Review Article

Infective endocarditis risk scores: a narrative review

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Background and Objective: Despite modern advancements, infective endocarditis remains a devastating disease with high mortality and morbidity rates. Given the heterogeneous patient background and the complexity of the condition, the decision for surgery is difficult. Traditional general cardiac surgery risk models, including EuroSCORE and Society of Thoracic Surgeons (STS) score, do not include disease-specific factors that often impact both the operability and frailty of patients. The aim of the study is to review the strength and limitations of current risk scores designed specifically for patients with infective endocarditis.

Methods: A search in PubMed and OVID databases was conducted for articles and abstracts published from inception to 1st June 2024 using the terms "infective endocarditis" AND "risk score" or "surgical futility" or "operative mortality".

Key Content and Findings: Various risk scores have therefore been developed to help stratify the operative risks of these patients by incorporating endocarditis-specific features. This review aims to analyse the applicability and usefulness of risk scores in the setting of surgical management of infective endocarditis, which in turn helps to identify patients who would benefit from interventions. From 2007, a total of 18 risk scores have been designed specifically for patients with infective endocarditis. These scores however have low generalisability since different patient characteristics, disease factors and validation strategies are used. In various validation cohorts and comparative studies, the discrimination performances of these scores are unsatisfactory. Most of the studies focused on early, or in-patient mortality, while the intermediate and long-term mortality was not well studied.

Conclusions: Risk stratification for the group of patients who are indicated for surgery, but only received medical treatment due to perceived futility or were too unstable to proceed to operation, is pertinent. This population is not frequently recruited to current studies, and more research is needed.

Keywords: Infective endocarditis; risk scores; surgical futility; operative mortality

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Introduction

First described by Sir Willian Osler in 1885, endocarditis is defined as an inflammatory process that affects the endocardium and may have an infective or non-infective origin. The incidence and mortality of infective endocarditis has increased over the past 30 years in developed countries; with a mortality up to 30% in the first year (1). The rise in mortality, despite advancements in treatment, has been attributed to increasing prosthetic valve or device-related infections, as well as a growing elderly population with multiple comorbidities.

Table 1 The search strategy summary

Items	Specification
Date of search	10th October 2024
Databases and other sources searched	PubMed and OVID
Search terms used	"Infective endocarditis" and "Risk score" or "Surgical futility" or "Operative mortality"
Timeframe	Inception to 1st June 2024
Inclusion and exclusion criteria	Inclusion: original articles including retrospective and prospective studies, meta-analysis, and conference abstracts in the English language
	Exclusion criteria: studies of paediatric or congenital population, studies on diagnosis or prevention of infective endocarditis; case reports, literature reviews; not in English language
Selection process	The selection process was conducted by C.S.Y.C. and K.L. independently. Duplicate results were eliminated. Consideration for additional studies and review of the final references were performed by all authors

A multidisciplinary approach is therefore required in the management of infective endocarditis, involving physicians, microbiologists and surgeons. Up to 30% of patients with endocarditis require surgical intervention in addition to antibiotics; and even so the mortality is high. The current indications for surgery as discussed in the European Society of Cardiology guideline include heart failure, uncontrolled infection and prevention of septic embolization.

Though surgical indications are clearly listed in current guidelines, in reality the decision is often complex. How do we decide which patients will benefit from an ultra-major surgery?

There are multiple risk scoring systems in the modern world for open heart surgeries; as well as infective endocarditis-specific scores for perioperative risk stratification. This article will review the strengths and limitations of such risk scores, and how they can be included in our decision-making process as physicians.

Surgical indications and candidacy

Up to one-fourth of patients with indications ultimately do not receive surgery, due to perceived futility from comorbidities or marginal preoperative status. This group of patients carry an even higher mortality than the usual endocarditis patients, with a 30-day mortality at 60% (2-4).

History of pre-existing valvular lesion, indwelling cardiac devices, intravenous drug users, poor dental health and immunocompromised state are considered to be risk factors of infective endocarditis. The demographics has, however, changed over the past decades due to an older population, with over one-third of patients with endocarditis over 70 years old in Western countries, as well as the increasing use of intracardiac devices and hemodialysis (5,6). The controversy therefore lies at how we stratify those at extreme risk for operation. We present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2024-2041/rc).

Methods

We searched Medline via PubMed, Embase via OVID databases from inception to 1st June 2024 and conducted a literature search on the keywords "infective endocarditis" AND "risk score" or "surgical futility" or "operative mortality". The search strategy is detailed in *Table 1*.

Evaluation of endocarditis specific risk scores

Eighteen relevant risk scores have been described since 2007 to quantify risks of infective endocarditis. They are listed in *Figure 1* and discussed in the following in a chronological manner. *Table 2* lists the characteristics of each study and *Table 3* summarizes the variables in each risk score.

Costa

Developed by Costa *et al.* in Brazil (7), the scoring system was designed based on a retrospective study from 186 consecutive cases of definite infective endocarditis. A

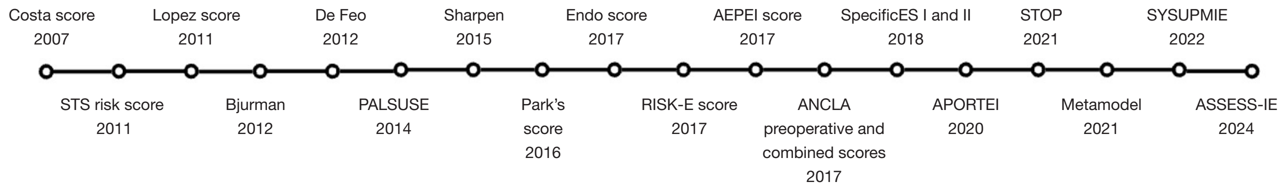

Figure 1 Timeframe of the 18 risk scores regarding infective endocarditis. STS, Society of Thoracic Surgeons; STOP, STratification risk analysis in OPerative management.

multivariate analysis was performed and a mortality risk index was designed. A total of seven factors predictive of in-hospital mortality were included: age, presence of New York Heart Association (NYHA) class IV heart failure or cardiovascular shock, arrhythmia, conduction disorders, complicated valve or prosthesis, uncontrolled sepsis and large vegetation larger than 10 millimeter. Mortality is at 5.26% when the cumulative score is less than 10, but rises to 32.7% at 11 to 15 points, 56.5% at 16 to 20 points and 78.9% at over 20 points. The receiver operating characteristic (ROC) curve for the risk index was at 0.835, compared to 0.872 for the probability of death, showing a good predictive performance of the risk index.

