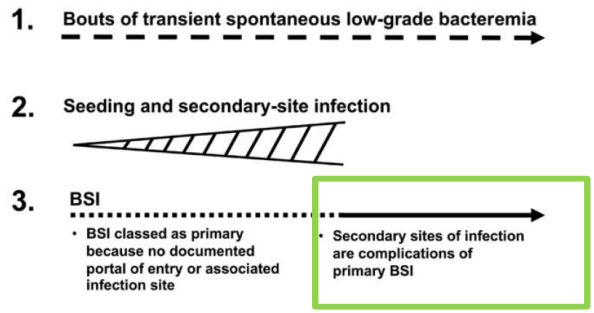
Eduardo López Cortés. Unidad Clínica de Enfermedades Infecciosas y Microbiología Clínica. HU Virgen Macarena. Sevilla.

5. ¿Riesgo de EI en pacientes con BSA de foco bien definido?

- El desarrollo de complicaciones hematógenas es (tras la gravedad clínica en su presentación) la consecuencia más temida de la BSA



- Sabemos que el riesgo depende **en gran parte del foco primario** de la bacteriemia:

	Metastatic infection		
	Present (n = 14), n (%)	Absent (n = 59), n (%)	*P*
Primary site of infection			
Intravascular catheter	1 (7.1)	24 (40.7)	0.140
Central venous catheter	0 (0)	21 (35.6)	0.005
Skin and soft tissue infection	3 (21.4)	12 (20.3)	0.591
Respiratory tract	0 (0)	4 (6.8)	0.418
Urinary tract	3 (21.4)	5 (8.5)	0.175
Unknown	7 (50.0)	14 (23.7)	0.056

Horino T, et al. Am J Med Sci. 2015;349(1):24-8.
Del Río A, et al Clin Infect Dis. 2009 May 15;48 Suppl 4:S246-53.

Predicting Risk of Endocarditis Using a Clinical Tool (PREDICT): Scoring System to Guide Use of Echocardiography in the Management of *Staphylococcus aureus* Bacteremia

- Unicentre (Minnesota), adults hospitalized with SAB from 2006 to 2011
- 757 patients screened → 85 (13%) IE
- Risk factors for infective endocarditis and **development of infective endocarditis**:

Model/Variable	Multivariable Result Odds Ratio (95% Confidence Interval) [*P* Value]	β	β′	$c \times \beta'$	Points^
Day 5 Model				$c = 2$	
CIED					
ICD	5.00 (2.09, 11.94) [<.001]	1.61	1.20	2.40	2
PPM	8.60 (4.18, 17.67) [<.001]	2.15	1.60	3.21	3
Neither	1.0 (reference)	. . .		. . .	0
Onset of SAB					
Community	3.83 (1.64, 8.96) [.002]	1.34	1.00	2.00	2
Healthcare	1.79 (.80, 4.03) [.159]	0.58	0.43	0.87	1
Nosocomial	1.0 (reference)	. . .		. . .	0
Prolonged bacteremia (≥72 h)	5.23 (2.85, 9.61) [<.001]	1.65	1.23	2.47	2

Palraj BR, et al. Clin Infect Dis. 2015;61(1):18-28.

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¿Riesgo de EI en pacientes con BSA de foco bien definido?

- Multicenter, prospective, observational study 884 hospitalized patients
- Patients were grouped by bacteremia duration (BD):
  - Short (1-2d): 63%
  - Intermediate (3-6d): 28%
  - Prolonged (≥7d) : 9%

- **Results**:
  - **Metastatic complications** and 30-day mortality were progressively worse as BD increased (p<0.0001).
  - Every continued day of bacteremia ↔ RR of death of 1.16 (95% CI 1.10-1.22, p<0.0001), with significant **increase in risk starting at 3 days** as determined by ROC analysis.
  - **EI cases: duration ≥ 3 days. Median: 4d for MSSA and 5d MRSA.**

Minejima E, et al. *Clin Infect Dis* 2019. In press.

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¿Riesgo de EI en pacientes con BSA de foco bien definido?

