

# A bedside scoring system (“Candida score”) for early antifungal treatment in nonneutropenic critically ill patients with *Candida* colonization\*

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**Objective:** To obtain a score for deciding early antifungal treatment when candidal infection is suspected in nonneutropenic critically ill patients.

**Design:** Analysis of data collected from the database of the EPCAN project, an ongoing prospective, cohort, observational, multicenter surveillance study of fungal infection and colonization in intensive care unit (ICU) patients.

**Setting:** Seventy-three medical-surgical ICUs of 70 teaching hospitals in Spain.

**Patients:** A total of 1,699 ICU patients aged 18 yrs and older admitted for at least 7 days between May 1998 and January 1999 were studied.

**Interventions:** Surveillance cultures of urine, tracheal, and gastric samples were obtained weekly. Patients were grouped as follows: neither colonized nor infected (n = 719), unifocal or multifocal *Candida* colonization (n = 883), and proven candidal infection (n = 97). The odds ratio (OR) for each risk factor associated with colonization vs. proven candidal infection was estimated. A logistic regression model was performed to adjust for possible confounders. The “Candida score” was obtained according to the logit method. The discriminatory power was

evaluated by the area under the receiver operating characteristics curve.

**Measurements and main results:** In the logit model, surgery (OR = 2.71, 95% confidence interval [CI], 1.45–5.06); multifocal colonization (OR = 3.04, 95% CI, 1.45–6.39); total parenteral nutrition (OR = 2.48, 95% CI, 1.16–5.31); and severe sepsis (OR = 7.68, 95% CI, 4.14–14.22) were predictors of proven candidal infection. The “Candida score” for a cut-off value of 2.5 (sensitivity 81%, specificity 74%) was as follows: parenteral nutrition, +0.908; surgery, +0.997; multifocal colonization, +1.112; and severe sepsis, +2.038. Central venous catheters were not a significant risk factor for proven candidal infection ( $p = .292$ ).

**Conclusions:** In a large cohort of nonneutropenic critically ill patients in whom *Candida* colonization was prospectively assessed, a “Candida score” >2.5 accurately selected patients who would benefit from early antifungal treatment. (Crit Care Med 2006; 34:730–737)

**KEY WORDS:** *Candida* colonization; intensive care unit; critically ill patients; *Candida* score; preemptive antifungal therapy; invasive candidiasis

The incidence of infections caused by *Candida* species in the critical care setting has substantially increased in recent years (1–3). Invasive candidiasis has been associated with severe sepsis, septic shock, and multiorgan failure with clinical characteristics resembling those caused by bacterial pathogens (4–7). Signs of invasive candidiasis might be

apparent early, but the disease is usually diagnosed late in the course of intensive care unit (ICU) stay, representing a diagnosis challenge with an estimated mortality rate of 40% despite the development of new antifungal drugs (8).

Different risk factors for invasive candidiasis, including prior *Candida* species colonization, could allow recognition of patients at highest risk. Such patients

may be potential candidates for preemptive antifungal therapy. An important proportion of patients are admitted or become colonized in the ICU, but only few subsequently develop systemic candidal infection (9). *Candida* species colonization assessment based on multiple-body-site screening is now performed routinely in many ICUs. The value of positive surveillance cultures and of several

**\*See also p. 913.**

See Appendix for list of EPCAN Study Group participants.

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developed colonization indexes to predict the risk for invasive candidiasis and to indicate preemptive antifungal therapy is currently a matter of active investigation (10). Therefore, the objective of this study was to obtain a simple scoring system (named "Candida score") that may assist clinicians in differentiating between *Candida* species colonization and proven candidal infection when they are considering preemptive antifungal treatment for non-neutropenic critically ill patients.

## METHODS

### Study Population

This study was performed in the context of the EPCAN project (Estudio de Prevalencia de CANDidiasis, Candidiasis Prevalence Study), a surveillance study of fungal infection and colonization in critically ill patients (11, 12). A total of 1,765 patients over the age of 18 yrs who were admitted for at least 7 days to 73 medical-surgical ICUs in 70 tertiary care hospitals in Spain between May 1998 and January 1999 were included. The study was approved by the institutional review board of the participating centers.

