

ABC Stenosis Morphology Classification and Outcome of Coronary Angioplasty

Reassessment With Computing Techniques

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Background—The American College of Cardiology/American Heart Association (ACC/AHA) stenosis morphology classification (MC) stratifies coronary lesions for probability of success and complications after coronary angioplasty (PTCA). Modern computing techniques were used to evaluate the individual predictive value of MC in random PTCA cases.

Methods and Results—MC was attributed to the target lesions by consensus of 2 observers. The predictive value regarding procedural success (PS) and major adverse cardiac events (MACE) of MC was analyzed by conventional logistic regression analyses and by inductive machine learning models. The study was adequately powered for the methods applied with 325 target lesions of 250 cases. Overall, PS decreased and MACE increased from type A to type C lesions. Regression analysis identified no single factor as predictive. Logistic regression showed an error rate of 42%. Machine learning techniques achieved an individual predictive error of only 10%, which could be further reduced to 2% by addition of parameters. For PS, MC parameters showed a high ranking for building the model. For MACE, variables of the medical history showed more impact.

Conclusions—MC per se cannot individually predict PS or MACE. However, when all MC parameters are integrated together with additional lesion-specific and history variables, a high individual predictive value can be achieved. This technique may be clinically helpful for risk stratification in the catheterization laboratory and improvement of classification systems in interventional cardiology. (*Circulation*. 2001;103:1225-1231.)

Key Words: angioplasty ■ complications ■ computers ■ prognosis

Computer technology has facilitated the creation of algorithms that integrate the knowledge of a scientific discipline and use artificial intelligence to make decisions.¹ In interventional cardiology, the ABC stenosis morphology classification of the American College of Cardiology/American Heart Association (ACC/AHA) task force^{2,3} has been used for more than a decade as a clinical tool for predicting success and complications in coronary interventions.⁴⁻⁶ Recently, the progress of techniques has engendered higher overall success rates for all lesion types.⁷ In parallel, computing techniques for determination of associations between classifiers and procedural outcomes (ie, variables pertinent to success or failure) have been refined. There have been repeated propositions of modified predictive indices.⁸⁻¹⁰ Notwithstanding these advances, the original criteria for classification of the target lesions continue to be used widely.

Additionally, the issues of quality control and outcomes assessment have emerged to provide justification for the steadily growing expenditure for coronary interventions. In

this context, an international quality control study in interventional cardiology was designed in Europe.¹¹ Given the interventions of the late 1990s, the purpose of the present study was to assess the individual predictive value of the ABC criteria by conventional logistic regression analyses and decision-tree algorithms (see Appendix).¹ An extension of the data model (given by the availability of all study parameters to the decision-tree algorithms) might improve the predictive performance. We also analyzed whether specific parameters help predict the procedural result versus major adverse cardiac events (MACE) during the intervention-related hospital stay.

Methods

Case Selection

A total of 250 angioplasty cases randomly selected across Europe and audited on-site were subjected to an expert panel assessment. They form the basis of the AQUA (Audit and Quality control in

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Data: AHA Classification Assignment + Complete AQUA Data Pool

