

ESC Working Group on Valvular Heart Disease Position Paper: assessing the risk of interventions in patients with valvular heart disease

Raphael Rosenhek^{1*}, Bernard Jung², Pilar Tornos³, Manuel J. Antunes⁴,
Bernard D. Prendergast⁵, Catherine M. Otto⁶, Arie Pieter Kappetein⁷,
Janina Stepinska⁸, Jens J. Kaden⁹, Christoph K. Naber¹⁰,
Esmeray Acartürk¹¹, and Christa Gohlke-Bärwolf¹²

¹Department of Cardiology, Medical University of Vienna, Vienna, Austria; ²Cardiology Department, Bichat Hospital and Paris 7 University, Paris, France; ³Cardiology Department, University Hospital Vall d'Hebron, Barcelona, Spain; ⁴Cardiothoracic Surgery, University of Coimbra, Coimbra, Portugal; ⁵Department of Cardiology, The John Radcliffe Hospital, Oxford, UK; ⁶Division of Cardiology, Department of Medicine, University of Washington, Seattle, WA, USA; ⁷Department of Cardio-Thoracic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands; ⁸Institute of Cardiology, Warsaw, Poland; ⁹Medical Faculty Mannheim, University of Heidelberg, Heidelberg, Germany; ¹⁰International Heart Center Essen, Essen, Germany; ¹¹Department of Cardiology, Çukurova University, Adana, Turkey; and ¹²Herzzentrum Bad Krozingen, Bad Krozingen, Germany

Received 26 September 2010; revised 28 December 2010; accepted 1 February 2011; online publish-ahead-of-print 15 March 2011

Aims

Risk scores provide an important contribution to clinical decision-making, but their validity has been questioned in patients with valvular heart disease (VHD), since current scores have been mainly derived and validated in adults undergoing coronary bypass surgery. The Working Group on Valvular Heart Disease of the European Society of Cardiology reviewed the performance of currently available scores when applied to VHD, in order to guide clinical practice and future development of new scores.

Methods and results

The most widely used risk scores (EuroSCORE, STS, and Ambler score) were reviewed, analysing variables included and their predictive ability when applied to patients with VHD. These scores provide relatively good discrimination, i.e. a gross estimation of risk category, but cannot be used to estimate the exact operative mortality in an individual patient because of unsatisfactory calibration.

Conclusion

Current risk scores do not provide a reliable estimate of exact operative mortality in an individual patient with VHD. They should therefore be interpreted with caution and only used as part of an integrated approach, which incorporates other patient characteristics, the clinical context, and local outcome data. Future risk scores should include additional variables, such as cognitive and functional capacity and be prospectively validated in high-risk patients. Specific risk models should also be developed for newer interventions, such as transcatheter aortic valve implantation.

Keywords

Valvular heart disease • Risk assessment • Risk scores • Risk factors • Aortic stenosis

Introduction

The range of interventions available for the management of adults with valvular heart disease (VHD) is increasing. Risk assessment is required for optimal decision-making and should be specific to the individual patient, taking account of patient factors, clinical outcomes, and local resources. Risk stratification for adults with

VHD in whom intervention is contemplated effects the decision to proceed as well as the timing and choice of procedure. This information enables the patient and family to participate in the management plan. Decision-making is particularly difficult in elderly patients who often have extensive comorbidity and differing expectations. Current risk scores are increasingly used to estimate the risk of valve surgery, define high-risk subgroups in which

* Corresponding author. Tel: +43 1 40400 4614, Fax: +43 1 40400 4216, Email: raphael.rosenhk@meduniwien.ac.at

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novel transcatheter techniques may be more appropriate, and adjudicate enrolment in clinical trials and registries. Beyond individual patients, risk scores are also increasingly used as a 'gold standard' to assess and compare outcomes between different populations, techniques, and medical centres. The recent VARC statement provides a standardized definition for endpoints after transcatheter aortic valve implantation, thus enabling a uniform assessment of outcome and future comparisons between different trials and devices.¹ In contrast, the present position paper provides clinical guidance for the general risk assessment of patients with VHD in whom intervention is being considered. The potential use of risk scores is discussed and the importance of the estimated in-hospital 30-day mortality is highlighted in this context. In this position statement, we summarize the strengths and weaknesses of currently available 'scores' used to estimate perioperative mortality following surgery in adults with VHD, and provide guidance for future development of new risk stratification methods.

