Chapter

Management and Clinical Aspects of Burned Patients Affected by SARS-COV2

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Abstract

At the end of January 2020, SARS-CoV-2 started escalating worldwide. COVID-19 can exert its effects on immunity, inflammation, and multi-organ system disease, common denominators with the burn injury. The pandemic required major efforts to Burn centres in order to preserve burn patients' care and contribute to the health care response. In our Burn Unit we autonomously developed a protocol for patients acceptance and surveillance of the hospitalized ones and the personnel. We briefly describe our experience with six cases of burn patients infected by SARS-CoV-2 highlighting the overlap between medical treatment of burn patients and COVID-19 patients. To avoid viral spreading epidemiologic control is essential, especially preventive measures such as isolation of infected patients and identification of the source of infection. In our surgical practice, we increased the use of enzymatic debridement avoiding procedures with a high risk of viral particles spreading. Personnel protection and dedicated pathways have been planned, optimizing air circulation and disinfection. Vaccines represent the best hope for the global population to stop the viral spread, despite new variants outbreaks.

Keywords: COVID-19, Burn Unit, Burn Patients, Preventive measures, Clinical and surgical management, experience

1. Introduction

1.1 Background

At the beginning of December 2019 was reported for the first time, in the city of Wuhan, Central China, a pneumonia of unknown origin, named "coronavirus disease 2019" (COVID-19), caused by an agent initially known as 2019 novel coronavirus (2019-nCOV) and later referred as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1].

1.2 Epidemiology

Since the end of January 2020, SARS-CoV-2 started escalating worldwide until it was declared a pandemic disease by the World Health Organization on

March 11th, 2020. By the end of May 2020, the disease reached 188 countries causing nearly 370000 deaths. In Italy, clusters of cases were detected on 21th and 22th of February 2020 only in the regions of Lombardy and Veneto. At the beginning of March 2020, the virus was present in all regions of Italy leading the government to quarantine the whole population. For more than a year, Italy has been burdened by a huge number of cases and deaths with a related increase in hospitalizations and ICU admissions leading to a consequent constant hard stress for the National Health System. Meanwhile, scientists from all over the world intensively strived to unravel virus characteristics and develop new therapeutic and preventive approaches.

1.3 SARS-CoV-2 and burned patients

Since the COVID-19 epidemic onset, SARS-CoV-2 demonstrated a major contagious capability [2] with recent findings demonstrating possible similar pathophysiological features with SARS-CoV [3].

The mechanism of infection among humans is based on inhaled respiratory droplets with the virus replicating in the nasopharyngeal mucosa, spreading then into the lungs with lower respiratory tract infection capability. Close contact could also represent an infection source through mucosal surfaces of the nose, mouth, and eyes [4, 5]. Besides, there is also the chance of aerosol transmission in a closed environment.

Viremia, after the entrance of the virus in the circulatory system, can provoke secondary involvement of various target organs (e.g., heart, kidney, and central nervous system) with pathophysiological effects of SARS-CoV-2 ranging from acute lung injury to systemic and pulmonary hypertension, heightened inflammation, vascular hyperpermeability, coagulopathy and cardiovascular and gastrointestinal complications [3, 6].

Among the various types of trauma, extended burns can be considered as one of the most dramatic ones, characterized by a state of hypermetabolism with a catabolic shift, a state of hyperdynamic circulation and inflammation, subsequently linked to multiorgan failure and poor outcome [7, 8]. Additional pathophysiologic changes include vascular leaking mediated by polymorphonuclear activation and hemodynamic instability [9]. Moreover, immunosuppression, reported in major burn injuries [10], can determine a higher risk of infections which in turn can degenerate into sepsis, multiorgan failure and death.

Patient's age, total body surface area with burns, inhalation injury, and arising organ dysfunction are some of the principal prognosis predictors of burns [4, 11, 12].

In this way, COVID-19 can exert its effects on immunity, inflammation, and multi-organ system disease, common denominators with the burn injury, especially because SARS-CoV-2 infection might be a concurrent disease in a patient presenting to the medical attention for burns, needing immediate evaluation and medical attention even before COVID- 19 can be ruled out.

2. Burn unit experience during the pandemic period

COVID-19 disease, when symptomatic, usually presents itself with fever, cough, and myalgia or fatigue. Less common presentations are sputum production, sore throat, nasal congestion, anosmia, headache, hemoptysis, and diarrhea [13]. The severe pattern of evolution is characterized by worsening dyspnoea with hypoxemia and lymphopenia after which septic shock, ARDS, metabolic acidosis, and coagulation dysfunction can rapidly develop [14].

The actual pandemic pushed Burn centres efforts forward, keeping a fair balance between preserving burn patients' care and contributing to the health care response.

Due to the lack of really effective therapies and prevention measures such as vaccination during the virus initial outbreak, the major and most effective ways for disease spreading control were the isolation of affected patients, tracing of infected, hands hygiene, respiratory airways protection, and surface sterilization [15].

Our Burn Center, located in the North-East of Italy, a third level facility responsible for the acceptance and treatment of all major burns in an area with a population of approximately 5 million people, consists of three separate units: an ICU, a semi-ICU, and a Burn and Plastic Surgery Ward. There is also an outpatient clinic for post-discharge follow-up and small interventional procedures.

Due to the high demand of personnel and resources in the semi-ICUs and ICUs, all non-emergent activity was reduced in order to allocate the resources needed. In Plastic Surgery, only major oncological and trauma cases were scheduled [16]. Our Burn Unit reduced its elective activity of correction of burn sequelae. However, urgent and emergent activities greatly increased at the beginning of the pandemic since burn patients could not be accepted by all other centres in Italy.

The incessant incoming of patients from different locations within the pandemic epicenter represented an increased risk both for patients in the Burn Unit and for healthcare workers, due to COVID19 rapid spreading inside and outside the University Hospital.

In order to face the risk of viral spread, since the beginning of the emergency period, we autonomously developed in our Burn Unit a protocol for the acceptance of all the new patients and the surveillance of the hospitalized ones and the personnel, with distinctions made for the pediatric population [17]. These measures were later followed by the general prevention and management indications established by the Medical Direction of our University Hospital. Both these protocols were in accordance and regularly updated with the most recent Italian Government and International literature guidelines [18, 19].

2.1 Burn unit admission management and COVID-19 protocol

The burn-injured patient is firstly transferred from the place of injury to the closest hospital with an emergency facility. Here, the first treatment is provided to the patient. Meanwhile, our Unit is activated and we give our first telephone consultation, predisposing the transfer to our facility if deemed necessary.

