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TREATMENT OF PATIENTS WITH CHRONIC WOUNDS DURING THE COVID-19 PANDEMIC IN REPUBLIC OF NORTH MACEDONIA

ТРЕТМАН НА ПАЦИЕНТИТЕ СО ХРОНИЧНИ РАНИ ВО ТЕК НА ПАНДЕМИЈАТА НА КОВИД-19 ВО РЕПУБЛИКА СЕВЕРНА МАКЕДОНИЈА

Nikola Gramatnikovski[1], Iva Stankovic[2], Elizabeta Markoska[3], Nina Apostolovska[4] and Andzela Vitanova[4]

[1]University Clinic for Thoracic and Vascular Surgery, Faculty of Medicine in Skopje, [2]University Clinic for Surgical Diseases "St. Naum Ohridski"-Skopje, [3]Biomedika dijagnostika Ltd., Skopje, [4,1]University Clinic for TOARICEC, Cyril and Methodius University in Skopje, Faculty of Medicine in Skopje, Republic of North Macedonia

Abstract

Introduction. The COVID-19 pandemic has had an impact on the routine management of the chronic wounds which are defined as wounds that have not proceeded through orderly and timely reparation to produce anatomic and functional integrity after three months.
Aim. The aim of the study was to evaluate the clinical characteristics and outcomes of patients with chronic wounds managed through a modified treatment protocol during the COVID-19 pandemic.
Methods. This retrospective study included a sample of 224 patients with chronic wounds, 152 males (67.9%) and 72 females (32.1%), aged 32 to 94 years (mean age of 64.4±10.5 years), examined during the period of 11 March to 30 November 2020. Demographic data, comorbidities, laboratory and imaging findings, photographs, and clinical outcomes (persistent lesions, healed wounds, amputations and lethal outcome) were analyzed. For statistical data analysis we used Chi-square test with level of significance $p<0.05$.
Results. The most common type of chronic wound was arterial ulcer (44.2%) treated in outpatients settings ($p=0.026$). Diabetic, venous, and pressure ulcers were represented with 32.6%, 14.7%, and 8.5%, respectively. The current ongoing treatment of patients is 53.1%, whereby 37.5% of patients' wounds have healed, 8.5% resulted in amputations, and three patients (1.3%) have lost their lives.
Conclusion. A specific triage pathway and modified treatment protocol for patients with chronic wounds during the COVID-19 pandemic were beneficial and showed adequate management of chronic wounds. The proposed algorithm reduced the exposure to SARS-CoV-2 of both, medical staff and patients, while providing a good healing rate in all chronic wounds types.

Correspondence to: Nikola Gramatnikovski, University Clinic for Thoracic and Vascular Surgery, Vodnjanska 17, Skopje, R. N. Macedonia; Phone: +389 2 31 47 031; E-mail: dr.gramatnikovski@gmail.com

Keywords: chronic wounds, COVID-19, SARS-CoV-2, patient management

Апстракт

Вовед. Пандемијата на Ковид-19 има влијание врз вообичаениот начин на лекување на хроничните рани, кои се дефинираат како рани кај кои нема уредно и навремено заздравување кое ќе доведе до анатомски и функционален интегритет по три месеци.
Цел. Целта на студијата беше да се евалуираат клиничките карактеристики и резултатите од третманот на пациентите со хронични рани лекувани преку модифицираниот протокол за време на пандемијата на Ковид-19.
Методи. Оваа ретроспективна студија вклучува примерок од 225 пациенти со хронични рани, 152 мажи (67,9%) и 72 жени (32,1%), на возраст од 32 до 94 години (средна возраст 64,4±10,5 години), прегледани во периодот од 11 март до 30 ноември 2020 година. Беа анализирани демографските податоци, коморбидитетите, лабораториски и дијагностички наоди, фотографии и резултатите од третманот (перзистентни лезии, излекувани рани, ампутации и летален исход). За статистичка анализа на податоците го користевме Хи-квадрат тестот со ниво на значајност $p<0,05$.
Резултати. Најчест тип на хронична рана беше артерискиот улкус (44,2%) лекуван во амбулантски услови ($p=0.026$). Дијабетичните, венските улкуси и декубиталните рани беа застапени во 32,6%, 14,7%, и 8,5%, последователно. Кај 53,1% третманот е во тек, кај 37,5% од пациентите раните се излекувани, 8,5% со ампутација на екстремитет и тројца пациенти (1,3%) починаа.
Заклучок. Специфичната тријажна патека и модифицираниот протокол за третман на пациентите со хронични рани за време на пандемијата на Ковид-19 беа корисни и покажаа адекватно лекување на

