Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
COVID-19 and peripheral arterial complications in people with diabetes and hypertension: A systematic review

Ashu Rastogi a, *, Himika Dogra a, Edward B. Jude b

a Deptt of Endocrinology, PGIMER, Chandigarh, 160012, India
b Tameside and Glossop Integrated Care NHS Foundation Trust, Tameside on Lyne, UK

A R T I C L E   I N F O

Article history:
Received 28 June 2021
Received in revised form 5 July 2021
Accepted 7 July 2021

Keywords:
COVID-19
Diabetes
Gangrene
Heparin
Peripheral arterial disease
SARS-CoV2

A B S T R A C T

Aims: Identify the prevalence, risk factors and outcomes of lower extremity ischemic complications.
Methods: A systematic review was conducted by searching PubMed and SCOPUS databases for SARS-CoV-2, COVID-19 and peripheral arterial complications.
Results: Overall 476 articles were retrieved and 31 articles describing 133 patients were included. The mean age was 65.4 years. Pain and gangrene were the most common presentation. Hypertension (51.3%), diabetes (31.9%) and hypercholesterolemia (17.6%) were associated co-morbidities. Overall, 30.1% of patients died and amputation was required in 11.8% patients.
Conclusions: COVID-19 patients with diabetes or hypertension are susceptible for lower limb complications and require therapeutic anti-coagulation.

© 2021 Diabetes India. Published by Elsevier Ltd. All rights reserved.

Introduction

The global pandemic of COVID-19 has stirred the scientific community not only because of the scale of infection affecting millions of individuals but also because of the varied presentations involving multiple organ systems. Though, COVID-19 characteristically involves the respiratory system causing acute respiratory distress syndrome (ARDS) even more distinctive is the complications of COVID-19 pertaining to the vascular system. COVID-19 is associated with cytokine storm that precipitates disseminated intravascular coagulation and thrombotic microangiopathy involving the medium and small size vessels.[1] Multiple thrombotic complications and presentations have been ascribed to COVID-19 mainly acute coronary syndrome, pulmonary thromboembolism, stroke, mesenteric ischemia, renal artery thrombosis and peripheral arterial disease (PAD) [2].

Involvement of the peripheral vasculature is relatively uncommon but there has been a surge in reported cases of peripheral gangrene after COVID-19 infection [2,3]. The cutaneous changes in COVID-19 secondary to arterial and venous thrombotic events manifest as gangrene of the extremities. The risk factors for peripheral gangrene in COVID-19 may be directly related to SARS-CoV-2 infection or secondary to cytokine storm, disseminated intravascular coagulation, hypercoagulability, thrombotic microangiopathy, use of inotropes in critically ill patients, cold antigen induced auto-immune phenomenon and complement activation or worsening of pre-existing diabetic peripheral vascular disease [4]. Peripheral gangrene in COVID-19 is more likely in patients with prior endothelial dysfunction secondary to hypertension or diabetes [4]. Patients with diabetes and foot complications are known to have poor survival and limb outcomes in the presence of co-existing peripheral arterial disease [5]. Studies have shown that patients with acute arterial thromboembolic lower limb complications due to COVID-19 are likely to have higher mortality (around 50%) compared to compared to similar patients without COVID-19 [6]. Therefore, we performed a systematic review of the reported cases of peripheral gangrene in COVID-19 patients, co-existing comorbidities, specific treatment given, and outcomes of limb amputations or death.

Methods

We conducted a literature search in the electronic database of PubMed central and SCOPUS using MeSH terms “COVID-19”; SARS-CoV-2”AND “gangrene”, “peripheral gangrene”, “peripheral arterial disease”. The words were used interchangeably for articles
published in any language from Jan 2020 until June 5, 2021. Two authors conducted an independent search for case reports, case series, intervention studies, original articles reporting peripheral gangrene as outcome in COVID-19 patients. Papers that included patients who became COVID-19 positive after the occurrence of peripheral ischemia were excluded from the analysis. All articles retrieved were collated, duplicates were removed and final list prepared. In addition, reference list of the included articles were checked for additional cases. The demographic characteristics of patient population, symptom onset and duration, risk factors for peripheral arterial disease other than COVID-19 like the presence of diabetes, hypertension, hyperlipidaemia, coronary artery disease, and smoking status were noted. The duration of hospital stays, treatment offered for peripheral gangrene and outcomes in the form of limb amputation, mortality and reasons for mortality were noted.

