Validation of three myocardial jeopardy scores in a population-based cardiac catheterization cohort

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Background The Jeopardy Score from Duke University and the Myocardial Jeopardy Index from the Bypass Angioplasty Revascularization Investigation (BARI) have been validated but never applied to a large unselected cohort. We assessed the prognostic value of these existing jeopardy scores, along with that of a new Lesion Score developed for the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH), a clinical data collection initiative capturing all patients undergoing cardiac catheterization in the province of Alberta.

Methods The predictive value of these three scores were compared in a cohort of >20,000 patients (9922 treated medically, 6334 treated with percutaneous intervention, and 3811 treated with bypass surgery). Scores were considered individually in logistic regression models for their ability to predict outcome and then added to models containing sociodemographic data, comorbidities, ejection fraction, indication for procedure, and descriptors of coronary anatomy.

Results All scores were found to be predictive of 1-year mortality, especially when patients are treated medically or with percutaneous intervention. In these patients, the APPROACH Lesion Score performed slightly better than the other jeopardy scores. The Duke Jeopardy Score was most predictive in those patients undergoing coronary bypass surgery.

Conclusions Myocardial jeopardy scores provide independent prognostic information for patients with ischemic heart disease, especially if those patients are treated medically or with percutaneous intervention. These scores represent potentially valuable tools in cardiovascular outcome studies. The APPROACH Lesion Score may perform slightly better than previously developed jeopardy scores. (Am Heart J 2001;142:254-61.)
eral vascular disease, chronic pulmonary disease, elevated creatinine level, renal dialysis, hyperlipidemia, hypertension, liver disease, gastrointestinal disease, or malignancy. The database also tracks therapeutic interventions such as previous thrombolytic therapy and revascularization by coronary artery bypass graft surgery (CABG) or PCI. Coronary anatomy is stored as a computerized data template (Heartview, HeartWare, Durham, NC), a copy of which becomes part of the patient medical record. Mortality is ascertained through semiannual linkage to Alberta Bureau of Vital Statistics records. After exclusion of those patients undergoing catheterization for valvular heart disease and those patients with previous bypass surgery, 1-year follow-up information was available for a total of 20,067 patients who underwent cardiac catheterization from January 1, 1995, to December 31, 1998. For patients undergoing more than one catheterization during this time period, only the first was considered for this analysis of jeopardy scores.

Computer algorithms were developed to calculate the jeopardy scores as follows.

**Duke Jeopardy Score**

The Duke Jeopardy Score was developed by Dash et al and validated by Califf et al. The coronary tree is divided into 6 segments: the left anterior descending coronary artery (LAD), diagonal branches of the LAD, septal perforating branches, the circumflex coronary artery, obtuse marginal branches, and the posterior descending coronary artery (PDA). All segments distal to ≥70% stenosis are considered to be at risk. Each such segment is assigned 2 points. The maximum possible number of points is 12.

**Myocardial Jeopardy Index (BARI)**

Myocardial jeopardy was calculated from an anatomic representation of the size and distribution of the coronary arteries. Distal terminating portions of the LAD, circumflex coronary, artery, and right coronary (RCA) arteries are assigned units of 1, 2, or 3 on the basis of length and size. Major branch vessels—diagonals, obtuse marginals, ramus, posterior descending, and left ventricular branches—were sized in a similar fashion. Septal perforators are arbitrarily assigned a maximum of 3 units. Units jeopardized by ≥50% stenosis are summed and divided by total left ventricular territory units to define the extent of jeopardy.

**APPROACH Lesion Score**

This score is based on a scoring system developed at the Green Lane Hospital, with modifications from pathologic data as reported by Kalbfleisch and Hort and Lee et al. These autopsy studies suggested that the LAD generally subtends 41% of the left ventricle, with the circumflex and RCA supplying the remainder, to different degrees depending on vessel dominance. To calculate the APPROACH Lesion Score, the left ventricle is divided into regions according to the percentage of myocardium supplied by a vessel or its branches (see Appendix). Jeopardized territories are those supplied by vessels with ≥70% stenoses (>50% stenosis of the left main coronary artery). All jeopardized territories are summed for a maximum score of 100.