During the pandemic, non-essential visits to inpatients were suspended. To partially compensate for the loss of direct contact, we provided our patients with the possibility of phone or video calls, improving the communication of the medical personnel with their relatives about clinical conditions and future therapeutic programs.

Cornerstones of our admission protocol are the use of PPE, patients' history, rapid disease screening and identification in a dedicated room until the test response and further patient isolation with frequent reevaluations during the following 14 days after admission in the BU.

Patient admission in our centre is performed exclusively in the operating room, using PPE when necessary [20]. All patients referred to our Burn Unit, before admission to the Ward, semi-ICU and ICU, must be tested through RT-PCR nasopharyngeal swab in the sending hospital when the response timing does not interfere with patient's care or in our hospital.

Immediately after collection, samples are sent for examination at the Microbiology lab and the results are available in about 90 minutes.

In addition, only for pediatric cases, also the caregiver is tested: outside the operating room if the arrival of the patient and the caregiver is simultaneous, in the monitoring room if it is delayed.

A history of fever, cough, other COVID-19 presentation symptoms [13] or contact with suspected or confirmed COVID-19 cases, are the first indicators of the necessity of isolation of a patient even if the test performed is negative.

During the wait for the result, the patient is treated as a suspect case, in a dedicated room or in the operating room, if intubated.

Chest X-ray and routine panel of blood tests including C-Reactive Protein are performed in patients requiring admission, regardless of symptoms.

Moreover, hospital personnel employs all the appropriate protections according to the specific-setting contagion risk [21, 22], which, in particular, is higher during aerosol-generating procedures as collection of diagnostic respiratory specimens for COVID-19, intubation, extubation, manual ventilation, suctioning of the respiratory tract, tracheostomy, bronchoscopy and surgery [23, 24].

In the case of a ventilated patient, we also perform a BAL which can allow the detection of a positive case even with a negative swab result. At the end of the admission procedure, the patient is managed according to the test result (**Table 1**). If the patient is intubated, during the test waiting period he is not moved from the operating room with any more emergencies treated in the same operating block in order to avoid contamination risk to other health workers and patients.

In some cases, when the number of required tests inside the Hospital is substantial, particularly in the period of acute emergency when the waiting time for the result was prolonged, the non-intubated patient could be temporarily moved to a dedicated and isolated room equipped as a Burn Unit room.

In the case of a pediatric positive patient and a negative caregiver, only the patient is hospitalized in a "COVID-19 room", a room designed for positive patients outside Burn Unit, supplied with the same equipment as the Burn Unit rooms and assistance guaranteed by Burn Unit personnel.

Instead, if the pediatric patient is negative and the caregiver positive, the patient is hospitalized in the monitoring room for up to 48 h and a new caregiver is designated. The former caregiver is invited to return home and adopt isolation measures keeping in contact with the local authorities. The Burn Unit physician has to inform the Epidemiology service of the caregiver positivity. The new caregiver and the patient have to be tested with the nasopharyngeal swab and if the result is negative they are both admitted outside the Burn Unit and placed in the isolation room for 14 days.

If the pediatric patient is intubated, no caregiver is included as in ICUs access is denied to anyone who does not belong to healthcare personnel.

Confirmed SARS-Cov-2 affected patients are admitted to the COVID-19 Unit, in separate airborne infection isolation rooms. Critical Burn patients are placed in the COVID-19 ICU.

Infectious disease specialists are consulted early with constant participation in patient care.

Burn patients who develop symptoms after admission are isolated and undergo swab PCR analysis and chest X-ray. Isolation is maintained until definitive results are received.

Negative patients are finally moved to the Burn Unit and quarantined for the following 14 days in a single-bed room. During this period, they are tested daily for fever and COVID-19-like symptoms. These measures are also effective for the caregiver of the pediatric patient. Moreover, a second nasopharyngeal swab is performed after 48 h in suspect cases and every 7 days after admittance, according to the fact that incubation period of SARS-CoV-2 is estimated to be 3–7 days

