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Fluconazole Survival Benefit in Invasive Candidiasis: A Retrospective Cohort Study Linking Biomarkers, Infection Source, and Outcomes

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Abstract

Background

Invasive candidiasis (IC), particularly candidemia (56.7% mortality), faces diagnostic delays with blood cultures. Early identification of infection sources and biomarkers (PCT, IL-6, β-D-glucan) could enable prompt intervention.

Methods

A 12-month retrospective cohort study analyzed 223 hospitalized IC patients (2013–2024; incidence 31.9/100,000 patient-years) confirmed by sterile-site mycological evidence. Biomarkers, microbiology (BD/Vitek, CLSI susceptibility), and mortality predictors were assessed using regression and Kaplan-Meier analysis (SPSS).

Results

Patients were predominantly male (1.45:1), median age 60.1 years. Blood culture was the primary diagnostic tool (33.5%); 35.2% were polymicrobial. Among 88 blood culture-positive cases, 77.3% detected solely in aerobic bottles (mean TTP 39.1h). C. albicans predominated (52.6% of isolates); resistance: fluconazole 5.8%, itraconazole 11.0%, voriconazole 7.0%. Primary infection sources: abdominal (46.6%), catheter (18.8%). Overall mortality was 46.2%, varying by focus: bloodstream infection (BSI: 70.3%), abdominal (43.2%), catheter (26.1%); joint infections: 0%. In single-species infections (n = 140), Procalcitonin (PCT) demonstrated highest diagnostic value (AUC 0.827; sensitivity 0.667, specificity 0.862 at 0.778 μg/mL). Fluconazole conferred superior 90-day survival vs. caspofungin (0.815 vs 0.330; $p < 0.001$). Regression identified significant mortality predictors: PCT ≥ 0.778 ng/mL (OR 3.800, 95% CI 1.995–7.237, $p < 0.001$), IL-6 ≥ 25.375 pg/mL (OR 3.667, 95% CI 1.372–9.795, $p = 0.01$), BSIs (OR 4.431, 95% CI 2.438–8.054, $p < 0.001$), ICU admission (OR 2.351, 95% CI 1.269–4.356, $p = 0.007$); Fluconazole was protective (OR 0.102, 95% CI 0.033–0.316).

Conclusion

Invasive candidiasis (IC) high mortality. Elevated PCT, IL-6, and BSI are significant predictors. Fluconazole is protective. C. albicans (52.6%) and abdominal infections (46.6%) predominated.

Introduction

Invasive candidiasis (IC), a group of infectious syndromes caused by *Candida spp*., is associated with significant morbidity and mortality. Candidemia, a severe form of IC characterized by bloodstream invasion and disseminated infection, carries a particularly high mortality rate of 56.7% [1]. Definitive

diagnosis of candidemia relies on blood culture isolation of *Candida spp.* However, false-negative blood cultures remain a major diagnostic challenge. Identifying the source of infection, which often precedes candidemia, is crucial for the early recognition of IC. Biomarkers such as procalcitonin (PCT), white blood cell count (WBC), and interleukin-6 (IL-6) are transforming microbiological diagnosis and infection assessment [2]. Nevertheless, their diagnostic value for IC specifically remains uncertain. Therefore, this study aims to investigate infection sources and evaluate the potential of these biomarkers for the early diagnosis of IC.

Materials and Methods

1.1 Study Design

1.2 Annotation: Selection criteria for confirmed cases of invasive candidiasis [3]

 A positive Candida culture from at least one specimen obtained from a sterile site (including blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, joint fluid, or pus).

 Abdominal drainage fluid and joint cavity drainage fluid (<24 h) for cultivation to obtain Candida.

 Indwelling venous catheter ≥ 15CFU/tube of Candida at the 5 cm tip and the patient had clinical symptoms (elevated infection indicators or positive 1,3-beta-D-glucan).

  These data excluded all suspected cases of Candida infection identified in bile, abdominal drainage fluid, wound secretions, and the upper urinary tract. Recovery of Candida species from peritoneal fluid obtained via intra-abdominal drains likely represents colonization of the drain from the skin rather than true intra-abdominal infection.

1.3 Setting

This retrospective study analyzed clinical data from the 940th Hospital of the Joint Logistics Support Force of the People's Liberation Army. The cohort comprised patients diagnosed with culture-positive invasive Candida infection. Statistical analyses were performed on pathogen distribution, sample sources, admitting departments, underlying comorbidities, infection biomarkers, incidence rates, and in-hospital mortality.

1.4 Ethics approval and consent to participate

We confirm that the need for individual informed consent was waived by the approving ethics committee the 940th Hospital of the Joint Logistics Support Force of the People's Liberation Army (Clinical trial number: not applicable). Due to the retrospective nature of the study and the use of anonymized data and the committee waived the requirement for informed consent. The study was conducted in accordance with the ethical standards of the responsible institutional review board and the principles of the Declaration of Helsinki (1975, and its later amendments).

1.5 Participants

Following a meticulous selection process, 223 participants were deemed eligible for the 12-month study period. A flowchart outlining participant eligibility and reasons for exclusion is presented.

1.6 Exposure Variables

This study selected the following demographics and clinical characteristics as exposure variables: age, sex, coinfection, Fluconazole resistance, ICU hospitalization, bloodstream infection, *Candida albicans* infection, cancer, malignant hematological diseases, Usage of antifungal drugs,

medical related infection,and laboratory biomarkers including procalcitonin (PCT), interleukin-6 (IL-6), serum (1,3)-β-D-glucan (β-D-glucan test), and neutrophil percentage (NEU%).