хроничните рани. Предложениот алгоритам го намали изложувањето на SARS-CoV-2 на медицинскиот персонал и на пациентите, истовремено обезбедувајќи висок процент на заздравување кај сите видови хронични рани.

Клучни зборови: хронични рани, Ковид-19, SARS-CoV-2, третман на пациенти

Introduction

Chronic wounds are defined as wounds that have not proceeded through an orderly and timely reparation to produce anatomic and functional integrity after three months, or barrier defects that have not healed in three months [1,2]. In developed countries, it is estimated that 1 to 2% of the population will experience a chronic wound during the lifetime [3]. Chronic, non-healing wounds can be debilitating for the affected individual and place a massive financial burden on healthcare system [4].
The physiological process of wound healing is divided into four phases. The first phase *hemostasis* is characterized by vasoconstriction and clotting. The subsequent *inflammation* phase is mediated through neutrophil granulocytes which prevent bacterial contamination and cleanse the wound from cell debris. The *proliferation* phase is primarily characterized by tissue granulation and formation of new blood vessels. During the last phase *remodeling*, the provisional wound matrix is replaced by more rigid scar tissue [5]. Wound healing depends on many factors, including adequate tissue perfusion, an intact immune system, appropriate level of wound hydration, removal of necrotic tissue and management of infection, if present [6].
All wounds have potential to become chronic wounds. They are classified by etiology into four categories: arterial, diabetic, pressure, and venous ulcers [7]. Despite differences in etiology at the molecular level, chronic wounds share certain common features, including excessive levels of proinflammatory cytokines, proteases, reactive oxygen species, and senescent cells, as well as the existence of persistent infection, and a deficiency of stem cells that are often also dysfunctional [8]. Comorbid illnesses induce adverse effects on the healing process of wounds and may need different strategies such as modification of drug therapy, diet, or behavior to promote wound healing. Diabetes, obesity, autoimmune diseases, malnutrition, cardiovascular disease, end-stage renal disease and cancer are the most common comorbidities that impact wound healing [9]. The presence of bacteria is most likely to influence the wound healing. The most common bacterial species detected in chronic venous leg ulcers were *Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa,* coagulase-negative staphylococci, anaerobic bacteria, *Enterobacter cloacae,* and *Escherichia coli* [10].
The effective care of chronic wounds requires a multimodal approach, including wound bed optimization, management of chronic medical conditions, and consistent follow-up. Advanced wound therapies, such as negative pressure wound therapy (NPWT), can have benefit in some patients, but evidence to support the use of one specific advanced dressing type over another is limited [11]. A primary aspect in effective wound care is exudates management. The excessive presence of exudate in the wound bed acts to delay healing. An effective dressing must maintain a moist wound bed, but not wet; absorb and retain excess exudate; maintain normal tissue temperatures at and around the wound bed and be impermeable to external pathogens and fluids, but allow gas exchange between the wound bed and the environment [12].
The spread of COVID-19 pandemic and limited hospital access caused significant limitation of patients' access to treatment, affecting in particular chronic wounds patients [13]. The current general strategy is to minimize the number of nonessential hospitalizations for three main reasons: providing intensive care units (ICU) the capacity for COVID-19 patients requiring intensive care, preserving medical staff due to the shortage of medical personnel, and reducing the risk of infection for hospitalized patients and medical staff [14]. Wound care practitioners should take necessary steps to minimize hospital admission of patients with chronic wounds. A specific triage is required to differentiate between critical, severe and stable patients. The first priority should be given to critical patients with ICU care. Alternative services like telemedicine with proper patient education should be adopted and homecare services should be provided as continuity of care [15].
The COVID-19 pandemic had an impact on the routine management of the chronic wounds in North Macedonia. There are several challenges faced by any clinician while managing chronic wounds during this pandemic. Since the beginning of the pandemic, we have modified our triage pathway accordingly, both chronic wound severity and comorbidities in patients to provide an appropriate chronic wound management and reduce the risk of SARS-CoV-2 exposure. The aim of the study was to evaluate the clinical characteristics and outcomes of patients with chronic wounds managed through specific triage pathway and modified treatment protocol during the COVID-19 pandemic.

