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Effect of (1→3)-β-D glucan false-negative results on outcomes in critically ill patients with catheter-related bloodstream infection due to candidiasis

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Abstract

The purpose of this study was to determine how a false-negative result on the (1→3)-β-D glucan (BG) test affected the prognosis and 30-day mortality in patients with a catheter-related bloodstream infection (CRBSI) in association with an invasive fungal infection (IFI).

A total of 107 adult candidemia patients were retrospectively studied. Among these 35 who were diagnosed with proven or probable CRBSI due to infection with Candida species, and who had undergone further BG tests before producing a positive result on blood culture met the study criteria. The patients' clinical features, risk factors, indwelling time for a central venous catheter, and initiation of antifungal therapy associated with 30-day mortality as the main outcome were investigated.

No significant differences were observed in baseline characteristics or risk factor scores between the BG-positive and -negative groups. However, the difference in the 30-day mortality rate between BG-negative patients (7/11, 63.6%) and BG-positive patients (7/24, 29.2%) was almost significant ($p = 0.08$).

These findings indicate that, even if the result of the BG test is negative, treatment should be initiated immediately after consideration of the characteristics of each patient, especially in those with a suspected IFI.

Introduction

In recent years, morbidity and mortality due to invasive fungal diseases (IFDs) have been unacceptably high, especially in patients with a significantly more severe clinical status[1)]. Candida species are the most common cause of invasive fungal infections (IFIs), and are associated with a high incidence of severe sepsis and septic shock[2)]. When associated with biofilm on medical devices, *Candida* is highly resistant to antimicrobial agents, and can lead to serious life-threatening complications and mortality[3)4)].

Early initiation of therapy is an essential prerequisite in obtaining successful treatment and outcomes in IFIs, especially in immunosuppressed individuals. However, early diagnosis of IFIs is usually difficult due to large variation in how they may present, which will depend on any underlying concomitant disease that may be present or low sensitivity of the blood culture used[5-8)].

Clinicians usually consider empirical treatment before

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diagnosing an IFI in patients considered at risk of developing such a condition. The final judgement in such cases will be arrived at after consideration of both clinical factors and evidence from a range of tests. This will include microbiological or serum tests for fungal antigens, such as (1→3)-β-D glucan (BG) and galactomannan ; PCR-based assays ; and risk factors particular to the patient concerned (prior surgery, or a prolonged stay in an intensive care unit, for example).

Detection of serum BG, which is widely present in the fungal cell wall and acts as a specific biomarker for fungal infection, is considered to be simple and useful. This assay is currently indispensable in arriving at a presumptive diagnosis of an IFI[9)10)].

In the United States, the U.S. Food and Drug Administration approved an alkali treatment, a chromogenic automated kinetic assay (Fungitell® ; Associates of Cape Code, Inc., East Falmouth, MA, USA) in 2004 as a BG assay[11)]. The European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Disease Mycoses Study Group included BG assays as microbiological criteria in their revised definitions of IFD in 2008, and indicated its adaptation to candidiasis[12)].

A presumptive diagnosis based on a positive result in a BG assay tends to be a trigger for initial treatment, especially in cases of catheter-related bloodstream infection (CRBSI) due to Candida species. However, false-positive and false-negative cases still remain a concern due to limitations in the accuracy of BG tests[9)13)]. False-negative results may lead to inadequate empiric treatment, which is associated with a delay in starting antifungal therapy or decision making for catheter management (exchange or removal). Although factors and unnecessary treatment in cases with false-positive results in a BG assay have been investigated[9)13)], few studies have investigated these in cases where the result was a false-negative. Therefore, this study investigated how false-negative BG results affected the prognosis and mortality in patients with an IFI diagnosed as a CRBSI.

Materials and Methods

A total of 107 adult patients aged 20 years or older with candidemia were retrospectively investigated. All had been admitted to the Tokyo Medical University Hospital in Japan (a tertiary hospital) between October 1st, 2009 and September 30th, 2016. The inclusion criteria were as follows : a diagnosis of proven or probable CRBSI due to Candida species ; and submission to a BG test conducted between 10 days before the first blood culture collection and a positive result from that blood culture.