### Design

This was a prospective, cohort, observational, multicenter study. For all patients, screening cultures for *Candida* species were performed on ICU admission and once a week thereafter until discharge from the ICU or death. Samples were obtained from tracheal aspirates, pharyngeal exudates, gastric aspirates, and urine, as part of the EPCAN surveillance study. Other samples, taken from peripheral blood, intravascular lines, feces, wound exudates, surgical drains, or other infectious foci, were obtained at the discretion of the attending physician. Samples were processed by the different reference clinical microbiology laboratories of the participating hospitals according to standard procedures, including seeding of the samples in Sabouraud dextrose agar culture medium and Sabouraud agar with cycloheximide and chloramphenicol (mycobiologic agar) and incubation at 35°C for 7 days. Blood cultures were processed with an automated system (BACTEC, Becton Dickinson Diagnostic Instrument Systems, Paramus, NJ). Identification of yeasts at the species level was made with the API 20C, API 32C, or the YST card of the Vitek system (bioMérieux España, Madrid, Spain) whenever possible (13).

A case report form was completed for each patient and data were prospectively included in the EPCAN database. For the purpose of this study—that is, to develop the "Candida score" system for deciding the use of early antifungal

treatment when *Candida* colonization is diagnosed in nonneutropenic critically ill patients—the following data were collected from the database: age, gender, underlying disease, reason for ICU admission, concomitant infections, presence and duration of risk factors for *Candida* species colonization and infection, antifungal treatment, and vital status at discharge (survival vs. death). Neutropenia was an exclusion criterion. Severity of illness on ICU admission was calculated with the Acute Physiology and Chronic Health Evaluation II (APACHE II) system (14). According to diagnoses at the time of ICU admission, patients were classified as surgical, trauma, or medical. Surgical patients were those for whom the reason of ICU admission was the postoperative control of an elective or urgent procedure, trauma patients were those admitted for trauma-related acute lesions, and medical patients were those admitted for any other reason.

Only insulin-treated patients were considered to have diabetes mellitus. Chronic bronchitis was defined as the presence of a productive cough or expectoration for >90 days a year (although on separate days) and for >2 (consecutive) yrs, provided that a specific disorder responsible for these symptoms was not present. Chronic liver disease was confirmed by liver biopsy or signs of portal hypertension, such as esophageal varices or ascites. Chronic renal failure was considered in patients requiring hemodialysis or peritoneal dialysis at the time of admission to the hospital. Severe heart failure was defined as grades III and IV of the New York Heart Association (NYHA) classification (15). Other risk factors included the following: arterial catheter, central venous catheter, total parenteral nutrition, enteral nutrition, urinary catheter, antibiotic treatment (when given within 10 days before ICU admission), extrarenal deputation procedures (hemodialysis or continuous hemofiltration), and use of steroids (a daily dose equivalent to 20 mg prednisone for at least 2 wks or 30 mg for at least 1 wk before isolation of *Candida* in cultures). The development of organ failure, sepsis, and septic shock was also recorded (16).

### Definitions of Colonization and Infection

Colonization was defined as the presence of *Candida* species in nonsignificant samples obtained from the oropharynx, stomach, urine, or tracheal aspirates. Colonization was considered unifocal when *Candida* species were isolated from one focus and multifocal when *Candida* species were simultaneously isolated from various noncontiguous foci, even if two different *Candida* species were isolated. Oropharynx and stomach were considered one site (digestive focus). Unifocal and multifocal colonization persistence was defined by at least