**Statistical analysis**

Logistic regression models were used to assess the associations between jeopardy scores and mortality at 1 year. Logistic regression assumes that the log(odds) of the outcome is linear in the independent variables. To test this, the BARI and APPROACH scores were broken into intervals with a width of 10 points. Within each interval, the proportion of cases dying within 1 year was transformed by taking the natural logarithm of the odds corresponding to this proportion. This transformation was also used for the proportion dying in the 7 levels of the Duke score. Plotting these log(odds) against their corresponding levels or intervals assessed linearity.

The jeopardy scores were assessed for their individual ability to predict outcome. They were also assessed for their ability to increase the predictive power of a baseline risk model that included sociodemographic variables, comorbidity information, indication for procedure, ejection fraction, and traditional descriptions of coronary anatomy. Patients were analyzed in treatment groups according to first treatment received within 1 year of the index catheterization. Each score was examined separately for each initial treatment strategy (CABG, PCI, and medical therapy). The C statistic (equal to the area under the receiver operating characteristic [ROC] curve) and the drop in deviance accounted for by the measures were used to assess the importance of each jeopardy score as a predictor of outcome. For an individual score, the drop in deviance is the decrease in the residual deviance from the null model that occurs when the score is placed in the model. Improvements over the baseline model were assessed with use of the drop in residual deviance associated with the addition of the variable to the baseline model. Drops in deviance were tested for significance with a χ² distribution with 1 degree of freedom. (All statistics were performed with SAS for Windows, version 7, SAS Institute, Cary, NC).

**Results**

The 3 jeopardy scores were calculated for each of the 20,067 patients. Patients were grouped according to the initial treatment strategy: medical therapy in 9922 patients, percutaneous intervention in 6334 patients, and bypass surgery in 3811 patients. Table I illustrates the baseline characteristics of each treatment subset and for the overall group. Differences among the treatment groups for the categorical baseline variables and for death at 1 year were tested with χ² tests of independence. Differences among the mean ages of the treatment groups were tested with a 1-way analysis of variance. With the exception of dialysis dependence (P < .001), liver disease (P = .716), and malignancy (P = .146), all tests were significant at P < .0001. Table II shows the distribution of jeopardy scores in the 3 treatment groups. Scores tended to be higher in those patients undergoing CABG, midrange in those treated with percutaneous intervention, and lowest in those receiving medical therapy.

Figure 1 relates 1-year mortality to jeopardy score. For each of the jeopardy scores mortality tended to rise with incremental increases in myocardial jeopardy.
Figure 2 shows the linear fit of the logistic regression for each of the 3 scores according to initial therapy. The APPROACH Lesion Score appears to be clustered closer to the line than either the Duke Jeopardy Score or the BARI Jeopardy Index for both the PCI and medical treatment groups.

Table III presents the C statistics and changes in deviance for each jeopardy score in each of the 3 treatment cohorts. When modeled alone as a predictor of mortality, each of the jeopardy scores was a significant predictor of outcome, particularly in patients treated medically (Duke Jeopardy Score $C = 0.740$, BARI Jeopardy Index $C = 0.745$, and APPROACH Lesion Score $C = 0.744$) or with PCI (Duke Jeopardy Score $C = 0.674$, BARI Jeopardy Index $C = 0.699$, and APPROACH Lesion Score $C = 0.708$). In these patients the APPROACH Lesion Score, which also demonstrates larger deviance drops, has the best predictive value. However, in patients treated with bypass surgery, the Duke Jeopardy Score appears to be more predictive of mortality (Duke Jeopardy Score $C = 0.611$, BARI Jeopardy Index $C = 0.601$, and APPROACH Lesion Score $C = 0.598$). When the scores are added to a baseline model that included traditional descriptors of coronary anatomy and other variables listed in Table I, there were modest improvements in the C statistics and significant drops in deviance, particularly for the APPROACH Lesion Score. For CABG patients, the Duke Jeopardy Score is again most predictive.

