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A multicenter retrospective analysis of the antifungal susceptibility patterns of *Candida* species and the predictive factors of mortality in South Korean patients with candidemia

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Abstract

As detection rates of non-albicans *Candida* species are increasing, determining their pathogen profiles and antifungal susceptibilities is important for antifungal treatment selection. We identified the antifungal susceptibility patterns and predictive factors for mortality in candidemia.

A multicenter retrospective analysis of patients with at least 1 blood culture positive for *Candida* species was conducted. *Candida* species were classified into 3 groups (group A, *Candia albicans*; group B, *Candida tropicalis*, and *Candida parasilosis*; group C, *Candida glabrata* and *Candida krusei*) to analyze the susceptibility patterns, first-line antifungal administered, and mortality. Univariate and multivariate comparisons between outcomes were performed to identify mortality risk factors.

In total, 317 patients were identified, and 136 (42.9%) had recorded mortality. Echinocandin susceptibility was higher for group A than group B (111/111 [100%] vs 77/94 [81.9%], $P < .001$). Moreover, group A demonstrated higher fluconazole susceptibility (144/149 [96.6%] vs 39/55 [70.9%], $P < .001$) and lower mortality (68 [45.3%] vs 34 [61.8%], $P = .036$) than those of group C. In the multivariate analysis, the sequential organ failure assessment score (odds ratio OR 1.351, 95% confidence interval 1.067–1.711, $p = 0.013$) and positive blood culture on day 7 of hospitalization (odds ratio 5.506, 95% confidence interval, 1.697–17.860, $P = .004$) were associated with a higher risk of mortality.

Patients with higher sequential organ failure assessment scores and sustained positive blood cultures have an increased risk of mortality.

Abbreviations: C albicans = Candida albicans, C glabrata = Candida glabrata, C krusei = Candida krusei, C parapsilosis = Candida parasilosis, C tropicalis = Candida tropicalis, CI = confidence interval, CLSI = Clinical and Laboratory Standards Institute, CVC = central venous catheters, EUR = Europe, ICU = intensive care unit, MICs = minimal inhibitory concentrations, NA = North America, OR = odds ratio, SOFA = sequential organ failure assessment.

Keywords: antifungal, candida, mortality, susceptibility

1. Introduction

Candida species are normal flora of the gastrointestinal and genitourinary tracts. However, in hosts with a decreased immune response, widespread dissemination can result in multi-organ failure.[1] The term candidemia refers to the presence of *Candida* species in the blood.[2] *Candida* species identified from blood should never be considered contaminants, because that is the most common manifestation of invasive candidiasis.[2] Risk factors for candidemia include patients who have been treated in an intensive care unit (ICU) and those who are immunocompro-

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mised.[3] Identified risk factors for developing candidemia are patients in the ICU with indwelling central venous catheters (CVC), those receiving total parental nutrition, and those who have undergone gastrointestinal procedures.[4]

Although infection with *Candida albicans* (*C albicans*) is most common, the identification of the casual species is important, because some species are more resistant to azole antifungal agents.[2] The isolation of non-albicans *Candida* species has been increasing, and they have been frequently identified in the following order: *Candida glabrata* (*C glabrata*) and *Candida parapsilosis*, followed by *Candida tropicalis* (*C tropicalis*) and *Candida krusei* (*C krusei*).[5,6] Some *C glabrata* isolates are resistant to fluconazole, and all *C krusei* isolates are considered to be intrinsically resistant to fluconazole.[7] The minimal inhibitory concentrations (MICs) for echinocandins for *Candida parasilosis* (*C parapsilosis*) are higher than those of other Candida species. Moreover, resistance to fluconazole is highly predictive of resistance to voriconazole.[7] Therefore, the identification of changes in pathogen profiles and antifungal susceptibilities is important for antifungal treatment selection. Our study specifically compared the clinical, epidemiological, and antifungal susceptibility patterns in candidemia and identified risk factors for mortality.

