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Simple Scoring System to Predict In-Hospital Mortality After Surgery for Infective Endocarditis

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***Background*—**Aspecific scoring systems are used to predict the risk of death postsurgery in patients with infective endocarditis (IE). The purpose of the present study was both to analyze the risk factors for in-hospital death, which complicates surgery for IE, and to create a mortality risk score based on the results of this analysis.

***Methods and Results*—**Outcomes of 361 consecutive patients (mean age, 59.1±15.4 years) who had undergone surgery for IE in 8 European centers of cardiac surgery were recorded prospectively, and a risk factor analysis (multivariable logistic regression) for in-hospital death was performed. The discriminatory power of a new predictive scoring system was assessed with the receiver operating characteristic curve analysis. Score validation procedures were carried out. Fifty-six (15.5%) patients died postsurgery. BMI >27 kg/m^2 (odds ratio [OR], 1.79; *P*=0.049), estimated glomerular filtration rate <50 mL/min (OR, 3.52; *P*<0.0001), New York Heart Association class IV (OR, 2.11; *P*=0.024), systolic pulmonary artery pressure >55 mm Hg (OR, 1.78; *P*=0.032), and critical state (OR, 2.37; *P*=0.017) were independent predictors of in-hospital death. A scoring system was devised to predict in-hospital death postsurgery for IE (area under the receiver operating characteristic curve, 0.780; 95% CI, 0.734–0.822). The score performed better than 5 of 6 scoring systems for in-hospital death after cardiac surgery that were considered.

***Conclusions*—**A simple scoring system based on risk factors for in-hospital death was specifically created to predict mortality risk postsurgery in patients with IE. **(*J Am Heart Assoc*. 2017;6:e004806. DOI: 10.1161/JAHA.116.004806.)**

Key Words: cardiac valvular surgery • critical care • infective endocarditis • mortality • predictors • pulmonary hypertension • quality control • treatment outcome

Outcome in patients with infective endocarditis (IE) is a complex process, mediated by the immune system, and a function of interactions between patient-related factors (eg, demographic data, risk factors for cardiovascular disease, underlying cardiac disease, and comorbidities) and the properties of the causal agent (eg, nature, virulence, and antibiotic resistance). In 25% to 30% of cases, medical treatment alone is inadequate and must be combined with surgery, which aims to control infection by debridement and removal of necrotic tissue, and to restore cardiac morphology by surgical repair and/or valve replacement. Cardiac operations in some of these critically ill patients may be challenging and yield poor early and late results, even when carefully performed. Mortality rates have been reported to range

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Accompanying Tables S1 through S4 are available at http://jaha.ahajournals.org/content/6/7/e004806/DC1/embed/inline-supplementary-material-1.pdf

*A complete list of the AEPEI Study Group members can be found in the Appendix at the end of the article.

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between 10% in elective patients and up to 30% in urgent surgery. Prolonged invasive ventilation, low cardiac output, acute kidney injury, sepsis, and bleeding are frequent postoperative complications.[1–3] Consequently, for patients with IE, risk stratification is important not only for the surgeon for decision making, but also for counseling of the patient and comparative assessment of quality of care.

Currently, the risk of mortality postsurgery for IE is estimated using predictive scoring systems that have been derived from patient databases where most of the patients had had cardiac operations other than those for endocarditis.[4–7] Because of this inherent limitation, the utility of these aspecific predictive systems for patients with IE has been called into question.[8–13] In fact, specific scores to predict in-hospital death postsurgery in patients with IE have also been devised,[14–16] but with no external validation, and their impact in clinical practice is unclear.

In this context, we performed a prospective, population-based observational study in 8 European centers of cardiac surgery. The aims of the study were both to analyze the risk factors for hospital death and create a risk score based on the results of this analysis.

Methods

Study Patients

The study population consisted of 361 patients who underwent surgery for IE: (1) 138 consecutive patients (mean age, 60.6±8.5 years; 19.6% females) who were operated on between 2000 and 2015 at the Cardiovascular Department of the University Hospital of Trieste, Trieste, Italy; (2) 223 consecutive patients (mean age, 58.2±15.6 years; 22% females) who underwent surgery in 2008 in 7 French administrative areas: greater Paris, Lorraine, Rhône-Alpes, Franche-Comté, Marne, Ille-et-Vilaine, and Languedoc-Roussillon. The adult population in these areas (15.3 million inhabitants) covers 31.9% of the overall French population aged >18 years.[11] The French centers are grouped in the Association for the study and prevention of IE (Association pour l'Étude et la Prévention de l'Endocadite Infectieuse; AEPEI). Since 2001, the members of the AEPEI (see Appendix for full list of members) are enrolling patients with IE in each of the French administrative areas in an ad-hoc prospective registry.[17] In 2008, the data collection was particularly exhaustive, comprehensive, and accurate because it coincided with an epidemiological study performed by the AEPEI to update national data regarding the epidemiology of IE in France. Only definite cases of IE, as defined by the modified Duke criteria,[18] were included into the present study. For all patients, baseline characteristics, surgical and endocarditis-related features, as well as postoperative complications were prospectively recorded in a computerized data registry. For each center, approval to conduct the study was acquired from the local ethics committee. Patients were informed about the study, but were not required to provide individual consent, in accord with French and Italian legislation.

A risk factor analysis for in-hospital death postsurgery for IE was performed and a predictive scoring system, named the AEPEI score, was devised from the results of the analysis. External validation was performed using data from the AEPEI registry of patients with definite IE who underwent surgery between 2001 and 2015. The validation sample comprised 161 AEPEI patients for whom there were sufficient data to calculate the AEPEI score. The 223 AEPEI patients operated on in 2008 and included in the present study had been excluded preventively from the validation sample.

Definitions

Unless otherwise stated, the definitions and cut-off values of the preoperative variables were those used for the European System for Cardiac Operative Risk Evaluation (EuroSCORE). In particular, critical state was defined as the presence of ventricular tachycardia/ventricular fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before anesthetic room, preoperative inotropes or intra-aortic balloon pump, and preoperative acute renal failure (anuria or oliguria <10 mL/h).[5,6] Myocardial infarction (MI) was defined according to the recent definition criteria of type V MI by Moussa et al.[19] Acute kidney injury was defined as an increase in serum creatinine of 1.5 to 1.9 times the baseline level or serum creatinine increase ≥26.5 μmol/L within 7 days postsurgery.[20] Sternal wound infections were graded according to the Centers for Disease Control and Prevention definitions of surgical site infections. In brief, superficial incisional infection involves only skin or subcutaneous tissues, deep incisional infection involves deep soft tissues (fascial and muscle layers) with or without the sternal bone, and organ/space infection involves the mediastinum (mediastinitis).[21] For the purposes of this study, deep incisional infection and mediastinitis were considered to be deep sternal wound infections. Any sternal wound infection occurring within 3 months postsurgery was considered as postoperative wound infection.

Statistical Analysis

Continuous variables with normal distribution are expressed as mean±SD and those without normal distribution as median [interquartile range]. Categorical variables are expressed as number and percentage. Statistical comparison of baseline characteristics was performed using Pearson's chi-square or Fisher's exact test for categorical variables, and Student *t* test or the Mann–Whitney *U* test for continuous variables. Backward step-wise multivariable logistic regression analysis was used to identify independent predictors of in-hospital mortality. All variables with a $P<0.1$ by univariable analysis were included in the multivariable model. For each variable, the odds ratio (OR) and the corresponding 95% CI were calculated. Each of the risk indices had the variable weighted according to its regression coefficient. Goodness of fit of the model was evaluated with the Hosmer–Lemeshow test. The discriminatory power of the model was assessed with the receiver operating characteristic (ROC) curve and the calculation of the area under the curve (AUC). The new predictive scoring system, the AEPEI score, was compared (using De Long's method) with 3 existing scoring systems for in-hospital mortality after cardiac surgery, namely the EuroSCORE II,[5] the logistic EuroSCORE,[16] and the Ontario Province Risk (OPR) score,[17] as well as with 3 existing scores specifically designed to predict early mortality postsurgery for IE, namely the PALSUSE score (the prosthetic valve, age ≥70, large