Materials and methods

This retrospective study included a sample of 224 patients with chronic wounds, 152 males (67.9%) and 72 females (32.1%), aged 32 to 94 years (mean age of 64.4±10.5 years), examined at the University Clinic for Thoracic and Vascular Surgery, Faculty of Medicine-Skopje and University Clinic for Surgical Diseases "St. Naum Ohridski"-Skopje, during the period of 11

March to 30 November 2020. Inclusion criteria were: presence of chronic wound, follow-up of at least one month, both hospital and outpatient treatment settings. Demographic data, comorbidities, laboratory and imaging findings, consultation history, photographs, and clinical outcomes (persistent lesions, healed wounds, amputations, and lethal outcome) were analyzed. For statistical data analysis we used Chi-square test with level of significance $p<0.05$.

Results

The total number of patients with chronic wounds was 224,152 males (67.9%) and 72 females (32.1%). Majority of patients (39.7%) were in 61-70 age range. The most common comorbidities were cardiovascular diseases (57% of all comorbidities). Three patients (1.3%) were infected with SARS-CoV-2. Demographic and clinical characteristics of the patients are displayed in Table 1. Chronic wounds were classified into four categories: arterial, venous, diabetic, and pressure ulcers. Types of chronic wounds in all patients and treatment settings are presented in Table 2. The most common type of chronic wound was arterial ulcer (44.2%), and most of the wounds were treated in outpatient settings (p=0.026). Only patients who needed surgeries were hospitalized.

Table 1. Demographic and clinical characteristics of patients

Characteristics	No (%)
Age (Years)	64.4±10.5 (Mean±SD)
32-40	3(1.3%)
41-50	20(8.9%)
51-60	51(22.8%)
61-70	89(39.7%)
71-80	50(22.3%)
≥ 81	11(4.9%)
Gender	
Male	152(67.9%)
Female	72(32.1%)
Comorbidities*	
Cardiovascular disease	183(57%)
Diabetes	73(22.7%)
Obesity	45(14%)
Chronic kidney disease	9(2.8%)
COPD	8(2.5%)
Cancer	3(0.9%)
COVID-19 positive	3(1.3%)

*There were several comorbidities in some patients (Percentage calculated from the total number of comorbidities: 321)

Table 2. Types of chronic wounds and treatment settings

Type of chronic wound	Outpatient treatment No (%)	Hospital treatment No (%)	Total No (%)	p*
Arterial ulcer	74 (33)	25 (11.2)	99 (44.2)	0.026
Diabetic ulcer	65 (29)	8 (3.6)	73 (32.6)	
Venous ulcer	28 (12.5)	5 (2.2)	33 (14.7)	
Pressure ulcer	12 (5.4)	7 (3.1)	19 (8.5)	
Total	179 (79.9)	45 (20.1)	224 (100)	

*Chi-square test

The statistical analysis showed that there was a statistically significant difference between the type of chronic wound and treatment settings (χ^2=9.258, df=3, p=0.026). The types of chronic wounds and clinical outcomes in all patients were illustrated in Table 3. Persistent lesions, the rate of healing (complete wound closure), amputation, and lethal outcome were evaluated. There was still a need for wound treatment in majority of patients (53.1%) during the period surveyed. In total of 84(37.5%) patients, the wounds healed, 19(8.5%) patients had worsened ulcers and unavoidable amputations. Three patients have died. They had serious comorbidities, and one of them was positive for COVID-19.

