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### Original article

# Analysis of risk factors and prognosis of fluconazole-resistant *Candida tropicalis* bloodstream infection

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### ABSTRACT

**Background:** In China, the isolation rate of fluconazole-resistant isolates of *Candida tropicalis*, together with fatality in cases of bloodstream infections due to this yeast, have increased annually.

**Aims:** This study investigates the clinical characteristics, risk factors, and prognostic factors of fluconazole-resistant *C. tropicalis* bloodstream infections (BSI).

**Methods:** A retrospective study analyzed clinical data of patients with *C. tropicalis* BSI from July 2013 to June 2019, focusing on clinical characteristics, risk factors, treatment regimens, and prognosis. Univariate analysis of risk factors and prognosis was conducted using  $\chi^2$  test or Fisher's exact tests. Binary logistic regression model for risk factors, and Cox regression method for prognosis, were used for multivariate analysis.

**Results:** The study enrolled 100 patients with *C. tropicalis* BSI, including 44 fluconazole-resistant and 56 fluconazole-sensitive cases; 64 patients were cured and 36 died, resulting in a mortality rate of 36%. Logistic regression analysis identified exposure to azole antifungal agents during the 2 weeks prior to the onset of the BSI as a risk factor for fluconazole resistance. Cox regression analysis showed that hematological malignancy, fluconazole-resistant strains, indwelling catheters, and chronic obstructive pulmonary disease were independent risk factors for patient mortality. Conversely, targeted therapy with sensitive antifungal agents and removal of drainage tubes were protective factors for survival.

**Conclusions:** Azole exposure led to the development of fluconazole resistance in *C. tropicalis* BSI; hematologic malignancies, azole resistance, chronic obstructive pulmonary disease and having intravenous catheters increased mortality rate. The use of echinocandins or amphotericin B and catheter removal improved outcomes, underscoring the need for early resistance detection and targeted treatment.

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## Análisis de los factores de riesgo y pronóstico en la candidemia por *Candida tropicalis* resistente al fluconazol

### RESUMEN

**Antecedentes:** En China, el aislamiento de cepas de *Candida tropicalis* resistentes al fluconazol ha aumentado anualmente, así como la mortalidad en casos de infecciones del torrente sanguíneo causadas por esta levadura.

**Objetivos:** Este estudio investiga las características clínicas, los factores de riesgo y los factores pronósticos de candidemias debidas a aislamientos de *C. tropicalis* resistentes al fluconazol.

**Métodos:** Entre julio de 2013 y junio de 2019 se realizó un estudio retrospectivo en el que se analizaron los datos clínicos de pacientes con candidemia por *C. tropicalis*, con especial relevancia en las características

#### Palabras clave:

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clínicas, los factores de riesgo, los regímenes de tratamiento y el pronóstico. Se llevó a cabo un análisis univariante de los factores de riesgo y del pronóstico mediante la prueba  $\chi^2$  o la prueba exacta de Fisher. Para el análisis multivariante se utilizó un modelo de regresión logística binaria para los factores de riesgo y el método de regresión de Cox para el pronóstico.

**Resultados:** En el estudio fueron incluidos 100 pacientes con candidemia por *C. tropicalis*, entre los que se encontraban 44 casos con resistencia al fluconazol y 56 sensibles al fluconazol. Sesenta y cuatro pacientes se curaron y 36 fallecieron, lo que supuso una tasa de mortalidad del 36%. Según el análisis de regresión logística, la exposición a agentes antifúngicos azólicos en las dos semanas previas a la aparición de la candidemia fue un factor de riesgo para desarrollar resistencia al fluconazol. El análisis de regresión de Cox mostró que la neoplasia hematológica maligna, las cepas resistentes al fluconazol, portar catéteres permanentes y la enfermedad pulmonar obstructiva crónica eran factores de riesgo independientes de mortalidad de los pacientes. Por el contrario, la terapia dirigida con los agentes antifúngicos adecuados y la retirada de los tubos de drenaje fueron medidas que incrementaron la supervivencia.

**Conclusiones:** La exposición a azoles puede provocar la aparición de resistencia al fluconazol en casos de candidemia por *C. tropicalis*; las neoplasias hematológicas, la resistencia a los azoles, la enfermedad pulmonar obstructiva crónica y la presencia de catéteres intravenosos aumentaron la tasa de mortalidad. El uso de equinocandinas o anfotericina B y la retirada del catéter mejoró el pronóstico, lo que subraya la necesidad de detectar precozmente la resistencia y aplicar un tratamiento específico.

