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Original article

Predictive model of in-hospital mortality in left-sided infective endocarditis

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ABSTRACT

Introduction and objectives: Infective endocarditis (IE) is a complex disease with high in-hospital mortality. Prognostic assessment is essential to select the most appropriate therapeutic approach; however, international IE guidelines do not provide objective assessment of the individual risk in each patient. We aimed to design a predictive model of in-hospital mortality in left-sided IE combining the prognostic variables proposed by the European guidelines.

Methods: Two prospective cohorts of consecutive patients with left-sided IE were used. Cohort 1 (n = 1002) was randomized in a 2:1 ratio to obtain 2 samples: an adjustment sample to derive the model (n = 688), and a validation sample for internal validation (n = 314). Cohort 2 (n = 133) was used for external validation.

Results: The model included age, prosthetic valve IE, comorbidities, heart failure, renal failure, septic shock, *Staphylococcus aureus*, fungi, periannular complications, ventricular dysfunction, and vegetations as independent predictors of in-hospital mortality. The model showed good discrimination (area under the ROC curve = 0.855; 95%CI, 0.825-0.885) and calibration (*P* value in Hosmer-Lemeshow test = 0.409), which were ratified in the internal (area under the ROC curve = 0.823; 95%CI, 0.774-0.873) and external validations (area under the ROC curve = 0.753; 95%CI, 0.659-0.847). For the internal validation sample (observed mortality: 29.9%) the model predicted an in-hospital mortality of 30.7% (95%CI, 27.7-33.7), and for the external validation cohort (observed mortality: 27.1%) the value was 26.4% (95%CI, 22.2-30.5).

Conclusions: A predictive model of in-hospital mortality in left-sided IE based on the prognostic variables proposed by the European Society of Cardiology IE guidelines has high discriminatory ability.

Modelo predictivo de mortalidad hospitalaria en endocarditis infecciosa izquierda

Palabras clave:
Endocarditis infecciosa
Endocarditis infecciosa izquierda
Mortalidad hospitalaria
Modelo predictivo

RESUMEN

Introducción y objetivos: La endocarditis infecciosa (EI) es una enfermedad compleja con elevada mortalidad. La evaluación pronóstica es esencial en el tratamiento de la enfermedad; sin embargo, las guías internacionales no aportan una evaluación objetiva del riesgo individual. Se desarrolló un modelo predictivo de mortalidad hospitalaria en EI izquierda combinando las variables pronósticas propuestas por la guía europea.

Métodos: Se utilizaron 2 cohortes prospectivas de pacientes con EI izquierda. La cohorte 1 (n = 1.002) se aleatorizó 2:1 para obtener 2 muestras: muestra de derivación (n = 688) y muestra de validación interna (n = 314). La cohorte 2 (n = 133) se utilizó para la validación externa.

Resultados: El modelo incluyó edad, endocarditis protésica, comorbilidades, insuficiencia cardiaca, insuficiencia renal, *shock* séptico, *Estafilococo aureus*, hongos, complicaciones perianulares, disfunción

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ventricular y vegetaciones como predictores independientes de mortalidad hospitalaria. El modelo mostró buena capacidad discriminativa (área bajo la curva ROC = 0,855; IC95%, 0,825-0,885) y calibración (p valor test Hosmer-Lemeshow = 0,409) que se ratificaron en la validación interna (área bajo curva ROC = 0,823; IC95%, 0,774-0,873) y externa (área bajo curva ROC = 0,753; IC95%, 0,659-0,847). Para la muestra de validación interna (mortalidad 29,9%) el modelo predijo una mortalidad de 30,7% (IC95%, 27,7-33,7) y para la muestra de validación externa (mortalidad 27,1%) 26,4% (IC95%, 22,2-30,5). *Conclusiones:* Se presenta un modelo predictivo de mortalidad hospitalaria en EII basado en las variables pronósticas propuestas por la guía europea de EI y con alta capacidad discriminativa.

