



ORIGINAL ARTICLE

Comparison of epidemiology and treatment outcome of patients with candidemia at a teaching hospital in Northern Taiwan, in 2002 and 2010



Pao-Yu Chen^{a,b}, Yu-Chung Chuang^{a,b}, Jann-Tay Wang^{a,b},
Wang-Huei Sheng^{a,b}, Chung-Jen Yu^{a,c,d}, Chen-Chen Chu^e,
Po-Ren Hsueh^{a,f}, Shan-Chwen Chang^{a,b,c}, Yee-Chun Chen^{a,b,c,*}

^a Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

^b Center for Infection Control, National Taiwan University Hospital, Taipei, Taiwan

^c Department of Medicine, National Taiwan University, College of Medicine, Taipei, Taiwan

^d Medical Information Management Office, National Taiwan University Hospital, Taipei, Taiwan

^e Department of Pharmacy, National Taiwan University Hospital, Taipei, Taiwan

^f Department of Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan

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KEYWORDS

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Background: The incidence of candidemia varied between hospitals and different study periods. Few, if any, studies provide the reasons. This hospital-based population study aimed to describe and compare the patient population hospitalized in 2002 and 2010 and determine the disease-specific incidences of candidemia and evaluate the impact of time to initiate anti-fungal therapy on 30-day mortality.

Patients and methods: All patients hospitalized at a 2300-bed teaching hospital in Taiwan in 2002 and 2010 were analyzed for the distribution of age, sex, and type of underlying diseases (maximum of six diagnoses). All patients with blood isolates that were collected in 2002 and 2010 and yielded *Candida* species were included for analysis of the demographic and clinical characteristics, distribution of *Candida* species, length of hospital stay before candidemia, stay in the intensive care units at onset of candidemia, time of initiating systemic antifungal agent, antifungal regimen, and 30-day crude mortality.

Results: In 2010, the hospitalized patients were older ($p < 0.001$), had a higher Charlson Comorbidity Index ($p < 0.001$), and more underlying disease/status, including chronic pulmonary

* Corresponding author. Department of Internal Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei 10016, Taiwan.

E-mail address: yeechunchen@gmail.com (Y.-C. Chen).

diseases, moderate-to-severe renal diseases, leukemia, lymphoma, and gastrointestinal malignancies ($p < 0.001$) than those seen in 2002. Multivariate analysis identified the following host factors were associated with the occurrence of candidemia in 2010: neonate (adjusted odds ratio [OR], 3.67), 45–64 year (OR, 2.18) and the elderly (OR 2.64), compared with young adult (20–44 year); patients with moderate-to-severe renal diseases (OR, 8.08), leukemia (OR, 4.58) and lymphoma (OR 3.98) and gastrointestinal malignancies (OR 2.80). The incidence density of candidemia was 0.34 and 0.41 per 1000 patient-days in 2002 and 2010, respectively ($p = 0.04$). The majority of characteristics of patients with candidemia and disease-specific incidences of candidemia did not differ between 2002 and 2010. Despite more patients in 2010 receiving antifungal therapy on the same day or 1 day after onset (27.5% vs. 41.2%, respectively, $p = 0.002$), the 30-day mortality remained high (45.9% in 2002 and 44.4% in 2010). Moreover, time to initiate antifungal therapy had no impact on 30-day mortality.

Conclusion: This hospital-based population study demonstrated that the incidence density of candidemia was high and increased in 2010 compared with 2002, which was at least in part due to the increase in the proportion of patients at a higher risk of candidemia. Although antifungal therapy was initiated earlier in 2010, the 30-day mortality remained high.

