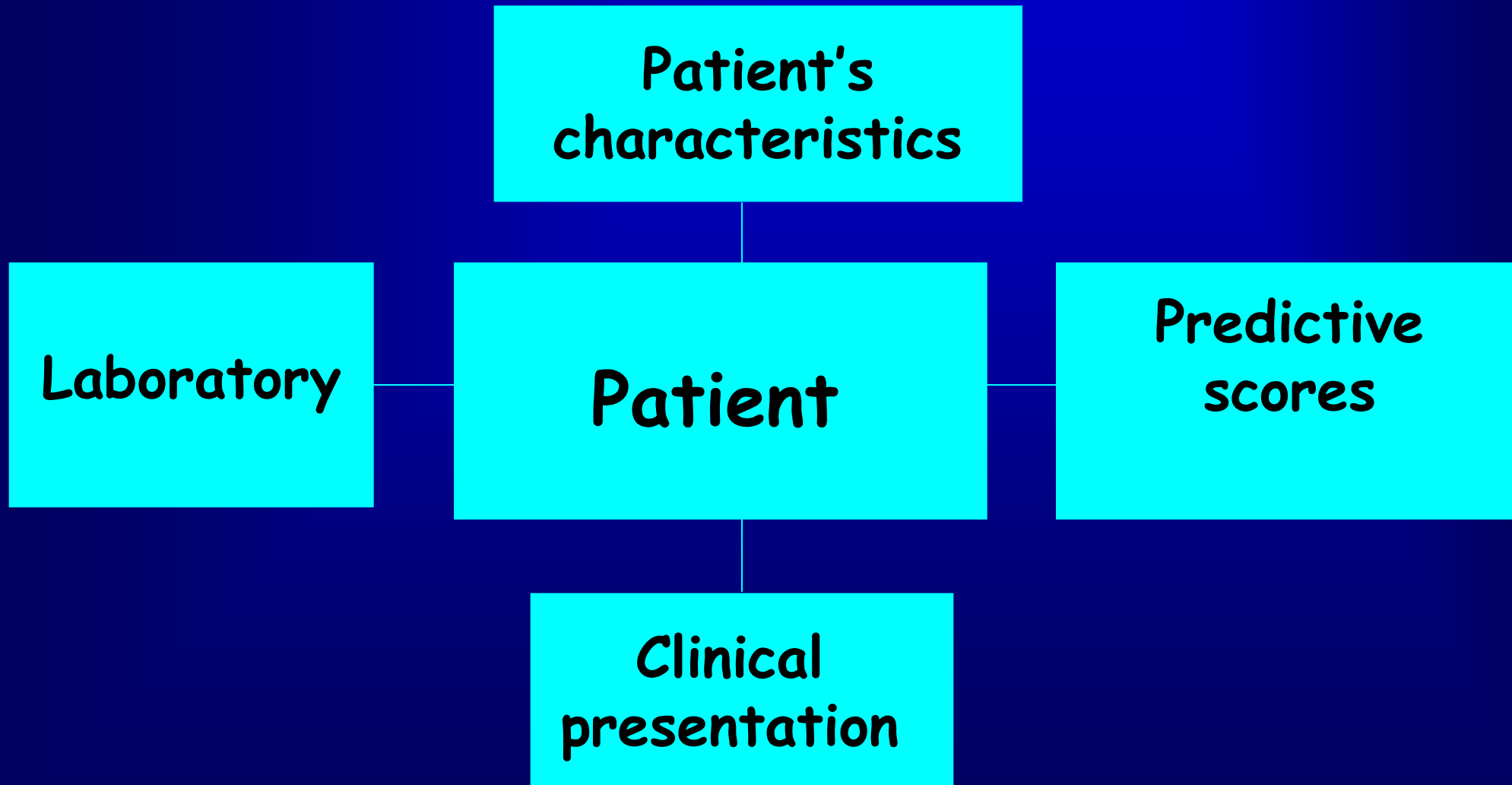# INFEZIONI FUNGINE E PERCORSI TERAPEUTICI IN ICU

Claudio Viscoli

Professor of Infectious Disease

University of Genoa

What I would like to discuss with you today
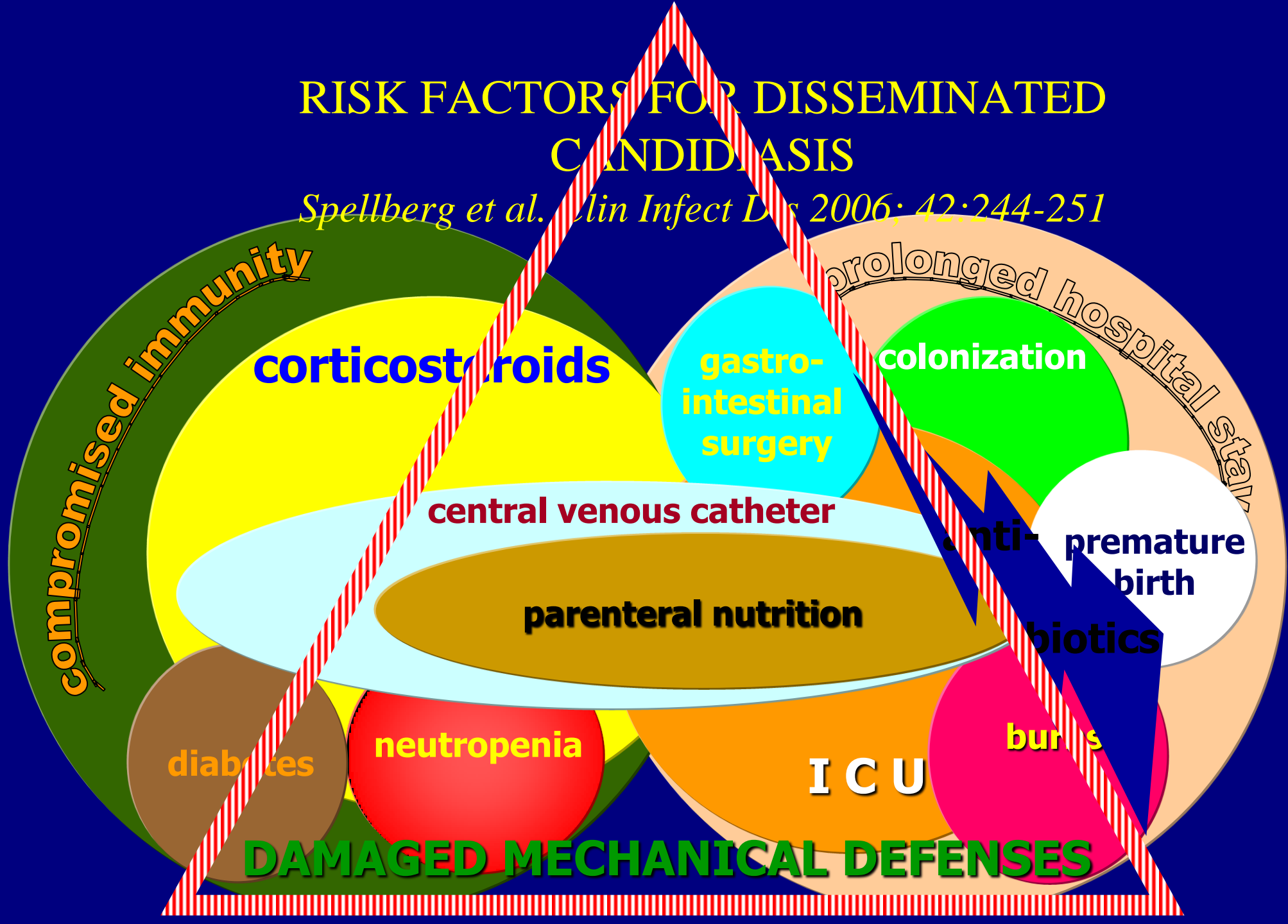
- – When to start an antifungal therapy (before symptoms? At symptoms? Upon documentation?)
- – What to give
- – What else to do
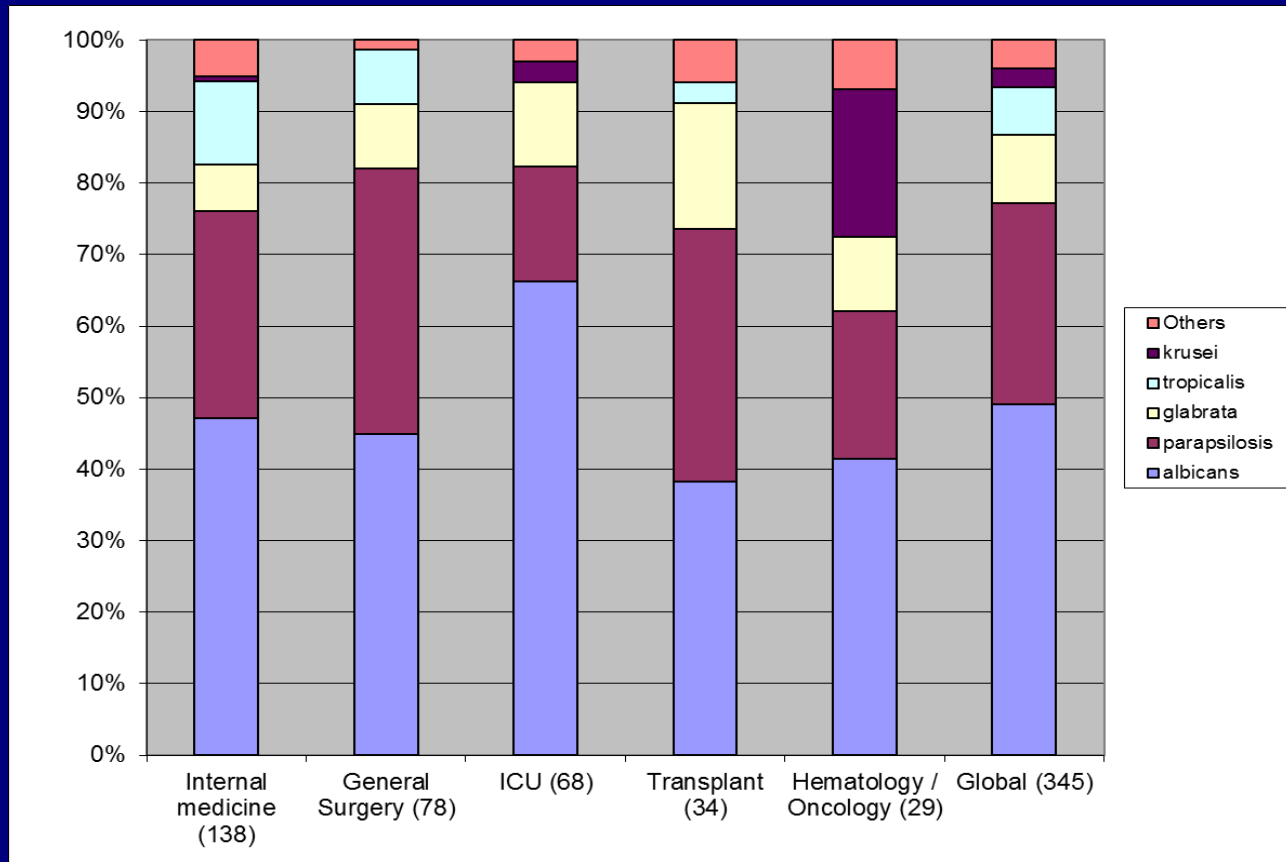
When to start: a comprehensive approach