Table 1. Baseline Characteristics of Patients (n=361)*

Variable	Trieste Database (n=138)	AEPEI Registry (n=223)	*P* Value
Age, y	60.6±8.5	58.2±15.6	0.15
Female sex	27 (19.6)	49 (22.0)	0.58
Hypertension	21 (15.2)	90 (40.4)	<0.0001
Current smoker	11 (8)	54 (24.2)	<0.0001
BMI, kg/m^2	25.5±4.1	25.4±5.4	0.88
Diabetes mellitus	22 (15.9)	48 (21.5)	0.19
Diabetes mellitus on insulin	9 (6.5)	18 (8.1)	0.58
Anemia†	113 (81.9)	171 (76.6)	0.95
White blood cell, 10^3/mm^3	12±5.9	14.9±10.5	0.0032
CRP, mg/L	193.6±81.3	140.4±85.5	<0.0001
Poor mobility‡	2 (1.4)	18 (8.1)	0.0075
Chronic lung disease‡	13 (9.4)	20 (9.0)	0.88
eGFR, mL/min§	67.7±37.3	69.4±35.4	0.67
Dialysis	13 (9.4)	2 (0.9)	<0.0001
Extracardiac arteriopathy‡	22 (15.9)	28 (12.6)	0.36
NYHA class IV	55 (39.9)	81 (36.3)	0.5
CCS class 4	20 (14.5)	3 (1.3)	<0.0001
Recent MI‡	0	1 (0.4)	1
Left ventricular ejection fraction <50%‡	32 (23.2)	43 (19.3)	0.37
sPAP >55 mm Hg‡	3 (2.2)	15 (12.4)	0.053
Coronary artery disease	18 (13)	25 (18.1)	0.6
Previous cardiac surgery	37 (26.8)	17 (7.6)	<0.0001
Critical state‡	27 (19.6)	35 (15.7)	0.34
Length of the preoperative hospital stay (days)‖	6 [2–19]	13 [5–25]	0.16

CCS indicates Canadian Cardiovascular Society; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; MI, myocardial infarction; NYHA, New York Heart Association; ROC, receiver operating characteristic; sPAP, systolic pulmonary artery pressure.
*Unless otherwise stated, values are mean±SD, or number (percentage).
†Defined as haemoglobin <12 g/dL for women and <13 g/dL for men.
‡The definitions and the cut-off values are those used for the EuroSCORE II.[5]
§The creatinine clearance rate, calculated according to the Cockcroft–Gault formula, was used to estimate GFR.
‖Median [interquartile range].

Table 2. Surgical Features (n=361)*

Variable	Trieste Database (n=138)	AEPEI Registry (n=223)	*P* Value
Reason for surgery			
Refractory heart failure attributed to valvular dysfunction	32 (23.2)	59 (26.5)	0.49
Persistent infection	18 (13)	28 (12.6)	0.89
Embolism	58 (42)	106 (47.5)	0.31
Recurrent	4 (2.9)	49 (22)	<0.0001
Perivalvular complications†	40 (29)	67 (30)	0.82
Surgical priority‡			<0.0001
Elective	26 (18.8)	107 (48.0)	
Urgent	90 (65.2)	94 (42.2)	
Emergency	22 (15.9)	11 (4.9)	
Salvage	0	11 (4.9)	
Valve involvement			
Aortic valve	86 (62.3)	138 (61.9)	0.93
Mitral valve	60 (43.5)	107 (48.0)	0.40
Tricuspid valve	7 (5.1)	28 (12.6)	0.02
Multivalvular	23 (16.7)	55 (24.7)	0.07
Large intracardiac destruction§	57 (41.3)	119 (52)	0.08
Weight of the intervention‡			
Combined CABG	25 (18.1)	13 (5.8)	<0.0001
Single non-CABG	89 (64.5)	126 (56.5)	0.13
Two procedures	46 (33.3)	82 (36.8)	0.51
Three procedures	3 (2.2)	15 (6.7)	0.053
Surgery on thoracic aorta	9 (6.5)	15 (6.7)	0.94

CABG indicates coronary artery bypass grafting; EuroSCORE, European System for Cardiac Operative Risk Evaluation.
*Number (percentage).
†Perivalvular leak, annular or aortic abscess, sinus of Valsalva aneurysm, aortic fistula, and prosthetic valve detachment.
‡The definitions are those used for the EuroSCORE II.[5]
§Defined as extensive valve destruction, perivalvular complications, or multivalvular involvement.

Table 3. Endocarditis-Related Features (n=361)*

Variable	Trieste Database (n=138)	AEPEI Registry (n=223)	*P* Value
Endocarditis			<0.0001
Active†	72 (52.2)	203 (91)	
Treated†	66 (47.8)	20 (9.0)	
Type of endocarditis			
Native valve	103 (74.6)	182 (81.6)	0.78
Prosthetic valve	27 (19.6)	41 (18.3)	0.78
Intracardiac device or other side	12 (8.7)	36 (16.1)	0.043
Causal agents			0.014
Streptococcus species	45 (32.6)	89 (39.9)	
Staphylococcus aureus	23 (16.7)	49 (22)	
Coagulase-negative Staphylococci	10 (7.2)	23 (10.3)	
Enterococcus species	13 (9.4)	24 (10.8)	
Gram-negative bacteria	6 (4.3)	9 (4)	
Fungi	2 (1.4)	2 (0.9)	
Not identified	39 (28.3)	27 (12.1)	

EuroSCORE indicates European System for Cardiac Operative Risk Evaluation.
*Number (percentage).
†The definitions are those used for the EuroSCORE II.[5]

intracardiac destruction, *Staphylococcus* spp, urgent surgery, sex [female], and EuroSCORE ≥10),[18] the De Feo score (for native valve IE),[19] and the Society of Thoracic Surgeons (STS) score for IE.[20] Both internal validation, based on the 0.632 bootstrap method, and external validation were performed. In addition, a new set of statistical analyses was carried out as follows: (1) In order to verify the stability of the original 5-variable model of the AEPEI score without the variable linked to pulmonary artery pressure, an alternate model of the AEPEI score was created by removing systolic pulmonary artery pressure (sPAP) >55 mm Hg from the original set of variables from which the score was generated. The goodness of fit and the discriminatory power of this alternate model were measured. (2) Because all the variables of the AEPEI score except BMI >27 kg/m^2 were also components of the EuroSCORE II, we added BMI >27 kg/m^2 to EuroSCORE II and investigated its incremental value with continuous net reclassification improvement and integrated discrimination improvement measures.[22] (3) Given the ratio of events to potential predictor variables, Akaike's information criterion (AIC), which accounts for the small number of events relative to the number of covariates, was analyzed.[23] Statistical

Table 4. In-Hospital Mortality and Perioperative Complications*

Complication	n=361
In-hospital death	56 (15.5)
30-day death	42 (11.6)
Stroke	9 (2.5)
Prolonged (>48 hours) invasive ventilation	482 (22.7)
Pneumonia	30 (8.3)
Atrial fibrillation, new onset	38/358† (10.6)
MI[19]	2 (0.6)
Immediate reoperation for acute prosthetic failure	9 (2.5)
Low cardiac output‡	32 (8.9)
Intraoperative and postoperative use of IABP	9 (2.5)
Use of ECMO	6 (1.7)
Acute kidney injury[20]	67 (18.6)
Renal replacement therapy	23 (6.4)
Bleeding peptic disease	4 (1.1)
Mesenteric ischemia	7 (1.9)
Acute pancreatitis	2 (0.6)
Multiorgan failure (3 or more organs)	11 (3.0)
Sepsis	22 (6.1)
Mediastinal re-exploration§	38 (10.5)
Deep sternal wound infection[21]	10 (2.8)
Length of the postoperative hospital stay, days	23.9 [12.7–42.4]‖

ECMO indicates extracorporeal membrane oxygenator; IABP, intra-aortic balloon pumping; KDIGO, Kidney Disease: Improving Global Outcomes; MI, myocardial infarction.
*Unless otherwise stated, values are number (percentage).
†Patients with preoperative stable sinus rhythm or paroxysmal atrial fibrillation.
‡Defined as 3 consecutive cardiac index measurements <2.0 L/min per m^2 despite adequate preload, afterload and inotropic support, or IABP.
§Through resternotomy or subxifoid window.
‖Median [interquartile range].

analyses were performed using SPSS for Windows (version 13.0; SPSS, Inc, Chicago, IL).

