group 2 versus 10.14% of cases in group 1, p=0.039). The study groups had the same frequency of bleeding (group 1 — one case (1.4%), group 2 — one case (1.6%). The use of preventive compression at the inpatient stage of treatment of a new coronavirus infection makes it possible to prevent VTEC in patients with bleeding when anticoagulant therapy is not possible.

**Keywords:** new coronavirus infection, thrombosis, bleeding, elastic compression, venous thromboembolic complications, COVID-19

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ACT – anticoagulant therapy
ALV – artificial lung ventilation
APTT – activated partial thromboplastin time
BA – bronchial asthma
CAD – coronary artery disease
COPD – chronic obstructive pulmonary disease
CRP – C-reactive protein
CT – computed tomography
CVD – chronic venous disease
DIC – disseminated intravascular coagulation
DVT – deep vein thrombosis
EC – elastic compression
ESR – erythrocyte sedimentation rate
HFOT – high flow oxygen therapy
ICU – intensive care unit
NIV – non-invasive ventilation
PCR – polymerase chain reaction
PCT – procalcitonin
PE – pulmonary embolism
PICS – post-infarction cardiosclerosis
PT – prothrombin time
UFH – unfractionated heparin
VTEC – venous thromboembolic complications
X-ray CT – X-ray computed tomography

## RELEVANCE

*COVID*-19-associated coagulopathy, which underlies the pathogenesis of the pandemic of the last three years, is a consequence of an inflammatory response to the viral load, which leads to the activation of immune complexes [1]. At the beginning of the disease, an adaptive mechanism is activated, hemostasis is activated and fibrin is deposited. Further exposure to the virus leads to the formation of a hyperinflammatory response due to the cytokine storm and macrophage activation syndrome [2].

These pathogenic mechanisms lead to thrombosis at the microcirculatory level, a high incidence of venous thromboembolic complications (VTEC) and mortality [1, 2].

The main method of preventing VTEC is anticoagulant therapy (ACT). However, it is not always possible. For example, in patients with large and significant bleeding. The only method of prevention in this case is elastic compression (EC) [3]. This method is underestimated in real clinical practice, but its use is justified by the fact that patients are on prolonged bed rest for oxygen therapy.

**Aim of study:** to evaluate the effectiveness of the use of EC of the lower extremities in the prevention of VTEC in patients with a new coronavirus infection.

## MATERIAL AND METHODS

The clinical study was conducted on the basis of the "covid hospitals" of the Regional Clinical Hospital and the Ryazan Emergency Hospital from July to November, 2021. The study included 69 patients without EC (Group 1) and 65 patients who used prophylactic compression (stockings) *˝Tonus Elast˝* (group 2). The study was approved by the local ethics committee of the FSBEI HE RyazSMU of the Ministry of Health of Russia and registered on the *ClinicalTrials.gov platform* (identifier *NCT* 05143567).

Inclusion criteria for the study: men or women over 18 who were treated in a covid hospital for bilateral viral pneumonia according to X-ray computed tomography (CT) of the chest; with suspected *COVID*-19 or confirmed novel coronavirus infection according to the PCR test (polymerase chain reaction); signed a voluntary consent to the use of preventive compression stockings. The selection of knitwear (stockings) was carried out individually according to the measurements of the circumference of the upper third of the thigh and lower leg, the lower third of the lower leg, growth indicators and according to the manufacturer's instructions.

Exclusion criteria from the study: men or women under 18 years of age with decompensated somatic pathology, pregnancy or lactation (women), as well as patients who are contraindicated in the use of compression therapy. Contraindications to elastic compression: heart failure of a high functional class, condition after bypass surgery on the arteries of the lower extremities, systolic pressure at the ankle level less than 70 mm Hg, severe peripheral neuropathy, dermatitis, allergic reactions to components of compression products, thinned skin over the bones deformations.