Patient's characteristics

Laboratory

Patient

Predictive scores

Clinical presentation

RISK FACTORS FOR DISSEMINATED CANDIDIASIS

Spellberg et al. Clin Infect Dis 2006; 42:244-251

compromised immunity

prolonged hospital stay

corticosteroids

gastro-intestinal surgery

colonization

central venous catheter

anti-biotics

premature birth

parenteral nutrition

diabetes

neutropenia

I C U

burns

DAMAGED MECHANICAL DEFENSES

Candida distribution in hospital

# Caratteristiche cliniche di pazienti con candidemia

Area medica

> 70 aa, comorbidità (diabete, IRC, neoplasie) terapie (steroidi, antibiotici), ricoverato da almeno 14 gg

ICU

40-60 aa, intervento di chirurgia maggiore complicato, NPT, antibiotici, ricoverato da almeno 7 gg

When to start: a comprehensive approach

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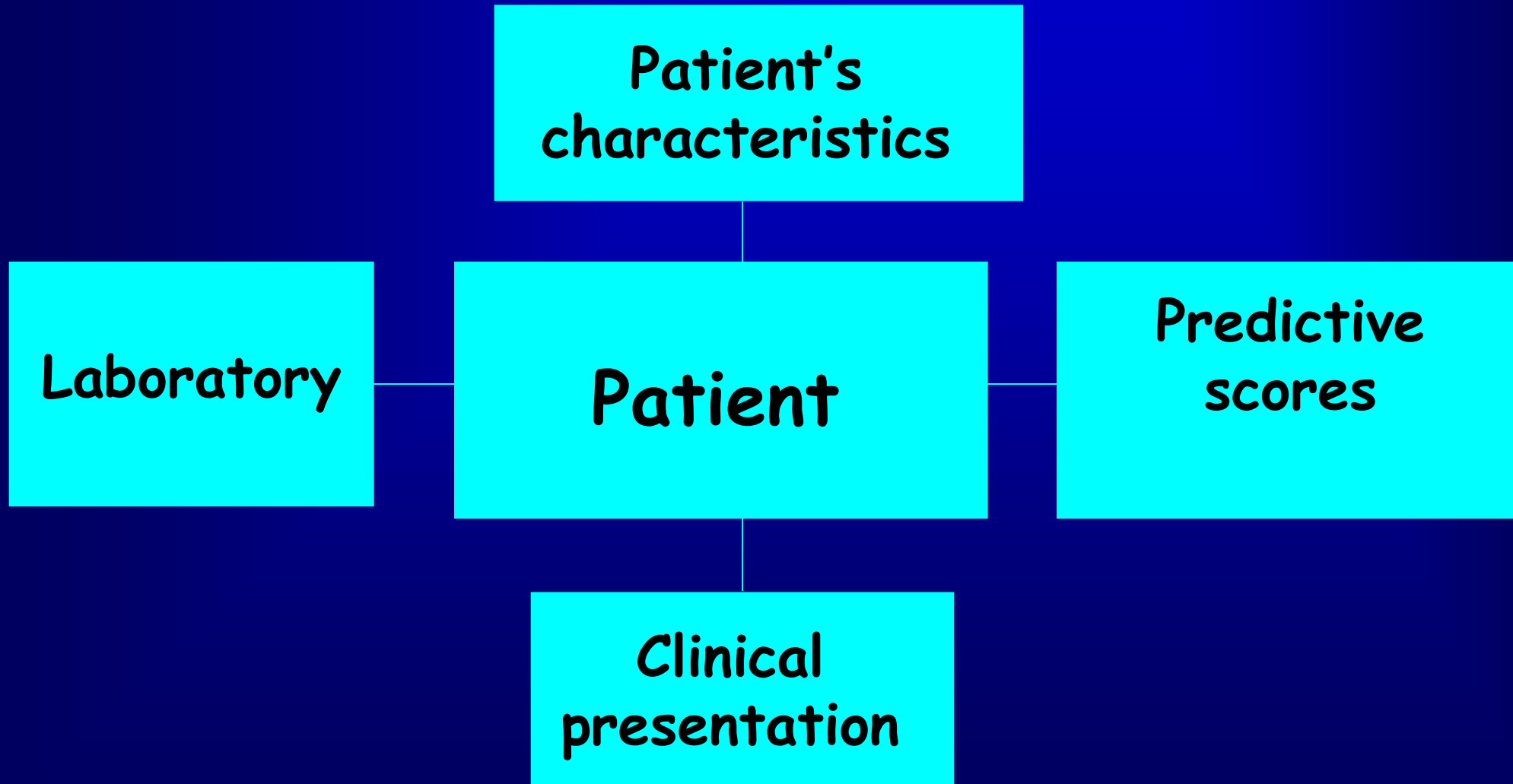
CONCISE ARTICLE

Multicenter retrospective development and validation of a clinical prediction rule for nosocomial invasive candidiasis in the intensive care setting

L. Ostrosky-Zeichner · C. Sable · J. Sobel ·
B. D. Alexander · G. Donowitz · V. Kan ·
C. A. Kauffman · D. Kett · R. A. Larsen · V. Morrison ·
M. Nucci · P. G. Pappas · M. E. Bradley · S. Major ·
L. Zimmer · D. Wallace · W. E. Dismukes · J. H. Rex

Study overview

Retrospective analysis of 2,890 medical and surgical ICU patients (stayed ≥4 days) to assess predictive factors for nosocomial invasive candidiasis

Overall incidence of invasive candidiasis, 3.0%

Rate of invasive candidiasis among patients meeting the rule, 9.9%

Rule captured 34% of cases of invasive candidiasis

Predictive rule

Patients in the ICU >4 days

       AND

Any systemic antibiotic (days 1–3)

       OR

Central venous catheter (days 1–3)

       AND

at least two among:

Total parenteral nutrition (days 1–3)
**Any dialysis (days 1–3)**
Major surgery (days -7–0)
Pancreatitis (days -7–0)
Any use of steroids (days -7–3)
Immunosuppressive agents (days -7–0)

MSG-01: A randomized, double-blind, placebo controlled trial of caspofungin prophylaxis followed by pre-emptive therapy for invasive candidiasis in high-risk adults in the critical care setting

Luis Ostrosky-Zeichner[1], Shmuel Shoham[2], Jose Vazquez[3], Annette Reboli[4], Robert Betts[5], Michelle A. Barron[6], Mindy Schuster[7], Marc A. Judson[8], Sanjay G. Revankar[9], Juan Pablo Caeiro[10], Julie E. Mangino[11], David Mushatt[12], Roger Bedimo[13], Alison Freifeld[14], Minh Hong Nguyen[15], Carol A. Kauffman[16], William E. Dismukes[17], Andrew O. Westfall[18], Jeanna Beth Deerman[19], Craig Wood[20], Jack D. Sobel[21], Peter G. Pappas[22]
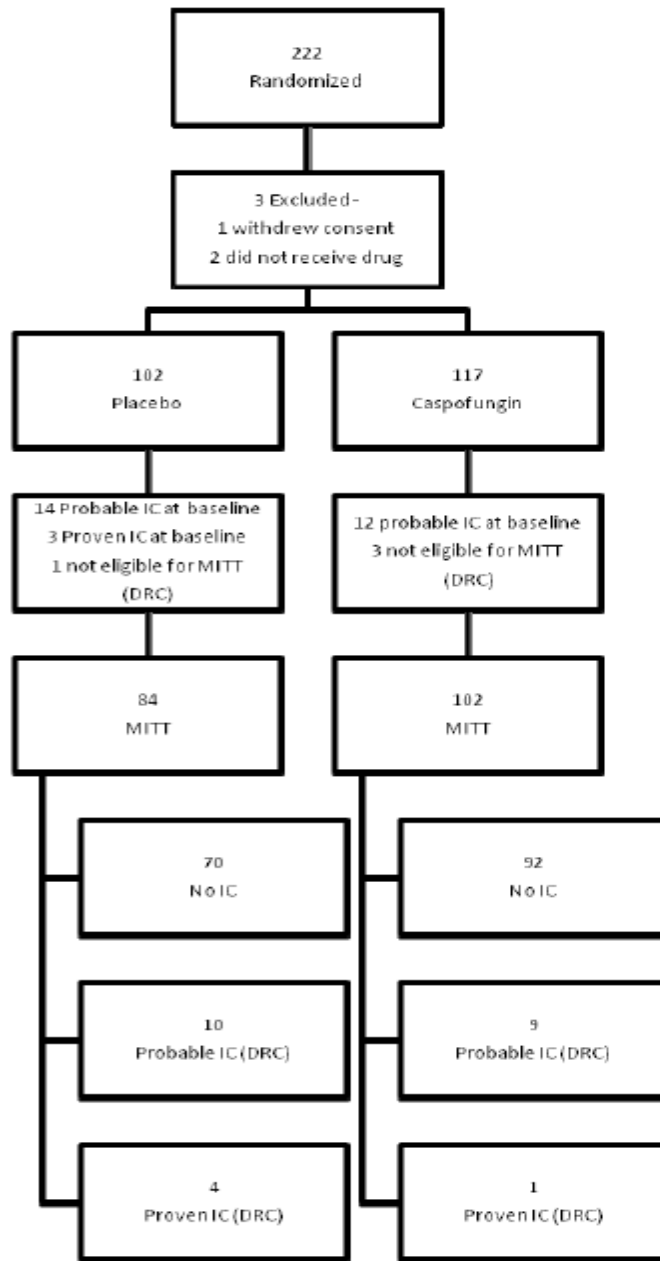
OUT of 16000 screened

A total of 29/219 patients
had candidemia at baseline

Table 3. Study endpoints and outcomes in ICU patients receiving caspofungin vs. placebo followed by pre-emptive therapy for invasive candidiasis.

Variable	Prophylaxis/MITT population		
	Caspofungin (n=102)	Placebo (n=84)	p value
Incidence of proven or probable IC by DRC (%)	9.8	16.7	0.14
Incidence of proven IC by DRC (%)	1.0	4.8	0.11
Use of antifungals within 7 days EOT (%)	13.7	17.9	0.35
All-cause mortality within 7 days EOT(%)	16.7	14.3	0.78

Table 3. Results of multivariate analysis: Risk factors for proven candidal infection in 1,669 adult patients

Variable	Proven Candidal Infection %	p Value	Crude Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)
Surgery on ICU admission				
No	6.9			
Yes	16.5	<.001	2.69 (1.76–4.10)	2.71 (1.45–5.06)
Total parenteral nutrition				
No	2.8			
Yes	15.5	<.001	6.46 (3.48–11.98)	2.48 (1.16–5.31)
Severe sepsis				
No	4.5			
Yes	28.8	<.001	8.63 (5.49–13.56)	7.68 (4.14–14.22)
Candida species colonization				
No	4.2			
Yes	12.3	<.001	3.20 (1.85–5.53)	3.04 (1.45–6.39)

Leon C. Crit Care Med, 2006

Candida Score

Predictive factor	Rounded risk score
Surgery	1
Multifocal colonisation*	1
Total parenteral nutrition	1
Severe sepsis	2

Cut-off value 2.5 (sensitivity 81%, specificity 74%) equates to sepsis plus any one of the three other remaining risk factors; or the presence of all of them together except sepsis.

