Efficacy of a bundle intervention on the clinical evolution of patients with *Candida* bloodstream infection

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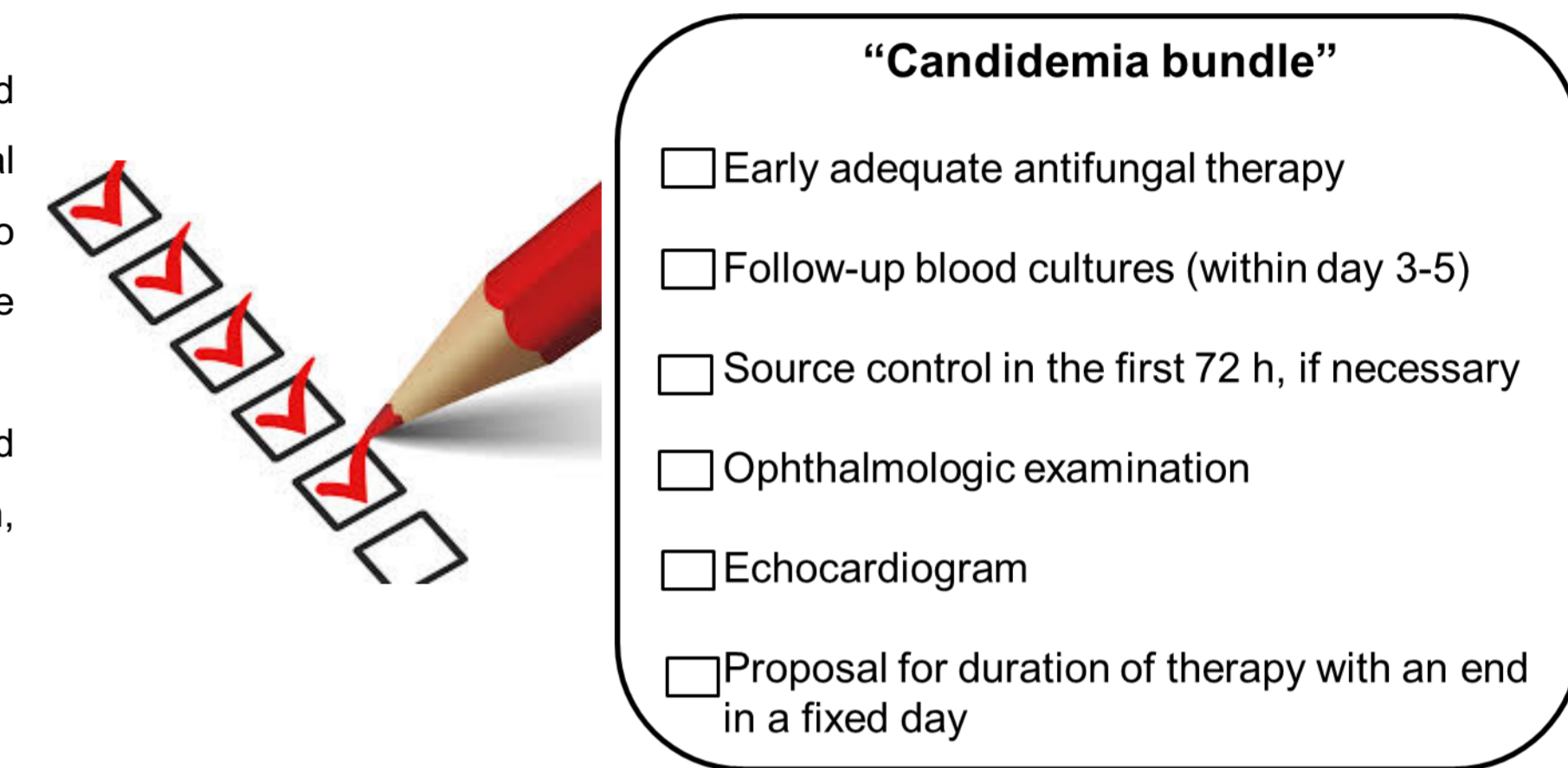
INTRODUCTION

• Candidemia is a life-threating disease associated with significant morbidity and mortality that may benefit from regular ID consultation and antifungal stewardship recommendations.

• Prompt diagnosis, early administration of appropriate antifungal therapy and adequate source control of infection have been shown to be key factors that improve the prognosis of *Candida* bloodstream infection. However, those recommendations are not always carried out in due time, despite such programs.

• The aim of this study was to evaluate the clinical impact of implementing routine stewardship measures with a bedside **check list care bundle** immediately after the detection of candidemia.

MATERIAL AND METHODS

• *Study design and setting.* Prospective quasi-experimental study performed at Hospital General "Gregorio Marañon", Madrid, Spain.