Patients were treated according to the Interim Guidelines of the Ministry of Health of the Russian Federation "Prevention, diagnosis and treatment of a new coronavirus infection" [4]. Patients underwent complex therapy aimed at treating the underlying and concomitant diseases, as well as correcting the conditions caused by the severity of the disease and the treatment being carried out.

Drugs from various pharmacological groups were prescribed: anticoagulant, antiviral, antibacterial, hormonal therapy, drugs from the group of monoclonal antibodies, proton pump blockers, insulin therapy according to indications, antitussives, infusion therapy up to 1500 ml per day, oxygen insufflation depending on the level of saturation and severity underlying disease. All patients underwent duplex ultrasound scanning according to generally accepted protocols for examining the veins of the lower extremities upon admission, upon transfer to the intensive care unit (if any), and upon discharge [5]. We assessed the frequency of VTEC, hemorrhagic complications, and mortality at the inpatient stage of treatment. The classification of the Committee of the International *Society on Thrombosis and Haemostasis* (*ISTH)* was used to assess the severity of bleeding [6].

The statistical analysis of the data was carried out using the program *Statistica* 10 for Windows. Quantitative variables were described by the following values: the number of cases, absolute and relative values (percentages). The accepted level of statistical significance is $p < 0.05$. Numerical data are presented as arithmetic mean and standard deviation.

## RESULTS

Clinical and anamnestic characteristics of patients included in the study are presented in Table 1. The average age of patients without knitwear (Group 1) was 56.1±14.4 years, with knitwear (Group 2) — 57.5±11.9 years. By gender: in the group using knitwear, there were 61 women (96.8%) and two men (3.2%). In the group without EC (Group 1), there were also more women — 46 (66.7%); men — 23 (33.3%) (Table 1).

*Table 1*

**Clinical and anamnestic characteristics of patients**

| Index | 1st group, *n* =69 | 2nd group, *n* =63 | *R* |
|---|---|---|---|
| Age | 56.13±14.4 years | 57.5±11.9 years | 0.548 |
| Men | 23 (33.3%) | 2 (3.2%) | 0.001 |
| Women | 46 (66.7%) | 61 (96.8%) | |
| Positive PCR test upon admission | 55 (79.7%) | 55 (87.3%) | 0.217 |
| Severity of COVID -19 | | | |
| – mild | 9 (13.04%) | 1 (1.6%) | 0.013 |
| – moderate | 30 (43.5%) | 23 (36.5%) | 0.415 |
| – severe | 21 (30.4%) | 31 (49.2%) | 0.028 |
| – extremely severe | 9 (13.04%) | 8 (12.7%) | 0.841 |
| CT-1 | 17 (24.6%) | 6 (9.6%) | 0.022 |
| CT-2 | 33 (47.8%) | 28 (44.4%) | 0.697 |
| CT-3 | 16 (23.2%) | 26 (41.2%) | 0.026 |
| CT-4 | 3 (4.3%) | 3 (4.8%) | 0.909 |
| Oxygen requirement | 57 (83%) | 55 (87%) | 0.453 |
| ICU | 14 (20.3%) | 8 (12.7%) | 0.242 |
| Transferred from ICU | 3 (4.3%) | 1 (1.6%) | 0.602 |
| HFOT | 3 (4.3%) | 1 (1.6%) | 0.602 |
| NIV | 3 (4.3%) | 1 (1.6%) | 0.602 |
| ALV | 8 (11.6%) | 6 (9.5%) | 0.699 |
| Bed day | 16.6±10.14 | 20.9±13.52 | 0.015 |
| Mortality | 11 (15.9%) | 7 (11.1%) | 0.419 |

Notes: PCR, polymerase chain reaction; CT, computed tomography; ICU, resuscitation and intensive care unit; HFOT, high-flow oxygen therapy; NIV, non-invasive ventilation of the lungs; ALV, artificial lung ventilation

According to the severity of coronavirus infection in both groups, patients with moderate and severe forms of the disease were most common, and the severe form was more common in patients of the 2nd group (21 (30.4%) in the 1st group, 31 (49 .2%) in the 2nd group, $p = 0.028$). The severity of the disease is directly related to the volume of lung tissue damage according to CT of the chest: group 1 is CT-3 in 16 patients (23.2%), group 2 is CT-3 in 26 (41.2%), $p = 0.026$.

