

# Predictive Capacity of Different Surgical Risk Scores in Infective Endocarditis

## Capacidad predictiva de diferentes puntuaciones de riesgo quirúrgico en la endocarditis infecciosa

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### ABSTRACT

**Background:** Infective endocarditis (IE) is a life-threatening disease that may require surgical treatment. Despite being fundamental in decision making, surgical scores were not generated specifically to stratify the risk of this disease.

**Objectives** The objective of this study was to: To evaluate the predictive capacity of surgical risk scores adjusted for IE.

**Methods:** Single-center observational and retrospective study of 270 patients > 18 years, hospitalized for active IE from 06/2008 to 02/2023, of which 70 (26%) underwent central cardiac surgery. Device-associated endocarditis and patients who did not undergo cardiac surgery were excluded. The surgical risk scores analyzed were: EuroSCORE II, EURO-IE, STS-IE and PALSUSE (Prosthesis, Age >70, large cardiac destruction, Staphylococcus, Urgency, Female gender, EuroScore >10). The predictive capacity of each score was evaluated using the C statistic, calculating the area under the curve of the sensitivity/1-specificity relationship with their respective 95% confidence intervals (CI), and statistical significance.

**Results:** The median age (interquartile range, IQR) was 60 years (48-67) and the number of days of hospitalization were 23 (17-39). Forty-one patients (58.57%) had a prosthetic valve. Regarding the causative germs, Staphylococcus was responsible for 30% of the infections. The main indications for surgical treatment were heart failure (44%), abscess (19%) and prosthetic dysfunction (12%). Annular abscess was observed in 28.57% of patients. Urgent surgery was performed in 45.71% and emergency surgery was performed in 7.14%. Hospital mortality was 21.42%. The predictive capacity of all scores was statistically significant, except for the STS-IE. The STS-IE score presented an area under the curve (AUC) of 0.586 (95% CI 0.429-0.743). The EuroSCORE II, an AUC of 0.685 (95% CI 0.541-0.830); the EURO-IE presented an AUC of 0.695 (95% CI 0.556-0.834) and the PALSUSE an AUC of 0.819 (95% CI 0.697-0.941).

**Conclusions:** The results of this study suggest that the PALSUSE score was a better predictor of surgical risk in patients with active IE, compared to the Euroscore II, EURO-IE and STS-IE scores.

**Keywords:** Infective Endocarditis - Heart Valve Surgery - Mortality - Risk Score

### RESUMEN

**Introducción:** La endocarditis infecciosa (EI) es una enfermedad potencialmente mortal que puede requerir tratamiento quirúrgico. A pesar de ser fundamentales en la toma de decisiones, los puntajes de riesgo quirúrgico no fueron generados específicamente para estratificar el riesgo de esta enfermedad.

**Objetivo:** Evaluar la capacidad predictiva de los puntajes de riesgo quirúrgico ajustados a la EI.

**Material y métodos:** Estudio unicéntrico observacional y retrospectivo de 270 pacientes mayores de 18 años que cursaron internación por EI en actividad desde 06/2008 hasta 02/2023, de los cuales 70 (26%) fueron sometidos a cirugía cardíaca central. Se excluyeron las endocarditis asociadas a dispositivos, y los pacientes que no se sometieron a cirugía cardíaca. Los puntajes de riesgo quirúrgico analizados fueron: EuroSCORE II, EURO-IE, STS-IE y PALSUSE (Prótesis, Edad >70, (Large) gran destrucción, Staphylococcus, Urgencia, Sexo femenino, EuroSCORE >10). La capacidad predictiva de cada puntaje se evaluó por medio del estadístico C, calculando el área bajo la curva de la relación sensibilidad/1-especificidad, con sus respectivos intervalos de confianza (IC) 95%, y su significación estadística.


**Resultados:** La mediana (rango intercuartílico, RIC) de edad fue de 60 años (48-67) y la de los días de internación fue de 23 (17-39). Cuarenta y un pacientes (58,57%) tenían una válvula protésica. Respecto a los gérmenes causales, el Staphylococcus fue responsable del 30% de las infecciones. Las principales indicaciones de tratamiento quirúrgico fueron la insuficiencia cardíaca (44%), el absceso (19%) y la disfunción protésica (12%). Se objetivó absceso anular en el 28,57% de los pacientes. La necesidad de cirugía de urgencia fue del 45,71% y de emergencia del 7,14%. La mortalidad hospitalaria fue del 21,42%. La capacidad predictiva de todos los puntajes

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fue estadísticamente significativa, excepto el STS-IE. El STS-IE presentó un área bajo la curva (ABC) de 0,586 (IC 95% 0,429-0,743). El EuroSCORE II, un ABC de 0,685 (IC 95% 0,541-0,830); el EURO-IE presentó un ABC de 0,695 (IC 95% 0,556-0,834) y el PALSUSE un ABC de 0,819 (IC 95% 0,697-0,941).