*Colonisation was defined as the presence of *Candida* species in non-significant samples from the oropharynx, stomach, urine or tracheal aspirates. Colonisation was considered multifocal when *Candida* species were simultaneously isolated from various non-contiguous foci, even if two different *Candida* species were isolated.

Validation of candida score

- Prospective study
- 1107 pts. In 37 ICUs for 7 days

Table 4. Rates of invasive candidiasis according to the *Candida* score

Cutoff Value	Incidence Rate (%) (95% CI)	Relative Risk (95% CI)
<3	2.3 (1.1–3.5)	1
3	8.5 (4.2–12.7)	3.7 (1.8–7.7)
4	16.8 (9.7–23.9)	7.3 (3.7–14.5)
5	23.6 (12.4–34.9)	10.3 (5.0–21.0)

Table 5. *Candida* score vs. colonization index discriminatory power

	Candida Score ≥3 (95% CI)	Colonization Index ≥0.5 (95% CI)
Area under ROC curve	0.774 (0.715–0.832)	0.633 (0.557–0.709)
Sensitivity	77.6 (66.9–88.3)	72.4 (60.9–83.9)
Specificity	66.2 (63.0–69.4)	47.4 (44.0–50.8)
Predictive positive value	13.8 (10.0–17.5)	8.7 (6.2–11.3)
Predictive negative value	97.7 (96.4–98.9)	96.1 (94.2–98.0)
Relative risk for invasive candidiasis	5.98 (3.28–10.92)	2.24 (1.28–3.93)

Leon et al, Crit Care Med 2009

β-Glucan Antigenemia Anticipates Diagnosis of Blood Culture–Negative Intraabdominal Candidiasis

Frederic Tissot[1], Frederic Lamoth[1], Philippe M. Hauser[2], Christina Orasch[1,3], Ursula Flückiger[3], Martin Siegemund[4], Stefan Zimmerli[5], Thierry Calandra[1], Jacques Bille[2], Philippe Eggimann[6]*, Oscar Marchetti[1]*, and the Fungal Infection Network of Switzerland (FUNGINOS)

TABLE 1. PATIENT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS
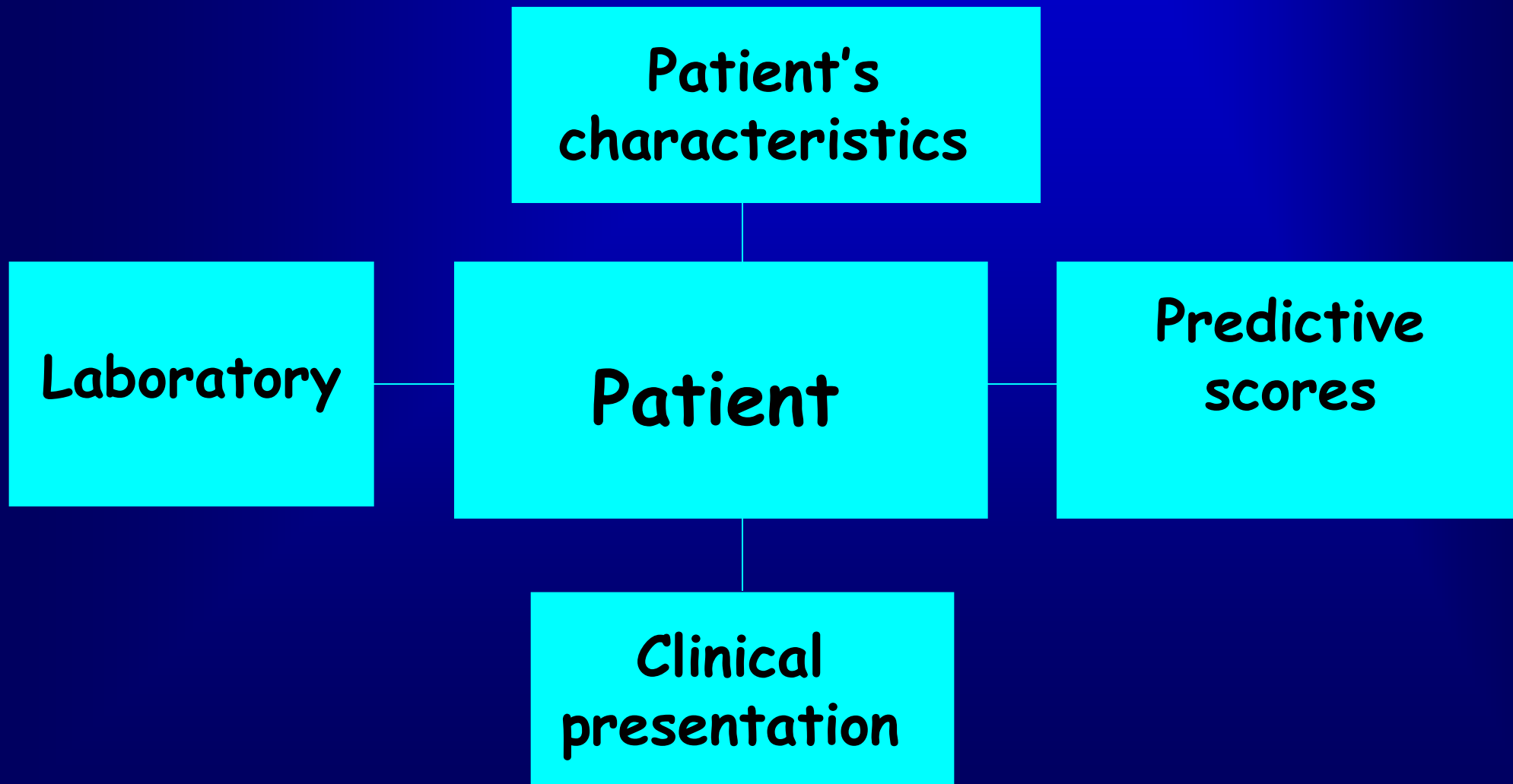
	Value (n = 89)
Sex, male/female	59 (66)/30 (34)
Age, median yr (range)	62 (22–86)
Primary diagnosis at ICU admission:	
Intraabdominal tumor	23 (26)
Intestinal ischemic disorder	20 (22)
Acute necrotizing pancreatitis	20 (22)
GI perforation	10 (11)
GI bleeding	5 (6)
Ruptured aneurysm of abdominal aorta	4 (4)
Others*	7 (8)
Inclusion criteria	
Recurrent GI tract perforation[†]	68 (76)
Acute necrotizing pancreatitis[‡]	21 (23)
Total hospital stay, median (range), d	44.5 (9–176)
Hospital stay before inclusion, median (range), d	8 (1–74)
Total ICU stay, median (range), d	13 (3–74)
ICU stay before inclusion, median (range), d	2 (0–54)
Abdominal surgery during study	78 (87)
No. of operations, median (range)	3 (0–9)
Sites of abdominal surgery during study (≥1 site/patient)	
Stomach	7 (8)
Small intestine	42 (47)
Colon	42 (47)
Biliary tract	18 (20)
Pancreas	17 (19)
Bacterial infections during study	
No. of patients	86 (97)
No. of episodes[§]	151
Severity at inclusion	
SAPS II, median (range)	51 (13–87)
APACHE II, median (range)	23 (5–37)
Severe sepsis or septic shock	50 (56)
Mortality	15 (17)

18

TABLE 2. RISK FACTORS FOR *Candida* COLONIZATION AND INFECTION

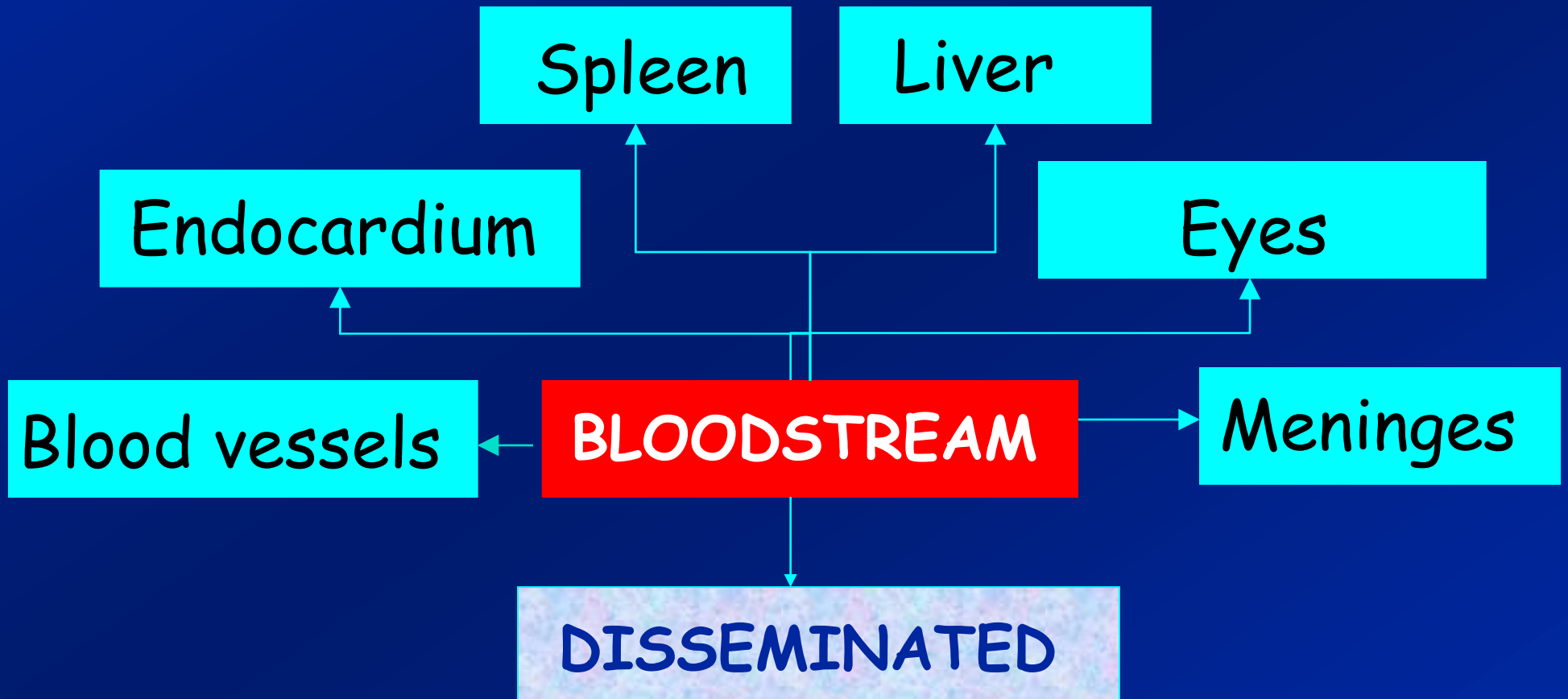|	Value (n = 89)
Risk factors for *Candida* infection at inclusion	
Central venous catheter	87 (98)
Proton-pump inhibitor	86 (97)
Urinary catheter	86 (97)
Total parenteral nutrition	84 (94)
Antibacterial therapy	77 (86)
Mechanical ventilation > 24 h	61 (68)
Renal replacement therapy: CRRT/intermittent HD	16/3 (21)
Immunosuppressive therapy*	6 (7)
Candida colonization	
Colonization at any site: at inclusion/during study	75 (84)/87 (98)
Colonization index ≥ 0.5: first wk/during study	51 (57)/71 (80)
Corrected colonization index ≥ 0.4: first wk/during study	34 (38)/49 (55)
Candida score ≥ 3: first wk/during study	44 (49)/78 (88)
Candida infection	
IAC	29 (33)
Pure culture from intraoperative specimens	7/29 (24)
Mixed-flora abscess	8/29 (27.5)
Mixed-flora peritonitis	14/29 (48.5)
Secondary candidemia	2/29 (7)
Median days from hospital admission to infection (range)	12 (0–74)
Median days from ICU admission to infection (range)	7 (0–70)
Candida species (≥1 isolate/patient)	
C. albicans	23/29 (79)
C. tropicalis	5/29 (17)
C. glabrata	3/29 (10)
C. kefyr	1/29 (3)
C. lusitaniae	1/29 (3)
Other non-*albicans* Candida species	1/29 (3)
Severity of *Candida* infection	
No sepsis, sepsis	2/29 (7), 12/29 (41)
Severe sepsis, septic shock	4/29 (14), 11/29 (38)
Mortality	5/29 (17)
Antifungal therapy	
All included patients (n = 89)	
No therapy	45 (51)
Preemptive therapy for suspected IAC	18 (20)
Therapy for documented infection	26 (29)
Patients with documented IAC (n = 29)	
Median days of therapy (range)	16 (4–48)
Antifungal agent (≥1 agent/patient)	
None	3/29 (6)
Fluconazole	26/29 (89)
Caspofungin (before or after fluconazole)	6/29 (12)