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Introduction

Candida species are important pathogens causing healthcare-associated infections and are associated with high mortality, excess lengths of hospital stay, and medical

costs.^{1,2} A nation-wide surveillance data in Taiwan showed that *Candida* species was the leading pathogens of healthcare-associated infections in the intensive care units (ICUs) of the medical centers and ranked second in regional hospitals in 2010.³ The incidence of bloodstream

Table 1 Characteristics of patients hospitalized at National Taiwan University Hospital in 2002 and 2010

Parameters	2002	2010	<i>p</i> value
Number of acute care beds	2200	2300	—
Total number of admissions	66,763	79,710	—
Total number of patient-days	632,318	691,692	—
Age, y	47.3 ± 23.6	51.2 ± 22.9	<0.001
Sex, male (%)	34,514 (54.58)	39,669 (57.35)	<0.001
Charlson Comorbidity Index	2.10 ± 3.45	3.18 ± 4.33	<0.001
Underlying disease/status, <i>n</i> (%)			
Congestive heart failure	1264 (18.93)	2595 (32.56)	<0.001
Cerebrovascular diseases	3230 (48.38)	3682 (46.19)	0.04
Chronic pulmonary diseases	2629 (39.38)	3372 (42.30)	0.005
Connective tissue diseases	828 (12.40)	2002 (25.12)	<0.001
Moderate-to-severe liver diseases	4076 (61.05)	3302 (41.43)	<0.001
Moderate-to-severe renal diseases	3568 (53.44)	3063 (38.43)	<0.001
Diabetes mellitus without end organ damage	5447 (81.59)	10,530 (132.10)	<0.001
Diabetes mellitus with end organ damage	918 (13.75)	1177 (14.77)	0.10
Any tumor ^a	13,330 (199.66)	26,312 (330.10)	<0.001
Lymphoma	865 (12.96)	1776 (22.28)	<0.001
Leukemia	1186 (17.76)	1779 (22.32)	<0.001
Gastrointestinal malignancy ^b	1250 (18.72)	3377 (42.37)	<0.001
Metastatic solid tumor	4451 (66.67)	10,090 (126.58)	<0.001
Acquired immunodeficiency syndrome	260 (3.89)	346 (4.34)	0.19
Neutropenia	909 (13.62)	1231 (15.44)	0.004
Solid organ transplantation (kidney, liver, heart, pancreas)	392 (5.87)	662 (8.31)	<0.001
Hematopoietic stem cell transplantation	29 (0.43)	106 (1.00)	<0.001
Incidence density of candidemia (per 1000 patient-days)	218 (0.34)	286 (0.41)	0.04

^a Any tumor is defined as any solid malignancy excluding gastrointestinal malignancy, metastatic malignancy, leukemia and lymphoma.

^b Gastrointestinal malignancy indicates malignancies involving any part of the following organs: esophagus, stomach, small or large intestines, and rectum.

infections with fungi (especially *Candida* species) has increased substantially during recent decades.^{4–7} The potential reasons include increase in patient population at risk, and more extensive use of invasive procedures and devices, broad-spectrum antimicrobial agents, advanced life-support, and aggressive chemotherapy. The incidence of candidemia varies between countries, patient populations, and study periods.^{4–7} The incidence of candidemia in a multicenter study of healthcare-associated bloodstream infection in Taiwan varied widely between hospitals, and the highest incidence was observed in a cancer center.⁷

In a hospital-wide surveillance study we observed an average of 15.0% increase annually in incidence of healthcare-associated bloodstream infection during 1981 and 2007,⁶ and *Candida* species have become the leading healthcare-associated bloodstream pathogens since 1993.⁸ A prospective observational study during 1994 and 1995 showed high incidences of candidemia in surgical and medical intensive care units and hemato-oncology units (9.4, 6.3 and 2.4 per 1000 discharges, respectively), and no antifungal therapy was an independent factor associated with mortality.⁹ Since then, we adopted empirical antifungal therapy for high-risk patients using either amphotericin B or fluconazole.¹⁰

In a recent study, we observed a significant increase of hospitalized patients with neoplasms from 22.0% during January 1999 and March 2004 to 31.7% during April 2004 and December 2007.¹¹ Therefore, we retrospectively analyzed the hospital-wide prospective surveillance data at this 2300-bed teaching hospital in Taiwan and aimed to describe and compare the patient population hospitalized in 2002 and 2010 and determine the disease-specific incidences of candidemia, as well as evaluate the impact of time to initiate antifungal therapy on 30-day mortality.