Abbreviations

IE: infective endocarditis
LSIE: left-sided infective endocarditis

INTRODUCTION

Left-sided infective endocarditis (LSIE) is a rare disease with high mortality, ranging from 15% to 40%.[1–4] Prognosis may be improved by some recent advances, such as new indications for imaging techniques, potent new antibiotics, and early surgery. However, although adjusted mortality may have decreased, absolute mortality remains steady.[5–7]

With such a bleak prognosis, early identification of patients with poor short-term outcome is crucial and could have influence the natural history of the disease. Although the European guidelines for infective endocarditis (IE) insist on prognostic assessment, they only provide a list of 19 individual variables associated with poor outcome, and evidence for some of these variables is weak. The American guidelines do not provide any recommendations in this regard.[8,9]

The prognostic factors provided by the European guidelines are divided into 4 groups: 4 variables are related to patient characteristics (older age, prosthetic valve IE, diabetes mellitus, and comorbidity); 5 to clinical complications (heart failure, renal failure, moderate area of ischemic stroke, brain hemorrhage, and septic shock); 3 to the causative microorganism (*Staphylococcus aureus*, fungi, and Gram-negative bacilli); and 7 are echocardiographic findings (periannular complications, severe left-sided valve regurgitation, low left ventricular ejection fraction, pulmonary hypertension, large vegetation, severe prosthetic valve dysfunction, and premature mitral valve closure, and other signs of elevated diastolic pressures). For some of these variables, there is almost no evidence supporting their prognostic value. In addition, the prognostic impact of each variable is not weighted and some of them undoubtedly carry a worse prognosis than others.

We aimed to derive and validate a model to predict the short-term outcome of patients with LSIE based on these variables by using a large population of patients with LSIE.

METHODS

Study population

Two prospective cohorts of consecutive patients with LSIE from 4 tertiary university hospitals were used in this study. The first cohort (cohort 1) included all patients consecutively diagnosed with definite LSIE between 2000 and 2017 from 3 hospitals and was used to derive and internally validate the predictive model. The second cohort (cohort 2), used for the external validation, included all patients with a final diagnosis of LSIE between 2012 and 2017 admitted to another hospital. All the centers are tertiary university hospitals with immediate cardiac surgery facilities, and are leaders in treatment and research in IE.

The participating centers have ongoing prospective local databases including all consecutive patients with IE admitted to their institutions. A standardized case report form for each patient was recorded at each site. The protocols conformed to the ethics guidelines of the 1975 Declaration of Helsinki and its subsequent revisions and were approved by the local ethics committees. The proportion of missing data was $< 10\%$ in all analyzed variables.

We included only patients with definitive LSIE according to the Duke criteria until 2002 and the modified Duke criteria thereafter.[10,11]

Study design

The predictive model was derived and internally validated using data from cohort 1 (n = 1002). This population was randomized in a 2:1 proportion for the derivation and internal validation samples. Approximately two thirds of the population were used to derive the model (derivation sample, n = 688) and the other third to validate it (internal validation sample, n = 314). The predictive model was designed on the basis of the results of a multivariable analysis of in-hospital mortality including all the prognostic variables proposed by the European guidelines. The model was externally validated in cohort 2 (n = 133). The study design is presented in figure 1.

Definition of variables

A total of 17 out of the 19 prognostic variables proposed in the European Society of Cardiology (ESC) IE guidelines were included in our analysis. Variables were recorded during hospital admission,

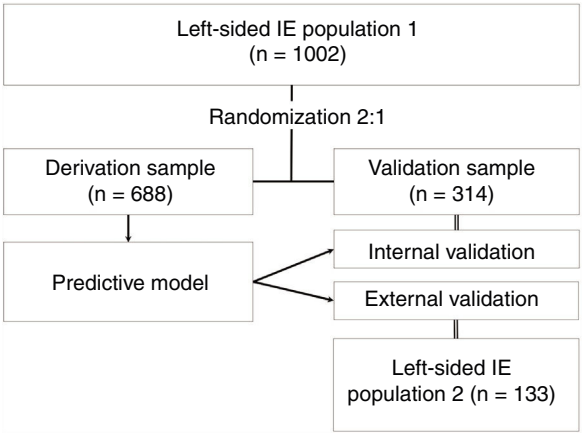

Figure 1. Study design. IE, infective endocarditis.