Importance of risk assessment

Individualized decision-making

Determination of the optimal timing of intervention (valve surgery or percutaneous procedures) in adults with VHD is based upon cumulative assessment of the natural history of the disease, the option of alternative treatments, the patient's life expectancy, risk of the intervention, and long-term post-procedural outcomes. While this decision-making process is generally based upon clinical experience, the availability of more objective means of risk assessment is desirable. Risk scores are increasingly used across the broad range of indications for cardiac surgery (including VHD), although most of them have been primarily defined and validated in patients undergoing coronary artery bypass surgery. However, more accurate risk prediction is needed as demand for therapeutic interventions increases, particularly in high-risk patients with VHD. The average older adult can be expected to live several years after effective intervention and estimation of risk can be adjusted to

the individual patient based on comorbidity and functional evaluation.^{2,3} Average life expectancy according to age should be considered (Table 1), but may be shorter in certain patients with valve disease, in particular in young patients, when compared with the normal population.⁴ Decision-making in high-risk patients requires a team approach, including cardiologists, cardiac surgeons, and anaesthesiologists, especially when percutaneous techniques are being considered.⁵

Timing of surgery

There are several established Class I indications for surgery in patients with VHD,^{6,7} although many patients are not referred promptly even when these indications are present. The reasons for this failure include misconceptions of the risk of intervention or a lack of knowledge of current guidelines. Late referral is frequently associated with higher surgical risk and may preclude intervention in some patients. Accurate risk assessment in these patients is critical for decision-making concerning the choice between valve surgery, transcatheter intervention, or medical therapy alone.

Conversely, some patients may benefit from earlier elective intervention when the risk is low, despite minimal or absent symptoms. Clinical approaches are being explored to allow identification of patients at high risk of functional deterioration and those in whom delayed surgery may result in a higher operative risk or impaired long-term outcome. This decision-making depends on an accurate estimate of the operative risk for an individual patient in a specific centre.

Choice of procedure (conventional surgery vs. transcatheter techniques)

The development of transcatheter aortic valve implantation was fuelled by the fact that elderly patients with severe symptomatic aortic stenosis (AS) and significant comorbidity have high operative mortality and frequent postoperative complications following conventional surgery. As a result, about one-third of patients with

Table 1 Average life expectancy (years) in the general population of the European Union and the USA

Age	European Union			USA		
	Overall	Men	Women	Overall	Men	Women
65	18.9	17.0	20.5	18.5	17.0	19.7
70	15.2	13.5	16.5	14.9	13.6	15.9
75	11.8	10.5	12.7	11.6	10.5	12.3
80	8.8	7.9	9.4	8.7	7.8	9.3
85	6.5	5.9	6.8	6.4	5.7	6.8
90				4.6	4.1	4.8
95				3.2	2.9	3.3
100				2.3	2.0	2.3

Sources: Eurostat. European Commission. Life Expectancy by Sex and Age. Queries for Survival performed for the year 2007 for the European Union (27 countries). Accessed (12 July 2010) at: http://epp.eurostat.ec.europa.eu/portal/page/portal/product_details/dataset?p_product_code=DEMO_MLEXPEC. US National Center for Health Statistics, National Vital Statistics Reports (NVSR), US Decennial Life Tables for 1999–2001, United States Life Tables, Volume 57, Number 1, 5 August 2008. Accessed (10 July 2010) at: http://www.census.gov/compendia/statab/cats/births_deaths_marriages_divorces/life_expectancy.html.

symptomatic severe AS do not undergo surgery.^{8–10} Percutaneous techniques are currently recommended in patients in whom conventional valve surgery is contraindicated or poses very high risk.⁵ The European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgery (STS) score have been used in several series to estimate the risk of conventional surgery, to determine a threshold for enrolment in clinical trials, and to justify the choice of new procedures in patients with a high estimated surgical risk.^{11–13} However, it is unclear whether their use can be extrapolated to predict the risk of percutaneous interventions. Risk assessment may also influence the choice of percutaneous approaches to mitral regurgitation, although experience in this field is very limited.

Risk scores should be included in guidelines to identify high-risk patients who may benefit from additional work-up or alternative treatment. They may also be useful for administrative, logistic, and budget planning, especially when high-risk patients are identified.