• *Study population.* All consecutive adult patients with candidemia managed according to a pre-established bundle (Bundle group) were compared with a historical group, including patients with candidemia from January 2011 to December 2014. During this period a non-restrictive antifungal stewardship program was implemented in our hospital and patients with candidemia were visited by an ID specialist as soon as possible who provided diagnostic and therapeutic advice. Patients who died in the first 72 hours (not subject to intervention) and patients receiving palliative care for terminal conditions were excluded from both cohorts.

• The **candidemia bundle** is reported in **Figure 1.** Briefly, intervention consisted of six recommendations provided in a structured form and checked with a list that included: 1) **early (<72 h)** adequate antifungal therapy, 2) follow-up blood cultures (within day 3 to 5), 3) source control in the first 72 h, if necessary, 4) ophthalmologic examination, 5) echocardiogram, and a 6) proposal for duration of therapy with an end in a fixed day.

• *Outcomes*: **Rates of 14-day mortality** (attributable mortality) and **30-day mortality** (non attributable mortality).
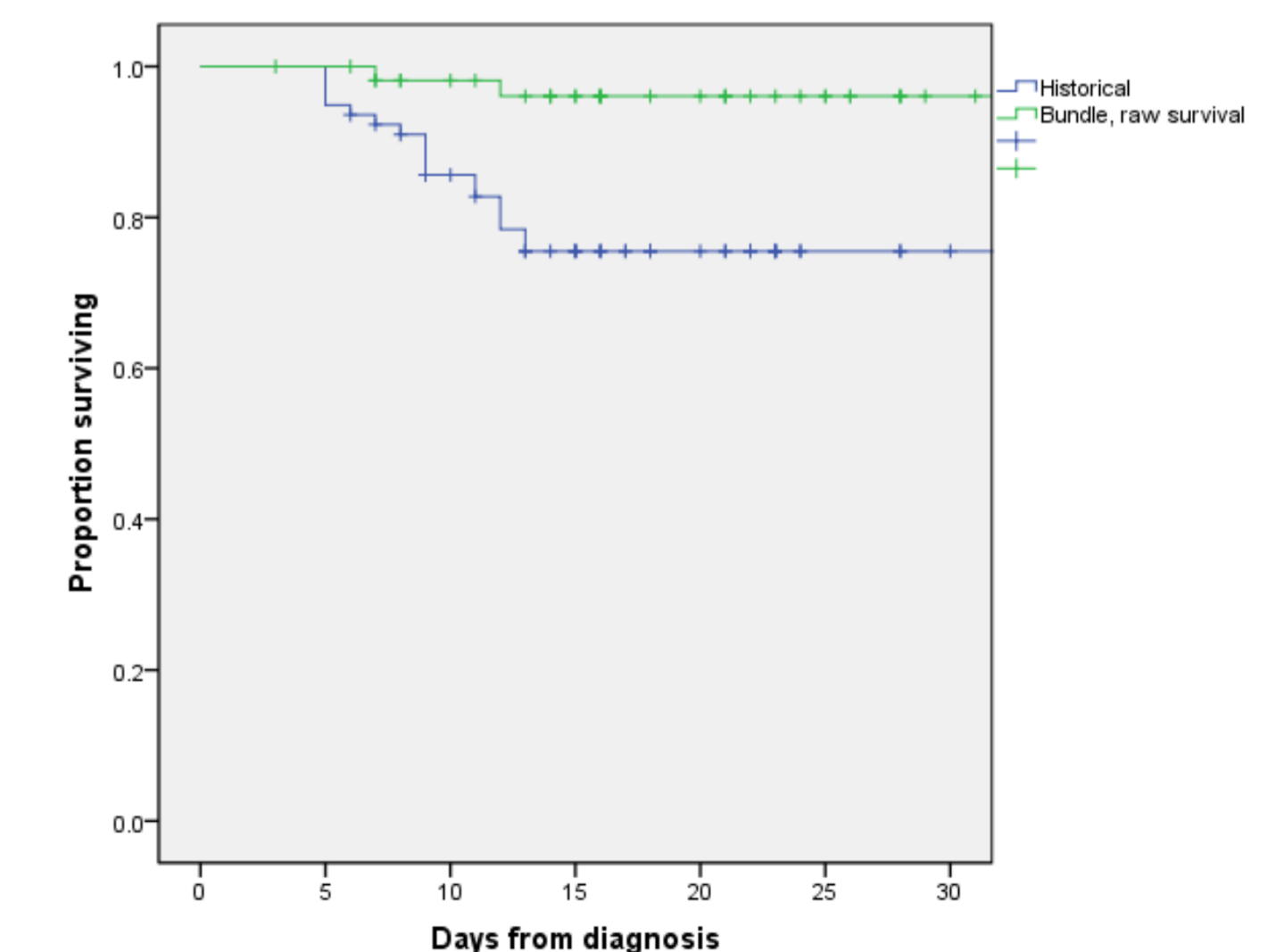
"Candidemia bundle"

☐ Early adequate antifungal therapy

☐ Follow-up blood cultures (within day 3-5)

☐ Source control in the first 72 h, if necessary

☐ Ophthalmologic examination

☐ Echocardiogram

☐ Proposal for duration of therapy with an end in a fixed day

RESULTS

• Diagnosis of candidemia: 68 patients. Of these **56 patients** were treated according to "candidemia bundle".