Respiratory support for all patients was performed according to the recommendations of the Russian Federation of Anesthesiologists and Resuscitators [7]. Oxygen insufflation was used in 83% of cases in group 1 and in 87% of cases in group 2. Fourteen patients (20.3%) were transferred to the intensive care unit without the use of EC (Group 1), and in the group using EC, 8 patients (12.7%) patients were transferred to the ICU.

In the intensive care unit, methods were used to help delay the switch to artificial lung ventilation (ALV). Thus, high-flow oxygen therapy (HFOT) was used in all patients in the ICU, but due to the severity of the condition, not all of them remained with it, and there was a need for non-invasive lung ventilation (NIV). Three patients (4.3%) of the 1st group and one (1.6%) patient of the 2nd group remained on HFOT. These patients were transferred from the ICU to the wards. With the ineffectiveness of NIV, violation of hemodynamics and consciousness, mechanical ventilation was performed. All patients in both NIV and ALV groups died. Thus, the switch to mechanical ventilation and NIV was accompanied by high mortality in the ICU.

When analyzing comorbidity, it was noted that all patients were statistically comparable to each other ($p$ >0.05). The most common in hospitalized patients are: cardiac disesase (hypertension), type 2 diabetes mellitus and obesity (Table 2).

*Table 2*

**Concomitant disorders in patients of the 1st and 2nd groups**

| Related diseases | 1st group ($n$ =69) | 2nd group ($n$ =63) | *R* |
|---|---|---|---|
| **Hypertensive disease** | **47 (68)** | **46 (73%)** | 0.336 |
| Coronary artery disease | 10 (14%) | 7 (11%) | 0.376 |
| PICS | 3 (4%) | 4 (6%) | 0.449 |
| Rhythm disturbance | 4 (6%) | 2 (3%) | 0.384 |
| **Diabetes** | **24 (35%)** | **21 (33%)** | 0.504 |
| Lung diseases (COPD, BA) | 4 (6%) | 5 (8%) | 0.443 |
| Rheumatological diseases | 4 (6%) | 3 (5%) | 0.551 |
| Oncological diseases | 4 (6%) | 5 (8%) | 0.443 |
| Gastroenterological diseases | 3 (4%) | 4 (6%) | 0.449 |
| **Obesity** | **19 (28%)** | **15 (24%)** | 0.387 |
| CVD | 7 (10%) | 6 (10%) | 0.569 |
| History of VTEC | 2 (3%) | 3 (5%) | 0.457 |

Notes: CAD, coronary artery disease; PICS, postinfarction cardiosclerosis; COPD, chronic obstructive pulmonary disease; BA, bronchial asthma; CVD, chronic venous disease; VTEC, venous thromboembolic complications

Diabetes mellitus in patients with coronavirus infection is exacerbated by the use of hormone therapy. And such a factor as obesity contributes to an increase in respiratory failure.

According to the dynamics of laboratory parameters in both groups, high values of CRP and ferritin were noted , which indicates the presence of active inflammation in the body (Table 3). Also, at admission, all patients had coagulopathy with an increase in the level of fibrinogen and D-dimer. When patients were admitted to the intensive care unit, an increase in the concentration of inflammatory markers (leukocytosis, CRP, ferritin, procalcitonin) was observed. In the coagulogram, an increase in activated partial thromboplastin time (APTT), prothrombin time was observed, which may be associated with intravenous heparin infusion through an infusion pump. Also, all patients had hyperglycemia, associated with the high incidence of type 2 diabetes mellitus or was a consequence of taking glucocorticosteroids. Upon discharge from the hospital, there was a decrease in markers of inflammation and hemostasis. Thus, according to our data, the most sensitive routine markers of inflammation and coagulation are the concentration of CRP, WBC, procalcitonin, ferritin, fibrinogen, D-dimer.