Results

Overall, 474 articles that described ischemic complications in COVID-19 patients were retrieved from PUBMED and SCOPUS. After removing duplicates, the title and abstract of 424 publications were studied. We further excluded publications that were unrelated to peripheral gangrene but focused on gangrene of other organs example intestine, Fournier gangrene etc. Of the selected publications, 76 were review articles, commentaries or editorial and were excluded (Fig. 1). Finally, 31 articles describing 133 patients with peripheral gangrene in COVID-19 were included for analysis as shown in Table 1 [7–37]. The mean age of the subjects was 65.4 years with 81 males and 35 females (gender was not mentioned for 17 subjects). Mean duration of symptoms before hospital presentation was 7.4 days. Pain, paraesthesia, and gangrene of the affected extremity were the most common symptoms in addition to the COVID-19 related symptoms of fever, cough and respiratory complaints. Other presentations related to peripheral extremities included swelling of leg, acrocyanosis, limb weakness, asthenia and ischemic ulcer. Majority of the articles did not mention the time from SARS-CoV-2 positivity to the onset of gangrene.

Details of pre-existing co-morbidities were available for 119 patients; hypertension was the most common associated co-morbidity present in 61 patients (51.3%), followed by diabetes in 38 (31.9%), hypercholesterolemia in 21 (17.6%), prior CAD in 19 (16.0%), COPD in 6 (5.0%), chronic kidney disease in 4 (3.4%), atrial fibrillation and prior stroke in 2 subjects each and hypothyroidism (0.8%) in one patient (Fig. 2). Anticoagulants were added to the COVID specific treatment for peripheral ischemia in 78.9% (n = 105) of patients. Heparin was the most prescribed anti-coagulant (n = 98), followed by dual anticoagulants (apixaban along with heparin) in 5 patients, warfarin only and apixaban only in one patient each. Overall, 30.1% of patients (n = 40) died during the hospital stay. COVID related ARDS and multiorgan failure (n = 26, 65%) were the most common cause of death followed by acute coronary event (n = 9, 22.5%) followed by invasive aspergillosis, pulmonary thromboembolism, stroke, terminal ileal perforation and intestinal bleeding in one patient each. All deaths were ascribed to severe COVID-19 illness. Amputation of the affected digit/limb was required in 11 of the 93 surviving of participants (11.8%).

Discussion

We analyzed the prevalence, presentation and outcomes of peripheral vascular complications in people with COVID-19. Although millions of people are afflicted with COVID-19 globally, peripheral extremity complications are uncommon. Lower limb pain and gangrene are the most frequent presentations amongst those with peripheral arterial complications. More than two-third of patients had risk factor for peripheral arterial disease including hypertension and diabetes. Almost one-third of the patients died and one in ten required limb amputations during the illness suggesting a poor prognosis.

COVID-19 is associated with a prothrombotic state and various thrombotic events predominantly involving the pulmonary and coronary vasculature in critically ill patients [38,39]. The thrombotic events in COVID-19 may manifest as pulmonary thromboembolism and acute coronary events. The incidence of clinically manifest thrombotic events is much higher in SARS-CoV-2 infection as compared to other respiratory infections such as acute influenza or other viral infections [40]. However, autopsy studies have shown that alveolar microthrombi are nine times more common in COVID-19 patients [41]. The risk of arterial thrombotic events in COVID-19 correlates with the severity of the illness as most of the events are described in critically ill patients. The risk of thrombotic events prevails in COVID-19 patients despite thromboprophylaxis with heparin or low molecular weight heparin that is routinely administered to all admitted patients [39]. A good correlation has been found between systemic markers of inflammation like D-dimer, fibrinogen levels and risk of thrombosis in COVID-19 [42]. However, a study by Tan et al. found a similar incidence of venous thromboembolic episodes in COVID-19 and non-COVID-19 patients admitted during the COVID-19 pandemic and no correlation between D-dimer or fibrinogen and thromboembolic events [35]. The coronary, pulmonary and venous thromboembolism are found to be more common than arterial thrombosis in COVID-19 which is testimony to very few cases of peripheral arterial manifestations in the literature. Peripheral arterial disease may manifest as acute lower limb pain, paraesthesia, livido reticularis, gangrene, or asymptomatic chilblain like lesions. We found that pain in the affected extremity and gangrene were the most common presenting features of peripheral arterial involvement in COVID-19 patients.