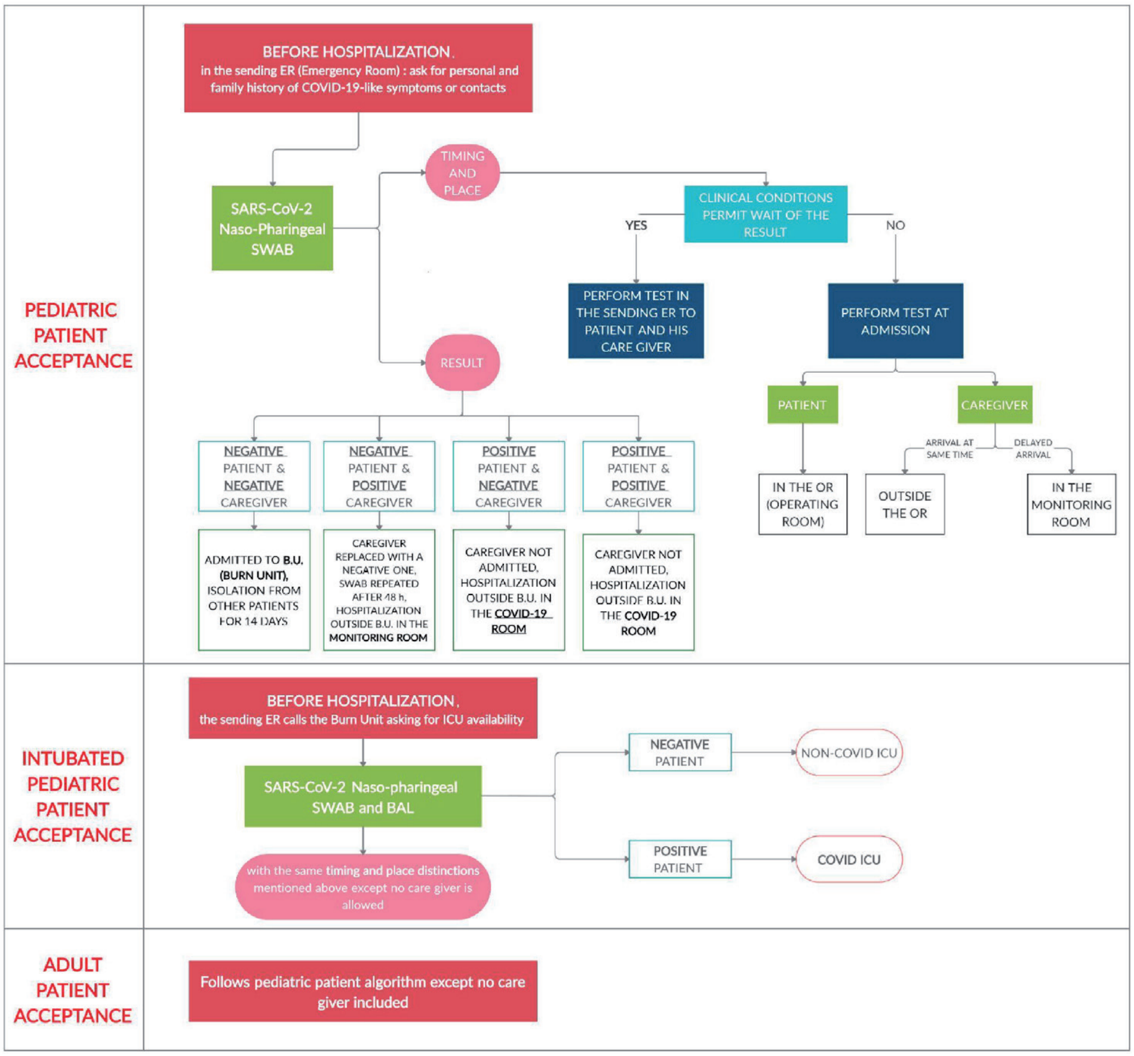

Table 1.
Acceptance protocol for pediatric and adult patients admitted to Padua university hospital burn unit.

with a range period from 2 to 14 days [25]. Both patients and caregivers are not permitted to leave the Burn Unit.

The temperature of all staff is measured at the entrance and exit from the Unit.

Unnecessary meetings are avoided with the preference given to the video conference modality.

On discharge, telemedicine follow-up is emphasized with special attention to rehabilitation.

After the initial viral pandemic spreading, in which all elective activity was suspended, we progressively began to reschedule this activity since May 2020. In order to achieve it, we have decided to screen patients first by phone and again immediately before the hospital admittance for travel history, presence of affected family members, evidence of fever or any respiratory tract symptoms in the previous weeks. In addition, asymptomatic patients undergo RT-PCR Sars-CoV-2 test before hospital admission.

2.2 Burn unit COVID-19 case series

Since the pandemic began, the main goal of our protocol was to preserve burn patients from infection and to avoid viral spread in such a delicate unit.

In the last year, from the beginning of the pandemic, 93 patients were hospitalized in our Burn Unit, including six cases of burn patients affected by SARS-CoV-2:

three of them were hospitalized with a molecular swab positive for COVID-19, while three of them were infected during the hospitalization (**Table 2**).

In April 2020 an extensive burned patient was the first to test positive for COVID-19.

She was a 56-year-old female who got burned after a domestic accident (explosion of a gas cylinder) on April 5th 2020 with 70% of TBSA. She was immediately intubated, a urinary catheter was introduced, a central line was put and fluid resuscitation was immediately commenced.

She reported a 70% TBSA burn involving face (II degree burn), neck, trunk, and upper and lower limbs (III degree burns). Once she arrived in our operating room, she immediately underwent surgical debridement of all third-degree burns and xifo–pubic and both upper limbs fasciotomies were performed. She also underwent enzymatic debridement (Nexobrid®) on her third-degree burns on the neck, shoulders, and abdomen.

A molecular swab and a BAL were performed at the arrival in the operating room and the patient stayed there until the result showed positivity for SARS-CoV-2. Finally, the patient was transferred to our COVID-19 ICU. Before the burn accident, the patient had only a mild fever (38°C), with no other symptoms reported. She got infected by her sister with whom she lived.

Once she arrived in our COVID-19 ICU her vital parameters were stabilized and she immediately underwent specific treatment for burn patient: intravenous fluid resuscitation with Ringer lactate's solution according to Parkland formula, empiric intravenous antibiotics, Low Molecular Weight Heparin (LMWH) 4000 UI once a

Age	Sex	TBSA	Covid test at hospitalization	ICU	Surgical treatment	Days of hospitalization	Positivity	Outcome
56	F	70%	+	YES	Proteolytic debridement, surgical debridement, tracheostomy, skin graftings	105	12 days	death
73	M	60%	+	YES	Proteolytic debridement, surgical debridement, skin graftings	105	3 days	death
54	M	25%	—	YES	Arm amputation, surgical debridement, skin graftings	144	52 days	healed
61	M	51%	—	YES	Surgical debridement, skin graftings	170	52 days	healed
51	F	10%	+	NO	Grafing with amniotic membrane	6	6 days	healed
25	F	41%	+	YES	Surgical debridement, skin graftings	96	5 days	healed

Table 2.
Features of our Covid-positive patients.

day, analgesic therapy and human endovenous Immunoglobulin (Pentaglobin®). In order to stabilize the vital parameters, it was necessary to perform blood and plasma transfusions and to administer noradrenaline. She was also set on an air fluidized bed (Clinitron®) for extensive burns of her back.

Initial assessment included a routine blood test, Arterial Blood Gas (ABG) every two hours, chest x-ray twice a day and rectal swab searching for MDROs.

Blood tests showed mild leukocytosis (12,02 10^9/L), implementation of PCT (0,65 ug/L), important augmentation of myolysis markers (P-CPK 5.813 U/L, P-myoglobin 3.814 ug/L).

Because of the important muscular necrosis, she rapidly developed acute kidney insufficiency and needed immediate CVVH-DF substitutive renal therapy.

Even though she initially had no Covid-like symptoms but fever, her chest x-ray showed an interstitial involvement, her lungs were less expanded and her costo-phrenic sinuses were poorly evaluable. Because of the risk of ARDS, fluid resuscitation has been kept lower than a 70% TBSA burn patient would necessitate.

During the hospitalization, several cutaneous swabs were performed and intravenous antibiotic treatment was changed based on antibiograms.

Blood and plasma were transfused routinely both during surgery and hospitalization.

Medical treatment of burn patients and COVID-19 patients shows an overlap.

Treatment with LMWH is mandatory because both burn condition and COVID-19 infection increase the risk of thrombosis.

Significant inflammation is present in patients with SARS-CoV-2 infection. There is the elevation of IL-6 levels, C-reactive protein, erythrocyte sedimentation rate, and fibrinogen. Since the tropism of the virus is for ACE2 receptors, this determines endothelial cell activation and disruption of the antithrombotic state [26].

