

Supplementary Table S1. Common risk factors for neonates to acquire candidemia

Risk factors	Neonates (n = 9)
Male	6 (66.7)
Age (days)	14.4 ± 9.6 (range: 0.0–28.0)
Premature birth	8 (88.89)
Perinatal conditions	
Gestational age (weeks)	31.5 ± 2.4 (range: 29.0–37.0)
Birth weight (g)	1528.3 ± 281.9 (range: 1090.0–1920.0)
Maternal age (years)	34.7 ± 2.1 (range: 32.0–38.0)
Maternal disease	
Gestational diabetes mellitus	1 (11.1)
Infections	1 (11.1)
Fetal intrauterine distress	3 (33.3)
Premature rupture of fetal membrane	3 (33.3)
Hemoglobin (g/L)	131.1 ± 17.1 (range: 107–166)
Albumin (g/L)	29.0 ± 4.8 (range: 21–37)
Neonatal respiratory distress syndrome	3 (33.3)
Hydrocephaly	1 (11.1)
Iatrogenic factors	
Corticosteroids/immunosuppressant	0 (0.0)
Use of CVC	9 (100.0)
Mechanical ventilation	8 (88.9)
Candida Score	1.2 ± 1.2
Sepsis	2 (22.2)
Surgery	1 (11.1)
TPN	6 (66.7)
Multi-focal colonization	0 (0.0)

Note. Normally distributed variables are presented with mean ± standard deviation while categorical variables are presented with the patient number (percentage, %). Abbreviations: CVC: Central venous catheter; TPN: Total parenteral nutrition.

Supplementary Table S2. The unsterile sites detected with *Candida* colonization

Colonization sites	Frequency
Sputum/BALF/tracheal secretions	28
Urine	20
Stool	18
Pharynx	4
Skin	1
Drained abdominal fluid (tubes placed for over 24 h)	3

Note. BALF: Bronchoalveolar lavage fluid.