two weekly consecutive sets of *Candida*-positive cultures. Proven candidal infection required one of the following criteria: presence of candidemia, that is, documentation of one blood culture that yielded a *Candida* species; ophthalmic examination consistent with candidal endophthalmitis in a patient with clinical sepsis; isolation of *Candida* species in significant samples (e.g., pleural fluid, pericardial fluid) or candidal peritonitis; or histologically documented candidiasis. Ophthalmic examination was done routinely for every patient with sepsis. Candidal peritonitis was defined by the isolation of *Candida* species in a peritoneal sample obtained by laparotomy or percutaneous puncture in patients with associated clinical findings, including perforation of an abdominal organ, dehiscence of an intestinal suture with peritonitis, severe acute pancreatitis, or presence of a peritoneal catheter for dialysis. Catheter-related candidemia was considered in those patients who had an intravascular device and one or more positive cultures of blood samples obtained from the peripheral vein, clinical manifestations of infection (e.g., fever, chills, and/or hypotension), and no apparent source for bloodstream infection (with the exception of the catheter), as well as a positive catheter culture, either semiquantitative ( $\geq 15$  colony-forming units [cfu] per catheter segment) or quantitative ( $\geq 10^2$  cfu per catheter segment), whereby the same organism (species and susceptibility) was isolated from a catheter segment and a peripheral blood sample (17).

Patients were classified into three groups as follows: neither colonized nor infected, unifocal or multifocal *Candida* species colonization without proven infection, and proven candidal infection.

### Statistical Analysis

To estimate the predictive model that will allow us to differentiate between *Candida* species and proven candidal infection, the crude odds ratio (OR) for each risk factor associated with colonization vs. proven candidal infection was estimated. In order to estimate the multivariate model, the dataset was subdivided into two groups: a training set to fit the model, composed of 65% of the sample, and a validation set to validate the model, made up of 35% of the sample (18). Based on the cases of the training set, a logistic regression (logit) model was performed to adjust for possible confounders. Statistically significant variables in the univariate analysis were included in the model, and through a stepwise elimination process, the so-called "Candida score" was obtained. The discriminatory power of this score was evaluated by the area under the receiver operating characteristics (ROC) curve and the 95% confidence interval (CI). Then, a cut-off value to estimate the diagnostic sensitivity and

Table 1. Risk for death in the study population, according to colonization and infection status ( $n = 1,669$ )

Patient group	Nonsurvivors		Odds Ratio (95% Confidence Interval) <sup>a</sup>	
	No.	Mortality Rate <sup>b</sup>	Crude	Adjusted <sup>c</sup>
Neither colonized nor infected, $n = 719$	239	33.2%	1	1
<i>Candida</i> species colonization, $n = 883$				
Unifocal, $n = 388$	103	26.5%	1.02 (0.8–1.4)	1.04 (0.8–1.4)
Multifocal, $n = 495$	252	50.9%	1.55 (1.3–2)	1.54 (1.2–1.9)
Candidal infection, $n = 97$	56	57.7%	2.74 (1.8–4.2)	3.2 (2.0–5.0)

<sup>a</sup>Estimated by logistic regression analysis; <sup>b</sup> $p < .001$ , linear association test; <sup>c</sup>for Acute Physiology and Chronic Health Evaluation (APACHE II) score.

specificity in the validation set was selected. Statistical significance was set at  $p < .05$ . Data were analyzed with the SPSS statistical program (11.5, SPSS, Chicago, IL) for Windows.

## RESULTS

Of the initial 1,765 patients included in the study, 96 (5.4%) were excluded because of inadequate data collection. The study population consisted of 1,669 patients, 66.5% men, with a mean (SD) age of 57.8 (17.2) yrs.

There were 719 (43.1%) patients in the neither-colonized-nor-infected group, 67.9% men, with a mean age of 57.5 (17.0) yrs. The median (5th to 95th percentile) APACHE II score on ICU admission was 18 (6.6–33). A total of 239 died, for a mortality rate of 33.2%.

Colonization solely by *Candida* species was diagnosed in 883 patients. There were 577 men and 306 women in this group, with a mean age of 58.9 (17.0) yrs and a median APACHE II score of 18 (8–32.4). Unifocal *Candida* species colonization was diagnosed in 388 patients (43.9%) and multifocal *Candida* species colonization in the remaining 495 patients (56.0%). The overall mortality rate was 40.2%. There were 103 deaths (mortality rate, 26.5%) among patients with unifocal *Candida* colonization and 252 deaths (mortality rate, 50.9%) among patients with multifocal colonization.

