

Table S1: Items evaluated by PREDICT (5-day model), POSITIVE and VIRSTA scores.

	ITEM	PREDICT (5-DAY MODEL)	POSITIVE	VIRSTA
ACQUISITION	Community	2 points	-	2 points
	Healthcare-associated	1 point	-	
	Nosocomial	0 point	-	0 points
CARDIAC DEVICES	Prosthetic valve	-	5 points for any of them	4 points any of them
	Pacemaker	3 points		
	Defibrillator	2 points		
PERSISTENT BACTEREMIA		2 points (>72 hours)	-	3 points (>48 hours)
TIME TO POSITIVITY	Less than 9 hours	-	5 points	-
	9-11 hours		3 points	
	11-13 hours		2 points	
	More than 13 hours		0 points	
PREEXISTING NATURAL CARDIAC PREDISPOSITION		-	5 points*	3 points
INTRAVENOUS DRUG ABUSE		-	3 points	4 points
VASCULAR PHENOMENA/EMBOLI		-	6 points	5 points
PREVIOUS INFECTIVE ENDOCARDITIS		-	-	4 points**
MENINGITIS		-	-	5 points
VERTEBRAL OSTEOMYELITIS		-	-	2 points
SEVERE SEPSIS OR SHOCK		-	-	1 points
C-REACTIVE PROTEIN >190MG/L		-	-	1 points
POSSIBLE PUNCTUATION		0-7	0-19	0-20
CUT-OFF POINTS (HIGH RISK)		Greater than 1 point	Greater than 4 points	Greater than 2 points

*In POSITIVE score, cardiac device, preexisting natural valve disease and other cardiac predisposition are considered as the same item: "predisposing heart disease"

**In VIRSTA score, previous infective endocarditis and cardiac devices are considered as the same item: "permanent intracardiac device or previous infective endocarditis"

Table S2: Evaluation of alternative cut-off points of different clinical prediction rules to identify IE among SAB patients. IE: infective endocarditis. SAB: Staphylococcus aureus bacteriemia. Sens: sensitivity. Spec: Specificity. PPV: Positive Predictive Value. NPV: Negative Predictive Value. PLR: Positive likelihood-ratio. NLR: Negative likelihood-ratio. AUC: Area under de curve.

Score	Cut-off point	Sens.	Spec.	PPV	NPV	NLR	PLR
PREDICT (5-day model)	> 0 points	90.0%	31.0%	15.9%	95.6%	0.32	1.30
POSITIVE	> 0 points	92.0%	35.6%	16.8%	96.9%	0.22	1.43
	> 3 points	84.0%	50.6%	19.4%	95.7%	0.32	1.70
VIRSTA	> 0 points	94.0%	24.0%	14.9%	96.5%	0.25	1.24
	> 1 point	94.0%	33.6%	16.7%	97.5%	0.18	1.42

Table S3: Individual characteristics of patients identified as low risk of IE by means of VIRSTA score but who finally were diagnosed of IE. IE: infective endocarditis. CIED: Cardiac implantable electronic device, PVC: peripheral venous catheter. ATB: antibiotic. TTE: transthoracic echocardiography, TEE: transesophageal echocardiography

VARIABLE	Patient 1	Patient 2	Patient 3	Patient 4
Age (YEARS)	91	91	72	75
Sex	Male	Male	Female	Female
Charlson index	1	0	7	0
Chronic heart failure	No	No	Yes	No
Natural cardiac valve disease	No	No	No	No
Prosthetic heart valve disease	No	No	No	No
CIED	No	No	No	No
Hemodialysis	No	No	No	No
Liver cirrhosis	No	No	No	No
Intravenous drug user	No	No	No	No
Previous IE	No	No	No	No
Acquisition	Nosocomial	Nosocomial	Nosocomial	Community
Primary source	PVC related	PVC related	Unknown*	Unknown
Symptoms duration prior to ATB	48 hours	24 hours	24 hours	48 hours
Sepsis/shock	No	No	No	No
Fever defervescence within 48h	Yes	Yes	Yes	Yes
Septic emboli	No	No	No	No
Thrombophlebitis	No	No	No	No
Acute cardiac failure	No	No	No	No
Time to positivity	18 hours	17 hours	13 hours	16 hours
Persistent bacteriemia	No	No	No	No
Early source control (if necessary)	Yes	Yes	Yes*	-
TTE	Positive	Positive	Negative	Not done
TEE	Not done	Not done	Positive	Positive
Outcome	IE-related death	IE-related death	Alive No relapse	Alive No relapse
PREDICT score classification	Low risk	Low risk	Low risk	High risk
POSITIVE score classification	Low risk	Low risk	Low risk	Low risk

*Patient 3 had a central venous catheter which was presumed to be the probable source of infection, although it could not be demonstrate. The catheter was retired 1 week previously to symptoms onset.