Table 3. Types of chronic wounds and clinical outcomes

Type of wound	Ongoing care No (%)	Healed No (%)	Amputation No (%)	Death No (%)	Total No (%)
Arterial ulcer	46 (20.5)	35 (29.4)	16 (7.1)	2 (0.9)	99 (44.2)
Diabetic ulcer	40 (17.9)	29 (12.9)	3 (1.3)	1 (0.4)	73 (32.6)
Venous ulcer	20 (8.9)	13 (5.8)	/ (0)	/ (0)	33 (14.7)
Pressure ulcer	12 (5.4)	7 (3.1)	/ (0)	/ (0)	19 (8.5)
Total	118 (52.7)	84 (37.5)	19 (8.5)	3 (1.3)	224 (100)

The case of healed lower limb arterial ulcers infected with *Pseudomonas aeruginosa* is shown in Figure 2. The patient was treated ambulatory in a period of five months. There was also a good home care in this case. Since the beginning of the COVID-19 pandemic, we modified our triage pathway in accordance with both chronic wound severity and comorbidities in patients. The main goal in this activity was to provide an appropriate chronic wound management and reduce the risk of SARS-CoV-2 exposure. In Figure 3 our algori-

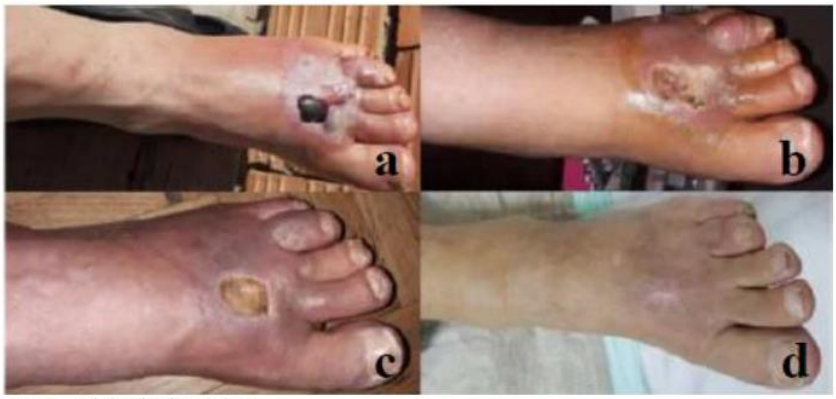

Fig. 1. Diabetic foot ulcer
a) First examination, **b**) after three weeks, **c**) after four weeks, **d**) after three months

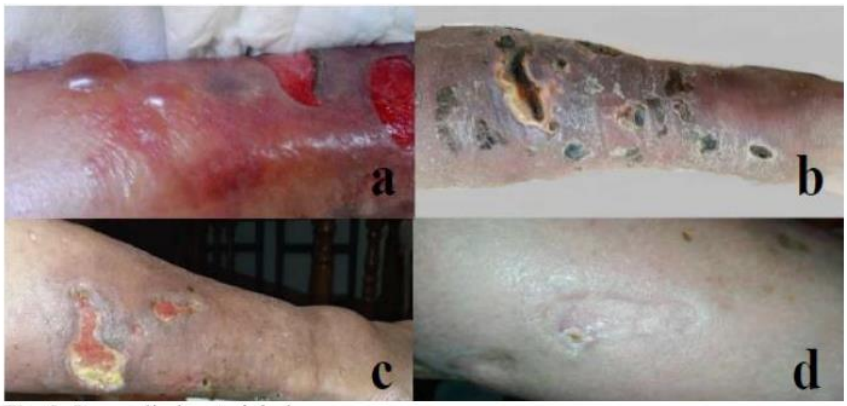

Fig. 2. Lower limb arterial ulcer
a) First examination, **b**) after five weeks, **c**) after three months, **d**) after five months