Prerevascularization and postrevascularization scores were assessed in 6256 patients undergoing PCI. The remaining 78 patients treated with PCI did not have computerized descriptions of anatomy available both before and after the procedure. To investigate improvements in prediction associated with postrevascularization scores, they were added to baseline models including prerevascularization scores. Addition of the postrevascularization scores did not improve the C statistics.
and resulted in small decreases in deviance (Duke Jeopardy Score 2.34, BARI Jeopardy Index 1.89, APPROACH Lesion Score 0.45). This would indicate that outcome in patients undergoing angioplasty is determined more by the preintervention score.

**Discussion**

Compared with simple considerations of the number of diseased vessels, the calculation of jeopardy scores allows for the variability in importance of each of the 3 major coronary arteries in individual patients. The Duke Jeopardy Score and BARI Myocardial Jeopardy Index are very different from each other. The Duke Jeopardy Score is, arguably, the simplest score available and is therefore easy to use clinically. Despite its simplicity, it has been reported to provide significant prognostic information in a group of 462 patients.7 The current study confirms its value in a cohort of >20,000 patients.

The BARI Myocardial Jeopardy Index is significantly more complex because it seeks to calculate the amount of myocardium supplied by stenotic vessels. Of interest, it describes significance to vessels with >50% stenosis.16 Although this does not follow classical clinical teaching, it does allow for the potential for moderately diseased vessels, which are prone to disease progression,16 to have an impact on survival during long-term follow-up.

The APPROACH Lesion Score is based on pathologic studies evaluating the relative proportion of myocardium perfused by each coronary artery. For this score,
with a significant stenosis and may represent a more physiologic assessment of degree of risk. Despite the differences among these 3 scores, it is apparent that each is capable of providing prognostic information over and above that available from simple descriptions of coronary anatomy. This benefit persists after the inclusion of traditional risk factors in the outcome model. For patients who are treated medically and for patients who undergo percutaneous intervention, the Myocardial Jeopardy Index and the APPROACH Lesion Score best predict survival. This advantage is likely the result of considering the amount of myocardium supplied by a diseased artery and its major branches.

The BARI group reported a series of 270 patients who underwent protocol-driven angiography at 1 year after revascularization. The Myocardial Jeopardy Index was significantly decreased by either form of revascularization but to a greater extent by CABG. The presence of angina at 1 year was predicted by the degree of residual myocardial jeopardy, and there was a nonsignificant trend toward increased mortality with each increment of myocardial jeopardy. However, in the current large study population, none of the scores fared as well for patients treated with CABG as they did for patients undergoing percutaneous intervention or for patients treated medically. This may reflect the failure of each of the scores to include the extent of distal disease and size of the distal vessel. Of course, these are very important determinants of the ability of the surgeon to successfully complete a distal anastomosis. In addition, successful CABG completely restructures anatomy. Thereafter, assessments of degree of myocardium supplied by a native coronary may no longer be of critical importance.

In the current analysis postprocedure jeopardy scores provided additional prognostic information in those patients undergoing PCI. However, the contribution of these postintervention data to model prediction was less than that of preprocedure jeopardy scores. This highlights the considerable prognostic importance of baseline coronary anatomy (and specifically myocardial jeopardy) regardless of modifications in jeopardy score achieved through percutaneous intervention.

One limitation of this study was that it focused only on mortality at 1 year as the outcome for validating these jeopardy scores. A second limitation, more of the jeopardy scoring systems than of study design, is that the volumes of myocardium at risk estimated by these jeopardy scores are derived for a “typical” heart. Although variations in coronary anatomy, including vessel dominance or the presence of collaterals, are dealt with by convention in each score, the results are still only approximations of true jeopardy.