Thromboembolic risk in COVID-19 seems to be a systemic phenomenon secondary to disseminated intravascular coagulation as highlighted by markedly increased levels of inflammatory cytokines like IL-6 and TNF-a. Also, there is a consistently increased level of fibrinogen, D-dimer, factor VIII, von Willebrand factor (vWF), and decreased antithrombin leading to a prothrombotic milieu in COVID-19. It is known that immobilized patients with critical illness are at heightened risk of thromboembolism, and COVID-19 further heightens the risk owing to a unique hypercoagulable milieu through a profound pro-inflammatory state [43]. It is proposed that viral entry into pneumocytes incites an inflammatory response that sets off a cascade of thrombosis initially localised to pulmonary vasculature and subsequent systemic response. COVID-19 is associated with endothelial injury as SARS-CoV-2 docking sites are the ACE2 receptor present on endothelial cells. It is known that SARS-CoV2 docks through its spike protein on to angiotensin-converting enzyme (ACE-2) present on the cell membrane and enters the cells. ACE-2 degrades angiotensin −II (Ang-II) and deletion of ACE-2 after binding of SARS-CoV2 to ACE-2 is associated with excess Ang-II. Ang-II binds to the Angiotensin receptor −1 and exacerbates the hypercoagulable state by increasing cytokine levels and induction of plasminogen activator inhibitor 1 (PAI-1) expression on endothelial cells. People with hypertension, diabetes and prior cardiovascular disease have reduced expression of ACE-2 that additionally contributes to high Ang-II levels in COVID-19. In addition, it has been proposed that heightened activation of monocytes and complement system confirmed by histopathological demonstration of pauci-inflammatory vasculitis with complement deposits in the affected
vessel may also contribute to thrombotic microangiopathy [41] and peripheral gangrene in COVID-19.

We found that almost two-thirds of patients with reported peripheral arterial complications in COVID-19 had background hypertension, diabetes or dyslipidaemia. The risk of thrombotic peripheral arterial complications is increased manifold in patients with pre-existing endothelial dysfunction like hypertension and diabetes [44]. Diabetes (odds ratio of 2.72) and smoking (odds ratio of 1.88) are considered as the strongest risk factor for PAD [45]. It is known that diabetes being a pro-inflammatory state contributes to endothelial dysfunction, abnormal vascular smooth muscle cell (VSMC) migration into the intima layer of vessels, decreased endothelial nitric oxide synthase (eNOS) activity and platelet dysfunction that adds to hypercoagulability of COVID-19 [46].

Almost one-fifth to one-third of people with diabetes have PAD that is related to the duration and severity of diabetes [47]. People with uncontrolled diabetes are more susceptible to severe COVID-19, requiring hospitalisation, thus increased likelihood of detection of peripheral arterial complications. We noticed that 10% of the subjects required limb amputation over a short duration of hospital stay and almost one fourth of the patients with COVID-19 identified in the present systematic review died due to acute coronary events that may be or not related to COVID-19. This emphasises the need for heightened screening for thrombotic complications amongst hospitalised patients with diabetes and COVID-19.

We found that almost all the patients were on therapeutic anticoagulation in the form of subcutaneous heparin (most frequent). Considering increased thrombotic risk in COVID-19, prophylactic or therapeutic anticoagulation is routinely prescribed in clinical practice. Though, the doses and duration of anticoagulation were inadequately described amongst the reported cases suggesting lack of consensus. Similarly, there is controversy regarding the prophylactic or therapeutic use of anticoagulation especially for people with co-morbidities like diabetes. The risk of thrombotic complications persists despite appropriate prophylactic anticoagulation with increased thrombotic events especially in