but only preoperatively in the case of cardiac surgery. Premature mitral valve closure and echocardiographic signs of elevated diastolic pressures were not included, as these factors were considered as surrogates of heart failure. In addition, the definition of some variables was adapted to achieve higher simplicity and reproducibility in the use of the predictive model. Severe left-sided valve regurgitation and severe prosthetic valve dysfunction were grouped together and valvular vegetation was considered irrespective of their length since there is no clear evidence-based cutoff point to consider a vegetation as large. The prespecified predictors and their definitions are summarized in table 1.

In-hospital mortality was used as the main event and included all-cause mortality during hospital stay. Antibiotic treatment and indications for surgery followed the recommendations of the European guidelines and decisions were taken by multidisciplinary experienced groups on IE. We considered urgent surgery to be surgery performed during the active phase of the disease, before the end of antibiotic treatment.[12]

Statistical analysis

Categorical variables are reported as frequency (No.) and percentages and continuous variables as the mean ± standard deviation or median and [interquartile range] in cases of nonnormal distribution. Normal distribution of quantitative variables was verified with the Kolmogorov-Smirnov test and visually through Q-Q plot graphics. Qualitative variables were compared with the chi-square test and Fisher exact test. Continuous variables were compared with the Student *t* test or its equivalent for nonparametric tests, the Mann-Whitney *U* test, for variables that were nonnormally distributed.

Randomization of cohort 1 was done by individual simple assignment of each episode with a probability of 0.67 for the derivation sample and a probability of 0.33 for the validation sample. We used the C4 Study Design Pack V 1.1 Glaxo Wellcome S.A. program.

Univariable analysis was performed in the derivation sample (cohort 1) to test the linear relation of each variable with the outcome, in-hospital mortality. To derive the predictive model, a logistic regression model with the maximum likelihood method using backward stepwise selection was adjusted, which included the prognostic factors shown in table 1. The ratio variable/event was controlled to avoid overfitting. For the final model, odds ratios (OR) adjusted for each of the variables included were calculated, along with their 95% confidence intervals (95%CI). This model was internally validated in the validation sample (cohort 1) and externally in cohort 2.

Table 1
Definition of each prognostic factor used in the predictive model construction

Prognostic factor	Definition
Patient characteristics	
Age	Age at the beginning of the infection in years
Prosthetic valve IE	Prosthetic material infection determined by any imaging technique
Diabetes mellitus	Patient already diagnosed with diabetes mellitus by the American Diabetes Association criteria and under treatment with either diet, oral antidiabetic agents, or insulin
Comorbidity	At least 1 of the following conditions: chronic kidney disease (creatinine clearance < 60 mL/min), chronic pulmonary obstructive disease, or immunosuppression
Clinical complications	
Heart failure	Signs and symptoms according to Framingham criteria for the diagnosis of heart failure An echocardiographic finding of premature mitral valve closure or other signs of elevated diastolic pressures has been considered equivalent to the presence of heart failure
Renal failure	Increase in serum creatinine by at least 0.3 mg/dL in 48 h, or an increase greater than 1.5 times the baseline value in 7 d with or without concomitant diuresis decrease
Ischemic stroke	Neurological deficit with evidence of a moderate area of necrosis in any imaging technique (CT scan or magnetic resonance)
Brain hemorrhage	Neurological deficit with evidence of brain hemorrhage in any imaging technique (CT scan or magnetic resonance)
Septic shock	Acute circulatory failure in sepsis with concomitant persistent hypotension (systolic blood pressure less than 90 mmHg or mean blood pressure less than 65 mmHg) which needs vasopressors despite volume overload or in the presence of serum lactic acid increase above 2 mmol/L
Types of microorganism	
Staphylococcus aureus	*Staphylococcus aureus* growing in at least 2 separate blood culture samples
Fungi	Fungi growing in at least 3 separate blood culture samples
Non-HACEK Gram-negative bacilli	Non-HACEK Gram-negative bacilli growing in at least 3 separate blood culture samples
Echocardiographic findings	
Vegetation	Intracardiac mass on valvular endocardium or any other cardiac structure or prosthetic material with different echogenicity from proximal structures and with erratic and independent movement
Periannular complication	Presence of either abscess, pseudoaneurysm, or fistula - Abscess: perivalvular cavity with necrosis and purulent material not communicating with cardiovascular lumen. Thickened, nonhomogeneous perivalvular area with echodense or echolucent appearance, and no Doppler signal inside - Pseudoaneurysm: perivalvular cavity communicating with the cardiovascular lumen - Fistula: communication between 2 neighboring cavities through a perforation
Severe left-sided valve or prosthesis dysfunction	Aortic or mitral, native or prosthetic valve severe regurgitation according to the European guidelines on heart valve disease management
Pulmonary hypertension	Mean pulmonary pressure higher than 35 mmHg in a right heart catheterization or echocardiographic measure of systolic pulmonary artery pressure above 60 mmHg or less in cases of other signs of right ventricle overload
Low left ventricular ejection fraction	Left ventricular ejection fraction on echocardiogram under 45%