**Conclusiones:** Los resultados de este estudio sugieren que el score PALSUSE fue mejor predictor de riesgo quirúrgico en pacientes con EI activa, en comparación con los puntajes Euroscore II, EURO-IE y STS-IE.

**Palabras clave:** Endocarditis infecciosa - Cirugía cardíaca valvular - Mortalidad - Puntuación de riesgo

## INTRODUCTION

Infective endocarditis (IE) is a potentially fatal cardiovascular disease. During 2019, the estimated global incidence of IE was of 13.8 cases per 100 000 subjects per year, and IE accounted for 66 300 deaths. (1) Although it is a relatively rare pathology, it has a great impact on the morbidity and mortality of patients. (2-4) In this context, medical treatment alone is often inadequate and must be combined with surgical intervention. However, in critically ill patients, cardiovascular interventions can be challenging and have poor outcomes. (5) According to the EIRA III registry, the median length of hospital stay in patients admitted for IE was 28 days and during that period, surgery was indicated for 56.9% of the patients, with 22% mortality rate of the operated patients. (4)

The risk of surgical treatment during the active phase of IE is strongly influenced by pre-existing comorbidities. (6,7) Currently, the decision to indicate surgery must be made by the endocarditis team (made up of cardiologists, imaging specialists, cardiovascular surgeons, infectologists and microbiologists), (8) considering the urgency of the clinical condition, the perioperative risk, the potential for recovery from infection and the associated long-term prognosis of the patient. (9,10) For this reason, it is crucial to have precise tools to predict the outcome of the intervention.

Risk prediction scores for cardiovascular surgery (e.g., STS or EuroSCORE II) may not be ideal for IE, a rare situation in the population that originated these risk scales. (11-13) Therefore, there are scores specifically designed for this pathology, which include the STS-IE, the PALSUSE score and the EURO-IE, among others. These scoring systems have been developed based on retrospective data and their performance is variable. (13-15)

Taking this into account, choosing the appropriate score to predict mortality in a specific population of patients with IE constitutes a fundamental tool for decision making. The objective of the present work was to analyze the group of patients who undergo cardiovascular surgery for active IE, to reveal the complications related to the procedure and to evaluate the capacity of different risk scores to predict them.

## METHODS

An observational and retrospective study was carried out in patients admitted between June 2008 and February 2023, with a diagnosis of definite or possible IE, according to the Duke criteria, (16) in the Hospital Universitario Fundación Favaloro, a referral center for cardiovascular surgery of the

Autonomous City of Buenos Aires, Argentina. Those over 18 years of age who were hospitalized for active IE were included, and those undergoing central cardiac surgery were taken into account for the evaluation of risk scores. Patients with IE associated to devices (pacemakers, cardioresynchronizers) and IE in percutaneously implanted valves were excluded.

Anthropometric data, laboratory values, clinical characteristics, and hospital outcomes were collected prospectively from the medical records. Acute renal failure (ARF), increase in serum creatinine  $\geq 0.3$  mg/dL in 48 hours), the requirement for hemodialysis (HDL), complete atrioventricular block (CAVB), stroke, transient ischemic attack (TIA), reoperation, and surgery-related infection were considered post-surgical complications.

Four risk scores specifically designed to predict in-hospital mortality after cardiovascular surgery were used (Table 1): EuroSCORE II, (11) modified EuroSCORE (EURO-IE), (13) the Society for Thoracic Surgery risk score for infective endocarditis (STS-IE) (14) and the PALSUSE scoring system. (15)

The different risk scores were compared in their predictive capacity for in-hospital mortality. Alternatively, we evaluated whether these scores were useful for predicting major complications defined as stroke, ARF, HDL, reoperation, infections, CAVB, pacemaker requirement; major complications or death; or prolonged hospitalization defined as greater than 30 days.