When to start: a comprehensive approach

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                    ┌─────────────────┐
                    │   Patient's     │
                    │ characteristics │
                    └────────┬────────┘
                             │
┌──────────────┐    ┌────────┴────────┐    ┌──────────────┐
│  Laboratory  │────│     Patient     │────│  Predictive  │
│              │    │                 │    │    scores    │
└──────────────┘    └────────┬────────┘    └──────────────┘
                             │
                    ┌────────┴────────┐
                    │    Clinical     │
                    │  presentation   │
                    └─────────────────┘
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When to start: a comprehensive approach

Patient's characteristics

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Patient

Predictive scores

Clinical presentation

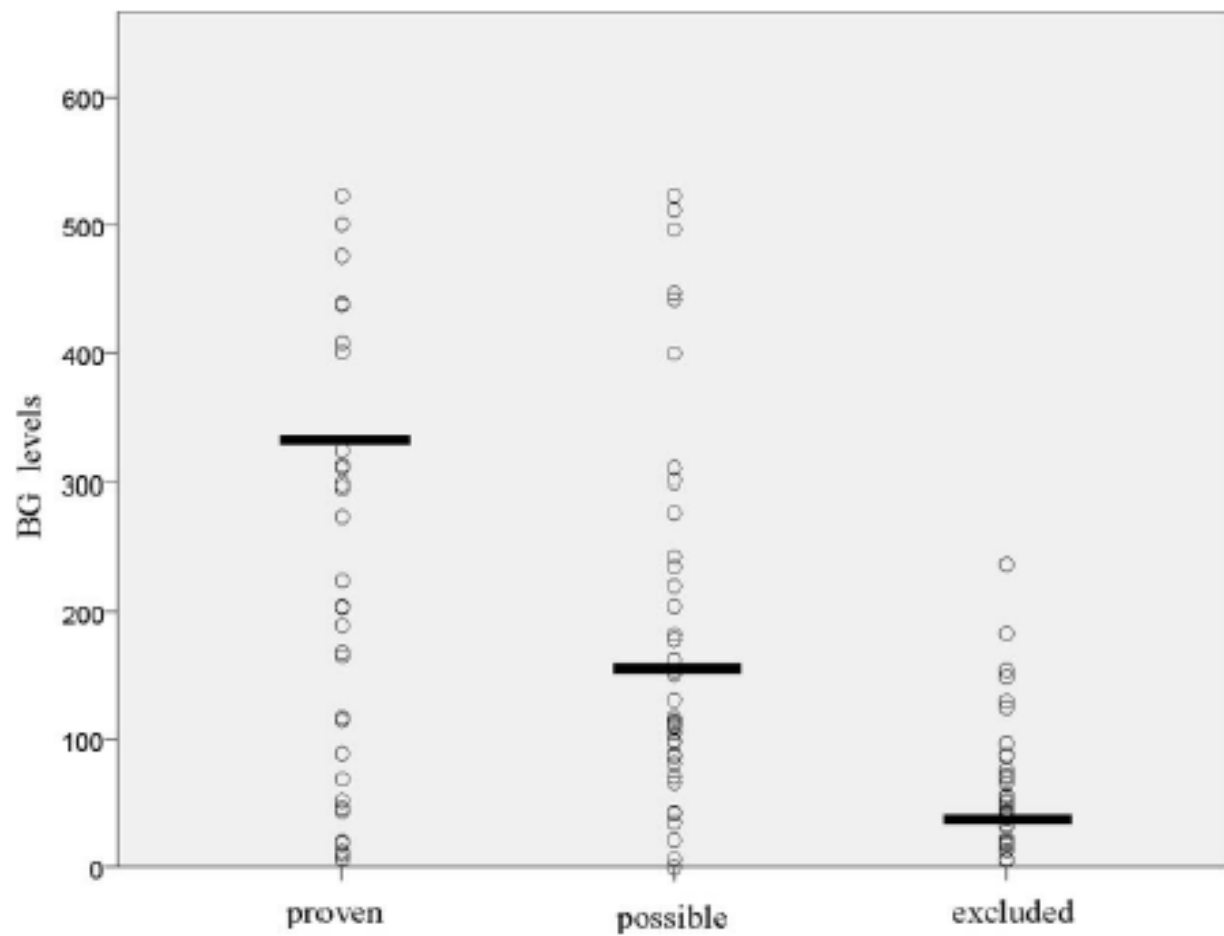# Clinical Performance of the (1,3)-β-D-Glucan Assay in Early Diagnosis of Nosocomial *Candida* Bloodstream Infections[▽]

Valerio Del Bono,[1*] Emanuele Delfino,[1] Elisa Furfaro,[1] Malgorzata Mikulska,[1] Elena Nicco,[1]
Paolo Bruzzi,[2] Alessandra Mularoni,[3] Matteo Bassetti,[4] and Claudio Viscoli[1]

TABLE 1. Demographic and clinical characteristics and BG levels of study patients

| Parameter	Value for group[a] with:			P
	Proven candidemia	Possible candidemia	Candidemia excluded	
No. of patients ($n = 152$)	53	47	52	NS
Median age, yr (range)	72 (35–88)	64 (18–88)	59.5 (19–92)	0.013
Gender (no. male/no. female)	27/26	27/20	32/20	NS
Median total hospital stay, days (range)	60 (11–398)	56 (9–600)	45 (10–268)	NS
Median days to BG assay[b] (range)	28 (4–182)	21 (3–398)	15.5 (3–187)	0.010
Median days to blood culture[c] (range)	27 (4–179)	NA[f]	NA	NA
No. (%) of patients with:				
ICU stay[d]	11 (20.7)	7 (14.9)	6 (11.5)	NS
Abdominal surgery	17 (32)	18 (38)	13 (21)	NS
Multifocal colonization[e]	38 (72)	25 (53)	19 (52)	<0.001
Positive BG test	41 (77)	38 (81)	9 (17)	<0.001
Median BG value, pg/ml (range)	324 (6–523)	162 (6–523)	27 (6–237)	<0.001
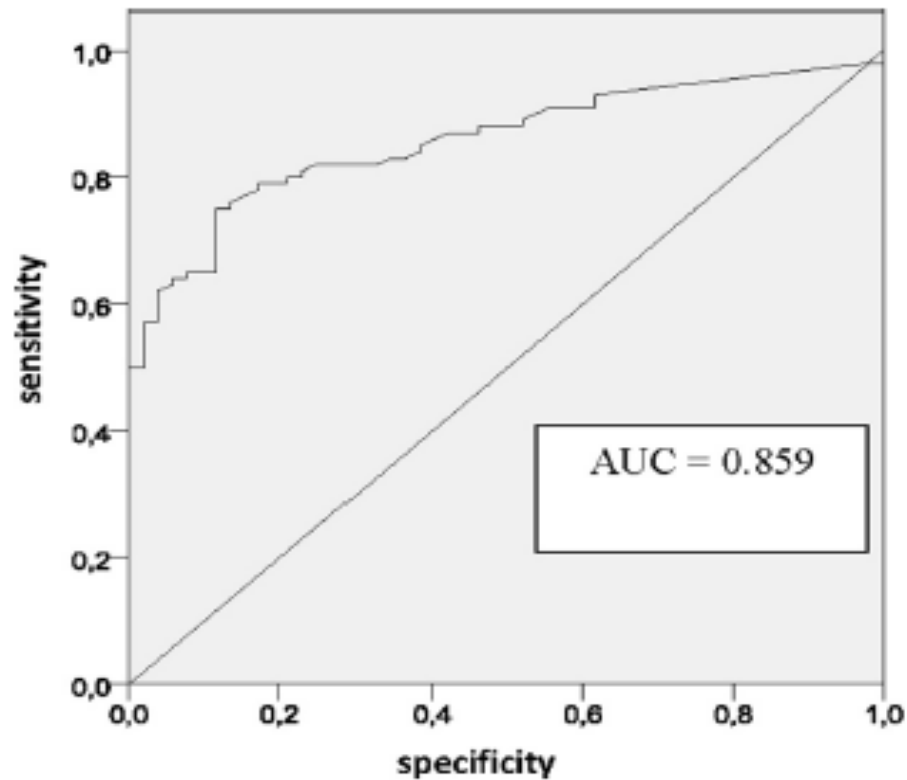
Sensibilità 79% specificità 83%

Clinical Performance of the (1,3)-β-D-Glucan Assay in Early Diagnosis of Nosocomial Candida Bloodstream Infections[∇]

Valerio Del Bono,[1]* Emanuele Delfino,[1] Elisa Furfaro,[1] Malgorzata Mikulska,[1] Elena Nicco,[1]
Paolo Bruzzi,[2] Alessandra Mularoni,[3] Matteo Bassetti,[4] and Claudio Viscoli[1]

TABLE 2. Sensitivity, specificity, PPV, and NPV of the BG assay at different cutoff levels

Cutoff (pg/ml)	No./total[a]		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	Above cutoff (cases)	Below cutoff (controls)				
>10	92/100	11/52	92	21	69.2	57.9
>20	89/100	25/52	89	48	76.7	69.4
>40	87/100	30/52	87	58	79.8	69.8
>60	82/100	39/52	82	75	86.3	68.4
>80	79/100	43/52	79	83	89.8	67.2
>100	73/100	46/52	73	88	92.4	63.0
>120	65/100	46/52	65	88	91.5	56.8
>140	64/100	48/52	64	92	94.1	57.1
>160	62/100	51/52	62	98	98.4	57.3

[a] Cases, patients with proven or possible candidemia; controls, patients with candidemia excluded.