CT, computed tomography; HACEK, *Haemophilus* spp, *Aggregatibacter* spp, *Cardiobacterium* spp, *Eikenella* spp, *Kingella* spp; IE, infective endocarditis.

Noncollinearity was verified among the variables included in the model. The area under the receiver operating characteristic curve (ROC curve) was used to measure how well the model discriminated between patients with a high and low risk of in-hospital mortality. A value of 0.5 indicates no discrimination and a value equal to 1 indicates perfect discrimination. Calibration was evaluated with the Hosmer-Lemeshow test and with plots comparing predicted and observed mortality for different levels of risk.

P values are bilateral and were considered statistically significant with a *P* value $< .05$. Analyses were performed with the use of SPSS software, version 24.0 (IBM), and R software, version 3.4.3 (R Foundation for Statistical Computing).

RESULTS

Baseline features of patients with left-sided infective endocarditis

The description of the main features in cohort 1 and the comparison between the derivation and internal validation samples resulting from its randomization are shown in table 1 of the supplementary data. There were no relevant differences and the distribution of prognostic variables was homogeneous.

In addition, the main features of cohort 1 and cohort 2 were compared (table 2).

Table 2
Comparison of populations in cohorts 1 and 2

	Cohort 1 (n = 1002)	Cohort 2 (n = 133)	*P*
Epidemiological features			
Age, y	65.1 ± 14.3	65.8 ± 13.4	.589
Male sex	666 (67)	82 (62)	.271
Nosocomial origin	253 (25)	38 (30)	.307
Previous heart disease			
None	168 (17)	46 (35)	< .001*
Degenerative	193 (19)	15(11)	.024*
Prosthesis	404 (40)	62 (47)	.165
Rheumatic	91 (9)	5 (4)	.045*
Comorbidities	259 (26)	59 (44)	< .001*
Chronic kidney disease	148 (15)	17 (13)	.538
COPD	84 (8)	24 (18)	< .001*
Immunosuppression	61 (6)	33 (25)	< .001*
Diabetes mellitus	256 (26)	35 (26)	.849
Clinical course			
Acute onset (< 15 d)	490 (49)	86 (71)	< .001*
Fever	811 (81)	102 (77)	.246
Heart failure	571 (57)	60 (45)	.010*
Renal failure	415 (41)	62 (47)	254
Septic shock	158 (16)	15 (11)	.176
Ischemic stroke	180 (18)	32 (24)	.090
Brain hemorrhage	67 (7)	4 (3)	.100
In-hospital death	301 (30)	36 (27)	.481
Microbiology			
Positive blood cultures	884 (88)	104 (78)	.001*
Streptococcus spp	272 (27)	26 (20)	.074
Streptococcus bovis	55 (6)	8 (6)	.803
Viridans streptococci	159 (16)	9 (7)	.005*
Other streptococci	58 (6)	9 (7)	.653
Enterococcus spp	130 (13)	16 (12)	.760
Staphylococcus spp	382 (38)	49 (37)	.849
Staphylococcus aureus	210 (21)	23 (17)	.326
Coagulase-negative staphylococcus	172 (17)	26 (20)	.496
Gram-negative non-HACEK bacillus	48 (5)	4 (3)	.355
Fungi	16 (2)	2 (2)	.999
HACEK group	7 (1)	0 (0)	.999
Anaerobes	32 (3)	3 (2)	.790
Polymicrobial infective endocarditis	49 (5)	0 (0)	.009*
Other microorganisms	41 (4)	3 (2)	.303
Negative blood cultures	118 (12)	29 (22)	.001*

