Catheter-related Candida bloodstream infection in intensive care unit patients: a subgroup analysis of the China-SCAN study

Bo Hu1, Zhaohui Du1, Yan Kang2, Bin Zang3, Wei Cui4, Bingyu Qin5, Qiang Fang6, Haibo Qiu7 and Jianguo Li1*

Abstract

Background: In patients hospitalized in intensive care units (ICU), Candida infections are associated with increased morbidity, mortality and costs. However, previous studies reported confused risk factors for catheter-related Candida bloodstream infection (CRCBSI). The objective was to describe the risk factors, microbiology, management and outcomes of CRCBSI in the China-SCAN population.

Methods: Patients with ≥1 Candida-positive peripheral blood culture were selected from the China-SCAN study. Peripheral and catheter blood samples were collected for Candida isolation. Patients with the same strain of Candida in peripheral and catheter blood samples were considered as being with CRCBSI, while patients with Candida-positive peripheral blood cultures only or different strains were considered as non-CRCBSI. Data were collected from the China-SCAN study.

Results: CRCBSI incidence in ICU was 0.03% (29/96,060), accounting for 9.86% of all candidemia observed in ICU (29/294). The proportion of CRCBSI due to Candida parapsilosis reached 33.3%, more than that of Candida albicans (28.6%). In univariate analyses, older age (P = 0.028) and lower body weight (P = 0.037) were associated with CRCBSI. Multivariate analysis showed that the sequential organ failure assessment (SOFA) score was independently associated with CRCBSI (odds ratio (OR) = 1.142, 95% confidence interval = 1.049-1.244, \( P = 0.002 \)). Catheter removal and immune enhancement therapy were often used for CRCBSI treatment.

Conclusions: In China, CRCBSI was more likely to occur in old patients with low body weight. SOFA score was independently associated with CRCBSI. Candida parapsilosis accounted for a high proportion of CRCBSI, but the difference from non-CRCBSI was not significant.

Keywords: Catheter related infection, Candidemia, Candida parapsilosis, Candida albicans

Background

Candida sp. represent the third most common family of pathogens causing bloodstream infections in intensive care units (ICU) patients in the United States [1-3]. The global incidence of candidemia is reported to be 6.7-54 per 1000 ICU patients [4-6]. Untreated candidemia typically results in eye lesions, skin lesions and abscesses, and often lead to multiple organ failure. The mortality rate is 30–61.8% in Europe and America [5-8]. In addition, candidemia can extend hospital stay by 10–30 days, and increase inpatient hospital costs by about $40,000 in the United States [8]. Candidemia requires treatment with an antifungal agent, and removal of the catheter alone is not an adequate therapy for candidemia [9]. The large prospective China Survey of Candidiasis (China-SCAN) study showed that most candidemia in China were caused by non-albicans species (58.2%), and that first-line antifungal therapy decreased mortality [10].

Catheters are commonly used in ICU patients, and represent an easy entry route for pathogens, including Candida sp. In general, patients with candidemia are inserted with catheters, most commonly central venous catheter (CVC), with a placement rate of 80-89% in Europe and America [11,12]. CVC placement can significantly increase
the risk of candidemia in hospitalized patients [13],
and is an independent risk factor for candidemia in
the United States [14]. Candidemia caused by catheter
placement is named Candida catheter-related bloodstream
infection (CRCBSI). In addition to CVC, studies in Europe
and America identified a number of risk factors that are
associated with CRCBSI such as surgical trauma, cancer,
parenteral nutrition, diabetes mellitus, urinary catheter,
age, vancomycin use, and impaired acute physiology and
chronic health evaluation (APACHE) score [8,15-19].

The epidemiology of candidemia varies with geography,
but is mostly dominated by Candida albicans; however,
the proportion of non-albicans candidemia is increasing
each year [20], sometimes reaching higher rates than that
of albicans candidemia in European countries [21]. In
many countries, Candida parapsilosis contributes to
15-20% of candidemia, and is often associated with
CRCBSI [22,23]. Therefore, a better understanding of the
CRCBSI epidemiology could lead to better first-line
treatments, and to decreased morbidity and mortality.

