ORIGINAL PAPERS

Candida Infections in Severely Burned Patients: 1 Year Retrospective Study

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Abstract

Infections represent the most common complication occurring during the evolution of the severely burned patient, hence requiring closer study and targeted result analysis. The fungal infections are one of the most aggressive types of existing infections, their opportunistic character enabling them to cause invasive infections, ultimately leading to a higher morbidity and a higher rate of mortality. The present study focuses on the presence of Candida spp. in 19 out of a total of 70 patients admitted to the Critical Care Burn Unit in the Clinical Emergency Hospital Bucharest, between 01.01.2019-31.12.2019. No other fungal species, besides Candida spp., were identified in this patient lot.
The aim of this study was to analyze the risk factors and the dynamics of the biological parameters of the patients presenting Candida spp. infections, in order to determine how these contribute to the prognostic and final outcome of these patients. We can conclude that a precise diagnostic and prompt treatment can make a significant difference in the outcome of severely burnt patients presenting with a fungal infection.

Keywords: burns, fungal infections, Candida spp., severity, treatment.

Rezumat

Infecțiile reprezintă cea mai frecventă complicație ce apare în evoluția pacientului ars grav, motiv pentru care necesită studii specializate cu analiza atentă a rezultatelor. Infecțiile fungice sunt unele dintre cele mai agresive tipuri de infecții existente, caracterul oportunist al acestora făcându-le capabile de a determina infecții invazive, ducând în final la morbiditate crescută și o rată crescută a mortalității. Prezentul studiu se concentrează pe prezența Candida spp. la 19 dintr-un total de 70 pacienți care au fost admiși în Unitatea de Îngrijire a Arșilor Grav a Spitalului Clinic de Urgență București în perioada 01.01.2019-31.12.2019. Nu au fost identificate alte specii de fungi în afară de Candida spp.
Scopul acestui studiu a constat în analizarea factorilor de risc și a dinamicii parametrilor biologici ale pacienților cu infecție Candida spp., în vederea stabilirii contribuției acestora la prognosticul și evoluția acestor pacienți. Putem concluziona că stabilirea unui diagnostic concret și instaurarea unui tratament prompt poate realiza o diferență semnificativă în evoluția pacientului ars cu prezență de infecție fungică.

Cuvinte cheie: arsuri, infecții fungice, Candida spp., severitate, tratament.

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INTRODUCTION

In recent years, fungal infections have gradually become more frequent and complex, especially among severely burned patients.[1] In this context, Candida spp., a ubiquitous fungus, was identified as a significant cause of morbidity and mortality among these patients. Although Candida spp. is a normal component of commensal flora, it can turn into an opportunistic pathogen given favorable conditions, such as those provided by severe burns.[2,3]

An alarming fact is the development of antifungal resistance, which hinders infection management.[4,5] In this study, we aim to study the prevalence of Candida spp. in severely burned patients admitted in the Critical Care Burn Unit of the Clinical Emergency Hospital Bucharest, as well as the resistance of this fungus to different antifungal drugs. Moreover, we will analyze the risk factors associated with development of Candida spp. infections in this cohort and also the evolution of the patients. The results of this study aim to optimize Candida spp. infection prophylaxis and therapeutic management in burn units dealing with severe cases.

MATERIALS AND METHODS

For this study, data were collected retrospectively from hospital files, both physical and electronical (hospital's informatic system – Hipocrate), pertaining to patients admitted in the Critical Care Burn Unit of the Clinical Emergency Hospital Bucharest, between January 1st and December 31st, 2019. Inclusion criteria were patients who had positive fungal culture results, (Candida spp. in this study) during hospital stay. Demographical data, health-related data, burn-related data, as well as fungal antibiogram results were collected and analyzed.

Microsoft Excel was used to organize, analyze, and illustrate data distribution. Variables such as age, gender, associated pathologies, TBSA, burn depth, Candida spp. sites and fungal antibiogram results were the main data categories.

Candida spp. strains ware isolated through various culture methods, depending on the sampling site: burn wounds, blood, urine, tongue, tracheal, catheter, bronchi, vagina and external ear. Sensitivity to different drugs was quantified with the help of the fungal antibiogram.

RESULTS

Between 01.01.2019-31.12.2019, out of 70 total patients admitted to the Critical Care Burn Unit of the Clinical Emergency Hospital Bucharest, 19 tested positive for Candida spp. No other fungal pathogen was identified.

