A validated simple model to predict coexistent coronary disease in patients undergoing mitral valve surgery

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Objective: The primary limitation of the American Heart Association/American College of Cardiology guidelines is specificity. To improve the selection process, we proposed a simple additive model including age (1 point for every 5 years above 50), male sex (2 points), hypercholesterolemia (2 points), angina (3 points), and electrocardiographic evidence of ischemia (3 points). We recommend screening angiography at 3 or more points. This model was previously derived from 359 patients at Papworth Hospital.

Methods: The validation cohort was a consecutive series of patients who underwent mitral valve surgery at the Royal Brompton Hospital. Preoperative coronary angiography reports were obtained, and coronary disease was defined as luminal narrowing of 50% in 2 or more views. Sensitivities and specificities were calculated for the American Heart Association/American College of Cardiology criteria, the simple additive model, and a logistic regression model. Receiver operating characteristic curves were used to validate accuracy and compare discrimination with logistic regression.

Results: From 1998 through 2003, angiographic details were available for 342 (86%) of 396 patients who underwent mitral valve surgery. The sensitivity and specificity of the American Heart Association/American College of Cardiology guidelines were 100% and 5%, respectively; those of the simple additive model were 91% and 44%, respectively; and those of logistic regression were 93% and 41%, respectively. The receiver operating characteristic areas for the simple additive and logistic regression model were 0.78 (95% confidence interval, 0.73-0.84) and 0.80 (95% confidence interval, 0.74-0.85), respectively.

Conclusions: This is the third independent cohort to highlight the poor specificity of the American Heart Association/American College of Cardiology guidelines. Although high sensitivity is achieved, the cost is the majority of patients requiring screening angiography. Our validated simple model improved the specificity and selection; however, this was achieved at the expense of decreased sensitivity.

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Screening for coexistent coronary disease remains an important aspect of the assessment of patients before mitral valve surgery. Coronary and mitral valve disease are inextricably linked as a causative agent for mitral valve disease (eg, ischemic mitral regurgitation), a coexistent agent that modifies operative strategy (eg, concomitant coronary disease in patients with degenerative mitral valve disease), and an adverse prognostic predictor of survival.¹

The primary limitation of the widely used American Heart Association/American College of Cardiology (AHA/ACC) guidelines² is specificity (previously estimated at 1%).³ The inability to accurately rule in coexistent coronary disease (the selection

TABLE 1. Baseline characteristics*

Sample size	342
Mean (SD) age, y	65 (11)
Male sex	194 (57)
Diabetes	6 (2)
Hypercholesterolemia	51 (15)
Smoker	125 (37)
Family history of IHD	34 (10)
Angina	7 (2)
Previous myocardial infarction, n (%)	8 (2)
ECG evidence of ischemia	5 (1)
NYHA class III-IV	199 (58)
Cause of mitral valve disease	
Degenerative	226 (66)
Rheumatic	64 (19)
Ischemic	18 (5)
Endocarditis	10 (3)
Other†	22 (7)
Mitral valve repair	182 (61)
Mitral valve replacement	114 (39)
Any coronary disease	82 (24)
Concomitant coronary bypass surgery	69 (20)

IHD, Ischemic heart disease; ECG, electrocardiography; NYHA, New York Heart Association. *All data except age are presented as numbers (percentages). †Other includes revision operations and congenital mitral valve disease.

process) leads to almost universal recommendation for preoperative screening angiography.

A number of proposals have been made to improve selection criteria and increase the discriminatory ability achieved with sophisticated statistical models.⁴ Although mathematically accurate, they are difficult to implement at the bedside or consulting room. In 2003, we proposed a simple additive model derived from a cohort of patients in Cambridge, with the following 5 variables: age (1 point for every 5 years above 50), male sex (2 points), hypercholesterolemia (2 points), angina (3 points), and electrocardiographic evidence of ischemia (3 points). We recommend screening angiography at 3 or more points.

The aim of this study was to validate and assess the discriminatory value of our simple additive model on a different cohort of patients who underwent mitral valve surgery at the Royal Brompton Hospital in London, United Kingdom.