Risk-benefit analysis

A score that predicts both in-hospital and long-term outcome will guide risk-benefit analysis and the choice of treatment. One therapy may have higher operative mortality but better long-term outcome (e.g. aortic valve replacement in a high-risk patient with AS), while an alternative option may have lower hospital mortality but less favourable or questionable long-term outcome (e.g. medical therapy or balloon valvuloplasty in the same patient). The risk-benefit analysis in a younger population will differ from that in an older population with more comorbidities.

Quality of care

Episodic evaluation of clinical outcomes in a given centre is an increasingly important part of quality control. The risk profile of patients may vary greatly between different institutions and this variation needs to be considered when outcome measures are compared. Standardization using risk scores allows comparison of the quality of care between institutions at national or international level and also between operators within a single institution. The availability of an accurate risk score for a specific patient population and procedure is also fundamental before the introduction of new technologies and their evaluation in relation to established techniques.

Risk scores

A number of risk scoring models for the prediction of perioperative mortality have been proposed. Most were initially developed and validated in large cohorts of patients, most of whom were undergoing coronary artery bypass surgery. The use of risk scores is recommended by the ESC guidelines⁷ for decision-making in patients with VHD. The most widely used measure in the decision-making process is 30-day in-hospital mortality, although these risk scores also may be used for estimating the length of intensive care unit stay and overall costs as well as 1-year mortality.

The European system for Cardiac Operative Risk Evaluation (EuroSCORE)

The European System for Cardiac Operative Risk Evaluation (EuroSCORE) provides an estimate of in-hospital mortality following cardiac surgery¹⁴ and was developed from a large database of patients undergoing cardiac surgery (mostly coronary surgery, 30% valve surgery) in 1995¹⁵ with subsequent validation in Europe¹⁶ and North America.¹⁷ The additive EuroSCORE is calculated using simple mathematics, while the logistic EuroSCORE requires a computer. The additive EuroSCORE is calculated incrementally by adding risk points for 17 individual risk factors. However, the additive EuroSCORE has been shown to overpredict risk in contemporary coronary surgery and has poor predictive ability in high-risk patients. The logistic EuroSCORE (which uses a more complex algorithm based on the same variables) avoids some of these limitations and its use has been recommended, in particular for research studies.¹⁸ Surgical techniques and results have improved since then and data collection for an updated version began in early 2010.¹⁹

The Society of Thoracic Surgeons' risk models (STS)

The US Society of Thoracic Surgeons (STS) risk model and calculator were developed to estimate the risk of mortality or serious postoperative complications following cardiac surgery and specifically consider the type of valve or coronary artery surgery. The current STS risk model includes a broad range of variables (*Table 2*) making it the most detailed risk score available. The score is updated on a regular basis and can only be calculated via the STS website—it is thus important to specify and consider the date of calculation when applied for clinical purposes.

Ambler score

The first European risk model specifically dedicated to the prediction of in-hospital mortality in patients undergoing heart valve surgery (aortic and/or mitral) was proposed by Ambler *et al.*²⁰ in 2005. In contrast to the EuroSCORE, the Ambler score includes body mass index, need for dialysis, and the type of valve surgery. On the other hand, it does not take account of neurological dysfunction or previous cerebrovascular accident. The Ambler score is based upon a list of risk factors and a ready-reckoner table and is very quick and simple to calculate. Although not widely used, this tool is available through online medical information resources.

Other risk scores

Other risk models specifically designed for the prediction of in-hospital mortality after heart valve surgery have been proposed.^{18,21–25} Because of their limited dissemination in the scientific literature, these will not be addressed in further detail. Other risk scores have also been derived for heart surgery in general but not specifically validated in patients with VHD.^{26–30}

