Prognostic Value of Angiographic Indices of Coronary Artery Disease from the Coronary Artery Surgery Study (CASS)

IVAR RINGQVIST, LLOYD D. FISHER, MICHAEL MOCK, KATHRYN B. DAVIS, HANS WEDEL, BERNARD R. CHAITMAN, EUGENE PASSAMANI, RICHARD O. RUSSELL, JR., EDWIN L. ALDERMAN, NICHOLAS T. KOUCHOUKAS, GEORGE C. KAISER, THOMAS J. RYAN, THOMAS KILLIP, and DAVID FRAY,
Cardiac Disease Branch, National Heart, Lung, and Blood Institute, Bethesda, Maryland 20014; Department of Biostatistics, University of Washington, Seattle, Washington 98195; Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55901; Cardiology, Montreal Heart Institute, Montreal H1T1C8, Quebec, Canada; Department of Medicine and Surgery, University of Alabama in Birmingham, Alabama 35294; Cardiology Division, Stanford University School of Medicine, Stanford, California 94305; Department of Surgery, St. Louis University School of Medicine, St. Louis, Missouri 63104; Department of Medicine, Boston University Medical Center, Boston, Massachusetts 02118; Department of Medicine, Henry Ford Hospital, Detroit, Michigan 48202

ABSTRACT The Coronary Artery Surgery Study, CASS, enrolled 24,959 patients between August 1975 and June 1979 who were studied angiographically for suspected coronary artery disease. This paper compares the prognostic value for survival without early elective surgery of eight different indices of the extent of coronary artery disease: the number of diseased vessels, two indices using the number of proximal arterial segments diseased, two empirically generated indices from the CASS data, and the published indices of Friesinger, Gensini, and the National Heart and Chest Hospital, London. All had considerable prognostic information. Typically 80% of the prognostic information in one index was also contained in another. Our analysis shows that good prediction from angiographic data results from a combination of left ventricular function and arteriographic extent of disease. Prognosis may reasonably be obtained from three simple indices: the number of vessels diseased, the number of proximal arterial segments diseased, and a left ventricular wall motion score. These three indices account for an estimated 84% of the prognostic information available. 6-yr survival varies between 93 and 16% depending upon the values of these three indices.

Received for publication 10 March 1982 and in revised form 14 February 1983.

INTRODUCTION

Interventions such as bypass surgery and the use of potent drugs emphasize the need for a thorough understanding of the natural history of coronary artery disease. Identification of high risk groups of patients who may benefit from certain treatments depends upon adequate evaluation of the characteristics that influence survival. Analysis of high quality coronary arteriograms and ventriculograms offers a good assessment of the anatomical consequence of coronary artery disease and left ventricular function. Since the introduction of coronary angiography many different arteriographic indices have been developed to predict survival in subsets of patients (1–5). In addition, it has been earlier shown (6–8) that left ventricular function has an important effect on prognosis even if the patients are grouped into different arteriographic classes.

This study was undertaken to: (*a*) compare the prognostic value of different arteriographic indices including some empirically constructed from the Coronary

 J. Clin. Invest. © *The American Society for Clinical Investigation, Inc.* · *0021-9738/83/06/1854/13* $1.00
Volume 71 June 1983 1854–1866

Artery Surgery Study (CASS)[1] in subsets of patients with coronary artery disease and varying degrees of left ventricular dysfunction; (*b*) estimate the overlap in predictive information between different arteriographic indices; and (*c*) construct a simple index from angiographic data that is clinically useful in identifying subsets of patients at different levels of risk.

METHODS

CASS carried out under the auspices of the National Heart, Lung, and Blood Institute contains a registry of 24,959 patients enrolled from August 1975 to June 1979. At the 15 cooperative centers, all patients who were studied angiographically for suspected or proven coronary artery disease were enrolled in the registry (subject to their informed consent). Angiographic findings were recorded on standardized forms, and readings were quality controlled. The percentage narrowing of arterial segments was estimated by visual assessment. Vital status is known in 99.8% of the registry patients. A detailed description of CASS has been previously published (9). This study is based on analysis of 8,773 registry patients with at least minimal coronary artery disease who did not have surgery, or who had very late surgery.

Description of indices

Eight indices of the arteriographic extent of disease were examined. The descriptions below are given in more detail in Appendix I.

1. *Number of vessels diseased.* The possible scores of this index range from zero to three vessels diseased. The criterion for one, two, or three vessel disease is a 70% or more reduction in the internal diameter of the right, left anterior descending, or left circumflex system. A 50% or more reduction in the internal diameter of the left main coronary artery is considered two vessel disease. Patients with less severe disease, that is obstructions causing <70% reduction in the right, left anterior descending, or left circumflex coronary artery and <50% reduction in the left main coronary artery, are classified as zero vessel disease for the purposes of this index. In this paper the zero vessel disease patients have minimal or moderate coronary artery disease.

2. *Number of proximal arterial segments diseased.* This index ranges from zero to three proximal segments diseased. The criteria for the presence of proximal vessel disease are the same as for the number of vessels diseased (Index 1), but restricted to the proximal portion of the vessels. (Definitions of the coronary artery segments are given in Appendix I.)

