The Impact of COVID-19 Pandemic on Vascular Leg Ulcers

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Abstract
The aim of this study was to evaluate the impact of 2 lockdown periods during coronavirus disease 2019 (COVID-19) on the course and management of nonhealing vascular ulcers of lower limbs. A total of 41 patients were included in the study. Before the pandemic began they had been seen at our unit at weekly intervals. During lockdown from March 9, 2020, to May 18, 2020 subjects were not allowed to enter the hospital unless they needed urgency or emergency surgery, or oncological management. During the second lockdown, from October 19, 2020, to December 11, 2020 patients could be followed up at distance by direct outreach including telephoning contacts. Data obtained early after each lockdown were compared with those obtained prior to the pandemic. Data for the first lockdown show that pain intensified and there was an increase in the recurrence rate of wounds, of their severity, and of superimposed infections as compared with the prelockdown period. The risk of lower-limb amputation was also considerably greater. During the second and less restrictive lockdown, patients were followed up by telemedicine and data indicate that skin lesions had not worsened any further. The management of vascular wounds was impacted by the pandemic unfavorably with health care failures in the hospital as well as in the primary care settings. In conclusion, the treatment of vascular leg ulcers is challenged by the COVID-19 pandemic as this spreads worldwide. This seems to be in keeping with what happens for other diseases. The data we obtained indicate that the pandemic-related lockdown has a deleterious effect on vascular skin wounds, with an increase of severity and mortality risk. The impact appears to be proportional to the number and the degree of limitations imposed on people.

Keywords
chronic wound, nonhealing ulcer, COVID-19 pandemic, wound care, vascular leg ulcer

Introduction
During the coronavirus disease 2019 (COVID-19) pandemic, which spread all over the world, Italy had to face one of the most severe infection clusters.1 Due to the exponential growth of infected cases and deaths registered in Italy from March 9, 2020, to March 28, 2020, and from October 19, 2020, to December 4, 2020, the hospital organization was remodeled to guarantee adequate assistance to COVID-19 patients. In turn, a considerable number of beds, including those in the intensive care unit, were dedicated to COVID-19 patients and taken away from other disease areas. Daily clinical work for non-COVID cases was interrupted and all health care resources were used to treat COVID patients and to decrease the risk of transmission among patients and health care workers as much as possible.2,3

The above-mentioned measures were found to have a great impact on the management of all non-COVID conditions resulting in an increase in morbidity and mortality.4-6

The field of vascular diseases, included that of leg ulcers, was expected by us to be similarly affected since patients were missing their weekly care at our unit.

The aim of the present study was to investigate the effect of the COVID-19 lockdown on the management and course of nonhealing vascular leg ulcers.

Materials and Methods
Included in the study were 41 patients, with a total of 46 ulcers, treated for nonhealing vascular leg ulcers during COVID-19 events. Of 41 cases, 18 were females and 23 males; mean age 62 years ± 9.5. Inclusion criteria were wound depth ≥ 1.5 cm, wound area ≥ 3 cm², and duration of ulceration ≥ 6 weeks. Exclusion criteria were wound etiology

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different from ischemia, chronic venous insufficiency, and diabetes; COVID-19 positivity; allergy or hypersensitivity to animal origin proteins preventing us from using porcine-derived dermal substitutes to cover lesions and promote wound healing. Demographic and wound data are given in Table 1. Prior to the pandemic, patients were treated at our unit at regular intervals separated by 4 to 7 days. To control pandemic spread, government and local institutions imposed a first stringent lockdown, from March 9, 2020, to May 18, 2020, during which period non-COVID patients were not allowed to get into our hospital except those who needed urgency or emergency surgery and/or oncology management. Moreover, during this period, people were not allowed to leave their homes unless they had to get basic needs such as food and medicines. In such an instance, everybody had to show his/her identification card to a policeman and sign a formal certificate attesting all the details about moving outside the home. In addition, work activities were stopped and only grocery stores and food markets were allowed to stay open. Schools, universities, theaters, cinemas, gyms, and swimming pools were closed. The second lockdown from October 19, 2020, to December 11, 2020, was less restrictive, let us say partial lockdown, during which the Italian National Health Care Institute divided Italy into different areas depending on the risk of infection, whether high, intermediate, or low, the restrictions being proportional to the risk. Each area could change its risk level approximately every 3 weeks: depending on the changing epidemiology of the pandemic. In addition, there was a nationwide curfew at night, from 10 PM to 5 AM. During the second lockdown, our geographic area, Campania Region, was at a high-risk level. Due to the renewed allocation of health care resources to non-COVID diseases, we could not see COVID-free patients in the presence, but we could do so at distance by direct outreach, by telephoning, and by web contacts.