Table 2 Variables required for current risk scores

	STS score	EUROSCORE additive/logistic*	Ambler Score
Patient characteristics			
Age	+	+	+
Gender	+	+	+
Height	+		
Weight	+		
Body mass index			+
Ethnicity	+		
Comorbid conditions			
Diabetes	+		
Hypertension	+		+
Chronic lung/pulmonary disease	+	+	
Extracardiac arteriopathy	+	+	
Peripheral vascular disease	+		
Neurological dysfunction	+	+	
Cerebrovascular accident	+		
Serum creatinine	+	+	+
Dialysis-dependent renal failure	+		+
Immunosuppressive therapy	+		
Cardiac history			
NYHA classification	+		
Unstable angina	+	+	
Recent myocardial infarction	+	+	
Arrhythmias	+		+
Previous cardiac surgery		+	+
Previous CABG	+		
Previous valvular surgery	+		
Previous PCI	+		
Active endocarditis	+	+	
Number of diseased coronary vessels	+		
Type and severity of valvular disease (stenosis/regurgitation, aortic/mitral)	+		
Haemodynamic state			
Systolic pulmonary pressure > 60 mmHg		+	
Ejection fraction	+	+	+
Critical pre-operative state		+	
Cardiogenic shock	+		
Resuscitation	+		
Inotropic agents	+		
Intra-aortic balloon pump	+		
Procedure			
Emergency	+	+	
Surgery on thoracic aorta	+	+	
Aortic valve surgery ^a	+		+
Mitral valve surgery ^a	+		+
Aortic and mitral valve surgery ^a	+		+
Tricuspid surgery ^a	+		
Surgery for congenital heart disease	+		
Rhythmologic surgery	+		
Concomitant CABG	+		+

Continued

Table 2 Continued

	STS score	EUROSCORE additive/logistic*	Ambler Score
Concomitant tricuspid valve surgery	+		+
Post-infarct septal rupture		+	

*The same variables are used for the additive and logistic EuroSCORE.

STS, The Society of Thoracic Surgeons; CABG, coronary artery bypass grafting; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

^aIn the STS score, the type of valvular surgery (valve replacement or repair) is taken into account.

Table 3 Predicted and observed mortality rates using different risk scores in high-risk patients (modified from reference³⁹)

	STS score	Additive EuroSCORE	Logistic EuroSCORE	Ambler score
N	64	84	64	97
Predicted mortality (%)	13.3	14.0	50.9	19.0
Observed mortality (%)	18.7	11.9	15.6	13.4
Ratio of observed to predicted mortality	1.41	0.85	0.31	0.71
Observed late mortality (%)	45.3	33.3	29.7	26.8

Performance of risk scores validated in valvular heart disease

The EuroSCORE, the STS score, and the Ambler score have all been tested in large patient populations with VHD. Although their ability to predict perioperative morbidity^{31–33} and long-term outcome³⁴ has been reported, most published data refer to perioperative mortality.

Discrimination

The discriminatory power of a risk score refers to its ability to differentiate between low- and high-risk patients and is assessed using the area under the ROC curve or the c-index.^{19,35} Exact comparison of the discriminatory power of the different scores would require their validation in the same population. Such an analysis has not been performed to date. A meta-analysis assessing the utility of the logistic and additive EuroSCOREs in valve surgery reported an average area under the ROC curve of 0.72,³⁶ whereas a recent report of the STS found an area of 0.80 for isolated valve surgery³⁷ and of 0.75 for combined valve and coronary artery bypass surgery.³⁸ Similarly, the area under the curve for the Ambler score was 0.77.²⁰

Calibration

Calibration refers to the comparison between predicted and observed mortality.¹⁹ The logistic EuroSCORE tends to overestimate operative mortality, particularly in high-risk patients.^{34,36,39–43} One study compared the calibration of the additive and logistic EUROSCORE, the Ambler and STS risk scores in the same population of high-risk patients with AS.³⁹ In this group (who exceeded the 90th risk percentile), the risk of mortality was underestimated by the STS score and

Table 4 Predicted operative mortality of six hypothetical patients scheduled to undergo isolated aortic valve replacement for aortic stenosis derived using different risk scores

Age	45	70	75	80	75	80
Gender	m	f	f	m	m	f
Size, cm	182	165	164	180	170	162
Weight, kg	75	60	68	70	80	50
Creatinine, mg/dL	0.9	1.6	2.0	2.3	2.8	2.5
Ejection fraction, %	70	60	65	58	38	42
Pulmonary artery systolic pressure, mmHg	35	34	44	38	50	64
Concomitant CABG	No	No	Yes	No	No	No
Redo surgery	No	No	No	No	Yes	No
Additive EuroSCORE, %	2.0	3.0	7.0	9.0	12.0	13.0
Logistic EuroSCORE, %	1.5	2.1	5.8	10.6	26.1	35.2
STS score, %	0.4	7.1	3.4	7.7	9.0	14.3
Ambler risk score, %	0.2	2.1	4.1	5.5	14.3	9.3

overestimated by the other two (Table 3). The discrepancy between these estimations of risk is illustrated by the predicted mortality using different risk scores for specific patients with a given risk profile (Table 4). The logistic EuroSCORE predicts the highest mortality in most cases. Furthermore, recent series demonstrate suboptimal performance of the additive^{44,45} and the logistic^{44–46} EuroSCORE in specific national populations.