*Table 3*

**The dynamics of laboratory parameters in patients**

| Indicator (norm) | Upon admission | | *R* | IN THE ICU | | *R* | Discharge/death | | *R* |
|---|---|---|---|---|---|---|---|---|---|
| | 1st group | 2nd group | | 1st group | 2nd group | | 1st group | 2nd group | |
| RBC 3.5–5.5x10 $^{12}$/l | 4.6 (3.4–6) | 4.6 (3.1–5.5) | 0.973 | 4.7 (4.2–5.8) | 4.4 (2.2–5.3) | 0.781 | 4.4 (2.8–5.9) | 4.3 (3.2–5.9) | 0.476 |
| Hemoglobin 110–160 g/l | 139 (85–188) | 135.4 (90–170) | 0.429 | 143 (118–176) | 126.1 (72–158) | 0.074 | 133.9 (78–181) | 126.4 (90–185) | 0.699 |
| Platelets 100–400x10 $^{9}$/l | 216.1 (34–520) | 244.5 (55–690) | 0.149 | 246.7 (57–426) | 231.8 (34–401) | 0.358 | 244.2 (34–568) | 249.5 (39–474) | 0.567 |
| WBC 4.0–10.0x10 $^{9}$/l | 7.2 (2–32.6) | 8.3 (2–23.5) | 0.206 | **11.9 (6.2–20.1)** | **17.8 (1.4–41.8)** | 0.004 | 12.5 (3.5–69) | 12.9 (2–43.8) | 0.437 |
| ESR 2–18 mm/h | 24.3 (1–63) | 22.3 (1–60) | 0.479 | 14.1 (1–30) | 34.7 (14–55) | 0.001 | 12.9 (1–60) | 19.3 (1–77.1) | 0.042 |
| Glucose 3.5-6.3 mmol/l | 8.8 (2–38.2) | 8.63 (3.6–24.6) | 0.361 | **19.1 (4.1–33)** | **7.4 (1.9–16.3)** | 0.109 | **11.3 (2–31.4)** | **10.7 (2.8–40.4)** | 0.422 |
| CRP ⩽5 mg/l | 78.7 (6.6–356) | 75.7 (3.2–205.5) | 0.531 | **73.4 (10–197)** | **105.2 (16-200)** | 0.372 | 28.3 (0.3–197.9) | 20.1 (1–207) | 0.031 |
| Ferritin 10–200 mkg/l | 843.2 (310–1064) | 720.9 (312–1040) | **0.013** | **1128 (562–1467)** | **1089 (428–1367)** | 0.458 | 903.7 (570–1059) | 484.9 (292–945) | 0.024 |
| PCT ⩽0.5 ng/ml | 0.104 (0.02–0.4) | 0.101 (0.002–0.4) | 0.793 | **1.56 (0.036–14.7)** | **1.1 (0.068–3.9)** | 0.493 | 0.25 (0.02–4.6) | 0.09 (0.04–0.48) | 0.124 |
| APTT 12.6–28.7 sec | 39.6 (19.9–155.9) | 33.9 (21.1–70.2) | **0.012** | **74.4 (26.6–155.9)** | **40.8 (27.8–75)** | 0.110 | 42.9 (17.4–158) | 35.4 (11.8–105.5) | 0.271 |
| PT 9.8–12.2 sec | 12.1 (9.4–20.1) | 12.5 (10–21.5) | 0.138 | **15.2 (11.2–25.2)** | **17.3 (11.8–45.6)** | 0.329 | 15.7 (9.4–36.8) | **18.9 (9.8-39)** | 0.457 |
| Fibrinogen 1.8–3.5 g/l | **3.6 (1.1–7.4)** | **4.4 (1.1–7.8)** | **0.003** | 3.3 (1.1–8) | **4.6 (1.2–8)** | 0.224 | 2.5 (1.1–7.2) | 3.12 (1.01–7.3) | 0.009 |
| D-dimer ⩽0.5 mg/l | 1.2 (0.9–5.5) | 0.56 (0.12–2.1) | **0.008** | 3.23 (0.6–5) | 1.2 (0.6–2.4) | 0.033 | 1.4 (0.2–5.6) | 0.6 (0.12–4.4) | 0.001 |