2. Materials and methods

2.1. Study population and definitions

A multicenter retrospective analysis of episodes of candidemia in adults, collected from the electronic databases of 2 tertiary care hospitals in South Korea, was performed over a 4-year (2012–2015) period. Patients with at least 1 positive blood culture for a *Candida* species were included in the analysis. Patients with isolated yeasts other than *Candida* species were excluded from the study.

Intravenous catheter-related candidemia was defined in patients who had an intravascular device and ≥1 positive blood culture result, such that the same organism was isolated from the catheter and a peripheral blood culture, with clinical manifestations of infection (fever, chills, and/or hypotension) and no other apparent source for the bloodstream infection.[8] An intra-abdominal source of candidemia was considered for the patients who had a recent abdominal surgery or intra-abdominal events, such as peritonitis, abdominal abscess, and a purulent or necrotic infection at sites of gastrointestinal perforation or anastomotic leak, as confirmed by computed tomography scans.[1] Cardiovascular disease in patients was defined as the presence of hypertension, valvular heart disease, ischemic heart disease, or heart failure. Central nervous system disorder in patients was defined by a history of cerebrovascular accident or hemorrhage. Renal disease in patients was defined by chronic renal failure, stage 3 or 4, requiring hemodialysis or peritoneal dialysis. Lung disease in patients was defined as the presence of asthma, chronic obstructive lung disease, or idiopathic pulmonary fibrosis. Hematologic disease in patients was defined by aplastic anemia, lymphoma, or leukemia. The use of echinocandin was defined in patients who received first-line antifungal treatment with caspofungin, anidulafungin, or micafungin.

The demographic data, comorbidities, hospitalization and ICU stay, laboratory results, treatment outcomes, *Candida* species distribution, antifungal susceptibility results, first-line antifungal agents administered, and the complications (endocarditis, bone or joint infection, hepatosplenic candidiasis, and endophthalmitis) related to the candidemia were compared among the outcomes. The severity of illness was estimated by the sequential organ failure assessment (SOFA) score and the Charlson index. The laboratory data obtained on the first day of admission were analyzed. The presence of CVC insertion at the time of the positive blood culture and whether the patient was admitted to the ICU or the general ward were compared between outcomes. Blood culture results positive for a *Candida* species, obtained on the 7th, 14th, and 28th hospital day, were analyzed. The appropriate antifungal treatment was considered when the treatment was started within 48 hours, after the first blood culture was performed.[9] Univariate and multivariate comparisons between outcomes were performed.

Candida species were classified as *C albicans* (group A) and non-albicans *Candida* species groups (groups B and C). Among the non-albicans group, species with reduced susceptibility to fluconazole were classified as group C (*C glabrata* and *C krusei*), and species susceptible to fluconazole classified as group B (*C tropicalis* and *C parapsilosis*). The clinical and demographic factors, susceptibility patterns, first-line antifungal treatment, and mortality of each groups were analyzed.

2.2. Laboratory testing

Using the BACTEC 860 system (Becton Dickinson, Inc., Sparks, MD), isolated *Candida* were detected from blood cultures. *Candida* species were identified using the API-32C system (BioMerieux Vitek, Inc., St. Louis, MI). The commercial VITEK-2 yeast susceptibility test (BioMerieux, Hazelwood, MO) was used to derive the MICs for *Candida* species. Susceptibility to echinocandin and fluconazole was defined as follows according to the clinical breakpoints for interpreting the MICs from the Clinical and Laboratory Standards Institute (CLSI) guidelines. Susceptibility to echinocandins was defined in isolates of *C albicans*, *C tropicalis*, and *C krusei* with an MIC ≤0.25 mcg/mL, and *C parasilosis* with an MIC ≤2 mcg/mL for all 3 echinocandins (anidulafungin, caspofungin, and micafungin). *C glabrata* isolates with an MIC ≤0.12 mcg/mL to caspofungin and anidulafungin, and an MIC ≤0.06 mcg/mL to micafungin were considered susceptible.[10] The CLSI does not currently provide a susceptible breakpoint of fluconazole for *C glabrata*, with the intermediate breakpoint defined as MIC ≤32 and resistance as MIC ≥64. Susceptible was an MIC ≤2 mcg/mL for fluconazole in all species of Candida, except for *C glabrata* and *C krusei* (Supplementary Table 1, http://links.lww.com/MD/D953).[11]

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to and the appropriate ethical review committee approval has been received.