## Statistical analysis

Quantitative variables were expressed as mean  $\pm$  standard deviation (SD) or median and interquartile range (IQR), according to the normal distribution evaluated by the Shapiro-Wilk test. Qualitative variables were expressed as number and percentage. Comparisons between groups were made with the Student t test for continuous variables and using the Chi2 test or Fisher's exact test for categorical variables. The Hosmer-Lemeshow test was used to evaluate the goodness of fit of the risk scores. The discrimination capacity of the models was measured by the C statistic and the receiver operating characteristic (ROC) curve, with the respective area under the curve of the sensitivity/specificity relationship, their 95% confidence intervals (CI) and statistical significance. The discrimination ability of the area under the curve (AUC) was considered excellent (AUC 0.90-1), good (AUC 0.80-0.90), reasonable (AUC 0.70-0.80), poor (AUC 0.60-0.70) or null (AUC 0.50-0.60). The De Long test was used to compare risk scores. A two-tailed p value  $< 0.05$  was considered statistically significant. Statistical analysis was performed using SPSS software version 16 (SPSS Inc, Chicago, Illinois, USA), and R version 4.3.1.

## Ethical considerations

The protocol was evaluated and approved by the Institution's Ethics Committee.

**Table 1.** Risk scores for infective endocarditis

EuroSCORE II	EURO-IE	STS-IE	PALSUSE
Age	Previous cardiac surgery	Previous CABG	Prosthetic valve endocarditis
Gender	Critical preoperative situation	Urgency (No cardiogenic shock)	Age>70
Insulin-requiring diabetes	Creatinine clearance	Emergency/Cardiogenic Shock	Intracardiac destruction
COPD	NYHA >1	Preoperative Balloon/Inotropes	Staphylococcus spp
Extra cardiac arthropathy	Age	Multivalvular surgery	Emergency surgery
Creatinine clearance	Emergency surgery	Insulin-requiring diabetes	Female gender
Active endocarditis	Fistula	Non-insulin-requiring diabetes	EuroSCORE>10%
Previous cardiac surgery	Staphylococcus spp	Hypertension	
Pulmonary hypertension	Pulmonary hypertension	Chronic lung disease	
Recent heart attack (<90 days)	Emergency surgery	Active endocarditis	
Angor functional class		Kidney failure or Creatinine >2	
Functional class of dyspnea		mg/dL	
Reduced mobility		Arrhythmia	
Critical preoperative situation		Previous valve surgery	
Ejection fraction			
Surgical priority			
Associated intervention			
Thoracic aorta surgery			

CABG: Coronary artery bypass grafting; COPD: Chronic obstructive pulmonary disease; NYHA: New York Heart Association scale.

## RESULTS

In the analyzed period, 270 patients were admitted with a diagnosis of active IE, of whom 70 required valve surgical treatment. Table 2 shows the characteristics of this population. Patients undergoing surgery were younger: 60 (IQR 48-67) vs. 69 (IQR 57-76) years;  $p=0.001$ , with a more frequent prosthetic valve involvement (58.5% vs. 42%;  $p=0.01$ ), and a higher percentage associated with dyspnea (42.8% vs. 19.5%;  $p=0.001$ ) and heart failure (55.7% vs. 28.5%;  $p<0.0001$ ). On the other hand, patients who did not undergo surgical treatment had a higher prevalence of neoplastic diseases (11.5% vs. 1.4%;  $p<0.0001$ ). A similar frequency of previous endocarditis and previous predisposing procedure was observed.

Regarding the group undergoing valve replacement, the presurgical ultrasound showed that 18.5% of the population had a reduced left ventricular ejection fraction (LVEF), with mild to moderate dysfunction in 17.1% and severe in 1.4% of cases. Vegetation was observed in 77% ( $n=54$ ), located in the aortic valve in 66.6%, of cases, in the mitral valve in 31.5% of cases and only 1 patient with mitro-aortic location. Prosthetic IE represented 58.6% of cases, and aortic involvement was the most frequent (80.5%). This location was also the most common among native IE (55%). The presence of abscesses was observed in 28.6% of cases, again aortic location was the most prevalent (70%). The indications for surgical treatment were heart failure (44.3%), abscess (18.6%), prosthetic dysfunction (11.5%), persistent fever

(7.2%), recurrent embolism (4.3%)., sepsis (2.9%), and others (11.2%).