---

**Fig. 1.** PRISMA flowchart depicting records screened and study included for data synthesis.
| NAME OF THE AUTHOR | PLACE | NO. OF PATIENTS | AGE | GENDER | COMORBIDITY | DURATION OF SYMPTOMS (IN DAYS) | TREATMENT | OUTCOME |
|-------------------|-------|----------------|-----|--------|-------------|-----------------------------|-----------|---------|
| Zhang et al. [7] | CHINA | n = 7 | 71  | F      | DM, HTN, CAD | 11                          | Antibiotics | 5 DEATH |
|                   |       |       | 63  | F      |             |                             | Antiviral  |         |
|                   |       |       | 59  | M      |             |                             | Anticoagulant |         |
|                   |       |       | 49  | M      |             |                             | Other      |         |
|                   |       |       | 56  | M      |             |                             |            |         |
|                   |       |       | 65  | M      |             |                             |            |         |
| Novara et al. [8] | ITALY | n = 1 | 78  | F      |             | 7                          | Y, Antiviral | DEATH  |
|                   |       |       |     | F      |             |                             | Amiodarone |         |
| Alonso et al. [9] | SPAIN | n = 24 | 74  | F      | DM, HTN, CAD | 13                          | Interferon, | 3 DEATH |
|                   |       |       |     | F      |             |                             | Glucocorticoids, |       |
|                   |       |       |     | F      |             |                             | Tocilizumab, |       |
|                   |       |       |     | F      |             |                             | Cyclosporine, |       |
|                   |       |       |     | F      |             |                             | Colchicine  |         |
| Mathilde et al.  | GERMANY | n = 1 | 73  | F      | DM, HTN, CAD | 14                          | Y, Antiviral | IMPROVED |
|                   |       |       |     | F      |             |                             | Anticoagulant |         |
|                   |       |       |     | F      |             |                             | Other      |         |
|                   |       |       |     | F      |             |                             |            |         |
| Khalid et al. [11] | UAE | n = 1 | 41  | M      |             | 14                          | Tocilizumab, | AMPUTATION |
|                   |       |       |     | M      |             |                             | Interferon Beta |       |
| Bamghoje et al. | USA | n = 1 | 61  | M      |             | 14                          | Y, Antiviral | IMPROVED |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Singh et al. [13] | India | n = 1 | 64  | F      | DM, HTN, CAD | 14                          | Y, Antiviral | IMPROVED |
|                   |       |       |     | F      |             |                             | Anticoagulant |         |
|                   |       |       |     | F      |             |                             | Other      |         |
|                   |       |       |     | F      |             |                             |            |         |
| Ramachandran et al. [14] | India | n = 1 | 44  | M      |             | 3                           | Y, Antiviral | AMPUTATION |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Shubhra et al. [15] | India | n = 1 | 65  | M      |             | 10                          | Y, Antiviral | DEATH |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Chaudhary et al. [16] | India | n = 1 | 8   | M      |             | 7                           | Y, Antiviral | IMPROVED |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Adekiigbe et al. [17] | USA | n = 1 | 47  | M      |             | 10                          | Y, Antiviral | AMPUTATION |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Baccellieri et al. [18] | Italy | n = 1 | 67  | M      |             | 5                           | Y, Antiviral | IMPROVED |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Chun et al. [19] | USA | n = 1 | 51  | M      |             | 2                           | Y, Antiviral | AMPUTATION |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Sores et al. [20] | Brazil | n = 1 | 67  | M      |             | 9                           | Y, Antiviral | DEATH |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Qian et al. [21] | China | n = 1 | 53  | M      |             | 9                           | Y, Antiviral | IMPROVED |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Martino et al. [22] | Italy | n = 1 | 86  | F      |             | 2                           | Y, Antiviral | AMPUTATION |
|                   |       |       |     | F      |             |                             | Anticoagulant |         |
|                   |       |       |     | F      |             |                             | Other      |         |
|                   |       |       |     | F      |             |                             |            |         |
| Ilonzo et al. [23] | USA | n = 4 | 62  | M      |             | 2                           | Y, Antiviral | AMPUTATION |
|                   |       |       |     | M      |             |                             | Anticoagulant |         |
|                   |       |       |     | M      |             |                             | Other      |         |
|                   |       |       |     | M      |             |                             |            |         |
| Study            | Country   | Gender | Age | Condition                      | Event | Follow-up |
|------------------|-----------|--------|-----|--------------------------------|-------|-----------|
| Valle et al. [24] | Spain     | M/F   | 18-25 | Gastroesophageal Reflux        | Death | 14        |
| Mascia et al. [25] | Italy     | F/M   | 14-25 | Hyperlipidemia, CKD, Smoking, Dyslipidemia | Improved | 24    |
| Etkin et al. [26] | USA       | F/M   | 18-25 | Dyslipidemia                   | Improved | 25    |
| Perini et al. [27] | Italy     | M/F   | 18-25 | CKD, Smoking, Dyslipidemia     | Death | 5        |
| Maurere et al. [28] | USA       | M/F   | 18-25 | Dyslipidemia                   | Improved | 6      |
| Borrelli et al. [29] | Italy     | M/F   | 18-25 | Dyslipidemia                   | Improved | 5      |
| Singh et al. [30] | USA       | M/F   | 18-25 | Dyslipidemia                   | Improved | 6      |
| Kathryn et al. [31] | USA       | M/F   | 18-25 | Dyslipidemia                   | Death | 5        |
| Veyre et al. [32] | France    | M/F   | 18-25 | Dyslipidemia                   | Improved | 6      |
| Khattab et al. [33] | Egypt      | M/F   | 18-25 | Dyslipidemia                   | Death | 6        |
| Ali et al. [34] | USA       | M/F   | 18-25 | Dyslipidemia                   | Improved | 6      |
| Mohammed et al. [35] | UK         | M/F   | 18-25 | Dyslipidemia                   | Death | 5        |
| Patel et al. [36] | USA       | M/F   | 18-25 | Dyslipidemia                   | Improved | 6      |
| Showers et al. [37] | USA        | M/F   | 18-25 | Dyslipidemia                   | Improved | 2      |