Results

Italian Versus French Study Patients

There were some differences in baseline characteristics, surgical data, and endocarditis-related features between the Italian and French patients of the study. The rates of preoperative dialysis, Canadian Cardiovascular Society (CCS) class 4, previous cardiac surgery, urgent/emergency priority, and combined coronary surgery were higher in Italian patients, whereas poor mobility, recurrent embolism, and active endocarditis were more frequent in French patients. Baseline levels of C-reactive protein were higher in Italian

Table 5. Risk Factor Analysis for In-Hospital Death After Surgery for IE (n=361)

Variable	Univariable Analysis*	Original Multivariable Analysis[†]			Alternate Multivariable Analysis[‡]		
	P Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age >70 years	0.016	1.14	0.52 to 2.53	0.74	1.18	0.55 to 2.55	0.67
BMI >27 kg/m^2[§]	0.039	2.15	1.06 to 4.37	0.034	1.91	0.96 to 3.81	0.065
eGFR <50 mL/min[‖,¶]	<0.0001	3.62	1.78 to 7.78	<0.0001	3.19	1.59 to 6.41	<0.0001
Dialysis	0.066	1.04	0.27 to 3.96	0.96	1.47	0.41 to 5.27	0.56
NYHA class IV	0.0001	2.43	1.14 to 5.18	0.022	2.07	1.00 to 4.27	0.05
CCS class 4	0.015	1.13	0.38 to 3.3	0.83	1.19	0.41 to 3.45	0.74
Left ventricular ejection fraction, 30% to 50%[¶]	0.036	1.37	0.65 to 2.9	0.41	1.29	0.61 to 2.72	0.51
sPAP >55 mm Hg[¶]	0.044	3.29	1.13 to 9.53	0.028	...	...	...
Coronary artery disease	0.052	1.33	0.1 to 17.9	0.83	1.46	0.11 to 18.6	0.77
Previous cardiac surgery	0.022	1.29	0.48 to 3.48	0.61	1.30	0.50 to 3.38	0.59
Critical state[¶]	<0.0001	2.52	1.11 to 5.73	0.027	2.49	1.11 to 5.78	0.026
Length of the preoperative hospital stay <10 days[§]	0.061	1.12	0.52 to 2.44	0.77	1.06	0.51 to 3.39	0.87
Urgent surgical priority[¶]	0.006	1.62	0.76 to 3.47	0.21	1.80	0.84 to 3.83	0.13
Combined CABG	0.052	1.49	0.12 to 2.34	0.77	1.26	0.09 to 17.8	0.87
Surgery on thoracic aorta	0.075	2.44	0.69 to 8.67	0.17	2.55	0.78 to 8.31	0.12
Prosthetic valve endocarditis	0.043	1.49	0.61 to 6.34	0.38	1.45	0.61 to 3.45	0.4

CABG indicates coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New York Heart Association; OR, odds ratio; ROC, receiver operating characteristic curve; sPAP, systolic pulmonary artery pressure.
*All the variables that were considered for the univariable analysis are listed in Table S1.
[†]All variables with a $P<0.1$ by univariable analysis were included in the multivariable model.
[‡]All variables with a $P<0.1$ by univariable analysis except sPAP >55 mm Hg were included in the multivariable model.
[§]The best discriminative value for in-hospital mortality by ROC analysis.
[‖]The creatinine clearance rate, calculated according to the Cockcroft–Gault formula, was used to estimate GFR.
[¶]The definitions and cut-off values are those used for EuroSCORE II.[5]

patients (Tables 1 through 3). Overall, the expected operative risk was higher in Italian patients than in the French series (mean EuroSCORE II, 15.9±18.7% versus 9.9±3.6%; $P<0.0001$). In-hospital mortality was higher in Italian than in French patients (20.3% versus 12.6%; $P=0.049$); 30-day mortality was also higher in the Italian series (18.1% versus 7.6%; $P=0.0025$).

Risk Factors for Hospital Death and Multivariable Analysis Model

A total of 56 (15.5%) patients died in hospital after surgery (Table 4). Baseline characteristics and operative data of these patients and the corresponding endocarditis-related features (Table S1) were compared with those of survivors of the in-hospital phase postsurgery (Tables S2 through S4). Risk factor analysis for in-hospital death postsurgery for IE was performed. A multivariable model with 16 variables was created using all the variables with a $P<0.1$ by univariable analysis. BMI >27 kg/m^2, estimated glomerular filtration rate (eGFR) <50 mL/min, New York Heart Association (NYHA) class IV, sPAP >55 mm Hg, and critical state were found to be independent predictors of postoperative in-hospital death (Tables 5 and 6).

The AEPEI Score: Performance and Validation

By multivariable analysis (Table 5), a new scoring system, the AEPEI score, was created to predict in-hospital mortality postsurgery for IE (Table 6). The new score includes 5 variables and consists of 7 risk classes (Table 7); its performance is summarized in Tables 8 and 9. In the study population, the AEPEI score had equivalent discriminatory power to that of the EuroSCORE II ($P=0.4$). It was found to be better than the logistic EuroSCORE ($P=0.0026$) and OPR score ($P=0.065$) and better than each of the 3 specific predictive systems (De Feo score, $P=0.054$, PALSUSE score, $P=0.047$, and STS risk score for IE; $P=0.027$), albeit without reaching statistical significance for the De Feo score (Figure 1). There was no difference in performance of the AEPEI score between

Table 6. The AEPEI Score: the Risk Factors for In-Hospital Death (by Backward Multivariable Logistic Regression) and the Scoring (n=361)

	The Original Model*						The Alternate Model†					
Variable	Regression Coefficient	SE	OR	95% CI	*P* Value	Points‡	Regression Coefficient	SE	OR	95% CI	*P* Value	Points‡
BMI >27 kg/m²§	0.58	0.34	1.79	1.02 to 3.45	0.049	1	...	...	...	...	...	...
eGFR <50 mL/min‖,¶	1.26	0.33	3.52	1.84 to 6.73	<0.0001	2.2	1.32	0.33	3.75	1.97 to 7.14	<0.0001	1.8
NYHA class IV	0.75	0.33	2.11	1.10 to 4.05	0.024	1.3	0.75	0.33	2.12	1.12 to 4.02	0.021	1
sPAP >55 mm Hg¶	0.58	0.58	1.78	1.06 to 5.61	0.032	1	...	...	...	...	...	...
Critical state¶	0.86	0.36	2.37	1.16 to 4.82	0.017	1.5	0.85	0.36	2.35	1.17 to 4.74	0.017	1.1
Constant	−3.065						−1.411					

eGFR indicates estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New York Heart Association; ROC, receiver-operating characteristic curve; sPAP, systolic pulmonary artery pressure.
*All variables with a *P*<0.05 by the original multivariable analysis (Table 5) were included.
†All variables with a *P*<0.05 by the alternate multivariable analysis (Table 5) were included.
‡Dividing each regression coefficient by the lowest coefficient and approximating to the first decimal place.
§The best discriminatory value for in-hospital mortality by ROC analysis.
‖The creatinine clearance rate, calculated according to the Cockcroft–Gault formula, was used to estimate GFR.
¶The definitions and cut-off values are those used for EuroSCORE II.[5]

the Italian and French series (*P*=0.37; Table 10). The logistic equation of the AEPEI final model was:

$$p = \frac{e^{(\beta_0 + \sum \beta_i X_i)}}{1 + e^{(\beta_0 + \sum \beta_i X_i)}}$$

where β_0 is the constant of the logistic regression equation (ie, −3.0645) and β_i the coefficient of the variable X_i. The coefficients and variable values are: for BMI, β_i=0.58 and X_i=1 if BMI >27 kg/m², or 0 if BMI ≤27 kg/m²; for eGFR, β_i=1.26 and X_i=1if eGFR <50 mL/min, or 0 if eGFR ≥50 mL/min; for NYHA class IV, β_i=0.75 and X_i=1 in case of NYHA class IV, or 0 if not; for sPAP, β_i=0.58 and X_i=1 if sPAP ≥55 mm Hg, or 0 if sPAP <55 mm Hg; for critical state, β_i=0.86 and X_i=1 if the patient is in critical state, or 0 if not (Table 6).

All the AEPEI score variables remained significant by bootstrap internal validation (Table 11). By external validation, there were no significant differences between expected and observed deaths (χ^2=2.7; 5 *df*; *P*=0.75; Table 12) and the discriminatory power of the score was confirmed to be good (AUC, 0.715; 95% CI, 0.638–0.783; Figure 2).

