

BACKGROUND

- Echinocandins are often used as initial antifungal therapy for the treatment of candidemia with eventual de-escalation (DE) to oral azoles based on clinical response and susceptibilities¹
- Currently, there are no universally accepted DE criteria, but rapid diagnostic testing (RDT) allows for earlier *Candida* sp. identification²
- At NewYork-Presbyterian Hospital (NYPH), fluconazole-susceptible *Candida* sp. are rapidly identified using BioFire® Blood Culture Identification Panels
- Objective:** To compare outcomes between early DE (≤ 2 days) and late DE (> 2 days) from an echinocandin to an oral azole using RDT as an antifungal stewardship strategy

METHODS

Design: Retrospective cohort study of adult patients with an azole-susceptible candidemia from January 2017 to June 2021

Inclusion criteria

- Positive blood culture for *C. albicans*, *C. tropicalis*, or *C. parapsilosis*
- At least one dose of micafungin followed by at least two consecutive days of treatment with micafungin or fluconazole

Exclusion criteria

- Infection caused by *Candida* sp. without evidence of source control
- Osteomyelitis endocarditis, meningitis, or endophthalmitis due to *Candida* sp.
- Switch to another systemic antifungal agent following DE to an azole
- Neutropenia, defined as an absolute neutrophil count of < 1000 cells/mm³
- Patients requiring hospice or comfort care during treatment

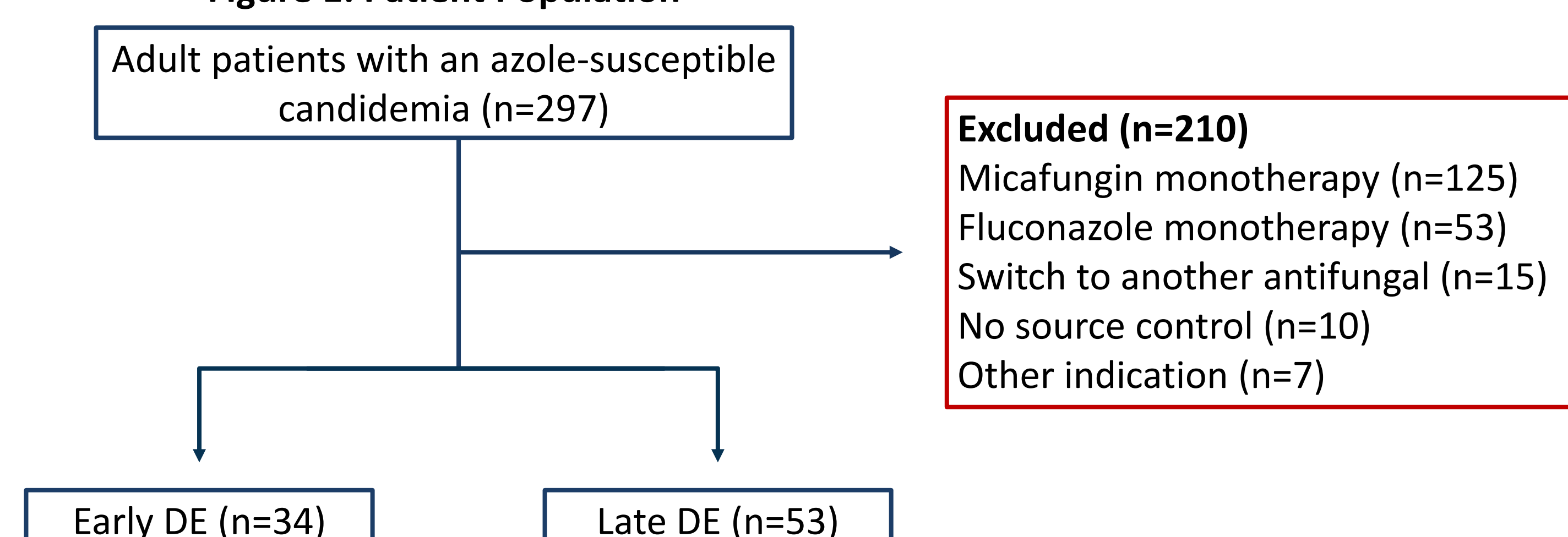
Primary outcome

- Global response at 30 days (clinical and microbiological success with survival)

Secondary outcomes

- Clinical success and microbiological success at end of treatment
- Length of stay after candidemia
- Recurrence of infection within 30 days of treatment
- Development of echinocandin or azole resistance during and/or within 90 days of treatment
- 30-day mortality