Patients and methods

Hospital setting and infection control surveillance program

National Taiwan University Hospital (NTUH) is a 2300-bed major teaching hospital in Taiwan that provides both primary and tertiary medical care. Prospective, hospital-wide on-site surveillance of Healthcare-associated infections (HAIs) had begun since 1981, and it was conducted by weekly visits of full-time infection control nurses to all patient units. The clinical and microbiologic data of all hospitalized patients were reviewed, healthcare-associated infections were defined according to the definitions provided by the U.S. Centers for Disease Control and Prevention,^{12,13} and relevant information were collected.⁶

There was no cluster of *Candida* colonization or infection documented during the study period. Besides, a previous active microbial surveillance study conducted during 1996–1997 when the incidence of invasive candidiasis increased rapidly at NTUH showed that *Candida* colonization was common in adult patients stayed in the intensive care units (ICUs).¹⁴ In addition, molecular epidemiologic study based on pulse-field gel electrophoresis findings did not identify cross-transmission between these patients.¹⁴

Data collection or sources

All patients hospitalized at NTUH in 2002 and 2010 were analyzed for the distribution of age, sex, type of underlying diseases, and source of patients (from outpatient clinics, emergence services, or transfer from other hospitals). Underlying diseases, comprising a maximum of six diseases, were recorded and classified according to International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes, which were coded by Medical Information Management personnel when patients were discharged from the hospital.

All patients with blood isolates which were collected in 2002 and 2010 and yielded *Candida* spp. were included for analysis of the demographic and clinical characteristics, distribution of *Candida* species, length of hospital stay before and after onset of candidemia, ICU stay at the onset of candidemia, use of antifungal agent, time of initiating systemic antifungal agent, antifungal regimen, and 30-day crude mortality and in-hospital mortality. We did not record the therapeutic factors other than antimicrobial agents (such as parenteral nutrition, indwelling central lines) and delayed complications after discharge due to candidemia. The laboratory methods for blood culture,