1.6 Endpoint

Inpatients with invasive candidiasis (IC) died during hospitalization.

1.7 Microbiology Methods

Infection biomarkers were collected from IC infection patients, specifically those detected within 24 hours of initial admission or within 24 hours of a positive Candida culture. The biomarkers and their detection methods were: procalcitonin (PCT; Roche chemiluminescence), C-reactive protein (CRP; Beckmann immunoturbidimetry), Interleukin-6 (IL-6; Roche chemiluminescence), white blood cell count (WBC; Mindray 6900), neutrophil percentage (N%; Mindray 6900), 1,3-beta-D-glucan (Beijing Jinshanchuan immunoturbidimetric method), and D-dimer (Hiesenmikon immunoturbidimetric assay). To prevent data duplication, only one biomarker result per patient was included. A negative control group comprised 200 uninfected patients.

1.8 Blood culture and General Fungal Culture

Following a standard aseptic procedure, 16-20 mL of blood was collected from adult patients and promptly aliquoted into two BD Bactec blood culture bottles: 8-10 mL into an aerobic bottle and 8-10 mL into an anaerobic bottle. Laboratory processing involved numbering, registering, and loading samples into a BD FX blood culture instrument. Upon positive alarm, staff observed the growth curve, aseptically extracted culture medium with a sterile syringe for Gram staining/microscopy, and reported results to clinicians. The medium was simultaneously inoculated onto plates for aerobic incubation at 35°C (24h). Following colony formation, organisms were identified using YST cards on a Vitek Compact-2 automated system.

Routine Fungal Culture: Tissue samples (1 cm^3) obtained from sterile surgical sites were inoculated onto sheep blood agar plates. Sterile fluid specimens (including ascites, puncture fluids, and pus) were inoculated onto sheep blood agar, China Blue agar, and/or Sabouraud agar plates. Cultures were examined after 24 hours of incubation; positive results prompted immediate antifungal susceptibility

testing, while negative cultures were re-examined after extended incubation for up to 48–72 hours. Following colony formation, yeast isolates were identified using YST cards on the Vitek Compact-2 automated system.

Candida Identification and Susceptibility Testing: Clinical samples underwent routine culture. Suspected Candida-positive cultures were incubated for 24 hours. After colony formation, bacterial identification was performed using YST cards on the Vitek Compact-2 automated system. Additionally, antifungal susceptibility testing against 5-fluorocytosine, amphotericin B, fluconazole, itraconazole, and voriconazole was performed using the BioMérieux ATB FUNGUS 3 microdilution method, following CLSI M27-A guidelines for testing and interpretation.

1.9 Statistical Methods.

Statistical analyses were performed using SPSS 22.0. Categorical variables (age, sex, and ICU status) were analyzed using Pearson's χ^2 test. Multiple regression analysis identified statistically significant predictors of crude mortality ($p < 0.05$), with several factors reaching significance at $p < 0.001$. Survival curves for invasive candidiasis were generated using the Kaplan-Meier method. Finally, the sensitivity and specificity of clinical infection biomarkers were assessed via receiver operating characteristic (ROC) curve analysis, and calculating sensitivity and specificity by maximum Jordan index.

Results

3.1 Clinical features of IC patients

A cohort of 223 inpatients with invasive candidiasis (IC), diagnosed by microbiological confirmation between 2013 and 2024, was analyzed. The incidence rate was 31.9 per 100,000 patient-years. The healthcare-associated infection (HAI) at 60%.The male-to-female ratio was 1.45:1, and the median age was 60.1 years (IQR 49.0–72.0).Blood culture was the primary diagnostic specimen (33.5%, 78/223 cases), followed by ascites (27.0%), pus (18.0%), and catheter tips (9.9%). Polymicrobial infections (Bacteria combined with candida) occurred in 35.2% of cases, with 10 patients confirmed by specimens from two distinct sites. Among 88 blood culture-positive IC cases, 77.3% were detected in aerobic bottles only (mean time-to-positivity: 39.1 ± 26.7 hours; range 3–140 hours), 18.2% in both aerobic and anaerobic bottles, and 4.5% in anaerobic bottles only (mean time-to-positivity: 24.1 ± 15.2 hours; range 3–54 hours).A total of 247 strains were isolated from the 223 patients. *Candida albicans* was predominant (52.6%). Antifungal susceptibility testing revealed resistance rates of 5.8% to fluconazole, 11.0% to itraconazole, and 7.0% to voriconazole. Resistant strains included *C. albicans* (n=7), *C. tropicalis* (n=7), *C. glabrata* (n=3), and *C. parapsilosis* (n=2) (**Fig.1**).

3.2 Infection source and underlying diseases in IC patients

Analysis of infection sources revealed abdominal infection as the primary site (46.6%). This was followed by catheter-related infections (18.8%), joint infections (5.4%), maxillofacial space infections

(4.0%), and chest infections (2.7%). The source remained unknown in 35 cases (15.7%) (**Fig. 2**). Analysis of underlying diseases/comorbidities identified over 30 distinct conditions among IC patients. The most prevalent critically ill conditions were peritonitis (15.6%, n=31), malignant hematological diseases (7.6%), intestinal malignancies (7.2%), digestive tract perforation (6.7%), and postoperative gastric malignancies (4.9%) (**Table 1**).