• Reason for exclusion were: death within 72 hours (9 pts) and palliative care (3 pts).

• Patients managed according to bundle were compared with 112 historical cohort (**Table 1**).

• No differences were observed regarding origin of infection and *Candida* species.

• Fulfillment of the items of "candidemia bundle" in both cohorts and its impact on clinical outcome is reported in **Table 2.**

• **Risk factors for 14-day mortality**

➢ **Univariate analysis:** being admitted to a surgical ward, previous immunosuppression therapy, high Pitt score, Septic shock at presentation and management according to candidemia bundle.

➢ **Multivariate analysis:** management according to candidemia bundle (OR 0.25, 95%IC: 0.05-0.94, p=0.04)

• **Risk factors for 30 day mortality**

➢ **Univariate analysis:** higher PITT bacteremia score, fungemia due to *C. krusei* and persistent candidemia.

➢ **Multivariate analysis:** Persistent candidemia (OR 2.89, 95%IC: 1.01-8.28, p=0.05)

TABLE 1. *Comparison of demographic and clinical data*

VARIABLE	Historical Group, n=112	Intervention Group, n=56	p
Age (years), mean ± SD	66.4 ± 14.0	67.8 ± 13.5	0.55
Male sex	43 (38.4)	17 (30.4)	0.39
Ward of admission			
Intensive care	23 (20.5)	12 (21.4)	0.99
Onco-hematological	20 (17.9)	4 (7.1)	0.07
Medical	36 (32.1)	20 (35.7)	0.72
Surgical	35 (31.2)	20 (35.7)	0.60
Underlying disease			
Neoplasia	55 (51.8)	29 (51.8)	0.87
Renal disease	24 (21.4)	(13 (23.2)	0.84
Diabetes	31 (27.7)	16 (28.2)	0.99
Neurological	24 (21.4)	14 (25.0)	0.69
Risk factors for *Candida* BSI			
Previous antibiotic therapy	104 (92.4)	51 (91.1)	0.76
CVC	71 (63.4)	46 (82.1)	**0.003**
TPN	54 (48.2)	40 (71.4)	**0.01**
Surgery within previous 3 m	53 (47.3)	26 (46.4)	0.87
Neutropenia	7 (6.2)	3 (5.4)	0.99
Clinical presentation			
Sepsis	82 (72.3)	26 (46.4)	**0.001**
Severe sepsis	19 (17.0)	26 (46.4)	**0.001**
Septic shock	10 (8.9)	4 (7.1)	0.77
Origin			
CVC related	55 (49.1)	36 (64.3)	0.07
Intra-abdominal	19 (17.0)	11 (19.6)	0.67
Primary	17 (15.2)	3 (5.4)	0.08
Urinary tract	14 (12.5)	4 (7.1)	0.42
Other	5 (4.5)	2 (3.6)	0.99

TABLE 2 *Microbiological and diagnostic workup, therapeutic management and outcome*

VARIABLE	Historical Group, n=112	Interventional Group, n=56	p
Early source control (<72 horas)	53 (63.1)	31 (68.9)	0.56
Follow-up blood cultures	86 (76.8)	55 (98.2)	**<0.001**
Ophthalmoscopic examination	77 (68,8)	56 (100)	**<0.001**
Echocardiography	92 (82.1)	56 (100)	**<0.001**
Early AF therapy (<72 h)	94 (83.9)	53 (94.6)	**0.05**
Treatment duration according to the complexity of infection	36 (45.6)	40 (74.1)	**0.001**
Full adherence to all indicators	19 (17.0)	28 (50.0)	**<0.001**
Candidemia related complication			
ICU admission	10 (8.9)	1 (1.8)	0.10
Ocular candidiasis	8 (9.8)	9 (16.2)	0.30
Endocarditis	3 (3.3)	0 (0)	0.29
Other septic metastasis	5 (4.5)	11 (19.6)	**<0.001**
Persistent candidemia	19 (21.8)	14 (25.5)	0.68
Clinical outcome			
14-day mortality	18 (16.1)	2 (3.6)	**0.02**
30-day mortality	29 (25.9)	9 (16.1)	0.17

FIG 1. Kaplan Meyer estimates of 14-day survival in bundle patients and historical cohort

CONCLUSION

• Reinforcement of routine antifungal stewardship program with a simple check list bundle, focused on increasing adherence to a few evidence-based interventions, provided bedside immediately after the diagnosis of candidemia, is able to further reduce 14-day (related) mortality in patients with candidemia.