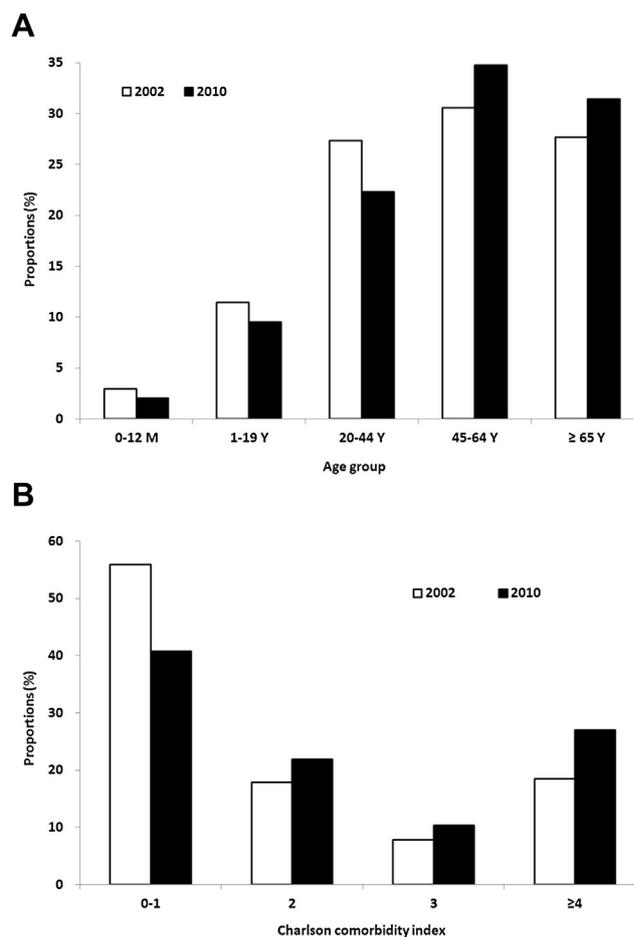


Figure 1. Distribution of patients hospitalized at the National Taiwan University Hospital in 2002 and 2010 by (A) age group; and (B) Charlson Comorbidity Index. The proportions in each age group or Charlson Comorbidity Index changed significantly ($p < 0.001$) as compared with those in 2002 and in 2010.

Candida spp. identification and antimicrobial susceptibility were described previously.^{15,16}

Antifungal strategy

We adopted empirical antifungal therapy for high-risk patients using either amphotericin B or fluconazole¹³ as a series of studies showed clinical isolates of *Candida* spp. collected at NTUH remained highly susceptible to fluconazole and amphotericin B.^{10,17,18} Besides, Golan et al demonstrated that empirical fluconazole therapy was the most cost-effective strategy for ICU patients with high risks for candidemia if fluconazole resistance rate was low.¹⁹ Antifungal prophylaxis was limited to allogeneic hematopoietic stem cell transplant recipients using fluconazole¹⁹ or micafungin (since 2008).

Definitions

The severity of underlying diseases, comprising a maximum of six diseases, was scored using the Charlson Comorbidity

Index.²⁰ *Candida* colonization was defined as any *Candida* isolated from any decision-driven clinical specimens collected from the patients in the preceding 1 month of candidemia. The timing to initiate antifungal therapy was determined as the date to initiate antifungal agents following the date when the first *Candida*-positive blood sample for culture was drawn (Day 0). We segregated these times as being on the same calendar day, 1 day later, 2 days later, 3 days or more days later. No treatment was defined as no systemic antifungal agents used during hospitalization after the onset of candidemia. Breakthrough candidemia indicated the patients had been on systemic antifungal agents at the time when the first *Candida*-positive blood sample for culture was drawn.

Statistical analysis

The difference in patient population and patients with candidemia during the two study periods was examined using Student's t-test (continuous variables) and a chi-squared test (categorical variables). The incidences of

Table 2 Risk factors of patients who developed candidemia in 2010 by characteristics

Parameters	Univariate analysis				Multivariate analysis			
	Odds ratio	95% confidence interval		p value	Odds ratio	95% confidence interval		p value
		Lower	Upper			Lower	Upper	
Age								
0–12 mo	2.54	1.04	6.17	0.04	3.67	1.50	8.97	0.004
1–19 y	1.08	0.54	2.14	0.82	1.07	0.54	2.13	0.85
20–44 y (as reference)								
45–64 y	2.65	1.73	4.07	<0.001	2.18	1.42	3.30	<0.001
≥65 y	3.70	2.43	5.64	<0.001	2.64	1.72	4.06	<0.001
Sex, male								
	1.48	1.17	1.88	0.001				
Charlson Comorbidity Index								
0–1 (as reference)								
2	2.57	1.68	3.92	<0.001				
3	3.94	2.49	6.21	<0.001				
≥4	6.62	4.63	9.47	<0.001				
Underlying diseases/status								
Congestive heart failure	2.24	1.42	3.54	0.001				
Cerebrovascular diseases	1.39	0.86	2.24	0.18				
Chronic pulmonary diseases	2.27	1.52	3.41	<0.001	1.90	1.25	2.89	0.003
Connective tissue diseases	1.12	0.55	2.26	0.76				
Moderate-to-severe liver diseases	1.37	0.83	2.28	0.22				
Moderate-to-severe renal diseases	8.76	6.70	11.46	<0.001	8.08	6.11	10.67	<0.001
Diabetes mellitus without end organ damage	1.46	1.08	1.98	0.01				
Diabetes mellitus with end organ damage	0.95	0.35	2.55	0.92				
Any tumor	1.16	0.91	1.48	0.23				
Lymphoma	3.33	2.11	5.25	<0.001	3.98	2.49	6.35	<0.001
Leukemia	3.68	2.38	5.71	<0.001	4.58	2.90	7.23	<0.001
Gastrointestinal malignancy	3.93	2.83	5.46	<0.001	2.80	1.93	4.05	<0.001
Metastatic solid tumor	2.51	1.93	3.26	<0.001	2.32	1.72	3.14	<0.001
Neutropenia	3.06	1.75	5.35	<0.001				
Acquired immunodeficiency syndrome	2.44	0.78	7.66	0.12				
Solid organ transplant (kidney, liver, heart, pancreas)	1.70	0.63	4.57	0.29				