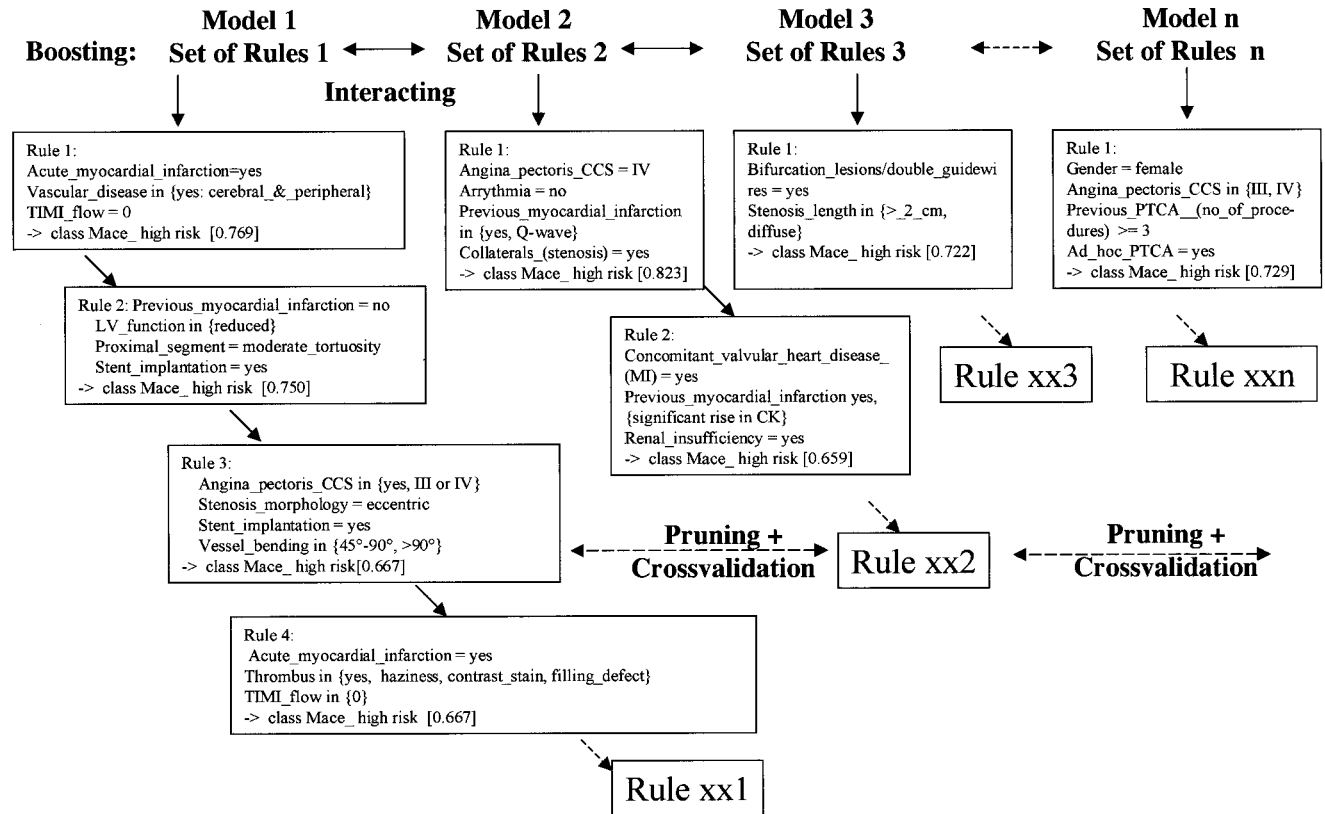


Figure 1. Schematic representation of machine-learning process with some exemplary rules and interaction of subtasks in algorithm. CCS indicates Canadian Cardiovascular Society; CK, creatine kinase.

Angioplasty) study.¹¹ This quality assurance program provides highly scrutinized data of real-life cases from multiple hospital types.

Stratified Sampling

The selection was performed according to the necessities of a stratified sampling technique. The sample should parallel the population with respect to certain key characteristics that are important to the respective investigation.¹²

Case Analysis

Case records and imaging material, including reports and image documentation from preceding hospital stays, were collected. A dedicated computer program (AQUA Intervent) was used to record pertinent data.¹¹ A total of 301 variables per case were available for electronic analysis. The majority rating of an expert panel determined the end-point procedural success (see below).

All imaging material was analyzed by 2 independent observers blinded to the clinical outcome. The ACC/AHA classification^{2,3} was attributed to the target lesions by a third consensus rating in case of disagreement. Each target lesion was systematically documented according to the classification table in the AQUA Intervent program. Caliper measurements were performed for angulation and length. As additional parameters, for each lesion, TIMI flow¹³ and the status of the lesion with regard to previous infarction were documented.