The Costa score, however, did not undergo formal external validation. In a comparative study by Wang and Pemberton (8) comparing STS-IE, Costa, De Feo-Cotrufo and PALSUSE scores, the Costa score performed the worst with an area under the curve (AUC) of 0.596. Varela *et al.* (9) also demonstrated that the prognostic ability of Costa score was inferior to the above three infective endocarditis-specific scores.

Interestingly, it is the only study discussed in this review demonstrating a higher mortality among operated patients, at 31.9% compared to 16.4% in the non-operative group. None of the patients who had surgical indications were denied an operation, regardless of the risk profile; 64% of the cases were treated with surgery during the acute phase; and the relatively high-risk profile of this cohort could contribute to the worse predictive power of the risk score in other populations.

Society of Thoracic Surgeons (STS)

This was the largest study focusing on endocarditis patients with surgery done. Analysing a total of 19,543 surgical patients from 2002 to 2008, 70% of patients were selected randomly to develop the STS score for IE (10), while the remaining data were used for validation of the score. Logistic regression analysis was performed with 13 predictive factors identified for operative mortality. Emergency, salvage status or with cardiogenic shock was the most important parameter, and remaining variables included renal failure, active endocarditis, preoperative use of inotropes or intra-aortic balloon pump, urgent or emergency surgery with no cardiogenic shock, prior coronary artery bypass grafting, multiple valve procedure, prior valve surgery, insulin-dependent and non-insulin dependent diabetes, hypertension, chronic lung disease and arrhythmia. A score exceeding 35 would lead to a 10% operative mortality. A good predictive ability was seen with a C-statistic of 0.75784 compared to observed mortality.

In a comparative study including 324 surgical patients with infective endocarditis by Gatti *et al.* (11), the STS risk score for IE showed fairly accurate prediction for in-hospital mortality with an area under curve at 0.697. In the study by Varela *et al.* (9), the discriminatory power of STS-IE (AUC 0.76) was better than the three other endocarditis-specific scores (De Feo-Cotrufo: AUC 0.68, PALSUSE: AUC 0.73, Costa: AUC 0.65).

In another single-centre retrospective review by Fernández-Cisneros *et al.* (12) with 142 patients diagnosed with acute left-sided endocarditis undergoing surgery, however, STS-IE score was noted to have the worst performance out of 11 endocarditis and general cardiac risk scores, with an area under the curve of 0.6. Brizido *et al.* (13) reviewed 128 patients receiving operative treatment and noted the STS-IE risk score (AUC 0.75) had a weaker discriminative power compared to EuroSCORE II (AUC 0.83).

One limitation of this score is that the authors fail to include certain endocarditis specific factors in the process of creating a risk score. Microbiological factors were not provided in the database. Out of the total 416,227 valvular procedures performed in the STS database, only 4.7% (n=19,730) were performed for infective endocarditis. The dataset was not designed with the mind to study endocarditis patients; thus certain specific characteristics,

Table 2 Comparison of risk scores and their performances

Risk scores	Populations considered	Number of patients	Time scale	Endpoint	Study type	AUC	Validation
Costa score, 2007	All medical and surgical IE patients diagnosed according to modified Duke's criteria	186	1988–1999	In-hospital mortality	Retrospective	0.835	No
STS risk score (Gaca), 2011	Surgical patients with definite IE (modified Duke's): left sided active IE, native and prosthetic valve active IE including implantable cardiac devices. Medical patients with definite IE (modified Duke's) including all valves and devices	19,543	2002–2008	Postoperative mortality and morbidity	Retrospective	C statistic 0.72870	Internal validation
López, 2011	Surgical patients with definite IE as defined by modified Duke criteria left sided active IE	317	1996–2003	In-hospital mortality or requiring urgent surgery	Retrospective	0.67 in both internal and external validation cohorts	External and internal validation
Bjurman (Cystatin-C score), 2012	Medical and surgical patients, including prosthetic valves and cardiac devices	125	1999–2005	90-day and 5-year mortality	Retrospective	0.70–0.74	No
De Feo, 2012	Surgical patients with definite IE as defined by modified Duke's criteria, including active IE, left-sided active IE, native and prosthetic valve active IE including implantable cardiac devices. Medical patients with definite IE (modified Duke's) including all valves and devices	440	1980–2009	In-hospital mortality	Prospective	0.88	No
PALSUSE, 2014	Surgical patients with definite IE as defined by modified Duke's criteria, including active IE, left-sided active IE, native and prosthetic valve active IE including implantable cardiac devices. Medical patients with definite IE (modified Duke's) including all valves and devices	437	2008–2010	In-hospital mortality	Prospective	0.84	No
Sharpen, 2015	All medical and surgical IE patients diagnosed according to modified Duke's criteria	233	2001–2011	In-hospital mortality	Retrospective	0.86	No
Park's score, 2016	Medical patients not considered for surgery, including all valves and devices. Surgical patients, excluding prosthetic valve	4,049	2000–2006	6-month mortality	Prospective	Harrell's C statistic 0.715	External validation
EndoScore, 2017	Surgical patients with definite IE as defined by modified Duke criteria, including native and prosthetic valves. Medical patients with definite IE (modified Duke's) including all valves and devices	2,715	2000–2015	30-day mortality	Retrospective	0.851	No
RISK-E, 2017	Surgical patients with definite IE as defined by modified Duke's criteria: left-sided active IE	671	1996–2014	In-hospital mortality	Prospective	0.82 in the derivation cohort; 0.76 in external validation cohort	External validation
AEPEI score, 2017	Surgical patients with definite IE (modified Duke's) including implantable cardiac devices. Medical patients with definite IE (modified Duke's) including all valves and devices	361	2000–2015	In-hospital (or 30-day) mortality	Prospective	0.780	External validation
ANCLA preoperative score, 2017	Surgical patients with definite IE (modified Duke's)	138	2000–2015	Operative mortality	Retrospective	0.828	Internal validation
ANCLA combined score, 2017	Surgical patients with definite IE (modified Duke's)	138	2000–2015	Operative mortality	Retrospective	0.823	Internal validation
SpecificES (Specific EuroSCORE) I, 2018	Surgical patients with definite IE (modified Duke's) during active phase of infection, excluding pacemaker leads	775	2000–2011	Operative mortality	Retrospective	C-statistic 0.7728	No

Table 2 (*continued*)

Table 2 (*continued*)