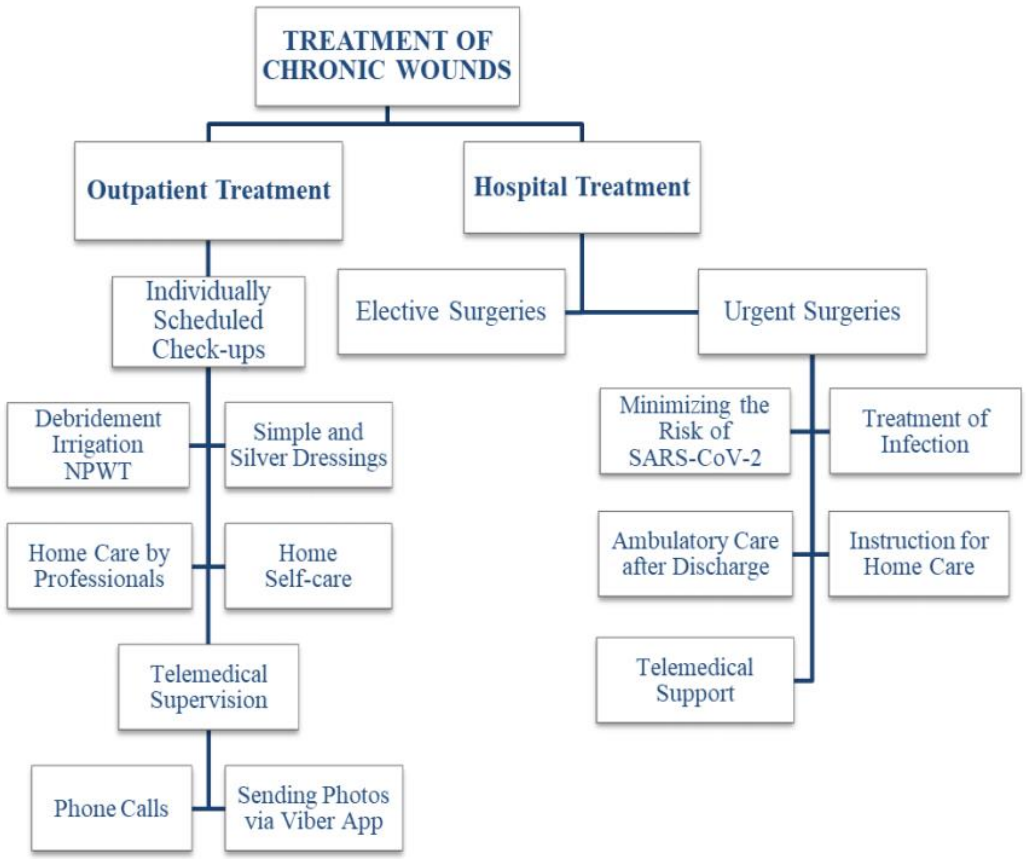

Fig. 3. Algorithm for chronic wounds management during COVID-19 pandemic

thm for chronic wound management during COVID-19 pandemic is presented.

Discussion

Managing patients during COVID-19 pandemic has been modified for all patients with chronic wounds, including patients with peripheral arterial disease, chronic venous insufficiency, diabetic foot, and pressure ulcers in terms of restricted visits to hospital facilities and applying simplified self-care. It is crucial to minimize probability of exposure to SARS-CoV-2, having in mind that the most critical preventive measures are keeping physical distance and avoiding contacts, as well as, wearing a mask. This is beneficial for both patients and healthcare providers. Patients with chronic wounds fit several of the high-risk criteria for COVID-19 infection and mortality. They are often older, immunocompromised, and have multiple comorbidities. The answer is not to avoid clinical evaluation and wait for wound infection, but to mitigate the risk of COVID-19 and ulcer infection [16]. Many patients have always been ambivalent about the need of referral to hospital and would often prefer to be managed in the community if possible, but this ambivalence during COVID-19 pandemic is magnified by a very real fear of being exposed to potential risk of infection in crowded waiting rooms and increased difficulty of transport [17].