3.3 ROC curve analysis for the biomarker diagnostic value for IC

The discriminatory ability of biomarkers for invasive candidiasis (IC) was evaluated in a cohort of 140 cases with single-species *Candida spp.* infection. Diagnostic performance, determined by the AUC-ROC for each biomarker, is presented in **Fig. 3** and **Table 2**. The most useful biomarker was procalcitonin (PCT), achieving an AUC-ROC of 0.827. At its optimal cut-off value of 0.778 μg/mL, PCT demonstrated a sensitivity of 0.667 and a specificity of 0.862. D-dimer showed superior discriminatory power with an AUC-ROC of 0.913. At its optimal cut-off of 2.600 mg/L, D-dimer yielded a sensitivity of 0.833 and a specificity of 0.914. When using a cut-off of 100 pg/ml, the G test demonstrated a sensitivity of 50% in patients with invasive candidiasis.

3.4 Kaplain Meier Survival Curve and mortality risk factors in IC patients

The overall hospital mortality rate for invasive candidiasis (IC) patients was 46.2% (103/223). Mortality varied significantly by infection focus (χ^2=33.099, p<0.001): highest in bloodstream infections (BSIs) (70.3%, 52/74), followed by abdominal infections (43.2%, 38/88) and catheter-related infections (26.1%, 6/23). No mortality occurred in joint infections (0/12).Kaplan-Meier analysis demonstrated: No significant 30-day survival difference between antifungal-treated (capsafungin/fluconazole/voriconazole; 0.666±0.057) and untreated groups (0.671±0.053; Log-rank χ^2=0.003, p=0.958; **Fig.4A**).Superior 90-day survival with fluconazole (0.815±0.090) versus caspofungin (0.330±0.093; Log-rank χ^2=12.244, p<0.001; **Fig.4B**).Multiple regression identified significant mortality predictors (**Fig.5**, **Table 3**):PCT ≥ 0.778 ng/mL (OR 3.800, 95% CI 1.995-7.237, p < 0.001),IL-6 ≥ 25.375 pg/mL (OR 3.667, 95% CI 1.372-9.795, p = 0.01),BSI diagnosis (OR 4.431, 95% CI 2.438-8.054, p < 0.001), ICU admission (OR 2.351, 95% CI 1.269-4.356, p = 0.007)**,**Fluconazole usage (OR =0.102 ; 95% CI: 0.033–0.316)**.**

Discussion

Invasive candidiasis (IC), a severe infectious disease caused by Candida species, demonstrated a hospital mortality rate of 46.2% in our study. This aligns with Logan C [4], who reported IC crude mortality rates of 40-55% in ICU settings over the past decade. Our observed incidence rate of 31.9 per 100,000 persons exceeds the 2–14 per 100,000 reported by Soriano A [5].Laboratory-based diagnosis revealed blood culture as the most common method (33.5%). Consistent with this finding, bloodstream infections (BSIs) exhibited the highest mortality among IC patients in our cohort (70.3%), significantly exceeding rates for abdominal infections (43.2%), catheter-related infections (26.1%), and joint infections (0%). This underscores BSIs as the most severe manifestation of IC, warranting heightened therapeutic attention.

Among IC patients with positive blood cultures, 77.3% of detections occurred in aerobic bottles alone (mean time to positivity: 39.1 ± 26.7 hours), while 18.2% were detected in both aerobic and anaerobic bottles. Only 4.5% were detected solely in anaerobic bottles, with a significantly shorter mean time to positivity (24.1 ± 15.2 hours). These findings support the necessity of extending blood culture incubation to at least 7 days and utilizing both aerobic and anaerobic bottles for suspected candidemia.We isolated 247 strains representing 10 Candida species. C. albicans was the predominant pathogen (52.6%), and 8.5% of isolates were acquired resistant strains, consistent with prior reports [6-8].

Abdominal infections constituted the most common infection source (46.6%), followed by catheter-related infections (18.8%). The high prevalence of abdominal involvement likely relates to intestinal colonization by Candida species, which occurs in up to 60% of individuals [9]. Disruption of the commensal microbial equilibrium or intestinal damage can facilitate Candida overgrowth and invasion into the abdominal cavity. Patients presented with over 30 underlying conditions predisposing to IC. Peritonitis was the predominant comorbidity, followed by malignant hematological diseases, intestinal malignancies, digestive tract perforation, and postoperative gastric malignancies. This pattern reflects the established risk associated with abdominal surgery (particularly cases involving anastomotic leakage or repeat laparotomies), hematologic malignancies, solid-organ tumors [6], and catheter-related bloodstream infections [10].

We evaluated the diagnostic performance of biomarkers for invasive candidiasis (IC) in patients with single-species infections (n=140). Procalcitonin (PCT) demonstrated significant discriminatory power with an AUC-ROC of 0.827. At the optimal cut-off value of 0.778 μg/mL, PCT yielded a sensitivity of 0.667 and specificity of 0.862. In this cohort, PCT was the only biomarker showing clinically useful diagnostic value for IC. This finding contrasts with León C [11], who reported no significant diagnostic utility for PCT (p=0.179).