In 36 out of 41 cases of proven candidemia with positive BG results, the BG assay was performed within 48 h from the day when blood for the first positive culture for *Candida* was drawn, thus potentially allowing for an earlier initiation of antifungal treatment. The timing of BG assay performance in these 36 cases was as follows: in 7 cases before day 0 (day of blood culture sampling), in 12 on day 0, and in 17 between days 1 and 2.
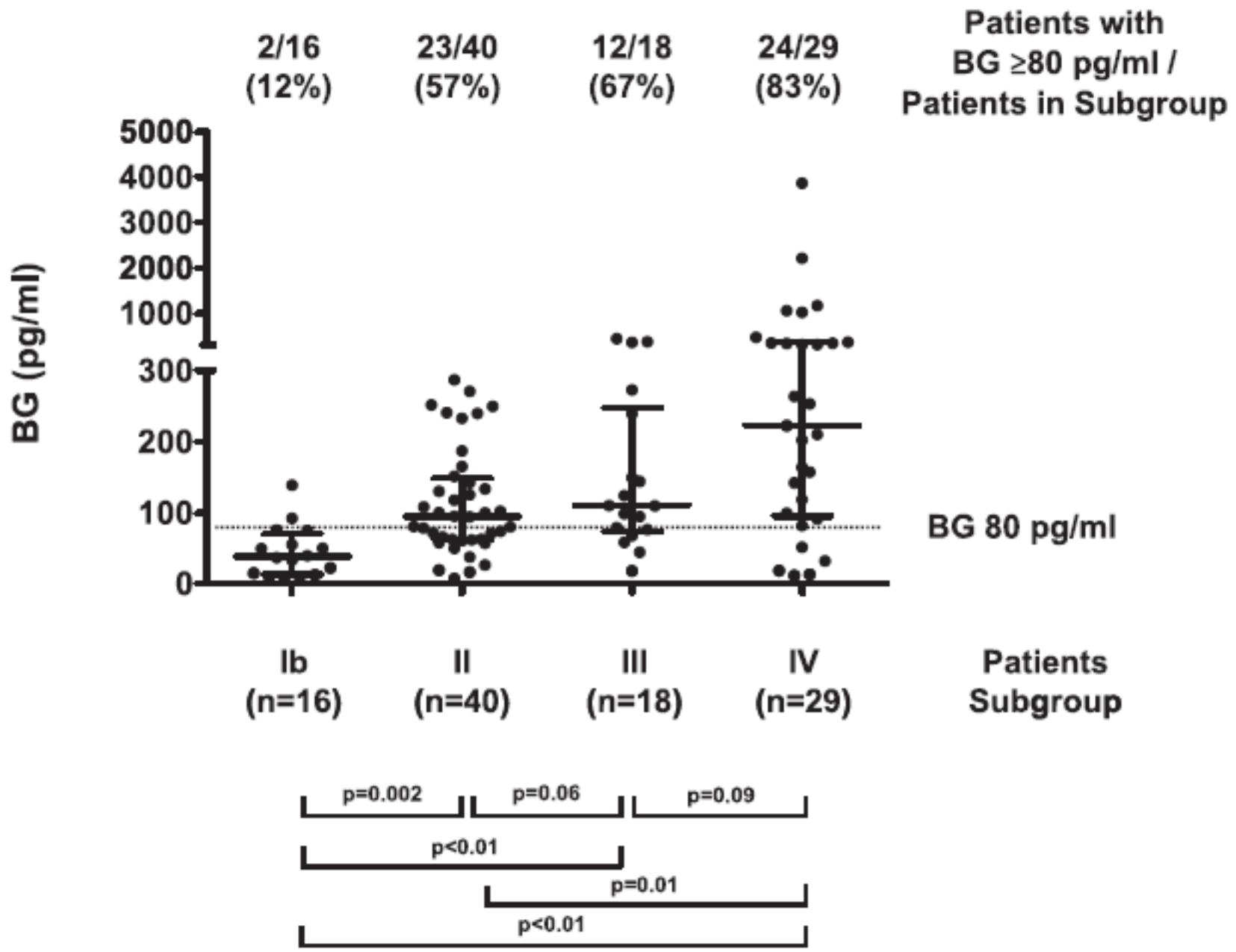
β-Glucan Antigenemia Anticipates Diagnosis of Blood Culture–Negative Intraabdominal Candidiasis

Frederic Tissot[1], Frederic Lamoth[1], Philippe M. Hauser[2], Christina Orasch[1,3], Ursula Flückiger[3], Martin Siegemund[4], Stefan Zimmerli[5], Thierry Calandra[1], Jacques Bille[2], Philippe Eggimann[6]*, Oscar Marchetti[1]*, and the Fungal Infection Network of Switzerland (FUNGINOS)

434 Patients :

Abdominal Surgery / Acute Pancreatitis
AND
Surgical ICU Stay ≥ 72h

101 Eligible Patients (23%) :

Recurrent GI Tract Perforation /
Anastomotic Leakage
OR
Acute Necrotizing Pancreatitis

12 Patients not Included (3%) :

Informed consent not obtained :	7
Transferred before inclusion :	2
Died before inclusion :	3

89 Patients Included (20%) :

Not colonized by *Candida* (subgroup Ia) :	2
Colonized by *Candida* and not receiving antifungals (subgroup II) :	40
Colonized by *Candida* and receiving pre-emptive antifungals for suspected intra-abdominal candidiasis, IAC (subgroup III) :	18
Documented intra-abdominal candidiasis, IAC (subgroup IV) :	29