Proven candidal infection was diagnosed in 97 patients (5.8%). There were 68 men and 29 women in this group, with a mean age of 58.5 (16.9) yrs and a median APACHE II score of 17 (10.6–30.8). Fifty-eight patients developed candidemia, 30 peritonitis, 6 endophthalmitis, and 3 candidemia and peritonitis concomitantly. Fifty-six patients died, for a mortality rate of 57.7%. Eighty-five pa-

tients (87.6%) received antifungal treatment. The median (5th to 95th percentile) time elapsed between the onset of proven candidal infection and the beginning of the antifungal therapy was 12 (0.3–37.8) days. The median (5th to 95th percentile) APACHE II score at the start of the antifungal treatment was 18 (4.9–29.3). Eighteen patients (18.6%) had catheter-related candidemia, and the catheter was removed from all of them.

There were no statistically significant differences in the APACHE II scores between the groups who were noncolonized, noninfected, colonized with *Candida* species, and infected by *Candida* species (Kruskal-Wallis test,  $p = .145$ ). However, when the risk for death was estimated (Table 1), there were statistically significant differences between the variable indicating patient group and the variable indicating the mortality in the Mantel-Haenszel test for linear association ( $p < .001$ ).

As shown in Table 2, patients with candidal infection compared with those with *Candida* species colonization alone showed statistically significant differences in the following variables: length of ICU stay, patient category, surgery on ICU admission, total parenteral nutrition, extrarenal deputation procedures, unifocal or multifocal colonization, and severe sepsis. Central venous catheters were not found to be a significant risk factor for proven candidal infection ( $p = .292$ ).

In the logit model adjusted for possible confounding variables, surgery on ICU admission, total parenteral nutrition, multifocal *Candida* species colonization, and severe sepsis were independently associated with a greater risk for proven candidal infection (Table 3). Through a stepwise elimination process, the *Candida* score was obtained (Table 4). The

discriminatory power of this score, assessed by the area under the ROC curve and its main cut-off values, is shown in Figure 1.

## DISCUSSION

This study shows that the new *Candida* score allows differentiating between *Candida* species colonization and candidal infection in nonneutropenic ICU patients. Multifocal colonization, total parenteral nutrition, surgery as the reason of ICU admission, and clinical symptoms of severe sepsis were found to be independent predictors of systemic candidiasis in this population. Accordingly, it is possible to stratify the risk of proven candidal infection in a large population of critically ill patients and to select those patients who will most benefit from starting antifungal therapy (i.e., early antifungal administration given to patients with evidence of colonization in the presence of multiple risk factors for candidal infection).

An important finding of the study is that multifocal fungal colonization is really an independent risk factor of proven candidal infection in this large cohort of both medical and surgical critically ill patients at various centers. In the National Epidemiology of Mycoses Survey (NEMIS) study conducted in surgical ICUs at six sites in the United States (19), recovery of *Candida* species in rectal and/or urine surveillance cultures was not associated with an increased risk of candidal bloodstream infections. The fact that fungal colonization assessment was based on multiple-site cultures performed weekly in the present study could account for the discrepant results, since only two sites were cultured in the NEMIS study.

Nosocomial fungal infections in nonneutropenic critically ill patients are caused by mainly *Candida* species. The proposed definitions of “probable,” “possible,” and “proven” opportunistic fungal infections intended for immunocompromised patients (20) may be unreliable for nonneutropenic patients (21). The clinical significance of *Candida* species colonization as a determinant risk factor for invasive candidiasis has been largely recognized, and recent efforts have been directed toward developing a predictor for the diagnosis of systemic infection based on colonization density. A colonization index with a 0.5 threshold, defined as the ratio of the number of culture-positive

Table 2. Results of univariate analysis: Risk factors for invasive candidiasis according to colonization and infection status (n = 1,669)