2.3. Statistical analysis

Categorical variables have been presented as numbers and percentages, and continuous variables have been expressed as the mean ± standard deviation, unless otherwise indicated. Categorical variables were compared using a χ^2 analysis, and continuous variables with normal distributions were compared using the Student *t* test. Single linear univariate correlations (Pearson correlation coefficients) and stepwise multivariate regression analyses were performed to evaluate the relationship between

mortality and other variables. The covariates inserted in this model included the variables that differed with a $P < .05$ in the univariate analysis, which ensured the absence of significant multicollinearity. Multiple differences among groups of *C albicans* and non-albicans species were evaluated using a 1-way Analysis of Variance (ANOVA) with Tukey multiple comparison test. All categories were calculated as a percentage with a 95% confidence interval (CI). All statistical tests were performed using IBM SPSS software for Windows, version 20. *P*-values $< .05$ were considered statistically significant.

3. Results

During the study period, a total of 317 patients (88 cases originating from indwelling intravenous catheter, 89 cases from an intra-abdominal source, and 140 cases with an unidentifiable source of candidemia) were analyzed. Among these patients, mortality was observed for 136 (42.9%) patients.

The baseline characteristics and demographic data of the study population are presented in Table 1. Among the study patients, 198 (62.5%) were male with a median age of 68.3 ± 13.5 years. Patients with renal failure (36 [19.9%] vs 60 [44.1%], $P < .001$), chronic lung diseases (71 [39.2%] vs 93 [68.4%], $P < .001$), and hematologic disorders (48 [26.5%] vs 62 [45.6%], $P < .001$) presented with higher rates of mortality. Moreover, higher mortality was observed in the patients with higher SOFA scores (2.9 ± 2.9 vs 6.2 ± 4.3, $P < .001$), higher Charlson index (3.1 ± 1.8 vs 3.8 ± 1.9, $P = .003$), a CVC in place at the time of candidemia (74 [40.9%] vs 75 [55.1%], $P = .012$), and those admitted to the ICU (49 [27.1%] vs 67 [49.3%], $P < .001$). Patients with positive culture results on the 7th day of hospitalization demonstrated higher mortality rates than those with negative culture results (21 [35.6%] vs 21 [77.8%], $P < .001$).

Table 2 presents the predictive factors associated with an increased risk of mortality. Higher SOFA scores (odds ratio [OR] 1.351, 95% CI 1.067–1.711, $P = .013$) and positive culture results on the 7th day of hospitalization (OR 5.506, 95% CI, 1.697–17.860, $P = .004$) were associated with an increased risk of mortality. The multivariate analysis demonstrated that there was no statistically significant difference in mortality based on the

Table 1

Baseline characteristics of the study population.