patients with candidemia by age group, Charlson Comorbidity Index, and underlying diseases were compared by Poisson regression analyses.⁶ As regards to the risk factors of candidemia, the univariate analyses were undertaken using logistic regression. All variables significant at $p < 0.05$ in univariate analyses were considered as possible predictor variables for the multivariable analyses, which was performed by stepwise logistic regression. However, Charlson Comorbidity Index were not included in multivariate analyses model because of collinearity with underlying diseases. All statistical tests were considered two-tailed and were significant at $p < 0.05$. Statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC, USA).

Ethics statement

We followed the principles expressed in the Declaration of Helsinki. This study was approved by the Institutional Ethics Review Board of the National Taiwan University Hospital (NTUH-201204058RIC).

Results

Patient population

The characteristics of patients hospitalized in 2002 and 2010 are summarized in Table 1. In 2010, age ($p < 0.001$), Charlson Comorbidity Index ($p < 0.001$), and proportions of

most underlying illness including chronic pulmonary diseases, moderate-to-severe renal diseases, leukemia, lymphoma and gastrointestinal malignancies significantly increased ($p < 0.001$) compared with those in 2002. The distribution of all hospitalized patients by age groups and Charlson Comorbidity Index are shown in Fig. 1A and Fig. 1B. The proportions in each age group or Charlson Comorbidity Index changed significantly ($p < 0.001$) as compared with those in 2002 and in 2010. In 2010 more than one third of our patient populations had one or more neoplasms.

Candida species distribution

There were 218 and 286 patients who had candidemia during hospitalization in 2002 and 2010, respectively. The distributions of *Candida* species were similar in these two study periods ($p = 0.26$). The most common species were *C. albicans* (55.0% in 2002 vs. 53.2% in 2010), followed by *C. tropicalis* (20.2% vs. 23.1%), *C. glabrata* (15.6% vs. 18.5%), and *C. parapsilosis* (14.2% vs. 9.1%).

Risk factors of candidemia

The risk factors of candidemia among patients hospitalized in 2010 are shown in Table 2. By univariate analysis, odds ratios were higher in patients with extreme of age and higher Charlson Comorbidity Index. Multivariate logistic

Table 3 Comparison of characteristics of patients with candidemia and disease-specific incidence in 2002 and 2010