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Candidemia, caused by *Candida* species, represents a life-threatening complication in immunocompromised and critically ill patients,<sup>18,22</sup> with mortality rates exceeding 30% despite advances in antifungal therapies.<sup>16</sup> While *Candida albicans* remains the most common etiological agent, non-*C. albicans Candida* species now account for nearly half of invasive candidiasis cases globally, reflecting shifting epidemiological trends driven by prolonged ICU stays, broad-spectrum antibiotic use, and immunosuppressive therapies.<sup>26</sup> Among these emerging pathogens, *Candida tropicalis* has garnered significant clinical attention due to its rising incidence, intrinsic resistance patterns, and disproportionately high mortality rates,<sup>3,8,13</sup> particularly in subtropical and tropical regions.

Geographical disparities in *Candida* epidemiology further complicate management strategies. Surveillance data from Saudi Arabia found higher mortality in ICU-acquired *C. albicans*-candidemia, compared with cases due to non-*C. albicans Candida* species.<sup>2</sup> In contrast, Thai studies revealed *C. tropicalis* was the dominant pathogen in bloodstream infections (BSI).<sup>23</sup> The respiratory tract serves as a critical reservoir for *C. tropicalis* dissemination, particularly in patients with structural lung disease, prolonged mechanical ventilation, or compromised mucociliary clearance.<sup>29</sup> This species exhibits unique pulmonary tropism through biofilm formation on endotracheal devices, enhanced epithelial adhesion via Als3 virulence factors, and immune evasion mechanisms mediated by  $\beta$ -glucan masking.<sup>12</sup> According to the data from a surveillance study conducted to ascertain the degree of antifungal resistance in invasive candidiasis in China over the past 5 years, the fluconazole and voriconazole resistance rates of *C. tropicalis* increased from <8% in 2009–2010 to over 22% in 2013–2014.<sup>34</sup>

The World Health Organization has recently defined *C. tropicalis* as a critical fungal pathogen, necessitating targeted research into geography-dependent virulence, rapid molecular diagnostics, and inhaled antifungal delivery systems.<sup>27</sup> This study elucidates the epidemiological burden and prognostic impact of fluconazole-resistant *C. tropicalis* infections in a subtropical zone, aiming to inform regionally tailored prevention strategies and enhance awareness of this underrecognized threat in Zhejiang Province.

## Materials and methods

### Patients included

One hundred patients diagnosed with blood stream infection (BSI) caused by *C. tropicalis* through blood culture in the First Affil-

iated Hospital, Zhejiang University School of Medicine, from July 2013 to June 2019, were included. Inclusion criteria fulfilled the diagnostic criteria for invasive mycosis formulated by the European Cancer Treatment and Research Collaboration Group (EORTC/MSG) in 2008<sup>4</sup>; *C. tropicalis* had to be isolated from blood culture, having the patient clinical signs and symptoms of BSI. The isolation of *C. tropicalis* from a blood culture likely contaminated, patients younger than 18 years old, or having no detailed clinical data were the exclusion criteria. If the patient had multiple positive blood cultures, only the first one was considered. Long-term glucocorticoid therapy was defined as prednisone  $\geq 20$  mg/day for more than 7 days. Long-term immunosuppressive therapy was defined as using immunosuppressive agents for more than 2 weeks. Antibiotic exposure was defined as more than 5 days of antibiotic use within 2 weeks prior to the onset of the disease.

The records of all 100 patients were retrieved. Clinical data were collected including patients' gender, age, check-in desk, hospitalized time, length of hospital stay, blood culture results, comorbidities, invasive operation, parenteral nutrition, the usage of antibiotics, long-term use of glucocorticoids and/or immune inhibitors, tumor chemotherapy, empirical antifungal therapy, target antifungal therapy and pathogenic microbiology tests. Risk factors and prognosis were analyzed. Hypoproteinemia is defined as serum albumin less than 30 g/L<sup>11</sup>; agranulocytosis is defined as the absolute count of neutrophils in peripheral blood under  $0.5 \times 10^9$  cells/L<sup>30</sup>; and renal insufficiency was defined as glomerular filtration rate lower than 60 ml/min/1.73 m<sup>2</sup>.<sup>6</sup>

### Blood culture and strain identification and susceptibility tests

Bact/Alert 3D full-automatic blood culture instrument and the corresponding Bact/Alert culture flask were used for blood culture. VITEK 2 compact was used to identify strains, and ATB-Fungus susceptibility kit was used for susceptibility testing. The above instruments and reagents were all products from bioMérieux. The results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) standard M27, a method for testing the susceptibility to antifungal agents of yeasts that cause invasive fungal infections.<sup>15</sup> Susceptibility to 5-fluorouracil, amphotericin B, micafungin, caspofungin, fluconazole, voriconazole and itraconazole were published by CLSI M27-S2.