Patient data registered prior to COVID pandemic (T0) were obtained by reviewing their clinical records and the following variables were registered for further evaluation: sex, age, and ulcer etiology whether ischemic, diabetic, venous related to chronic venous insufficiency, or post-thrombotic syndrome. For data obtained after the first lockdown (T1) and after the second lockdown (T2), the recurrence of the ulcer was recorded. In addition, we used our clinical judgment to categorize ulcers.T1 and T2 data were compared with T0 data (Table 1). The primary endpoint was defined as an increase of clinical severity with worsening of at least 3 ulcer features. Secondary endpoints were the occurrence of at least one more amputation and/or one more all cause as well as vascular-related mortality.

Analysis of variance test was used for comparison of continuous variables and Fisher’s exact test for comparisons of categorical variables. P values of <.05 were considered statistically significant.

We had pictures taken before and after lockdown for all cases. After patient informed consent, we present some of those images that are more representative (Figure 1a–c).

### Results

Patient data prior to the beginning of pandemic (T0) and those obtained early after the 2 lockdowns, March 9, 2020, to May 18, 2020 (T1) and October 19, 2020, to

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### Table 1. Clinical Data of the 41 Patients Evaluated Before the COVID-19 Period (T0), Early After the First (T1), and the Second Lockdown (T2) for COVID-19.

| Baselines characteristics | T0            | T1            | T2            | P<          |
|---------------------------|---------------|---------------|---------------|-------------|
| Mean age (y) ± SD         | 62 ± 9.5      | 62 ± 9.5      | 62 ± 9.5      | NS          |
| Gender (male/female)      | 23/18         | 23/18         | 21/17         | NS          |
| Ulcer type                |               |               |               |             |
| 41% ischemic (n = 19)     | 41% ischemic  | 41% ischemic  | NS            |
| 20% diabetic (n = 9)      | 20% diabetic  | 20% diabetic  | NS            |
| 39% venous (n = 18)       | 39% venous    | 38% venous    | NS            |
| VAS score, mean ± SD      | 2.05 ± 0.38   | 8.0 ± 0.44    | 6.07 ± 0.26   | .0001a      |
| Superimposed infection    | 0%            | 89% (n = 34 of 41)| 44% (n = 17 of 38)| .0001b      |
| Healing                   | 85% (n = 35 of 41)| 12 % (n = 5 of 41)| 13% (n = 5 of 38)| .0001b      |
| Improvement               | 15% (n = 6 of 41)| 0% (n = 0 of 41)| 45% (n = 17 of 38)| .01b        |
| Worsening                 | 0.0% (n = 0 of 41)| 88% (n = 36 of 41)| 42% (n = 16 of 38)| .0001b      |
| Recurrence                | 0.0% (n = 0 of 41)| 74.0% (n = 30 of 41)| 42.0% (n = 16 of 38)| .0001b      |
| Minor amputation          | 0.0% (n = 0 of 41)| 19% (n = 8 of 41)| 0.0% (n = 0 of 38)| .002c       |
| Mortality                 | 0.0% (n = 0 of 41)| 2.5% (n = 1 of 41)| 0.0% (n = 0 of 38)| NS          |

*a Two patients were lost to follow-up and 1 patient died by T1.

NS = not significant.

P values calculated by analysis of variance test.