Risk scores	Populations considered	Number of patients	Time scale	Endpoint	Study type	AUC	Validation
SpecificES II, 2018	Surgical patients with definite IE (modified Duke's) during active phase of infection, excluding pacemaker leads involvement	775	2000–2011	Operative mortality	Retrospective	C-statistic 0.7700	No
APORTEI, 2020	Surgical patients with definite IE (modified Duke's): native and prosthetic valve active IE	1,338	2008–2018	In-hospital mortality	Retrospective	0.75	External validation
STOP, 2021	Surgical patients with a history of intravenous drug use	1,181	2011–2018	Operative morbidity (reintubation, prolonged ventilation, pneumonia, renal failure, dialysis, stroke, reop for bleeding, need for PPM) and mortality	Retrospective	0.941	Internal validation
Metamodel, 2021	Original studies with prognostic models, with or without external validation, to predict mortality after surgery	1,447	2011–2018	Operative mortality	Retrospective	C-statistic 0.79	No
SYSUPMIE, 2022	Surgical patients with definite IE as defined by modified Duke's	476	2013–2019	Operative mortality	Retrospective	0.810	Internal and external validation
ASSESS-IE, 2024	All medical and surgical IE patients diagnosed according to modified Duke's criteria	1,549	2009–2020	In-hospital and 6-month mortality	Retrospective	0.781 (in-hospital); 0.778 (6-month)	Internal validation

AUC, area under the curve; C statistics, concordance statistics; IE, infective endocarditis; PPM, permanent pacemaker; STOP, STratification risk analysis in OPerative management.

including echocardiographic and electrographic features, were probably overlooked. Patients with intracardiac device-related endocarditis were not included; and outcomes of prosthetic valve endocarditis were not discussed separately.

López

The López score (14,15) was designed with a derivation cohort of 317 patients diagnosed with infective endocarditis and verified, in a prospective manner, internally with 263 patients diagnosed at the same hospital as the derivation cohort and externally with 264 patients admitted to another hospital. Three risk factors, including *Staphylococcus aureus* infection, heart failure and periannular complications, were identified. Without any of the factors present, one-quarter of the patients were at risk of having an event, defined as in-hospital death or surgery during active endocarditis. With one variable present, the risk was as high as 49%, and increased to 79% when all 3 factors were present. The AUC of derivation and both validation samples were between 0.67 and 0.74.

All variables included in this study could be obtained within 72 hours of admission. This was designed to mirror the clinical approach where clinicians first encounter patients in the early phase of disease, allowing us to identify high-risk candidates early on.

This study is, however, not without limitations. The prognostic model consisted of one rule, where three independent predictors from each of clinical, echocardiographic and microbiological were chosen. This may create selection bias. The score was then calculated by a simple arithmetic sum of the number of variables present, instead of by weighting methods. The discrimination performance was suboptimal, with AUC less than 0.8. The method of calibration was also not shown.

Bjurman

A retrospective single-centre case control study by Bjurman *et al.* (16) in 2012 developed a multimarker score predicting 90-day and 5-year mortality. On multivariate analyses of 125 patients with definite infective endocarditis, cystatin C (CysC) level, N-terminal pro-brain natriuretic peptide (NT-proBNP), age and presence of mitral valve insufficiency

Table 3 Comparison of variables included in risk scores

Risk scores	Epidemiological	Medical	Laboratory	Electrographic	Echocardiographic	Embolic events	Microbiological
Costa score, 2007	Age >40 years (OR: 4.61; 95% CI: 1.63–10.80; four points)	1) Presence of NYHA class IV heart failure or cardiovascular shock (OR: 4.93, 95% CI: 1.86–13.05; five points). 2) Uncontrolled sepsis (OR: 5.97, 95% CI: 1.95–18.35; six points)		1) Arrhythmia (OR: 8.17, 95% CI: 2.60–25.71; eight points). 2) Conduction disorders (OR: 5.07, 95% CI: 1.67–15.35; five points)	1) Complicated valve or prosthesis (OR: 4.77, 95% CI: 1.44–15.76; five points). 2) Large vegetation >10 mm (OR: 4.36, 95% CI: 1.55–12.90; four points)		
STS risk score (Gaca), 2011	1) Insulin-dependent diabetes mellitus (OR: 1.727, 95% CI: 1.68–1.78; 8 points). 2) Previous valvular surgery (OR: 1.602, 95% CI: 1.57–1.64; 7 points). 3) Non-insulin-dependent diabetes mellitus (OR: 1.539, 95% CI: 1.50–1.58; 6 points). 4) Hypertension (OR: 1.408, 95% CI: 1.38–1.43; 5 points). 5) Chronic lung disease (OR: 1.411, 95% CI: 1.38–1.44; 5 points)	1) Emergency, salvage status, or cardiogenic shock (OR: 3.17, 95% CI: 3.03–3.31; 17 points). 2) Preoperative hemodialysis, renal failure, or creatinine level >2.0 mg/dL (OR: 2.29, 95% CI: 2.24–2.33; 12 points). 3) Preoperative inotropic or balloon pump support (OR: 1.958, 95% CI: 1.89–2.03; 10 points). 4) Urgent status without cardiogenic shock (OR 1.525, 95% CI: 1.50–1.55; 6 points)		Arrhythmia (OR: 1.656, 95% CI: 1.62–1.69; 8 points)	Multiple valve procedure (OR: 1.826, 95% CI: 1.79–1.86; 9 points)		Active (*vs.* treated) endocarditis (OR: 2.00, 95% CI: 1.97–2.04; 10 points)
López, 2011		Heart failure (OR: 2.9, 95% CI: 1.8–4.8)			Periannular complications (OR: 1.8, 95% CI: 1.1–3.1)		*Staphylococcus aureus* infection (OR: 2.0, 95% CI: 1.1–3.8)
Bjurman (Cystatin-C score), 2012	Age (OR: 1.06, 95% CI: 1.03–1.10)		1) CysC level (OR: 2.55, 95% CI: 1.37–4.76). 2) NT-proBNP (OR: 5.91; 95% CI: 2.43–14.4)		Presence of mitral valve insufficiency (OR: 2.94, 95% CI: 1.30–6.67)		
De Feo, 2012	Age (OR: 1.042, 95% CI: 1.015–1.020)	1) Renal failure (OR 3.033, 95% CI: 1.338–6.876). 2) NYHA class IV symptoms (OR: 5.913, 95% CI: 2.569–13.612). 3) Ventilatory support (OR: 9.784, 95% CI: 3.178–30.117)			Perivalvular involvement (OR: 3.033, 95% CI: 1.338–6.876)		Positive latest pre-operative blood culture (OR: 2.982, 95% CI: 1.304–6.821)
PALSUSE, 2014	1) Age (OR: 1.03, 95% CI: 1.003–1.047). 2) Prosthetic valve IE (OR: 2.2, 95% CI: 1.2–4.0). 3) Female sex (OR: 2.1, 95% CI: 1.1–3.6)	1) Urgent surgery (OR: 2.0, 95% CI: 1.2–3.1). 2) EuroSCORE (OR: 1.02, 95% CI: 1.01–1.03)			Substantial intracardiac destruction (OR: 1.9, 95% CI: 1.1–3.4)		*Staphylococcus* species (OR: 2.3, 95% CI: 1.3–4.1)