Statistical data regarding the age of the patients admitted to our Burn Unit who tested positive for Candida spp. showed that there were 9 female patients and 10 male patients, with ages between 29 and 99 years, most of them in the 6th-8th decades and a mean age of 64 years (Figure 1).

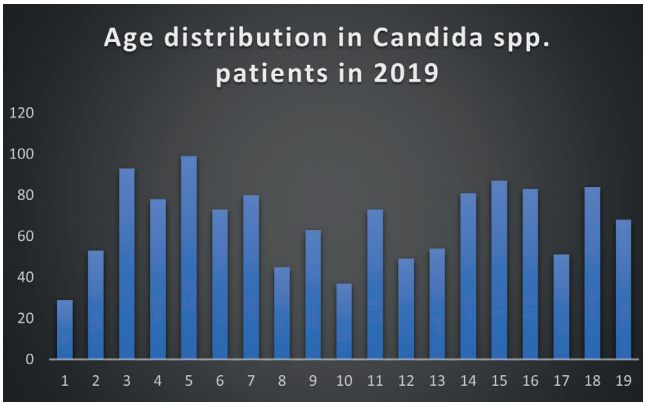

Figure 1. Patient distribution based on age

When it comes to the associated pathologies of the studied patients, 11 of them suffered from arterial hypertension, 5 from cardiac arrhythmias, 5 from ischemic cardiac disease, 2 from diabetes mellitus, as well as multiple singular comorbidities: valvular insufficiency, depression, anxiety, gastric/duodenal ulcer, dyslipidemia, dementia, vertigo, peripheral polyneuropathy, osteoarthritis, alcoholic hepatitis, COPD, benign prostatic hyperplasia, stroke sequelae, paranoid schizophrenia, sleep apnea, history of pancreatic tumor resection in the last month and, lastly, chronic tobacco use. The mechanism was thermal injury in 15 patients, electrocution in one case and 3 patients were victims of explosions.

Regarding the TBSA, it appeared that the patients who tested positive for Candida spp. had TBSA values ranging between 18% and 60%, with a mean of 39% TBSA. There were 15 patients who also presented with third-degree burns and 9 patients who had additional inhalation injury (Figure 2). Tracheostomy was required for 4 patients of the 19 patients with Candida spp.

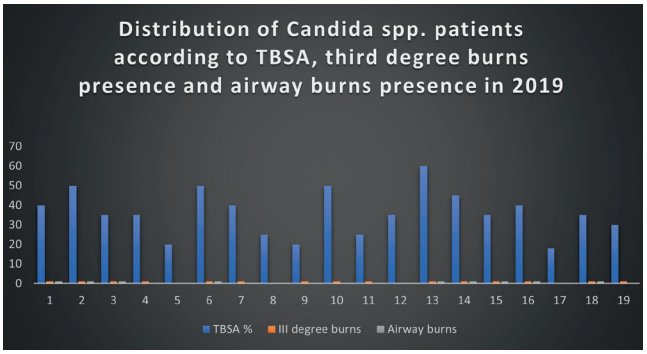

Figure 2. Patient distribution based on TBSA, presence of inhalation injury and third-degree burns

Out of 19 patients with Candida spp, there were 11 deaths and 8 survivals. All the deceased patients presented cardiac comorbidities and other previous systemic disorders. Also, severity of the lesions was higher in the deceased patients group: 9 of the 11 deceased patients presented third degree burns, also 9 of 11 deceased patients presented extensive burns with over 35% TBSA, 7 patients from these 11 patients presented airway burns.

When analyzing the fungal distribution among the patients, 7 patients tested positive for Candida spp. on admission, 4 patients on day 7, 5 patients on day 14 after admission, 1 patient on day 28 and 2 patients on day 35. (Figure 3).

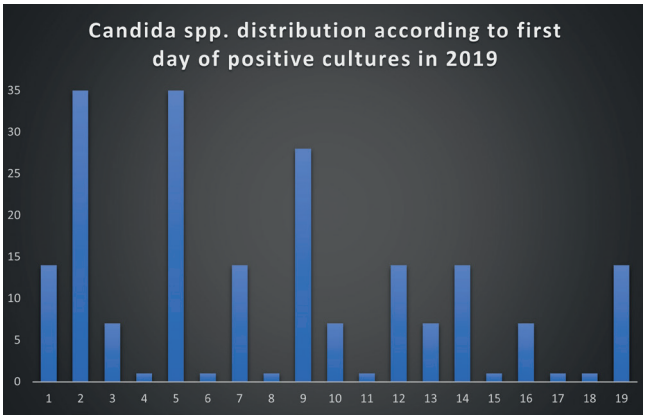

Figure 3. Patient distribution based on the day of the first positive testing for Candida spp.