P values calculated by Fisher’s exact test: T0 versus T1 and T0 versus T2. P values for the 2 comparisons were equal.

Fisher’s exact test comparing T0 versus T1.

Abbreviations: COVID-19, coronavirus disease 2019; VAS, visual analog scale.
December 11, 2020 (T2), respectively, are presented in Table 1. It is noteworthy that clinical data at T1 differ from those at T2, and all differ from T0 data. Taken together, they show that wounds worsened during the lockdown and, more so during the first and more restrictive one. The etiology of a vascular leg ulcer, whether ischemic, diabetic, or venous, and its severity are very important factors that predict nontreatment prognosis and indeed they influenced the outcome observed in the present study. Ischemic ulcers were the most common type of leg ulcers accounting for 41% (n = 19) of cases followed by venous ulcers 39% (n = 18), and diabetic ulcers 20% (n = 9). Ischemic ulcers were associated with better prognosis due to the complete wound healing obtained after successful endovascular or surgical revascularization procedures for critical limb ischemia, while diabetic ulcers highly worsened during T1 leading to digital or forefoot amputation. In fact, during the lockdown, we registered an increase in the amputation rate due to superimposed infection among diabetic patients. Foot care, control of diabetes, offloading, medical care, and walking all were made more difficult by the pandemic thus increasing the worsening rate. Venous ulcers increased clinical severity during T1 without risk of limb loss. Venous ulcers showed increased recurrence rate and reduced healing rate as compared with ulcers of a different etiology. We believe that this is essentially due to the absence of a walking program and to a sedentary lifestyle with a subsequent increase of venous hypertension and edema. During the pandemic, walking opportunities were reduced and compression elastic bandage was not possible since it has to be done by professional personnel. We used compression stockings to obtain a somewhat standardized pressure and to make wearing easier. Out of 46 lesions, 38 (83%) were as severe as indicated by the presence of at least 2 inclusion criteria. Pandemic was associated with a sharp increase of pain as indicated by the visual analog scale (VAS) score that raised from 2.05 at the beginning to 8.0 at T1 and 6.07 at T2 (P < .0001). During the pandemic, the proportion of healed lesions dropped from 85% (T0) to 12% (T1) and 13% (T2) consistent with the increased rate of recurrences from 0% to 74% and 42%, respectively (P < .0001). Improvement occurred in no one lesion at T1 and in 45% of ulcers at T2 (P < .01). Worsening increased from 0% (T0) to 88% (T1) and 42% (T2) significantly (P < .0001). At T0, we registered no one superimposed infection, which went up to 89% and 44% at T1 and T2, respectively (P < .0001). Eight patients presented with irreversible toe or forefoot gangrene without sepsis and digital or forefoot amputation was required. Five patients were allowed to get into hospital since they presented with limb-threatening ischemia, were treated with surgical or endovascular revascularization, and healed without complications. One nonvascular-related death occurred in a patient who had received surgery for hepatocarcinoma and could not be followed up for >1-year post-COVID. The degree of worsening at T2 was lower than that at T1 and this is likely to be due to telemedicine that we could use to follow-up patients (Figure 2a–c).

Two patients were lost to follow-up (7.5%). The overall primary endpoint was reached in 30 patients after the first lockdown and in 16 patients after the second lockdown. At least 1 of the second endpoints was fulfilled in 9 patients and 0 patients, respectively.

Discussion

Worsening of nonhealing vascular leg ulcers was observed in May 2020 soon after the first lockdown and to a lower extent in December 2020 soon after the second lockdown which was less restrictive. The natural history of chronic leg ulcers is frequently characterized by an increase of severity, recurrence, and superimposed infections, which may result in loss of limb and even of life. Particularly in our study, due to the absence of weekly wound care service, we registered an increased rate of superimposed infection, recurrence, and amputation rate.

Figure 1. (a) A 52-year-old male with a nonhealing ulcer caused by chronic venous insufficiency and postthrombotic syndrome healed before the pandemic (T0), (b) recurrence of ulcer after the first lockdown (T1), and (c) recurrence of ulcer after the second lockdown (T2).