Table 3 (*continued*)

Table 3 (*continued*)

Risk scores	Epidemiological	Medical	Laboratory	Electrographic	Echocardiographic	Embolic events	Microbiological
Sharpen, 2015	1) Age (OR: 1.053, 95% CI: 1.030–1.087; 2–6 points). 2) Non-intravenous drug abuser (OR: 5.6, 95% CI: 1.2–25.5; 3 points)	1) Systolic blood pressure <90 mmHg at presentation (OR: 6.3, 95% CI: 2.1–18.8; 3 points). 2) Heart failure (OR: 3.8, 95% CI: 1.3–10.6; 2 points). 3) Raised serum creatinine >200 µmol/L (OR: 1.003, 95% CI: 1.001–1.005; 2 points). 4) Pneumonia (OR: 4.9, 95% CI: 1.5–16.1; 2 points)	Elevated peak CRP >200 mg/dL (OR: 1.005, 95% CI: 1.001–1.009; 2 points)				
ICE, 2016	1) Age (46–60 years: HR 1.51, 95% CI: 1.29–1.78; 61–70 years: HR 1.87, 95% CI: 1.58–2.20; >70 years: HR 2.90, 95% CI: 2.50–3.37). 2) History of dialysis (HR 2.04, 95% CI: 1.80–2.31). 3) Nosocomial IE (HR 1.47, 95% CI: 1.33–1.63); prosthetic IE (HR 1.20, 95% CI: 1.09–1.32). 4) IE symptom onset to admission more than 30 days (HR 0.74, 95% CI: 0.65–0.84). 5) Aortic vegetation (HR: 1.21, 95% CI: 1.09–1.33); mitral vegetation (HR 1.20, 95% CI: 1.08–1.32). 6) Surgical treatment (HR 0.66, 95% CI: 0.60–0.74)	NYHA class 3–4 (HR 2.19, 95% CI: 2.0–2.39)			Paravalvular complications (HR 1.47, 95% CI: 1.34–1.61)	Stroke (HR 1.76; 95% CI: 1.60–1.94)	1) *Staphylococcus aureus* IE (HR 1.42, 95% CI: 1.29–1.56). Viridans group IE (HR 0.63, 95% CI: 0.53–0.75). 2) Persistent bacteremia (HR 1.53, 95% CI: 1.35–1.72)
EndoScore, 2017	1) Age >80 years (OR: 4.65, 95% CI: 2.80–7.73). 2) Female gender (OR: 1.67, 95% CI: 1.26–2.23). 3) COPD (OR: 1.98, 95% CI: 1.23–3.18). 4) Number of treated valves or prostheses equal to 3 (OR: 4.49, 95% CI: 2.02–9.99)	Preoperative shock (OR: 4.31, 95% CI: 3.0–6.21)	Elevated creatinine (OR: 1.66, 95% CI: 1.08–2.53)		1) LVEF (OR: 0.97, 95% CI: 0.96–0.98). 2) Presence of abscess (OR: 2.97, 95% CI: 2.04–4.31)		*Pseudomonas aeruginosa* isolated (OR: 3.11, 95% CI: 1.35–13.93). *Staphylococcus aureus* isolated (OR: 3.45, 95% CI: 2.52–4.73). Fungal disease (OR: 5.26, 95% CI: 2.15–12.90)
RISK-E, 2017	1) Age (51–60 years: beta coefficient 0.916; 61–65 years: 1.336; >72 years: 1.362). 2) Prosthetic IE (0.645)	Septic shock (0.702). Acute renal insufficiency (0.542). Cardiogenic shock (1.486)	Thrombocytopenia (0.655)		Periannular complications (0.541)		*Staphylococcus aureus* or fungal infection (0.903)
AEPEI score, 2017	BMI >27 kg/m^2 (OR: 1.79, 95% CI: 1.02–3.45)	1) eGFR <50 mL/min (OR: 3.52, 95% CI: 1.84–6.73). 2) NYHA class IV (OR: 2.11, 95% CI: 1.10–4.05). 3) Critical state (OR: 2.37, 95% CI: 1.16–4.82)			sPAP >55 mmHg (OR: 1.78, 95% CI: 1.06–5.61)		
ANCLA preoperative score, 2017	Surgery of the thoracic aorta (OR 7.51, 95% CI: 1.09–51.8)	1) NYHA class IV (OR 2.61, 95% 0.86–7.92). 2) Critical state (OR 4.97, 95% CI: 1.34–18.4)	Anaemia (OR 11.0, 95% CI: 1.18–102.9)		Large intracardiac destruction (OR 6.45, 95% CI: 2.05–20.3)		

Table 3 (*continued*)

Table 3 (*continued*)