This study reaffirms the moderate and variable diagnostic performance of the (1,3)-β-D-glucan (BDG) assay for invasive candidiasis (IC). In our cohort, using a cutoff of 100 pg/mL, the G test demonstrated an overall sensitivity of only 50% for IC. Notably, candidemia—which represented 33.5% of IC cases in this study—constituted the largest subgroup. This observed sensitivity is substantially lower than the pooled estimate of 0.73 (95% CI: 0.66–0.80) reported for candidemia in a recent meta-analysis [12]. The discrepancy may arise from differences in patient characteristics, a higher prevalence of non-Candida albicans species with distinct BDG expression profiles, or a greater proportion of localized rather than disseminated infections in our cohort.

Kaplan-Meier analysis revealed a 28-day survival rate of 0.591 ± 0.036 in our candidemia cohort, corresponding to a mortality rate of 50.1%. This exceeds the 35.1–40.0% mortality rates reported in prior studies [13,14].Multiple regression modeling identified significant mortality risk factors for invasive candidiasis(IC):Procalcitonin (PCT) ≥ 0.778 ng/mL (OR 3.800, 95% CI 1.995–7.237; p< 0.001),IL-6 ≥ 25.375 pg/mL (OR 3.667, 95% CI 1.372–9.795; p = 0.01).Bloodstream infection (OR 4.431, 95% CI 2.438–8.054; p< 0.001),ICU admission (OR 2.351, 95% CI 1.269–4.356; p = 0.007),Fluconazole use

(protective: OR 0.102, 95% CI 0.033–0.316; p < 0.001).Notably, fluconazole administration significantly reduced IC mortality. However, antifungal initiation was delayed (mean culture time: 35.7 ± 25.7 h), highlighting the importance of early treatment—consistent with literature establishing prompt antifungal therapy and catheter removal as mortality-reduction cornerstones [15]. For ICU patients failing antibiotic therapy, empirical fluconazole may reduce mortality at acceptable cost [16].Our findings contrast with Zeng et al. [17], where C. albicans infection predicted mortality (HR 3.35; 95% CI 1.13–9.92; p = 0.029); our analysis showed no such association (p = 0.135). Regarding ICU admission, while Leroy et al. [18] reported no mortality difference by admission type, our results align with Al-Dorzi et al. [19] (OR 2.87; 95% CI 1.22–6.74). This study provides novel evidence for PCT, IL-6, and bloodstream infection as significant IC mortality predictors—factors infrequently reported in existing literature.

Conclusion, invasive candidiasis (IC) high mortality (46.2%) and identifies elevated PCT, IL-6, and bloodstream infection (BSI) as novel, significant mortality predictors. Fluconazole use was strongly protective but treatment initiation was often delayed. BSI had the highest mortality (70.3%). C. albicans predominated (52.6%); abdominal infections were most common (46.6%).

Limitation

Although this article collected cases within the past 10 years, the sample set is still relatively small. And due to the difficulty in diagnosing invasive candidiasis, we did not track samples suspected of contamination. Another limitation is the fact that the findings are applicable to the epidemiology of the area. ie in other areas that have many fluconazole resistant isolates ,as C. auris or C. parapsilosis, fluconazole is not the bast option as compares to Echinocandins.

Declarations

The study was approved by the 940th Hospital of the Joint Logistics Support Force of People's Liberation of the PLA Committee for Medical and Health Research Ethics. All participants provided written informed consent for publication of the clinical data and associated images. All identifying information has been removed to protect patient anonymity.The Ethics Committee waived the need for informed consent, as this was an observational study, the treatment of the patients was standard, and no samples were taken for the study.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FENG Qiang-sheng conceived the study and participated in the design, data collection, statistical analysis, data interpretation, and drafting of the manuscript. SONG Yue and Juan participated in the design, statistical analysis, data interpretation, and manuscript drafting. XiaoQin-ha participated in the design, statistical analysis, data interpretation, and manuscript drafting. All the authors have read and approved the final manuscript.

Data availability statement

The datasets generated during this study derive from de-identified patient records in Hospital (HIS) and Laboratory (LIS) Information Systems. Due to patient privacy requirements, the volume of source data, and their original documentation in Chinese (requiring translation for accessibility), these data are not publicly available. Processed datasets are available from the corresponding author upon reasonable request.

Consent for publication

Not Applicable

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Tables

Table 1

Underlying diseases in patients with invasive candidiasis(n = 223case)

Underlying diseases	Case	%	Underlying diseases	Case	%
Peritonitis	31	13.9	Postoperative lung cancer	4	1.8
Malignant hematological diseases	17	7.6	Autoimmune diseases	3	1.4
Malignant tumors of the intestine	16	7.2	Diabetes	3	1.4
Digestive tract perforation	15	6.7	Skin and soft tissue	3	1.4
Postoperative gastric malignant tumor	11	4.9	Infectious endocarditis	3	1.4
Infection of the maxillofacial muscle space	10	4.5	Liver abscess	3	1.4
Joint replacement surgery Infection	10	4.5	Intestinal obstruction	3	1.4
Cirrhosis	10	4.5	Bladder tumor	3	1.4
Multiple injuries	10	4.5	Neonate	2	0.9
Gallbladder cancer	8	3.6	Intracranial infection	2	0.9
Severe pneumonia	8	3.6	Viral pneumonia	2	0.9
Severe acute pancreatitis	6	2.7	Alzheimer's disease	2	0.9
Uremia	6	2.7	Acute cerebrovascular disease	2	0.9
Pancreatic cancer	4	1.8	Gallstones and cholecystitis	2	0.9
Postoperative esophageal cancer	4	1.8	Others	20	9.0

Table 2

AUC for the biomarker diagnostic value in invasive candidiasis (Single infection,n = 140 case) Notes: G test: 1,3-β-D glucan test; PCT: procalcitonin; IL-6: Interleukin- 6; WBC: White blood cell; NEU%: Neutrophil %.