Table 2 *(Continued)*
Comparison of populations in cohorts 1 and 2

	Cohort 1 (n = 1002)	Cohort 2 (n = 133)	*P*
Imaging techniques findings			
Vegetation	870 (87)	87 (65)	< .001*
Periannular complication	302 (30)	47 (35)	.222
Abscess	184 (18)	25 (19)	.905
Pseudoaneurysm	165 (17)	18 (14)	.452
Fistula	34 (3)	2 (2)	.424
Severe valvular/prosthesis dysfunction	619 (62)	36 (27)	< .001*
Left ventricular ejection fraction < 45%	78 (8)	10 (7)	.914
Pulmonary hypertension	136 (14)	8 (6)	.014*
Localization			
Native aortic valve	359 (36)	26 (25)	.027*
Native mitral valve	381 (38)	36 (35)	.495
Mechanical aortic prosthesis	118 (12)	19 (18)	.056
Mechanical mitral prosthesis	192 (19)	17 (16)	.485
Biological aortic prosthesis	108 (11)	13 (13)	.592
Biological mitral prosthesis	21 (2)	0 (0)	.250
Concomitant right-sided involvement	23 (2)	2 (2)	.759
Multivalvular	215 (22)	15 (11)	.006*
Treatment			
Cardiac surgery	614 (61)	72 (54)	.113
Urgent	367 (60)	71 (99)	< .001*
Elective	247 (40)	1 (1)	
Indications			
Heart failure	428 (72)	27 (47)	< .001*
Uncontrolled infection	335 (56)	38 (66)	.180
Prevention of embolism	139 (23)	6 (10)	.022*
Antibiotic treatment			
Correct antibiotic treatment	879 (95)	123 (93)	.220
Weeks of treatment	5 [3.3-6.6]	5.4 [4-6.1]	.784

CPOD, chronic obstructive pulmonary disease; HACEK, *Haemophilus* spp, *Aggregatibacter* spp, *Cardiobacterium* spp, *Eikenella* spp, Kingella spp.
Data are expressed as No. (%), mean ± standard deviation, or median [interquartile range].
* Statistically significance ($P < .05$)

Construction of the predictive model

Table 3 shows the relationship between the variables proposed by the European guidelines and in-hospital mortality in the derivation sample (n = 688). All variables, except ischemic stroke, cerebral hemorrhage, fungi, non-HACEK Gram-negative bacilli (*Haemophilus spp*, *Aggregatibacter spp*, *Cardiobacterium spp*, *Eikenella spp*, *Kingella spp*) and severe valve/prosthesis dysfunction, were statistically associated with in-hospital mortality in the univariable analysis.

Then, a multivariate analysis was undertaken (table 3). Independent predictors of in-hospital mortality were age, prosthetic valve IE, comorbidities, heart failure, renal failure, septic shock, *Staphylococcus aureus*, fungi, periannular complications, ventricular dysfunction, and vegetations. The model showed good discriminatory ability with an area under the ROC curve of 0.855 (95%CI, 0.825-0.885) and good calibration (figure 2A).