Risk scores	Epidemiological	Medical	Laboratory	Electrographic	Echocardiographic	Embolic events	Microbiological
ANCLA combined score, 2017	1) Surgery of the thoracic aorta (OR 6.05, 95% CI: 0.83–44.1). 2) Aortic cross-clamping time >150 minutes (OR 2.81, 95% CI: 1.00–7.91)	1) NYHA class IV (OR 2.31, 95% 0.74–7.24). 2) Critical state (OR 5.37, 95% CI: 1.40–20.5)	Anaemia (OR 10.3, 95% CI: 1.02–104.2)		Large intracardiac destruction (OR 5.11, 95% CI: 1.57–16.6)		
SpecificES (Specific EuroSCORE) I, 2018	1) Age. 2) Previous cardiac surgery. 3) Mitral valve involvement	1) Cardiogenic shock. 2) NYHA >I. 3) Emergent surgery. 4) Renal failure			1) Pulmonary hypertension. 2) Fistula		*Staphylococci* infection
SpecificES II, 2018	1) Age. 2) Previous cardiac surgery. 3) Mitral valve involvement	1) Cardiogenic shock. 2) NYHA >I. 3) Emergent/urgent surgery. 4) Renal failure			Fistula		
APORTEI, 2020	1) Age (OR 1.04). 2) Female (OR 1.39). 3) Previous cardiac surgery (OR 1.95). 4) Prosthetic valve (OR 2.14). 5) Multivalvular involvement (OR 1.13)	1) Urgent surgery (OR 2.09). 2) NYHA class 3–4 (OR 2.15). 3) Cardiogenic shock (OR 3.44). 4) Renal failure (OR 2.42)			Abscess formation (OR 1.48)		*Staphylococcus aureus* infection (OR 2.38)
STOP, 2021 (Mortality)	1) Lung disease (OR 2/70, 95% CI: 1.25–5.43). 2) Prosthetic valve endocarditis (OR 2.15, 95% CI: 1.24–3.69). 3) Aortic valve replacement (OR 2.87, 95% CI: 1.49–5.92). 4) Multivalvular involvement (OR 1.72, 95% CI: 1.00–2.95)	1) Dialysis-dependent renal failure (OR 2.81, 95% CI: 1.29–5.74). 2) Emergent surgical intervention (OR 3.41, 95% CI: 1.69–6.60)					Active endocarditis (OR 2.94, 95% CI: 1.32–7.83)
(Morbidity)	1) Multivalve procedure (OR 1.41, 95% CI: 1.01–1.98). 2) Type of valve procedure (aortic: OR 1.51, 95% CI: 1.07–2.15; mitral: OR 1.45, 95% CI: 1.03–2.05; tricuspid: OR 1.77, 95% CI: 1.21–2.60)	1) Dialysis-dependent renal failure (OR 1.80, 95% CI: 1.16–2.82). 2) Emergent surgical intervention (OR 2.91, 95% CI: 1.83–4.73)					Causative organisms other than *Streptococcus* (OR 1.48, 95% CI: 1.09–2.02)
Metamodel, 2021	1) Age. 2) Gender. 3) Previous surgery. 4) COPD. 5) Number and location of valves	1) Renal failure. 2) Shock. 3) NYHA. 4) Urgency of operation			1) Pulmonary hypertension. 2) LVEF. 3) Paravalvular complications		Etiology
SYSUPMIE, 2022	1) Multivalvular IE. 2) Tricuspid IE	Heart failure	1) Platelet count. 2) Urine occult blood		1) Diastolic dysfunction. 2) Vegetations >10 mm		
ASSESS-IE, 2024	1) Prosthetic valve (OR 4.35, 95% CI: 2.20–8.63). 2) Aortic involvement (OR 2.10, 95% CI: 1.23–3.58)	1) Clinical course of less than a month (OR 2.25, 95% CI: 1.34–3.82). 2) NYHA class III–IV (OR 2.98, 95% CI: 1.75–5.09)	1) Elevated direct bilirubin (OR 3.22, 95% CI: 1.90–5.46). 2) Anaemia (OR 1.82, 95% CI: 1.08–3.07)				

BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CysC, cystatin C; eGFR, estimated glomerular filtration fate; HR, hazard ratio; IE, infective endocarditis; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; NYHA, New York Heart Association; OR, odds ratio; sPAP, systolic pulmonary artery pressure; STOP, STratification risk analysis in OPerative management.

were noted to be independent predictors. The AUC for predicting 5-year mortality was 0.70 for CysC levels on admission and 0.74 after 2 weeks of treatment.

This was one of the few studies that emphasised the use of laboratory markers in risk stratification. CysC has also been described in other studies to be an independent prognostic marker for both acute and chronic heart failure (17,18).

The patient population was small compared to other studies. There were also issues on data collection. Hemodynamic parameters on admission and during hospital stay were not collected, and 36.2% of patients did not have stored blood samples. This could all lead to selection bias. As for the discrimination performance, the AUC for 90-day mortality was not included.

De Feo

Four hundred and forty patients with native infective endocarditis who were treated surgically were prospectively entered into a multivariable logistic regression model to assess for predictors of early mortality (19). A total of six factors were identified, including: age, renal failure, NYHA class IV symptoms, ventilatory support, positive latest preoperative blood culture and perivalvular involvement. The AUC was 0.88, with a P value for the Hosmer and Lemeshow test at 0.52. The AUC of a subpopulation (n=252) operated from 2000 to 2010 for the new scoring system was at 0.91 while the AUC for the logistic EuroSCORE in the same population was 0.84.

De Feo score was also the only risk score quoted in the 2015 European Society of Cardiology (ESC) guidelines for infective endocarditis. The overall mortality was lower in this cohort compared to other studies, at 9.1%. This was probably contributed by the fact that 17% of patients had surgeries done during the inactive phase.

Despite high discriminative power demonstrated, the model was neither validated internally nor externally. In multiple comparative studies assessing the efficacy and feasibility of risk scores, De Feo, however, did not show promising results. In the study by Varela *et al.* (9) as mentioned above, the discriminatory power of De Feo score was lower than two out of the four scores calibrated, with an AUC of only 0.68. This is likely due to the small population size.

PALSUSE

PALSUSE score (20) was developed from a Spanish multicentre prospective cohort study (PCS), including 437 patients who underwent surgery for infective endocarditis. seven independent predictors of in-hospital mortality were found, including age, prosthetic valve IE, substantial intracardiac destruction, female sex, urgent surgery, *Staphylococcus species* and EuroSCORE. The AUC was 0.84, higher than that of EuroSCORE in the same cohort (AUC 0.73).

It was one of the few multicentre studies, including data from 26 Spanish hospitals, to have included endocarditis-specific variables during derivation of the scoring system. A spectrum of patients were included, such as native, prosthetic valves and pacemaker leads with no clear valve involvement, reflecting a more heterogeneous population.

Three major limitations were noted. First, 630 patients were initially indicated for operation, but one-third of patients (n=193) were considered inoperable or passed away prior to surgical intervention. It was also noted that compared to the group who received only medical therapy, surgical patients were significantly younger and presented with fewer comorbidities. The in-hospital mortality for patients after surgery was lower than those with medical therapy. This could contribute to survivorship bias, with those presenting with more complex diseases, or poor premorbid excluded from the analysis. Second, one of the independent predictors in this study was a high logistic EuroSCORE, which can lead to multicollinearity since other predictors including age, gender and timing of surgery have already been incorporated into the EuroSCORE. Third, there was neither internal nor external validation.

Sharpen

A Singaporean single-centre study (21) including 233 patients with definite infective endocarditis over 11 years, the SHARPEN clinical risk score stratifies patients to low (score less than seven), moderate (score seven to 10) and high (score exceeding 10); with 100% mortality in those scoring 15 or above.

Seven parameters were independently associated with in-patient mortality, including hypotension at presentation, heart failure, age, raised serum creatinine, pneumonia, elevated peak C-reactive protein (CRP), non-intravenous drug abuser.

Among 182 patients indicated for surgery, only 49 (26.9%) received surgical intervention, with an in-hospital mortality of this subgroup of 7.8% only (n=4), compared to 23% (n=54) in the entire cohort. There is thus the possibility of survivor bias, where those who eventually had surgery performed were inherently more likely to survive.