Biomarkers	AUC value	Cut-off value	Sensitivity	Specificity	95% Confidence interval	
					Lower bound	Upper bound
PCT(ng/ml)	0.827	0.778	0.667	0.862	0.720	0.933
IL-6(ng/ml)	0.788	25.375	0.958	0.603	0.686	0.891
WBC(×109/L)	0.746	8.395	0.75	0.759	0.600	0.892
NEU%(%)	0.869	79.9	0.792	0.983	0.742	0.995
D-Dimer(mg/L)	0.913	2.6	0.833	0.914	0.849	0.978
G test(pg/ml)		> 100	0.500	0.600		

Table 3

Demographic, clinical and laboratory, findings of patients on admission

Demographics and clinical characteristics	Total(n = 218)	Nonsurvivor (n = 101)	Survivor (n = 117)	p value
Age, years	60(49.0–72.0)	59.0(50.0-70.5)	60.0(47.5–73.0)	0.685
Sex				0.073
Female	89(41%)	48(54%)	41(46%)	
Male	129(59%)	53(41%)	76(59%)	
Age				0.504
>=60	110(50%)	48(44%)	62(56%)	
< 60	108(50%)	52(48%)	56(52%)	
Co-pathogen				0.091
Yes	87(40%)	46(53%)	41(47%)	
No	131(60%)	54(41%)	77(59%)	
Fluconazole	189			
Drug resistance or intermediary	17(9%)	11(65%)	6(35%)	0.105
Sensitive	172(91%)	89(44%)	112(56%)	
ICU Hospitalization				0.005
Yes	56(26%)	35(63%)	21(37%)	
No	162(74%)	66(41%)	96(59%)	
Bloodstream infection				< 0.001
Yes	74(34%)	52(70%)	22(30%)	
No	144(66%)	49(34%)	95(66%)	
Candida albicans				0.135
Yes	118(54%)	49(42%)	69(58%)	
No	100(46%)	52(52%)	48(48%)	
Procalcitonin, ng/mL				< 0.001

Data are median (IQR) or n (%). p values were calculated by Mann-Whitney U test, $\chi 2$ test, or Fisher's exact test,as appropriate. The administration time of antifungal drugs is calculated by the time of submitting positive microbial samples.

Demographics and clinical characteristics	Total(n = 218)	Nonsurvivor (n = 101)	Survivor (n = 117)	p value
PCT > = 778	96(55%)	56(58%)	40(42%)	
PCT < 0.778	78(45%)	21(27%)	57(73%)	
G test(pg/ml)				0.239
G value > = 100	51(%)	28(55%)	23(45%)	
G value < 100	49(%)	21(43%)	28(57%)	
Cancer and Malignant hematological diseases				0.102
Yes	65(30%)	36(55%)	29(45%)	
No	153(70%)	65(42%)	88(58%)	
IL-6(pg/ml)				0.007
>=25.375	102(79%)	51(50%)	51(50%)	
< 25.375	28(36%)	6(21%)	22(79%)	
NEU%				0.078
>=79.9	145(76%)	70(48%)	75(52%)	
< 79.9	45(24%)	15(30%)	30(70%)	
Medical related infection				0.127
Yes	128(60%)	63(48%)	66(52%)	
NO	87(40%)	33(38%)	54(62%)	
Usage of antifungal drugs				0.824
Yes	86(46%)	32(37%)	54(63%)	
NO	101(54%)	36(36%)	65(64%)	
Types of antifungal drugs				< 0.001
Caspofungin	31(36%)	19(61%)	12(39%)	
Fluconazole	43(50%)	6(14%)	37(86%)	
Voriconazole	12(14%)	7(58%)	5(42%)	

Data are median (IQR) or n (%). p values were calculated by Mann-Whitney U test, $\chi 2$ test, or Fisher's exact test,as appropriate. The administration time of antifungal drugs is calculated by the time of submitting positive microbial samples.

Demographics and clinical characteristics	Total(n = 218)	Nonsurvivor (n = 101)	Survivor (n = 117)	p value
Administration time of antifungal drugs				0.104
24h	29(34%)	14(48%)	15(52%)	
48h	12(14%)	6(50%)	6(50%)	
≥ 72h	45(52%)	13(29%)	33(71%)	
Data are median (IQR) or n (%). p values were calculated by Mann-Whitney U test, χ2 test, or Fisher's exact test,as appropriate. The administration time of antifungal drugs is calculated by the time of submitting positive microbial samples.				