Supplementary Table S3. Risk factors by common infected *Candida* species

Risk factors	<i>Candida</i> species						P-value
	<i>C. albicans</i> (n = 87)	<i>C. parapsilosis</i> (n = 37)	<i>C. glabrata</i> (n = 27)	<i>C. tropicalis</i> (n = 26)	<i>C. krusei</i> (n = 7)	Others (n = 6)	
Male	58 (66.7)	29 (78.4)	15 (55.6)	18 (69.2)	6 (85.7)	4 (66.7)	0.431
Age	67 (49–81)	65 (32–73)	73 (51–88)	64 (39–78)	66 (28–78)	65 (0–70)	0.663
Age > 75 years	29 (33.3)	6 (16.2)	13 (48.1)	8 (30.8)	2 (28.6)	1 (16.7)	0.140
Age < 1 month	8 (9.2)	6 (16.2)	4 (14.8)	0 (0.0)	0 (0.0)	2 (33.3)	0.103
Hemoglobin (g/L)	102.0 ± 21.9	101.3 ± 21.5	94.5 ± 28.6	93.6 ± 21.1	81.4 ± 31.9	86.2 ± 19.2	0.080
Hemoglobin < 80 g/L	12 (13.8)	5 (13.5)	12 (44.4)	9 (34.6)	4 (57.1)	3 (50.0)	0.007**
Albumin (g/L)	30 (28–35)	30 (28–35)	30 (27–36)	32 (30–35)	31 (28–35)	28 (21–31)	0.379
Albumin < 25 g/L	6 (6.9)	3 (8.1)	1 (3.7)	3 (11.5)	1 (6.9)	2 (33.3)	0.259
Diabetes mellitus	25 (28.7)	8 (21.6)	15 (55.6)	8 (30.8)	2 (28.6)	0 (0.0)	0.033*
Solid organ malignancies	35 (40.2)	7 (18.9)	6 (22.2)	5 (19.2)	1 (14.3)	0 (0.0)	0.031*
Hematologic malignancies	0 (0.0)	0 (0.0)	0 (0.0)	7 (26.9)	1 (14.3)	2 (33.3)	< 0.001***
Neutropenia	1 (1.1)	0 (0.0)	0 (0.0)	6 (23.1)	3 (4.3)	2 (33.3)	< 0.001***
Organ failure	47 (54.0)	23 (62.2)	18 (66.7)	13 (50.0)	7 (100.0)	1 (16.7)	0.042*
Heart failure	27 (31.0)	6 (16.2)	10 (37.0)	7 (26.9)	3 (42.9)	1 (16.7)	0.399
Respiratory failure	25 (28.7)	17 (45.9)	16 (59.3)	7 (26.9)	1 (14.3)	1 (16.7)	0.020*
Renal failure	21 (24.1)	10 (27.0)	8 (29.6)	6 (23.1)	6 (85.7)	0 (0.0)	0.010*
Hepatic failure	6 (6.9)	2 (5.4)	0 (0.0)	2 (7.7)	1 (14.3)	0 (0.0)	0.649
Other deep-seated bacterial infection	38 (43.7)	20 (54.1)	18 (66.7)	13 (50.0)	2 (28.6)	1 (16.7)	0.135
Pancreatitis	4 (4.6)	0 (0.0)	2 (7.4)	2 (7.7)	1 (14.3)	0 (0.0)	0.482
Iatrogenic factors							
Long-term hospitalization (≥ 90 days)	11 (12.6)	12 (32.44)	9 (33.3)	7 (26.9)	0 (0.0)	0 (0.0)	0.021*
ICU hospitalization	39 (44.8)	20 (54.1)	17 (63.0)	3 (11.5)	2 (28.6)	2 (33.3)	0.004**
Hemodialysis	5 (5.7)	5 (13.5)	2 (7.4)	4 (15.4)	0 (0.0)	0 (0.0)	0.426
Long-term use of broad spectrum antibiotics	24 (27.6)	22 (59.5)	16 (59.3)	12 (46.2)	2 (28.6)	3 (50.0)	0.006**
Corticosteroids/immunosuppressant	7 (8.0)	2 (5.4)	1 (3.7)	7 (26.9)	3 (42.9)	1 (16.7)	0.004**
CVC	51 (58.6)	27 (73.0)	18 (66.7)	19 (73.1)	2 (28.6)	5 (83.3)	0.145
Mechanical ventilation	21 (24.1)	17 (45.9)	15 (55.6)	8 (30.8)	0 (0.0)	3 (50.0)	0.006**
<i>Candida</i> Score	1.0 (1.0–2.0)	1.5 (0.0–2.0)	1.0 (0.5–2.0)	1.0 (0.0–2.5)	1.0 (0.0–1.0)	0.0 (0.0–3.0)	0.816
Sepsis	17 (19.5)	10 (27.0)	7 (25.9)	9 (34.6)	1 (14.3)	2 (33.3)	0.636
Surgery	49 (56.3)	15 (40.5)	7 (25.9)	9 (34.6)	3 (42.9)	0 (0.0)	0.011*
TPN	40 (46.0)	15 (40.5)	15 (55.6)	8 (30.8)	2 (28.6)	2 (33.3)	0.474
Multifocal colonization	6 (6.9)	5 (13.5)	6 (22.2)	2 (7.7)	0 (0.0)	0 (0.0)	0.185
Antifungal-drug exposure							
Fluconazole	3 (3.4)	10 (27.0)	9 (33.3)	7 (26.9)	0 (0.0)	3 (50.0)	< 0.001***
Voriconazole	1 (1.1)	5 (13.5)	3 (11.1)	5 (19.2)	1 (14.3)	1 (16.7)	0.032*
Echinocandins	2 (2.3)	3 (8.1)	3 (11.1)	1 (3.8)	1 (14.3)	0 (0.0)	0.351
Amphotericin B	1 (1.1)	0 (0.0)	1 (3.7)	1 (3.8)	0 (0.0)	0 (0.0)	0.769
Sites							
Blood/CVC	54 (62.1)	34 (92.0)	23 (85.2)	19 (73.1)	4 (57.1)	4 (66.7)	0.011*