Parameters	2002 (n = 218)	2010 (n = 286)	p value
Characteristics			
Age, y	56.7 ± 23.1	60.3 ± 19.9	0.07
Sex, male, n (%)	130 (59.6)	170 (59.4)	0.96
Charlson Comorbidity Index	5.38 ± 5.77	5.66 ± 5.39	0.56
Prior <i>Candida</i> colonization within 1 month, n (%)	89 (40.8)	131 (45.8)	0.03
Prior antibiotics use within 1 month, n (%)	203 (93.1)	279 (97.6)	0.02
Prior antifungal agents use within 1 month, n (%)	179 (82.1)	254 (88.8)	0.03
Length of hospital stay before onset, d	35.6 ± 54.4	25.8 ± 29.8	0.02
Intensive care unit onset, n (%)	66 (30.3)	87 (30.4)	0.25
Disease-specific incidence (per 1000 admissions)			
Congestive heart failure	10 (7.91)	20 (7.71)	>0.99
Cerebrovascular diseases	22 (6.81)	18 (4.89)	0.37
Chronic pulmonary diseases	22 (8.37)	26 (7.71)	0.89
Connective tissue diseases	2 (2.42)	8 (4.00)	0.81
Moderate-to-severe liver diseases	20 (4.91)	16 (4.85)	>0.99
Moderate-to-severe renal diseases	54 (15.13)	73 (23.83)	0.01
Diabetes mellitus without end organ damage	21 (3.86)	52 (4.94)	0.41
Diabetes mellitus with end organ damage	3 (3.27)	4 (3.40)	>0.99
Any tumor	52 (3.90)	104 (3.95)	>0.99
Lymphoma	11 (12.72)	20 (16.99)	0.56
Leukemia	17 (14.33)	22 (12.37)	0.76
Gastrointestinal malignancy	36 (28.80)	42 (12.44)	<0.001
Metastatic solid tumor	53 (11.91)	76 (7.53)	0.01
Neutropenia	11 (11.54)	13 (8.67)	>0.99
Acquired immunodeficiency syndrome	3 (12.10)	3 (10.56)	0.89
Solid organ transplantation (kidney, liver, heart, pancreas)	2 (5.10)	4 (6.04)	>0.99
Hematopoietic stem cell transplantation	0 (0.00)	0 (0.00)	—

analysis, chronic pulmonary diseases, moderate-to-severe renal disease, leukemia, lymphoma, gastrointestinal malignancies and metastatic malignancies were significant predictors of candidemia.

Characteristics of patients with candidemia

The demographic and clinical characteristics of the patients with candidemia are shown in Table 3. The proportions of prior antibiotics or antifungal use within one month were high and both increased significantly in 2010 than those in 2002 ($p = 0.02$ and $p = 0.03$, respectively). Length of hospital stay before onset of candidemia was shorter by 10 days in 2010 ($p = 0.02$).

The incidences of candidemia were 2.78 per 1000 admissions in 2002 and 2.88 per 1000 admissions in 2010 ($p = 0.71$). The incidence density was 0.34 and 0.41 per 1000 patient-days ($p = 0.04$), respectively. The incidences of patients with candidemia per 1000 admissions in each age group and Charlson Comorbidity Index are shown in Fig. 2A and Fig. 2B. There was no difference between these two study years. The disease-specific incidences of patients with candidemia increased among patients with moderate-to-severe renal diseases ($p = 0.01$), but decreased among those with gastrointestinal malignancy ($p < 0.001$), and metastatic malignancy ($p = 0.01$) in 2010 (Table 3).

Antifungal therapy and outcomes evaluation

As shown in Table 4,² there was considerable variation in the time to initiate antifungal therapy in 2002 and 2010, and the most significant difference was more patients received antifungal therapy one day later in 2010 (18.8% in 2002 vs. 30.4% in 2010, $p = 0.003$). Antifungal therapy was prescribed in 185 (84.9%) patients in 2002 and in 256 (89.5%) patients in 2010. Choice of the first antifungal agent showed uprising trend of fluconazole use ($p = 0.02$) and declining trend in amphotericin deoxycholate use ($p = 0.03$). In 2002, no echinocandins were used due to not yet approval for candidemia in Taiwan. With regard to outcome, the 30-day mortality was 45.9% in 2002 and 44.4% in 2010 ($p = 0.74$). The outcome was not better for those treated earlier. The mortality was highest among those received antifungal therapy one day later in 2002 (56.1%), and among those with breakthrough candidemia in 2010 (52.2%).