From the beginning of COVID-19 crisis in the Republic of North Macedonia we have switched to a modified managing of patients with chronic wounds, to reduce their visits and therefore minimize the risk of transmission of SARS-CoV-2. Patients urgently admitted to the hospital were considered and treated as positive to SARS-CoV-2 until the test results proved to be negative. The approach to treat these patients was time consuming requiring additional medical equipment as well as more staff engagement. These preventive measures were critical to minimize the risk of exposure for both patients and medical staff within the hospital. Three patients in our sample were positive for COVID-19. Patients who have been infected with COVID-19 combined with chronic infective wound should be closely monitored and isolated for treatment, negative pressure wards should be used during the surgery, and standardized preoperative, intraoperative, and postoperative treatment should be carried out to improve their prognosis [18].

During this period, majority of our patients were treated in outpatient settings. First of all, it was crucial to establish rigorous criteria during the process, which means to distinguish patients that require hospital admission and reduce the admission as much as possible only for urgent and critical patients (sepsis, chronic limb-threatening ischemia and gas gangrene). In terms of the wound type, the most common wounds were arterial ulcers, followed by diabetic, venous, and pressure ulcers. In relation to age, majority of patients were older than 60 years. In a study about the incidence of chronic wounds, Goh *et al.* reported an increased trend across all wound types, with the highest increase of incidence rate among the oldest age groups. The burden of wounds is expected to increase as the population ages [19]. During the period surveyed there was an ongoing treatment in majority of patients. In 37.5% of patients the wounds healed, 8.5% had amputations, and three patients (1.3%) have died.

We presented our algorithm for chronic wound management during the COVID-19 pandemic. The treatment was reorganized to treating patients in outpatient conditions, as infrequent as possible, and self-care with instructions from healthcare professionals as well. After the initial examination and decision that the patient can be treated ambulatory, a sharp surgical debridement to the vital margins of the wound was done. Thorough lavage was done mostly with saline, and usually after wards silver hydrocolloid dressings were applied. For signs of infection the patients were treated with antibiotics, non-steroid anti-inflammatory drugs and anti-edematous enzyme-based drugs. Some of the treatment strategies utilized in chronic wounds include offloading, compression, warming, and vacuum-assisted closure devices [20].

After ambulatory treatment, the patients were advised not to open the wound for three days at least if silver hydrocolloid dressing was applied, or if simple dressing with betadine gauze pads were applied. Then, after removing those, simple shower with medical antibacterial soap or betadine baths should be done. In some cases, patients were advised to perform irrigation of wound with hypochlorous acid-based solutions after doing a shower and apply simple sterile dressing as a final step. These patients were also instructed to notice every important change and signs if the wound was getting worse and to inform their surgeon immediately. Meloni *et al.* proposed a new triage pathway for management of persons with diabetes and foot ulcers (DFUs) according to ulcer features and comorbidities. Critical patients with severely complicated DFUs were urgently referred to a hospital. Patients with complicated DFUs received outpatient evaluation. Patients with uncomplicated ulcers were only managed by telemedicine after the first outpatient evaluation [21]. Shankhdhar presented a case of preventing diabetic foot amputation during COVID-19. The author and his diabetes care team managed the patient using online services and phone calls. The patient's self-care at home was successful and his ulcer healed completely, saving his toe from amputation [22].