**Table 1**  
Single factor analysis of risk factors for bloodstream infection with fluconazole resistant *C. tropicalis*.

Factors	Patients with fluconazole resistant <i>C. tropicalis</i> n = 44 (%)	Patients with fluconazole sensitive <i>C. tropicalis</i> n = 56 (%)	$\chi^2$	p-Values
Age (mean $\pm$ SD)	53.14 $\pm$ 15.96	52.96 $\pm$ 18.88		0.9615
$\geq 60$ years old	16 (36.4)	19 (33.9)	0.064	0.8
Male gender	28 (63.6)	36 (64.3)	0.005	0.946
<i>Underlying disease</i>				
Hematological malignancy	22 (50)	18 (32.1)	3.274	0.07
Solid organ tumor	6 (13.6)	10 (17.9)	0.327	0.568
Diabetes	6 (13.6)	9 (16.1)	0.115	0.735
Renal insufficiency	7 (15.9)	16 (28.6)	2.231	0.135
Solid organ transplantation	12 (27.3)	6 (10.7)	4.577	0.032
Agranulocytosis	16 (36.4)	13 (23.2)	2.069	0.15
Chronic obstructive pulmonary disease	14 (31.8)	22 (39.3)	0.596	0.44
Hypoproteinemia	15 (34.1)	18 (32.1)	0.042	0.837
<i>Related treatment and others</i>				
Deep vein catheterization	16 (36.4)	28 (50)	1.860	0.173
Indwelling gastric tube	10 (22.7)	18 (32.1)	1.084	0.298
Indwelling catheter $\geq 7$ days	14 (31.8)	20 (35.7)	0.167	0.683
Mechanical ventilation	11 (25)	19 (33.9)	0.935	0.333
Parenteral nutrition $\geq 5$ days	28 (63.6)	36 (64.3)	0.005	0.946
Indwelling cavity drainage tube	11 (25)	15 (26.8)	0.041	0.840
Surgery	13 (29.5)	21 (37.5)	0.695	0.405
Use of broad-spectrum antibiotics $\geq 5$ days	38 (86.4)	42 (75)	1.989	0.158
Hemodialysis	4 (9.1)	11 (19.6)	2.152	0.142
Stay in hospital for more than 4 weeks	28 (63.6)	30 (53.6)	1.025	0.311
Recent exposure to azoles $\geq 2$ weeks	25 (56.8)	12 (21.4)	13.239	<0.001
Long-term use of glucocorticoids and/or immunosuppressants	19 (43.2)	13 (23.2)	4.515	0.034
Chemotherapy	25 (56.8)	20 (35.7)	4.434	0.035

SD: standard deviation.

### Statistical methods

SPSS19.0 software was used for statistical analysis. Data conforming to a Normal distribution were represented by mean  $\pm$  standard deviation and *t*-test, while counting data were tested by chi-square test or two-sided Fisher exact probability test. Factors in univariate analysis ( $p < 0.05$ ) were included in logistic regression model for multivariate analysis. In order to perfect the analysis of the risk factors that may be related to the prognosis of the patients, Cox regression model was used for multi-factor analysis.  $p < 0.05$  was considered statistically significant.

## Results

### Demographic and clinical characteristics of patients with *C. tropicalis* BSI

Of the 100 patients, 64 were male (64%), with an average age of 53.0  $\pm$  17.4 years. According to the results of the drug susceptibility test of *C. tropicalis*, 44 isolates were resistant to fluconazole. The comorbidities included hematological malignancy (40%), chronic obstructive pulmonary disease (36%), hypoalbuminemia (33%), agranulocytosis (29%), impairment of renal function (23%), solid organ transplantation (18%), solid organ tumor (16%), diabetes (15%).

Before the onset of *C. tropicalis* candidemia, eighty cases (80%) were treated with broad-spectrum antibiotics for at least 5 days, 64 cases (64%) had parenteral nutrition for at least 5 days, 45 cases (45%) were treated with chemotherapy, indwelling catheterization was present for at least 7 days in 34 cases (34%), glucocorticoids and/or immunosuppressive treatments were used in 32 cases (32%), mechanical ventilation was used in 30 cases (30%), ICU length-of-stay for 7 days or more occurred in 17 cases (17%), and hemodialysis was performed in 15 cases (15%) (Table 1).