Proven CRBSI was defined in accordance with the guidelines of the Infectious Diseases Society of America : when the same organism was recognized on the catheter surface and in blood cultures, or both blood samples from a catheter hub and a peripheral vein met CRBSI criteria for quantitative blood cultures or the differential time to positivity[14)]. The differential time to positivity was considered positive and thus suggestive of CRBSI if blood culture from the central venous catheter (CVC) was positive > 120 min before a peripheral blood culture. Probable CRBSI was defined as when blood culture was positive and the source was presumed to be the CVC, even in the absence of catheter-tip cultures.

Candidiasis was defined as a positive culture from at least one of a pair of blood samples. If a patient had multiple episodes of Candida fungemia during the study period, only the first episode was included. CHROmagar Candida medium (Kanto Chemical Co., Ltd., Tokyo, Japan) was used to identify Candida species. The BG serum level was determined with the β-glucan test Wako (Wako Pure Chemical Industries, Ltd., Tokyo, Japan). A BG value of ≥ 6.0 pg/mg was defined as positive within the manufacturer's standard assay range.

The baseline patient characteristics were collected. These comprised clinical features such as age, Candida species, and organ failure ; 30-day mortality as the main outcome ; the indwelling time for CVC management (removal or retention) ; and time to initiation of antifungal therapy from the day of blood culture collection in BG-positive and BG-negative patients.

Risk assessment was also performed[15)16)]. Each known risk factor for an IFI was awarded a score of 1 point. These factors comprised the following : antimicrobial agents, adrenal corticosteroids, older than 70 years, cancer chemotherapy, malignancy, previous use of antimicrobial agents, gastric acid suppression, total parenteral nutrition, neutropenia (< 500/mm^3), prior surgery (especially gastrointestinal), mechanical ventilation, malnutrition, renal failure or hemodialysis, and prolonged stay in an intensive care unit.

The Sequential Organ Failure Assessment (SOFA) scores were also determined at the time of blood sample collection to assess organ dysfunction. Scores were calculated based on the definitions for sepsis (Sepsis-3) as revised in the International Sepsis Definitions Conference convened by the Society of Critical Care Medicine and the European Society for Intensive Care Medicine in 2016[17)].

Statistical testing was carried out to compare the two groups using SPSS (version 24.0 ; IBM Corp., Armonk, NY, USA). For the variables of age and number of days, the median values and standard errors (SEs) were obtained, and the t-test was conducted for analysis. The chi-square ($\chi 2$) test was carried out for rates. A p-value of < 0.05 was considered statistically significant.

All procedures used in this study were approved by the Ethics Committee of Tokyo Medical University (approval number : 2017-230).

Results

Among the total number of 107 patients investigated, 40 (37.3%) had undergone a BG test. Five of these 40 patients were excluded from the analysis as no CVC had been installed. Finally, a total of 35 patients met the inclusion criteria. These comprised 32 with proven (91.4%) and 3 with probable (8.6%) CRBSI due to infection by Candida species. The results of the BG test in these 35 patients were negative in 11 (31.4%), including 2 with probable CRBSI, and positive in 24 (68.6%),