Park's score

The simplified risk score for predicting six-month mortality in infective endocarditis was arguably one of the most structured studies. The score was first derived using the International Collaboration on Endocarditis (ICE)-PCS registry (22), which included 5,676 patients from 64 centres in 28 countries over 16 years; then externally validated using the ICE-PLUS registry including 2,124 patients from 34 centres in 18 countries over 4 years.

Fourteen prognostic variables were included in the risk score calculation, divided into host factors (age, history of dialysis), endocarditis factors (nosocomial, prosthetic infective endocarditis, symptom onset more than one month before admission, *Staphylococcus aureus*, viridans group streptococci, aortic or mitral vegetation), endocarditis complications (NYHA class III or IV heart failure, stroke, paravalvular complications, persistent bacteremia) and treatment with or without surgery.

With large derivation and validation cohorts, the study has improved generalizability compared to the others. Results from both groups were seen consistent with the inclusion of a rather heterogeneous population.

The other major difference compared to other risk scores discussed is the primary endpoint. A 6-month mortality, rather than in-hospital mortality, was measured, which gives a better sense of the intermediate-term survival and prognosis. There are only two other retrospective studies performed with the aim of identifying independent predictors of six-month mortality. Hasbun *et al.* (23) conducted a multicentre retrospective observational cohort study including 513 patients over 10 years with complicated left-sided native valve endocarditis. Independent prognostic factors include comorbidity, abnormal mental status, moderate to severe congestive heart failure, bacterial aetiology other than viridans streptococci except *Staphylococcus aureus* and medical therapy without valve surgery.

Another study with 273 patients (24) identified six independent predictors for 6-month mortality, including heart failure, thrombocytopenia, severe comorbidity, age, tachycardia, renal impairment and severe embolic events. All of the variables were collected on days 1, 8, and 15 from admission. Three of these predictors were time-dependent, meaning that the clinical factors can vary over time, allowing more accurate estimation of the intermediate term mortality. The rationale behind this study design was that the critical phase of infective endocarditis lasts for two weeks during which complications may arise and important management decisions are made.

EndoSCORE

This was a retrospective study including 2,715 surgical patients from 26 Italian cardiac surgery centres between 2000 and 2015 (25). A mixed effect logistic regression identified 10 independent factors associated with early mortality, including age, female, left ventricular ejection fraction, elevated creatinine, chronic obstructive pulmonary disease, preoperative shock, three treated valves or prostheses, presence of abscess, *Pseudomonas aeruginosa* isolated, *Staphylococcus aureus* isolated and fungal disease. The final model was validated by bootstrapping with the bootstrapping corrected AUC at 0.851.

The difference of the EndoSCORE from other risk models is that the beta coefficients and intercepts were used in designing the score, instead of purely additive in nature. However, in the comparative study by Gatti *et al.* (11), the predictive ability and goodness-of-fit are poorer than other models including ANCLA and AEPEI discussed below.

RISK-E

Olmos *et al.* (26) prospectively recruited 671 patients with infective endocarditis and included only those who underwent surgery with definite, left sided endocarditis in the active phase of disease (n=671). The cohort were further randomised into the development (n=424) and validation (n=247) groups. The final logistic regression model has a total score of 68 made up of eight variables, including age, prosthetic endocarditis, virulent microorganism, septic shock, thrombocytopenia, acute renal insufficiency, cardiogenic shock and periannular complications. Their weightings were obtained by multiplying the beta coefficients of each variable. The predicted mortality of patients with a score of zero was 3%, rising to 40% with a score of 30 and to 97% with a maximum score of 68. The predictive performance of RISK-E score (AUC 0.802) was compared to three existing cardiac surgical risk scores, including EuroSCORE (AUC 0.766), STS-IE (AUC 0.739) and PALSUSE (AUC 0.641) scores with all 671 patients.

This study has its limitations. Firstly, 472 patients with left sided infective endocarditis who were treated medically were excluded. Among this group, 19.9% (n=94) had surgical indications but did not receive surgical treatment due to prohibitive operative risk. The applicability in this group of patients is therefore questionable. Secondly, despite including an external validation cohort, the population size was small, with only 18 events. These affect the predictive ability of the score in the high-risk group.

AEPEI score

A prospective, population-based observational study including 361 patients from eight European cardiac centres over 15 years was conducted by Gatti *et al.* (27). It was externally validated from a cohort of 161 patients from the AEPEI registry between 2001 and 2015. A backward stepwise logistic regression model identified five independent predictors for in-hospital mortality, including obesity, deranged renal function, NYHA class IV, pulmonary hypertension and critical state. The AUC was 0.780.

An alternative model eliminating body mass index (BMI) and systolic pulmonary artery pressure (sPAP) as independent variables was also introduced in this study, showing equivalent discriminatory power but lower goodness of fit. This was created since pulmonary artery pressure (PAP) measurement requires right heart catheterization, which is an invasive procedure and not always available in critically-ill patients. The AUC of the alternative model was 0.774. The AEPEI incremented-EuroSCORE II, which included BMI, however showed no improvement in the predictive ability of EuroSCORE in infective endocarditis patients.

The study was however not without flaws. The sample size was relatively small, pathogens were not identified in 18% of cases and there were frequent co-infections which could result in misclassification of causative microbes. These could explain why microbiological factors were not found to be significant predictors of mortality. Though it was externally validated, it was a relatively small sample size with only 21 events noted.

ANCLA preoperative and combined scores

Created by the same first author of the AEPEI score, the ANCLA scores (28) were devised from a retrospective review of 138 patients in an Italian cardiac surgery centre between 1999 and 2015. In the preoperative model, five independent predictors of in-hospital death were included: anemia, NYHA class IV, critical state, large intracardiac destruction and surgery of the thoracic aorta. The combined score additionally includes aortic cross-clamping time. Compared to other endocarditis-specific and nonspecific scores including STS-IE score, De Feo score, PALSUSE and EuroSCORE, the ANCLA preoperative model (AUC 0.828) and combined model (AUC 0.823) both showed improved discrimination power, with other scores unable to achieve an AUC greater than 0.8 in the same cohort of patients.

The in-patient mortality was also higher at 20%. The authors attributed this to a relatively “sicker” group; 36.2% of patients had severe preoperative renal impairment, compared to 13.6% in De Feo score and 23.3% in STS-IE score; 62.4% had NYHA class III to IV symptoms, compared to 15.9% in De Feo and 52.3% in PALSUSE; 21.7% had perivalvular complications, compared to 15.9% in De Feo and 14.4% in PALSUSE. By including patients who are often considered more critical who might eventually not undergo surgical treatment despite being indicated, the ANCLA score could provide a better estimation of this group.