Broad-spectrum intravenous antibiotics are administered both for the increased risk of sepsis in burn patients and prophylactically in COVID-19 patients to avoid opportunistic infections.

Besides this treatment, which is common in burn patients and COVID-19 patients, she also received specific treatment for COVID-19 pneumonia. In order to improve her ventilation, she was set in a prone position leading to a slow improvement of her gas exchanges [27]. The change to prone position generates a more even distribution of the gas–tissue ratios and a more homogeneous distribution of lung stress and strain. It is also accompanied by an improvement in arterial blood gases, due to a better overall ventilation/perfusion matching [3].

It was then started endovenous corticosteroid therapy, with the goal of improving gas exchanges. Corticosteroid therapy given to COVID-19 patients could have a favorable effect by reducing pro-inflammatory cytokines, decreasing lung vascular permeability, improving epithelial barrier integrity, and promoting alveolar oedema fluid clearance [28].

The patient also started medical treatment with Chloroquine/hydroxychloroquine *(CQ/HCQ)*. Possible mechanisms of action of HCQ are multiple and not fully understood. It probably reduces viral entrance by increasing endosomal pH and inhibits glycosylation of the cellular ACE2 receptor, interfering with viral binding in the lungs [29].

On the twelfth day of hospitalization, her swabs and BALs were negative and the patient showed no more COVID-19 positivities until her last day of hospitalization.

After the negativization of two consequent BALs, the patient was transferred to a non-COVID-19 ICU, according to the fact that her clinical conditions required ICU treatment. In fact, she stayed feverish with temperature oscillating in a range from 37.5°C and 39°C, her chest x-rays showed pleural effusion and her blood tests revealed an overall augmentation of inflammatory parameters.

During the hospitalization, her general conditions were initially quite stable but she slowly developed a septic status, which led the patient to death on her 105th day of recovery.

From a surgical point of view, the day after the hospitalization the patient underwent a massive surgical debridement of all burned areas, removal of proteolytic enzymes, and a total body change of dressing.

Frequent change of dressings in a dedicated operating room was planned (three times a week) and the patient underwent several surgical debridements and homologous and autologous skin grafting procedures.

In order to avoid long-term intubation complications, on the 5th day after hospitalization a tracheostomy was performed.

During hospitalization, we assisted to a gradual re-epithelialization of the burned area, with total healing of her upper left limb but the permanence of not fully healed areas on her chest and dorsum.

Our second COVID-19 positive patient was a 73-year-old man who set himself on fire with turpentine once he found out that his wife had contracted COVID-19 infection. His medical history included blood hypertension, diabetes, and depression.

The patient lived in Bergamo, one of the worst-hit cities by COVID-19 in Italy. He immediately was transferred to his city ER, where he was stabilized, intubated and a BAL was performed with a positive result. The day after, May 7th 2020, he was transported by helicopter to our dedicated operating room, where a new BAL was performed.

He had II and III degree circumferential burns on his lower limbs, III degree burns on the perineum and scrotum, III degree burns on the half of the flanks, chest, and left side of the back, III degree burns on half neck and upper limb with a TBSA of 60%.

The patient was immediately transfused with plasma and underwent double decompressive fasciotomies on his right lower limb. Then surgical and enzymatic debridement was performed on all third-degree burns.

The patient was then transferred to our COVID-19 ICU.

As he showed no COVID-19 symptoms, no pneumonia, and initial negative BAL, a BAL per day was repeated for the next three days and all of them resulted negative. It was also performed a serological test that showed high IgG levels and low IgM levels, a sign of a previous positivity.

As his clinical condition required an ICU, the patient stayed in our COVID-19 ICU, even though he did not develop a COVID-19 infection, and never contracted it during his hospitalization in COVID-19 ICU.

In his hospitalization in COVID-19 ICU, the patient was set on an air fluidized bed (Clinitron®) as adjuvant therapy for his back burns, and standard treatment for burn patient was started: hydration with Ringer lactate's solution for the first 24 hours, then with rehydration solution, antithrombotic therapy with LMWH, broad-spectrum intravenous antibiotics according to microbial cultures, Immunoglobulin therapy for three days (Pentaglobin®) and antalgic therapy.

His vital parameters were monitored, water balance was kept positive, and specific parenteral alimentation rich in proteins and oligo-elements was started.

Routine blood tests and x-rays were made and various microbiological samples were sent.

Thanks to the ICU care we assisted in a gradual recovery of vital parameters, stabilization of the hemodynamic system, and the restoration of spontaneous breathing.

From a respiratory point of view, the patient has been intubated until the 15th of May, when a tracheostomy was performed and he was ventilated through it. Since the 28th of June, he has been spontaneously breathing.

Hemodynamically he required therapy with norepinephrine for about one month.

His recovery in COVID-19 ICU, which in the meantime returned to a non-COVID-19 ICU as the first wave of COVID-19 was about to end, lasted 52 days and then he was transferred to our Burn Unit.

During his hospitalization in our Burn Unit, we assisted in gradual healing and re-epithelialization of all burned areas and the patient was going to be transferred to the Burn Centre of his belonging region for the continuation of treatment.

On the 19th of August the patient complained of dyspnea, he had a fever (41°C) which did not respond to antipyretics. His saturation was 86% with 6 L/min of 02, his blood pressure was 72/32 mmHg, heath rate 105 bpm, and respiratory rate 42 breaths per minute. A septic shock was developing. He was immediately transferred to the ICU and intubated but he died some days later because of the worsening of the septic shock.

It is clear that death in this patient is related to the severity of his burns and not to COVID-19.

Nevertheless, this case remarks once again how fundamental is the management of a COVID-19 burn patient since the beginning, with the use of a dedicated operating room and the recovery in a COVID-19 ICU.

In the month of October 2020, all of Italy was affected by the second wave of COVID-19, with the viral spread and the crescent burden on ICUs. This led to the diffusion of the infection inside the hospitals and the genesis of clusters of infection.

As a matter of fact, between October 8th and November 30th 2020, two of our patients got infected by the virus several weeks after their hospitalization.

Thanks to our protocol, which contemplates the repetition of antigenic and molecular COVID-19 swabs weekly, we managed to identify and immediately isolate patients affected by COVID-19, in order to reduce the spread of infection inside our Burn Unit.

None of our patients who contracted the infection showed any COVID-19-like symptoms. They had only a mild fever, which wasn't imputable to the virus. In fact, all of them had a mild augmentation of inflammatory parameters and microbiological growth (*Pseudomonas aeruginosa* above all) on their burns. In fact, fever is one of the most frequent symptoms in burn patients.