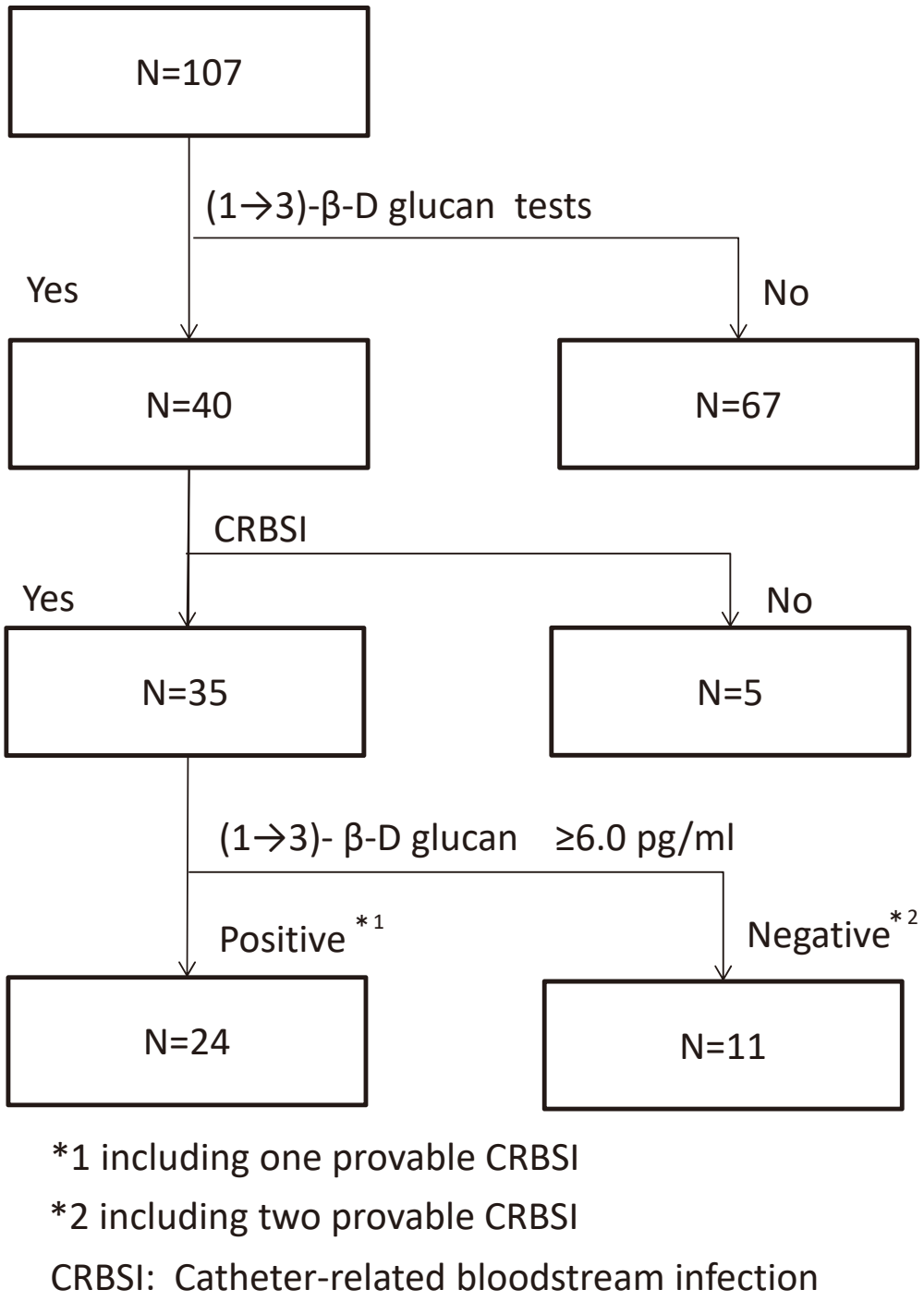

Fig. 1 BG test was performed in 40 of 107 candidemia patients. Five of those 40 patients without CRBSI were excluded from study. Finally, 35 patients with proven or probable CRBSI due to Candida species infection met inclusion criteria. Among these 35, BG test results were negative in 11, including 2 with probable CRBSI, and postive in 24, including 1 with probable CRBSI.

Table 1 Characteristics of

No.	Candida species	Other species in blood culture isolates	Underlying disease	30-day death	Time to blood culturecollection from BG test (days)	Second BG test between blood culture collection and blood culture positivity (BG result)
1	*C. glabrata*	*Coagulase-negative Staphylococcus*	Aortic dissection	No	1	no
2	*C. glabrata*	-	Congestive heart failure	No	4	no
3	*C. albicans*	*Staphylococcus aureus (MSSA)*	Myocardial infarction	Yes	1	yes (negative)
4	*C. albicans*	-	Pneumonia	Yes	0	no
5	*C. albicans*	-	Intestinal obstruction	Yes	0	no
6	*C. albicans*	-	Stomach cancer	Yes	3	no
7	*C. albicans*	-	Cholangiocarcinoma	No	2	yes (negative)
8	*C. tropicalis*	*Enterococcus faecalis*	Hematologic malignancy	Yes	2	no
9	*C. parapsilosis*	-	Hematologic malignancy	No	2	no
10	*C. parapsilosis*	-	Intestinal obstruction	Yes	3	no
11	*Candida.sp*	-	Pneumonia	Yes	0	no

Table 1 shows characteristics of BG-negative patients.
Two of 11 BG-negative patients underwent second BG test between time of blood culture collection and appearance of negative result
glabrata (2 cases, 18%), *C. parapsilosisis* (2 cases, 18%), *C. tropicalis* (1 case, 9%), and an unidentified Candida species (1 case, 9%).
Two patients with CVC were included in analysis of 30-day mortality.
One patient had not received antifungal therapy.
Average time to positive blood culture was 3.45 ± 0.41 days.
Three of 11 patients (27.2%) underwent BG test on day of blood culture collection.

including 1 with probable CRBSI (Figure 1). Two of the 11 BG-negative and 1 of the 24 BG-positive patients underwent a second BG test between the time of initial blood culture collection and the result, but the BG results were consistent (Table 1, negative ; Table 2, positive).