The median hospital stay of the operated patients was 23 (IQR 17-39) days; 40% stayed more than 30 days, and 4.2% more than 60 days. Postoperative complications in order of frequency were: ARF (32.9%), CAVB (22.9%), HDL (11.4%), stroke (8.6%), requirement for reoperation (8.6%), infection (8.6%), others (24.3%). In-hospital mortality was 21.4%, 4.3% mortality within 48 hours after surgery. Of the deceased patients, 53.5% had ARF, while 27.5% of the survivors presented this complication ( $p$  NS). Similarly, more patients who died were complicated with HDL (33% vs. 5.5%;  $p<0.01$ ). *Staphylococcus* spp was the most frequently found germ (30%).

In the individualized analysis of the prediction scores, PALSUSE presented as the most frequent variables: prosthetic valve involvement (58.9%), urgency (45.6%), intracardiac destruction (34.3%), EuroSCORE>10% (32.9%), rescue of *Staphylococcus* spp. (30%), female gender (21.4%) and age over 70 years (20%). The most frequent variables of STS-IE were: presence of active endocarditis (100%), arterial hypertension (68.6%), previous cardiovascular surgery (57.2%), urgency (45.7%) and renal failure (31.5%). Regarding the EURO-IE and EuroSCORE II scores, the most frequent shared variables were previous cardiovascular surgery (57.2%), age  $\leq 60$  years (45.7%), urgency of the intervention (45.7%) and New York Heart Association functional class (CF NYHA) >1 (41.4%). Among the specific variables, the presence

	Surgical treatment (n=70)	Medical Treatment (n=200)	p
Age	60 (48-67)	69 (57-76)	0.001
Male sex	55 (78,5%)	145 (72.5%)	0.346
Hospitalization days	23 (17-39)	19 (12-36)	0.294
Diabetes Mellitus	16 (22.8%)	44 (22%)	0.868
Chronic renal failure	9 (12.8%)	25 (12.5%)	1.000
Prosthetic valve	41 (58.5%)	84 (42%)	0.018
Previous endocarditis	10 (14.2%)	28 (14%)	1.000
Predisposing prior procedure	24 (34.2%)	53 (26.5%)	0.221
Fever	58 (82.8%)	163 (81.5%)	0.858
Dyspnoea	30 (42.8%)	39 (19.5%)	<0.001
Leukocytes/mm <sup>3</sup>	9700 (6600-11900)	8900 (6550-12750)	0.566
Anemia	53 (75.7%)	158 (79%)	0.614
Driving disorder	12 (17.1%)	29 (14.5%)	0.568
Heart failure	39 (55.7%)	57 (28.5%)	<0.0001
Acute kidney failure	14 (20%)	44 (22%)	0.865
Sepsis	5 (7.1%)	31 (15,5%)	0.101
Embolism	17 (2.2%)	31 (15.5%)	0.104
Persistent fever	10 (14.2%)	26 (13%)	0.838
Anticoagulation	19(27.1%)	55 (27.5%)	1.000
Cancer	1(1.4%)	23 (11.5%)	0.007
Previous cardiovascular disease	55 (78.5%)	149 (74.5%)	0.523
Splenomegaly	8 (11.4 %)	9 (4.5 %)	0.048

**Table 2.** Comparative analysis of patients with active IE, whether or not undergoing surgical treatment.

of fistula (34.3%), *Staphylococcus* spp. (30%) and mitral valve involvement (25.7%), are added as the most frequently present in EURO-IE, and a LVEF greater than 50% (81.4%) in the EuroSCORE II.

All models presented good goodness of fit: the Hosmer-Lemeshow test did not show statistical significance for any of the proposed scores (PALSUSE df=4,  $p=0.912$ ; EuroSCOREII df=8,  $p=0.175$ ; STS-EI df=7,  $p=0.200$ ; EURO-EI df=8,  $p=0.595$ ). Figure 1 shows the ROC curves for mortality corresponding to the four scores. The PALSUSE score was the one that showed the highest AUC (AUC 0.819, 95% CI 0.697-0.941;  $p<0.001$ ), behaving as a score with good discrimination capacity for mortality. Although they retained statistical significance, EuroSCORE II (AUC 0.685, 95% CI 0.541-0.830;  $p=0.029$ ) and EURO-IE (AUC 0.695, CI 0.556-0.834;  $p=0.022$ ), showed poor discrimination capacity. The STS-IE score was not useful as a discriminative tool (AUC 0.596, 95% CI 0.429-0.743;  $p=0.310$ ). In the comparison between scores, PALSUSE showed a statistically significant difference with respect to STS-IE in predicting mortality ( $p<0.001$ ), while when compared with EuroSCORE II and EURO-IE, the benefit of this score was of borderline statistical significance ( $p=0.05$ ).