When to start: a comprehensive approach

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Clinical presentation
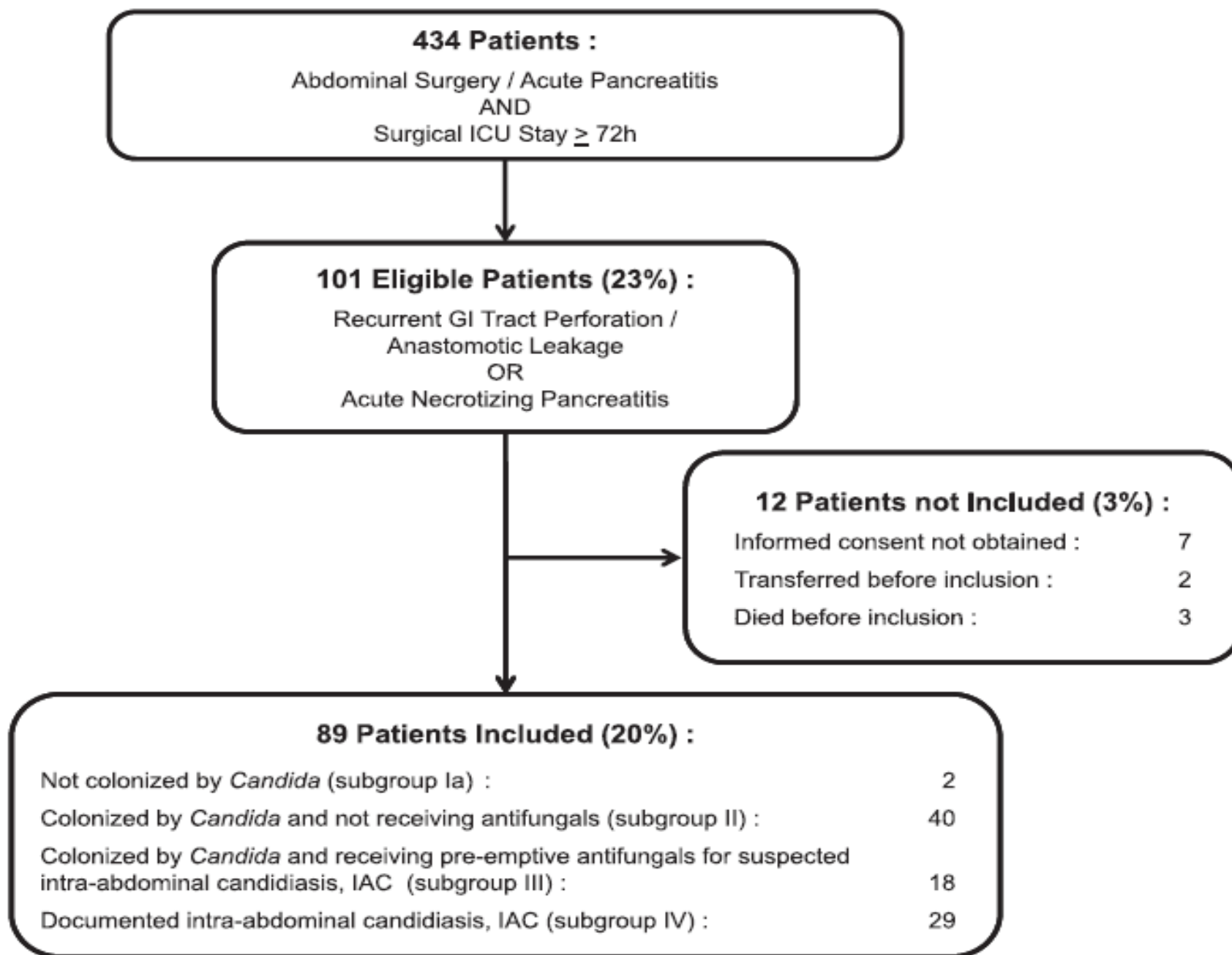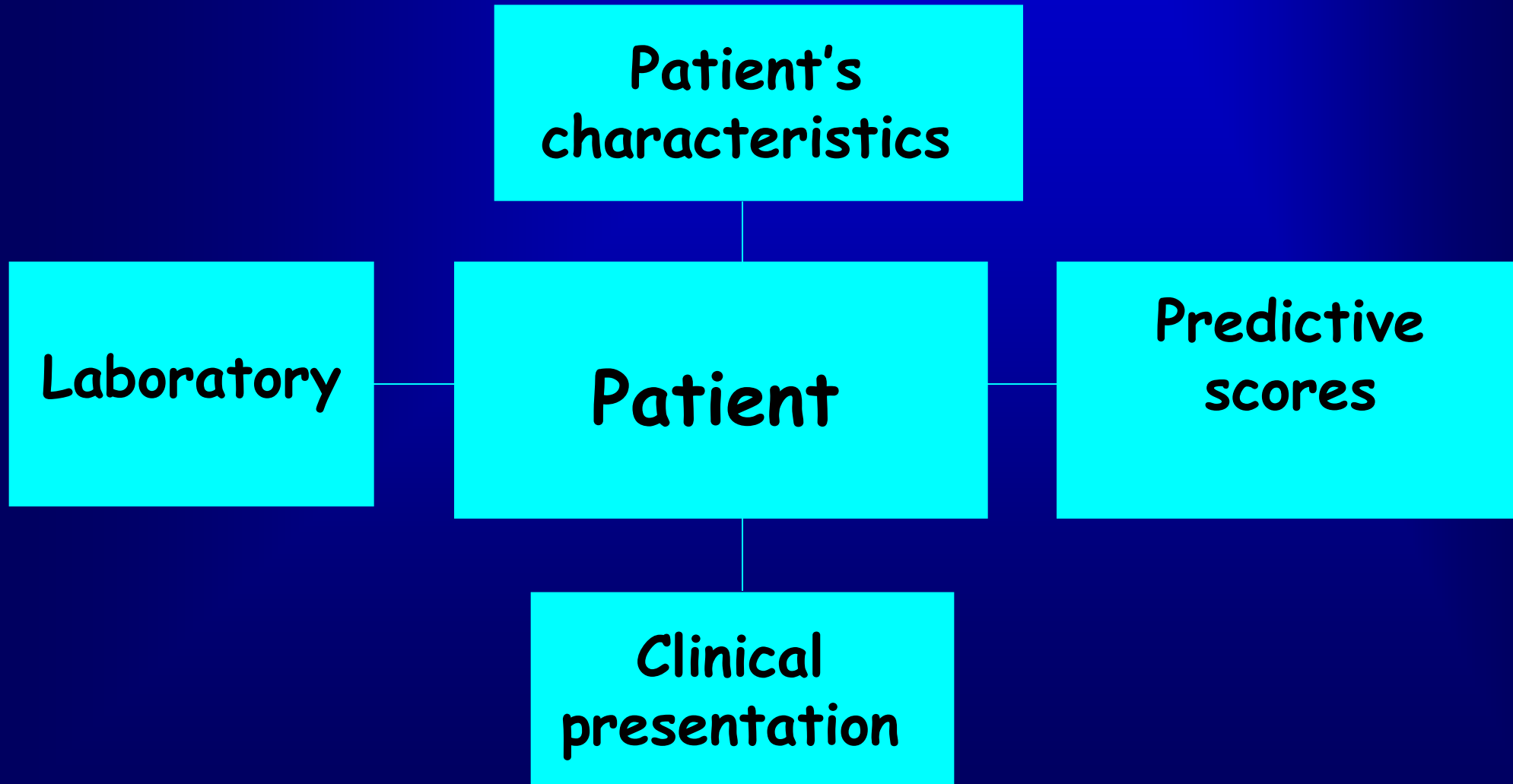
Relationship between hospital mortality and the timing of antifungal treatment in internal medicine wards
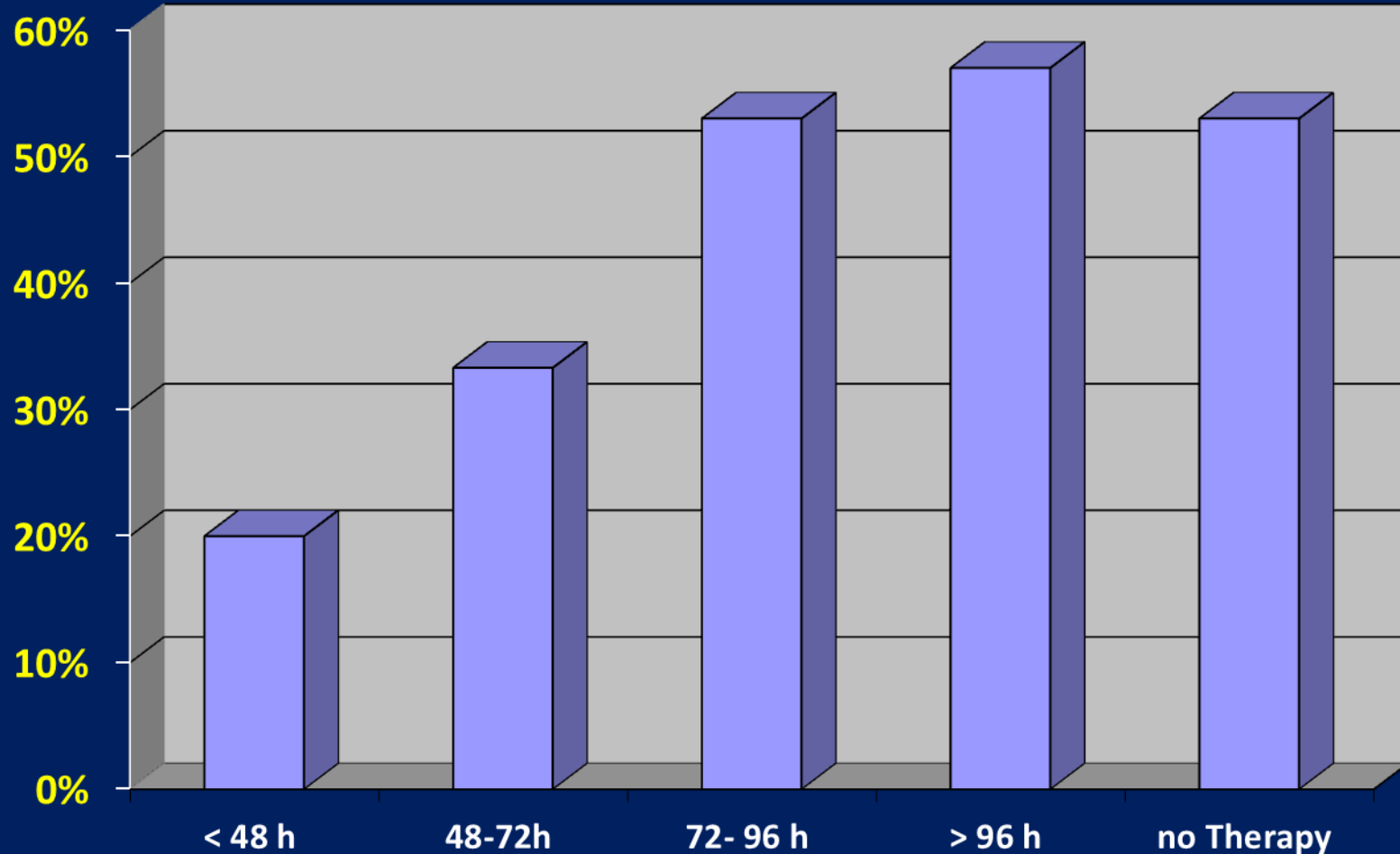
To treat early

- Act on risk factors
- Treat pre-emptively based on all the above mentioned
- Beta-glucan is a useful toll
- Other tools will come soon (????)
- **No single receipt, but a comprehensive approach**

What I would like to discuss with you today

– When to start (before symptoms? At symptoms? Upon documentation?)
– What to give
– What else to do

Treatment of candida in non-neutropenic patients according to ESCMID guidelines 2011-12
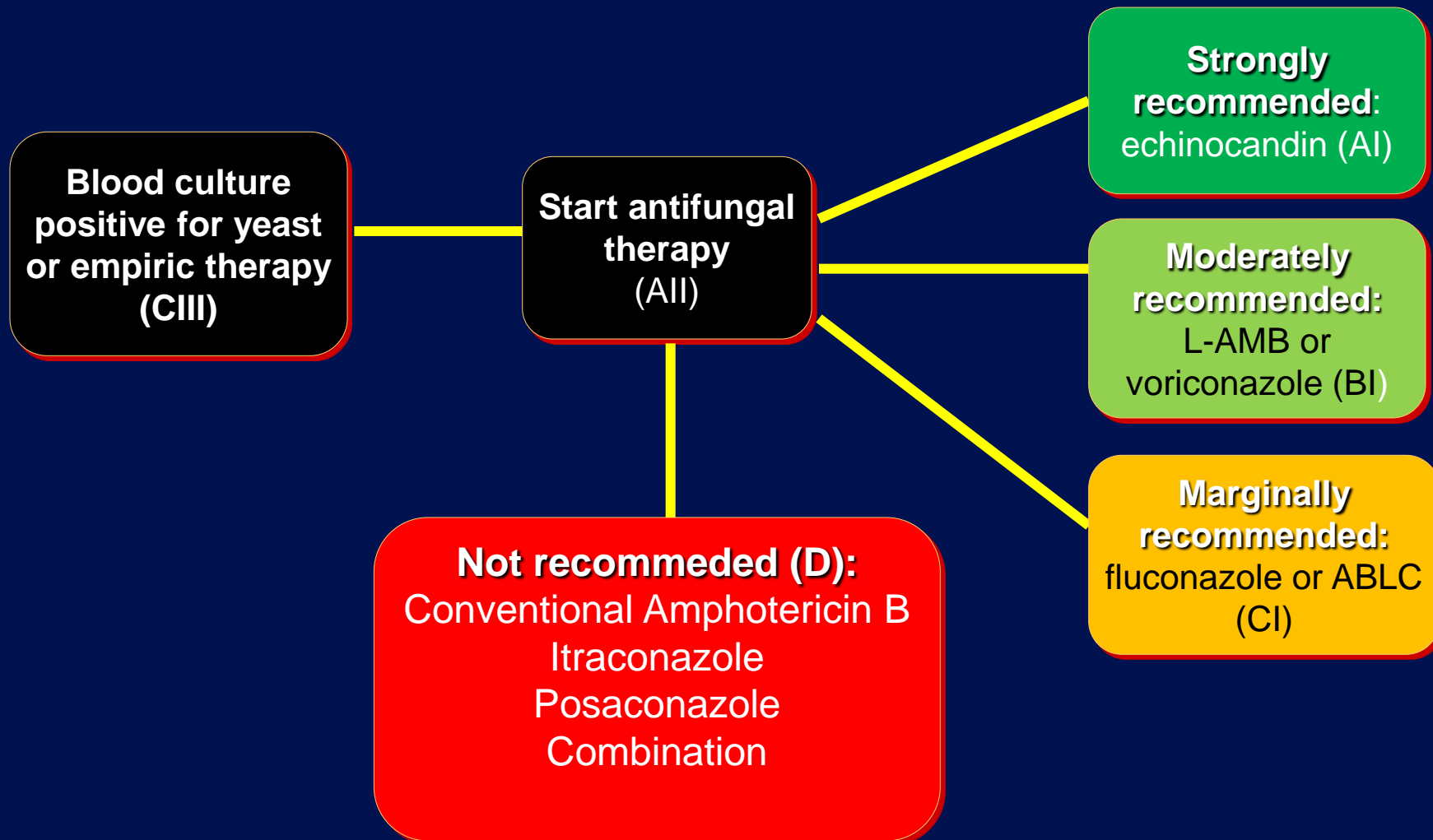
Blood culture positive for yeast or empiric therapy (CIII)