- Chang FY: 505 consecutive patients with SAB (6 tertiary hospitals) → 64 IE → 7 **(1,3%) new endocarditis** (catheter was the most frequent)

- Souli M: longitudinal study 1995-2015 in Duke Clinical Research Institute (North Carolina)
- 2,348 participants: 36,7% metastatic infection, **13,7% IE**

Characteristic[a]	Number of Patients (%)[b]	Annual Change (%)[c]	*P* Value[d]
Any metastatic infection	860 (36.7)	0.94	**.019**
Endocarditis	320 (13.7)	0.45	**.049**
Abscess (other than the types below)	197 (8.4)	0.40	**.004**
Psoas abscess	47 (2.0)	0.05	.272
Epidural abscess	69 (2.9)	0.20	**.004**
Septic emboli	138 (5.9)	0.62	**<.0001**
Vertebral osteomyelitis	105 (4.5)	0.30	**.002**
Septic arthritis	163 (7.0)	0.17	.154
Septic thrombophlebitis	96 (4.1)	0.20	**.044**
Meningitis	20 (0.9)	−0.08	.087
Other metastatic infection[e]	108 (4.6)	0.21	.144

1. Chang FY, et al. Medicine (Baltimore). 2003;82(5):322-32
2. Souli M, et al Clin Infect Dis. 2019. In press

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Risk Factors For Hematogenous Complications of Intravascular Catheter–Associated *Staphylococcus aureus* Bacteremia

- Duke University Medical Center: consecutive patients with CRB SAB were prospectively recruited (91 months)
- 324 patients → 42 (13%) hematogenous complications → **31 (9,6%) IE**

Table 3. Final multivariable analysis of patient and bacterial characteristics associated with hematogenous complications of intravascular catheter–associated *Staphylococcus aureus* bacteremia.

Independent variable	OR (95% CI)	*P*
Hemodialysis dependence only[a]	72 (8.2–630)	<.001
Permanent foreign body only[b]	4.2 (1.1–17)	.04
Both hemodialysis dependence and permanent foreign body[c]	11 (3.2–38)	<.001
Duration of symptoms before diagnosis[d]	1.15 (1.06–1.24)	<.001
Methicillin-resistant bacterial isolate	2.3 (1.1–4.7)	.03

Fowler VG Jr, et al. Clin Infect Dis. 2005;40(5):695-703

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Conclusiones

1. No hay estudios con realización sistemática de ecocardio → NO es posible definir con precisión el riesgo de endocarditis 2aria ya que ésta se realiza fundamentalmente en "bacteriemias complicadas"

2. El riesgo parece estar comprendido entre 9,6 y 13,7%, aunque…

3. Depende directamente **de la duración de la bacteriemia**, que a su vez depende **del foco 1ario y el tiempo hasta el control del mismo**

4. El riesgo se incrementa si existe:
   - Retraso hasta el tratamiento adecuado
   - Presencia de dispositivos endovasculares (y tiempo desde el implante) / cardiopatía predisponente
   - Hemodiálisis
   - SARM

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6. ¿Qué pacientes con candidemia no ameritan excluir endocarditis?

- Muy escasa bibliografía, la mayoría centrada en tratamiento
  - Alta frecuencia de citación recíproca
- **Baja incidencia:**
  - *International Collaboration on Endocarditis—Prospective Cohort Study* 2000-2005: **1,2% (33/2749).**
  - Fernández Cruz A, et. al; GAME: **5,9% (11/187)**
- **Mortalidad**: 50-55%

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

Population	Intention	Intervention	SoR	QoE
Candidaemia with no organ involvement detected	To avoid organ involvement	Treat for 14 days after the end of candidaemia	B	II
		Take at least one blood culture per day until negative	B	III
	To detect organ involvement	Transoesophageal echocardiography	B	II_a
		Fundoscopy	B	II

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Endocarditis should be suspected when:

- Blood cultures are persistently positive
- Persistent fever despite appropriate treatment
- New heart murmur, heart failure, or embolic phenomena

Cornely OA, et al. Clin Microbiol Infect. 2012; 18: 19–37
Pappas PG, IDSA. Clin Infect Dis. 2016; 62: 409.