It is curious that they had their first positive molecular swab on the 8th of October and continued to alternate positive and negative molecular swabs until the 30th of November.

These patients never showed any significant symptoms and had been isolated in a single room for all the positivity period. Further examinations were made, in fact, a sputum culture examination was performed and within approximately one week we had the result: no SARS-CoV-2 growth. So all the molecular swabs which resulted positive after the sputum examination were false positive and the patients were not considered contagious anymore.

Until an effective circumscription of positive cases has been achieved, it was taken the hard decision not to hospitalize other burn patients which did not come, of course, from our ER.

Spatial isolation, the use of PPE, the weekly screening program, and the disinfection of all common spaces were fundamental to circumscribe the COVID-19 cluster which was born in our Burn Unit.

Once safety was finally achieved it was restarted regular hospitalization, always according to our COVID-19 protocol.

The third COVID-19 burn patient was a 51-year-old female who burned her face due to a backfire, reporting only II-degree burns. At the arrival, an ENT consultation was made and it stated intubation wasn't necessary. A molecular swab was made and it tested positive for COVID-19. The patient was completely asymptomatic and was hospitalized in our Burn Unit.

She underwent surgical debridement and an amniotic membrane grafting was performed. Her hospitalization lasted for 6 days and then she was dismissed.

Our last burn patient affected by COVID-19 was a 25-year-old female.

She had contracted the infection ten days before the burn and she was in home isolation, as her conditions did not require hospitalization. Her home treatment included antipyretics, Azithromycin once a day for six days, no LMWH or corticosteroids were necessary. No other significant medical history was reported.

Due to this injury, she reported second-degree burns on her neck and cheeks; third-degree burns circumferential on her upper limbs, second-degree on her chest and breasts; second-degree on her abdomen with a TBSA of 41%. We decided to immediately perform enzymatic debridement with Nexobrid® (**Figure 1**), and after 24 hours we performed coverage within homologous skin grafts and amniotic membrane. The patient was then transferred to a COVID-19 ICU.

During her hospitalization in ICU, she did not present any COVID-19-like symptoms and her BALs negativized five days after her hospitalization, so no specific treatment for COVID-19 was started and she received standard therapy for burn patients. In two weeks the patient was stabilized and transferred to our Burn Unit and her skin injuries were definitely closed by an autologous skin graft.

This case series reported how the novel SARS-CoV-2 afflicted our Burn Unit and how we managed to adapt our Burn Unit admission because of the pandemic. It is important to underline that none of our patients affected by COVID-19 ever developed interstitial pneumonia and so COVID-19 infection did not directly influence the outcome of our patients.

What actually was influenced by the pandemic was the management of the patient, the preparation of the operating room, and the surgical act itself.

2.3 Surgical treatment of Sars-CoV-2 patients

For most burn patients coming to the OR, the need for surgical intervention is imperative. Patients urgently admitted to any Burn Unit generally need immediate transfer to the OR for the primary care of their wounds and, mostly, will need subsequent surgical reassessments and re-interventions until an acceptable cover of the wounds has been achieved and the patient may be followed up as an outpatient.

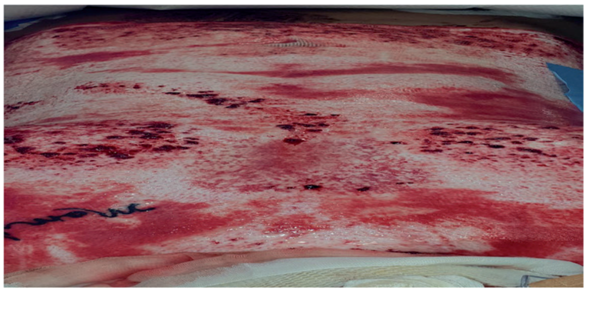

Figure 1.
Third degree burn abdoment and chest 4 hour after enzimatic debridment with Nexobrid.

The urgent admission and the subsequent surgical revisions expose medical personnel involved in burned patient care to an increased risk of contracting SARS-CoV-2 due to prolonged exposure in the OR and in the Burn Unit itself. Besides, the exposure risk also applies to the other patients admitted to the OR or the wards due to proximity.

As vaccine rollout proceeds, more and more people are getting immunized to SARS-CoV-2, however, as vaccination efforts are still underway, screening at admission, isolation protocols for positive patients and safe surgical and anesthesiologic procedures for the personnel are still to be enforced to ensure spread avoidance.

In our experience, the protocol enforced to screen SARS-CoV-2 patients entering our ward has worked fine in avoiding admission of positive patients and in avoiding spreading of the infection among inpatients and to or from healthcare workers [17].

In general, struggling with a pandemic and having hospitals overwhelmed by SARS-CoV-2 positive patients in various degrees of severity, required careful organization, and eventual re-organization, of the health care staff activity from nurses to medical doctors to support personnel in order to avoid exhaustion of resources. This is especially true for surgical equipment which cannot be easily replaced with new, less trained staff or by staff taken from other branches of medicine without the risk of reducing senior surgical expertise hence the standard of care. From here, the need to work on skeleton personnel in order to spare as many units as possible in case of health care personnel contagion. In general, this type of approach has been required to minimize almost all elective surgical activities and to postpone them to the moment when contagion levels start, slowly, to reduce in number. The only elective patients that kept on being admitted were the oncological ones and only after submission of a negative SARS-CoV-2 RT- PCR test dated no more than 3 days before admission. However, obviously, emergent patients did not disappear during COVID-19 pandemic and their management has been the greatest concern of all in order to guarantee assistance, but to avoid excessive personnel exposure.

In Italy, the major medical societies involved in the care of surgical patients have produced indications for the management of potential SARS-CoV-2 patients [30] which often are the backbone of each hospital-specific protocol.

As the emergent need for surgery does not allow time to wait for SARS-CoV-2 swab results, all patients admitted in emergency must be treated as if they were positive.

As, usually, transport is needed to bring the patient from the ward or from elsewhere to the theater, clear and pre-designed pathways should be available. These paths should be the shortest possible and the most isolated possible, as this is clearly not always possible, anyone crossing these paths should be alerted preemptively or these paths should be cleared before passage and sanitized afterwards. Transport personnel should be trained to wear appropriate PPE at all times.

In general, patients going to theater should not stop anywhere for any reason but should be brought to the designated theater where all procedures pre, peri, and post-operational should be performed and that designated theater should be the one closest to theater entry in order to minimize transit contagion risk. Entry and exit pathways to the theater should be different from negative patients' routes. Potentially positive patients should wear the protective masks until anesthesiologic procedures for tubing begin, otherwise, if there is no need for intubation, the protective mask should be worn at all times. Clearly, the personnel that will care for the patient, needs to be trained in donning, doffing, and in the disposal of protective equipment (**Figure 2**).