Definitions and End Points

The ACC/AHA ABC classification criteria were applied according to Ryan et al^{2,3} and Ellis et al.⁴ Flow was determined according to the TIMI study group.¹³ The additional parameter “vessel related to infarction” was attributed when the target lesion was part of an

infarcted vessel by any definition (previous, subacute, acute, or non-Q-wave infarction).

For assessment of the predictive value of the ACC/AHA ABC classification criteria, the following end points were considered: (1) procedural outcome; (2) MACE during the intervention-related hospital stay (death, myocardial infarction [MI], need for urgent bypass surgery [CABG], or hemodynamic compromise); and (3) extended MACE during the intervention-related hospital stay (death, MI, CABG, or hemodynamic compromise, plus the following out-of-laboratory complications: stable angina [Canadian Cardiovascular Society class II-IV], unstable angina, bleeding requiring transfusion or surgical intervention, cardiac arrest, cardiovascular collapse, recatheterization, reintervention, stent thrombosis, or abrupt closure).

Procedural success was defined by the expert panel as a residual diameter stenosis <50% by visual estimate. Visual estimate was chosen because this was a clinical quality control trial, and angiograms had been made without a quantitative coronary angiography protocol. The rationale for expert analysis was that even if quantitative coronary angiography had been performed, a <50% diameter stenosis at the end of the procedure alone would not completely fulfill the criteria of procedural success in the intended sense of the ACC/AHA criteria concept. Therefore, clinical expert judgment was implemented by setting the majority vote of the panel as reference.

MI was defined according to established criteria by clinical, ECG, or enzymatic changes.¹⁴ Non-Q-wave MIs were included if creatine kinase elevations $\geq 3\times$ the upper normal limit with positive cardiac isoenzymes were present. The study was not designed for assessment of minimal myocardial damage through serial enzyme assessments.

Hemodynamic compromise was defined as prolonged hemodynamic instability (systolic pressure <80 mm Hg, including pro-

TABLE 1. Baseline Patient Characteristics

Patients, n	250
Male, %	82
Stable AP, %	49
Unstable AP, %	32
Positive stress test, %	39
(Sub)acute MI, %	13
Previous MI, %	36
Previous PTCA, %	28
Previous CABG, %	12
Target lesions, n	325

AP indicates angina pectoris.

longed vasovagal reactions) and new pulmonary congestion or edema.

Machine Learning Techniques

Machine learning addresses the question of how to construct computer programs that automatically improve with experience (see Figure 1 and Appendix). It has proved to be of great practical value in a variety of application domains. Machine learning techniques are especially useful in (1) data-mining problems for which (large) databases may contain valuable regularities that can be discovered automatically (ie, to analyze outcomes of medical treatments from patient databases), (2) poorly understood domains where humans might lack the knowledge to develop effective algorithms, and (3) domains where the program must dynamically adapt to changing conditions.

The techniques used in this study for improving the predictive accuracy were “boosting”¹⁵ and “cost functions.” The Pearson χ^2 or likelihood-ratio tests were used for calculation of probability values. Accuracy was measured in connection with n-fold cross-validation (see Appendix).¹

Software and Hardware

Conventional statistics were computed with SAS (SAS Institute Inc). The decision-tree techniques were based on C4.5 (RuleQuest Research). The AQUA Intervent program was developed with Delphi.

Results

Patient Characteristics

The baseline characteristics of all patients are summarized in Table 1. Among the 250 patients included, 325 of 556 significant stenoses represented target lesions.

Descriptive Statistics: Distribution of Target Lesions and Complication Rates Versus Morphological Types

Figures 2 and 3 show the overall distribution of morphological types relative to target lesions and unsuccessful procedures or complications. The majority of target lesions (64%) were classified as B1/B2 lesions (Figure 2). The overall percentage of unsuccessful procedures and MACE increased from type A to type C lesions (Figure 3).