Variable	Unifocal or Multifocal <i>Candida</i> Species Colonization n = 883	Proven Candidal Infection n = 97	p Value
Age, yrs, mean (SD)	58.9 (17.0)	58.5 (16.9)	.825
Male/female	577/306	68/29	.337
APACHE II score on admission, median (range)	19 (1–67)	17 (6–45)	.203
Length of ICU stay, days, median (range)	20 (7–166)	28 (7–138)	<.001
APACHE II score, no. (%)			
<15	302 (34.2)	37 (38.5)	.137
15–25	408 (46.3)	48 (50.5)	
>25	173 (19.5)	12 (11.0)	
Diagnosis on ICU admission, no. (%)			
Medical	449 (50.8)	34 (35.1)	<.001
Surgical	258 (29.2)	51 (52.6)	
Trauma	176 (19.9)	12 (12.4)	
Underlying disease, no. (%)			
Chronic bronchitis	197 (22.3)	14 (14.4)	.073
Diabetes mellitus	136 (15.4)	14 (14.4)	.801
Chronic liver disease	40 (4.5)	2 (2.1)	.255
Chronic renal failure	44 (5.5)	4 (4.1)	.710
Heart failure	40 (4.5)	2 (2.1)	.255
Risk factors, no (%)			
Broad spectrum antibiotics	866 (98.0)	97 (100)	.380
Central venous catheter	873 (98.9)	97 (100)	.292
Urinary catheter	870 (98.5)	93 (95.9)	.078
Mechanical ventilation	837 (94.8)	92 (94.8)	.982
Enteral nutrition	695 (78.7)	68 (70.1)	.053
Arterial catheter	666 (75.4)	68 (70.1)	.251
Total parenteral nutrition	462 (52.3)	85 (87.6)	<.001
Corticosteroids	214 (24.2)	22 (22.7)	.734
Hemodialysis or continuous hemofiltration	106 (12.0)	29 (29.9)	<.001
Severe sepsis, no. (%)	156 (17.7)	63 (64.9)	<.001
<i>Candida</i> species colonization, no. (%)			<.001
Unifocal	390 (44.1)	17 (17.5) <sup>a</sup>	
Multifocal	493 (55.8)	69 (71.1) <sup>a</sup>	

APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit.  
<sup>a</sup>Eleven patients in the proven candidal infection group did not have previous *Candida* colonization.

Table 3. Results of multivariate analysis: Risk factors for proven candidal infection in 1,669 adult patients

Variable	Proven Candidal Infection %	p Value	Crude Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)
Surgery on ICU admission				
No	6.9			
Yes	16.5	<.001	2.69 (1.76–4.10)	2.71 (1.45–5.06)
Total parenteral nutrition				
No	2.8			
Yes	15.5	<.001	6.46 (3.48–11.98)	2.48 (1.16–5.31)
Severe sepsis				
No	4.5			
Yes	28.8	<.001	8.63 (5.49–13.56)	7.68 (4.14–14.22)
<i>Candida</i> species colonization				
No	4.2			
Yes	12.3	<.001	3.20 (1.85–5.53)	3.04 (1.45–6.39)

ICU, intensive care unit.

sites to the number of sites cultured, and its corrected version with a 0.4 threshold (22) have been used as tools to start preemptive antifungal treatment in ICU patients (10). In a before/after intervention study of 2-yr prospective and 2-yr histor-

ical-control cohorts carried out by Piarroux et al. (10), patients with a corrected colonization index  $\geq 0.4$  received early preemptive antifungal therapy, and only 18 cases (3.8%) of proven candidiasis were diagnosed; all were imported infec-

tions. The incidence of ICU-acquired proven candidiasis significantly decreased from 2.2% to 0% ( $p < .001$ , Fisher test). The authors concluded that targeted preemptive strategy may efficiently prevent acquisition of proven candidiasis in patients admitted to a surgical ICU. It should be noted that the *Candida* score takes in account other relevant risk factors of candidiasis, in addition to colonization, to improve the specificity of the test.

For patients considered “heavily” colonized by *Candida* species, there are no biological markers that may assist clinicians in deciding to prescribe or not prescribe antifungal agents. According to the results of a survey in medical-surgical ICUs in France, most of the units showed a homogeneous antifungal prescription pattern. Furthermore, most intensivists interviewed prescribed antifungal treatment in the presence of multifocal *Candida* colonization, clinical signs of sepsis, and several other risk factors for invasive candidiasis (23). In agreement with these

data, 79% of 135 Spanish intensivists in 45 ICUs reported that they would start antifungal treatment for nonneutropenic critically ill patients if clinical signs of infection and multifocal *Candida* isolates were noted (24).