In-hospital mortality formula

The formula to predict in-hospital mortality was built by using the logarithms of adjusted OR from the predictive model:

$$p = \frac{e^z}{1 + e^z}$$

Where z = – 6.288 + 0.033 x Age + 0.602 x Prosthetic valve IE + 0.485 x Comorbidity + 1.210 x Heart failure + 0.800 x Renal failure + 1.742 x Septic shock + 1.195 x *Staphylococcus aureus* + 1.847 x Fungi + 0.690 x Periannular complication + 0.747 x Low left ventricular ejection fraction + 0.850 x Vegetation.

Model validation

The model was internally and externally validated with the internal validation sample from cohort 1 (n = 314) and from cohort 2 (n = 133), respectively. Internal validation showed an area under the ROC curve of 0.823 (95%CI, 0.774-0.873). The model predicted an in-hospital mortality of 30.7% (95%CI, 27.7-33.7) and observed mortality was 29.9% (figure 2B).

External validation showed an area under the ROC curve of 0.753 (95%CI, 0.659-0.847). The model predicted an in-hospital mortality of 26.4% (95%CI, 22.2-30.5) and observed mortality was 29.9% (figure 2C).

Presentation of the model

The model can be accessed as an informatic application via internet at ENDOVAL score web[13] and via google play store ("ENDOVAL score").

Table 3
Association between in-hospital mortality and variables proposed by the European guidelines on IE in cohort 1 (derivation sample)

Derivation sample (n = 688)	Nonsurvivors (n = 207)	Survivors (n = 481)	*P*	OR	95%CI		*P*
					Inferior	Superior	
Patient characteristics							
Age, y	69.6 ± 11.6	62.6 ± 15.1	< .001*	1.034	1.017	1.051	< .001*
Prosthetic valve IE	96 (46)	182 (38)	.036*	1.825	1.188	2.803	.006*
Diabetes mellitus	72 (35)	110 (23)	.001*				
Comorbidity	79 (38)	100 (21)	< .001*	1.624	1.034	2.549	.035*
Clinical complications							
Heart failure	155 (75)	225 (47)	< .001*	3.355	2.158	5.214	< .001*
Renal failure	141 (68)	145 (30)	< .001*	2.226	1.448	3.421	< .001*
Ischemic stroke	43 (21)	80 (17)	.194				
Brain hemorrhage	15 (7)	28 (6)	.479				
Septic shock	80 (39)	30 (6)	< .001*	5.707	3.280	9.932	< .001*
Type of microorganism							
Staphylococcus aureus	83 (40)	65 (14)	< .001*	3.304	2.025	5.389	< .001*
Gram-negative non-HACEK bacillus	10 (5)	20 (4)	.692				
Fungi	5 (2)	6 (1)	.321	6.338	1.425	28.184	.015
Echocardiographic findings							
Periannular complication	77 (37)	131 (27)	.009*	1.994	1.289	3.084	.002*
Severe valvular/prosthesis dysfunction	118 (57)	294 (61)	.312				
LVEF < 45%	28 (14)	28 (6)	.001*	2.111	1.063	4.194	.033*
Pulmonary hypertension	38 (18)	52 (11)	.007*				
Vegetations	190 (92)	408 (85)	.013*	2.341	1.180	4.642	.015*
Constant				0.002			< .001*

95%CI, 95% confidence interval; IE, infective endocarditis; HACEK, *Haemophilus* spp, *Aggregatibacter* spp, *Cardiobacterium* spp, *Eikenella* spp, *Kingella* spp; LVEF, left ventricular ejection fraction; OR: odds ratio.
Data are expressed as No. (%) or mean ± standard deviation.
* Statistical significance (P < .05).

DISCUSSION

We present the first predictive model of in-hospital mortality in LSIE derived by using the prognostic factors proposed by the European guidelines on the management of IE. Our results show that the model has high discriminatory ability.