Figures

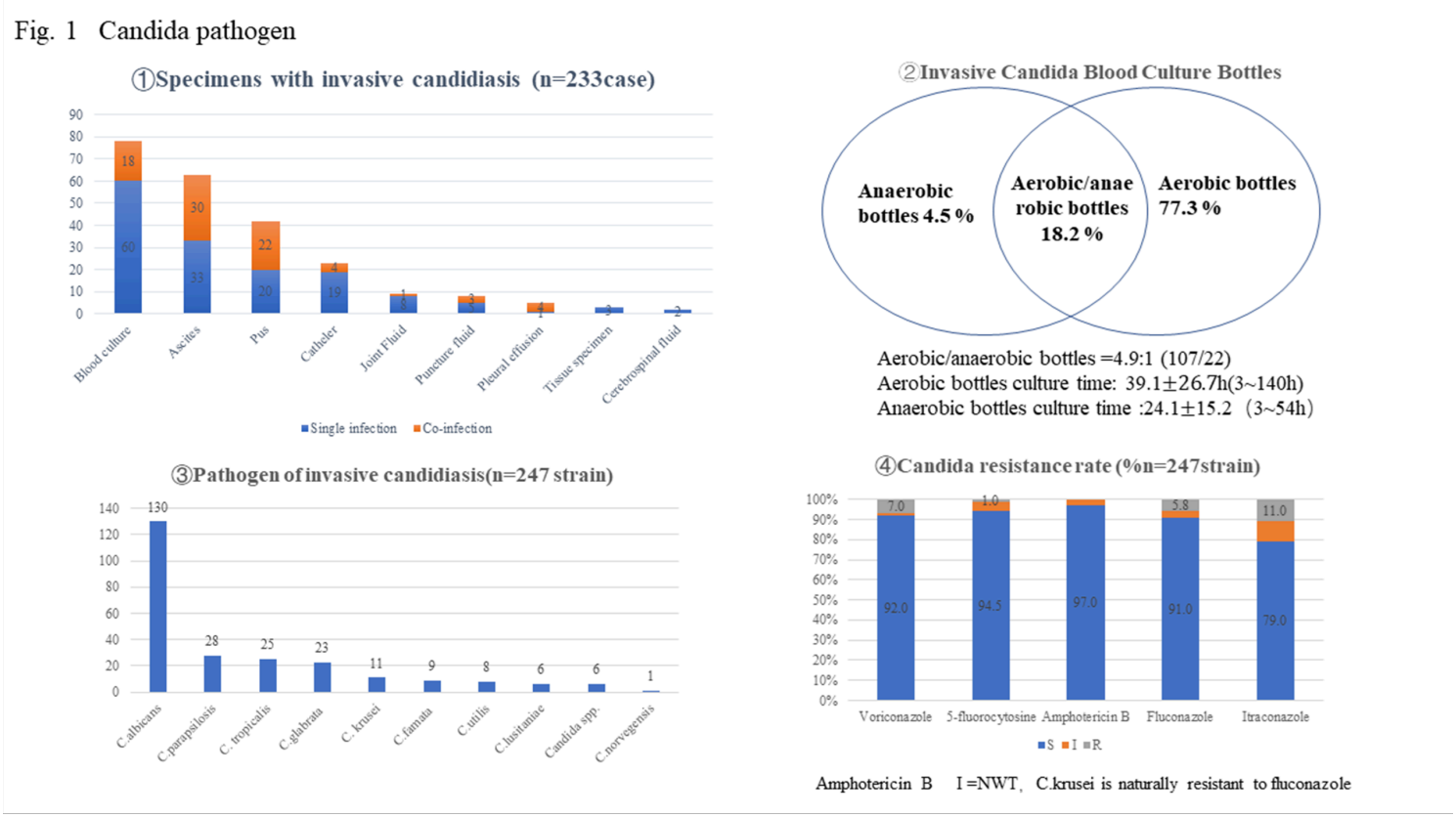


Figure 1

 Specimen Distribution & Co-pathogens:

Among confirmed invasive candidiasis (IC) cases, blood culture was the most frequent initial diagnostic specimen (33.5%), followed by ascitic fluid (27.0%), catheter tips (18.0%), and pus (9.9%,42 cases pus

main contained abdominal abscess 26 cases, maxillofacial space infection abscess7 cases, 3 cases of liver abscess). Polymicrobial infections (co-pathogens) were identified in 35.2% of total cases. Ten cases were confirmed using ≥2 specimen types.

 Blood Culture Characteristics:For culture-positive IC bloodstream infections, 77.3% were detected only in aerobic bottles (mean time-to-positivity: 39.1 ± 26.7 hours; range: 3–140 hours).

 Pathogen Distribution:We isolated 247 Candida strains representing 10 species. C. albicans was the predominant pathogen (52.6%).

Resistance Patterns:Acquired resistance was observed in 17 isolates (6.9% of total). All isolates were wild-type for Amphotericin B. As expected, C. krusei isolates demonstrated intrinsic resistance to fluconazole.