Discussion

This hospital-based population study demonstrated that the incidence density of candidemia increased in 2010 comparing to that in 2002. The reason for this trend, at least in part, was due to the increase in the proportion of patients at higher risk of candidemia (Table 1, Fig. 1) including older patients, and patients with chronic pulmonary diseases, leukemia, lymphoma, gastrointestinal malignancies, and metastatic solid tumors (Table 2). However, the majority of age group-specific and disease-specific incidences of candidemia did not change significantly (Table 3, Fig. 2). Although more patients in 2010 were treated earlier (Table 4), the 30-day mortality rate

remained high and time to initiating antifungal therapy had no impact on 30-day mortality.

In this study we showed the incidence density of candidemia up to 0.34 to 0.41 per 1,000 patient-days in 2002 and 2010, respectively, were higher than those in the United States, Europe, and Australia,^{5,21–26} and were comparative to those in Latin America^{27,28} and a recent study in a medical center in Taiwan.²⁹ A multicenter study involving 11 teaching hospitals in Taiwan also showed relatively high incidences of healthcare-associated candidemia compared with those worldwide.¹⁰ However, few if any study providing data to explain this variation between hospitals/countries/regions or time trends. In 2010 more than one-third of our patient populations had one or more neoplasms. Thus, composition of patient populations should be taken into consideration when comparing disease burden between hospitals or study periods.

Few population level studies provided age group-specific or underlying disease/status-specific incidences of candidemia.^{30–33} With these data available, it is possible that the disease burden can be adjusted and compared between hospitals and study periods. In addition, we could predict

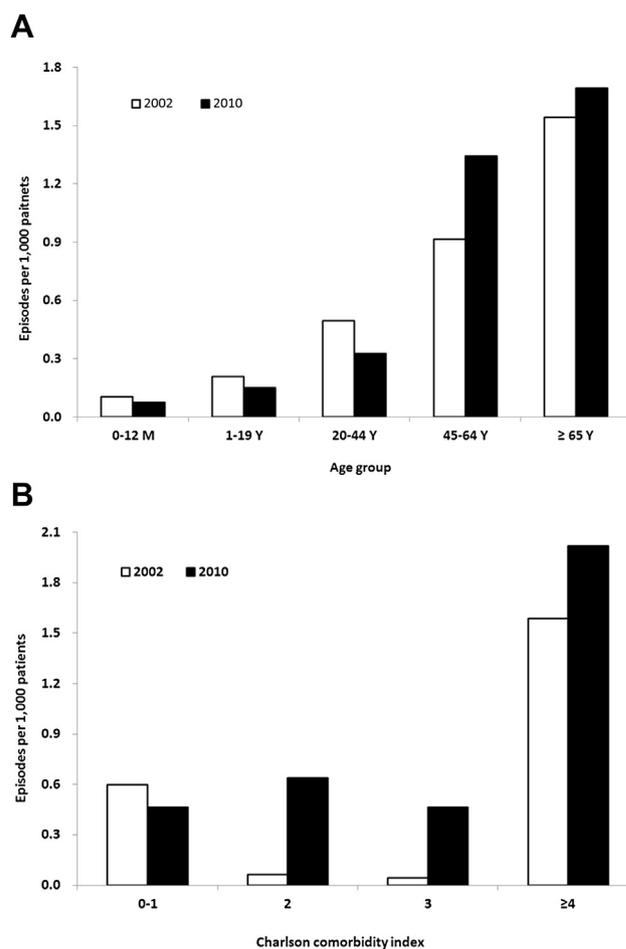


Figure 2. Incidences of candidemia (per 1000 admissions) among patients hospitalized at National Taiwan University Hospital in 2002 and 2010 by (A) age group and (B) Charlson Comorbidity Index. There was no difference between these two study years.