**Notes:**
- AGE: 58-75
- Mean: 6
- IMPROVED
- DEATH
- CKD: Chronic Kidney Disease; DM: Diabetes mellitus; HTN: Hypertension; IVIG: Intravenous immunoglobulin.

**Additional Information:**
- CAD: Chronic Artery Disease; CKD: Chronic Kidney Disease; DM: Diabetes mellitus; HTN: Hypertension; IVIG: Intravenous immunoglobulin.
people with diabetes, though less frequent in those receiving therapeutic doses of anticoagulants [48]. On the other hand, there is a risk of fatal bleeding episodes on higher or therapeutic anticoagulation which require careful evaluation. However, a recent study found reduced rate of thrombotic complications without bleeding risk with therapeutic anticoagulation of LMWH (dose. (100 IU/kg/12 h SC) or (UFH (500 IU/kg/24 h) [49]. Also, a systematic review found a slightly reduced mortality in patients of COVID-19 receiving therapeutic anticoagulation [50]. Thus, people with heightened risk of thrombotic complications like diabetes may be offered therapeutic anticoagulation immediately on hospitalisation with severe COVID-19 (Table 2).

In conclusion, COVID-19 is a unique thrombo-inflammatory condition and patients with background diabetes or hypertension are more susceptible for lower limb complications due to peripheral arterial disease presenting as gangrene. The outcomes of COVID-19 with peripheral arterial complications are poor in terms of limb preservation and mortality. Considering the heightened risk of peripheral thrombotic complications in COVID-19, therapeutic anticoagulation must be considered. Future studies are urgently needed to assess such treatments to reduce amputation and mortality.

Table 2
Clinical management of pro-thrombotic state in COVID-19.

| Thromboprophylaxis and COVID-19 |
|---------------------------------|
| 1. Consider thromboprophylaxis* in |
| • Acutely ill hospitalized patients with COVID-19 |
| • Critically ill patients with COVID-19 |
| *Contraindicated in those with active bleeding and platelet count less than 25 x 10^9/L |
| 2. How to provide thromboprophylaxis? |
| • Anticoagulant thromboprophylaxis with low-molecular-weight heparin (LMWH) or fondaparinux may be preferred over unfractionated heparin (UFH) |
| • Antiplatelet agents are not given for VTE prophylaxis |
| • Standard dose anticoagulant thromboprophylaxis is preferred over intermediate doses of LMWH BID or weight-based dosing except in patients with heightened risk of thrombosis like diabetes |
| 3. How long to continue thromboprophylaxis? |
| • Only for the duration of the hospital stay and discontinued at discharge |
| 4. Routine ultrasound for detection of DVT is not required unless clinically indicated |

Table 2. Pre-existing co-morbidities in patients with COVID-19 and peripheral arterial complications.