Prognosis assessment in left-sided infective endocarditis

Diagnosis and treatment of IE is a clinical challenge. Early identification of patients with LSIE at high risk is crucial to change the natural course of the disease.[8] Previous important research has focused on the prognosis of IE.[1,4,5,7,14–16] Although some of these classic studies on IE present a very good overview of the disease, they have important methodological limitations. First, these studies did not differentiate between left- and right-sided IE episodes, despite having very different profiles and prognosis.[1,4,14] Furthermore, most studies focused on evaluating a single or a limited number of prognostic factors.[3,11,12,17–31] The European guidelines summarize the most important prognostic factors in an attempt to reflect current knowledge and help clinicians in their daily practice; however, the information is not sufficiently accurate and its practical usefulness is limited. We tested the prognostic power of these prespecified variables, as we consider that all of them have clinical importance and have the scientific support of the authors and reviewers of the guidelines.

Practical implications

Our group published a very simple prognostic stratification of patients with LSIE determined at admission and based on the presence of heart failure, *Staphylococcus aureus*, and periannular complications.[15] Our new predictive model is a simple tool to help obtain a quick and accurate estimate of patient prognosis. This should not be regarded as definitive but as a complementary source of prognostic information that, together with other variables, will help clinicians decide whether and when surgery is indicated. It can be inferred from our results that in-hospital mortality risk can be assessed for the same patient at different time points in the course of the disease, but this hypothesis must be confirmed in prospective studies. In addition, the model also may help patients and families to obtain accurate information and a better understanding of the disease and its complications.

Differential features of our work

Our work has some strengths. This study includes only patients with definite LSIE. The number of episodes is high in a disease that has a low incidence, and information from 4 tertiary hospitals has been included. The information is homogeneous and of high quality. Finally, the study focused on the prognostic factors proposed by the European guidelines, and demonstrates their prognostic power for the first time. This methodology precludes