The Alternative 3-Variable AEPEI Score Model

According to the alternate multivariable model (Table 5), an alternate model of the AEPEI score was created (Table 6). This model includes 3 variables and consists of 4 risk classes (Table 7). Its discriminatory power was equivalent to that of the original 5-variable model (*P*=0.49); calibration was slightly lower (Tables 8 and 13; Figure 3). There was no significant difference in the performance of the alternate model of the AEPEI score between the Italian and the French series (*P*=0.29; Table 10). The logistic equation of the alternate AEPEI model was:

$$p = \frac{e^{(\beta_0 + \sum \beta_i X_i)}}{1 + e^{(\beta_0 + \sum \beta_i X_i)}}$$

where β_0 is the constant of the logistic regression equation (ie, −1.411) and β_i the coefficient of the variable X_i. The coefficients and variable values are: for eGFR, β_i=1.32 and X_i=1if eGFR <50 mL/min, or 0 if eGFR ≥50 mL/min; for NYHA class IV, β_i=0.75 and X_i=1 in case of NYHA class IV, or 0 if not; for critical state, β_i=0.86 and X_i=1 if the patient is in critical state, or 0 if not (Table 6).

The 3 variables of the alternate model of the AEPEI score remained significant by bootstrap internal validation (Table 14). By external validation, there were no significant differences between expected and observed deaths (χ^2=2.1; 1 *df*; *P*=0.15; Table 15) and the discriminatory power of the score was satisfactory (AUC, 0.690; 95% CI, 0.613–0.761).

The AEPEI Incremented EuroSCORE II

The variable BMI >27 kg/m² was added to the EuroSCORE II. The integrated discrimination improvement was 0.027

Table 7. Specific Predictive Scoring Systems for In-Hospital Mortality After Surgery for IE

Scoring System	Study Population	Variables (Points)	Discrimination Power	Expected Hospital Mortality
AEPEI score, the original model* (2016)	361 pts. (mean age, 59.1±15.4 years); AEPEI registry (223 pts., 7 French hospitals, 2008) & Cardiovascular Department of Trieste, Italy (138 pts., 2000–2015); Hospital mortality, 15.5%; 30-Day mortality, 11.6%	5 variables: BMI >27 kg/m^2 (1) eGFR <50 mL/min (2.2) NYHA class IV (1.3) sPAP >55 mm Hg (1) Critical state (1.5)	AUC, 0.780 (95% CI, 0.734–0.822)	Score, 0 to 1 point: expected mortality, 4.5% to 7.7%; Score, 1.3 to 2 points: expected mortality, 9% to 12.9%; Score, 2.2 to 2.8 points: expected mortality, 14.1% to 18.9%; Score, 3.2 to 3.8 points: expected mortality, 22.6% to 29.4%; Score, 4.5 to 5 points: expected mortality, 38.2% to 45.1%; Score, 5.5 to 6 points: expected mortality, 52.5% to 59.4%; Score, 7 points: expected mortality, 72.4%
AEPEI score, the alternate model* (2016)	Idem	3 variables: eGFR <50 mL/min (1.8) NYHA class IV (1) Critical state (1.1)	AUC, 0.774 (95% CI, 0.727–0.816)	Score, 0 to 1 point: expected mortality, 19.6% to 34.1%; Score, 1.1 to 1.8 points: expected mortality, 36.6% to 47.7%; Score, 2.1 to 2.9 points: expected mortality, 55% to 68.3%; Score, 3.9 points: expected mortality, 82%
PALSUSE score[14] (2014)	437 pts. (mean age, 61.4±15.5 years); GAMES registry (26 Spanish hospitals, 2008–2010); Hospital mortality, 24.3%	7 variables: Prosthetic valve (2) Age ≥70 years (1) Large intracardiac destruction (2) *Staphylococcus* spp (2) Urgent surgery (2) Sex, female (2) EuroSCORE II ≥10% (1)	AUC, 0.84 (95% CI, 0.79–0.88)	Hospital mortality ranged from 0, in patients with score=0, to 45.4% in patients with score >3
De Feo score (for native valve IE)[15] (2012)	440 pts. (mean age, 49±16 years); Department of Cardiothoracic Surgery of Naples, Italy (1980–2009); Hospital mortality, 9.1%	6 variables: Age, 5 classes (5–13) Renal failure (5) NYHA class IV (9) Preop. ventilator support (11) Positivity of latest preop. blood cultures (5) Perivalvular involvement (5)	AUC, 0.88 (95% CI, 0.82–0.93)	Score, 0 to 5 points: expected mortality ≤4.55%; Score, 7 to 13 points: expected mortality, 4.55% to 9.1%; Score, 14 to 19 points: expected mortality, 9.2% to 27.3%; Score ≥20 points: expected mortality >27.3%
STS risk score for IE[16] (2011)	19 543 pts. (mean age, 55 years); STS database (2002–2008) 30-day mortality, 8.2%	12 variables: Emergency, salvage status, or cardiogenic shock (17) Preop. hemodialysis, renal failure, or creatinine level >2.0 mg/dL (12) Preop. inotropic or balloon pump support (10) Active (vs treated) endocarditis (10) Multiple valve involvement (9) Insulin-dependent diabetes mellitus (8) Arrhythmia (8) Previous cardiac surgery (7) Urgent status without cardiogenic shock (6) Non-insulin-dependent diabetes mellitus (6) Hypertension (5) Chronic lung disease (5)	AUC, 0.758	...

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse; AUC, area under the receiver operating characteristic (ROC) curve; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; GAMES, Grupo de Apoyo al Manejo de la Endocarditis infecciosa en España; IE, infective endocarditis; NYHA, New York Heart Association; PALSUSE, Prosthetic valve, Age ≥70, Large intracardiac destruction, *Staphylococcus* spp, Urgent surgery, Sex [female], EuroSCORE II ≥10%; Preop., preoperative; pts., patients; sPAP, systolic pulmonary artery pressure; STS, the Society of Thoracic Surgery.
*Table 6.

Table 8. Performance of the AEPEI Score (2 Models) and of 6 Other Specific/Nonspecific Predictive Scoring Systems for In-Hospital Mortality After Surgery for IE in the Original Series of Patients

	Original Series (n=361)					
	Goodness of Fit*			Discriminatory Power†		
System	Chi-square	DF	*P* Value	AUC	95% CI	AIC Value[23]
Specific						
AEPEI score, the original model	2.6	5	0.76	0.780	0.734 to 0.822	257.5
AEPEI score, the alternate model	3.9	3	0.27	0.774	0.727 to 0.816	266.9
PALSUSE score[14]	2.3	7	0.97	0.684	0.633 to 0.731	289.1
De Feo score (for native valve IE)[15]	2.8	6	0.9	0.722	0.654 to 0.790	296.8
STS risk score for IE[16]	7.9	8	0.44	0.709	0.659 to 0.756	300
Aspecific						
EuroSCORE II[5]	9.5	8	0.3	0.751	0.704 to 0.795	132.5
Logistic EuroSCORE[6]	14.3	8	0.068	0.632	0.580 to 0.682	306.9
OPR score[7]	12.1	8	0.15	0.698	0.647 to 0.745	288.7

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse; AIC, Akaike's information criterion; AUC, area under the receiver operating characteristic (ROC) curve; DF, degrees of freedom; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IE, infective endocarditis; NYHA, New York Heart Association; OPR, Ontario Province Risk; PALSUSE, prosthetic valve, age ≥70, large intracardiac destruction, *Staphylococcus* spp, urgent surgery, sex (female), EuroSCORE II ≥10%; STS, the Society of Thoracic Surgeons.
*By the Hosmer–Lemeshow test for logistic regression.
†By ROC analysis.

($P<0.01$). The continuous net reclassification improvement was 0.13 ($P=0.37$).

The AIC Analysis

With 56 events and 16 variables in the initial logistic regression (with multiple categories that further increase the dimension), the initial model was severely overfit (Table 5). However, according to the AIC,[22] each predictive system that was considered in this study except EuroSCORE II was <0.0001 times as probable as the AEPEI score to minimize the information loss. The alternate AEPEI model was 0.0091 times as probable as the original AEPEI model to minimize the information loss (Table 8).