The China-SCAN study assessed the epidemiology,
microbiology, management and outcomes of invasive
candidiasis in 67 ICUs across China, and the results
were published [10]. The aim of the present study was
to assess the risk factors, microbiology, management and
outcomes of CRCBSI in the China-SCAN sample. Results
might lead to a better identification of patients at high risk
of CRCBSI, and to adopt appropriate clinical strategies.

Methods

Study design and patients

The methods of the China-SCAN study including inclusion
and exclusion criteria were previously published [10]. The
present study focused on patients with at least one
Candida-positive peripheral blood culture rather than
those with positive Candida in histopathological specimen
or sterile body cavities fluid specimen culture. Hence,
from 306 patients recruited in the CHINA-SCAN study,
294 patients with Candida-positive peripheral blood
cultures (290 cases with Candida-positive peripheral blood
culture only, and 4 cases with Candida-positive peripheral
blood and sterile body cavities fluid specimens) were
selected for the present study. Peripheral blood and
catheter blood were sampled simultaneously to isolate the
Candida strains; the same isolated Candida strain denoted
CRCBSI [21,24]. Patients with Candida-positive peripheral
blood culture only or with different Candida isolates were
considered as non-CRCBSI (NCRCBSI) (Figure 1).

The study was approved by the Ethics Committee
of Zhongda Hospital of Southeast University, the lead
investigation site. Other participating hospitals accepted
the central ethics committee review or conducted a
further, independent, ethics review, according to their own
institutional policy (20 hospitals). The study complied
with the Declaration of Helsinki regarding ethical principles
of human subjects research and the relevant ethical require-
ments of the International Conference on Harmonisation/
Good Clinical Practice guidance and national regulations.
All patients provided written informed consent. The
China-SCAN study is registered with ClinicalTrials.
.gov (NCTT01253954).

Sample management and strain identification

All participating centers used the same transportation
method. Personnel from each center were trained
together to standardize our procedures. Peripheral and
catheter blood samples were sampled using strict aseptic
methods, and then each sample collected in aerobic and
anaerobic blood culture vials (10 ml each). Interval
between peripheral and catheter blood sampling was no
more than 5 minutes. Blood samples were immediately
sent to the sub-center's laboratory for preliminary
screening. After preliminary screening, strains were
grown in SDA or PDA plastic tubes at 28-30°C and
cultured for 2–3 days. After growth, strains were stored at
room temperature. Within 1–2 months, strains were
transported to the central laboratory. Clinical research
assistants at each sub-center were responsible for the
regular collection of strains. Strains were shipped to the
central laboratory (Research Center for Medical Mycology,
Peking University First Hospital, Beijing, China) overnight,
at room temperature, by professional courier companies
in leak-proof, sealed, unbreakable containers. At the
central laboratory, the exact strain and its drug sens-
sibility were determined, as previously described for
the China-SCAN study [10,25].

Strains were identified as previously described for the
China-SCAN study [10,25]. Briefly, species were identified
using chromogenic culture media (CHROMagar, Paris,
France) and the API 20C AUX yeast identification kit
(bioMérieux SA, Marcy l'Étoile, France). When necessary,
large-subunit (26S) ribosomal rRNA gene D1/D2 domain
sequencing was performed. Candida haemulonii, Candida
pelliculosa, Candida ernobii, Candida norvegensis, Candida
metapsilosis and Lodderomyces elongisporus were identified
by sequencing.

![Figure 1 Flow chart of patients.](http://www.biomedcentral.com/1471-2334/14/594)
Data collection and management

All data were from the databases of the China-SCAN study. The content and management of the database had been reported in details [10]. Data were collected from case report forms, and analyzed for comparison between CRCBSI and NCRCBSI.

The APACHE II was evaluated within 24 h of ICU admission. An integrated score from 0 to 71 was calculated. Higher scores indicate more severe disease and higher risk of death [26].

The SOFA score is an ICU scoring system based on organ function or failure rate. The score is based on scores for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems [27]. This score was calculated within 24 h of ICU admission.

Chronic hepatic insufficiency was defined as in APACHE II: 1) biopsy-proven cirrhosis and documented portal hypertension; 2) history of upper gastrointestinal bleeding attributed to portal hypertension; or 3) history of hepatic failure/encephalopathy/coma.