Morphological Classification and Device Use

Morphological classification did not predict device use. The overall stent rate per case was 54%. Other so-called new devices accounted for a negligible 3%. The distribution of morphology types among target lesions and stented lesions did not differ: A, target lesions 12%, stented lesions 14%; B1,

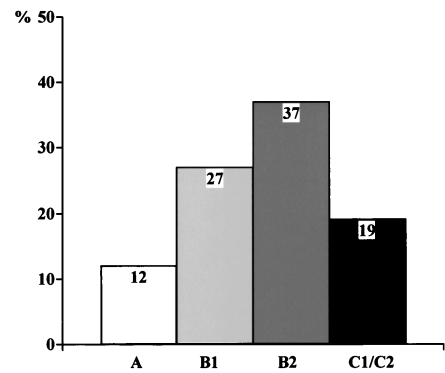


Figure 2. Percentage of morphological types among target lesions.

27% and 25%; B2, 37% and 36%; and C1/2, 19% and 19%, respectively.

Stenosis length was found to be relevant for stent placement only in connection with diffuse disease. Vessels related to infarction were found to be slightly preferred for stenting (target 35%, stented 39%). There was less stenting in bifurcation lesions (target 14%, stented 9%). Procedural success in bifurcation lesions was 100% with stenting and 89% with PTCA.

The only approved glycoprotein IIb/IIIa receptor antagonist (abciximab) represented an element of the extended database. It was used in 3% of patients.

Univariate and Multivariate Regression of Procedural Success Versus Morphological Classification

For univariate regression, no single factor enabled the satisfactory prediction of any end point. Multivariate regression showed an error rate of 42% (percentage of misclassified, 95% confidence).

Morphological Classification, Procedural Success, and MACE: Assessment With Machine Learning Techniques

Probability of Procedural Success Based on a Maximally Extended Data Model

Starting with all parameters, the decision-tree algorithm extracts the relevant ones. The training data are correctly

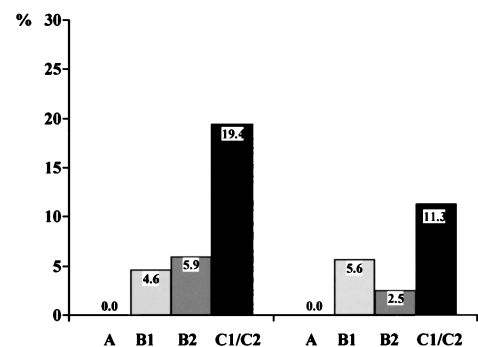


Figure 3. Morphological types and percentage of unsuccessful procedures (left) or major complications (death, need for CABG, MI, hemodynamic compromise) (right).

TABLE 2. Procedural Success: Model Building With All Available Data

Trial	Size	Decision Tree		Rules		
		Errors	Cost	No.	Errors	Cost
0	27	5 (1.6%)	0.04	11	7 (2.3%)	0.06
1	38	10 (3.3%)	0.11	17	6 (2.0%)	0.11
2	34	17 (5.6%)	0.18	17	19 (6.2%)	0.18
.....						
7	38	9 (2.9%)	0.63	14	8 (2.6%)	0.59
8	16	34 (11.1%)	0.81	5	23 (7.5%)	0.80
9	33	35 (11.4%)	0.93	16	18 (5.9%)	0.95
Boost		0 (0.0%)	0.00		0 (0.0%)	0.00
	(a)	(b)	← classified as			
	283		(a): class procedural success: yes			
		23	(b): class procedural success: no			

Size is the number of leaves in the decision tree and "No." is the number of rules of model n (n = 0→9); cost is the value of the cost function for a model. Procedural success is not calculated directly but via minimizing a cost function. In this case, the misclassification costs associated with each combination of real class and predicted class were predefined to yield a 5× higher "cost" in case of misclassification of an unsuccessful procedure as successful, compared with the converse condition, ie, misclassification of a successful procedure as unsuccessful.

Extended model based on availability of AHA/ACC criteria and all collected data items. The trained model gives a 100% correct classification.

classified. Table 2 shows the error rates of the 10 different models generated in connection with boosting and the overall error rate when a case is analyzed simultaneously by application of these 10 different models (error rate of the various models: minimum 2%, maximum 8% on trained data). A 10-fold cross-validation gives an overall error rate of 10%; each time, a different partitioning of the data into a training set (90% of the data) and a validation set (the remaining 10% of the data) is used. Figure 1 shows a flow chart representing the machine learning process with some exemplary rules and the interaction of the subtasks in the algorithm.