Fever was the most common clinical manifestation (91/100, 91%), accompanied by cough, sputum or shortness of breath in 42

cases (42%), disturbance of consciousness in 15 cases (15%), abdominal pain, diarrhea or gastrointestinal bleeding in 8 cases (8%), and shock in 8 cases (8%).

*C. tropicalis* was also recovered from other specimens than blood in 37 patients, including sputum (12 cases), ascites (7 cases), urine (7 cases), drainage fluid (3 cases), sputum + ascites (2 cases), drainage fluid + urine liquid (2 cases), sputum + urine (1 case), lumbar puncture fluid + disc necrosis (1 case), bile (1 case), bile + ascites (1 case). Twenty four patients had also bacteremia: *Pseudomonas aeruginosa* in 6 cases, *Acinetobacter baumannii* in 6 cases, *Escherichia coli* in 5 cases, *Klebsiella pneumoniae* in 5 cases, *Enterococcus* in 5 cases, *Burkholderia* in 2 cases, *Staphylococcus aureus* in one case, and *Enterobacter aerogenes* in one case. Four patients (4%) suffered other fungal BSI with the following species: *Candida glabrata*, *Candida albicans*, *Candida famata*, *Candida glabrata* + *Candida krusei*.

### Risk factors of fluconazole resistant *C. tropicalis* BSI

Univariate analysis showed that solid organ transplantation, exposure to azole for weeks, long-term use of glucocorticoids and/or immunosuppressants, and having received chemotherapy were the risk factor associated to fluconazole resistant *C. tropicalis* BSI ( $p < 0.05$ ) (Table 1). According to the results obtained with the multivariate logistic analysis azole exposure (OR = 5.725,  $p = 0.001$ ) was an independent risk factor for suffering a BSI with *C. tropicalis*–fluconazole resistant strains, while other factors were not statistically significant in multivariate analysis (Table 2).

### Antimicrobial treatment and prognosis in patients with *C. tropicalis* BSI

In this group, isolates of *C. tropicalis* obtained from patients were all sensitive to 5-fluorouracil, amphotericin B and echinocandins in vitro, and the resistant rates of fluconazole, voriconazole and itraconazole were 44%, 47% and 60%, respectively.

**Table 2**  
Multivariate binary logistic analysis of risk factors in fluconazole resistant *C. tropicalis* bloodstream infection.

Factors	Regression coefficient (B)	Standard error (Sb)	Wald value	OR value (95% confidence interval)	p-Values
Solid organ transplantation	0.406	0.643	0.398	1.5 (0.426, 5.286)	0.528
Recent exposure to azoles $\geq 2$ weeks	1.745	0.524	11.102	5.725 (2.051, 15.979)	0.001
Long-term use of glucocorticoids and/or immunosuppressants	0.796	0.496	2.577	2.217 (0.839, 5.862)	0.108
Chemotherapy	0.381	0.476	0.64	1.464 (0.576, 3.722)	0.424

**Table 3**  
Univariate analysis of risk factors of death in patients with *C. tropicalis* bloodstream infection.

Factors	Total	Deceased patients <i>n</i> = 36 (%)	Non-deceased patients <i>n</i> = 64 (%)	p-Values
<b>Age</b>				
$\geq 60$ years	35	11 (30.6)	24 (37.5)	0.3215 0.485
<b>Underlying disease</b>				
Hematological malignancy	40	16 (44.4)	24 (37.5)	0.496
Solid organ tumor	16	5 (13.9)	11 (17.2)	0.666
Diabetes	15	3 (8.3)	12 (18.8)	0.161
Renal insufficiency	23	9 (25.0)	14 (21.9)	0.722
Solid organ transplantation	18	7 (19.4)	11 (17.2)	0.778
Lack of neutrophils	29	13 (36.1)	16 (25.0)	0.240
Chronic obstructive pulmonary disease	36	23 (63.9)	13 (20.3)	<0.001
Hypoproteinemia	33	18 (50)	15 (23.4)	0.007
<b>Related treatment</b>				
Deep vein catheterization	44	20 (55.6)	24 (37.5)	0.081
Indwelling gastric tube	28	12 (33.3)	16 (25)	0.373
Indwelling catheter $\geq 7$ days	34	18 (50)	16 (25)	0.011
Mechanical ventilation	30	16 (44.4)	14 (21.9)	0.018
Parenteral nutrition $\geq 5$ days	64	27 (75)	37 (57.8)	0.086
Indwelling cavity drainage tube	26	6 (16.7)	20 (31.3)	0.111
Use of broad-spectrum antibiotics $\geq 5$ d	80	31 (86.1)	49 (76.6)	0.252
Hemodialysis	15	7 (19.4)	8 (12.5)	0.351
Recent exposure to azoles $\geq 2$ weeks	32	16 (44.4)	16 (25)	0.045
Long-term use of glucocorticoids and/or immunosuppressants	32	19 (52.8)	13 (20.3)	0.001
Tumor chemotherapy	45	20 (55.6)	25 (39.1)	0.112
Empirically sensitive antifungal therapy	58	16 (44.4)	42 (65.6)	0.039
Target sensitive antifungal therapy	76	20 (55.6)	56 (87.5)	<0.001
<b>Fluconazole resistant <i>C. tropicalis</i></b>	44	21 (58.3)	23 (35.9)	0.03