In the OR minimal personnel should be allocated to a single infected case in order to minimize exposure and, if the case spans more than one shift, this could mean working after hours for the equipment involved. All personnel receiving the

Figure 2.
Preparation to a Covid burned patient surgery with all protective disposable.

patient should be wearing appropriate PPE. All non-necessary material must remain outside the OR including medical records which may be consulted either by doffing or by personnel non involved in the OR and then communicated inside the OR.

OR should be negative-pressurized with a high air exchange cycle rate. Materials available should be ready on a case-by-case basis before the procedure begins and, once it starts, all efforts should be made to use what is available in order to reduce to the least possible entry and exit of personnel to and from the OR. All trolleys should be replaced with dedicated ones in order to avoid possible surface contagion for procedures to come afterwards. Personnel must be reduced to the minimum number possible to perform the planned operation.

Anesthesiologists should have planned their strategy in advance in order to minimize risks associated with complex intubation procedures and techniques with the highest chance of first-time success should be used to reduce excessive manipulation of the airways. All staff must wear full PPE and these should be replaced after completing the procedure, especially if that has been complex.

More liberal use of intubation is acceptable to avoid risks associated with non-invasive ventilation. RSI could potentially reduce the need for manual ventilation and potential aerosol spreading, which could however be reduced by using small current volumes in manual ventilation. HEPA filters should be put between the patient's expiratory limb and the ventilator machine and between the patient and the gas sampling tube and replaced after each use.

As all materials should be ready before the procedure starts, all efforts must be made to use the material available. Entering or exiting the room should be discouraged at all times. Any need for additional material should be addressed by personnel outside the OR. Surgical masks are replaced by FFP2 all the remaining donning should be performed as protocols indicate. The patient is dressed according to the procedure to be performed.

For what concerns the procedure, no consensus exists on whether laparoscopy should be used or should be contraindicated [31]. There is the theoretical possibility of spreading the virus through smoke produced by energy devices, but this has not been demonstrated for SARS-CoV-2. The same applies to energy devices used in open surgery. No formal contraindication exists to perform laparoscopic procedures in SARS-CoV-2 patients either positive or suspected, however, all precautions must be applied to reduce potential exposures including reducing the use of electrosurgical devices, applying smoke evacuators and HEPA filters to exhaustion of surgical smoke, reducing pneumoperitoneum pressures [32] and, finally, deflating the abdomen using suction or smoke evacuation devices instead of letting pneumoperitoneum out from trocar incisions in the OR [33].

Otherwise, we need to perform a protection colostomy for burn legs in our second COVID-19 patient and we preferred to perform it by open laparotomy due to efforts to avoid gas diffusion on COVID-19 tissues and the presence of abundant abdomen's free liquid [34].

After the procedure, enough time should be allowed for air exchange in the OR according to the exchange cycle rate of the theater to avoid cross-contamination. All environments in which the patient has transited should be carefully sanitized. All waste should be disposed of in designated containers and should transported wearing full PPE.

2.4 Burned patient swab surveillance

Screening swabs on the healthcare workers were scheduled weekly while on hospitalized patients twice a week. In the first 6 months from the beginning of the pandemic, no outbreak occurred in the ward, neither among staff nor among patients.

For scheduled surgical interventions instead, a telephone triage was performed to find out if in the previous 2 weeks the patient had developed any symptoms compatible with a possible COVID-19 infection, such as fever, cough, breathing difficulties, asthenia, anosmia, or ageusia. If the patient did not report any symptoms or known positive contacts, molecular swabs were performed in the 96-72 h before hospitalization, requiring the patient to be isolated at home after the execution [16].

In early October, rapid antigenic swabs began to be used mainly by the infectious disease department and the emergency room. During the second week of October a small Coronavirus outbreak involving two healthcare workers as well as two patients, developed inside the Burn Unit. This led to the request to the infectious diseases department for a supply of rapid antigenic swabs, to obtain a faster and more efficient screening of patients and medical staff.

Up to that time, the standard hospital procedure, in case of unprotected contact with a patient positive for COVID-19, included the execution of a molecular swab: immediately after contact, on the 5th and the 10th day.

During this screening period, the operator, if asymptomatic and tested negative, was not required to stay in home isolation.

The main problem with this screening routine based on molecular swabs was the report timing. In fact, at that time, a screening swab, given the large amount of work to which the laboratory was subjected, was rarely reported before 2–3 days.

These timing of execution, considering the incubation period and the high percentage of asymptomatic patients with the COVID-19 infection, subjected the staff, who had to work daily with positive patients, to a concrete risk, if they had contracted the virus, to act as vectors before the swabs detected their positivity.

To reduce this risk, we decided that the screening for the viral detection in the major burn centre had to be carried out by performing a double swab: antigenic and molecular at the same time.

Although at that time many studies had already reported an antigenic swabs sensitivity varying between 30% and 80%, considerably inferior compared to the molecular swabs one, reported around 97%, the speed of execution made it possible to anticipate possible isolation by a few days, thus reducing the possibility of any intra-hospital infections and the onset of new outbreaks [35–37].

With the double swab method, screenings continued to be carried out every 7 days on healthcare workers, twice a week (usually on Monday and Friday) on hospitalized patients, at 0–5-10 days for unprotected contacts and as needed for personnel or patients who presented suggestive symptoms such as fever, arthralgia, anosmia or malaise.

The "double-swab" screening continued till the end of February when the healthcare workers got vaccinated. From that moment, weekly, only molecular swabs are performed, while "double-swabs" screening is still carried out nowadays for unvaccinated hospitalized patients.

From the beginning of this double swab protocol, no patient got infected during their hospitalization. We registered four cases of SARS-CoV-2 infection between healthcare personnel, all of them immediately quarantined with none of them contracting the infection in the workplace.

3. Therapeutic consideration in a COVID-19 burn patient

Burn-injured patients are deeply affected in nearly all their vital functions with pathophysiologic changes that can range from hemodynamic instability to altered metabolism, hypothermia, and, more importantly, airway and pulmonary impaired functions.

SARS-CoV-2 has represented in Italy an impressive public health threat, rapidly spreading among regions with Lombardy and Veneto as epidemic centres. Because of the high viral infectious rate and its capability to damage several organs, especially the lung with particular severe pneumonia, effective prevention and treatment are essential [12].