Start antifungal therapy (AII)

Strongly recommended: echinocandin (AI)

Moderately recommended: L-AMB or voriconazole (BI)

Marginally recommended: fluconazole or ABLC (CI)

Not recommeded (D):
Conventional Amphotericin B
Itraconazole
Posaconazole
Combination

Cornely OA et al. 21st ECCMID, Milano 20011
http://www.escmid.org/escmid_library/online_lecture_library/eccmid/21st_eccmid27th_icc_2011_milan/educational_workshops_2011/

Treatment of candida in non-neutropenic patients according to ESCMID guidelines 2011-12

Treatment with echinocandins (AI)

After 10 days:
-Stable
-Isolate susceptible to fluco
- PO suitable

Yes

Step-down to fluco (BII)

no

Treatment for at least 14 days after candidemia resolution (BII)

Remains in echinocandin

Diagnostic procedures recommended:
- 1 daily blood culture till negativization (BIII)
-Fundoscopic examination (BII)
- TEE (BII)

Cornely OA et al. 21st ECCMID, Milano 20011
http://www.escmid.org/escmid_library/online_lecture_library/eccmid/21st_eccmid27th_icc_2011_milan/educational_workshops_2011/
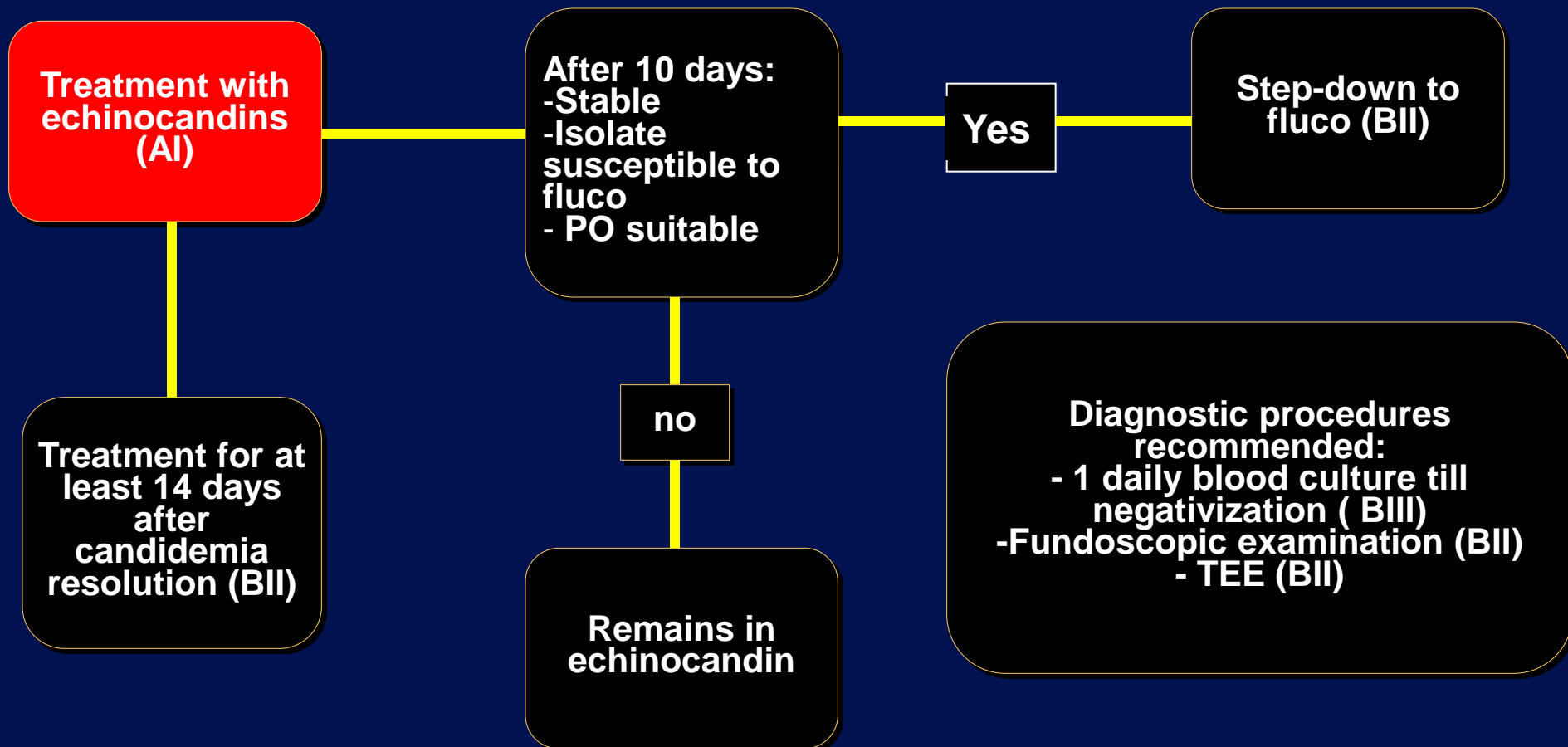
Impact of Treatment Strategy on Outcomes in Patients with Candidemia and Other Forms of Invasive Candidiasis: A Patient-Level Quantitative Review of Randomized Trials

David R. Andes,[1] Nasia Safdar,[1] John W. Baddley,[2] Geoffrey Playford,[6] Annette C. Reboli,[3] John H. Rex,[4] Jack D. Sobel,[5] Peter G. Pappas,[2] and Bart Jan Kullberg[7] for the Mycoses Study Group[a]

Table 4. Multivariate Analysis of Host, Disease, and Treatment Factors and Outcome in Patients With Invasive Candidiasis

Organisms[a]	Factor	Mortality			Factor	Success		
		P	OR	95% CI		P	OR	95% CI
All organisms (n = 978)	Age	.02	1.01	1.00–1.02	APACHE II	.0001	0.94	.93–.96
	APACHE II score	.0001	1.11	1.08–1.14	Echinocandin	.01	2.33	1.27–4.35
	Immunosuppressive therapy	.001	1.69	1.18–2.44	CVC removed	.001	1.69	1.23–2.33
	Candida tropicalis	.01	1.64	1.11–2.39	Study	NS		
	Echinocandin	.02	0.65	.45–.94				
	CVC removed	.0001	0.50	.35–.72				
	Study	NS						
Candida albicans (n = 408)	APACHE II score	.0001	1.09	1.05–1.13	APACHE II score	.005	0.92	.92–.99
	Immunosuppressive therapy	.002	2.22	1.30–3.70	Echinocandin	.005	3.70	1.49–9.09
	Surgery	.05	0.58	.34–.98	Study	NS		
	Malignancy	.03	1.89	1.05–3.45				
	Echinocandin	.03	0.55	.32–.95				
	CVC removed	.01	0.52	.31–.90				
	Study	NS						
Non-*albicans* species (n = 570)	APACHE II score	.0001	1.14	1.1–1.17	Age	.004	1.02	1.01–1.03
	Echinocandin	.04	0.52	.36–.78	APACHE II score	.0001	0.93	.91–.96
	CVC removed	.05	0.69	.48–.98	CVC removed	.007	1.74	1.16–2.61
	Study	NS			Study	NS		
Candida glabrata (n = 104)	CVC removed	.001	0.13	.04–.45	APACHE II score	.05	0.95	.90–.99
	Study	NS			Echinocandin	.05	2.63	1.10–625
					Study	NS		
Candida tropicalis[b]	APACHE II score	.0001	1.13	1.08–1.18	Age	.04	0.98	.96–.99
	Study	NS			APACHE II score	.0001	0.93	.89–.96
					CVC removed	.02	1.97	1.10–3.52
					Study	NS		
Candida parapsilosis[c]	APACHE II score	.001	1.11	1.04–1.19	APACHE II score	.01	0.95	.90–.99
	ICU admission	.02	2.63	1.12–6.25	Study	NS		
	Study	NS						

Step-down therapy in guidelines

If:
- the species is susceptible
- the patient is clinically stable
- the patient is able to take oral drug

Candidaemia (IDSA 2009):[1] 3–5 days

Candidaemia (ESCMID 2012):[2] 10 days

Intra-abdominal candidiasis (SITI/ISC 2013):[3] 5–7 days

1. Pappas PG, Kauffman CA, Andes D, et al. *Clin Infect Dis* 2009;48:503–35
2. Cornely OA, Bassetti M, Calandra T, et al. *Clin Microbiol Infect* 2012;18 Suppl 7:19–37
3. Bassetti M, et al. *Intensive Care Med* 2013. In press

BMC
Infectious Diseases

Evaluation of an early step-down strategy from intravenous anidulafungin to oral azole therapy for the treatment of candidemia and other forms of invasive candidiasis: results from an open-label trial

Jose Vazquez[1], Annette C Reboli[2], Peter G Pappas[3], Thomas F Patterson[4], John Reinhardt[5], Peter Chin-Hong[6], Ellis Tobin[7], Daniel H Kett[8], Pinaki Biswas[9] and Robert Swanson[9*]

Table 3 Responses at EOT and secondary timepoints in the MITT population and early switch subpopulation

Response	MITT population (n = 250) n/N (%) [95% CI][a]	Early switch subpopulation (n = 102) n/N (%) [95% CI][a]
Global response at EOT		
Success	170/203 (83.7) [78.7–88.8]	81/ 90 (90.0) [83.8–96.2]
Sensitivity analysis[a]	170/250 (68.0) [62.2–73.8]	81/ 102 (79.4) [71.6–87.3]
Failure	33	9
Missing/unknown	47	12

Echinocandins: 4 possible pitfalls

- *Candida parapsilosis* is less sensitive and one study showed that the use of echinocandins is associated with the emergence of infections due to species with higher MIC (Lortholary et al, CID 2011)

- Acquired rsistance has been described and it seems to be increasing (Pfaller et al, 2012)

- Echinocandins do not penetrate in eyes. The issue of Candida ophtalmitis

Recent Exposure to Caspofungin or Fluconazole Influences the Epidemiology of Candidemia: a Prospective Multicenter Study Involving 2,441 Patients[▽]

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Stéphane Bretagne,[1,2,5] Françoise Dromer,[1,2*] and the French Mycosis Study Group†

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Hôpital Necker-Enfants Malades, APHP, Paris,[3] Institut Pasteur, Unité d'Epidémiologie des Maladies Emergentes,
Paris,[4] and Laboratoire de Parasitologie-Mycologie, Université Paris-Est, and
Hôpital Henri Mondor, AP-HP, Créteil,[5] France