Sixty four patients recovered, and 36 died. Seventy-eight patients with *C. tropicalis* BSI received empirical antifungal therapy: azoles (42 cases), echinocandins (29 cases), azole + echinocandin (4 cases), polyene (2 cases), and echinocandin + polyene (1 case). Among them, isolates of 58 cases were sensitive to empirical antifungal drugs, and isolates of 20 cases were resistant. Statistical analysis showed that the case fatality rate of the empirically sensitive group was lower, as shown in Table 3.

#### Chronic obstructive pulmonary disease

Eighty five patients out of 100 received targeted antifungal therapy; 76 patients were treated with the appropriate antifungal (*C. tropicalis* was sensitive to the treatment) sensitive drugs and 9 patients were not. The statistical analysis showed that using the appropriate antifungal in the target treatment led to a lower fatality rate ( $p < 0.05$ ), as shown in Table 3.

Patients were divided in two groups according to the outcome (death or survival). The univariate analysis showed poor prognosis ( $p < 0.05$ ) associated with the following factors: chronic obstructive pulmonary disease, hypoalbuminemia, indwelling catheter  $\geq 7$  days, mechanical ventilation, recent exposure to azoles  $\geq 2$  weeks, long-term use of glucocorticoids and/or immunosuppressants, and infection with fluconazole resistant-*C. tropicalis* strains (Table 3). Empirical usage of antifungal drugs in cases of *C. tropicalis* resis-

tance led to poor outcome, whereas patients' prognosis could improve in cases of sensible *C. tropicalis* strains. This suggest that the early use of the proper antifungal may could reduce the mortality of patients.

The Cox regression model analysis showed that hematological malignancies (OR = 0.066,  $p = 0.023$ ), having an infection by a fluconazole resistant strain (OR = 0.137,  $p = 0.002$ ), suffering chronic obstructive pulmonary disease (OR = 0.205,  $p = 0.002$ ), or carrying an indwelling catheter (OR = 0.136,  $p = 0.007$ ) were independent risk factor for death in patients with *C. tropicalis* BSI. Targeted treatment with a proper antifungal agent (OR = 5.593,  $p = 0.002$ ) and the removal of drainage tubes (OR = 8.782,  $p = 0.012$ ) were protective factors (Table 4).

#### Discussion

In China, both the isolation rate of *C. tropicalis* and the resistance to fluconazole and voriconazole were significantly higher than the world average rates during the same period.<sup>14,32</sup> In this group of *C. tropicalis* BSI cases, the proportion of hematological malignancies was the highest, which was consistent with the literature reports.<sup>20</sup>

The risk factors of fluconazole resistant *C. tropicalis* BSI have been rarely reported. Studies have shown that *C. tropicalis* is prone to infect patients with tumors or patients affected with neutropenia.<sup>9,10</sup> It has been reported that *C. tropicalis* BSI is closely