In summary, the currently available scores achieve acceptable discrimination but sub-optimal calibration in estimating the operative mortality of contemporary heart valve surgery.

Limitations of risk scores

Differences in predicted mortality between the scores are significant for the following major reasons:

1. Different risk factors selected;
2. Different weighting of these risk factors;
3. Variable patient characteristics in the initial derivation cohort;
4. Differences in outcome data used for risk score development (partly related to caseload at enrolling centres);
5. Changing patient characteristics (age, comorbidity, and redo surgery) over time, resulting in a disproportionate number of high-risk patients;⁴⁷
6. Changing operative techniques and reduced mortality with time, resulting in discrepancies between estimated and observed outcome.⁴⁷

While scores may be consistent in low-risk patients, differences become more important in high-risk patients where there is greatest clinical need for reliable risk estimation. It is therefore important that high-risk patients are sufficiently represented in the derivation cohort. Inclusion of large numbers of low-risk patients results in distortion (or skewing) of the model, making it imprecise and inapplicable in high-risk patients. For example, high-risk patients (estimated mortality >20%) accounted for only 3.5% of the data set used to derive the Ambler score.²⁰ The heterogeneous nature of high-risk patients is another limitation. Given the number of possible comorbidities and their various combinations, it is difficult to accurately estimate the weight of each variable. Furthermore, most studies evaluating the predictive value of risk scores were performed in patients with AS.⁴² Limited data are available for patients with mitral regurgitation, which is the second most common manifestation of VHD.

In reality, treatment decisions for an individual patient relate to a specific centre (and specific surgeon) and it is therefore necessary to compare local outcomes to those predicted by a risk score.⁴⁸ Risk calculations can only be applied to a given patient population once the score is validated in this way—a strong argument in favour of regular audit, outcome assessment, and risk modelling for specific centres (and surgeons).⁴⁹

Variables affecting perioperative mortality and decision making in valvular heart disease

Several studies have demonstrated the numerous potential predictors of operative mortality after heart valve surgery.^{24,50–53} Despite this large range of variables, a risk assessment model based on just three factors (age, left ventricular ejection fraction, and creatinine) provided better prognostic value than the additive and logistic EuroSCORE, Parsonnet, Cleveland, and Northern New England scores in one recent study.⁵⁴ Furthermore, use of a single variable (age) matched the ability of the additive and logistic EuroSCORE to predict early mortality in a recent single centre analysis of patients undergoing isolated aortic valve replacement.⁵⁵ While these simpler predictors may be applicable to large populations,

they are not necessarily useful discriminators when applied to individual patients.

The ideal number of variables required to derive a risk score therefore deserves discussion. While a very limited number of variables may be sufficient to describe the risk of a certain population, a larger set of variables is needed to accurately predict the risk in an individual high-risk patient.²⁷ Clearly, a risk score should be accurate, reproducible, and practical, including a limited number of variables defined by the following characteristics:

1. Frequent representation in the derivation and validation cohorts to avoid inaccurate estimation of predictive power;
2. Easy and reproducible assessment;
3. Clinically relevant impact on operative mortality (but not surrogate endpoints).

The following variables fulfil these criteria:

- Age;
- Gender;
- Symptomatic status (NYHA class);
- Left ventricular ejection fraction;
- Pulmonary artery systolic pressure;
- Creatinine;
- Chronic pulmonary disease;
- Extracardiac arteriopathy (one or more of claudication, carotid occlusion or >50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries, or carotids);
- Neurological impairment affecting daily activity (disease severely affecting ambulation or day-to-day functioning);
- Concomitant coronary artery disease;
- Concomitant coronary artery bypass surgery;
- Type of valve surgery (aortic, mitral, aortic + mitral, additional tricuspid, repair vs. replacement);
- Concomitant surgery of the ascending aorta;
- Redo cardiac surgery;
- Emergency surgery.