Characteristic	Total (n = 317)	Survival (n = 181)	Mortality (n = 136)	*P*-value
Gender, male	198 (62.5)	105 (58.0)	93 (68.4)	.059*
Age, yr	68.3 ± 13.5	68.1 ± 13.4	68.7 ± 13.7	.696†
BMI	21.8 ± 4.1	21.5 ± 3.9	22.2 ± 4.2	.169†
Hospital, d	53.4 ± 63.4	62.9 ± 74.6	47.7 ± 43.0	.033†
ICU, d	19.5 ± 24.2	16.8 ± 21.4	22.7 ± 26.8	.059†
Charlson index	3.4 ± 1.9	3.1 ± 1.8	3.8 ± 1.9	.003†
SOFA score	4.3 ± 3.9	2.9 ± 2.9	6.2 ± 4.3	<.001†
Underlying disease				
Cardiovascular disease	179 (56.5)	100 (55.2)	79 (58.1)	.614*
CNS disorder	91 (28.7)	51 (25.2)	40 (29.4)	.810*
Solid organ cancer	109 (34.5)	66 (36.5)	43 (31.9)	.394*
Renal disease	96 (30.3)	36 (19.9)	60 (44.1)	<.001*
Liver disease	59 (18.6)	33 (18.2)	26 (19.1)	.841*
Lung disease	164 (51.7)	71 (39.2)	93 (68.4)	<.001*
Solid organ transplantation	8 (2.5)	6 (3.3)	2 (1.5)	.474‡
Hematologic disease	110 (34.7)	48 (26.5)	62 (45.6)	<.001*
Risk factor for infection				
CVC	149 (47.0)	74 (40.9)	75 (55.1)	.012*
ICU admission	116 (36.6)	49 (27.1)	67 (49.3)	<.001*
Laboratory data				
WBC ($\times 10^9$/L)	1949 ± 5023	2120 ± 4,798	1722 ± 5,316	.486†
Hb (g/dL)	10.3 ± 2.3	10.5 ± 2.7	10.1 ± 1.6	.071†
Platelet ($\times 10^9$/L)	40,098 ± 101,745	48,676 ± 105,095	28,681 ± 96306	.080†
AST (U/L)	121.3 ± 594.9	51.4 ± 64.2	224.7 ± 926.8	.068†
ALT (U/L)	54.6 ± 105.2	40.4 ± 59.1	75.9 ± 147.8	.028†
Total bilirubin	10.9 ± 131.3	2.1 ± 7.6	23.9 ± 206.4	.299†
BUN (mg/dL)	33.8 ± 28.1	26.4 ± 23.7	43.7 ± 30.6	<.001†
Creatinine (mg/dL)	1.6 ± 2.6	1.5 ± 3.2	1.7 ± 1.6	.690†
Microbiological data				
Culture positive on day 7	42 (48.8)	21 (35.6)	21 (77.8)	<.001*
Culture positive on day 14	10 (18.5)	7 (17.1)	3 (23.1)	.689‡
Culture positive on day 28	2 (6.5)	1 (4.3)	1 (12.5)	.456‡
Complication related to candidemia	9 (2.8)	7 (3.9)	2 (1.5)	.309‡

The data were expressed as the mean ± SD or median (interquartile range) or number of patients (%).

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, BUN = blood urea nitrogen, CNS = central nervous system, CVC = central venous catheter, Hb = haemoglobin, ICU = intensive care unit, SOFA = sequential organ failure assessment, WBC = white blood cell.

* Pearson χ-test.

† Student *t* test.

‡ Fisher exact test.

Table 2

Predictive factors for mortality.

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Hematologic disease	2.322	1.448–3.722	<.001	0.861	0.218–3.399	.830
Presence of CVC	1.778	1.134–2.787	.012	0.767	0.206–2.852	.767
ICU admission	2.616	1.636–4.184	<.001	1.371	0.303–6.200	.682
Hospital, days	0.995	0.990–1.000	.037	0.997	0.986–1.009	.655
SOFA score	1.294	1.199–1.396	<.001	1.351	1.067–1.711	.013
Charlson index	1.201	1.063–1.357	.003			
Culture positive on day 7	6.333	2.211–18.139	.001	5.506	1.697–17.860	.004
Candida species						
Candida albicans	1					
Candida tropicalis, Candida parasilosis	0.612	0.363–1.033	.066			
Candida glabrata, Candida krusei	1.665	0.872–3.181	.122			
Treatment						
No antifungal	1					
Fluconazole	0.636	0.383–1.055	.080			
Echinocandin	0.148	0.041–0.541	.004			

CI = confidence interval, CVC = central venous catheter, ICU = intensive care unit, Logistic regression analysis, OR = odds ratio, SOFA = sequential organ failure assessment.