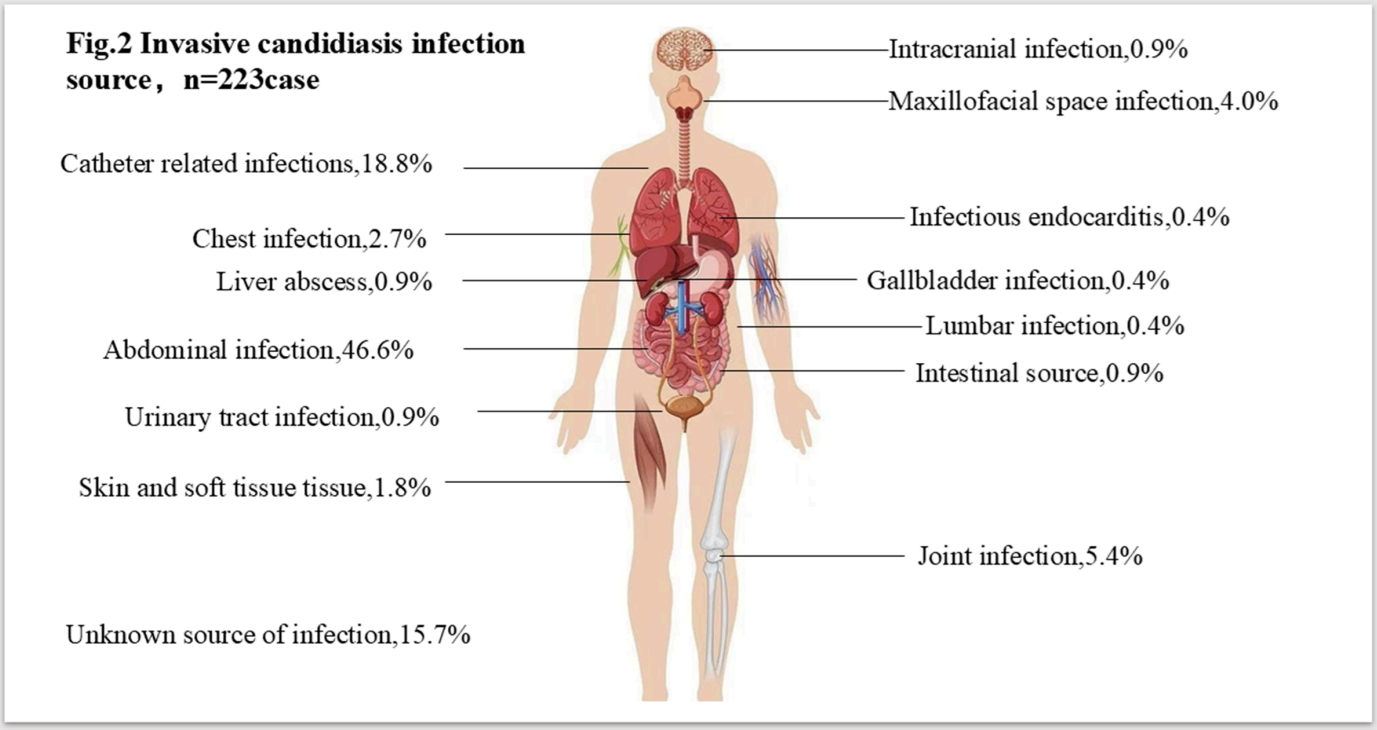


Figure 2

Invasive candidiasis infection source

Abdominal infections constituted the predominant source (46.6%), followed by catheter-related infections (18.8%). Less frequent sources included joint, maxillofacial space, and chest infections. Notably, 35 cases (15.7%) had undetermined infection origins.

Fig 3.ROC curve for the biomarker diagnostic value in invasive candidiasis

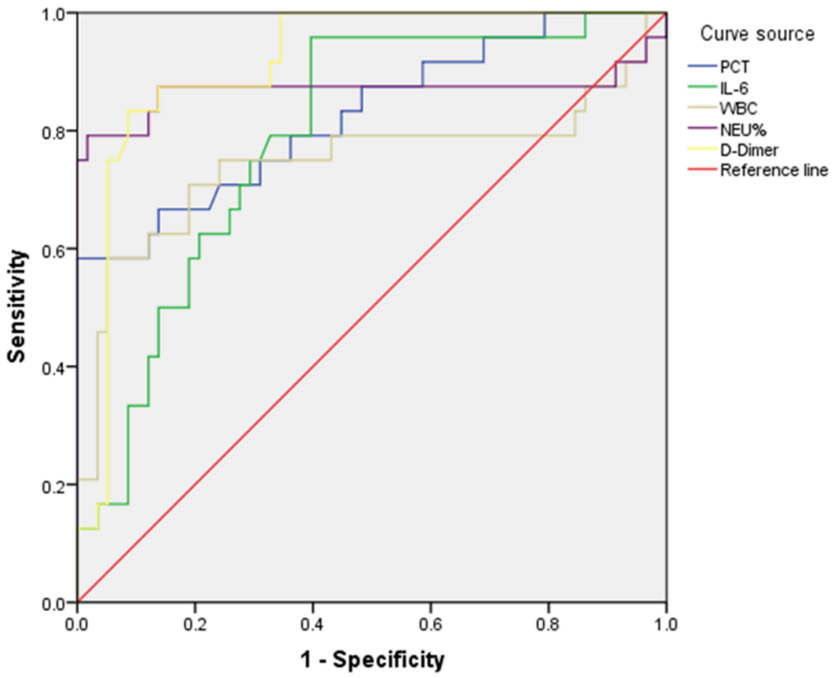
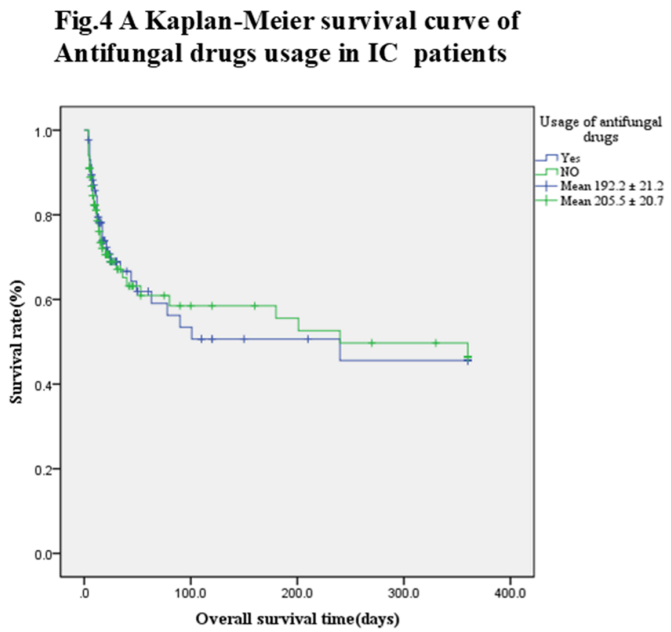


Figure 3

ROC curve for the biomarker diagnostic value in invasive candidiasis

This study enrolled 140 patients with a single infection type to evaluate biomarkers for invasive candidiasis. The area under the receiver operating characteristic curve (AUC-ROC) for procalcitonin (PCT) was 0.827; at a cut-off value of 0.778 μg/mL, sensitivity and specificity were 66.7% and 86.2%, respectively.