Statistical analysis

Statistical analysis was conducted using SAS 9.1 (SAS Institute, Cary, NC, USA). Continuous variables are presented as means ± standard deviation (SD) (normally distributed), or median (Q1, Q3) (non-normally distributed). Categorical variables are presented as frequencies and percentiles. Independent samples t-tests and Wilcoxon rank sum tests were used for continuous variables, as appropriate. Chi-square tests and Fisher's tests were used for categorical data, as appropriate. Variables with P-values <0.20 in univariate analyses were entered into a multivariate logistic regression analysis to identify factors that were independently associated with CRCBSI. P-values <0.05 were considered to be statistically significant.

Results and discussion

Incidence and patient characteristics

Among the 294 identified patients, there were 265 cases of NCRCBSI and 29 cases of CRCBSI. Patients with CRCBSI represented 9.86% of all candidemia patients. Based on the 96,060 ICU patients in the CHINA-SCAN study [10], CRCBSI incidence was 0.03% of ICU patients (29/96,060) (Figure 1).

The baseline characteristics of patients are compared in Table 1. Results from univariate analyses suggest that CRCBSI was associated with age (69.4 ± 19.1 vs. 60.7 ± 20.2 years, P = 0.028) and with body weight (58.0 ± 5.2 vs. 63.2 ± 11.0 kg, P = 0.037). SOFA score at candidemia diagnosis (P = 0.15), solid tumors (P = 0.18) and chronic hepatic insufficiency (P = 0.06) were also included in the multivariate analysis.

Catheter indwelling between the CRCBSI and NCRCBSI groups

Among CRCBSI patients, 26 were inserted with CVC, and the remaining three had peripheral arterial catheters. Among the NCRCBSI patients, 217 were inserted with CVC. There was no difference in the rate of CVC indwelling between CRCBSI and NCRCBSI patients (P = 0.438). CVC puncture was placed in the jugular, subclavian, or femoral vein, without difference between the groups (all P > 0.05). Indwelling time of the last catheter before candidemia diagnosis was not different between the groups (all P > 0.05) (Table 2).

Catheter removal between the CRCBSI and NCRCBSI groups

There was no difference between the two groups in the number of CVC removal from each position within two weeks before candidemia diagnosis (all P > 0.05). Significantly more catheters were removed in the CRCBSI group after diagnosis (82.8 vs. 60.0%, P = 0.016) (Table 2).

Microbiology

Because of the individual hospital policy and suboptimal storage or handling of isolates, not all isolates from other hospitals were sent to the central laboratory for review and identification, and a total of 237 isolates (21 from CRCBSI patients, and 216 from NCRCBSI patients) were identified in the central laboratory (Table 3). The proportion of Candida parapsilosis (33.3%) was higher than that of Candida albicans (28.6%) in the CRCBSI group, while the proportion of Candida albicans (40.3%) was the highest in the NCRCBSI group. However, there was no difference in the distribution of Candida strains between the two groups (P = 0.352). The results derived from the different hospitals were consistent with those obtained in the central laboratory. Additional file 1: Table S1 presents the strains distribution across study centers in China.

Multivariate analysis

Multivariate analysis showed that the SOFA score at candidemia diagnosis was independently associated with CRCBSI (odds ratio = 1.142, 95% confidence interval = 1.049-1.244, P = 0.002). Solid tumors (P = 0.08), chronic hepatic insufficiency (P = 0.82), age (P = 0.16) and body weight (P = 0.58) were not associated with CRCBSI (Table 4).

Antifungal treatment

Twenty-eight CRCBSI patients (28/29, 96.6%) received antifungal treatment, without difference from the NCRCBSI group (229/265, 86.4%; P > 0.05) (Table 1). The more frequently used drugs were fluconazole, followed by caspofungin and voriconazole. The course of antifungal therapy was similar between the two groups. More CRCBSI patients...
Table 1 Baseline characteristics of 294 patients with Candida bloodstream infection in the CHINA-SCAN study, according to CRCBSI and NCRCBSI