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Factores predisponentes asociados:

- Varón (51.5% vs 67.9%, p=0.04)[1]
- Endocarditis previa (21.2% vs. 7.8%, p=0.005)[1]
- Válvula protésica (48.8% vs. 19.6%, p=0.005)[1]
- Ojo a UDVP!! (16,7% vs 2,9%, p=0,014)[2]

Evolución clínica:

- Candidemia persistente (**RR 4.51, IC95% 1.83–11.11**)[3]

Risk factors predicting *Candida* infective endocarditis in patients with candidemia

- Retrospective analysis of all inpatients with candidemia (1315 beds hospital, Missouri)
- 1,873 patients with candidemia
- **56% patients with echo → 47 (2.5%)**

Table 2. Multivariable logistic regression predicting *Candida* infective endocarditis in patients with candidemia.

Variable	Adjusted odd ratio (95% CI)	*P* value
Valvular heart disease	7.66 (2.95, 19.84)	<.0001
Infection with *Candida glabrata*	0.17 (0.04, 0.69)	.013
Hematologic malignancy[a]	0.09 (0.01, 0.68)	.019
Receipt of TPN	0.38 (0.16, 0.91)	.030

1. Baddley JW. EJCMID 2008;27(7):519-29
2. Poowanawittayakom N. Emerg Infect Dis. 2018;24(4).
3. Fernández-Cruz A. EJCMID. 2015;34(8):1543-9
4. Foong KS. Med Mycol. 2019. En prensa

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Bundles in candidemia

Table 4. Adherence to Quality-of-Care Indicators

Quality-of-Care Indicator	Pre-intervention group (n = 385)	Intervention group (n = 263)	Median Improvement in Percentage of Adherence to QCI (IQR)	Relative Risk for Adherence to QCI (95% CI)	*P* Value
Early appropiate antifungal therapy	248 (64.4%)	203 (81.5%)	6.9 (4.3-33)	2.4 (1.7-3.6)	<.001
Initial treatment with echinocandins if septic shock*	47 (45.6%)	64 (71.1%)	26.1 (0-52.5)	2.5 (1.39-4.51)	<.001
Early source control**	165 (54.8%)	168 (85.7%)	29.5 (20.2-40.8)	4.9 (3.1-7.8)	<.001
Follow-up blood culture	293 (76.1%)	220 (87.6%)	17 (7.4-26.5)	2.2 (1.4-3.5)	<.001
Ophtalmoscopic evaluation	192 (52.5%)	221 (85.7%)	38.5 (28.3-62.2)	5.4 (3.6-8.1)	<.001
Echocardiography	319 (84.8%)	232 (91%)	9.4 (20.2-40.8)	1.8 (1.1-3)	.023
De-escalation	254 (69.2%)	210 (84.3%)	13.1 (1.6-22.2)	2.4 (1.6-3.6)	<.001
Adequate length of antifungal treatment	248 (65.3%)	237 (96.3%)	32.1 (23.1-41.9)	14.02 (6.9-28.2)	<.001

*193 patients
**477 patients. IF we only take into account those with catheter related-candidemia (253 patients), the early catheter removal rate was 44.2% vs 86.6%, p= <.001.

Echocardiography in patients with **complicated candidemia** or **cardiological risk factor** for endocarditis

Cardozo C, et al. 2019. JAC. In press.

Conclusiones

1. La recomendación de las Guías ESCMID tiene baja evidencia

2. Dado la incidencia < 5% la clave es determiner a qué pacientes es imprescindible realizar al menos una ETT:
   - Candidemia persistente
   - Portadores de válvulas protésicas o cardiopatía predisponente
   - Embolización, insuf. cardiaca de novo, soplo de novo
   - UDVP

3. Factores protectores:
   - *C. glabrata*
   - Neoplasia hematológica
   - Recibir NPT

4. El *bundle* de candidemias incluye la eco en "candidemia complicada"

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