Analysis of antifungal antibiograms showed that 9 patients had a strain of Candida spp. susceptible to Flucytosine and Amphotericin B and resistant to Fluconazole, Itraconazole and Voriconazole; 3 patients had strains of Candida spp. susceptible to all antifungals. Out of the 19 patients, 12 patients (6 male, 6 female) required systemic treatment with Anidulafungin. The sites from which Candida spp. was isolated were as follows: burn wound (10 patients), blood (1 patient), urine (9 patients), lingual swab (3 patients), tracheal secretions (4 patients), catheter surface (2 patients), bronchial aspirate (1 patient), vaginal swab (1 patient) and ear swab (1 patient); they were sampled on various days of hospital stay through screening, as per the hospital protocol for infection identifying and surveillance. Figure 4 presents the distribution of fungal determination situs, during the evolution of the patients.

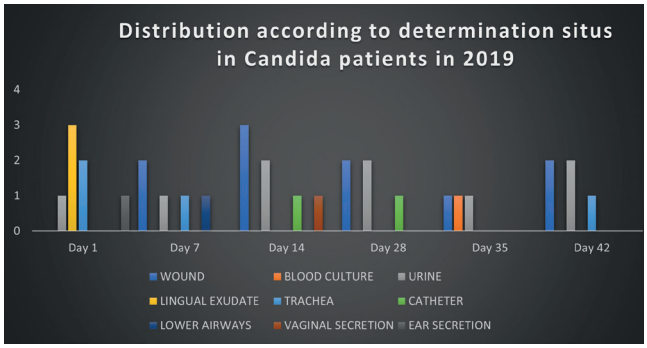

Figure 4. Patient distribution based on the day of the first positive testing for Candida spp. and the corresponding sampling site

Moreover, we correlated fungal infections with the patients' systemic evolution by determining some relevant biological markers.

Figure 5 shows the evolution of the average hemoglobin levels for the patients presenting with fungal infections:

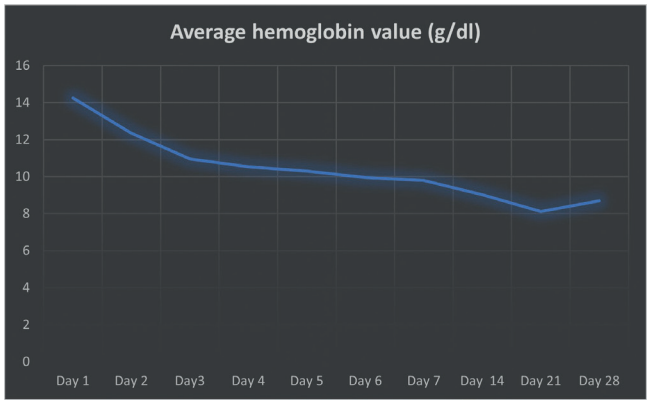

Figure 5. Average hemoglobin levels in patients with fungal infections

Figure 6 shows the average leucocyte levels dynamics in the Candida spp. patients, revealing an initial strong immune reaction at admission day 1, with a rather sudden drop of average leucocyte levels by day 4, and then a slight increase from day 5, followed by a plateau phase until day 28.

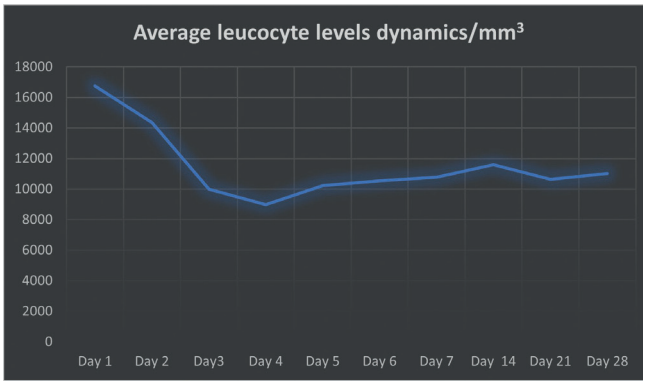

Figure 6. Average white blood cells count in patients with fungal infections

The following graphic analyses the dynamic of the platelet's average values, showing a steady drop of the thrombocytes starting from day 1 with normal values of 250000/mm^3, up to day 4 with almost 100000/mm^3. From day 5 there is a slight increase of the thrombocyte's values until the end of the first week of admission, followed by a progressive increase to 350000 until the second week, a value which lasts in a plateau phase up to 4 weeks of admission interval. (Figure 7).