| Variables                                      | CRCBSI     | NCRCBSI    | P-value  |
|------------------------------------------------|------------|------------|----------|
| N = 29                                         | N = 265    |            |          |
| Age (years), mean ± SD                         | 69.4 ± 19.1| 60.7 ± 20.2| 0.028*   |
| Gender, n (%)                                  |            |            | 0.527    |
| Male                                           | 22 (75.9)  | 181 (68.3) |          |
| Female                                         | 7 (24.1)   | 84 (31.7)  |          |
| Body weight (kg), mean ± SD                    | 58.0 ± 5.2 | 63.2 ± 11.0| 0.037*   |
| Symptoms, n (%)                                |            |            |          |
| Fever                                          | 27 (93.1)  | 243 (91.7) | 1.000    |
| Shivers                                        | 8 (27.6)   | 83 (31.3)  | 0.833    |
| Confusion                                      | 13 (44.8)  | 123 (46.4) | 1.000    |
| Concomitant disease, n (%)                     |            |            |          |
| Type 1 or 2 diabetes                           | 7 (24.1)   | 59 (22.3)  | 0.833    |
| Chronic cardiac dysfunction                    | 6 (20.7)   | 57 (21.5)  | 0.891    |
| Solid tumor                                    | 8 (27.6)   | 45 (16.9)  | 0.180    |
| Chronic obstructive pulmonary disease          | 4 (13.8)   | 31 (11.7)  | 0.762    |
| Chronic renal insufficiency                    | 5 (17.2)   | 27 (10.2)  | 0.259    |
| Chronic hepatic insufficiency                  | 4 (13.8)   | 12 (4.5)   | 0.060    |
| Hematological malignancy                      | 0 (0.0)    | 3 (1.2)    | 1.000    |
| Invasive procedures within 2 weeks prior to diagnosis, n (%) |            |            |          |
| Hemodialysis                                   | 2 (6.9)    | 15 (5.7)   | 0.259    |
| Invasive mechanical ventilation                | 24 (82.7)  | 204 (77.0) | 0.666    |
| Total parenteral nutrition                     | 14 (48.3)  | 115 (43.4) | 0.695    |
| Surgery                                        | 11 (37.9)  | 102 (38.5) | 1.000    |
| Immunosuppression                              | 2 (6.9)    | 15 (5.7)   | 0.679    |
| Illness severity at ICU admission, mean ± SD   |            |            |          |
| APACHE II score                                | 28.5 ± 7.6 | 27.0 ± 7.1 | 0.286    |
| SOFA score                                     | 10.6 ± 2.9 | 11.2 ± 3.5 | 0.330    |
| Illness severity at diagnosis, mean ± SD       |            |            |          |
| APACHE II score                                | 28.2 ± 7.2 | 27.0 ± 7.0 | 0.360    |
| SOFA score                                     | 9.8 ± 3.3  | 10.8 ± 3.5 | 0.147    |
| Immune enhancement therapy, n (%)a             | 21 (72.4)  | 102 (38.5) | <0.001** |
| Antibiotic use, n (%)                          |            |            | 0.963    |
| Monotherapy                                    | 8 (32.0)   | 75 (35.9)  |          |
| Two-drug combinations                          | 13 (52.0)  | 98 (46.9)  |          |
| Three-drug combinations                        | 4 (16.0)   | 35 (16.7)  |          |
| Antibiotic use period, mean ± SD               | 11.4 ± 4.2 | 10.6 ± 6.5 | 0.514    |
| Antibiotic therapy >5 days, n (%)              | 25 (86.2)  | 209 (78.9) | 0.469    |
| Antifungal therapy, n (%)                      | 28 (96.6%) | 229 (86.4%)| 0.118    |
| Initial antifungal treatment, n (%)            |            |            | 0.977    |
| Fluconazole                                    | 11 (39.3%) | 84 (36.7%) |          |
| Caspofungin                                    | 7 (25.0%)  | 54 (23.6%) |          |
| Voriconazole                                   | 4 (14.3%)  | 44 (19.2%) |          |
| Micafungin                                     | 3 (10.7%)  | 20 (8.7%)  |          |
received immune enhancement therapy (immunoglobulins and/or thymosin α1) (72.4% vs. 38.5%; \( P < 0.001 \)) (Table 1). However, because it only was an observational indicator, the types and doses of immunoglobulins and thymosin α1 were not recorded.

**Treatment outcomes**

CRCBSI patients showed a non-significant higher mortality (44.8% vs. 36.2%; \( P = 0.419 \)). Trends toward longer ICU stay (median: 34 vs. 25 days; \( P = 0.095 \)) and hospitalization (median: 54 vs. 39 days; \( P = 0.096 \)) were also observed. CRCBSI patients were more likely to experience microbiological recovery compared with NCRCBSI patients (67.9% vs. 50.0%; \( P < 0.001 \)) (Table 5).