Recommendations for starting antifungal treatment for nonneutropenic critically ill patients have also recently been reported in the literature (25–27). A predictive rule based on known risk factors, including colonization, that allow us

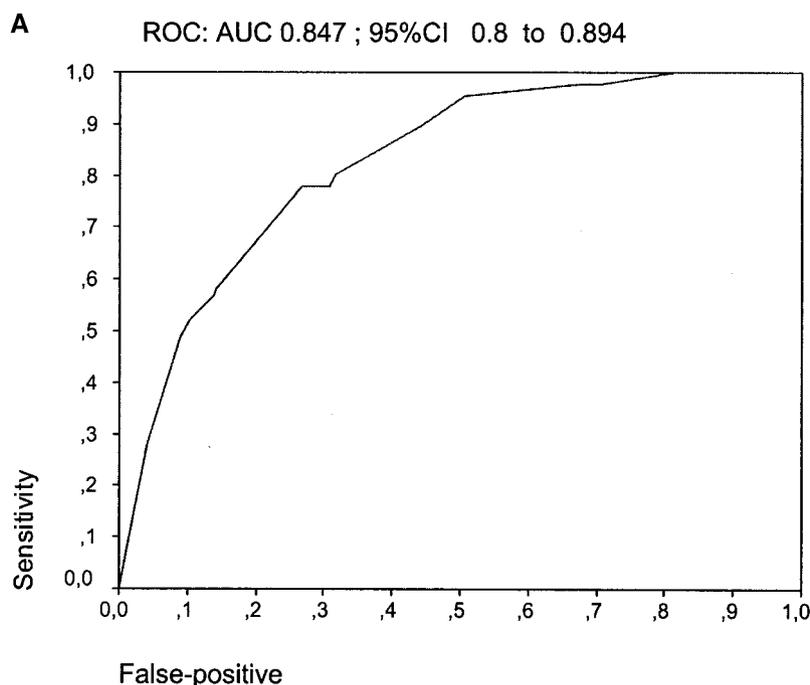
to differentiate between *Candida* species colonization and proven candidal infection would help clinicians more accurately than colonization alone to select those ICU patients who would benefit from early antifungal treatment. Paphitou and associates (28) and Ostrosky-Zeichner and colleagues (29) have proposed prediction rules for invasive candidiasis following a retrospective multicenter study in 12 ICUs at nine hospitals in the United States and Brazil. The best-performing rule required a combination of at least one “major” and at least two “minor” risk factors among several known for candidal infection in patients staying in the ICU for at least 48 hrs and who were expected to stay for  $\geq 2$  more days. Their clinical prediction rule identified ICU patients with a 10% risk of invasive candidiasis, but validation of this instrument is pending. Fungal coloniza-

Table 4. Calculation of the Candida score: Variables selected in the logistic regression model

Variable	Coefficient ( $\beta$ )	Standard Error	Wald $\chi^2$	<i>p</i> Value
Multifocal <i>Candida</i> species colonization	1.112	.379	8.625	.003
Surgery on ICU admission	.997	.319	9.761	.002
Severe sepsis	2.038	.314	42.014	.000
Total parenteral nutrition	.908	.389	5.451	.020
Constant	-4.916	.485	102.732	.000

ICU, intensive care unit.

Candida score =  $.908 \times$  (total parenteral nutrition) +  $.997 \times$  (surgery) + 1.112 (multifocal *Candida* species colonization) + 2.038 (severe sepsis). Candida score (rounded) =  $1 \times$  (total parenteral nutrition) +  $1 \times$  (surgery) + 1 (multifocal *Candida* species colonization) +  $2 \times$  (severe sepsis). All variables coded as follows: absent, 0; present, 1.