Discussion

Based on analysis of perioperative data from 361 patients from 8 European centers of cardiac surgery, we devised a weighted scoring system to predict in-hospital mortality postsurgery for IE, namely the AEPEI score. The score is composed of only 5 variables and consists of 7 classes of risk. It was derived from a backward step-wise logistic regression model that was created to find the independent predictors of in-hospital death in this series of patients with IE. Although the variables of the model were chosen from a pool of baseline characteristics of the patients, surgical data, and endocarditis-related features, all the variables of the AEPEI score (BMI >27 kg/m^2, eGFR <50 mL/min, NYHA class IV, sPAP >55 mm Hg, and critical state) refer to the patient's preoperative state and include an anthropometric measurement, a laboratory finding, an estimate of resting dyspnea, an invasive (or ultrasound) intracardiac pressure measurement, and a well-defined composite variable of events indicating the critical preoperative state of the patient.

The goodness of fit of the statistical model was satisfactory and the score showed a good discriminatory power. Both internal and external validation of the AEPEI score were performed. The results of the validation procedures confirmed satisfactory calibration and discriminatory power of the score. In the study population, the AEPEI score performed better than 3 specific scoring systems for in-hospital (or 30-day) mortality postsurgery for IE that were considered[18–20] and was superior to 2[14,16] of the 3 scoring systems for in-hospital (or 30-day) mortality after any cardiac operation that were used for comparison. These results were confirmed also according to a more-robust approach such as the AIC.[22] In addition, the AEPEI score is not intended only for native valve endocarditis, as is the De Feo score,[15] and the AEPEI score includes a composite variable, that is, critical state, similar to what applies in the PALSUSE and STS risk scores for IE.[18,20] The AEPEI score was found to be equivalent to EuroSCORE II, which consists of 18 (simple and composite) variables and was modeled from a contemporary surgical cohort of 22 381 patients, including 497 (2.2%) with active IE.[5] The EuroSCORE II performance in estimating perioperative risk of patients

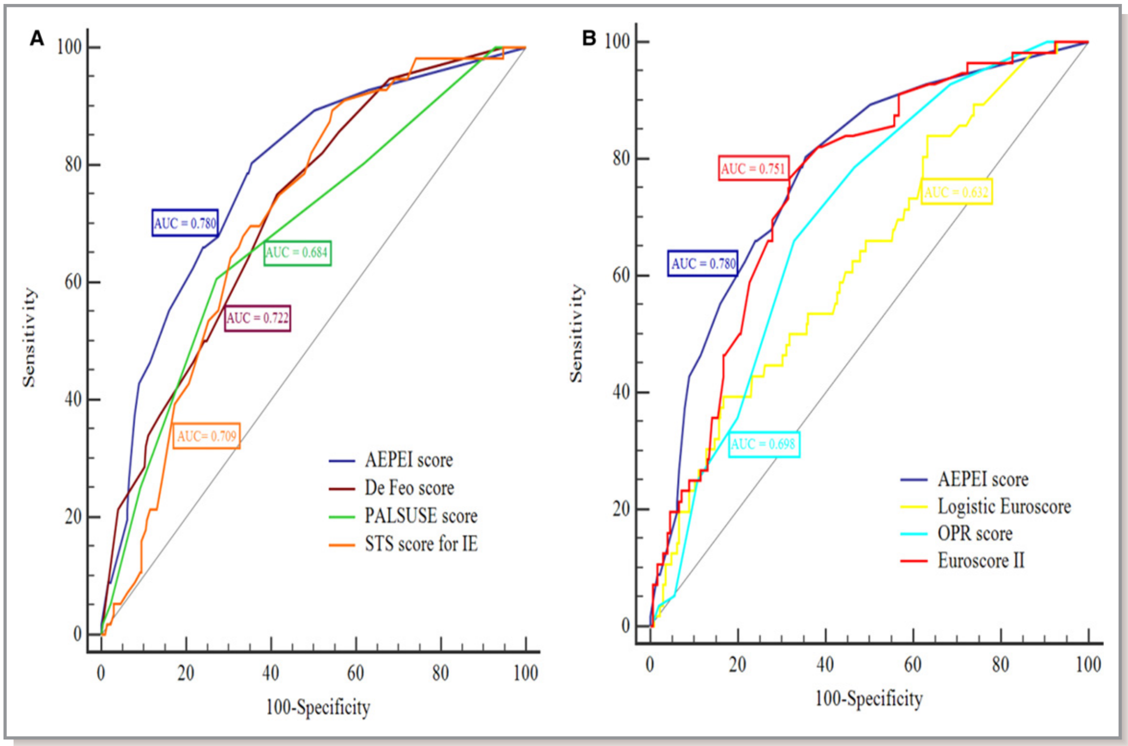

Figure 1. The new predictive scoring system for in-hospital death postsurgery for IE (the AEPEI score) vs (A) three scoring systems specifically created to predict in-hospital (or 30-day) mortality postsurgery for IE and (B) 3 predictive scoring systems for in-hospital (or 30-day) mortality after cardiac surgery. AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse; AUC, area under the receiver operating characteristic curve; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IE, infective endocarditis; OPR, Ontario Province Risk; PALSUSE, Prosthetic valve, Age ≥70, Large intracardiac destruction, *Staphylococcus* spp, Urgent surgery, Sex [female], EuroSCORE ≥10; STS, the Society of Thoracic Surgeons.

undergoing surgery for IE has been evaluated by other investigators. Some researchers think that it underestimates post–cardiac surgery mortality in these patients[7]; others have demonstrated poor calibration and comparatively poor discrimination of the system for emergency cardiac surgery.[8] Yet, others believe that the EuroSCORE II may be a useful and appropriate tool for estimating perioperative risk, even for IE patients, and that specific endocarditis features will increase model complexity without an unequivocal improvement in predictive ability.[6,9] Consequently, there is a lack of consensus on this issue. To improve the EuroSCORE II performance in IE, we added the only variable present in the AEPEI score that is not in the EuroSCORE II (namely, BMI >27 kg/m^2). Results showed that there was no added value to be derived from adding this variable to EuroSCORE II. Logistic EuroSCORE showed a poor performance in the present study, even though other researchers have reported different results.[21]

Table 9. The AEPEI Score, the Original Model: Contingency Table for the Hosmer–Lemeshow Test for Logistic Regression (n=361)

Group	Death		Survival		Total
	Observed	Expected	Observed	Expected	
1	4	5.2	113	111.8	117
2	2	3.2	39	37.8	41
3	5	4.5	45	45.5	50
4	7	4.5	26	28.5	33
5	7	8.0	33	32.0	40
6	11	10.2	26	26.8	37
7	20	20.4	23	22.6	43

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse.

sPAP was the sole hemodynamic parameter that was considered for analysis, which can be evaluated by echocardiography when even a trivial tricuspid regurgitation is present. In the absence of any grade of tricuspid regurgitation, the PAP measurement requires right heart catheterization. The fact that this method is invasive and could be a port of entry for infection make some practitioners reluctant to perform it presurgery. We therefore created an alternate model of the AEPEI score by removing sPAP >55 mm Hg from the original set of variables on which the original score was based. This procedure generated a 3-variable predictive scoring system (eGFR <50 mL/min, NYHA class IV, and

Table 10. Performance of the Considered Predictive Scores in the Trieste Database and in the AEPEI Registry

	Trieste Database (n=138)					AEPEI Registry (n=223)				
	Goodness of Fit*			Discriminatory Power†		Goodness of Fit*			Discriminatory Power†	
System	Chi-square	DF	*P* Value	AUC	95% CI	Chi-square	DF	*P* Value	AUC	95% CI
Specific										
AEPEI score, the original model	12.6	6	0.55	0.744	0.662 to 0.814	4.5	5	0.49	0.804	0.746 to 0.854
AEPEI score, the alternate model	5.03	4	0.28	0.732	0.650 to 0.804	1.5	3	0.68	0.802	0.744 to 0.852
PALSUSE score[14]	3.4	7	0.85	0.723	0.640 to 0.795	6.3	7	0.5	0.691	0.626 to 0.751
De Feo score (for native valve IE)[15]	1.6	6	0.95	0.730	0.648 to 0.802	5.2	6	0.63	0.720	0.656 to 0.778
STS risk score for IE[16]	3.3	8	0.92	0.706	0.623 to 0.780	3.1	8	0.93	0.740	0.677 to 0.796
Aspecific										
EuroSCORE II[5]	4.2	8	0.84	0.763	0.683 to 0.831	5.1	8	0.65	0.772	0.711 to 0.825
Logistic EuroSCORE[6]	15.5	8	0.05	0.658	0.572 to 0.736	13.8	8	0.088	0.500	0.433 to 0.568
OPR score[7]	13.8	8	0.087	0.637	0.551 to 0.717	3.9	8	0.87	0.694	0.656 to 0.753