**Discussion**

To our knowledge, the China-SCAN study is the largest prospective study of invasive candidiasis in Chinese ICUs, and possibly from anywhere. In addition, it is also one of the first to describe *Candida* catheter-related bloodstream infections in China. The present study aimed to determine the risk factors for catheter-related candidemia in Chinese ICU. Our results showed that CRCBSI incidence in ICU was 0.03%, accounting for 9.86% of all candidemia observed in ICU (29/294), mainly caused by *Candida parapsilosis* in CRCBSI patients (33.3%). Univariate analyses showed that older age and lower body weight were associated with CRCBSI. Multivariate analysis showed that the SOFA score was independently associated with CRCBSI (\( P = 0.002 \)). Catheter removal and immune enhancement therapy were more frequently used in CRCBSI than in NCRCBSI. Results of the present study provide clues for a better identification of CRCBSI patients.

Few studies reported large-scale epidemiological data on CRCBSI. In the present study, we reported a CRCBSI incidence in ICUs of 0.3/1000 patients, which was calculated based on the 96,060 ICU patients reported in the China-SCAN study. In the present study, some patients with NCRCBSI did not have blood sample in venous catheter; therefore, some of these patients might in reality be CRCBSI cases. In addition, some *Candida*-positive patients could have been excluded because of the strict inclusion criteria of the CHINA-SCAN study. Therefore, the real CRCBSI incidence may be higher.

In the present study, the mortality rate from CRCBSI was 44.8%, which was not significantly different from that of NCRCBSI (36.2%). These rates are in agreement with the published global mortality rates of 30–61.8% in hospital-based candidemia studies from western countries [5-8].

The CRCBSI and NCRCBSI groups were compared in order to identify risk factors for CRCBSI. Results showed that the two groups were similar in disease, invasive procedures, disease severity score, and the use of antibiotics within the past two weeks. However, in univariate analyses, there were significant differences in age and body weight. These results suggest that risk factors for CRCBSI, other candidemias and invasive candidiasis were similar in most ICU patients, except for those with an older age and lower body weight.

CVC is the most common type of catheter causing CRCBSI [28]. Studies have shown that CVC placement rate in candidemia patients is 80–96.7% [21]. Consistent with these results, the CVC placement rates in patients with CRCBSI and those with NCRCBSI in the present study were above 80% (89.7% and 81.9%), and there was no significant different between the two groups. The CVC placement position and indwelling period were similar in both groups, indicating that the initial placement position of catheter and catheter indwelling time were not the cause of CRCBSI. The catheter removal rate was not different within 2 weeks before diagnosis between the two groups, but was significantly higher after diagnosis in the CRCBSI group (82.8%) compared with the NCRCBSI group (60.0%), in compliance with previous studies and guidelines [18,29,30]. A recent study suggested that any delay in catheter removal and initiation of antifungal therapy was associated with increased mortality in CRCBSI patients; however, catheter removal had no impact on mortality of

---

**Table 1 Baseline characteristics of 294 patients with Candida bloodstream infection in the CHINA-SCAN study, according to CRCBSI and NCRCBSI (Continued)**

| Treatment duration, mean± SD | CRCBSI (n=213) | NCRCBSI (n=81) | P value |
|-----------------------------|---------------|---------------|---------|
| Antifungal therapy >5 days, n (%) | 19 (9.3%) | 20 (24.7%) | 0.005 |
| Time between ICU admission and diagnosis of Candida infection (days), median (Q1,Q3) | 11.0 (4.0, 26.0) | 10.00 (4.0, 21.0) | 0.544 |

*Use of immunoglobulins and/or thymosin α1.*

*Fluconazole + caspofungin: 2 patients; itraconazole + fluconazole: 1 patient; amphotericin B + caspofungin: 1 patient.*

CRCBSI: catheter-related Candida bloodstream infection; NCRCBSI: non-catheter-related Candida bloodstream infections; ICU: intensive care unit; APACHE: acute physiology and chronic health evaluation II; SOFA: sequential organ failure assessment.
NCRCBSI patients [18]. On the other hand, some studies argued that CVC removal do not affect prognosis of candidemia [31]. The 2012 ESCMID guidelines also pointed out that catheter removal is necessary for candidemia, but that antifungal treatment can be used if catheter removal is impossible [32].