Figure 2. (a) A 61-year-old female with chronic ulcer caused by venous insufficiency and postthrombotic syndrome partially healed before the pandemic (T0), (b) worsening of ulcer after the first lockdown (T1), and (c) worsening of ulcer after the second lockdown (T2).
Prior to the COVID-19 pandemic, patients with nonhealing vascular ulcers were seen and treated at our unit once or twice weekly. Advanced treatments were also used. For patients with severe comorbidities, the therapeutic approach was multidisciplinary. Deterioration of the underlying disease and/or of the local lesion required hospitalization. For critical limb-threatening ischemia, surgical or endovascular revascularization was the first line option with a prognosis of ischemic lesions being much improved. A walking program was strongly recommended. Special attention was paid to quality of life.

The above-mentioned treatment strategy that we had used in the past was drastically changed and somewhat disrupted by the COVID-19 crisis.\(^{8,9}\) It is noteworthy to consider that emergency vascular surgery is aimed at saving patient limb and even his/her life. Indeed vascular patients may require urgent surgery for several indications including limb-threatening ischemia, debridement, or abscess drainage.

Treatment of non-COVID patients was hampered by the need of coping with the pandemic. During that period non-COVID patients had none or limited access to hospitals in Italy unless they needed urgency or emergency or oncological treatment. Health, economic, territorial, and human resources were dedicated to control and treat COVID patients and their severe respiratory symptoms.\(^{10}\) However, patients with chronic vascular ulcers of the lower limbs should always be allowed to gain access to hospital through non-COVID dedicated pathways.\(^{11}\) This is because inside the hospital, they may receive adequate dressings for ulcers and wounds, advanced medications, and dermal regeneration substitutes. Indeed, before the pandemic, we had used a tailored and multistep therapy that included advanced dressings such as hydro fibers, collagen matrix, and lipocolloids; we obtained very satisfactory results with the application of porcine-derived dermal substitutes.\(^{12}\) Moreover, vascular skin lesions require a regular dressing and a frequent evaluation by an expert specialist able to recognize and treat superimposed infections they occur.

Treatment of chronic vascular leg ulcers has also to be directed toward the underlying systemic diseases involved in the pathogenesis of ulcers and toward any comorbidity. This implies a multidisciplinary approach that has been made very difficult in the context of lockdown which imposes social distancing measures.\(^{13}\) In fact, many patients get anxious about the risk of contracting coronavirus if they leave home and go to the hospital. As a consequence, they manage their lesions by themselves and use always the same standard medication since advanced dressings are expensive and not always sold to the public.

Due to lack of appropriate treatment and to drastic shortening of health care resources non-COVID patients with chronic vascular wounds were expected to worsen during lockdown periods. The data we presented are consistent with the expectation as they show that morbidity increased and outcome worsened up to foot amputation in some instances, and death. Data at T1 as compared with T0 showed an increase of minor amputations (19% vs 0%) and recurrence rate (74% vs 0%). Superimposed infections were observed much more frequently after the 2 COVID-19 waves even if patient and caregivers have been trained in recognizing signs and symptoms of a superimposed local infection such as warmth, redness, the appearance of exudate, increase of pain, tissue friability, enlargement of ulcer size, and foul-smelling. In these instances, an in-presence treatment given by an expert physician is suggested to control infection progression, because it is necessary to get a culture of a wound sample, peripheral blood cell count, erythrocyte sedimentation rate, and C-reactive protein. Should fever or other systemic manifestations be present blood cultures are to be taken. Patients have to be started on antibiotic therapy either empirical or based on sensitivity tests. Treatment may be local or systemic as appropriate. We suggest suspecting osteomyelitis as a possible complication of chronic, deep wounds, and use X-ray examination, bone scans, or magnetic resonance imaging to diagnose it. Wound care using iodine and silver-based dressings after an adequate debridement can be helpful to control local infection.