**Table 4**  
Cox regression analysis of correlation factors for mortality of *C. tropicalis* bloodstream infection.

Factors	Regression coefficient	Standard error	Wald value	OR value (95% confidence interval)	p-Values
Age ( $\geq 60$ years)	0.146	0.542	0.073	1.158 (0.4, 3.352)	0.787
Chronic obstructive pulmonary disease	-1.586	0.524	9.151	0.205 (0.073, 0.572)	0.002
Hypoproteinemia	-0.521	0.431	1.464	0.594 (0.255, 1.381)	0.226
Hematological malignancy	-2.713	1.193	5.173	0.066 (0.006, 0.687)	0.023
Solid organ tumor	-1.308	0.75	3.038	0.27 (0.062, 1.177)	0.081
Agranulocytosis	-0.896	0.843	1.129	0.408 (0.078, 2.131)	0.288
Renal insufficiency	-1.502	0.801	3.514	0.223 (0.046, 1.071)	0.061
Diabetes	1.45	0.75	3.735	4.265 (0.98, 18.563)	0.053
Solid organ transplantation	0.761	0.592	1.652	2.141 (0.671, 6.834)	0.199
Deep vein catheterization	-0.860	0.657	1.715	0.423 (0.117, 1.533)	0.19
Indwelling catheter $\geq 7$ days	-1.993	0.739	7.271	0.136 (0.032, 0.58)	0.007
Indwelling gastric tube	0.983	0.703	1.958	2.673 (0.674, 10.599)	0.162
Parenteral nutrition $\geq 5$ days	-0.456	0.555	0.675	0.634 (0.213, 1.881)	0.411
Indwelling cavity drainage tube	2.173	0.869	6.251	8.782 (1.599, 48.229)	0.012
Mechanical ventilation	0.552	0.949	0.338	1.736 (0.27, 11.152)	0.561
Tumor chemotherapy	1.242	0.796	2.434	3.462 (0.727, 16.479)	0.119
Hemodialysis	-0.492	0.706	0.486	0.611 (0.153, 2.438)	0.486
Recent exposure to azoles $\geq 2$ weeks	0.329	0.487	0.456	1.389 (0.535, 3.605)	0.5
Use of broad-spectrum antibiotics $\geq 5$ days	1.06	0.634	2.798	2.888 (0.834, 10.004)	0.094
Long-term use of glucocorticoids and/or immunosuppressants	-0.068	0.508	0.018	0.934 (0.345, 2.526)	0.893
Empirically sensitive antifungal therapy	0.177	0.541	0.107	1.193 (0.414, 3.444)	0.744
Target sensitive antifungal therapy	1.722	0.565	9.298	5.593 (1.850, 16.913)	0.002
Fluconazole resistant <i>C. tropicalis</i>	-1.991	0.658	9.166	0.137 (0.038, 0.496)	0.002

related to the formation of biofilms in urinary catheters.<sup>1</sup> Our study shows that exposure to azoles within the preceding two weeks was an independent risk factor for death in fluconazole resistant *C. tropicalis* BSI. Studies have confirmed that exposure to azole antifungal drugs can lead to the increase of fluconazole resistant strains.<sup>5,7,28,33</sup> Lortholary et al.<sup>19</sup> found that the recovery of fluconazole resistant strains from the blood of patients recently exposed to azoles was significantly higher than that of caspofungin resistant strains, suggesting that fluconazole resistant strains were prone to cause BSI when exposed to azole antifungal drugs.

Our data show that the mortality of patients with *C. tropicalis* BSI was 36%, which is consistent with the literature.<sup>25</sup> Several risk factors are associated with the prognosis of *C. tropicalis* BSI. These include multi-site *Candida* colonization, a high APACHE II score, and underlying conditions or complications such as malignant tumors, diabetes, hypoalbuminemia, sepsis, or septic shock. Additional factors involve the use of invasive devices-including central venous catheters and mechanical ventilation, as well as inappropriate antifungal.<sup>24</sup> Our study shows that hematological malignancies are an independent risk factor for death in patients with *C. tropicalis* BSI. Indwelling catheterization is also an independent risk factor of high mortality, both in this study and the literature.<sup>31,35</sup>

Notably, the role of fluconazole-resistant *C. tropicalis* strains on prognosis had not been reported widely. This study shows that fluconazole resistant *C. tropicalis* strains was an independent risk factor for death in patients with *C. tropicalis* BSI. The data in this study also show that chronic obstructive pulmonary disease is an independent risk factor for death.

According to our results, using the proper antifungal drug improved the survival rate and played a key role in improving prognosis as well. Studies have shown<sup>17</sup> that the high fatality rate of patients with fungal BSI has been related to both delayed or inadequate antifungal treatment. Therefore, early blood culture and targeted antifungal therapy are important to improve the prognosis. This study shows that resistance to echinocandins and amphotericin B in *C. tropicalis* is really low, suggesting that echinocandins and amphotericin B are still effective antifungal drugs to treat *C. tropicalis* BSI. It has been recommended that echinocandins should be used in critically ill patients with unstable conditions, especially in cases of BSI due to a fluconazole resistant *Candida* strain and previously treated with an azole antifungal.<sup>21</sup>

Amphotericin B was also preferred in patients with *Candida* BSI and neutropenia.<sup>21</sup> In the case of empirical use of fluconazole, the in vitro susceptibility test is important. The data in this study also show that the removal of drainage tubes favoured the survival of patients.