A third notable limitation is that there is potential for interobserver variability in physicians’ semiquantitative assessments of angiographic data. This potential problem is at least partially ameliorated by the fact that we
use a software package (HeartView) that provides standardized definitions and instructions for documenting the extent of coronary disease. However, we acknowledge that the use of explicit definitions in such a software package does not guarantee the validity and reliability of physicians' documentation of extent of coronary disease. To date, we have not performed an extensive validation study in APPROACH to assess the validity of quantitative information on extent of lesion stenosis. However, we did conduct a small validation study on APPROACH data from 1997 in which we used quantitative coronary angiography (QCA) to determine the accuracy of physicians' visual estimates of extent of stenosis in a small series of 90 lesions. In patients treated medically, the mean of physicians' estimates was 54.7%, whereas the mean stenosis estimated by QCA was 45.0%. In patients treated with PCI or bypass surgery for other significant lesions, the mean of physicians' estimates was 65.3% versus 60.7% for QCA. These findings suggest that physician estimates of lesion stenosis are reasonably accurate reflections of objectively derived estimates of stenosis.

It is also important to note that none of the 3 jeopardy scores described here consider minor “nonsignificant” proximal plaques that contribute to the overall degree of atherosclerosis. The progression of such plaques may have a significant impact over time, especially in diabetic patients. Diffuseness of disease is perhaps partially addressed by the BARI Jeopardy Index, which uses a >50% definition for significant lesions, but new tools need to be developed for better quantification of “nonsignificant” lesions in both proximal and distal locations. Existing measures of distal coronary disease have been considered subjective and prone to interobserver bias. Two studies have attempted to include a measure of distal disease status.

Figure 2

Plots of the logarithm of the odds of death associated with the jeopardy scores.
in models designed specifically for prediction of risk in bypass patients. One of these scored diffuse distal coronary disease as present if mentioned in the patient’s chart20 and the other if endarterectomy was planned as part of the procedure.21 Neither of these studies used an objective measure based on angiographic findings. A third model, using a quantitative approach,22 was not evaluated in this study because the system is not compatible with the HeartView software. An effective, reproducible, and easily applied index of diffuseness is still required.

In summary, the results of this study have validated 3 different jeopardy scores in a large population-based cohort of patients with ischemic heart disease. These scores represent potentially valuable tools for characterizing severity of illness in cardiovascular outcome studies. Myocardial jeopardy scores provide independent prognostic information, especially for patients who are treated medically or with percutaneous intervention. The APPROACH Lesion Score may perform slightly better than previously developed jeopardy scores.

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Figure 3

Weighting factors for myocardial regions for the APPROACH Lesion Score. RV, Right ventricle.
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Appendix

The APPROACH Lesion Score

The left ventricle is divided into regions according to the percentage of myocardium supplied by a vessel or its branches (Figure 3). Lesions in the proximal LAD jeopardize all the LAD septum, the LAD anterolateral region, and the anterolateral region supplied by diagonal branches. In addition, the apical contribution of a normal or large sized (type II or III) LAD is also compromised. A lesion in the mid-LAD jeopardizes two thirds of these regions. Distal LAD lesions similarly jeopardize one third of these territories.

A lesion in the proximal circumflex artery would jeopardize all regions supplied by the marginal, posterolateral, and PDA branches of the circumflex. A lesion in the mid-circumflex affects the regions supplied by the second marginal branch and all distal branches. Distal lesions jeopardize circumflex posterolateral branches in a codominant system and all distal posterolateral branches as well as the PDA distribution in a left dominant system.

All significant lesions in the RCA are deemed to jeopardize all regions supplied by the PDA and the posterolateral branches of the RCA. The PDA supplies a portion of the basol septum and 25% of the posterolateral free wall. A small PDA supplies one third of these territories, a normal-sized vessel two thirds, and a large vessel the entire territory.