T1 data show that complete wound healing without complications was obtained only in 12% of patients who underwent urgent endovascular or surgical treatment for critical limb ischemia while prior to pandemic 85% of patients completely healed and a better outcome was observed for venous ulcer. Also, the mean VAS score increased after the 2 lockdowns significantly indicating an impaired quality of life of already weak patients. The death of a vascular patient with hepatocarcinoma occurred because she did not present at the follow-up visit and was anxious for the risk of contracting coronavirus inside the hospital.

The degree of worsening at T2 was lower than that at T1 because considering the bad results obtained after the first lockdown we decided to follow-up patients remotely using telemedicine during the second lockdown. We treated chronic vascular wounds by phone contacts, video-call consultations, messages, and evaluation of wound pictures sent by patients. Crucial points to make this approach successful are patient education and appropriate wound self-care.

In particular, patient education regarding foot care may be highly effective in reducing ulcer recurrence, risks of amputation, and overall morbidity.\(^{14}\) Patients must adhere to medical prescriptions, inspect skin and wounds regularly, recognize signs of skin breakdown evaluating wound area and depth, perilesional inflammation, smell, and characteristics of the exudate that suggest superimposed infection. Obviously, patient compliance depends on his/her cultural and socioeconomic status. Unfortunately, it is not always easy to manage at distance complications due to poor
compliance. In these instances, an in-presence treatment given by an expert physician is essential to control disease progression. Moreover, during the second lockdown, home nursing gave a significant contribution to the decrease of the recurrence rate and the increase of the healing rate. Of course, the home nursing team may use telemedicine in cooperation with a physician in charge and a patient. Such cooperation is likely to improve health care further on.

The use of telemedicine may avoid many hospital admissions. However, any patient with high-risk, limb-threatening lesions should be seen by a vascular surgeon promptly to evaluate whether urgency or emergency revascularization, or surgical debridement is required.

We advocate that the activity of vascular wound services be not discontinued during the pandemic since it is targeted to fragile patients often affected by several comorbidities that impair wound healing (diabetes, cardiovascular diseases, renal diseases, or immunocompromised status). Although wound care best practice is challenged by the pandemic when amputation has to be avoided or sepsis has to be controlled in the presence of therapy is necessary.

In conclusion, the data of the present study show that the management of wound care was highly impaired by the pandemic and this resulted in worsening of the disease and increased amputation rate. Whenever possible telemedicine may be an alternative approach supposed that patients cooperate with a physician in a proper way and comply. On the other hand, it is often difficult for a physician to evaluate pictures for his decision-making. The role of services dealing with the treatment of vascular skin wounds turns out to be reinforced. Patients with vascular ulcers of lower limbs have poor health. They are at increased risk of infections due to the impaired immune response and if they do not receive appropriate therapy, including wound monitoring and debridement, are at risk of losing a limb or even life.

Guidelines or official recommendations about the management of patients with nonhealing vascular ulcers of lower limbs during the COVID-19 era are lacking. Therefore, it is extremely important that vascular units, wherever located, will share their experiences and strategies to agree on a common and best method of treatment that surely will be welcome by patients.

Conclusions
Therapy of nonhealing vascular ulcers is demanding and the COVID-19 pandemic has made it even more challenging. According to our experience, due to the lack of an appropriate multidisciplinary treatment, drastic reduction of health care resources, and restrictions imposed on people non-COVID patients with chronic vascular wounds worsened during lockdown periods and this resulted in impaired quality of patient life and an increase of morbidity and amputation rates. In such a framework, training patients in self-care may improve outcome greatly even when wounds are managed at distance, by telemedicine. Triage is of great help in establishing priorities based on clinical severity and selecting those patients who require hospitalization and perhaps emergency surgery. Even during the pandemic, this latter need should be met and medical care should be easily accessible and adequate.

In the future, national and local governments, as well as scientific committees and health care officials, should focus their attention on the impact of a biological storm, such as the COVID-19 pandemic is, on vulnerable patients to protect them at their best.

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