In the present study, multivariate analysis showed that the SOFA score was the only independent variable associated with CRCBSI. We explored a number of factors that have been shown to be associated with candidemia in previous studies, but we did not observe any association between these parameters and CRCBSI. The study by MacDonald et al. [19] showed that hyperalimentation was the only independent risk factor for candidemia in an ICU pediatric population. Another pediatric study showed that CVC, cancer, recent use of vancomycin, and use of agents against anaerobic bacteria were independent factors associated with candidemia [8]. A study showed that independent predictors of biofilm-forming candidemia were the use of CVC, the use of urinary catheters, parenteral alimentation, and diabetes [15]. Finally, a study showed that inadequate antifungal therapy, infection with biofilm-forming Candida species, and APACHE III scores were associated with higher Candida-related mortality [16]. However, these studies did not differentiate between CRCBSI and NCRCBSI. In addition, the only risk factor for candidemia that was common to these studies was the use of CVC.

Because there is variability in the resistance of Candida strains to storage and transport, some samples could not be tested in the central laboratory, and the exact distribution of the different Candida species might have suffered from this bias. However, we observed that CRCBSI was mainly associated with Candida parapsilosis, while NCRCBSI was mainly associated with Candida albicans, although the

| Strain                  | CRCBSI  | NCRCBSI | P-value |
|-------------------------|---------|---------|---------|
| Candida strains isolates, n (%) | 0.352   |         |         |
| Candida albicans        | 6 (28.6)| 87 (40.3)|         |
| Candida parapsilosis    | 7 (33.3)| 48 (22.2)|         |
| Candida tropicalis      | 2 (9.5 )| 37 (17.1)|         |
| Candida glabrata        | 2 (9.5 )| 25 (11.6)|         |
| Others                  | 4 (19.0)| 19 (8.7 )|         |
distribution of strains between the two groups was not different. This observation was consistent with previous studies on candidemia [6,25,33]. *Candida parapsilosis* is more prone to cause CRCBSI, which may be related to its ease of growing in intravenous infusion of high-sugar-based nutrition, to its growing in CVC biofilm that can easily be spread by the hands of medical personnel, and to its long-term survival [33]. Using catheter removal and appropriate antifungal therapy, CRCBSI microbiological clearance rate was significantly higher than that of NCRCBSI (67.9% vs. 50.0%), which was consistent with a previous study [18].

There was no difference in antifungal treatment between CRCBSI and NCRCBSI patients in respect to antifungal treatment. The most commonly used was fluconazole, followed by caspofungin and voriconazole. In the China-SCAN flora and sensitivity analysis, patients with non-*albicans* strains were more susceptible to require a therapy adjustment [10]. Considering the high proportion of *Candida parapsilosis* causing CRCBSI in the present study, we suggest to consider drugs with a higher efficacy against *Candida parapsilosis* in the treatment of CRCBSI.

Although there is no clear indicator of the presence of immunosuppression in the present study, ICU physicians rely on clinical experience to use immunotherapy. More CRCBSI patients received immune enhancement therapy (72.4% vs. 38.5%), suggesting that ICU physicians are concerned about CRCBSI-related immune suppression. From the previously identified risk factors in patients with CRCBSI [8,15-19], patients with old age and low body weight might be more prone to develop immunosuppression. Although no immune enhancement therapy is clearly recognized to improve CRCBSI patients’ prognosis, immunoglobulins and thymosin α1 were selected as immunotherapy since these drugs have a potential to improve prognosis in sepsis patients [34,35].

The China-SCAN study suffered from some limitations that also have an impact in the present study. Indeed, the lack of central validation for some samples could lead to an underestimation of the real CRCBSI incidence, as well as for the *Candida* strains causing CRCBSI. However, results based from the central laboratory clearly demonstrated that the proportion of *Candida parapsilosis* was higher in the CRCBSI group, while that of *Candida albicans* was higher in the NCRCBSI group. Differences in therapeutic strategies across the study centers may have contributed to biases in diagnosis, treatment and prognosis. Concerning the present study, the sample size of the CRCBSI group was small. Therefore, results need to be verified in further large-scale studies on CRCBSI.