Similar to the AEPEI score, the study is limited by the small sample size, retrospective nature and the fact that causative pathogens were not identified in 28% of cases.

Specific EuroSCORE I and II

The specific EuroSCORE I and II (29) were designed by adding endocarditis-specific features, including presence of fistulae, *Staphylococci* infection and mitral valve involvement, to the original scoring systems. Renal failure and pulmonary hypertension, which were already included in EuroSCORE II, were added to the specific EuroSCORE I. A total of 779 surgical patients with active and definite infective endocarditis were recruited from nine hospitals in Spain. All models were evaluated by bootstrapping and discriminative power assessed with C-statistic. Both specific scores showed improvement compared to the original version. The C-statistic of specific EuroSCORE I was at 0.7728 [95% confidence interval (CI): 0.7365–0.8091], compared to that of the original (0.7340, 95% CI: 0.6944–0.7736). The C-statistic of specific EuroSCORE II was 0.7700 (95% CI: 0.7333–0.8067), compared to 0.7442 (95% CI: 0.7060–0.7824) of the original. Net reclassification index, a percentage for patients who died in each risk subgroup as classified with the original EuroSCOREs being reclassified to a lower or higher-risk group with the new scores was 5.1% and 20.3% respectively for specific EuroSCORE I and II.

Since the patients were retrospectively recruited from three different databases, only variables clearly defined were entered in the models to minimise risk of heterogeneity, therefore certain endocarditis-specific and potential predictors of mortality such as duration of antimicrobial treatment and negative blood cultures before operation were not included.

A study by Madeira *et al.* in 2016 (30) reviewed the discriminatory power of both EuroSCORE I and II for perioperative mortality in patients with active endocarditis who underwent surgery. Independent predictors for mortality were also identified by binary logistic regression. One significant finding was that the addition of specific endocarditis features to the score did not result in a marked improvement in predictive ability, with only a 0.04 increase in AUC.

APORTEI

The APORTEI score was developed by systematic review and meta-analysis of a total of 16 studies on in-hospital mortality after surgery for acute IE including 7,484 patients, identifying 11 infective endocarditis-specific factors as significant predictors for in-hospital mortality after surgery for endocarditis (31). The 11 factors identified included age, female gender, surgery required on day of admission, previous cardiac surgery, NYHA class III–IV, cardiogenic shock, prosthetic valve, multivalvular involvement, renal failure, abscess and *Staphylococcus aureus* infection. The prognostic utility of the score was then verified with 1,338 patients in the Spanish GAMES national cohort from 2008 to 2018 (32), with an AUC of 0.75 and adequate calibration (Hosmer-Lemeshow test P=0.389). Compared to the prognostic accuracy of EuroSCORE I in the same population, where the AUC was 0.72 but the calibration was suboptimal [high level term (HLt) P=0.062].

The APORTEI score was first developed, then validated with over 9,000 patients across different hospitals. Though the AUC is lower than those in other studies when validated in the development sample, the APORTEI score showed better calibration, arguably had less selection bias and sampling error due to the large sample size.

However, there was selection bias during development of the score. Variables could only be included in the meta-analysis calculations if they are considered to be risk factors for mortality in two or more endocarditis-specific risk scores. Due to the retrospective nature of the study, certain general and endocarditis-specific factors, including vegetation size, embolic event or thrombocytopenia, were not included in the analysis due to missing or heterogenous data provided in the GAMES cohort. Only the EuroSCORE I could be used for comparison, limited again by the missing data.

STratification risk analysis in OPerative management (STOP)

STOP score was a retrospective study including 1,181 patients from 10 tertiary cardiac surgery centres in the US who underwent surgery for drug-associated IE from 2011 to 2018 (33). Multivariate analysis showed dialysis-dependent renal failure, active endocarditis, lung disease, emergent surgical intervention, prosthetic valve endocarditis, aortic valve replacement and multivalvular involvement as independent predictors for operative mortality. The predicted mortality at 27 points was 56.2% and at the highest possible score of 33, 81.2%.

Operative morbidities were also evaluated, including reintubation, prolonged ventilation, pneumonia, renal failure, dialysis, stroke, reoperation for bleeding and permanent pacemaker insertion. The independent predictors of morbidity were dialysis-dependent renal failure, emergent surgical intervention, multivalve procedure, causative organisms other than *Streptococcus* and type of valve procedure performed. The predicted morbidity ranged from 19.7% to 91%, with a score of 0 to 19 respectively.

The score was internally cross-validated with 10,000 bootstrap replications, with an AUC of 0.941 for early mortality and 0.94 for early morbidity, higher than other previous scoring systems.

There were a few limitations. Time from clinical diagnosis to intervention was not recorded, the proportion of patients failing initial medical therapy and requiring surgery versus those indicated for surgery during initial presentation were not stated, certain variables such as echocardiographic findings, operative details were not included. The inclusion of only intravenous drug-related endocarditis meant that this score is unlikely applicable to other subgroups.

Metamodel

This study by Fernandez-Felix *et al.* evaluated a total of 11 prognostic models used to estimate in-hospital or 30-day mortality after surgery for active infective endocarditis (34).

Eight of the models had a high risk of bias according to the PROBAST tool and only three models (EndoSCORE, specific EuroSCORE I and II) were included in the metamodel. The metamodel was then validated with the Spanish GAMES registry, the same registry used in the APORTEI study. The performance of the metamodel outperformed the original three models, with a C-statistics of 0.79 and a calibration slope of 0.98.

One of the major limitations of this study was that since both EuroSCORE I and II were derived with the same cohort of patients, the probability that certain variables were included as independent predictors were higher and this could magnify the associations of those with the outcome in the metamodel. All of the prediction models were considered with high risk of bias if the complete model equation was not available. As such, out of the 11 studies analysed, eight were classified as high risk of bias and excluded from the metamodel, which could lead to publication bias.

SYSUPMIE

This was a retrospective study, with the development cohort consisting 276 patients from two centres in southern China between 2013 and 2019 who received surgery for definite infective endocarditis (35). Eight variables were identified as independent predictors of early mortality among the 89 factors analysed: platelet count, serum albumin, current heart failure, urine occult blood (UOB), diastolic dysfunction, multiple valve involvement, tricuspid valve involvement and vegetation larger than 10 mm.

It was then validated with an internal cohort consisting 125 patients with an AUC of 0.813 and externally validated with 75 patients from another centre, with an AUC of 0.812. The predictive value of SYSUPMIE (AUC 0.810) was better than that of EuroSCORE II (AUC 0.619) in this cohort.