Notes: ESR, erythrocyte sedimentation rate; *CRP*, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; APPT, activated partial thromboplastin time

All patients received a therapeutic dose of heparin upon admission. A "starting" high dose of anticoagulants was prescribed to patients with obesity, high initial levels of D-dimer and fibrinogen, and a history of VTEC. In patients without EC (Group 1), a therapeutic dose of heparins was prescribed in 46 patients (67%), an increased dose was prescribed in 23 (33%) patients, and in patients using EC (Group 2), a therapeutic dose was prescribed in 43 patients ( 63%), increased — in 20 (37%), $p = 0.993$ (figure).

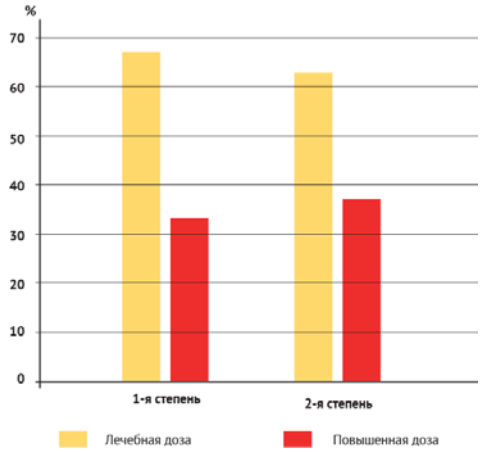


Figure. Anticoagulant therapy in patients of study groups

According to the results of the inpatient stage of treatment, it should be noted that mainly thrombotic events occurred in patients without the use of prophylactic compression stockings. VTEC in patients without knitwear (Group 1) occurred in 7 patients (10.14%), and in patients of the 2nd group using EC, the total incidence of VTEC was only one case (1.6%), which was presented by PE of small branches found at autopsy ($p = 0.039$).

Deep vein thrombosis (DVT) — 4 cases (5.8%, $p = 0.052$), PE — 3 (4.3%). All 6 patients (8.7%) with PE were fatal. The proximal border of a thrombus in patients with DVT without PE was found in 2 patients (2.8%) in the ileofemoral segment, and in 2 (2.8%) patients it was found in the femoropopliteal segment. In one patient with PE, thrombotic masses were located in the superficial veins and in the femoral vein. It was noted that 2 cases of PE (2.8%) were verified at autopsy, and not clinically.

Thus, in patients using prophylactic compression stockings, a low incidence of VTEC has been proven. The presence of VTEC is directly proportional to the severity of the disease and contributed to high mortality. Mortality in patients of the 1st group (without knitwear) was 11 patients (15.9%), in the 2nd group (with knitwear) — 7 (11.1%).

When analyzing the frequency of hemorrhagic complications, it was noted that large and significant bleeding was observed in the intensive care unit. In group 1, there was one pulmonary hemorrhage (1.4%), in group 2 there was also one (1.6%) case of intense intermuscular hematoma, which required blood transfusion (Table 4).