Candida species. Although the univariate analysis showed that echinocandin use resulted in a lower risk of mortality compared to no antifungal treatment (OR 0.148, 95% CI 0.041–0.541, $P = .004$), there was no statistically significant difference in the multivariate analysis.

Table 3 presents the characteristics of the *C albicans* (group A) and non-albicans *Candida* species groups (groups B and C). The isolates were identified as *C albicans, C parapsilosis* or *C tropicalis*, and *C glabrata* or *C krusei* in 150, 112, and 55 cases (*C albicans* [n = 150], *C parasilosis* [n = 60], *C tropicalis* [n = 52], *C glabrata* [n = 47], and *C krusei* [n = 8]), respectively. No other *Candida* species were isolated. No multiple *Candida* isolates were identified from the same patient, and no mixed infections were identified. Susceptibility to echinocandin was higher for group A than group B (111/111 [100%] vs 77/94 [81.9%], $P < .001$). Group A presented higher susceptibility to fluconazole than that of group C (144/149 [96.6%] vs 39/55 [70.9%], $P < .001$). There was no difference in mortality between groups A and B. However, lower mortality was observed for group A than group C (68 [45.3%] vs 34 [61.8%], $P = .036$).

Figure 1 presents the percentages for echinocandin and fluconazole susceptibility for each group of *Candida* species.

4. Discussion

Candidemia is 1 of the most common causes of health-care associated blood stream infections.[1] Among 1,314 *Candida* isolates tested from the Asia-Pacific region, *C albicans* (46.0%) was the most commonly isolated species followed by *C glabrata* (17.9%), *C tropicalis* (14.1%), *C parapsilosis* (12.9%), and *C krusei* (1.8%).[12] Although *C albicans* is the most commonly isolated species, an increase in non-*albicans Candida* species has been observed worldwide.[1]*C glabrata* was the most common non-*C albicans* species detected in all geographic regions except for Latin America, where *C parapsilosis* and *C tropicalis* were more common.[12] Both Europe (EUR) and North America (NA) demonstrated similar species distribution with *C albicans* (EUR 52.5%, NA 42.7%) the most commonly isolated species followed by *C glabrata* (EUR 16.0%, NA 24.3%).[12] In South Korea, although *C albicans* remains the leading Candida species that causes blood stream infection, an increase of *C glabrata* (from 21.3% to 28.5%) and a decrease of C parapsilosis (from 36.5% to 24.7%) over the past years were noticed.[13]*C auris* an emerging pathogen because it is intrinsically fluconazole resistant, and increasing numbers of infections have been identified in multiple countries.[14,15] This pathogen has caused invasive health care-associated infections, and it has been associated with high mortality rates.[15] The earliest known strain of *C auris* dates to 1996 in South Korea.[16] In this study, *C albicans* (n = 150) was the most commonly isolated pathogen, followed by *C parapsilosis* (n = 60), *C tropicalis* (n = 52), *C glabrata* (n = 47), and *C krusei* (n = 8).

A reduced dose-dependent susceptibility to fluconazole was observed for the *C glabrata* isolates compared to the other *Candida* species.[17] The highest rates of fluconazole resistant isolates were seen in *C glabrata* from North America (10.6%) and in *C tropicalis* from the Asia-Pacific region (9.2%).[12] Fluconazole resistance for *C albicans* was low in both North America (0.4%), and Asia-Pacific regions (0.2%).[12] In this study, 3.4% of *C albicans* were resistant to fluconazole, with *C glabrata*, and *C krusei* isolates exhibiting higher resistance to fluconazole than *C. albicans*. Due to an altered cytochrome *P450* isoenzyme, *C krusei* is intrinsically resistant to fluconazole.[18] In a large international surveillance study that included 326 bloodstream isolates of *C krusei*, all of the isolates were susceptible to echinocandins.[19] Echinocandin resistance ranged from 3.5% for *C glabrata* to 0.1% for *C albicans* and *C parapsilosis* across the globe.[12] In the present study, *C tropicalis* and *C parapsilosis* isolates were less susceptible to echinocandins, as has been reported in prior studies.[17,20]

Prior studies have identified increasing age, higher Acute Physiology and Chronic Health Evaluation II scores, the Candida species, underlying renal dysfunction, and the primary antifungal agent selected as factors that are associated with an increased risk of mortality.[21–23] Although a higher SOFA score demonstrated an association with an increased risk of mortality, which has been shown in prior studies, there was no statistically significant difference in mortality among the *Candida* species or the primary antifungal agent administered.