Table S4: Univariate analysis of 30-day mortality in patients with no diagnosed with infective endocarditis and who survived the first 48 hours after the index blood culture extraction. Qualitative variables are expressed as percentage (absolute number) and compared by means of chi-square (or Fisher exact test when necessary). Quantitative variables are expressed as median (interquartile range) and compared by means of Mann-Whitney's U. CIED: Cardiac implantable electronic device. SAB: *Staphylococcus aureus* bacteriemia.

Variable	Total (n=335)	Survivor (n=281)	Non survivor (n=54)	p	Missing
Demographic and comorbidity					
Age	70 (56-81)	68 (54-80)	77 (64-90)	<0.001	0
Sex (female)	31.9% (107)	32.0% (90)	31.5% (17)	1.000	0
Charlson index	2 (1-5)	2 (0-4)	4 (2-6)	0.001	2
Age-adjusted Charlson index	5 (3-7)	5 (2-7)	7 (5-8)	<0.001	2
Arterial hypertension	52.8% (177)	50.9% (143)	63.0% (34)	0.136	0
Diabetes mellitus	27.8% (93)	28.5% (80)	24.1% (13)	0.619	0
Chronic heart failure	27.5% (92)	25.3% (71)	38.9% (21)	0.046	0
Ischemic heart disease	17.3% (58)	15.7% (44)	25.9% (14)	0.078	0
Natural cardiac valve disease	14.3% (48)	12.8% (36)	22.2% (12)	0.088	0
Prosthetic heart valve disease	3.0% (10)	2.8% (8)	3.7% (2)	0.667	0
CIED	4.8% (16)	5.3% (15)	1.9% (1)	0.334	0
Chronic renal failure	21.5% (72)	19.9% (56)	29.6% (16)	0.146	0
Hemodialysis	6.9% (23)	7.2% (20)	5.6% (3)	0.789	0
Liver cirrhosis	3.0% (10)	2.5% (7)	5.6% (3)	0.209	0
Solid organ malignancy	22.2% (74)	21.8% (61)	24.1% (13)	0.722	1
Parenteral drug user	0.9% (3)	1.1% (3)	0	1.000	1
Clinical presentation					
Acquisition	Nosocomial	53.1% (178)	53.7% (151)	50.0% (27)	Ref.
	Healthcare associated	17.6% (59)	16.4% (46)	24.1% (13)	0.224
	Community	29.3% (98)	29.9% (84)	25.9% (14)	0.843
Source of infection	Catheter-related	35.5% (119)	37.0% (104)	27.8% (15)	ref
	Primary-Unknown	24.5% (80)	20.8% (57)	43.8% (23)	0.001
	Other	40.6% (136)	42.7% (120)	29.6% (16)	0.837
Fever	89.8% (300)	88.9% (249)	94.4% (51)	0.325	1
Sepsis/septic shock	23.1% (77)	18.9% (53)	44.4% (24)	<0.001	1
Fever defervescence within 72 hours	82.3% (276)	83.2% (234)	72.2% (39)	0.305	29
Septic emboli	9.0% (30)	9.3% (26)	7.4% (4)	0.799	0
Acute kidney injury	36.0% (119)	32.5% (90)	53.7% (29)	0.003	4
Acute cardiac failure	15.0% (50)	12.5% (35)	27.8% (15)	0.007	2
Pitt's bacteremia score	0 (0-1)	0 (0-1)	1 (0-3)	<0.001	1
SOFA	2 (0-4)	1 (0-3)	4 (2-5)	<0.001	2
Microbiology					
Time to positivity	12 (10-16)	12 (10-16)	12 (9-17)	0.423	0
Persistent bacteriemia	26.9% (71)	25.0% (58)	40.6% (13)	0.087	71
Meticilin-resistant SAB	20.6% (69)	18.9% (53)	29.6% (16)	0.057	0
Diagnostic work-up					
TTE and/or TEE	72.0% (237)	75.9% (211)	51.0% (26)	<0.001	6
TTE	62.3% (207)	66.4% (186)	40.4% (21)	0.001	3
TEE	28.0% (11)	29.1% (81)	21.6% (11)	0.311	6
PET-CT	8.1% (27)	8.9% (25)	3.8% (2)	0.279	3
Complicated SAB	28.1% (93)	26.1% (73)	39.2% (20)	0.042	4
VIRSTA score (high risk)	49.0% (164)	45.2% (127)	68.5% (37)	0.002	0
Source control necessary and not performed	11.3% (38)	10.7% (30)	14.8% (8)	0.252	0