In conclusion, we found that the exposure of azole antifungal agents was an independent risk factor for fluconazole resistant *C. tropicalis* BSI. Hematological malignancies, the infection with fluconazole-resistant strains, chronic obstructive pulmonary disease and portraying indwelling catheters were independent risk factors for death in patients with *C. tropicalis* BSI. An effective antifungal therapy was key to improve the prognosis and the removal of drainage tubes was a protective factor for the patients. Since this study was a single-center retrospective study and the sample size was relatively small, this conclusions needs to be further studied.

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## Conflict of interest

The authors declare that they have no competing interests.

## Data availability

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Data will be made available on request.

## References

- Achkar JM, Fries BC. *Candida* infections of the genitourinary tract. *Clin Microbiol Rev.* 2010;23:253–73.
- Al-Tawfiq JA. Distribution and epidemiology of *Candida* species causing fungemia at a Saudi Arabian hospital, 1996–2004. *Int J Infect Dis.* 2007;11:239–44.
- Aruna M, Jahappriya JD. Species distribution and antifungal susceptibility patterns of *Candida* isolates: a cross-sectional study from a tertiary care hospital in South India. *Cureus.* 2025;17:e79666.

4. Ben DP, Walsh TJ, Peter DJ, Stevens DA, Edwards JE, Thierry C, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Co. *Clin Infect Dis*. 2008;46:1813–21.
5. Ben-Ami R, Olshtain-Pops K, Krieger M, Oren I, Giladi M. Antibiotic exposure as a risk factor for fluconazole-resistant *Candida* bloodstream infection. *Antimicrob Agents Chemother*. 2012;56:2518–23.
6. Bladé J, Rosiñol L, Cibeira MT, de Larrea CF. Treatment of relapsed myeloma in a patient with renal insufficiency. *J Clin Oncol*. 2018;36, <http://dx.doi.org/10.1200/JCO.2017.77.6419>.
7. Canuto MM, Rodero FG. Antifungal drug resistance to azoles and polyenes. *Lancet Infect Dis*. 2002;2:550–63.
8. Cilo BD. Species distribution and antifungal susceptibilities of *Candida* species isolated from blood culture. *Cureus*. 2023;15:e38183.
9. Cisterna R, Zepeleta G, Telleria O, Guinea J, Esperalba J. Nationwide sentinel surveillance of bloodstream *Candida* infections in 40 tertiary care hospitals in Spain. *J Clin Microbiol*. 2010;48:4200–6.
10. Colombo AL. Epidemiology of opportunistic fungal infections in Latin America. *Clin Infect Dis*. 2010;51:561–70.
11. Conner BJ. Treating hypoalbuminemia. *Vet Clin North Am Small Anim Pract*. 2017;47:451–9.
12. de Souza CM, Dos Santos MM, Furlaneto-Maia L, Furlaneto MC. Adhesion and biofilm formation by the opportunistic pathogen *Candida tropicalis*: what do we know? *Can J Microbiol*. 2023;69:207–18.
13. Godoy P, Tiraboschi IN, Severo LC, Bustamante B, Calvo B, Almeida LPD, et al. Species distribution and antifungal susceptibility profile of *Candida* spp. bloodstream isolates from Latin American hospitals. *Memórias do Instituto Oswaldo Cruz*. 2003;98:401–5.
14. Guo F, Yang Y, Kang Y, Zang B, Cui W, Qin B, et al. Invasive candidiasis in intensive care units in China: a multicentre prospective observational study. *J Antimicrob Chemother*. 2013;68:1660–8.
15. Hazen KC, Dirks D, Masuoka J. Determination of echinocandin MICs for *Candida* species in less than 8 h: comparison of the rapid susceptibility assay with the Clinical and Laboratory Standards Institute's broth microdilution assay. *J Clin Microbiol*. 2009;47:4043–8.
16. Keighley C, Chen CA, Marriott D, Pope A, Slavin MA. Candidaemia and a risk predictive model for overall mortality: a prospective multicentre study. *BMC Infect Dis*. 2019;19:445.
17. Kumar A. Septic shock attributed to *Candida* infection: importance of empiric therapy and source control. *Clin Infect Dis*. 2012;54, 1739.
18. Liu T, Sun S, Zhu X, Wu H, Sun Z, Peng S. Epidemiology, clinical characteristics, and outcome in candidemia: a retrospective five-year analysis from two tertiary general hospitals. *BMC Infect Dis*. 2025;25:1–9.