Machine learning techniques generate a ranking of criteria for procedural success, shown in Table 3 (the subgroups represent parameters of the same level of importance, whereas the subgroups themselves are ordered in decreasing importance). For instance, vessel bending is less important than calcification, and calcification is less important than several stenoses per segment or total occlusion.

Procedural success is primarily defined by the classic ABC criteria and the additional parameters of left ventricular (LV) function, TIMI flow, vessel related to infarction, and the procedure (PTCA or stenting) itself. The most important parameter is stenting (yes or no). Depending on this decision, 2 different trees for procedural success are obtained. For example, stented patients showing the characteristic "several stenoses per segment" have no significantly different procedural success than those without ($P=0.6983$), in contrast to patients with PTCA-only strategy ($P=0.0004$). The parameters of the medical history play a secondary role, in contrast to the results for MACE (see below). Table 4 summarizes relevant parameters for procedural success derived from the boosting model.

For the "pure" ACC/AHA criteria, the following ranking in order of decreasing (or equivalent) importance for procedural

success can be derived from the decision trees: total occlusion; irregular vessel contour; severe calcification; proximal segment; severe tortuosity; bifurcation lesions/double guide-wires; and diffuse stenosis length.

By subsequently adding further parameters to the ACC/AHA criteria in the training model (which optimizes classification, in contrast to cross-validation, which analyzes the performance on unknown cases), the misclassification rate drops. With addition of the parameters LV

TABLE 3. Ranking of Criteria for Procedural Success

Stent implantation (yes or no)
Proximal segment
Total occlusion
Vessel contour
LV function (reduced)
Several stenoses per segment
Ad hoc PTCA
TIMI flow
Reintervention
Vessel related to infarction
Stenosis morphology
Calcification
Sex
Stenosis classification ACC/AHA
Stenosis length
Stenosis morphology
Vessel bending
Segment

Subgroups represent parameters of the same level of importance, whereas subgroups themselves are ordered in decreasing importance.

TABLE 4. Relevant Parameters for Procedural Success Derived From the Boosting Model

History Variables	Angiographic Variables	PTCA/Stent-Related Variables
Concomitant valvular heart disease	Several stenoses per segment	Stent implantation (is positive)
Arrhythmia	Total occlusion	Dissection after PTCA/stenting
Heart failure	Calcification	Perforation
Sex	Proximal segment	
Acute MI	Diameter stenosis before intervention >90%	
Subacute MI	Vessel related to infarction	
LV function	Several stenoses per segment	
Renal insufficiency	TIMI flow	
Unstable angina pectoris	Vessel contour	
Vascular disease: cerebral or peripheral	Stenosis morphology	
Smoker	Previous PTCA (number of procedures)	
Hypercholesterolemia	Previous CABG (number of procedures)	
	Segment	

function and vessel related to infarction, misclassification rates are only 6%. When the type of procedure is added, it further decreases to 5%, finally dropping to 2% with the addition of TIMI flow.

Probability of MACE Based on a Maximally Extended Data Model

The relevant parameters for MACE are nearly the same as for procedural success (Table 4), but the ranking is completely different. For MACE, history variables are of greater importance than the ACC/AHA criteria. Machine learning techniques generate the ranking of criteria for MACE shown in Table 5.

From the 10 different models calculated, a host of interesting rules ensue. The following rule (Rule 2/5) is an example:

TABLE 5. Ranking of Criteria for MACE

Acute MI
Previous MI
Unstable angina
Angina pectoris, Canadian Cardiovascular Society (III, IV)
Concomitant valvular heart disease
Significant rise in CK (Reduced) LV function
Stenosis morphology
Multivessel disease
TIMI flow
Occlusion
Calcification
Proximal segment
Bifurcation lesions/double guidewires
Several stenoses per segment
Stenosis length (diffuse)
Female sex
Age

CK indicates creatine kinase.