Fig. 2. Pre-existing co-morbidities in patients with COVID-19 and peripheral arterial complications.

References

[1] Tang Y, Liu J, Zhang D, Xu Z, Ji J, Wen C. Cytokine storm in COVID-19: the current evidence and treatment strategies. Front Immunol 2020;11:1708. https://doi.org/10.3389/fimmu.2020.01708.
[2] Guan W, Ni Z, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20.
[3] Sameni F, Hajikhani B, Yaslianifard S, Goudarzi M, Owlia P, Nasiri MJ, et al. COVID-19 and skin manifestations: an overview of case reports/case series and meta-analysis of prevalence studies. Front Med (Lausanne) 2020;7:573188. https://doi.org/10.3389/fmed.2020.573188. 2020 Oct 29.
[4] Han H, Yang L, Liu R, Wu KL, Li Z, Liu XH, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. Clin Chem Lab Med 2020;58:1116e20.
[5] Rastogi A, Goyal G, Kesavan R, Bal A, Kumar H, Mangalanandan, et al. Long term outcomes after incident diabetic foot ulcer: multicenter large cohort prospective study [EDF-FOCUS investigators] epidemiology of diabetic foot complications study. Diab Res Clin Pract 2020. https://doi.org/10.1016/j.diabres.2020.108113.
[6] Hemingway J, Emanuels D, Aarabi S, Quirroga E, Tran N, Starnes B, et al. Safety of transfer, type of procedure, and factors predictive of limb salvage in a modern series of acute limb ischemia. J Vasc Surg 2019;69:1174e9.
[7] Zhang Y, Cao W, Xiao M, Li YJ, Yang Y, Zhao J, et al. Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and acute ischemia. ZhonghuaXue Ye Xue Za Zhi 2020 Mar 28:41. https://doi.org/10.3760/cma.j.issn.0253-2772.2020.0006. Chinese.
[8] Novara E, Molinaro E, Benedetti I, Bonometti R, Lauritano EC, Boverio R. Severe acute dried gangrene in COVID-19 infection: a case report. Eur Rev Med Pharmacol Sci 2020 May;24(10):5769–71. https://doi.org/10.26355/eurrev_202005_21369.
Sena G, Gallelli G. An increased severity of peripheral arterial disease in the community: complications and clinical outcomes. J Cardiothorac Vasc Anesth 2020;34(10):2846–7. https://doi.org/10.1056/ijca.2020.03.063.

Sen A, Gallelli G. An increased severity of peripheral arterial disease in two young, non-atherosclerotic patients with COVID-19. J Cardiothorac Vasc Anesth 2020;34(10):2846–7. https://doi.org/10.1056/ijca.2020.03.063.

Sophia RA, Rozanz L, Sariyilmaz A, Sariyilmaz K, Aung KS, Aung AY, et al. Acute arterial thromboembolism in patients with COVID-19 in the New York City area. Ann Vasc Surg 2021;67:6736(13)61249-0.

Stevens JL, Granger DN, Rasmussen S, Eiser JR, Moher D, Stewart LA, et al. Comparison of global estimates of prevalence and risk factors for peripheral arterial disease in 2000 and 2010: a systematic review and analysis. Lancet 2013 Oct 19;382(9901):1329–38. https://doi.org/10.1016/S0140-6736(13)61249-0.

Stonier AD, Fearon DT, Sullins KJ, Sullins T, Sullins S, Sullins S, et al. Imaging in the evaluation of peripheral arterial disease. J Vasc Interv Radiol 2020 Dec;31(12):2150–3. https://doi.org/10.1016/j.jvir.2020.08.009.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.

Sorapar A, Miorini M, Musumeci M, Haddad B, Di Liberto CA, Rossetti A, et al. Incidence, characteristics, laboratory findings and outcomes in aco-ischmia in COVID-19 patients. Vasc Risk Manag 2020;16:467–78. https://doi.org/10.1417/VHRM.V16.S76530.