Continued

Risk factors	Candida species						P-value
	<i>C. albicans</i> (n = 87)	<i>C. parapsilosis</i> (n = 37)	<i>C. glabrata</i> (n = 27)	<i>C. tropicalis</i> (n = 26)	<i>C. krusei</i> (n = 7)	Others (n = 6)	
Drainage	20 (23.0)	1 (2.7)	2 (7.4)	5 (19.2)	3 (42.9)	1 (16.7)	0.025 [*]
CSF	8 (9.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.078
Other puncture fluids	5 (5.7)	2 (5.4)	2 (7.4)	4 (15.4)	1 (14.3)	1 (16.7)	0.562
Bone	2 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.793
90-day all-cause mortality ^a	22 (28.9)	9 (25.7)	11 (45.8)	9 (40.9)	1 (25.0)	1 (20.0)	0.507

Note. Normally distributed variables are presented with mean±standard deviation and compared using two-tailed student *t*-tests; Non-normally distributed variables are presented with median (interquartile range) and compared using one-way ANOVA; Categorical variables are presented with the patient number (percentage, %) and compared using chi-squared tests. Other *Candida* species in this table include *Candida inconspicua*, *Candida kefyr*, *Candida lipolytica*, *Candida carpophila*, *Candida guilliermondii*. Mixed infection with two *Candida* species were analyzed in both *Candida* species groups, thus the total number of isolates in this table was 190. ^aMortality data were available in 159 episodes including 76 episodes of *C. albicans* infection and 83 episodes of *C. non-albicans* infection. Abbreviations: CVC: Central venous catheter; CSF: Cerebrospinal fluid; TPN: Total parenteral nutrition. ^{*}*P* < 0.05; ^{**}*P* < 0.01; ^{***}*P* < 0.001.

Supplementary Table S4. *In vitro* resistance of the 212 yeast isolates to five antifungal agents in this study

Candida spp. (n = 208) ^a	Drug resistance					Non-wild type				
	FCZ (%)	VCZ (%)	AMB (%)	MICA (%)	CAS (%)	FCZ (%)	VCZ (%)	AMB (%)	MICA (%)	CAS (%)
<i>C. albicans</i> (n = 98)	4 (4.1)	3 (3.1)	–	3 (3.1)	1 (1.0)	–	–	0 (0.0)	–	–
<i>C. parapsilosis</i> (n = 44)	1 (2.3)	0 (0.0)	–	0 (0.0)	0 (0.0)	–	–	0 (0.0)	–	–
<i>C. glabrata</i> (n = 29)	7 (24.1)	–	–	3 (10.3)	3 (10.3)	–	17 (58.6)	0 (0.0)	–	–
<i>C. tropicalis</i> (n = 27)	10 (37.0)	0 (0.0)	–	2 (7.4)	2 (7.4)	–	–	0 (0.0)	–	–
<i>C. krusei</i> (n = 8)	IR	0 (0.0)	–	0 (0.0)	0 (0.0)	IR	–	0 (0.0)	–	–
<i>C. guilliermondii</i> (n = 1)	–	–	–	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	–	–
<i>C. kefyr</i> (n = 1)	–	–	–	–	–	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note. Variables are presented as number (percentage). ^aFour other isolates are not shown in this table including *Candida lipolytica*, *Candida inconspicua* and *Candida carpophila*, since the reference cut-off value to determine resistance has not been established due to its rarity. Abbreviations: AMB: Amphotericin B; CAS: Caspofungin; FCZ: Fluconazole; IR: Intrinsic resistance; MICA: Micafungin; VCZ: Voriconazole.