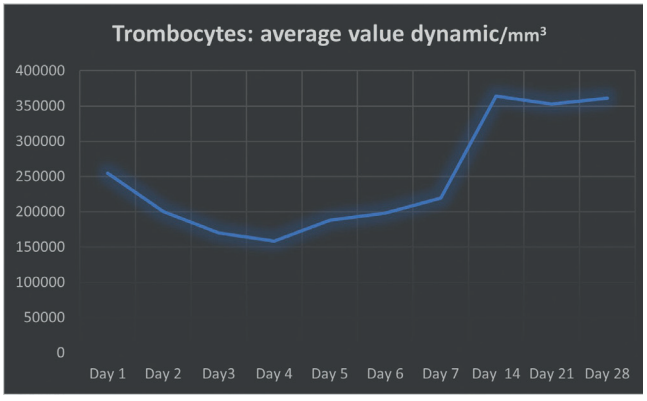

Figure 7. Average platelet count in patients with fungal infections

Figure 8 describes the evolution of the average glycemic values for the Candida spp. patients. Normal values are represented by a range of 60-99 mg/dl. The patients seem to present a rather high glycemic level on the admission day and during first three days and then there was observed a tendency to gradual decrease of glucose levels in these patients, by day 28.

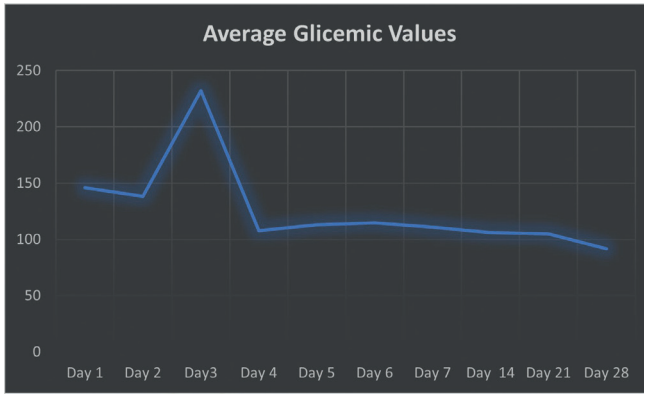

Figure 8. Evolution of the average glycemic values for the Candida spp. patients

The dynamics of the average values for the inflammatory markers in our burnt patients with Candida spp. infections is shown in Figure 9.

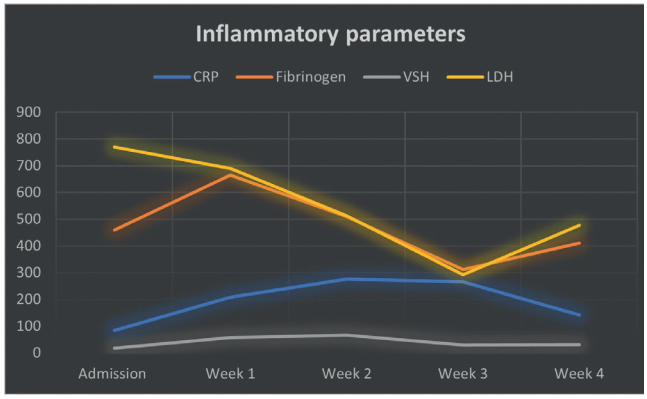

Figure 9. The dynamics of the average values for the inflammatory markers

We observed an already increased CRP average levels at admission (normal value < 0.5 mg/dl), with a more steep increase until the second week, followed by a plateau phase during the third week, and then a sudden drop until the fourth week of admission interval. As for fibrinogen, we can see an increase of the values in the first week, with a steady drop until the third week, followed also by a further increase until the fourth week. VSH levels were higher during the first two weeks of evolution. There are clearly high values

of LDH in these patients on the admission day which tend to drop steadily until the third week, where there is again a slight increase until day 28.