A prospective multicenter surveillance program on yeast bloodstream infections was implemented in the Paris, France, area without restrictions on ward of hospitalization (intensive care unit, hematology, and surgery) or age (adults and children). The present analysis concerns 2,618 isolates collected over 7 years from 2,441 patients. Centralized species identification and antifungal susceptibility testing using the EUCAST methodology were performed. Almost 10% (232/2,441) of the patients had recently ($\leq$30 days) been treated with antifungal drugs. We analyzed the effect of recent exposure to fluconazole ($n = 159$) or caspofungin ($n = 61$) on the proportions of the five major *Candida* species. For both drugs, preexposure was associated with a decreased prevalence of *Candida albicans* in favor of less drug-susceptible species (*C. glabrata* and *C. krusei* for the former and *C. parapsilosis* and, to a lesser extent, *C. glabrata* and *C. krusei* for the latter; $P = 0.001$). In the multivariate analysis, the risk of being infected with an isolate with decreased susceptibility to fluconazole was independently associated with an age of $\geq$15 years (odds ratio [OR] = 2.45; 95% confidence interval [CI] = 1.39 to 4.31; $P = 0.002$) and with recent exposure to fluconazole (OR = 2.17; 95% CI = 1.51 to 3.13; $P < 0.001$), while the risk of being infected with an isolate with decreased susceptibility to caspofungin was independently associated with an age <15 years (OR = 2.53; 95% CI = 1.43 to 4.48; $P = 0.001$) and with recent exposure to caspofungin (OR = 4.79; 95% CI = 2.47 to 9.28; $P < 0.001$). These findings could influence future recommendations for the management of candidemia.
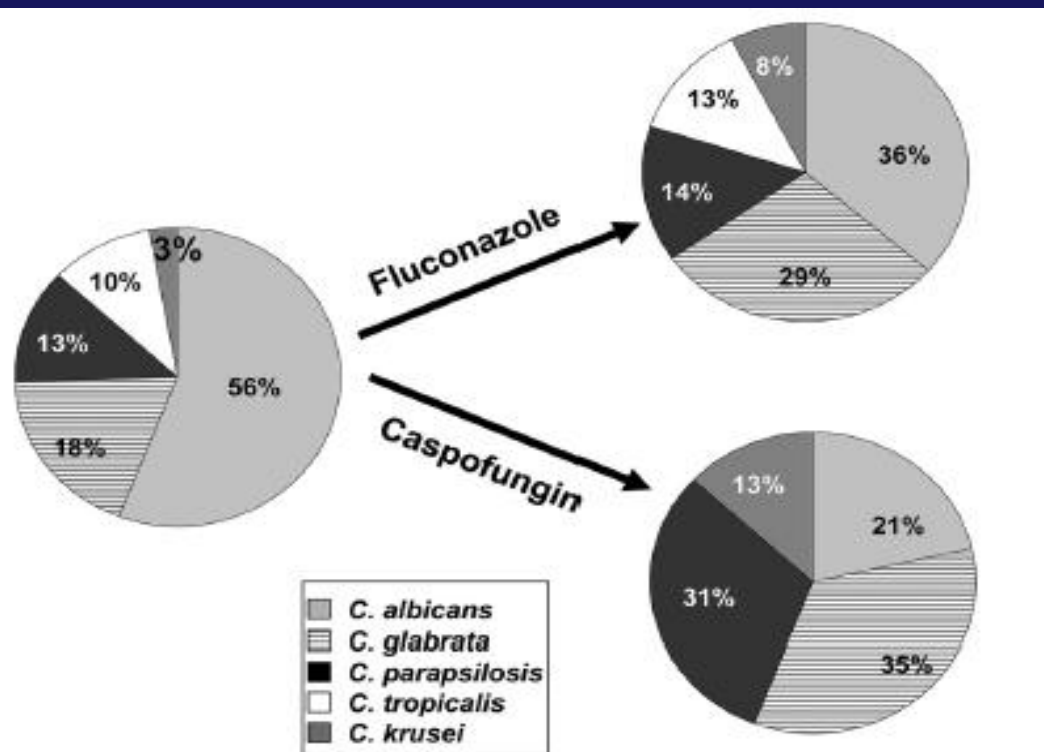
FIG. 2. Proportion of the five major *Candida* species responsible for fungemia in patients with ($n = 159$) or without ($n = 2,289$) prior exposure to fluconazole ($P = 0.001$) or with ($n = 61$) or without ($n = 2,387$) prior exposure to caspofungin ($P < 0.001$) (incident episodes and recurrences are included).

1

194 episodes C. parapsilosis candidemias

Initial use of echinocandins does not negatively influence outcome in *Candida parapsilosis* bloodstream infection: a propensity score analysis

Mario Fernández-Ruiz[1], José María Aguado[1], Benito Almirante[2], David Lora-Pablos[3,4], Belén Padilla[5], Mireia Puig-Asensio[2], Miguel Montejo[6], Julio García-Rodríguez[7], Javier Pemán[8], Maite Ruiz Pérez de Pipaón[9], and Manuel Cuenca-Estrella[10], on behalf of the CANDIPOP Project[*], GEIH-GEMICOMED (SEIMC) and REIPI.

Table 4. Univariate and multivariate logistic regression analyses of prognostic factors for clinical failure (all-cause mortality within days 3 to 30 or persistent BSI for ≥72 hours from the initiation of antifungal therapy) in 177 evaluable episodes of *C. parapsilosis* BSI.

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Orotracheal intubation at diagnosis	4.67	2.32 - 9.38	0.000	2.81	1.19 - 6.65	0.018
Septic shock	7.17	2.63 - 19.56	0.000	2.91	0.88 - 9.64	0.081
Haematogenous dissemination	6.75	1.32 - 34.56	0.016	7.42	0.67 - 82.44	0.103
Early CVC removal (≤48 hours)	0.41	0.20 - 0.86	0.016	0.43	0.19 - 0.96	0.040
Initial antifungal therapy						
Azole-based regimen	1	-	-	1	-	-
Echinocandin-based regimen	1.34	0.60 - 2.97	0.479	1.73	0.66 - 4.54	0.265
Amphotericin B-based regimen	0.99	0.40 - 2.45	0.989	0.99	0.34 - 2.89	0.996
Combination regimen	0.86	0.31 - 2.36	0.769	1.06	0.33 - 3.43	0.922

BSI: bloodstream infection; CI: confidence interval; CVC: central venous catheter; OR: odds ratio.

Hosmer-Lemeshow *P*-value = 0.653.

Table 5. Outcomes in 103 non-neonatal episodes of *C. parapsilosis* BSI treated with an echinocandin-based or an azole-based regimen as initial antifungal therapy (first 72 hours).

Variable	Azole-based regimen (n = 64)	Echinocandin-based regimen (n = 39)	*P*-value
Clinical failure[a]	20/62 (32.3)	13/37 (35.1)	0.769
Persistent BSI for ≥72 hours of therapy[b]	14/48 (29.2)	6/26 (23.1)	0.573
30-day all-cause mortality[c]	14/63 (22.2)	10/37 (27.0)	0.587
Early (<72 hours)	1/64 (1.6)	0/39 (0.0)	1.000
Non-early (days 3-30)	13/63 (20.6)	10/37 (27.0)	0.463

What I would like to discuss with you today

– When to start (before symptoms? At symptoms? Upon documentation?)
– What to give
– What else to do

Table 4. Univariate and multivariate logistic regression analyses of prognostic factors for clinical failure (all-cause mortality within days 3 to 30 or persistent BSI for ≥72 hours from the initiation of antifungal therapy) in 177 evaluable episodes of *C. parapsilosis* BSI.

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BSI: bloodstream infection; CI: confidence interval; CVC: central venous catheter; OR: odds ratio.
Hosmer-Lemeshow *P*-value = 0.653.

Impact of Treatment Strategy on Outcomes in Patients with Candidemia and Other Forms of Invasive Candidiasis: A Patient-Level Quantitative Review of Randomized Trials

David R. Andes,[1] Nasia Safdar,[1] John W. Baddley,[2] Geoffrey Playford,[6] Annette C. Reboli,[3] John H. Rex,[4] Jack D. Sobel,[5] Peter G. Pappas,[2] and Bart Jan Kullberg[7] for the Mycoses Study Group[a]

Factors Associated With Mortality and Treatment Response

The overall 30-day mortality was 31.4%, and composite treatment success at the end of treatment was 67.4%. Univariate

Table 4. Multivariate Analysis of Host, Disease, and Treatment Factors and Outcome in Patients With Invasive Candidiasis

Organisms[a]	Factor	Mortality			Factor	Success		
		P	OR	95% CI		P	OR	95% CI
All organisms (n = 978)	Age	.02	1.01	1.00–1.02	APACHE II	.0001	0.94	.93–.96
	APACHE II score	.0001	1.11	1.08–1.14	Echinocandin	.01	2.33	1.27–4.35
	Immunosuppressive therapy	.001	1.69	1.18–2.44	CVC removed	.001	1.69	1.23–2.33
	Candida tropicalis	.01	1.64	1.11–2.39	Study	NS		
	Echinocandin	.02	0.65	.45–.94				
	CVC removed	.0001	0.50	.35–.72				
	Study	NS						
Candida albicans (n = 408)	APACHE II score	.0001	1.09	1.05–1.13	APACHE II score	.005	0.92	.92–.99
	Immunosuppressive therapy	.002	2.22	1.30–3.70	Echinocandin	.005	3.70	1.49–9.09
	Surgery	.05	0.58	.34–.98	Study	NS		
	Malignancy	.03	1.89	1.05–3.45				
	Echinocandin	.03	0.55	.32–.95				
	CVC removed	.01	0.52	.31–.90				
	Study	NS						
Non-albicans species (n = 570)	APACHE II score	.0001	1.14	1.1–1.17	Age	.004	1.02	1.01–1.03
	Echinocandin	.04	0.52	.36–.78	APACHE II score	.0001	0.93	.91–.96
	CVC removed	.05	0.69	.48–.98	CVC removed	.007	1.74	1.16–2.61
	Study	NS			Study	NS		
Candida glabrata (n = 104)	CVC removed	.001	0.13	.04–.45	APACHE II score	.05	0.95	.90–.99
	Study	NS			Echinocandin	.05	2.63	1.10–625
					Study	NS		
Candida tropicalis[b]	APACHE II score	.0001	1.13	1.08–1.18	Age	.04	0.98	.96–.99
	Study	NS			APACHE II score	.0001	0.93	.89–.96
					CVC removed	.02	1.97	1.10–3.52
					Study	NS		
Candida parapsilosis[c]	APACHE II score	.001	1.11	1.04–1.19	APACHE II score	.01	0.95	.90–.99
	ICU admission	.02	2.63	1.12–6.25	Study	NS		
	Study	NS						

Recommendations on catheter removal in candidemia

Population	Intention	Intervention	SoR	QoE	Reference
Any patient with central venous catheter	To improve survival	Remove indwelling lines (not over a guidewire)	A	II	Andes CID 2012
Any patient in whom a central venous catheter cannot be removed	To clear candidaemia	Treat with echinocandin, liposomal amphotericin B, or amphotericin B lipid complex	B	II	Kucharikova AAC 2010 Kuhn AAC 2002 Mukherjee IJAA 2009 Nucci CID 2010 Rex CID 1995
		Treat with azole, or amphotericin B deoxycholate	D	II	Almirante JCM 2005 Leroy CCM 2009 Liu J Infect 2009 Rodriguez CMI 2007 Weinberger JHI 2005

Thank you for your attention!