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse; AUC, area under the receiver operating characteristic (ROC) curve; DF, degrees of freedom; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IE, infective endocarditis; NYHA, New York Heart Association; OPR, Ontario Province Risk; PALSUSE, prosthetic valve, age ≥70, large intracardiac destruction, *Staphylococcus* spp, urgent surgery, sex (female), EuroSCORE II ≥10%; STS, The Society of Thoracic Surgeons.
*By the Hosmer–Lemeshow test for logistic regression.
†By ROC analysis.

critical state) that had equivalent discriminatory power, but lower goodness of fit, compared to the original AEPEI score. Unlike other predictive systems,[14] no infectious agent was related to an increased in-hospital mortality postsurgery. However, in the present experience, there was an under-representation of potentially catastrophic organisms, such as

Table 11. Bootstrap Analysis of the Logistic Regression Model From Which the Original Model of the AEPEI Score was Generated*

		Bootstrap (No. of Samples: 1000)			
Variable	A	Bias	SE	95% CI	*P* Value
Age >70 years	0.40	−0.01	0.40	−0.41 to 1.15	0.27
BMI >27 kg/m²†	0.72	0.02	0.38	−0.02 to 1.43	0.03
eGFR <50 mL/min‡§	1.11	0.09	0.39	0.43 to 1.99	<0.01
Dialysis	0.19	−0.13	2.03	−2.09 to 2.06	0.83
NYHA class IV	0.81	0.08	0.43	0.03 to 1.76	0.028
CCS class 4	0.27	−0.02	0.67	−1.22 to 1.54	0.63
Left ventricular ejection fraction, 30% to 50%§	0.26	0.01	0.41	−0.51 to 1.06	0.48
sPAP >55 mm Hg§	−1.24	−0.21	1.10	−2.77 to −0.36	0.013
Coronary artery disease	0.33	−5.57	9.88	−20.8 to 3.25	0.502
Previous cardiac surgery	0.41	0.01	0.52	−0.60 to 1.41	0.41
Critical state§	0.97	0.06	0.51	−0.001 to 2.08	0.042
Length of the preop. hospital stay <10 days†	0.16	−0.04	0.48	−0.78 to 1.10	0.73
Urgent surgical priority§	0.65	0.04	0.40	−0.12 to 1.50	0.078
Combined CABG	0.28	5.59	9.89	−2.84 to 21.5	0.55
Surgery on thoracic aorta	1.11	0.05	0.76	−0.45 to 2.55	0.086
Prosthetic valve endocarditis	0.37	0.01	0.50	−0.60 to 1.29	0.44

CABG indicates coronary artery bypass grafting; CCS indicates Canadian Cardiovascular Society; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New York Heart Association; preop., preoperative; ROC, receiver operating characteristic; sPAP, systolic pulmonary artery pressure.
*All variables with a $P<0.1$ by univariable analysis were included in the model.
†The best discriminatory value for in-hospital mortality by ROC analysis.
‡The creatinine clearance rate, calculated according to the Cockcroft–Gault formula, was used to estimate GFR.
§The definitions and cut-off values are those used for the EuroSCORE II.[5]

Table 12. The AEPEI Score, the Original Model: Contingency Table for the Hosmer–Lemeshow Test for Logistic Regression (n=161)

Group	Death		Survival		Total
	Observed	Expected	Observed	Expected	
1	1	0.8	21	21.2	22
2	0	0.2	3	2.8	3
3	5	5.0	76	76.0	81
4	3	1.7	10	11.3	13
5	1	2.7	14	12.3	15
6	4	4.1	12	11.9	16
7	7	6.6	4	4.4	11

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse.

Table 13. The AEPEI Score, the Alternate Model: Contingency Table for the Hosmer–Lemeshow Test for Logistic Regression (n=361)

Group	Death		Survival		Total
	Observed	Expected	Observed	Expected	
1	6	8.5	153	150.5	159
2	6	6.5	55	54.5	61
3	11	8.9	41	43.1	52
4	17	13.1	30	33.9	47
5	16	19.0	26	23.0	42

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse.

fungi and multidrug resistant Gram-negative bacteria. Although 3 surgical features (urgent priority, combined coronary surgery, and surgery on thoracic aorta) and 1 endocarditis-related feature (prosthetic valve endocarditis) were found to be related (*P*<0.1) to in-hospital death by univariable analysis, they were not confirmed as risk factors by multivariable analyses. Contrary to other previous risk prediction models,[4–7,14,16] the variable "prosthetic valve endocarditis" was not found to be an independent risk factor for postoperative in-hospital death in either of the AEPEI scores. Our data do not provide any firm evidence to explain this discrepancy. No intraoperative features were associated with increased postoperative death, even when a composite variable, such as large intracardiac destruction, was considered. In our opinion, this is a strong point of the AEPEI score. Every practitioner is indeed well aware that results of combined cardiac operations in critically ill patients and the treatment of complex intracardiac lesions can be dependent on the surgeon's experience and expertise, which are both difficult to measure.

Despite the existence of some differences between the Italian and French patients of the study, such as the

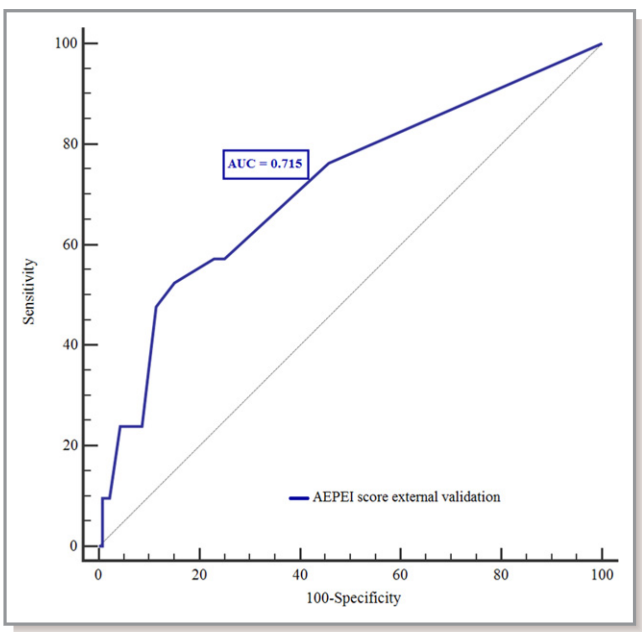

Figure 2. External validation of the AEPEI score in a validation sample of 161 patients: discriminatory power. AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse; AUC, area under the receiver-operating characteristic curve.

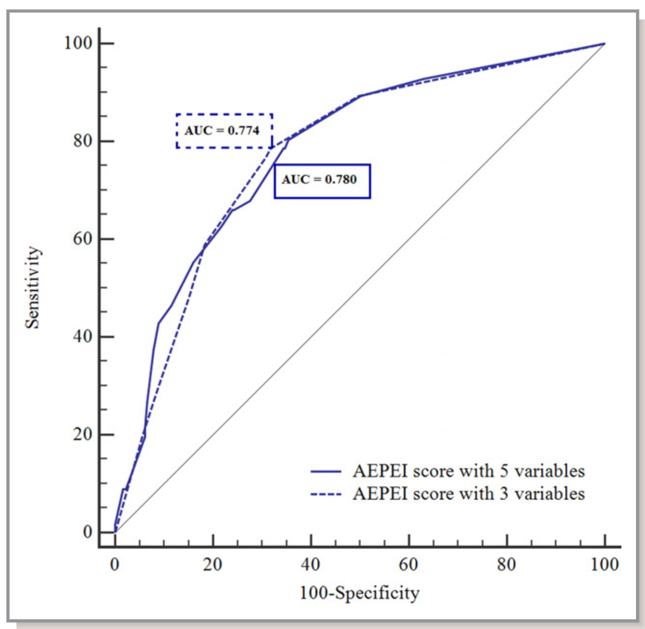

Figure 3. AEPEI score discriminatory power: the original 5-variable model vs the alternate 3-variable model. AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse; AUC, area under the receiver operating characteristic curve.