Table 3 shows the results of the different scores in predicting prolonged hospitalization, major complications, and major complications or death. Regarding prolonged hospitalization, EuroSCORE II and STS-IE

had poor discriminatory power, while it was null for EURO-IE and PALSUSE. On the other hand, STS-IE had a reasonable power for discrimination of major events, albeit poor in the rest of the scores. The predictive capacity of the 4 scores for major complications or death was reasonable.

## DISCUSSION

The treatment of IE is a challenge due to the complexity of this disease and the critical condition in which patients must face it. (4) Surgery can be curative, especially for those cases where medical treatment is ineffective; (8) hence, it is important to have a reliable tool to determine its risk. (5) Surgical risk prediction scores for general cardiovascular surgery may lose accuracy in less common diseases such as IE. For this reason, several specific scoring systems have been developed for this disease.(13-15) In our series, the PALSUSE score showed better ability to predict hospital death, therefore, it could be a good resource for decision making, a result similar to that published by other series. (5,17)

The evaluated population shares similar characteristics to the population registered in EIRA III, which is the largest series of studies on IE in Latin America, (4) although it is relevant to highlight that our population presented a greater proportion of patients with prosthetic valve IE, which may be related to the characteristics of our center. The mortality observed in our series is similar to the mortality detected in other reg-

**Table 3.** Results of the different scores in predicting prolonged hospitalization, major complications and major complications and death.

Name	AUC	CI 95%	p
Prolonged hospitalization EuroSCORE II	0.696	0.556-0.835	0.01
Prolonged hospitalization STS-IE	0.652	0.505-0.799	0.04
Prolonged hospitalization EURO-IE	0.517	0.336-0.667	0.83
Prolonged hospitalization PALSUSE	0.503	0.352-0.647	0.99
Major Complications EuroSCORE II	0.690	0.530-0.849	0.01
Major Complications STS-IE	0.788	0.658-0.918	<0.001
Major Complications EURO-IE	0.633	0.488-0.778	0.08
Major Complications PALSUSE	0.615	0.472-0.758	0.14
Major complications or death EuroSCORE II	0.720	0.591-0.849	0.002
Major complications or death STS-IE	0.742	0.622-0.863	0.001
Major complications or death EURO-IE	0.705	0.584-0.827	0.004
Major complications or death PALSUSE	0.727	0.606-0.848	0.001

AUC: area under curve; CI:confidence interval.

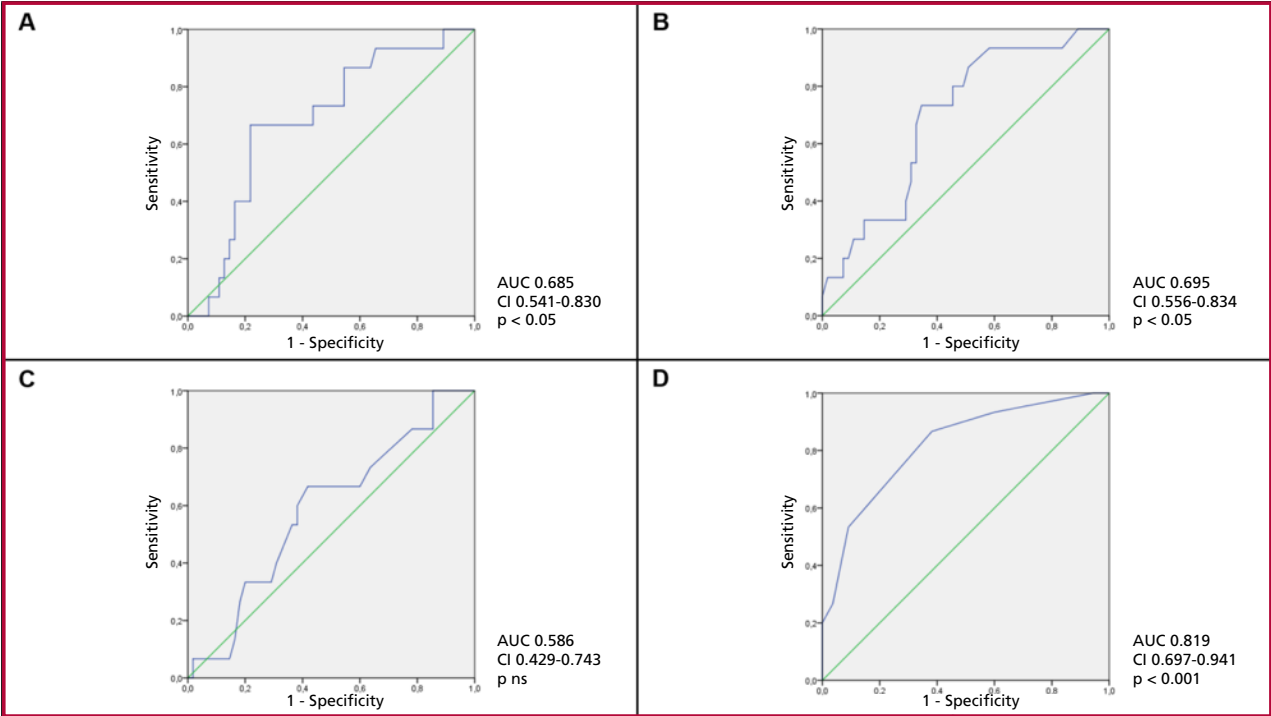
istries (4,5). In the EIRA III registry, the mortality of patients undergoing surgical treatment was 22%, (4) while the series reported by Gatti et al. was 25.6%. (5)