The SYSUPMIE study was the first large trial to be conducted in an Asian population. It was also the first study to identify UOB, diastolic dysfunction and tricuspid valve involvement as independent predictors of early mortality. UOB, despite being an uncommon factor to be considered in studies regarding infective endocarditis, were found to be present in 44.5% of patients. There were scattered case reports relating the presence of UOB with hemolytic anemia or glomerulonephritis (36,37), and more research is needed on whether this simple investigation can act as an accurate predictive tool for mortality.

Sixty-three percent of patients were found to have various degrees of diastolic dysfunction, again an echocardiographic feature not commonly documented. In the ESC guideline recommendations for echocardiography during IE, diastolic dysfunction was also discussed and could be a result of obstructive vegetation leading to functional valve stenosis, or major destructive lesions causing intracardiac shunts (38).

The authors postulated that since tricuspid valve endocarditis is associated with intravenous drug use, this group of patients are more likely to suffer from recurrence and thus, mortality. Tricuspid valve involvement was also an independent predictor for major comorbidity in the STOP trial focusing on patients with intravenous drug use.

Because of the small sample size, calibration of the score was not performed. The score might be inaccurate in patients who received platelet and albumin transfusions. Blood culture results were unavailable in 12% of patients and negative results in 21.6% were based only on 3-day blood cultures, where certain fastidious or intracellular microbes will require up to five to seven days or even different culture techniques.

ASSESS-IE

The final score is designed by Wei *et al.*, including 1,549 patients from China between 2009 and 2020 (39). The derivation cohort consists of 1,141 patients and validation cohort 408. Six variables were identified as independent predictors for in-hospital death, including clinical course of less than a month, prosthetic valve, NYHA class III–IV, elevated direct bilirubin, anemia and aortic involvement. Each of the factors is allocated one point. The patients are further divided according to low risk (score 0–2), moderate risk (score 3–4) and high risk (score >4). The mortality is up to 27.9% when reaching the maximum score.

This was the only study to identify direct bilirubin as an independent predictor. Apart from causing cardiac dysfunction and therefore acute cardiogenic liver congestion, infective endocarditis could result in systemic inflammation and multiorgan injury. Since the rise in direct bilirubin precedes that in total bilirubin, it is more useful as a predictor in the early phase of disease.

The discriminatory ability of the score was also compared to Park's score, where the AUC of both in-hospital (0.781 *vs.* 0.799) and 6-month mortality (AUC 0.778 *vs.* 0.814) were both lower in the ASSESS-IE score. This shows that although the ASSESS-IE score is arguably a user-friendly score with only 6 variables, compared to 14 in Park's, the accuracy may be lower. It is yet to be validated in a non-Chinese population. Certain clinical factors, including duration of antibiotics before operation, types of perivalvular complication and echocardiographic features were not considered.

Evaluation of general cardiac surgery risk scores

EuroSCORE is one of the most popular risk stratification models used to predict operative mortality and major morbidity following adult cardiac surgery. There have been contradictory reports on whether EuroSCORE can adequately predict early mortality after surgery for infective endocarditis (40,41). Both EuroSCORE I and II were modelled from a population of elective valvular and isolated coronary artery bypass graft (CABG) procedures. These general cardiac risk scores often fail to consider endocarditis-specific factors. The extent of local destruction leading to difficult procedure; sepsis-related haemodynamic disturbances, immunological dysfunction and clotting disorders; embolic events; active infection resulting in prosthetic valve endocarditis post-operatively can all complicate the decision of proceeding to surgical treatment in this group of patients. Madeira *et al.* argued that while it is undeniable that specific endocarditis features would alter the disease course and therefore, affect the prognosis, the addition of such can increase complexity of the model without an equivocal improvement in predictive performance (30).

Limitations

Obstacles to an all-encompassing endocarditis risk score

An important question that needs to be answered first and foremost is to what end does a risk scoring system serve for surgeons in the context of endocarditis. For the authors, the essential question is whether the patient will derive benefit in terms of life-years gained after surgery, given the patients' comorbidity burden and endocarditis severity.

Some patients obviously derive benefit from surgery. We would not hesitate to operate on a healthy 65-year-old woman with destructive *Streptococcus agalactiae* mitral valve endocarditis causing severe mitral regurgitation. However, we might hesitate to operate if the same 65-year-old was suffering from systemic lupus erythematosus, on long-term immunosuppressants, had caseating mitral annular calcification, was recently put on hemodialysis due to renal failure, with a partially treated spondylodiscitis due to hematogenous spread.

The obstacles to constructing a generalizable mortality scoring system for endocarditis are protean, and include patient heterogeneity, definition of surgical indication and candidacy, time horizon of mortality censorship, ease of use, and inherent geographical and temporal variances in disease pattern.

Although risk scores should account for patient comorbidities, including inherent differences in those undergoing surgery versus non-surgical management and how these comorbidities interact with endocarditis, this is easier said than done. When patients were divided into those who underwent surgery, those without a surgical indication, those with an indication but did not undergo surgery for some reason, the inherent differences in baseline characteristics between these subgroups may be often so dramatic that not even propensity score matching can adequately address them (2,27).

The traditional focus on surgical outcomes often overlooks an important patient subgroup: those with surgical indications who do not receive surgery. This group experiences unique risks that are often not captured in existing models, thereby reducing the discriminatory power of broad-applied risk scores.

The time horizon for mortality censorship is another critical factor. While most studies concentrate on in-hospital mortality, extending the timeframe to include intermediate outcomes, such as those seen at six months post-diagnosis as in Park's study, could provide a more comprehensive understanding of survival (22). Such an approach acknowledges that complications like embolic events and heart failure can manifest well beyond the acute and subacute period.

Additionally, changes in the epidemiology and treatment landscape of endocarditis complicate risk scoring. Increasingly older patients with comorbidities, or cases related to the use of cardiac implantable electronic devices and geographical variances in drug use, require that risk models are adapted to the location of practice, continually updated, and validated to reflect ever-changing demographics.

The balance between complexity and practicality must not be forgotten. While intricate models with numerous variables may promise greater accuracy, their practical application in fast-paced clinical environments remains limited. Therefore, risk scores should strive for the best balance between simplicity and precision, ensuring they remain user-friendly and accessible to clinicians.

Conclusions

To advance the development of reliable risk scores for infective endocarditis, future initiatives must ensure broad validation across diverse patient populations and incorporate a range of clinical factors. Instead of simple percentages of likelihood of survival with and without surgery, newer risk scores should address how much the patient will benefit in terms of life-years gained after surgery, given the patients' comorbidity burden and endocarditis severity. By harnessing the predictive power of these tools and addressing currently underrepresented patient subgroups, clinicians can make more informed decisions, ultimately improving patient outcomes.

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Footnote

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