*Table 4*

**Thrombotic and hemorrhagic complications**

| Patient groups | VTEC | | | | Hemorrhagic complications | | |
|---|---|---|---|---|---|---|---|
| | DVT | PE | | | Major | Significant | Minor |
| | | Total | PE+ DVT | PE without DVT | | | |
| 1st group ( *n* =69) | 4 (5.8%) | 3 (4.3%) | 1 (1.4%) | 2 (3%) | 1 (1.4%) | 1 (1.4%) | 11 (15.9%) |
| 2nd group ( *n* =63) | 0 (0%) | 1 (1.6%) | 0 (0%) | 1 (1.6%) | 1 (1.6%) | 3 (4.8%) | 8 (12.7%) |
| *R* | 0.052 | 0.355 | 0.338 | 0.614 | 0.729 | 0.268 | 0,390 |

Notes: VTEC, venous thromboembolic complications; DVT, deep vein thrombosis; PE, pulmonary embolism

A significant hemorrhagic complication in patients without elastic compression (group 1) was observed in one case (1.4%); represented by nosebleeds. This patient received a therapeutic dose of heparin in the ward for DVT. In the 2nd group, 3 patients (4.8%) experienced bleeding, which required discontinuation of ACT and were represented by intense intermuscular hematoma of the lower leg, hemorrhoidal bleeding, epistaxis. It should be noted that VTEC was not observed in patients using compression therapy after discontinuation of anticoagulants.

In the analysis of bleeding, subcutaneous hematomas of the anterior abdominal wall were not taken into account if they were not tense, because almost all patients received unfractionated heparin (UFH) at a dose of 5 thousand units 4 times a day and all had this undesirable phenomenon. Small bleeding (nasal and gingival) in the 1st group was observed in 11 patients (15.9%), in the 2nd — in 8 (12.7%). After completing the course of ACT at the outpatient stage, minor bleeding stopped.

## DISCUSSION

Before the pandemic, when understanding the pathogenesis of acute venous thrombosis, we were guided by the Virchow triad and the usual risk factors that clinicians paid attention to. There were immobilization, trauma, extensive surgical interventions, thrombophilia, hormone replacement therapy, oncology, and others [8, 9]. Currently, the process of hypercoagulability in patients with a new coronavirus infection proceeds together with a "cytokine storm", macrophage activation syndrome, thrombocytopathy, endothelial dysfunction, and in the literature is called "*COVID* -19-associated coagulopathy" [10, 11].

New factors contributing to thrombus formation today are viral intoxication, the presence of respiratory failure caused by volumetric lung damage [12]. However, previously known risk factors are also being discovered, only now they can be found in the treatment of *COVID*-19: physical inactivity, bed rest to obtain oxygen insufflation. In fact, this is the same immobilization of the patient, only with the presence of a viral disease. In our study, most of the patients received oxygen therapy (83% in group 1 and 87% in group 2, $p = 0.453$). All these factors make patients with coronavirus infection vulnerable to vascular thrombotic complications, so the use of VTEC prophylaxis is most justified in these patients.

The studied groups in our observation were comparable in terms of clinical and anamnestic data, treatment, but despite this, VTEC was most often observed in patients without elastic compression.

There is already enough data in the literature on the incidence of VTEC in patients with *COVID* -19. According to the results of the largest meta-analysis, which included 49 studies, the incidence of VTEC was 17.0% (95% CI 13.4–20.9), of which 12.1% (95% CI 8.4–16.4) were DVT and 7.1% (95% CI 5.3–9.1) were PE. VTEC were more often registered in intensive care units (27.9 vs. 7.1%). A feature of the results of this meta-analysis is that the frequency of VTEC did not depend on the nature of pharmacological prophylaxis: 21% without ACT, 18.2% with prophylactic doses of anticoagulants, 19.4% with high doses of anticoagulants [13].