Various treatment options are being tested, with a variety of studies investigating the utility of some off-label drugs. Currently, the major way to avoid virus spreading is epidemiologic control through preventive measures such as isolation of infected patients and identification of the source of infection. All categories of people are susceptible to SARS-CoV-2 but most severe cases are recognized in the elderly patients and those with underlying diseases or immune dysfunctions [6, 13]. Burn injuries must be considered similar to the above-mentioned conditions for their intrinsic immune and multiple organ dysregulation, in the context of a general severe illness affecting all vital functions [14].

The fast COVID-19 spread from China to European countries such as Italy, and particularly the region in which our centre is located, therefore imperatively required the implementation of every procedure and admission protocol in our Burn Unit.

COVID-19 treatment guidelines are continuously updating based on revising, legitimate national and international guidelines for optimal management. Antivirals such as Kaletra, Favipiravir and Remdesivir have been used by infectious disease consultants but are not part of our COVID-19 treatment guidelines yet. Oseltamivir or Ribavirin are not used any longer. Hydroxychloroquine has not been used anymore in the treatment of COVID-19 patients.

Interferon-Beta and/or IVIG have been given in case of excessive inflammatory responses, mostly in our burn critical care COVID-19 patients. Corticosteroids such as Dexamethasone and Methyl-prednisolone have recently been added to our COVID-19 treatment protocols in the setting of severe inflammatory responses and/or hypoxemia (blood oxygen saturation < 90%). Convalescent plasma has also been added to the therapeutic regimen of deteriorating burn critical care cases. All our adult patients (ward or ICU, with or without COVID-19) have been receiving pharmacological thromboprophylaxis (low molecular weight Heparin, standard-dose unfractionated Heparin) unless there were contraindications.

Frequent use of antibiotics without clear indications is not anymore recommended. However, they have often been used in burn critical care cases with worsening clinical conditions. All our patients receive the usual dose of daily vitamin C, per standard burn treatment protocols. Our current COVID-19 guidelines have not yet recommended high dose vitamin C.

Concomitant severe burn and COVID-19 might complicate the clinical presentation and hospital course.

This dictates multidisciplinary approaches to risk stratify, screen, assess, and manage coexisting diseases. Additionally, appropriate preparations and careful precautions need to be executed in burn units to prevent COVID-19 exposure and transmission to limit potential adverse outcomes.

The potential detrimental consequences of concomitant burn and COVID-19 suggest mandating extra precautions and sophisticated strategies which need to be implemented in burn units. Such policies help prevent infection, recognize different types of exposure, establish detailed and systematic protocols on proper diagnosis and management. The key steps include the fast and careful patient screening for COVID-19 on arrival, frequent screening of hospital staff, obtaining detailed history on travel risk factors in two weeks prior to the admission, assess for fever or other respiratory signs and symptoms before or during hospitalization with continuous clinical surveillance, personal protective equipment (PPE) in all areas with proper social distancing, provision of disinfectants and sanitation equipment, and staff travel restrictions [15, 16].

With an ongoing COVID-19 pandemic, SARS-CoV-2 infection might be a preceding, concomitant, or subsequent disease in addition to other various medical problems or traumas such as burns. Thorough risk stratification and multidisciplinary approaches to the strategic management of comorbid conditions are paramount to prevent possible worsening outcomes.

Current evidence demonstrated sensitivity rates of less than 70% for all COVID-19 diagnostic tests including RNA RT-PCR, total antibody, IgM, and IgG at the first week of symptom onset. In addition, the test-positive result rates of RNA RT-PCR tests (currently the most performed test in the UK) varies depending on the sampling technique (eg. oropharyngeal swab, NP swab, bronchoalveolar lavage) and timing of the test from symptom onset significant presence of false-negative tests should always be taken into consideration pending the development of validated, highly sensitive and specific tests.

All healthcare workers and patients should attempt to deliver care whilst ensuring protection from disease transmission by any means available. All burns services should anticipate and plan to continue delivering patient care whilst taking social distancing and shielding measures into account.

The shocking speed with which the COVID-19 pandemic has exploded, and the scale of strategic planning required to cope make it very difficult for systems to prepare adequately. In many places, the critical care demand will create sudden scarcity which will impact the capacity to provide critical care for burns. This obligates each burn centre to prepare for burn care under austere conditions. In cases of massive COVID-19 disease, the burn centre will become an important cache of personnel, space, and equipment. Burn centre leadership should actively engage in local and regional strategic planning. Importantly, the burn community should seek ways to help one another through the coming challenge. The present collection of experiences aims to achieve the goal of early communication among burn leaders in order to disseminate knowledge rapidly and fast-track best practices.

SARS-CoV-2 screening and prevention strategies need to be implemented at burn care centres, both outpatient and inpatient settings during the current COVID-19 pandemic. This is due to the substantial vulnerability of burn casualties to infection and the ease of transmission among them.

The effectiveness of the adopted measures during the COVID-19 epidemic outburst allowed our Burn Unit to preserve its clinical and surgical activity simultaneously safeguarding patients and hospital personnel from contagion risk, despite a high rate of admitted critical patients and the geographical position in the centre of an epidemic area.

3.1 Medical and surgical approach in the COVID-19 burn patient

Medical treatment of burn patients and COVID-19 patients show an overlap. The low number of treated cases could not allow any consideration about the absence of COVID-19 complications in burned patients. At the same time, we have to underline that several therapeutic approaches that seemed to improve Sars-CoV-2 affected patients are common to severely burned patients.

- **Low molecular weight heparin**: Treatment with LMWH is mandatory because both burn condition and COVID-19 infection increase the risk of thrombosis.

  Significant inflammation is present in patients with SARS-CoV-2 infection. There is the elevation of IL-6 levels, C-reactive protein, and erythrocyte sedimentation rate, and fibrinogen.

  Since the tropism of the virus is for ACE2 receptors, this determines endothelial cell activation and disruption of the antithrombotic state [2].

- **Antibiotic treatment**: Broad-spectrum intravenous antibiotics are administered both for the increased risk of sepsis in burn patients and prophylactically in COVID-19 patients to avoid opportunistic infections.

- **Plasma transfusion:** Plasma transfusion is a life-saving and fundamental treatment in burn patients because it represents the best resuscitation fluid due to its capability to restore intravascular volume status and treat the endotheliopathy. Hyperimmune plasma from COVID-19 convalescent was also suggested as a potential treatment for severe COVID-19 so, even though we have not experienced such treatment in our cases, it could be possible to consider the treatment of burn patients with severe SARS-CoV-2 infection by hyperimmune plasma.