**Conclusions**

In China, CRCBSI was more likely to occur in old patients with low body weight. SOFA score was independently associated with CRCBSI. *Candida parapsilosis* accounted for a high proportion of CRCBSI, but the difference from NCRCBSI was not significant.

| Table 4 Multivariate logistic regression analysis for exposure to potential risk factors for CRCBSI in ICU patients |
|---------------------------------------------------------------|
| Variables                        | Estimate | Standard Error | Wald chi-square | Odds ratio estimate | Lower 95% confidence limit | Upper 95% confidence limit | P-value |
| Solid tumors (yes vs. other Concomitant disease)   | 0.344    | 0.1954         | 3.1008          | 1.990              | 0.925                     | 4.279                   | 0.0783  |
| Chronic hepatic insufficiency (yes vs. other concomitant disease) | −0.1596  | 0.7118         | 0.0503          | 0.852              | 0.211                     | 3.44                    | 0.8226  |
| Age                                           | 0.0112   | 0.00808        | 1.9336          | 1.011              | 0.995                     | 1.027                   | 0.1644  |
| SOFA score at diagnosis                      | 0.1329   | 0.0436         | 9.2834          | 1.142              | 1.049                     | 1.244                   | 0.0023** |
| Body weight                                   | −0.00817 | 0.0149         | 0.3021          | 0.992              | 0.963                     | 1.021                   | 0.5825  |

**P<0.01

| Table 5 Treatment outcomes according to CRCBSI/NCRCBSI |
|--------------------------------------------------------|
| Category                                      | CRCBSI n = 29 | NCRCBSI n = 265 | P-value |
| Mortality, n (%)                               | 13 (44.8)     | 96 (36.2)       | 0.419   |
| ICU stay period (days), median (Q1,Q3)         | 34.00 (18.0, 71.0) | 25.00 (13.0, 44.0) | 0.095   |
| Hospital stays (days), median (Q1,Q3)          | 54.00 (26.0, 91.0) | 39.00 (18.0, 69.5) | 0.096   |
| Candida elimination, n (%)                     | 19 (67.9)     | 116 (50.0)      | 0.001** |
| Time from positive to negative blood culture (days), median (Q1,Q3) | 14.00 (6.0, 24.0) | 17.00 (12.0, 26.0) | 0.275   |

**P<0.01**
Additional file

Additional file 1: Table S1. Candida strains by center.

Competing interests
Haibo Qiu is a speaker for Pfizer and MSD China, and has received research grants from Pfizer, MSD China and Xian-Janssen. The remaining authors have no conflicts of interest to disclose. The funders participated in the design of the study, but had no role in study management, monitoring, data management, statistical analysis or development of this article. Authors accept direct responsibility for this paper.

Authors' contributions
BH, JL and HQ designed the study. BH, ZD contributed to the manuscript development. ZD, YK, BZ, WC, BO, QF and HQ were involved in patient recruitment and served as study investigators. All authors read and approved the final manuscript.

Acknowledgements
This study was supported by Merck Sharp & Dohme China.

Author details
1. Department of Intensive Care Unit, Zhongnan Hospital of Wuhan University, Wuhan, Hubei 430071, China. 2. Department of Intensive Care Unit, West China Hospital, Sichuan University, Chengdu, China. 3. Department of Intensive Care Unit, Shengjing Hospital, affiliated to China Medical University, Shenyang, China. 4. Department of Intensive Care Unit, The 2nd Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China. 5. Department of Intensive Care Unit, Henan Provincial People’s Hospital, Zhengzhou, China. 6. The First Affiliated Hospital of Medical School of Zhejiang University, Hangzhou, China. 7. Department of Intensive Care Unit, Nanjing Zhong-da Hospital, Southeast University School of Medicine, Nanjing, China.