Table 14. Bootstrap Analysis of the Logistic Regression Model From Which the Alternate Model of the AEPEI Score was Generated*

Variable	A	Bootstrap (No. of Samples: 1000)			
		Bias	SE	95% CI	*P* Value
Age >70 years	0.16	<0.001	0.47	−0.81 to 1.05	0.7
BMI >27 kg/m^2†	0.65	0.04	0.41	−0.13 to 1.55	0.08
eGFR <50 mL/min‡,§	1.16	0.14	0.41	0.49 to 2.13	<0.01
Dialysis	0.38	−0.08	1.66	−1.68 to 2.18	0.66
NYHA class IV	0.73	0.06	0.41	−0.004 to 1.66	0.05
CCS class 4	0.18	−0.01	0.74	−1.40 to 1.53	0.8
Left ventricular ejection fraction, 30% to 50%§	0.25	−0.01	0.47	−0.75 to 1.14	0.54
Coronary artery disease	0.38	−6.50	10.1	−20.2 to 3.13	0.44
Previous cardiac surgery	0.26	0.01	0.57	−0.82 to 1.44	0.6
Critical state§	0.91	0.08	0.53	−0.07 to 2.07	0.05
Length of the preop. hospital stay <10 days†	0.06	0.05	0.44	−0.76 to 0.99	0.89
Urgent surgical priority§	0.59	−0.01	0.44	−0.25 to 1.42	0.14
Combined CABG	0.23	6.51	10.1	−2.68 to 21.1	0.53
Surgery on thoracic aorta	0.94	0.01	0.76	−0.70 to 2.41	0.13
Prosthetic valve endocarditis	0.37	<0.001	0.49	−0.66 to 1.28	0.4

CABG indicates coronary artery bypass grafting; CCS indicates Canadian Cardiovascular Society; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New York Heart Association; preop., preoperative; ROC, receiver operating characteristic; sPAP, systolic pulmonary artery pressure.
*All variables with a $P<0.1$ by univariable analysis except sPAP >55 mm Hg were included in the model.
†The best discriminatory value for in-hospital mortality by ROC analysis.
‡The creatinine clearance rate, calculated according to the Cockcroft-Gault formula, was used to estimate GFR.
§The definitions and cut-off values are those used for the EuroSCORE II.[5]

preoperative characteristics of patients, surgical data, and endocarditis-related features, there was no significant difference in the discriminatory power of the AEPEI score between the 2 series of patients. Besides, the Italian series included patients operated on between 2000 and 2015. This could imply that the score works well even in populations of patients with different rates of comorbidities from other institutions, and operated on in different historical periods. Obviously, these hypotheses remain to be verified by new studies that take into consideration the impact on outcomes of the use of different surgical methods, different rates of use of surgical techniques, and different perioperative management of patients.

Table 15. The AEPEI Score, the Alternate Model: Contingency Table for the Hosmer–Lemeshow Test for Logistic Regression (n=161)

Group	Death		Survival		Total
	Observed	Expected	Observed	Expected	
1	10	9.0	110	111.0	120
2	1	3.1	21	18.9	22
3	10	8.9	9	10.1	19

AEPEI indicates Association pour l'Etude et la Prévention de l'Endocadite Infectieuse.

Overall, the performance of the predictive models considered and derived from large populations of patients from North America, that is, STS risk score for IE and OPR score, was lower than the European models. This could stress the concept that outcomes postsurgery for IE are influenced by epidemiological features both of the patient and the involved pathogen.

Study Limitations

The primary limitation of the present study was the small size of the sample. Actually, because the study patients were only 361, it is not surprising that only 5 variables were significant upon multivariable modeling. There may be indeed insufficient power to determine higher dimensional models. However, this is a problem common also to 2 other existing scoring systems that are being used to predict early mortality postsurgery for IE, namely the PALSUSE and the De Feo score,[14,16] and more generally to every predictive system of rare events occurring in patients having rare diseases. Although the present authors are aware that each score performs well in the data set in which it is fit, and the more-interesting comparison would be of the various scores in the external validation sample, this comparison was impossible because no other score than the AEPEI could be calculated in the validation sample with the available data. Because the pathogen was not identified in about 18% of cases, there is the possibility that some microorganisms were related to increased mortality rate postsurgery, especially because some infections may have been misclassified in terms of etiology because of the frequent rate of coinfections in endocarditis. This study did not evaluate the contribution to mortality risk of potentially important factors, such as antibiotic treatment and preoperative patient preparation. The impact of different strategies of myocardial protection and techniques, such as intraoperative ultrafiltration, on the risk of death was not taken into account.

Conclusions

Nonspecific scoring systems derived from large populations of patients are being used worldwide to predict adverse events after cardiac surgery, even in patients with IE. For this difficult subset of patients, however, risk stratification is of the utmost importance not only to aid the surgeon's decision making, but also to ensure true informed consent for patients and their family, and to allow comparative assessment of quality of care. Specific and simple predictive systems, such as the AEPEI score developed and validated here, could be useful to achieve these objectives. However, further larger validation studies are necessary before introducing the AEPEI score into the clinical practice.

Appendix

The Association pour l'Etude et la Prevention de l'Endocadite Infectieuse (AEPEI) Study Group Members

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None.

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SUPPLEMENTAL MATERIAL

Table S1. The variables entered in the analysis.

Group	Variable	Cut-points and subsets
Baseline characteristics of patients	Age (years)	<60, 60–70, >70
	Female sex	
	Hypertension	
	Current smoker	
	Body mass index (kg/m^2)	>27*
	Diabetes mellitus	Diabetes on insulin
	Anemia†	
	White blood cell ($10^3/mm^3$)	
	C-reactive protein (mg/l)	
	Poor mobility‡	
	Chronic lung disease‡	
	eGFR (ml/min)§	>85, 50–85, <50‡
	Dialysis	
	Extracardiac arteriopathy‡	

	NYHA class	I, II, III, IV
	CCS class	4
	Recent myocardial infarction‡	
	Left ventricular ejection fraction (%)	>50, 30–50, 20–30, <20‡
	Pulmonary artery pressure, systolic (mmHg)	<35, 35–55, ≥55‡
	Coronary artery disease	
	Previous cardiac surgery	
	Critical state‡	
	Length of the preoperative hospital stay (days)	>10*
	Era‖	2000–2005, 2006–2010, 2011–2015
Surgical features	Reason for surgery	Refractory heart failure due to valvular dysfunction
		Persistent infection
		Embolism (and recurrent embolism)
		Perivalvular complications#

	Surgical priority‡	Elective
		Urgent
		Emergency
		Salvage
	Valve involvement	Aortic
		Mitral
		Tricuspid
		Multivalvular
	Large intracardiac destruction	Extensive valve destruction
		Perivalvular complications
		Multivalvular involvement
	Weight of the intervention‡	Combined CABG
		Single non-CABG

		Two procedures
		Three procedures
		Surgery on thoracic aorta
Endocarditis-related features	Type of endocarditis	Active or treated‡
		Native valve
		Prosthetic valve
		Intracardiac device or other side
	Causal agents	Streptococcus species
		Staphylococcus aureus
		Coaagulase-negative Staphylococci
		Enterococcus species
		Gram-negative bacteria
		Fungi
		Not identified

*The best discriminative value for hospital mortality by ROC analysis.

†Defined as haemoglobin <12 g/dl for women and <13 g/dl for men.

‡The definitions and the cut-points are those used for the EuroSCORE II (*Suppl. Ref.* 1).

§The creatinine clearance rate, calculated according to the Cockcroft-Gault formula, was used to estimate eGFR.

||Only the Italian study patients are considered for this analysis.

#Perivalvular leak, annular or aortic abscess, sinus of Valsalva aneurysm, aortic fistula, and prosthetic valve detachment.