19. Lortholary O, Desnosollivier M, Sitbon K, Fontanet A, Bretagne S, Dromer F. Recent exposure to caspofungin or fluconazole influences the epidemiology of candidemia: a prospective multicenter study involving 2,441 patients. *Antimicrob Agents Chemother*. 2011;55:532–8.
20. Muñoz P, Giannella M, Fanciulli C, Guinea J, Valerio M, Rojas L, et al. *Candida tropicalis* fungaemia: incidence, risk factors and mortality in a general hospital. *Clin Microbiol Infect*. 2011;17:1538–45.
21. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Executive summary: Clinical Practice Guideline for the Management of Candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62:e1–50.
22. Posteraro B, Carolis ED, Criscuolo M, Ballanti S, Decembrino N. Candidaemia in haematological malignancy patients from a SEIFEM study: epidemiological patterns according to antifungal prophylaxis. *Mycoses*. 2020;63:900–10.
23. Pramodhini S, Srirangaraj S, Easow JM. Candiduria – study of virulence factors and its antifungal susceptibility pattern in tertiary care hospital. *J Lab Phys*. 2021;13:231–7.
24. Puig-Asensio M, Padilla B, Garnacho-Montero J, Zaragoza O, Aguado JM, Zaragoza R, et al. Epidemiology and predictive factors for early and late mortality in *Candida* bloodstream infections: a population-based surveillance in Spain. *Clin Microbiol Infect*. 2014;20:O245–54.
25. Rodríguez L, Bustamante B, Huaroto L, Agurto C, Illescas R, Ramírez R, et al. A multi-centric study of *Candida* bloodstream infection in Lima-Callao, Peru: species distribution, antifungal resistance and clinical outcomes. *PLoS One*. 2017;12, e0175172.
26. Ruhnke M. Epidemiology of *Candida albicans* infections and role of non-*Candida albicans* yeasts. *Curr Drug Targets*. 2006;7:495–504.
27. Sarika P, Aiken D, Yejin KH, Shukry Z, Ana-Alastruey I, Evelina T, et al. *Candida albicans* – a systematic review to inform the World Health Organization Fungal Priority Pathogens List. *Med Mycol*. 2024;62:myae040.
28. Shah DN, Yau R, Lasco TM, Weston J, Salazar M, Palmer HR, et al. Impact of prior inappropriate fluconazole dosing on isolation of fluconazole-nonsusceptible *Candida* species in hospitalized patients with candidemia. *Antimicrob Agents Chemother*. 2012;56:3239–43.
29. Tahtler JG, Cicvari A, Kourenti D, Karvouniaris M, Bogdan M, Kralik K, et al. Isolation of *Candida* species is associated with comorbidities, prolonged mechanical ventilation, and treatment outcomes in surgical ICU patients, a cross-sectional study. *Curr Tradit Med*. 2024;10:743.
30. Takata K, Kubota S, Fukata S, Kudo T, Nishihara E, Ito M, et al. Methimazole-induced agranulocytosis in patients with Graves' disease is more frequent with an initial dose of 30 mg daily than with 15 mg daily. *Thyroid*. 2009;19:559–63.
31. Vaidyanathan S, Soni B, Hughes P, Ramage G, Sherry L, Singh G, et al. *Candida albicans* fungaemia following traumatic urethral catheterisation in a paraplegic patient with diabetes mellitus and candiduria treated by caspofungin. *Case Rep Infect Dis*. 2013;2013:1–6.
32. Wang H, Xiao M, Chen CA, Kong F, Sun ZY, Liao K, et al. In vitro susceptibilities of yeast species to fluconazole and voriconazole as determined by the 2010 National China Hospital Invasive Fungal Surveillance Net (CHIF-NET) study. *J Clin Microbiol*. 2012;50:3952–9.
33. Whaley SG, Berkow EL, Rybak JM, Nishimoto AT, Barker KS, David RP. Azole antifungal resistance in *Candida albicans* and emerging non-*albicans Candida* species. *Front Microbiol*. 2016;7:2173.
34. Xin F, Meng X, Kang L, Timothy K, He W, Li Z, et al. Notable increasing trend in azole non-susceptible *Candida tropicalis* causing invasive candidiasis in China (August 2009 to July 2014): molecular epidemiology and clinical azole consumption. *Front Microbiol*. 2017;8:464.
35. Yapar N, Pullukcu H, Avkan-Oguz V, Sayin-Kutlu S, Kaya O. Evaluation of species distribution and risk factors of candidemia: a multicenter case-control study. *Med Mycol*. 2011;49:26–31.