Diameter stenosis after intervention=26% to 50%
 Stent implanation=yes
 → Classification of MACE as high risk [0.500]

The interesting aspect of this rule is the fact that in connection with stenting, the finding “diameter stenosis after intervention 26% to 50%,” which is usually still considered a successful procedure, nevertheless poses an increased risk for MACE. If the diameter of the target lesion (after intervention) is even 76% to 90%, the risk is 66% or, in other words, unsuccessful stenting carries a higher risk for MACE than unsuccessful PTCA.

Extended MACE

The results for extended MACE are similar to those for MACE. The ABC classification is not significant ($P=0.4139$). Taking abrupt closure as the dependent parameter, the corresponding P value is 0.8660. Only a combination of 3 different groups of parameters (medical history, morphological, and intervention-related criteria) characterize extended MACE. The most important parameter is again acute MI ($P<0.0001$). Other parameters are total occlusion, collaterals, vessel related to infarction, vessel bending, sex, concomitant valvular heart disease, and reduced LV function ($P<0.0001$ for the latter). Additional parameters for an adverse event of the type “extended MACE” are diameter before intervention (>90%), diameter after intervention (>50%), and length of stenosis (>2 cm and/or diffuse). Procedural success as an individual parameter is not significant ($P=0.2$).

Discussion

The present study integrates advanced computing techniques into a data model based on the ACC/AHA ABC stenosis morphology criteria, still widely used as a rough grading system. It addresses their overall and individual predictive value in a randomly selected, scrutinized population of a European audit survey.¹¹ Previous studies¹⁶ using an earlier and less refined version of the current methodology instead

tried to identify new classifiers on a different, not randomly selected patient population. The present study also proposes refined methods of prospective outcome analysis.

The distribution of target lesions to morphological types shows the majority in the type B group and more type C than type A lesions, in accordance with a recently reported series from a single US center.⁷ There is an association of cumulatively slightly decreasing procedural success and increasing procedural risk with lesion staging from A to C. However, ACC/AHA criteria do not predict individual outcome even when used as a set. With machine learning techniques, sets of different combinations (equivalent to sets of rules) of ACC/AHA criteria predict individual outcome with a misclassification rate of 10% in a retrospective analysis. For procedural success, the additional parameters of TIMI flow, vessel related to infarction, LV function, and most importantly, stenting (yes or no) are of high importance (reduction of misclassification rate from 10% to 2%). For predicting MACE, variables related to the medical history are more important than the ACC/AHA criteria.

Glycoprotein IIb/IIIa receptor antagonists, which were infrequently used, were not identified as major additional determinants. The reiterative self-improvement capacities of the algorithm, however, would allow the detection of any new variable that influences the outcome to a significant degree.

The high predictive performance is only achieved by the computer model as a whole and requires all techniques applied (eg, boosting, pruning, cross-validation, and cost functions). No single identified rule (as shown in Figure 1) is of individual predictive value. Because of their self-improvement capabilities, the predictive potency of the final algorithms could be expanded once more when applied to procedures performed in the same laboratory and by the same operators. This generates a "custom-tailored" set of rules for the respective group.

The outcome of coronary angioplasty has been documented in large-scale registries,¹⁷⁻¹⁹ which in part served as the basis for establishing the ACC/AHA criteria. An earlier retrospective study failed to predict the individual risk of abrupt vessel closure.⁸ The present study specifically deals with the individual predictive value of clinical or morphological conditions for outcome of PTCA using a detailed and highly scrutinized data set of a randomly selected patient population. TIMI flow, the relationship of the target vessel to MI, and stenting were identified as important additional classifiers. The established ACC/AHA criteria together with these newly identified classifiers can predict procedural success of PTCA with a misclassification rate of only $\approx 2\%$. Although many of the identified rules may appear familiar to the interventional cardiologist, others are puzzling. It must be emphasized that they are only applicable in the framework of the complex computer model. The predictive results, however, are generated by artificial intelligence independent of any interventional experience.