Candida species isolated from the BG-negative patients comprised *C. albicans* (5 cases, 46%), *C. glabrata* (2 cases, 18%), *C. parapsilosis* (2 cases, 18%), *C. tropicalis* (1 case, 9%), and an unidentified Candida species (1 case, 9%) ; while these species were observed in 14 (54%), 2 (8%), 5 (25%), 3 (13%), and 0 (0%) cases, respectively, among the BG-positive patients.

With regard to baseline characteristics, there were no significant differences in age (p = 0.18), proportion of male sex (p = 0.09), values of SOFA (p = 0.89), or risk factor scores (p = 0.94) (Tables 1, 2).

Micafungin (MCFG) was the major antifungal agent used (in 81.8% of patients in the BG-negative group and in 70.8% of patients in the BG-positive group). There was no significant difference in the time to initiation of antifungal therapy between the two groups (p = 0.31). However, a tendency towards a longer time to initiation of antifungal therapy was observed in the BG-negative group compared within the BG-positive group (1.8 ± 0.42 [SD, 1.5] vs 1.1 ± 0.35 [SD, 0.5]) (Table 3). The mean time to positivity of blood culture was longer than 3 days in both groups (3.45 ± 0.41 in the BG-negative group and 3.71 ± 0.29 in the BG-positive group ; p = 0.63) (Tables 1, 2). A total of 3 of 11 patients (27.2%) and 12 of 24 patients (50%) in the BG-negative and positive groups, respectively, underwent the BG test on the day of blood culture collection (Tables 1, 2). The mean time to blood culture collection was 1.64 ± 0.41 [SD, 2.0] and 1.54 ± 0.51 [SD, 0.5] in BG-negative and -positive groups, respectively (p = 0.91) (Table 3).

No significant difference was observed in the indwelling time for the CVC between the BG-negative and BG-positive groups (18.64 ± 2.90 vs 22.67 ± 3.03 ; p = 0.42). The proportion of patients who had had a CVC removed prior to a positive result on blood culture was higher in the BG-positive group (75.0%) than in the BG-negative group (45.5%, p = 0.08). Patients whose CVC was retained (2 in each group) were included in the analysis of 30-day mortality. Of these 4 patients, one in the BG-negative and 2 in the BG-positive group did not receive antifungal therapy.

Although the difference in the 30-day mortality rate between the two groups was not significant (p = 0.08), that in the BG-negative group was clinically higher than that in the BG-positive group (7/11 patients [63.6%] vs 7/24 patients [29.2%]) (Table 3).

Discussion

The present results revealed a greater likelihood of

BG-negative patients

Time to positivity of blood cultures (days)	Time to CVC removal after blood culturecollection (days)	Time to initiation of antifungal therapy after blood culturecollection (days)	Antifungal agent	Indwelling time for central venous catheter (days)	SOFA score	Risk factor score
3	4	2	MCFG	11	0	5
5	0	2	MCFG	20	4	9
4	4	1	MCFG	21	6	7
3	CVC retained	0	MCFG	44	10	7
2	1	1	MCFG	22	0	5
4	CVC retained	-	MCFG	10	5	7
4	1	1	MCFG	20	5	8
3	8	4	MCFG	12	6	9
1	1	1	L-AMB	14	4	8
6	3	4	L-AMB	20	11	7
3	0	2	MCFG	11	5	5

BG results remained, negative, however. Candida species isolated from BG-negative patients comprised *C. albicans* (5 cases, 46%), *C.*

early removal of a CVC prior to a positive result on blood culture and a lower 30-day mortality rate in the BG-positive group ; this despite no significant difference in baseline characteristics, risk factors, or SOFA scores between this and the BG-negative group. This suggests an association between higher mortality and inadequate or delayed treatment due to a BG-negative result, rather than to any other factor.

The European and USA guidelines recommend early CVC removal if Candida species bacteremia is recognized in non-neutrophilic patients[18]. One randomized, controlled trial reported that CVC retention had a negative effect on outcome or mortality in patients with candidemia (mortality of 28% for CVC removal vs 41% for CVC retention)[19]. Raad I et al. showed that early catheter removal ≤ 72 hr after onset was particularly beneficial in patients with CVC-related candidemia undergoing antifungal therapy[20].