Table 4 Comparison of antifungal therapy and outcome for patients with candidemia in 2002 and 2010

	2002 (n = 218)	2010 (n = 286)	p value
Time to initiation of antifungal therapy			
Same day	19 (8.72)	31 (10.84)	0.43
1 d later	41 (18.81)	87 (30.42)	0.003
2 d later	33 (15.14)	44 (15.38)	0.94
≥3 d later	38 (17.43)	35 (12.24)	0.10
No treatment	33 (15.14)	30 (10.49)	0.12
Breakthrough candidemia	54 (24.77)	59 (20.63)	0.27
First antifungal agent	185 (84.86)	256 (89.51)	0.12
Fluconazole ^a	162 (87.57)	242 (94.53)	0.009
Voriconazole ^a	0 (0.00)	1 (0.39)	>0.99
Amphotericin B ^a	18 (9.73)	5 (1.95)	<0.001
Lipid formulation amphotericin B ^a	1 (0.54)	0 (0.00)	0.42
Echinocandins ^a	0 (0.00)	6 (2.34)	0.04
Combination therapy ^a	4 (2.16)	2 (0.78)	0.24
30-day mortality	100 (45.87)	127 (44.41)	0.74
Same day ^b	7/19 (36.84)	14/31 (45.16)	0.56
1 d later ^b	23/41 (56.10)	35/87 (40.23)	0.09
2 d later ^b	15/33 (45.45)	16/44 (36.36)	0.42
≥3 d later ^b	12/38 (31.58)	11/35 (31.43)	0.99
No treatment ^b	13/33 (39.39)	20/30 (66.67)	0.03
Breakthrough candidemia ^b	30/54 (55.56)	31/59 (52.54)	0.75

^a Percentage by proportion of total patients receiving antifungal therapy.

^b Mortality stratified by time to initiate antifungal therapy.

time trends of incidences based on the composition of patient populations in order to make decision regarding antifungal strategy or to evaluate the impact of intervention targeting for preventing infection.

The high-risk patient population for of candidemia included neonate, the elderly, patients with moderate-to-severe renal diseases, gastrointestinal malignancies, or hematologic malignancies. These findings are consistent with those described in review articles.^{34–36} In this study there was no candidemia occurring among hematopoietic stem cell transplantation recipients, which support the success of antifungal prophylaxis before engraftment.

In this study we observed an unanticipated finding that timing of initiating antifungal agent had no impact on 30-day mortality. This finding was concordant to two recent reports^{37,38} but differed from others.^{39,40} As to this discrepancy, severity of illness, such as the Acute Physiology and Chronic Health Evaluation (APACHE) II score, should be taken into consideration. APACHE II score has been a well-known independent predictor of mortality, which might confound the impact of earlier initiating antifungal therapy on mortality.⁴¹ Furthermore, more patients in 2010 received antifungal therapy on one day later, which might reflect the effect of continuous education for our physicians to identify patients at risk and implement empirical strategy. In addition, the outcome was worse among patients without antifungal therapy in 2010 than those in 2002, probably because the majority of them died before confirmation of the diagnosis.

Although this population study provides robust information from epidemiological perspectives, there are several limitations. First, this study did not provide information regarding invasive procedure to adjust the disease-specific

incidence. Second, the lack of APACHE II score in this study might lead to more prudent interpretation of the impact of timing of initiating antifungal therapy on mortality. Third, the underlying diseases were retrieved from ICD-9 CM codes of discharge diagnosis and limited to six. Thus, disease-specific incidences might be underestimated or overestimated. Furthermore, this is a single-center study with study periods limited to 2002 and 2010.

In conclusion, this hospital-based population study demonstrated that the incidence density (and incidence) of candidemia was high and increased in 2010 compared with 2002, which, at least in part, was due to the increase in the proportion of patients at higher risk of candidemia. The 30-day mortality remained high in 2010, which is even earlier initiation of antifungal therapy.

Conflicts of interest

All authors declare that they have no conflicts of interest related to the material discussed in this article.

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