Supplementary Table S5. Association between risk factors and 90-day all-cause mortality

Risk factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Male	0.84 (0.41–1.72)	0.632	0.79 (0.26–2.39)	0.674
Age	1.02 (1.01–1.04)	0.001 ^{**}	1.01 (0.99–1.03)	0.347
Hemoglobin < 80 g/L	0.92 (0.40–2.12)	0.844	0.78 (0.20–3.08)	0.720
Albumin < 25 g/L	1.32 (0.41–4.24)	0.645	1.12 (0.21–5.85)	0.893
Diabetes mellitus	2.00 (0.99–4.06)	0.053	1.76 (0.64–4.81)	0.273
Solid organ malignancies	1.25 (0.60–2.60)	0.543	2.07 (0.62–6.93)	0.239
Hematologic malignancies	1.25 (0.29–5.44)	0.767	44.29 (2.38–825.37)	0.011 [*]
Neutropenia	1.03 (0.25–4.29)	0.967	38.31 (2.07–709.75)	0.014 [*]
Organ failure	8.86 (3.66–21.44)	< 0.001 ^{***}	2.62 (0.48–14.27)	0.264

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Risk factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Heart failure	4.63 (2.21–9.67)	< 0.001 ^{***}	3.62 (1.18–11.10)	0.025 [*]
Respiratory failure	6.90 (3.31–14.38)	< 0.001 ^{***}	7.13 (1.94–26.21)	0.003 ^{**}
Renal failure	4.54 (2.14–9.63)	< 0.001 ^{***}	2.40 (0.79–7.30)	0.122
Hepatic failure	0.87 (0.22–3.53)	0.851	1.01 (0.15–6.64)	0.994
Other deep-seated bacterial infection	2.13 (1.08–4.22)	0.009 ^{**}	0.31 (0.09–1.02)	0.054
Pancreatitis	0.68 (0.07–6.70)	0.741	0.14 (0.01–2.70)	0.191
Digestive tract perforation	1.52 (0.46–5.04)	0.494	13.02 (1.46–116.29)	0.022 [*]
Iatrogenic factors				
Long-term hospitalization (≥ 90 days)	1.66 (0.79–3.57)	0.195	0.12 (0.03–0.58)	0.006 ^{**}
ICU	2.02 (1.04–3.97)	0.039 [*]	1.28 (0.44–3.72)	0.656
Hemodialysis	1.37 (0.77–2.42)	0.287	0.48 (0.17–1.18)	0.104
Long-term use of broad-spectrum antibiotics	3.43 (1.71–6.85)	< 0.001 ^{***}	5.30 (1.55–18.08)	0.008 ^{**}
FCZ exposure	2.49 (1.10–5.60)	0.028 [*]	0.99 (0.23–4.17)	0.989
Corticosteroids/ immunosuppressant	0.91 (0.27–3.10)	0.877	1.76 (0.29–10.83)	0.543
Central venous catheter	0.88 (0.44–1.76)	0.719	0.12 (0.03–0.55)	0.006 ^{**}
Mechanical ventilation	3.05 (1.52–6.10)	0.002 ^{**}	0.71 (0.19–2.59)	0.602
<i>Candida</i> Score	1.44 (1.08–1.92)	0.013 [*]	1.43 (0.95–2.13)	0.084
Sepsis	2.67 (1.26–5.65)	0.011 [*]	1.25 (0.39–4.00)	0.709
Surgery	0.58 (0.29–1.15)	0.121	1.16 (0.35–3.87)	0.811
Gastrointestinal surgery	0.76 (0.36–1.58)	0.459	1.70 (0.40–7.20)	0.470
TPN	1.89 (0.96–3.71)	0.064	3.30 (1.18–9.22)	0.023 [*]
Multifocal colonization	2.28 (0.85–6.14)	0.103	0.77 (0.17–3.40)	0.728
Initial treatment				
FCZ	1 (reference)		1 (reference)	
VCZ	0.80 (0.20–3.20)	0.757	1.04 (0.12–9.34)	0.970
CAS	2.98 (1.07–8.31)	0.037 [*]	3.02 (0.47–19.38)	0.243
MICA	3.45 (1.14–10.38)	0.028 [*]	7.36 (1.20–45.02)	0.031 [*]
Main treatment				
FCZ	1 (reference)		1 (reference)	
VCZ	3.83 (1.11–13.30)	0.034 [*]	2.05 (0.25–17.02)	0.382
AMB	1.10 (0.20–6.05)	0.917	0.52 (0.05–5.20)	0.576
CAS	3.29 (1.09–9.88)	0.034 [*]	0.83 (0.12–5.85)	0.852
MICA	2.46 (0.73–8.31)	0.146	0.52 (0.06–4.70)	0.561
Echinocandins + Azoles	2.74 (0.72–10.34)	0.137	1.60 (0.14–18.35)	0.382
Amphotericin B + Azoles	1.53 (0.13–18.13)	0.734	25.10 (1.47–429.67)	0.026 [*]