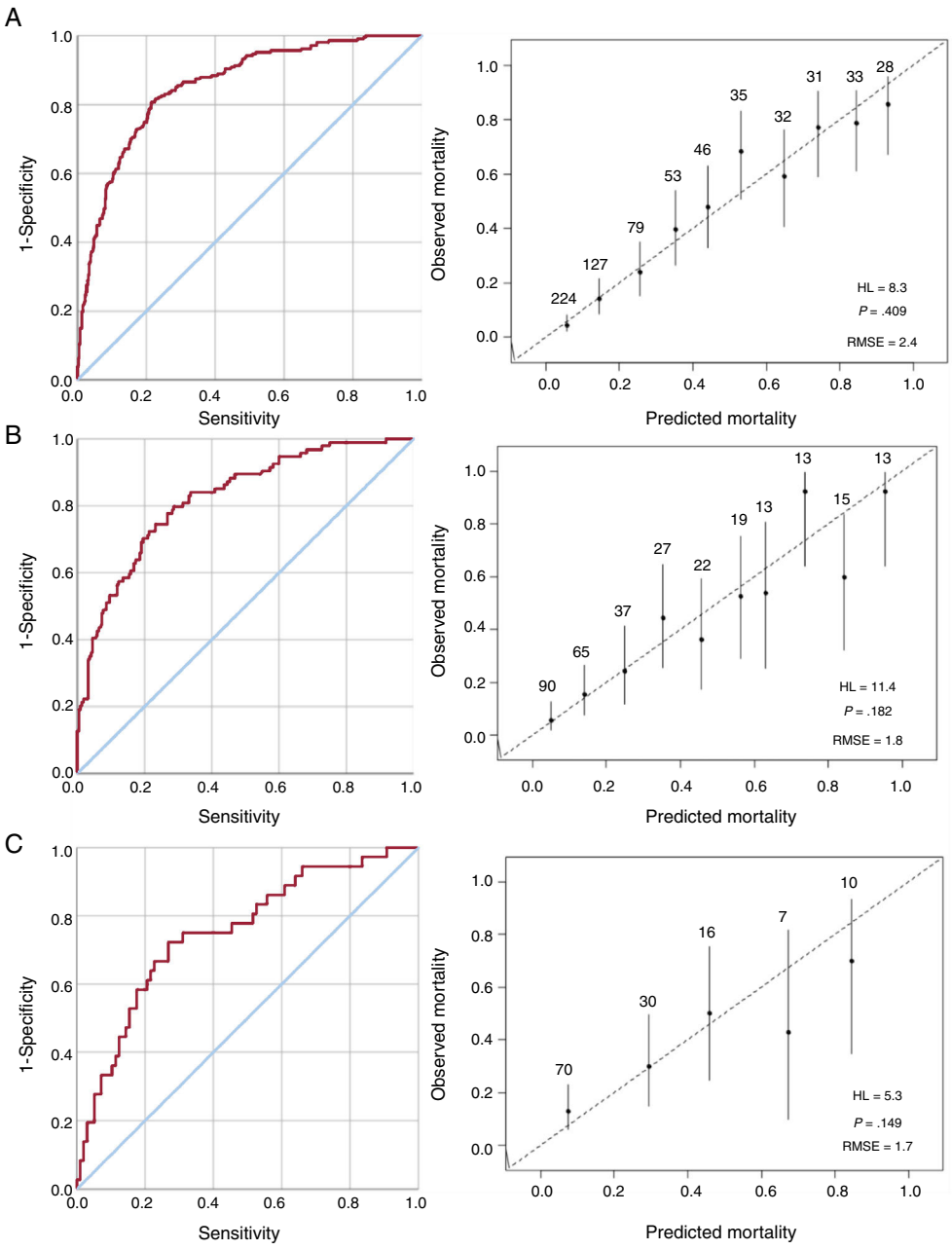

Figure 2. Discriminatory performance and calibration of the model. A: ROC curve and plot comparing predicted and observed in-hospital mortality in the derivation sample. B: ROC curve and plot comparing predicted and observed in-hospital mortality in the internal validation sample. C: ROC curve and plot comparing predicted and observed in-hospital mortality in the external validation sample. HL, Hosmer-Lemeshow; RMSE, root mean square error; ROC, receiver operating characteristic.

the bias that could exist in our population in the selection of variables for the construction of the predictive model, and favors the generalization of our results.

Limitations

This work also has some limitations. All centers are tertiary hospitals with cardiac surgery facilities and are leaders in IE management, which restricts the applicability of the model to hospitals with similar characteristics. Cohort 1 included patients between 2000 and 2017, a long period during which different forms of management have been tested, which could have limited the accuracy of the model. The external validation cohort is more recent, which could explain some of the differences between cohorts and could be considered as a methodological shortcoming. Although the good performance of the model in the validation cohort reinforces the clinical usefulness of our work, future external validations, particularly with larger sample sizes and different case-mix populations, would improve the applicability of the predictive model. The definition of variables in the European guidelines is sometimes somewhat simple and, at other times, includes small adaptations that could have limited the prognostic impact of those variables.

Finally, the inclusion of other prognostic variables may improve the predictive performance of the model; however, for the sake of simplicity and general applicability, we tested only variables proposed by the European guidelines. Future investigations will be necessary to validate the results and to explore the effect of including new variables.

CONCLUSIONS

Our predictive model of in-hospital mortality in left-sided IE based on the prognostic variables proposed by the ESC IE guidelines has high discriminatory ability.

FUNDING

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CONFLICTS OF INTEREST

None.

WHAT IS KNOWN ABOUT THE TOPIC?

- LSIE mortality is high and remains steady despite important medical advances. There are several known prognostic factors that are summarized by the European guidelines on IE in an attempt to reflect current knowledge and help clinicians in their daily practice; however, the information is not sufficiently accurate and its practical usefulness is limited.

WHAT DOES THIS STUDY ADD?

- This study adds a predictive model of in-hospital mortality in left-sided IE with high discriminatory ability, based on the prognostic variables proposed by the ESC IE guidelines. This model emerges as a tool to help in the decision-making process of the endocarditis team by giving a quick and accurate estimate about patient prognosis. In addition, the model may also help patients and families to obtain accurate information and a better understanding of the disease and its complications.

APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.1016/j.rec.2019.11.003

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