CABG=coronary artery bypass grafting; CCS=Canadian Cardiovascular Society; EuroSCORE=European System for Cardiac Operative Risk Evaluation; eGFR=estimated glomerular filtration rate; NYHA=New York Heart Association; ROC=receiver-operating characteristic curve

Table S2. Baseline characteristics of patients (n=361)*

Variable	Total (n=361)	In-hospital dead (n=56)	Alive (n=305)	p-Value
Age (years)	59.1±15.4	62.0±15.7	58.6±15.3	0.13
<60	169 (46.8)	16 (28.6)	153 (50.2)	
60–70	97 (26.9)	18 (32.1)	79 (25.9)	
>70	95 (26.3)	22 (39.3)	73 (23.9)	
Female sex	76 (21.1)	15 (26.8)	61 (20.0)	0.25
Hypertension	111 (30.7)	18 (32.1)	93 (30.5)	0.81
Current smoker	65 (18.0)	6 (10.7)	59 (19.3)	0.12
Body mass index (kg/m^2)	25.4±4.9	26.7±5.8	25.1±4.7	0.026
>27†	95 (26.3)	21 (37.5)	74 (24.3)	0.039
Diabetes	70 (19.4)	10 (17.9)	60 (19.7)	0.75
Diabetes on insulin	27 (7.5)	6 (10.7)	21 (6.9)	0.32
Anemia‡	284 (81.7)	50 (89.3)	245 (80.3)	0.13
White blood cell (10^3/mm^3)	14.9 ± 10.5	15.3 ± 6.7	14.8 ± 11.1	0.75
C-reactive protein (mg/l)	140.4±85.5	151.6±66.9	138.4±88.4	0.29
Poor mobility§	20 (5.5)	5 (8.9)	15 (4.9)	0.23
Chronic lung disease§	33 (9.1)	7 (12.5)	26 (8.5)	0.34
eGFR (ml/min)‖	68.8±36.1	47.1±31.2	72.8±35.6	<0.0001
>85§	99 (27.4)	5 (8.9)	94 (30.8)	
50–85§	141 (39.1)	14 (25.0)	127 (41.6)	
<50§	121 (33.5)	37 (66.1)	84 (27.5)	
Dialysis	15 (4.2)	5 (8.9)	10 (3.3)	0.066
Extracardiac arteriopathy§	50 (13.9)	10 (17.9)	40 (13.1)	0.35
NYHA class				<0.0001

I	105 (29.1)	7 (12.5)	98 (32.1)	
II	37 (10.2)	1 (1.8)	36 (11.8)	
III	83 (23)	14 (25.0)	69 (22.6)	
IV	136 (37.7)	34 (60.7)	102 (33.4)	
CCS class 4	23 (6.4)	8 (14.3)	15 (4.9)	0.015
Recent myocardial infarction§	1 (0.3)	0	1 (0.3)	1
Left ventricular ejection fraction (%)	56.6±3.5	54.6±12.1	57.2±10.3	0.29
>50§	289 (80.1)	39 (69.6)	250 (82.0)	
30–50§	67 (18.6)	16 (28.6)	51 (16.7)	
20–30§	4 (1.1)	1 (1.8)	3 (1)	
<20§	1 (0.3)	0	1 (0.3)	
Pulmonary artery pressure, systolic (mmHg)				<0.0001
<35§	273 (75.6)	44 (78.6)	229 (75.1)	
35–55§	70 (19.4)	6 (10.7)	64 (21)	
>55§	18 (5)	6 (10.7)	12 (3.9)	
Coronary artery disease	43 (11.9)	11 (19.6)	32 (10.5)	0.052
Previous cardiac surgery	54 (15.0)	14 (25.0)	40 (13.1)	0.022
Critical state§	62 (17.2)	23 (41.1)	39 (12.8)	<0.0001
Length of the preop. hospital stay (days)	9 [3–25]#	7 [4–16]#	10 [3–26]#	0.054
<10†	190 (52.6)	36 (64.3)	154 (50.5)	0.061
Era**				0.81
2000–2005	40/138 (30)	7/28 (25)	33/110 (30)	
2006–2010	43/138(31.1)	10/28 (35.7)	33/110 (30)	
2011–2015	55/138 (39.9)	11/28 (39.3)	44/110 (40)	

*Unless otherwise stated, values are mean ± standard deviation, or number (percentage).

†The best discriminative value for in-hospital mortality by ROC analysis.

‡Defined as haemoglobin <12 g/dl for women and <13 g/dl for men.

§The definitions and the cut-off values are those used for the EuroSCORE II (*Suppl. Ref.* 1).

||The creatinine clearance rate, calculated according to the Cockcroft-Gault formula, was used to estimate GFR.

#Median [interquartile range].

**Only the Italian study patients are considered for this analysis.

CCS=Canadian Cardiovascular Society; EuroSCORE=European System for Cardiac Operative Risk Evaluation; eGFR=estimated glomerular filtration rate; NYHA=New York Heart Association; ROC=receiver-operating characteristic curve

Table S3. Surgical features (n=361)*

Variable	Total (n=361)	In-hospital dead (n=56)	Alive (n=305)	p-Value
Reason for surgery				
Refractory heart failure due to valvular dysfunction	91 (25.2)	17 (30.4)	74 (24.3)	0.33
Persistent infection	46 (12.7)	6 (10.7)	40 (13.1)	0.62
Embolism	164 (45.4)	27 (48.2)	137 (44.9)	0.65
Recurrent	53 (14.7)	11 (19.6)	42 (13.8)	0.25
Perivalvular complications†	107 (29.6)	19 (33.9)	88 (28.9)	0.45
Surgical priority‡				<0.0001
Elective	133 (36.8)	10 (17.9)	123 (40.3)	
Urgent	184 (51.0)	38 (67.9)	146 (47.9)	
Emergency	33 (9.1)	7 (12.5)	26 (8.5)	
Salvage	11 (3)	1 (1.8)	10 (3.3)	
Valve involvement				
Aortic	224 (62.0)	34 (60.7)	190 (62.3)	0.82
Mitral	167 (46.3)	31 (55.4)	136 (44.6)	0.14
Tricuspid	35 (9.7)	4 (7.1)	31 (10.2)	0.48
Multivalvular	78 (21.6)	15 (26.8)	63 (20.7)	0.31
Large intracardiac destruction§	175 (48.5)	32 (57.1)	143 (46.9)	0.16
Weight of the intervention‡				
Combined CABG	38 (10.5)	10 (17.9)	28 (9.2)	0.052
Single non-CABG	215 (59.6)	28 (50.0)	187 (61.3)	0.11
Two procedures	128 (35.5)	24 (42.9)	104 (34.1)	0.21
Three procedures	18 (5.0)	4 (7.1)	14 (4.6)	0.49

Surgery on thoracic aorta	24 (6.6)	7 (12.5)	17 (5.6)	0.075

*Values are mean ± standard deviation, or number (percentage).

†Perivalvular leak, annular or aortic abscess, sinus of Valsalva aneurysm, aortic fistula and prosthetic valve detachment.

‡The definitions are those used for the EuroSCORE II (*Suppl. Ref.* 1).

§Defined as extensive valve destruction, perivalvular complications or multivalvular involvement.

CABG=coronary artery bypass grafting; EuroSCORE=European System for Cardiac Operative Risk Evaluation

Table S4. Endocarditis-related features (n=361)*

Variable	Total (n=361)	In-hospital dead (n=56)	Alive (n=305)	p-Value
Endocarditis				0.11
Active†	275 (76.2)	38 (67.9)	237 (77.7)	
Treated†	86 (23.8)	18 (32.1)	68 (22.3)	
Type of endocarditis				
Native valve	285 (78.9)	39 (69.6)	246 (80.7)	0.063
Prosthetic valve	68 (18.8)	16 (28.6)	52 (17)	0.043
Intracardiac device or other side	48 (13.3)	10 (17.9)	38 (12.5)	0.27
Causal agents				0.13
Streptococcus species	134 (37.1)	13 (23.2)	121 (39.7)	
Staphylococcus aureus	72 (19.9)	13 (23.2)	59 (19.3)	
Coagulase-negative	33 (9.1)	8 (14.3)	25 (8.2)	
Staphylococci	37 (10.2)	7 (12.5)	30 (9.8)	
Enterococcus	15 (4.2)	2 (3.6)	13 (4.3)	
Gram-negative bacteria	4 (1.1)	2 (3.6)	2 (0.7)	
Fungi	66 (18.3)	11 (19.6)	55 (18)	
Not identified				

*Number (percentage).

†The definitions are those used for the EuroSCORE II (*Suppl. Ref.* 1).

EuroSCORE=European System for Cardiac Operative Risk Evaluation

Supplemental Reference:

1. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, Lockowandt U. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734-744.

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