Figure 1: Patient Population



RESULTS

Table 1: Demographic Characteristics

	Early DE (n=34)	Late DE (n=53)	p-value
Male	20 (58.8)	32 (60.4)	1.000
Age (years), median (IQR)	66 (43-73)	64 (50-73)	0.879
SARS-CoV-2	3 (8.8)	4 (7.5)	1.000
Length of stay prior to candidemia (days), median (IQR)	9 (0-21)	9 (2-23)	0.497
Charlson comorbidity index	4 (2-5)	4 (2-6)	0.569
Comorbidities			
Chronic kidney disease	2 (5.9)	6 (11.3)	0.474
Diabetes	10 (29.4)	14 (26.4)	0.953
Liver disease	1 (2.9)	5 (9.4)	0.397
Malignancy	4 (11.8)	12 (22.6)	0.262
Campus			
Columbia	22 (64.7)	22 (41.5)	0.059
Cornell	12 (35.3)	31 (58.5)	

All values reported as n (%) unless otherwise specified; IQR: interquartile range

Table 2: Clinical Characteristics at Time of Candidemia

	Early DE (n=34)	Late DE (n=53)	p-value
Type of <i>Candida</i> sp.			
<i>C. albicans</i>	15 (44.1)	32 (60.4)	0.283
<i>C. parapsilosis</i>	14 (41.2)	17 (32.1)	
<i>C. tropicalis</i>	5 (14.7)	4 (7.5)	
Duration of candidemia (days), median (IQR)	2 (1-3)	1 (1-3)	0.283
Source			
Urinary	6 (17.6)	4 (7.5)	0.216
CVC/PICC/midline	16 (47.1)	23 (43.4)	
Abdominal	0 (0.0)	2 (3.8)	
Unknown	12 (35.3)	20 (37.7)	
Other	0 (0.0)	4 (7.5)	
Intensive care unit	6 (17.6)	20 (37.7)	0.079
SOFA score, median (IQR)	1 (1-3)	2 (0-6)	0.262
Antifungal duration (days), median (IQR)	16 (13-17)	16 (14-28)	0.086
Mechanical ventilation	6 (17.6)	14 (26.4)	0.492
Total parenteral nutrition	7 (20.6)	13 (24.5)	0.869
Continuous renal replacement therapy	2 (5.9)	5 (9.4)	0.700
Central venous catheter	17 (50.0)	29 (54.7)	0.834
Surgical intervention	13 (38.2)	28 (52.8)	0.267
Immunosuppressive medications	9 (26.5)	15 (28.3)	1.000
Prosthetic material	13 (38.2)	16 (30.2)	0.587
Hemodynamic instability*	15 (44.1)	24 (45.3)	1.000

*Hemodynamic instability at time of DE assessed using SIRS criteria, defined as ≥ 2 of the following:

Temp $> 38^\circ\text{C}$ or $< 36^\circ\text{C}$, Heart rate > 90 bpm, Respiratory rate > 20 or PaCO₂ < 32 mmHg, WBC $> 12,000/\text{mm}^3$, $< 4,000/\text{mm}^3$, or $> 10\%$ bands