In our sample, there was a good healing rate of diabetic ulcers. Patients with diabetes mellitus develop various microvascular and macrovascular complications, of which peripheral neuropathy and diabetic foot ulcers cause a significant negative impact on their quality of life [23]. Shin *et al.* reported a successful management of diabetic foot ulcers during the COVID-19 pandemic. Their approaches included virtual consultations using

physician-to-patient and physician-to-home nurse telemedicine as well as home podiatry visits [24]. Tao *et al.* suggested that in patients with small diabetic foot ulcers and mild infections, conservative treatment and small-scale debridement can be performed. In patients with irreversible injury and necrosis as the infection progresses, toxin absorption leads to a severe liver and kidney dysfunction. To save the lives of patients who cannot be stabilized by a non-surgical treatment, amputation must be performed. Patients with mild to moderate COVID-19 symptoms can tolerate more extensive or longer operations. For patients with severe or critical COVID-19, it is necessary to evaluate the potential risks of surgery [25].

Without an established public telemedicine system provided from wound or podiatric specialists in our country, the treatment of patients with wounds in general, especially vascular patients, is guided by the vascular surgeon in direct communication with the patient. Regular or video call, as well as, photos sent by patients are using for supervision and advice. It is of great importance that patients involved in this way of modified treatment have either previous basic medical knowledge or are educated for this purpose. Wang *et al.* presented their model for managing chronic wounds of outpatients during the COVID-19 pandemic. For stable wounds they recommended consulting through WeChat system online, teaching patients about basic wound managing skills, using foam dressings, and facilitating NPWT. For unstable and aggravated wounds they recommended multidisciplinary discussion online, choosing the nearest wound healing clinic, individual protection before going out, and fever and novel coronavirus screen [26]. COVID-19 has accelerated the adoption of telehealth among clinicians. Telehealth platforms make possible structured follow-up [27].

We provided telemedical support also for patients who underwent surgeries. After discharge they were scheduled for ambulatory check-ups and were advised for home care. Through efficient and effective application of telehealth strategies, health care providers can bypass infection risks while enabling the continuation of care for chronic wounds. Wound specialists, including physicians and registered nurses, can perform wound assessment through questions in text message format or phone calls, as well as photos and videos, to determine whether the lesions are stable, improving, or deteriorating [28]. It is important for the specialist to always keep the contact with the patients, assess by phone the presence of signs and symptoms: pain, redness, heat, swelling, drainage, fever, and increased pain, as well as, educate patients and their families how to perform the wound care [29]. We used Viber application in communication with our patients or their family members for sharing the photos of chronic wounds. Telehealth services can be used to screen patients who may have symptoms of COVID-19 and may provide the following: low-risk urgent care for non-COVID-19 conditions to identify those persons who may need medical consultation or assessment to make appropriate referrals; coaching and support for patients managing chronic health conditions; follow-up of patients after hospitalizations to decrease readmissions; and education of health care providers. Communication between healthcare providers and the population including telemedicine platforms can deliver healthcare and advice safely and quickly [30,31]. Persons with chronic wounds require regular care. As such, regular contact is inevitable not only for assessment but also for treatment (i.e. dressing changes). We can redesign the way in which wound care is delivered to fulfill the new norm of social distancing. Some elements, like self-care or family care, have existed for some time and others have been tested (e.g. telewound options), but none are the routine. That is about to change [32]. COVID-19 has reinforced that wound care is an essential service. Outpatients who do not receive frequent care, including wound monitoring and debridement, are at risk of loss of limb or even loss of life [33].

This model of providing surgical healthcare and treating of patients with chronic wounds in general can be absolutely beneficial even in normal circumstances, mostly because patients who are suffering from chronic wounds are weak and exhausted. Every visit to the hospital for them is an additional effort and psychological stress. Many of them are depended on transport to the hospital from their family members or other caregivers. In existing possibilities and circumstances we make efforts to provide safe and effective treatment of chronic wounds during the COVID-19 pandemic as our contribution to the global efforts to flatten the curve.

Conclusion

A specific triage pathway and modified treatment protocol for patients with chronic wounds during the COVID-19 pandemic were beneficial and showed an adequate management of chronic wounds. The proposed algorithm reduced the exposure to SARS-CoV-2 of both, medical staff and patients, while providing a good healing rate in all chronic wound types.

Conflict of interest statement. None declared.

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