DISCUSSION

Among the most severe complications of major burns patients are infections, mainly due to the barrier function loss of the skin, in addition to immunosuppression and gut translocation of micro-organisms leading to high rates of sepsis, multiple organ failure and death. Management of infectious complications is mandatory when dealing with severely burned patients. An accurate diagnosis and a prompt therapeutic intervention is essential to improve burned patients' prognosis.[6-9]

Reportedly, at least 1 out of 2 patients contracted an infection during hospital stay, the most frequent found pathogen being Staphylococcus aureus, followed by Pseudomonas aeruginosa and Acinetobacter baumannii.[10] In addition, an increase in fungal colonization has been observed because of the widespread use of topical antibiotic agents used during treatment of bacterial infections in major burns patients.[11,12] The incidence of fungal contamination was reported to be between 6.3% to 15% of the patients.[2] The main pathogen found were Candida-albicans species, strains that have developed antifungal resistance, reportedly sensitive to Amphotericin B and Voriconazole. Aspergillus species are the next most frequent invasive fungal infection species found, followed by Mucorales. The timing of the fungal infection was reported to be documented on day 10, however it can occur at any point after admission. It occurs most likely in high TBSA patients (>60%), and may determine very high mortality rates (>90%).[11-13]

Diagnostic is difficult in case of fungal infections, usually not having specific clinical signs to determine it, a particularity in the immunosuppressed burned patients.[2,11] Therefore, a standardized testing protocol is essential in establishing an accurate diagnosis, allowing prompt initiation of the antimycotic treatment.

In our study group of patients admitted to the Critical Care Burn Unit in the Clinical Emergency Hospital Bucharest in 2019, we performed microbiological screening at admission and further sequential testing once a week or when we had a clinical suspicion for a potential infection.

This study investigated the presence of Candida spp. among patients, as no other fungal pathogen was identified. The results of the study suggest a significant prevalence of Candida spp. on severely burned patients, with a total of 19 cases out of 70 patients (27.14%). In addition, the results showed a varied distribution regarding the timing of infection detection, which highlights the importance of continuous patient monitoring throughout the hospital stay.

The demographic analysis showed a relatively equal distribution among sexes, with ages ranging between 29 and 99 years and a mean of 64 years. Associated comorbidities were varied, predominantly arterial hypertension, cardiac arrhythmias and ischemic cardiac disease found in 11 patients which lead to increased mortality. Patients tested positive for Candida spp in our study were predominantly elder ones and presented extensive burns with an average of 39% TBSA. Increased TBSA and age were reported to be risk factors leading to burn complications including infections.[6,7] It is recognized that age over 60 years old, presence of extensive burns, full thickness burns and inhalation injury represent severity factors, increasing morbidity and mortality in burned patients.[14,15]

At microbiological screening performed at admission, 7 patients tested positive for Candida spp, representing more than one third of cases with fungal positive determinations and 10% of the total of 70 patients admitted in the Critical Care Burn Unit in 2019. As was previously shown, initial Candida colonization represents an important risk factor for developing further invasive candidiasis, the risk increasing considerably with the number of colonized sites.[2,16-19]

Antifungal resistance was a major problem also in our study group, most strains of Candida spp. being resistant to Fluconazole, Itraconazole and Voriconazole. This shows the importance of performing the fungal antibiogram for an appropriate course of treatment.

Burn injuries lead to systemic inflammatory response and metabolic disorders that can ultimately cause organ and system disfunction. The most severe situation is the development of sepsis and, even more so, sepsis complicated with multiple organ failure. Monitoring of immunobiochemical markers of burn injury leads to better understanding of burn injury progression, the final aim being to avoid worsening of vital prognosis. Early detection of complications may improve survival and functional recovery. Biological values measurement is mandatory for assessment of the burned patient evolution, especially in high severity mechanisms as electrocutions.[20-23]

The biological parameters of patients suffering from large burns and having fungal documented presence were analyzed in our study. Our data reveal that average hemoglobin drops from 14.25 g/dL during admission to 10.96 g/dL on day 3, maintaining a plateau until day 7, with drops to an average of 8.1 g/dL in day 14. It is remarkable to observe the progressive decrease of hemoglobin from normal to mediocre values (corresponding to sex and associated pathologies) in the first week, to almost half of the initial values until the fourth week. There was a clear tendency of the hemoglobin values to decrease, not abruptly, but rather rhythmically, very closely related to the physiopathological phenomenon encountered in severely burned patients. Severely burned patients often require multiple blood transfusions to correct anemia.[24]

Mean leukocyte count is high during admission (16 750 per microliter). However, it tends to normalize by day 3, falling within the normal threshold, followed by a plateau throughout the hospitalization. The thrombocytes average count remains within the normal ranges throughout the admission, with the lowest values just above the threshold during day 4 (average of 158 000 per microliter), increasing towards 360 000 per microliter at day 14.