**B**

Cutoff value	Sensitivity	False positive
1.055	.983	.653
1.509	.949	.495
1.963	.898	.426
2.069	.831	.312
2.074	.814	.301
2.528	.814	.259
2.982	.780	.231
3.026	.610	.132
3.093	.593	.130
3.547	.525	.092
4.001	.492	.077

Figure 1. A, receiver operating characteristics (ROC) curve and area under the ROC curve (AUC) for assessing the discriminatory power of the Candida score. B, cut-off values for the ROC curve.

tion was not included in this prediction rule proposed by Ostrosky-Zeichner et al. (29) because it was derived from the NEMIS study results (19). The Candida score presented here could therefore be considered to be more reliable, given the weight of fungal colonization in the pathogenesis of candidiasis.

DuPont and co-workers (30) carried out a retrospective systematic review of surgical intensive care patients, with a prospective follow-up in France. A scoring system was proposed with the following risk factors: female gender, upper gastrointestinal origin of peritonitis, cardiovascular failure, and use of antibiotics. A grade C score, defined as the presence of three qualifiers, was associated with a sensitivity of 84% and specificity of 50% for the detection of yeasts in the peritoneal fluid of patients with peritonitis. The main drawbacks of this study included its single-center setting and its potential application restriction to surgical patients.

We used the EPCAN database, which is a large cohort of nonneutropenic ICU patients for whom, among other goals, *Candida* colonization and invasive candidiasis were studied prospectively. As previously reported (21), the rate of proven candidal infection found in the present study was low, but the mortality rate was high. The mortality rate increased significantly according to the patient group, that is, with unifocal colonization (26.5%), multifocal colonization (50.9%), and candidal proven infection (57.7%). Although colonization does not define infection, these data support the well-known role of *Candida* colonization as a key factor in the decision to start early antifungal treatment for ICU patients.

The new Candida score was based on the respective predictive value of previously reported risk factors. In addition to multifocal *Candida* species colonization, three other risk factors were found to be significant predictors of proven candidal infection in the logistic regression model: use of total parenteral nutrition, surgery on ICU admission, and clinical manifestations of severe sepsis. The respective weight of colonization and these risk factors as shown in the Candida score allowed us to reliably differentiate between *Candida* species colonization and proven candidal infection. Although central venous catheters are repeatedly described as major risk factors for proven hematogenous candidiasis (19, 31), in this large dataset from a prospective multicenter study, venous catheters were not signifi-

cant predictors of proven candidal infection.

The medical literature is flooded with complicated prediction rules and scores (32–37), and there is a need to have available bedside easy-to-remember scores that would make daily tasks easier for clinicians. The simplified version of this score, after rounding up to 1 the weight for total parenteral nutrition, surgery, or multifocal *Candida* species colonization and up to 2 the weight for clinical severe sepsis, is a quite simple ready-to-use prediction rule. With a cut-off value of 2.5, that is to say, with a sensitivity of 81% and a specificity of 74%, we shall only need the presence of sepsis and any one of the three other remaining risk factors or the presence of all of them together except sepsis in order to consider starting antifungal treatment for one particular patient. Finally, the Candida score also identifies critically ill patients with proven candidiasis: patients with a score >2.5 are 7.75 times as likely to have proven infection (risk ratio = 7.75; 95% CI, 4.74–12.66) than patients with a Candida score up to 2.5.

Therefore, the easy rule of thumb for prescribing antifungals, according to a Candida score >2.5, will allow more efficient selection of patients who indeed will benefit from the increasing number of available antifungal drugs (38) and, at the same time, more adequate prevention of the development of new resistant species due to an excess of inappropriate and potentially detrimental antifungal treatments (39). Assessment with the Candida score should be performed at the time of ICU admission and any time candidiasis is suspected.

## CONCLUSIONS

A new score, the Candida score, which was calculated according to data collected in the EPCAN database (in which all cases of *Candida* species colonization and proven candidal infection were prospectively recorded), is an easy-to-remember bedside prediction rule. A score >2.5 will help intensivists select patients who will benefit from early antifungal administration. Finally, although the Candida score contributes to predicting proven candidal infection, the benefits of preemptive (prophylactic or empirical) antifungal therapy remain to be determined.

**A** score >2.5 will help intensivists select patients who will benefit from early antifungal administration.

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## APPENDIX

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