Two recent studies underscore the prevailing importance of factors, which we intend to address by use of the ABC criteria. Whereas the present study analyzed the individual predictive value of the ABC criteria on the immediate procedural success and on outcome during the procedure-

related hospital period, Kastrati et al²⁰ assessed the influence of a modified ACC/AHA score on long-term angiographic and clinical outcome after coronary stenting. They found a significant prognostic value for long-term outcome, which again argues in favor of the fact that the ABC criteria contain important determinants of outcome in interventional cardiology, which perhaps only need to be adequately weighted by methods of modern computing technique. In a large study population selected for stent or glycoprotein IIb/IIIa use, Ellis et al²¹ again were able to extract risk factors for complications of coronary interventions derived from the original ABC criteria. Our approach aims at modeling an individual risk profile from as many lesion and history characteristics as possible, using current tools of information technologies.

Applicability of the Algorithms for Routine Purposes

The software can be implemented into a catheterization report program running on standard Windows operating systems and standard hardware.

Limitations of the Study

A possible limitation of the study is the sample size. It was chosen to enable a scrutinized analysis of a representative cross section of European PTCA cases. Thus, a more detailed, cross-validated data set could be assessed. For definition of procedural success, the majority decision of expert interventional cardiologists was available in contrast to merely the operators' documentation in case of retrospective analysis of large-scale registries. Because of the stratified sampling for case selection according to opinion polls,¹² the samples can be considered representative.

For the conventional statistics, the traditional approach to sample-size estimation requires the smallest worthwhile effects to be statistically significant. We obtained a minimum sample size of 247, calculating the sample size over the parameter p of a binomial distribution with given type I errors and type II errors of 5% and 10%, respectively. The decision-tree techniques require a minimum sample size of 5 to 10 cases per relevant parameter, which is clearly met for the 26 AHA criteria by the current data set.

In summary, ACC/AHA class per se cannot predict individual outcome of angioplasty. However, inductive machine learning techniques are able to build models based on the ACC/AHA criteria that classify individual outcome with high accuracy. By implementation of additional (history, function, lesion-specific) parameters, accuracy can be improved stepwise. This technique provides an operator-independent risk stratification before coronary interventions. It is cost-effective and easily applicable in clinical routine provided that the necessary data are electronically documented and sufficiently scrutinized. With further progress of electronic data management in the medical environment, this technology might also be of value for building large-scale registries for future improvement of guidelines in interventional cardiology.

Appendix

Specific Methodologies

1. Decision Trees

The root of a tree is the top node, and examples are passed down the tree, with decisions being made at each node until a terminal node or leaf is reached. Each nonterminal node contains a question (eg, acute MI: yes or no) on which a split is based. Each leaf contains the label of a classification (eg, low risk or high risk). Equivalently, decision trees can also be represented by sets of if-then-else rules.

2. Cross-Validation

One way to get a more reliable estimate of predictive accuracy is by n-fold cross-validation.¹ The cases in the data file are divided into n blocks of roughly the same size and class distribution (we used n=10). For each block in turn, a classifier is constructed from the cases in the remaining blocks and tested on the cases in the holdout block.

3. Cost Function

Misclassification of a patient with complications as one without complications is more serious and “costs” more than the converse. Misclassification costs, represented by cost functions, are numeric penalties for classifying an item into one category when it really belongs in another. We calculated decision trees for which the total cost of misclassification was minimized.

4. Boosting

Boosting gives higher predictive accuracy.¹⁵ As the first step, a single decision tree or rule set is constructed as before from the training data. This classifier will usually make mistakes on some cases in the data, and the first decision tree possibly gives the wrong class for some cases. When the second classifier is constructed, more attention is paid to these cases. As a consequence, the second classifier will generally be different from the first. It also will make errors on some cases, and these will be focused on when the third classifier is constructed. This process continues for a predetermined number of iterations. When a new case is to be classified, each classifier votes for its predicted class, and the votes are counted to determine the final class.

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