- **Immunoglobulin:** Depressed serum immunoglobulin levels following severe burns may lead to subsequent infectious complications following such injuries so the administration of immunoglobulin in our therapeutic approach in major burns is common (*Pentaglobin*® at 100 ml rate three times a day for three days). At the same time immunomodulation with polyclonal preparation of immunoglobulins as adjuvant therapy in SARS-CoV-2 mild and severe pneumonia has been detected as efficacy in several cases [38, 39].

  At the same time about the medical approach, we have to emphasize the mismatch between the important fluid resuscitation necessary for burn patients and the fluid restriction that is needed in SARS-CoV-2 pneumonia.

  In the surgical approach to COVID-19 burned patients we have marked some important aspects to be considered:

- **Necrectomy approach:** Due to the necessity to reduce operating time and at the same time to be efficient with necrectomy we increased the use of enzymatic debridement (*Nexobrid* ®- Mediwound Germany GmbH) which allows an efficient and selective debridement with less blood loss [40].

- **Hydrodebridement:** We have avoided the use of hydro-debridement (such Versajet®) for wound bed preparation due to the necessity to have not spreading of virus particles into operating theater and on objects

- **Laparoscopic procedures:** When laparoscopic procedures were necessary (eg. Protection colostomy) we avoided performing because of the high risk of contamination with the insufflate air and we preferred the laparotomy approach

- **Tracheostomy:** To perform a tracheostomy on COVID-19 patients it's necessary a well-trained and experienced surgeon with a strict collaboration with an anesthesiologist in all parts of the procedure, in particular, to avoid any air spreading from the tube.

- **Personnel and equipment:** Personnel must be reduced to the minimum possible number with a very precise surgical planning. The equipment must be the same as in the COVID-19 ward unit and because of the high temperature needed during burn patient operations and the physical efforts, it's mandatory to perform early surgical procedures.

- **Pathways:** Dedicate pathways must be planned for COVID-19 positive patients from and to the OR and must be separated from regular pathways for non-COVID-19 patients.

- **Air circulation and operating room preparation:** Air circulation has to be achieved by using dedicated filters and numerous air exchanges. The OR must be equipped with the minimum instruments available and with easily sterilized tools, as it needs accurate disinfection after every procedure.

4. Conclusion

In the early weeks of the pandemic, with the first cluster of cases detected on 21th and 22th of February and a national quarantine declared on March 8th, the Italian National Health System found itself in a very stressful situation, counting a high number of the greatest number of cases and deaths and requiring an intense effort to secure bed availability in the hospitals and the ICUs.

Even if our elective activity was reduced to the correction of burn sequelae, urgent and emergent activities greatly increased since many other centres in North Italy could not accept burn patients anymore due to ICU bed lacking or furthermore for incapability to accept and treat COVID-19 positive patients.

To avoid a possible spreading of SARS-CoV-2 inside the Burn Unit, and to reduce the risk patients and health workers were submitted to, since the beginning of the emergency period we developed a protocol for the acceptance of all the new patients and the surveillance of the hospitalized ones [17].

This protocol was elaborated gathering guidelines and suggestions reported by the first Burn Centers involved in COVID-19 infection management [41, 42]. It anticipated the general prevention and management indications established by the Medical Direction of the University Hospital of Padua, which followed the most updated Italian Government and International literature guidelines at the time [18, 19].

Three principles are the pillars of this protocol: patients' history (suggestive symptoms or contact with cases are themself sufficient causes for isolation, even if the test performed is negative), rapid testing, and isolation in a dedicated room until the test response.

Our Burn Unit Centre is a third level facility, responsible for the acceptance and treatment of all major burns in an area with a population of approximately 5 million people. When the response timing did not interfere with the urgent treatment, we asked the patient to be tested by the sending hospital or by our emergency room.

For emergency cases instead, with major burns, our microbiological lab granted us a preferential route to obtain the results of the swabs within 90 minutes, while the patients were kept in isolation in a quarantine room or the operatory room if intubated, before being moved to the Ward, semi-ICU or ICU according to their conditions.

While since the beginning of the epidemic we decided to stop any outside visits to inpatient rooms, encouraging the use of phone or video calls to communicate with relatives, an exemption was made for pediatric cases, where the caregiver was tested simultaneously with the child or as soon as he arrived, staying in the monitoring room till the swab's result.

The nucleic acid detection through reverse transcription qualitative PCR was the only method accepted for the laboratory diagnosis, usually via the collection of nasal and pharyngeal swabs but also via BAL in ventilated patients, which proved to be a more sensible detector [43].

Once confirmed negative, the patients are finally moved to the Burn Unit strictly monitored for 14 days as recommended by the World Health Organization (WHO) [44].

Considering no SARS-CoV-2 outbreak has happened in our Burn Unit since the beginning of the double testing, despite the second wave of COVID-19 Italy has experienced from November 2020, we can consider it an appropriate way of managing SARS-CoV-2 screening on hospitalized patients and healthcare workers.

COVID-19 infection in burn patients might worsen the clinical outcome making medical care, even more, demanding, with the necessity of multidisciplinary care.

Management of surgical patients affected or potentially affected by SARS-CoV-2 requires clear protocols that must be shared with health care staff in order to be implemented. Careful observation of safety rules must be present at all times to avoid infection spread. All non-emergency procedures should be postponed until a negative RT-PCR test is available for the patient. Clearly, every measure is work-demanding and requires very high compliance to the rules applied, however, following protocols will be the only way to go back to normal activity in the shortest time possible.

Currently, the development of at least 7 different vaccines based on 3 platforms and their entry into the market represents the best hope for the global population to reach the herd immunity necessary to stop the viral spread.

The mass vaccination program started in December 2020. Despite clinical trials presenting high levels of efficacy of several COVID-19 vaccines, like all other vaccines, they will not be completely effective.

The development of other variants resistant to immunization and how many people get vaccinated are just a few of the possible variants to be included in the complex evaluation of the global success of the vaccination process.

Disclosures/conflict of interest

The authors declare no competing interests.

Abbreviations

COVID-19	coronavirus disease 2019
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
ARDS	acute respiratory distress syndrome
ICU	intensive care unit
BU	Burn Unit

OR	operation room
CT	computer tomography
BAL	broncho-alveolar lavage
RT-PCR	real time polymerase chain reaction
TBSA	total body surface area
ER	emergency room
PPE	personal protection equipment

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