Methods

The validation cohort was identified from a database of a consecutive series of patients who underwent mitral valve surgery from 1998 through 2003 at the Royal Brompton Hospital in a 3-surgeon series (J.P., A.D.S., and N.M.). Reports from preoperative screening coronary angiography were obtained from patients listed for elective mitral valve surgery. Experienced cardiologists had reviewed the coronary angiograms, and the degree of luminal nar-

TABLE 2. Sensitivity and specificity of AHA/ACC criteria, the simple additive model, and full logistic regression (Lin and colleagues⁴)

	Sensitivity (95% CI)	Specificity (95% CI)
AHA/ACC criteria	100% (100.0-100.0)	5% (2.9-7.6)
Simple additive model	91% (88.5-94.4)	44% (39.2-49.6)
Full logistic regression	93% (90.0-95.4)	41% (35.9-46.2)

AHA/ACC, American Heart Association/American College of Cardiology.

rowing was obtained by means of visual estimation. The presence of significant coronary disease was defined as luminal narrowing of 50% in 2 or more views.

Risk factors for coronary artery disease were defined as follows: age (≥ 35 years for men and ≥ 51 years for women), family history (first-degree relative with a myocardial infarction before the age of 50 years in men and 60 years in women), smoking, diabetes, and hypercholesterolemia (defined as receiving medication for hypercholesterolemia or serum cholesterol of ≥ 5.0 mmol/L [193 mg/dL]). Evaluated AHA/ACC indications were a history of angina or myocardial infarction or the presence of one or more risk factors for coronary artery disease. The presence of ischemic changes on echocardiography was defined as any resting ST-segment or T-wave abnormality. The cause of mitral regurgitation was determined by means of operative assessment in conjunction with histopathologic examination of valve specimens.

Statistical methodology for the development of our simple additive model (from logistic regression analysis) has been previously described.³ Sensitivities and specificities were calculated for the AHA/ACC criteria, our simple additive model, and a logistic regression model. Receiver operating characteristic (ROC) curves were used to validate the accuracy of our simple additive model and also to compare the discrimination of our model with that of a full logistic regression model derived by Lin and colleagues⁴ from the Cleveland Clinic (both models are detailed in the Appendix).

Results

From January 1, 1998, to January 1, 2003, a total of 396 patients underwent mitral valve surgery. Angiographic de-

TABLE 3. Utility of the different models to predict coexistent coronary disease

	No. (%) not requiring angiography	No. (%) of missed coronary disease*
AHA/ACC criteria	12 (3.5)	0 (0)
Simple additive model	123 (36.0)	7 (2.0)
Logistic regression	113 (33.0)	6 (1.8)

AHA/ACC, American Heart Association/American College of Cardiology.

*The percentages of missed coronary disease are expressed as a total of the cohort and not as a proportion of patients who did not require angiography because the aim is to evaluate the effect of the population-based approach on unselected patients.

Figure 1. ROC curves of the simple additive and logistic regression models.

tails were unavailable for 54 (14%) patients, 41 with and 13 without AHA/ACC-defined indications, leaving 342 patients. The validation cohort had a mean (SD) age of 65 (11) years, and a total of 182 (61%) had mitral valve repair, and 114 (39%) had mitral valve replacement (Table 1).

The sensitivities and specificities of the AHA/ACC guidelines were 100% and 5%, respectively; those of the simple additive model were 91% and 44%, respectively; and those of the logistic regression model were 93% and 41%, respectively (Tables 2 and 3).

The area under the ROC curves for the simple additive and logistic regression models were 0.78 (95% confidence interval [CI], 0.73-0.84) and 0.80 (95% CI, 0.74-0.85), respectively (Figure 1).

Discussion

This is now the third study (in 3 independent patient populations) that highlight the limitations of the AHA/ACC selection criteria for recommendations of preoperative screening angiography in patients before mitral valve surgery.^{3,4} The intrinsic problem lies in specificities that ranged from 1% to 5%, the latter achieved in this study. Our results demonstrate that it is possible to increase the specificity of the screening guidelines to 44% with more sophisticated statistical modeling. The results from our simple additive model, derived from logistic regression analysis and designed to be able to be used at the bedside without the requirement of a calculator, were comparable with prediction with full logistic regression analysis.

Optimum patient selection is the main drive to improve the criteria for screening coronary angiography, a procedure that carries a 1.7% risk of major complication, including a 0.11% risk of death, a 0.05% risk of myocardial infarction, and a 0.07% risk of stroke.⁵ Although the absolute risk increment itself might seem low, the low specificity of current AHA/ACC screening guidelines results in the vast majority of patients meeting the criteria. Therefore substantial mortality and morbidity might be experienced on a population basis when large numbers are exposed to these “low” risks.