Note. 159 episodes with mortality data were included in the analysis. Abbreviations: AMB: Amphotericin B; CAS: Caspofungin; FCZ: Fluconazole; ICU: Intensive care units; MICA: Micafungin; OR: Odds ratio; TPN: Total parenteral nutrition; VCZ: Voriconazole; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Supplementary Table S6. Information for patients who did not receive systematic antifungal drugs

Infected sites	Survived (n = 20)		Died (n = 8)		Missing outcome (n = 3)
	n	comments	n	comments	
Blood related (n = 15)	10		4		1
Blood (n = 10)	6	1. One patient acquired candidemia after surgery and recovered after changing a CVC. 2–4. Three patients acquired candidemia after surgery (two of the three received toe amputation for diabetic foot). However, no clinical abnormality was recorded in relation to fungal sepsis. 5. One patient re-admitted for renal abscess 20 days later, but culture for the abscess was negative for <i>Candida</i> species. 6. One patient was considered as acute abdomen induced candidemia and recovered after surgery.	3	1–2. Two patients gave up and both died four days later; 3. One patient died on the day when the culture result was obtained one day later.	1
CVC (n = 1)	1	1. The infection was hemodialysis-related and was cured by extubation.	0		0
Blood+CVC (n = 4)	3	1–3. Three patients acquired candidemia after surgery and recovered after extubation.	1	1. One patient gave up and died 18 days later;	0
Drains (n = 10)	6		3		1
Drainage after surgery (n = 5)	4	1–2. No clinical abnormality was recorded in these two patients regarding the intra-abdominal IC. 3–4. Two patients with acute abdomen (one perforation and one ileus) recovered after surgery.	0		1
Abscess (n = 3)	1	1. One patient with an abdominal abscess recovered after effective drainage.	2	1. One patient with a subcutaneous abscess recovered from antibiotics (Metronidazole) but died from STEMI afterwards. 2. One patient with an abdominal abscess died 12 days later.	0
Bile (n = 2)	1	1. The patient was diagnosed as acute cholecystitis and recovered after surgery and drainage.	1	1. The patient died before the culture results came back.	0
CSF (n = 1)	1	1. The original culture of CSF in this patient was negative while enrichment culture was positive for <i>Candida</i> species. Thus, the patient was not considered IC clinically.	0		0
Other fluids (n = 5)	3	1. One patient with infection in synovial fluid recovered after TKA surgery. 2. One patient with encapsulated pleural effusion recovered after effective drainage. 3. One patient with a tracheo-esophageal fistula recovered after drainage.	1	1. The patient did not add antifungal agents due to his hepatic failure, and died nine days later.	1

Note. There were 31 patients in this studies who did not receive any systematic antifungal drugs and were not included when comparing the drug effectiveness. The details for these patients, including their infected sites and other local treatment are listed below. Abbreviations: CSF: Cerebrospinal fluid; CVC: Central venous catheter; STEMI: ST-segment elevation myocardial infarction; TKA: Total knee arthroplasty.