According to the results of our study, VTEC was detected in patients without EC (Group 1) in 7 cases (10.14%) and in one case (1.6%) using EC represented by PE ($p = 0.039$). It should be noted that this single case of PE in the 2nd group and 2 cases of PE (3%) in the 1st group were identified at autopsy, in the absence of a source in the lower extremities. Widespread pulmonary microthrombosis is a unique feature of coronavirus infection. In a comparative study of autopsy material from patients with *COVID*-19 and patients with H1N1 influenza in the alveolar capillaries, microthrombi in the pulmonary arteries were found 9-foldmore often in patients who died from coronavirus infection [14].

In the area of pulmonary artery thrombosis, endothelial damage and the presence of intracellular viral particles were observed, which indicates the relationship between endothelial damage and inflammation, which is often the cause of primary pulmonary artery thrombosis [15].

When analyzing laboratory parameters, initially in both groups there is a high concentration of pro-inflammatory markers (ESR, CRP, ferritin) and coagulation parameters (D-dimer, fibrinogen), and the level of fibrinogen is significantly higher in patients using EC (Group 1 — 3.6 (1.1–7.4), group 2 — 4.4 (1.1–7.8), $p = 0.003$). The level of RBC, hemoglobin, and platelets was within normal limits in all patients. At the end of treatment, a regular decrease in pro-inflammatory markers was observed: CRP, procalcitonin, ESR (Table 3). However, the level of D-dimer remained high in all patients, which indicates a high risk of thrombotic complications in the hospital and at the outpatient stage of treatment.

In patients who were in intensive care, there was a sharp increase in inflammatory markers CRP, ferritin, procalcitonin. The level of procalcitonin is important in the diagnosis and prognosis of the course of sepsis [16]. According to our data, all patients in the ICU have high levels of procalcitonin (Group 1 — 1.56 (0.036–14.7) ng/mL and Group 2 — 1.1 (0.063–3.9) ng/mL, $p = 0.493$), which indicates the addition of bacterial co-infection in patients with *COVID*-19. In the coagulogram, an increase in the level of APTT, prothrombin time and D-dimer is observed. The increase in APTT in all patients may be associated with the management of these patients on intravenous heparin infusion. The level of prothrombin time reflects the time of blood clotting and its increase is observed in the 2nd phase of DIC (disseminated vascular coagulation), which is an integral part of severe patients with *COVID*-19 [17, 18].

There were particularly high indicators of prothrombin time in patients of the 2nd group (1st group — 15.2 (11.2-25.2) sec and 2nd group — 17.3 (11.8-45.6) sec). This indicator also signals a high risk of bleeding. According to the results of our study, one (1.4%) major pulmonary hemorrhage was observed in group 1 (Table 4). Despite conservative and surgical treatment of bleeding, the patient died. In patients of the 2nd group, one (1.6%) case of major bleeding (intermuscular hematoma) was observed, which required blood transfusion ($p = 0.729$).

There was one (1.4%) case of bleeding in group 1 and 3 (4.8%) cases in group 2 ($p = 0.268$). Considering that ACT is indicated for all patients with coronavirus infection, the impossibility of its use makes preventive compression stockings the only means of preventing VTEC.

The obtained data clearly show that the use of preventive compression stockings prevents the development of thrombotic complications. At the same time, an important observation was that the presence of VTEC was the cause of death in 6 patients with PE (8.7%). This relationship demonstrates the presence of severe microcirculatory disorders in the body with the development of fatal complications in patients with a new coronavirus infection.

## CONCLUSIONS

1. The mortality in patients with coronavirus infection without compression therapy is higher than in patients with compression stockings.

2. Patients wearing compression stockings in the hospital have a low incidence of venous thromboembolic complications (1.6% of cases in group 2 versus 10.14% of cases in group 1, $p = 0.039$).

3. The study groups had the same frequency of major bleeding: group 1 — one case (1.4%), group 2 — one case (1.6%).

4. The use of prophylactic stockings at the inpatient stage of treatment of a new coronavirus infection makes it possible to prevent venous thromboembolic complications in patients with bleeding when anticoagulant therapy is not possible.

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