Table 3

Characteristics of C albicans and non-albicans *Candida* species.

		Non-albicans groups				
	C albicans Group A (n = 150)	*C parasilosis*, *C tropicalis* Group B (n = 112)	*C glabrata*, *C krusei* Group C (n = 55)	*P*-value	*P*-value*	*P*-value†
Age, yr	74.6 ± 13.2‖	69.2 ± 13.3‖	73.8 ± 14.6	.004	.004	.923
Gender, male	88 (58.7)	76 (67.9)	34 (61.8)	.407‡	.128	.684
Hospital, d	48.9 ± 3.7	65.9 ± 87.6	57.4 ± 43.1	1.000	.082	.673
ICU, d	18.8 ± 21.6	21.4 ± 29.2	17.7 ± 19.7	.652	.716	.970
SOFA score	4.4 ± 4.0	4.2 ± 3.9	4.3 ± 3.5	.885	.874	.979
Charlson index	3.4 ± 1.8	3.1 ± 1.7	3.8 ± 2.2	.072	.382	.383
Underlying disease						
Cardiovascular disease	88 (58.7)	59 (52.7)	32 (58.2)	.721‡	.334	.950
CNS disorder	39 (26.0)	38 (33.9)	14 (25.5)	.706‡	.163	.937
Solid organ cancer	50 (33.6)	37 (33.0)	22 (40.0)	.484‡	.930	.393
Renal disease	48 (32.0)	28 (25.0)	20 (36.4)	.900‡	.217	.557
Liver disease	28 (18.7)	21 (18.8)	10 (18.2)	.951‡	.986	.937
Lung disease	89 (59.3)	51 (45.5)	24 (43.6)	.017‡	.027	.045
Solid organ transplantation	2 (1.3)	5 (4.5)	1 (1.8)	.503‡	.141§	1.000§
Hematologic malignancy	2 (1.3)	6 (5.4)	4 (7.3)	.028‡	.077§	.046§
Connective tissue disease	9 (6.0)	15 (13.4)	11 (20.0)	.003‡	.04	.003
Risk factor for infection						
CVC in place at time of positive blood culture	80 (53.3)	48 (42.9)	21 (38.2)	.031‡	.093	.055
ICU admission	59 (39.3)	43 (38.4)	14 (25.5)	.110‡	.877	.066
Laboratory data						
WBC ($\times 10^9$/L)	1874 ± 4411	2100 ± 5763	1847 ± 5058	.925	.931	.999
Hb (g/dL)	10.4 ± 2.9	10.3 ± 1.5	10.1 ± 2.1	.611	.883	.589
Platelet ($\times 10^9$/L)	35676 ± 81745	49810 ± 123832	32381 ± 89167	.446	.508	.977
AST (U/L)	85.6 ± 192.1	200.8 ± 967.6	54.8 ± 63.1	.287	.336	.954
ALT (U/L)	55.6 ± 116.9	57.7 ± 108.0	39.9 ± 49.2	.631	.990	.678
Total bilirubin	20.7 ± 194	3.05 ± 9.32	1.86 ± 4.93	.568	.616	.701
BUN (mg/dL)	37.0 ± 31.1‖	28.8 ± 24.9‖	35.2 ± 24.4	.059‡	.05	.904
Creatinine (mg/dL)	1.4 ± 1.4	1.8 ± 3.9	1.6 ± 1.7	.570	.544	.880
Microbiological data						
Culture positive on day 7	18 (31.0)	13 (28.3)	11 (50.0)	.369‡	.183§	.285
Culture positive on day 14	2 (6.7)	6 (24.0)	2 (15.4)	.768‡	1.000§	.658§
Culture positive on day 28	1 (5.0)	1 (5.0)	0 (0)	.368‡		.464§
Susceptibility						
Echinocandin S (n = 251)	111/111 (100)	77/94 (81.9)	45/46 (97.8)	.064‡	<.001	.293§
Fluconazole S (n = 316)	144/149 (96.6)	108/112 (96.4)	39/55 (70.9)	<.001‡	1.000§	<.001
Treatment						
Echinocandin (n = 67)	30 (20.0)	22 (19.6)	15 (27.3)	.350‡	1.000	.265
Fluconazole (n = 236)	114 (76.0)	88 (78.6)	34 (61.8)	.110‡	.624	.045
Complication	4 (2.7)	2 (1.8)	3 (5.5)	.443‡	1.000§	.388§
Mortality	68 (45.3)	34 (30.4)	34 (61.8)	.305‡	1.000§	.036