RESULTS

Figure 2: Primary Outcome, Global Response at Day 30

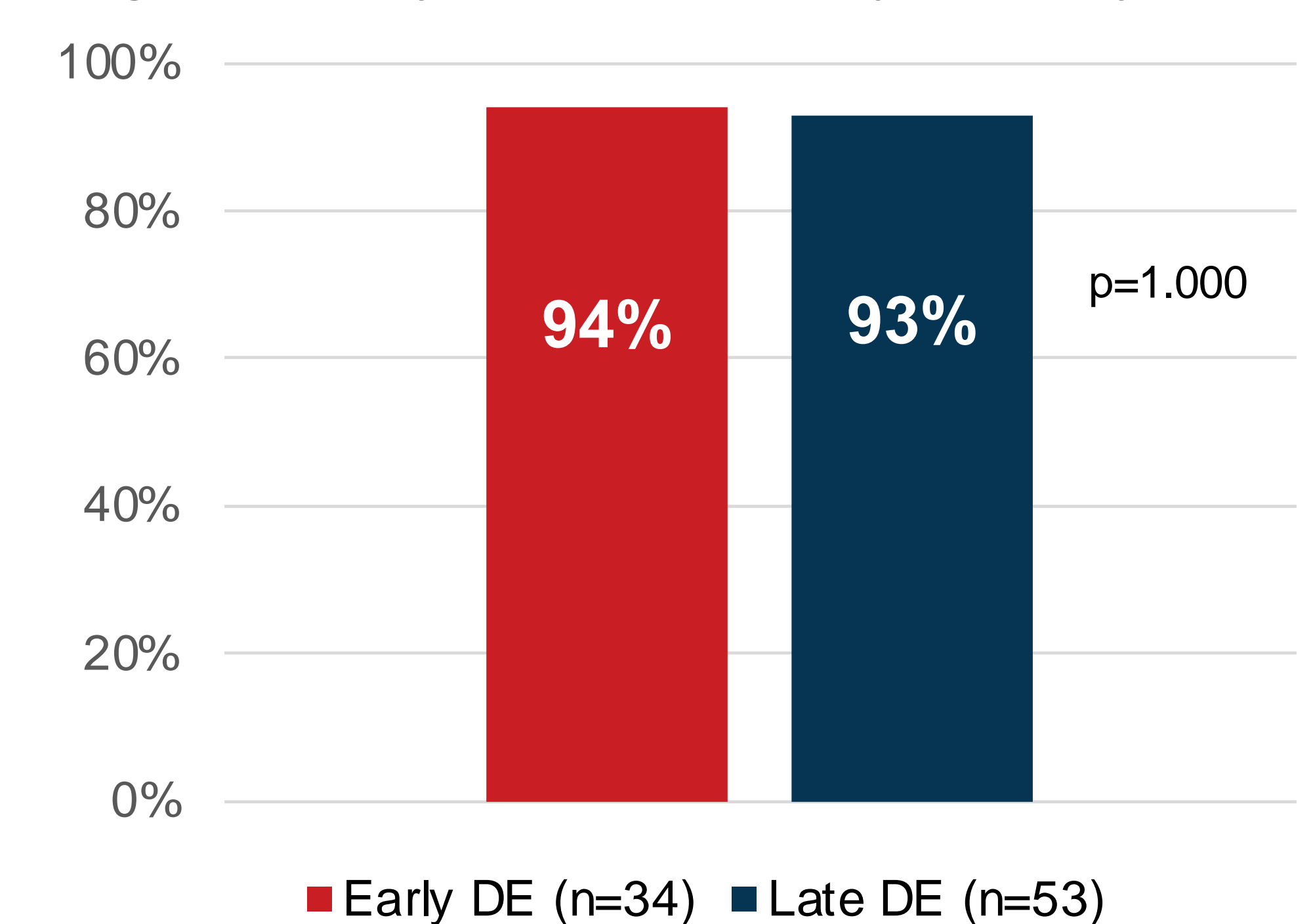


Table 3: Secondary Outcomes

	Early DE (n=34)	Late DE (n=53)	p-value
At end of treatment			
Clinical response	33 (97.1)	51 (96.2)	1.000
Microbiological response	33 (97.1)	53 (100)	0.822
LOS after candidemia (days), median (IQR)	15 (7-22)	14 (10-29)	0.300
30-day recurrence (different organism)	1 (2.9)	0 (0.0)	0.391
30-day mortality	1 (2.9)	3 (5.7)	1.000

All values reported as n (%) unless otherwise specified; LOS: length of stay

Table 4: Multivariable Analysis, Factors Associated with Global Response at Day 30

	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Late DE (> 2 days of micafungin)	0.766 (0.132, 4.427)	0.765	0.907 (0.096, 8.573)	0.932
Weill Cornell Campus	0.464 (0.080, 2.678)	0.391	0.299 (0.024, 3.676)	0.346
Age	0.925 (0.857, 0.999)	0.046	0.893 (0.792, 1.006)	0.063
LOS prior to candidemia	0.993 (0.965, 1.021)	0.607	0.986 (0.945, 1.029)	0.516
SARS-CoV-2 during hospitalization	0.052 (0.008, 0.344)	0.002	0.104 (0.006, 1.862)	0.124
SOFA score	0.820 (0.691, 0.972)	0.022	0.929 (0.669, 1.289)	0.658
CRRT	0.132 (0.019, 0.901)	0.039	0.160 (0.003, 7.987)	0.358

CRRT: continuous renal replacement therapy

DISCUSSION

- In non-neutropenic patients with azole-susceptible, uncomplicated candidemia, there were no differences in outcomes between early and late DE strategies
- Early DE within 2 days based on RDT should be considered as an antifungal stewardship strategy based on local susceptibilities
- SIRS criteria may be limited as a tool to assess hemodynamic instability to guide de-escalation practices
- Larger, prospective studies are needed to gain further understanding of the optimal duration of initial broad antifungal treatment

REFERENCES

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DISCLOSURES

The authors have nothing to disclose concerning financial or personal relationships with entities that may have an interest in this presentation