Previous reports have assessed the effect of delayed antifungal treatment on outcome or mortality in patients with candidemia. Morrell M et al. demonstrated that delayed antifungal treatment of ≥ 12 hr from the time when the first blood sample was drawn increased mortality 2.09-fold compared with that of < 12 hr[6]. Taur Y et al. showed that a 24-hr delay in blood culture positivity associated with first antifungal administration nearly doubled (1.823-fold increase) the risk of death[21].

Although BG assays are helpful in reaching an early diagnosis of an IFD, the diagnostic accuracy of such assays differs. This is due to differences in the performance of each type of assay with regard to the values measured, such as sensitivity, specificity, and positive and negative predictive values. Reports on screening performance are limited. Currently, in Japan, MK II (Nissui Pharmaceutical, Tokyo, Japan), Wako, and Fungitell® (Associates of Cape Code, Inc., East Falmouth, MA, USA) are commercially available as BG assays. The MK II, a successor to the MK assay (Nissui Pharmaceutical), was introduced in 2012, and uses the same reagents as Wako (derived from blood cells of *Limulus polyphemus*), but the measurement methods are different. Additionally, MK II is supposed to have equivalent efficacy to MK[22]. Fungitell® uses similar pretreatment and measurement methods to those of MK II, but the cutoff values are different[23].

In a previous report by Yoshida K et al., Wako, which was used in the present study, was described as having lower sensitivity and higher specificity than other assays[24]. They reported a sensitivity and specificity of 41.7% and 98.9% in Wako ; 75.0% and 91.6% in MK (Seikagaku Corporation, Tokyo) ; and 83.3% and 92.6% in Fungitell® ; respectively. The positive predictive value of Wako was the highest at 83.3%, compared with 52.9% for MK and 58.8% for Fungitell®[24].

Table 2 Characteristics of

No.	Candida species	Other species in blood culture isolates	Underlying disease	30-day death	Time to blood culturecollection from BG test (days)	Second BG test between blood culture collection and blood culture positivity (BG result)
1	*C. glabrata*	-	Pneumonia	No	0	no
2	*C. glabrata*	-	Malignant lymphoma	No	0	no
3	*C. albicans*	*Corynebacterium spp*	Gastrointestinal perforation	No	0	no
4	*C. albicans*	Staphylococcus aureus (MSSA)	Atypical Mycobacterial Infection	No	7	no
5	*C. albicans*	-	Brain tumor	Yes	0	no
6	*C. albicans*	-	Chronic obstructive pulmonary disease	No	3	no
7	*C. albicans*	-	Hematologic malignancy	Yes	0	no
8	*C. albicans*	-	Pancreatic cancer	No	0	no
9	*C. albicans*	-	Lung cancer	Yes	0	no
10	*C. albicans*	Corynebacterium spp	Colorectal cancer	Yes	0	no
11	*C. albicans*	-	Pneumonia	No	4	no
12	*C. albicans*	-	Ulcerative colitis	No	1	no
13	*C. albicans*	Acinetobacter baumanni	Burn	No	1	no
14	*C. albicans*	-	Colorectal cancer	Yes	3	no
15	*C. albicans*	-	Laryngeal cancer	No	2	no
16	*C. albicans*	-	Ovarian cancer	No	0	no
17	*C. tropicalis*	-	Tuberculosis	No	2	no
18	*C.t ropicalis*	Klebsiella oxytoca	Pneumonia	No	10	no
19	*C. tropicalis*	-	Esophagus cancer	Yes	0	no
20	*C. parapsilosis*	-	Pneumonia	No	0	yes (positive)
21	*C. parapsilosis*	-	Pneumonia	Yes	2	no
22	*C. parapsilosis*	-	Blood malignant tumor	No	1	no
23	*C. parapsilosis*	-	Aortic dissection	No	0	no
24	*C. parapsilosis*	-	Cholangiocarcinoma	No	1	no

Table 2 shows characteristics of BG-positive patients.
One of 24 BG-positive patients underwent second BG test between time of blood culture collection and appearance of positive result. BG results still remained positive, however. Candida species isolated from BG-positive patients comprised *C. albicans* (14 cases, 54%),
Two patients with CVC were included in analysis of 30-day mortality.
Two patients did not receive antifungal therapy.
Average time to positive blood culture was 3.71 ± 0.29 days.
Twelve of 24 patients (50%) underwent BG test on day of blood culture collection.