While most variables are easily assessable, some (e.g. chronic pulmonary disease, renal disease) have a wide range of values with continuous impact on risk and need more accurate definition. The additive and logistic EuroSCORE inappropriately categorizes creatinine and pulmonary arterial systolic pressure in a binary fashion defined by an arbitrary threshold, although these variables should be considered in a continuous way.

Certain conditions may not be suitable for inclusion in risk scores since they do not fulfil these criteria. However, given their key importance, they should be considered in clinical decision-making.

1. Conditions that are relative or absolute contraindications to conventional surgery (and are therefore very rare in surgical series):
 - Severe calcification of the ascending aorta (porcelain aorta, preferably defined using standardized imaging criteria);
 - Previous chest wall radiation;⁵⁶
 - Hepatic failure;
 - Chest wall malformation;

2. Complex conditions requiring an individual approach, including specific risk stratification:

- Frailty;^{57,58}
- Active endocarditis;
- Active cancer;
- Low-flow low-gradient AS.⁵⁹

Frailty is defined as a nonspecific state of vulnerability. The use of a standardized approach based on measurable factors⁶⁰ (weakness, weight loss, exhaustion, low physical activity, and slowed walking speed) and validated indices is recommended to limit subjectivity. However, predictive value needs to be evaluated in patients with VHD.

3. Conditions likely to be associated with increased operative mortality and/or morbidity with insufficient validation and requiring further study:

- Left ventricular hypertrophy;
- Left ventricular dilatation;
- Diastolic dysfunction;⁶¹
- Preoperative 6 min walk test;⁶²
- Hypoalbuminemia and poor nutritional status;⁶³
- Anaemia;⁶⁴
- Morbid obesity;⁶⁵
- Right ventricular dysfunction.

To date, the role of perioperative medical therapy has not been included or evaluated in scores dedicated to VHD. Preliminary evidence from non-randomized studies suggests that perioperative statin therapy may reduce the mortality of valve surgery.⁶⁶ Similarly, the potential benefits of stabilizing patients with medical therapy to treat heart failure and optimize loading conditions prior to intervention have not been formally studied.

Working group recommendations

Currently available risk scores should not be used as an isolated decision tool but as part of an integrated approach, which includes complete clinical evaluation, reference to local resources and surgical results, and the preferences of the patient and their family. Risk scores are not a substitute for clinical experience in the management of patients with VHD.

Limitations of current risk scores highlight the need for their improvement. The following proposals should be actively considered by professional groups involved in the management of patients with VHD:

- A simple, reliable, and reproducible score based on a limited number of variables is desirable.
- Variables specifically related to VHD should be considered.
- A multicentre international approach including patients with a broad spectrum of operative risk is mandatory for evaluation and validation.
- The score should be validated in both high- and low-volume centres.
- The score should be updated on a regular basis.⁶⁷
- Risk scores are particularly needed for decision-making in high-risk patients. We recommend the development of specific

scores generated and validated in large data sets of high-risk patients.

- Objective assessment of cognitive and functional capacity and indices of frailty should be evaluated.^{57,58}
- Risk scores should focus on the estimation of 30-day mortality following surgery. The development of scores aiming to predict morbidity may also be considered, but they should be based on standardized definitions of endpoints, such as the VARC criteria.¹ Specific risk evaluation models should be developed to predict outcomes after transcatheter aortic valve implantation (and other percutaneous valve procedures). Current surgical risk scores are inadequate and inappropriate in this setting.⁶⁸ Direct comparison of predicted mortalities for conventional surgery and transcatheter techniques may help determine the most appropriate treatment strategy for any individual patient.
- Risk scores should focus on operative mortality (in-hospital, or preferably 30-day mortality).

Acknowledgements

We are grateful to Dr Gaieta Permanyer-Miralda for his expert review of this manuscript.

Appendix: Links to Online Calculators for the EuroSCORE, STS score and Ambler score

EuroSCORE: <http://www.euroscore.org/calc.html>; STS score: <http://209.220.160.181/STSWebRiskCalc261/>; Ambler score: <http://www.ucl.ac.uk/stats/research/riskmodel/>.

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