The effect on cost-benefit analysis with improved selection has been considered previously by Lin and colleagues.⁴ Before consideration of finances, we would be more concerned in determining the effect of missing patients with potentially treatable coronary disease, and there is (not surprisingly) little in the literature to help guide this decision-making process. It is conceivable that a potential range of outcomes would include neither harm nor postoperative angina (no flow-limiting disease), residual postoperative angina, or inability to wean from cardiopulmonary bypass after surgical intervention, resulting in death. What price could possibly be attached to the (as yet unquantifiable) risk of death as a result of missing patients with potentially treatable coronary disease?

Where Is the Balance?

As we attempt to improve the specificity of the current AHA/ACC guidelines (to reduce the morbidity of patients undergoing unnecessary coronary angiography), we will inevitably reduce the sensitivity of the selection process (miss patients with potentially treatable coronary disease).³ This is due to the statistical properties of the relationship between sensitivity and specificity; as one increases, the other decreases, and vice versa.⁶

The guidelines of the AHA/ACC do not miss any patients with coexistent coronary disease (100% sensitivity), but this is achieved by almost universal recommendations for screening angiography (low specificity) and unnecessarily exposing patients to the risks of coronary angiography; as such, achieving the balance in this situation is extremely difficult. If the aim is not to miss any patients with coexistent coronary disease, then the AHA/ACC guidelines are successful in this regard. However, similar results can also be achieved by using age over 35 years alone as the sole indication (sensitivity, 100% [95% CI, 100.0%-100.0%]; specificity, 0.38% [95% CI, 0.0%-1.0%]), and detailed guidelines might not be required.

A similar but extreme counterargument, for example, would be to increase the specificity by performing angiography only on patients with a history of myocardial infarction, where the sensitivity would be close to 100% (allowing for misdiagnosis of myocardial infarction). However, this

would be undertaken with unacceptable loss to sensitivity (missing patients with coronary disease).

Therefore the balance does not rely on a test that would favor individual sensitivity or specificity but rather an approach that takes the balance of both into account. The crux of the argument lies in the individual surgeon’s opinion of the (unquantifiable) risks of untreated coronary disease weighted against the (known) risks of morality, morbidity, and cost associated with screening angiography in the majority (76% in this series) of patients who undergo mitral valve surgery without coexistent coronary disease.

Potential Limitations

In this study we have used the model of Lin and colleagues⁴ on an unselected cohort undergoing mitral valve surgery; its design and use was in patients with degenerative disease. However, when applied solely to the patients with degenerative disease in our cohort, the discriminating ability was similar (area under the ROC curve, 0.79 [95% CI, 0.71-0.87]).

Of the 7 patients without indications in the simple model for coronary angiography, 4 had single-vessel and 3 had double-vessel disease. Of the 6 patients without indications in the logistic regression model, 4 had single-vessel, 1 had double-vessel, and 1 had triple-vessel disease. It is important to note, however, that neither statistical model takes into account disease severity but merely the presence of significant coronary disease.

Conclusion

The high sensitivity of the AHA/ACC guidelines for screening angiography to detect coexistent coronary disease in patients before mitral valve surgery is achieved at a cost of poor specificity and results in the majority of patients requiring screening angiography. Our validated simple model has the discriminating ability of a more complex logistic regression model with the advantage of being easily implemented at the bedside and improved specificity over the AHA/ACC recommendations. This (and usually in other statistical models) is achieved by sacrificing sensitivity and carries the risk of missing patients with coexistent coronary disease.

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Appendix. Criteria for the simple additive and logistic regression model

Appendix TABLE 1. Simple additive model³

Variable	Score
Age	1 point for each 5 years over the age of 50 years
Male sex	2 points
Hypercholesterolemia	2 points
Angina	3 points
ECG evidence of ischemia	3 points
Angiography is recommended for a score of 3 or more. ECG, Electrocardiography.	

Appendix TABLE 2. Logistic regression model of Lin et al⁴

Model score (Ln OR) = (0.105 × Age) + (1.177 × Male sex) + (1.475 × Diabetes mellitus) + (1.750 × Hyperlipidemia) + (0.483 × Hypertension) – 10.070
Angiography is recommended for a risk of greater than 5% (model score of more than –2.95).

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