Although a cutoff value of 11 pg/mg is generally used for Wako[23], a minimum cutoff value of 6 pg/mg within the standard range is used at our hospital. This range still cannot exclude false-negatives in critically ill patients, however. Other assays with a higher sensitivity may avoid false-negatives, but may increase the possibility of false-positives. An understanding of the advantages and limitations in the performance of each of the various assays would aid in assessing the accuracy of these tests.

In the BG-positive group, the mean time from the BG test to blood culture collection was shorter, and a higher percentage of these patients underwent the BG test on the same day as blood culture collection. This suggests that the result of a BG test might change from negative to positive if the test were conducted on the same day as blood culture collection, which is usually undertaken by the attending physician, and that that might lead to a delay in treatment.

There are some limitations in this study. First, only a limited number of cases were investigated at a single hospital. Second, the selection of antifungal agents might have been inappropriate, as the susceptibility of Candida species to each agent was not examined.

The antifungal agents used in the present study comprised (echinocandin class), fosfluconazole (FLCZ, azole class), and liposomal amphotericin B (L-AMB, polyene class). *Candidda glabrata* is considered to have low

BG-positive patients

Time to positivity of blood cultures (days)	Time to CVC removal after blood culturecollection (days)	Time to initiation of antifungal therapy after blood culturecollection (days)	Antifungal agent	Indwelling time for central venous catheter (days)	SOFA score	Risk factor score
8	0	0	L-AMB	23	1	5
3	1	1	MCFG	60	3	6
3	1	0	MCFG	10	4	8
2	1	2	MCFG	34	3	5
4	4	0	MCFG	7	3	8
3	0	3	MCFG	15	3	8
4	CVC retained	-	-	24	10	9
5	8	0	MCFG	19	5	8
4	0	1	MCFG	12	7	8
3	6	6	MCFG	44	2	7
4	0	3	MCFG	24	1	6
2	1	0	MCFG	10	3	4
2	3	2	MCFG	17	3	8
4	3	3	MCFG	14	13	7
3	0	0	FLCZ	60	3	7
5	0	0	MCFG	16	1	5
2	1	1	MCFG	28	12	9
3	0	0	MCFG	21	5	7
4	CVC retained	-	-	4	16	7
2	0	0	MCFG	30	5	5
5	3	2	L-AMB	28	5	4
4	7	-1	L-AMB	14	12	9
4	0	3	L-AMB	7	12	7
6	0	0	MCFG	23	12	10

C. glabrata (2 cases, 18%), *C. parapsilosisis* (5 cases, 25%), and *C. tropicalis* (0 cases, 0%).

susceptibility to FLCZ[25-27] and increasing resistance to echinocandin[28-30]. *Candida parapsilosis* has resistance to echinocandin[31-33]. However, no patients with *C. glabrata* or *C. parapsilosis* who received FLCZ or MCFG were included in the analysis 30-day mortality (Table 1). Unidentified Candida species were found in 2 of the patients, and this may have affected outcomes due to differences in susceptibility in these two patients.

Conclusions

Thirty-day mortality in BG false-negative patients with CRBSI due to Candida species was higher than in BG-positive patients, and was associated with delayed treatment. This indicates that treatment solely based on BG-negative results can be a risk. These findings indicate that, even if the result of the BG test is negative, treatment should be initiated immediately after consideration of the characteristics of each patient, especially in those with a suspected IFI.

List of abbreviations

IFI : invasive fungal infection ; **BG** : (1→3)-β-D glucan ; **IFD** : invasive fungal disease ; **CRBSI** : catheter-related bloodstream infection ; **CVC** : central venous catheter ; **SOFA :** Sequential Organ Failure Assessment ; **MCFG :** micafungin ; **FLCZ** : fosfluconazole ; **L-AMB** : liposomal amphotericin B