Received: 19 May 2014 Accepted: 28 October 2014

Published online: 13 November 2014

References
1. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB: Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004, 39:309–317.
2. Richards MJ, Edwards JR, Culver DH, Gaynes RP: Nosocomial infections in combined medical-surgical intensive care units in the United States. Infect Control Hosp Epidemiol 2003, 23:105–10.
3. Jarvis WR: Epidemiology of nosocomial fungal infections, with emphasis on Candida species. Clin Infect Dis 1995, 21:1526–1530.
4. Kett DH, Azoulay E, Echeverria PM, Vincent JL: Extended Prevalence of Infection in ICU: Candida bloodstream infections in intensive care units: analysis of the extended period of prevalence in intensive care infection unit study. Crit Care Med 2011, 39:665–670.
5. Bougnoux ME, Kac G, Aegerter P, d’Enfert C, Fagon JY: Candida Study G: Candidemia and candiduria in critically ill patients admitted to intensive care units in France: incidence, molecular diversity, management and outcome. Intensive Care Med 2008, 34:292–299.
6. Dimopoulos G, Ntziora F, Rachiotis G, Armaganidis A, Falagas ME: Candida albicans versus non-albicans intensive care unit-acquired bloodstream infections: differences in risk factors and outcome. Antimicrob Agents Chemother 2006, 106:523–529. Table of contents.
7. Goddlaugsson O, Gillespie S, Lee K, Vanden Berg J, Hu J, Messer S, Herwaldt L: Rialf MA, Diekema DJ: Attributable mortality of nosocomial candidemia, revisited. Clin Infect Dis 2003, 37:1172–1177.
8. Zaoutis TE, Argon J, Chu J, Berlin JA, Walsh TJ, Feudtner C: The epidemiological and attributable outcomes of candidiasis in adults and children hospitalized in the United States: a propensity analysis. Clin Infect Dis 2005, 41:1232–1239.
9. Pappas PG, Kauffman CA, Andes D, Benjamin DK, Calandra TF, Edwards JR, Filler SG, Fisher JF, Kullberg BJ, Ostrosky-Zeichner L, Reboli AC, Rex JH, Walsh TJ, Sobel JD: Infectious Diseases Society of America: Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009, 49:503–533.
29. Mermet LA, Allon M, Bouza E, Craven DE, Flynn P, O’Grady NP, Raad II, Rijnders BJ, Sheeatts RJ, Warren DK: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 2009, 49:1–45.
30. Andes DR, Saffar N, Baddley JW, Playford G, Reboli AC, Rex JH, Sobel JD, Pappas PG, Kullberg BJ, Mycoses Study G: Impact of treatment strategy on outcomes in patients with candidemia and other forms of invasive candidiasis: a patient-level quantitative review of randomized trials. Clin Infect Dis 2012, 54:1110–1122.
31. Nucci M, Anaissie E, Betts RF, DuPont BF, Wu C, Buell DN, Kovanda L, Lortholary O: Early removal of central venous catheter in patients with candidemia does not improve outcome: analysis of 842 patients from 2 randomized clinical trials. Clin Infect Dis 2010, 51:295–303.
32. Cornely OA, Bassetti M, Calandra T, Garbinio J, Kullberg BJ, Lortholary O, Meersseman W, Akova M, Arendrup MC, Arikan-Akdagli S, Bille J, Castagnola E, Cuenca-Estrella M, Donnelly JP, Groll AH, Herbrecht R, Hope WW, Jensen HE, Lass-Flörl C, Petekias GS, Richardson MD, Rolides E, Verweij PE, Viscali C, Ullmann AJ, ESCMID Fungal Infection Study Group: ESCMID* guideline for the diagnosis and management of Candida diseases 2012: non-neutropenic adult patients. Clin Microbiol Infect 2012, 18(Suppl 7):19–37.
33. Trofa D, Gacser A, Nosanchuk JD: Candida parapsilosis, an emerging fungal pathogen. Clin Microbiol Rev 2008, 21:606–625.
34. Kreymann KG, de Heer G, Nierhaus A, Kluge S: Use of polyclonal immunoglobulins as adjunctive therapy for sepsis or septic shock. Crit Care Med 2007, 35:2677–2685.
35. Li Y, Chen H, Li X, Zhou W, He M, Chihi-Internati M, Wachtel XS, Frezza EE: A new immunomodulatory therapy for severe sepsis: Ulinastatin Plus Thymosin (alpha) 1. J Intensive Care Med 2009, 24:47–53.

doi:10.1186/s12879-014-0594-0
Cite this article as: Hu et al.: Catheter-related Candida bloodstream infection in intensive care unit patients: a subgroup analysis of the China-SCAN study. BMC Infectious Diseases 2014 14:594.