The initial high values of glucose should be related to the catabolic processes involving glucose levels and the metabolism of muscle protein. This normally translates with paraclinical findings such as hyperglycemia and in evolution, with clinical assessments such as steady loss of muscle mass, increasing morbidity and mortality.[25]

The role of procalcitonin and C-reactive protein in predicting the evolution of burned patients with infectious complications including fungal infection is evaluated by various studies, but their role is currently still under debate in case of fungal infections.[26,27] CRP measurements are a parameter useful to evaluate the post-burn inflammatory response, but there are not accurate in predicting the risk of sepsis.[28]

Promoting a series of prophylactic measures to avoid fungal infections complications as well as an adequate diagnostic and therapeutic strategy are essential for improving the vital prognosis of severely burned patients as we can see in Figure 10.[2,4,11]

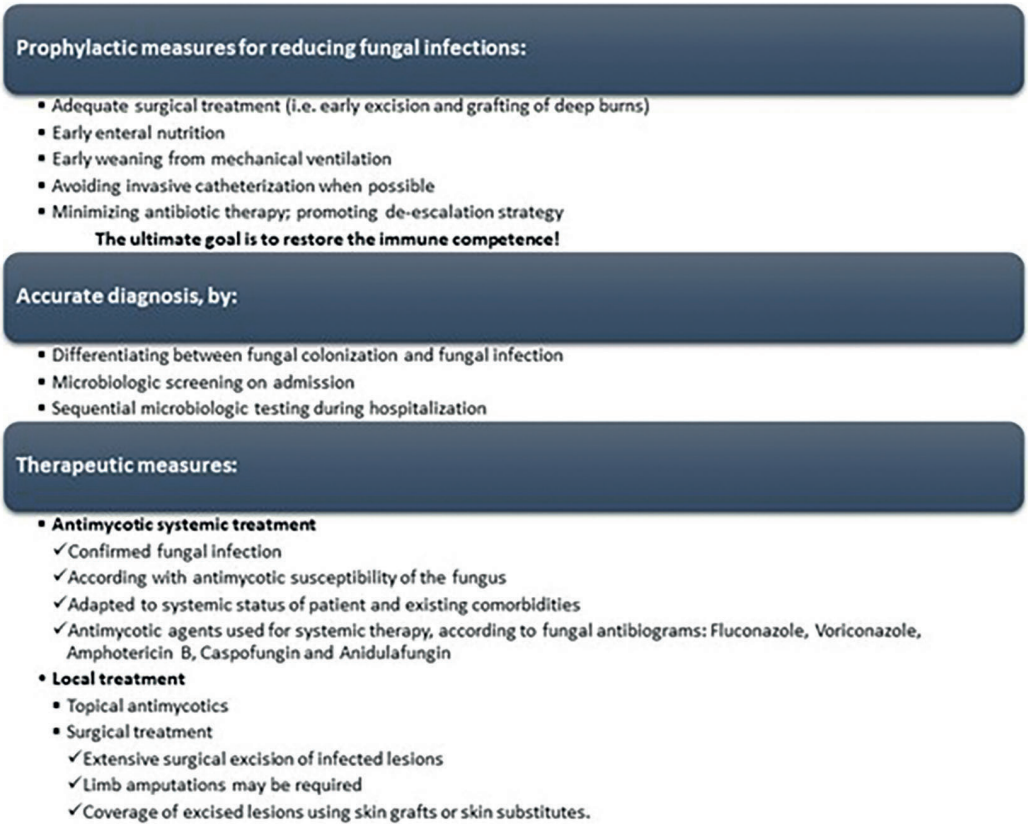

Figure 10. Comprehensive strategy to reduce fungal infections complications in severely burned patients

CONCLUSIONS

Fungal infections are one of the most severe complications in severely burned patients, ultimately leading to a higher morbidity and a higher rate of mortality.

Our study results highlight the relevance of Candida spp. infections in patients with major burns and the need for continuous monitoring in order to get an early diagnosis and an efficient treatment. They also suggest the need for a better approach in antifungal management, taking into account the development of antifungal resistance.

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