Table 3. Comparison of results between BG-nagative and BG-positive groups

	BG-negative group (n = 11)	BG-positive group (n = 24)	p-value*3
Sex : male	5 (45.5%)	18 (75.0%)	0.09
Age (years)[median]	75.0 ± 3.19 [76]	67.75 ± 3.26 [69]	0.18
C. albicans	5 (45.5%)	14 (58.3%)	0.48
Multiplebacteremia	3 (27.3%)	6 (25.0%)	0.88
30-day death	7 (63.6%)	7 (29.2%)	0.08
SOFA score [median]	5.09 ± 1.02 [5.0]	6.00 ± 0.93 [4.5]	0.59
Risk factor score [median]	7.00 ± 0.45 [7.0]	6.96 ± 0.34 [7.0]	0.94
Time to blood culture collection from BG test (days) [median]	1.64 ± 0.41[2.0]	1.54 ± 0.51 [0.5]	0.91
BG test on the of blood culture collection	3 (27.3	12 (50%)	0.28
Time to positivity of blood cultures (days) [median]	3.45 ± 0.41 [3.0]	3.71 ± 0.29 [4.0]	0.63
Time from blood sampling to device removal (days) [median]	2.44 ± 0.87 (n = 9)*1 [1.0]	1.77 ± 0.53 (n = 22)*1 [1.0]	0.50
Device removal prior to blood culture positivity	5 (45.5%)	18 (75.0%)	0.08
Time from blood sampling to initiation of antifungal therapy (days) [median]	1.8 ± 0.42 (n = 10)*2 [1.5]	1.1 ± 0.35 (n = 22)*2 [0.5]	0.31
Initiation of antifungal therapy prior to blood culture positivity	8 (72.7%)	18 (75.0%)	0.89
Indwelling time for central venous catheter (days) [median]	18.64 ± 2.90 [20]	22.67 ± 3.03 [20]	0.42

*1 Two cases with preserved devices were excluded
*2 Patients without antifungal therapy were excluded
*3 Chi-squared ($\chi 2$) test and t-test was carried out for rates.

Table 3 shows comparison of results between BG-negative and BG-positive groups.
There were no significant differences in baseline values for age (p = 0.18), male sex percentage (p = 0.09), SOFA value (p = 0.89), or risk factor score (p = 0.94).
Average time to blood culture collection was 1.64 ± 0.41 [SD, 2.0] and 1.54 ± 0.51 [SD, 0.5] in the BG-negative and -positive groups, respectively (p = 0.91).
MCFG was main antifungal agent used (in 81.8% of patients in BG-negative group and 70.8% of patients in BG-positive group). There was no significant difference in time to initiation of antifungal therapy between the two groups (p = 0.31).
Longer time to start of antifungal therapy was observed in BG-negative group compared with in BG positive group (1.8 ± 0.42 [SD, 1.5] vs. 1.1 ± 0.35 [SD, 0.5]).
Difference in CVC placement time was not significantly different between BG-negative and BG-positive groups (18.64 ± 2.90 vs 22.67 ± 3.03 ; p = 0.42). Proportion of patients from whom CVC was removed before positive blood culture was higher in BG-positive group (75.0%) than in BG-negative group (45.5%) (p = 0.08).
Higher mortality was observed in the BG-negative group, but this difference was not significant (p = 0.08).

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Conflict of interest

The authors declare that they have no competing interests.

Ethical approval

All procedures used in this study were approved by the Ethics Committee of Tokyo Medical University (TMU ; approval number : 2017-230). The need for consent was formally waived by the Ethics Committee of TMU.

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(1→3)-β-D グルカン偽陰性が、カンジダによるカテーテル関連血流感染症の重症患者の転帰に及ぼす影響

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【要旨】　この研究は、(1→3)-β-D グルカン（BG）偽陰性の結果が、侵襲性真菌感染（IFI）に関連するカテーテル関連血流感染（CRBSI）の予後と 30 日間の死亡率にどのように影響するかを検討した。

カンジダ血症の成人患者 107 人を遡及的に研究した。これらの患者のうち、35 人はカンジダにより確定診断または可能性の高い CRBSI と診断され、血液培養陽性が研究基準を満たす前に BG 検査を実施した。患者の臨床的特徴、危険因子、中心静脈カテーテル（CVC）の留置時間、および 30 日死亡率に関連する抗真菌療法の開始を主な結果として調査した。

グループ間でベースライン特性または危険因子スコアに有意差は認められなかった。ただし、BG 陰性患者（63.6％；7/11 患者）と BG 陽性患者（29.2％；7/24 患者）の 30 日間死亡率は有意に近かった (p 値 = 0.08)。

BG 陰性の結果に関係なく、特に IFI の可能性がある患者の場合、患者の特徴を考慮した治療の即時決定を下すべきである。

〈キーワード〉　(1→3)-β-D グルカン、カンジダ、侵襲性真菌感染、偽陰性、カテーテル関連血流感染症