Free wall branches (diagonals, ramus, obtuse marginals, posterolaterals) are given a size designation (small, normal, large) on the basis of an estimate of amount of myocardium supplied. Small vessels receive 1 point, normal vessels 2 points, and large vessels 3 points. The assumption is made that 25% of each free wall region is supplied by small branches and cannot be claimed in vessel size designations. Small vessels supply 25% of their free wall region, normal vessels 50%, and large branches 75%. In addition, there is a maximum of 9 possible points assigned to the entire free wall region. If the point value of one region exceeds 3, the total point value of another region must be reduced accordingly.
Inhibition by combined therapy with ticlopidine and aspirin of enhanced platelet aggregation during physical exercise in patients with coronary artery disease

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Background Strenuous exercise can be a major trigger for coronary thrombosis and it enhances platelet aggregation.

Methods We evaluated the effect of antiplatelet therapy on shear stress–induced platelet aggregation (SIPA), in addition to agonist-induced aggregation, before and immediately after ergometer exercise in patients with stable coronary artery diseases (CAD). Forty-eight patients with stable CAD were randomly distributed into 3 groups: no antiplatelet drug (patient control, n = 16), aspirin (ASA) monotherapy (n = 16), and combined therapy with ticlopidine (TIC) and ASA (n = 16).

Results There were significant increases in not only adenosine phosphate (ADP)- and collagen-induced platelet aggregation but also in SIPA during exercise by the patient control group. ASA monotherapy did not attenuate the enhanced ADP-induced aggregation nor SIPA. Combined ASA + TIC therapy significantly inhibited SIPA as well as ADP-induced aggregation both before and after exercise. Significant increases in levels of plasma von Willebrand factor (vWF) occurred during exercise, and these antiplatelet therapies had no apparent effect on increased vWF levels during exercise. Exercise induced a significant increase in the plasma thrombin-antithrombin III complex level with no significant changes in the level of plasmin-plasmin inhibitor complex level in all 3 groups.

Conclusions Combined therapy with ASA + TIC effectively inhibited increased platelet aggregability in response to acute exercise, with no effects on coagulant or fibrinolytic potentials in patients with CAD. The data suggest that TIC combined with ASA may be superior to ASA alone in preventing acute coronary events during exercise in patients with coronary atherosclerotic disease. (Am Heart J 2001; 142:e1.)

Secondary Prevention and Rehabilitation

The effect of pravastatin and atorvastatin on coenzyme Q10

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Background Coenzyme Q10 (CoQ10) is an antioxidant and plays an important role in the synthesis of adenosine triphosphate. Studies suggest that 3-hydroxy-3-methylglutaryl–coenzyme A (HMG-CoA) reductase inhibitors reduce CoQ10 levels; however, no studies have directly compared HMG-CoA reductase inhibitors in a randomized crossover fashion.

Methods Twelve healthy volunteers received either 20 mg pravastatin [P] or 10 mg atorvastatin [A] for 4 weeks in a randomized crossover fashion. There was a 4- to 8-week washout period between the 2 phases. CoQ10 levels and a lipid profile were obtained.

Results There was no difference in CoQ10 levels from baseline to post–drug therapy for either P or A [0.61 ± 0.14 vs 0.6 ± 0.12 mg/mL, respectively; P > .05]. There was a significant difference in low-density lipoprotein (LDL) levels from baseline to post–drug therapy for both P and A (97 ± 21 vs 66 ± 19 mg/dL and 102 ± 21 vs 52 ± 14 mg/dL, respectively; P < .01). There was no significant correlation between LDL and CoQ10.

Conclusions P and A did not decrease CoQ10 despite a significant decrease in LDL levels. These findings suggest that HMG-CoA reductase inhibitors do not significantly decrease the synthesis of circulating CoQ10 in healthy subjects. Routine supplementation of CoQ10 may not be necessary when HMG-CoA reductase inhibitor therapy is administered. (Am Heart J 2001; 142:e2.)

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