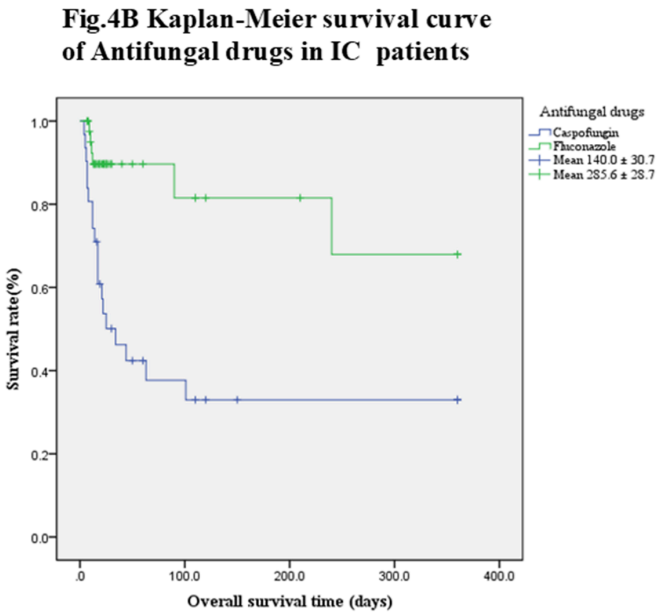


Figure 4

A Fig.2 A Kaplan-Meier survival curve of Antifungal drugs usage in IC patients

Antifungal drugs usage (Caspofungin, Fluconazole and Voriconazole) VS Non- Antifungal drugs usage 90 days survival rate 0.534±0.070 VS 0.585 ± 0.061, Log Rank (Mantel-Cox) χ=0.003, p=0.958.

B Kaplan-Meier survival curve of Antifungal drugs in IC patients

Antifungal drugs (Caspofungin, n=31cases) VS Antifungal drugs (Fluconazole, n=44cases) 90 days survival rate 0.330±0.093 VS 0.815 ± 0.090, Log Rank (Mantel-Cox) χ=0.003, p<0.001.

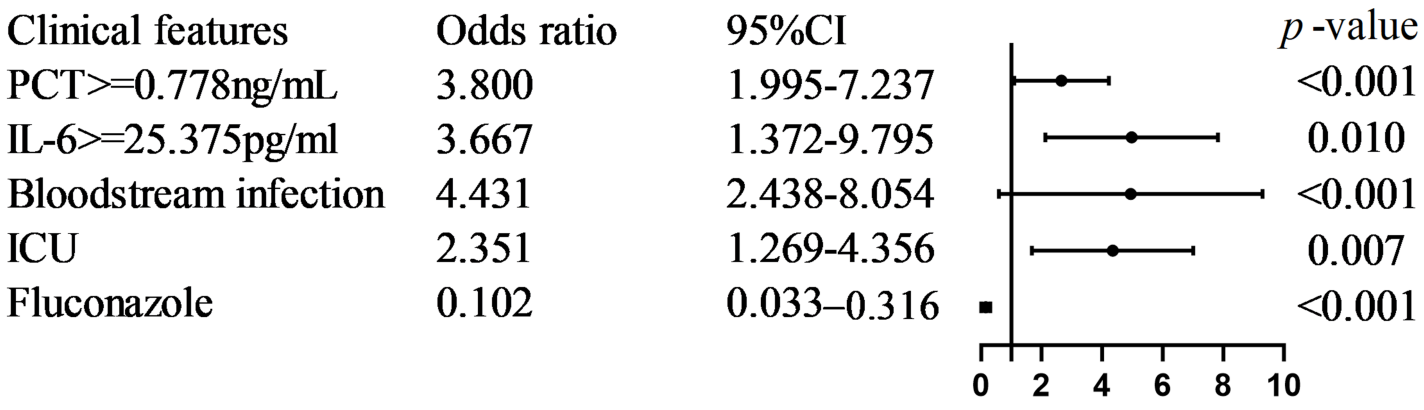


Figure 5

Mortality risk factors analysis in invasive candidiasis

Multiple regression analysis identified the following significant predictors of mortality in invasive candidiasis ($p < 0.01$):PCT ≥0.778 ng/mL (OR = 3.800; 95% CI: 1.995–7.237),IL-6 ≥ 25.375 pg/mL (OR = 3.667; 95% CI: 1.372–9.795),Bloodstream infection (OR = 4.431; 95% CI: 2.438–8.054),ICU admission/stay (OR = 2.351; 95% CI: 1.269–4.356), Fluconazole usage(OR =0.102 ;95% CI: 0.033–0.316).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Reviewer13.docx