In our work we performed a comparison of 4 surgical risk scores to predict mortality. Firstly, not all the compared scores were designed to evaluate surgical mortality in patients with IE, since EuroSCORE II evaluates the risk of cardiac surgery in general. (11) There is controversy based on the validity of this score to estimate surgical risk in IE. Patrat-Delon et al. conclude in their work that EuroSCORE II underestimates the surgical risk of IE since it does not eval-

uate variables that behave as independent predictors of mortality such as the presence of a prosthetic valve, septic shock or large vegetations. (18) While, in other series, EuroSCORE II was a useful tool to predict the surgical risk of this disease. (19)

Secondly, PALSUSE is a composite score, since within its 7 variables is the EuroSCORE, possibly generating an advantage in risk prediction. (15) It is worth clarifying that PALSUSE variables behaved as independent mortality factors in other series. In the study carried out by Costa et al, age, intracardiac destruction and prosthetic valve IE were independent

**Fig. 1.** ROC curve for the different risk scores predicting mortality. (A) EuroSCORE II. (B) EURO-IE. (C) STS-IE. (D) PALSUSE.



AUC: Area under the curve; CI: Confidence interval 95%.



predictor variables of mortality, (20) as well as the presence of heart failure, which, although not included as a dichotomous variable in PALSUSE, was the main indication for emergency surgery in our study. This fact could justify the good discrimination capacity for mortality that PALSUSE possesses.

It is important to note that ARF and the requirement for HDL were more frequent among patients who later died. This finding is in line with the presence of renal function assessment in the majority of the scores evaluated. Stahl et al. describe how renal failure prior to complex surgery is a predictor of mortality. (21) It is relevant to highlight that, although PALSUSE does not directly evaluate renal function, this is assessed in EuroSCORE.

The risk scores evaluated did not have a good predictive capacity for prolonged hospitalization and major complications. This finding should not be surprising, as has already been mentioned, most of these scores have been designed for the prediction of mortality, and mortality may precisely be a factor that censors the appearance of other complications. Therefore, we consider that these results do not invalidate the use of these scores, which are tools recommended by various consensus documents. (8,17,22)

### Limitations

The retrospective design and the participation of a single center constitute the major limitations of our study. Furthermore, the number of patients analyzed could be considered low, since it is a rare pathology, which is only operated on in a fraction of patients. Furthermore, the study cohort has been under prospective follow-up for 15 years. We must take into account that the constant evolution of indication, recommended treatments, implementation of surgical techniques and post-operative care of cardiovascular surgeries can influence the results.

### CONCLUSION

The surgical morbidity and mortality of IE depend on a variety of pre-, intra-, and postoperative factors. It is a serious, potentially fatal pathology, in which the option of surgical treatment carries a high risk. In this sense, recognizing specific risk prediction tools becomes an urgent need. The PALSUSE score was shown to be the most accurate in predicting in-hospital death and should be considered together with other risk prediction strategies for decision making in patients with IE. We consider that due to the importance and severity of the disease, research in this field should remain active; therefore, the multicenter registries in our environment are of fundamental relevance. Future studies may assess the prospective importance of these findings.

### Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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