The data were expressed as the mean ± SD or median (interquartile range) or number (%) of patients.

C albicans = Candida albicans, C glabrata = Candida glabrata, C krusei = Candida krusei, C parapsilosis = Candida parasilosis, C tropicalis = Candida tropicalis, CVC = central venous catheter, ICU = intensive care unit, R = resistant, S = susceptible, SOFA = sequential organ failure assessment.

* *P*-value between Group A and Group B.

† *P*-value between Group A and Group C. The *P*-value was evaluated by 1-way ANOVA among the 3 groups.

‡ Linear-by linear association.

§ Fisher exact test.

‖ Statistically significant difference between 2 groups based on Tukey post hoc test.

In this study, positive blood culture results obtained 1 week after hospitalization were associated with a nearly 5 times greater risk of mortality. For cases of deep-seated candidemia, blood culture positivity is estimated to be less than 50%.[24] Considering the low sensitivity of culture positivity in deep-seated candidemia, we believe that this finding raises awareness for clinicians, by indicating that *Candida* species isolated from blood should never be considered contaminants, and that patients with a positive blood culture after 1 week are at higher risk for a poor outcome.

There are several limitations to this study. First, this study is limited by its retrospective nature. Second, the clinical MIC breakpoints for both the echinocandins and fluconazole were defined according to the CLSI guidelines. Third, describing geometric means, MIC ranges, MIC 50 and MIC 90 values was not possible in this study.

The results of our study demonstrate the antifungal susceptibility patterns of *Candida* species at 2 hospitals in South Korea. Moreover, patients with higher SOFA scores at the time of

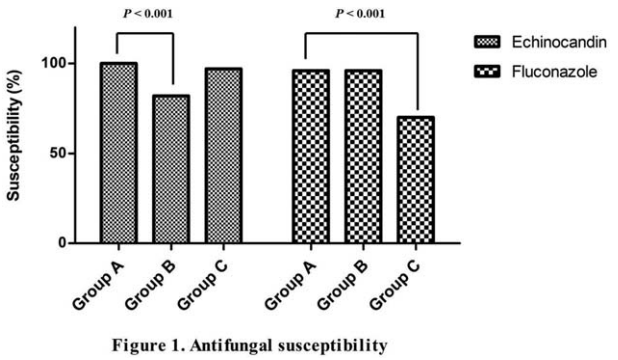

Figure 1. Antifungal susceptibility.

admission and a positive culture on the 7th day of hospitalization are at an increased risk of mortality.

Author contributions

IJY designed the study and acquired data, analyzed and interpreted the data, drafted the initial manuscript, reviewed, and critically revised and approved the final manuscript as submitted. SJS conceptualized the study and is responsible for the content of the manuscript, including the data and analysis. YKK, HYK, YGS, JMK, and JYC provided statistical assistance and revised and approved the final manuscript. All authors read and approved the final manuscript.

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