3. *Proximal arterial segments score.* The score of this index ranges from one to seven. The criteria for presence of proximal obstruction are the same as for the number of vessels diseased (Index 1). The score reflects both the number of proximal segments diseased and the location of the lesion. In this scheme, stenosis of the proximal left anterior descending artery is scored higher than stenosis of the proximal circumflex or the proximal right coronary artery. A score of seven is given when three proximal segments (with or without the left main coronary) are diseased.

4. *Friesinger index (3).* The scores in this index range from 0 to 15. Each of the three main coronary arteries is scored separately from zero to five. The scores are: 0, no arteriographic abnormalities; 1, trivial luminal narrowing <29%; 2, localized 30–68% luminal narrowing; 3, multiple 30–68% luminal narrowing; 4, 69–100% luminal narrowing without 100% occlusion of proximal segments; 5, total obstruction of a proximal segment.

5. *Modified Gensini index (4).* This index assigns a heavier weight to the more severe luminal narrowings. Weights are also assigned to each segment depending on vessel size and importance; segments serving larger regions of myocardium are more heavily weighted. For example, the left main coronary artery receives the heaviest weight. For each segment the two weights are multiplied. The sum of the products is the modified Gensini score.

6. *National Heart and Chest Hospital (NHCH) index.* Feuerlicht et al. (5) presented an index from the National Heart and Chest Hospital, London, based on a schematic diagram of the coronary artery tree. The product of the fraction luminal openings of the segments on each path on the coronary tree is calculated. The sum of these products, normalized to lie between 0 and 100, gives the index.

7. *Modified NHCH index.* This index uses the product of the luminal opening fractions as in the NHCH index. Before summation, each of the products is weighted by a factor that reflects the relative importance for myocardial blood flow of that coronary branch. For instance, the left anterior descending branch is weighted more heavily than the circumflex branch. The weighting factors were determined empirically from the CASS data.

8. *Arterial segments score.* This index is derived from a weighted sum of the luminal narrowings of specific segments of the coronary arteries. The segments are the left main, proximal and middle left anterior descending, proximal and middle right, proximal and distal circumflex, and first obtuse marginal coronary arteries. The left main coronary and the three proximal segments are weighted most heavily. The segments and weighting factors were determined empirically from the CASS data.

9. *Left ventricular score (9).* Left ventricular function is estimated by a score ranging from 5 to 30. The ventricle is divided into five segments: anterobasal, anterolateral, apical, diaphragmatic, and posterobasal. Left ventricular wall motion abnormalities were subjectively assessed and scored numerically as follows: 1, normal; 2, moderate hypokinesis, 3, severe hypokinesis; 4, akinesis; 5, dyskinesis; and 6, aneurysm. The score is the sum of scores for the five segments. A normally contracting left ventricle is scored five. The maximum possible score for a totally encompassing ventricular aneurysm is 30.

Statistical methods

For purposes of this study, medically treated patients are defined as those who did not have surgery, or who had very late surgery. The number of days after enrollment within which 95% of the first year bypass surgeries occurred was determined for each clinic. Patients with surgery within this period were excluded from this study. An alternative method was used wherein all 16,286 patients with at least minimal coronary artery disease were used. In this analysis, patients treated surgically were also included, but considered as lost to follow-up at the time of their bypass surgery.

To estimate the ability of each index to predict survival, each index was used to categorize patients into risk groups. The risk groups for an index were compared in a life table analysis to determine how distinctly the index could separate

[1] *Abbreviations used in this paper:* CASS, Coronary Artery Surgery Study; NHCH, National Heart and Chest Hospital, London.

the risk groups. For indices one through three, the risk groups were determined by the number of diseased vessels, the number of diseased proximal segments, or the proximal arterial segment score. For indices four through eight, which had a wider range of scores, each index was used to categorize the patients into five quintiles of risk. The first quintile was set to contain ~20% of the patients with the lowest scores for that index, the next quintile to contain the next 20%, and so on. The relation of the index to survival was rated by the separation of the risk groups as measured by the log-rank statistic.

Since the number of vessels diseased is an especially important categorization, in another analysis the other indices were used to divide patients into four risk groups with the same proportion of patients in each group as in the groups of zero, one, two, and three vessels diseased. The percentiles were 0–22, 23–54, 55–79, and 80–100%. For indices two through four, which have few categories, these percentiles could only be approximated. These indices and their percentiles were the number of proximal arterial segments (0–56, 57–86, 87–97, and 98–100%), the proximal arterial segments score (0–55, 56–73, 74–86, and 87–100%), and the Friesinger index (0–19, 20–53, 54–75, and 75–100%).

The indices were also rated by use of the Cox proportional hazards (or regression) model (10). The proportional hazards model for survival analysis assumes covariates influence survival by modifying the survival function by an exponent that contains a linear combination of covariates. The significance of a covariate in influencing survival is measured by a chi-square statistic that tests whether the coefficient for that covariate is actually zero. Each of the indices was examined separately by this method to measure its univariate predictive ability.

To compare and quantify the overlap among the eight indices, three methods of analysis were used: (*a*) an analysis based on information theory, (*b*) Cox stepwise regression analysis, and (*c*) a stratified life table, or actuarial, analysis.

Information theory (11) was used to quantify the amount of information for predicting 6-yr survival from each of the indices including left ventricular function score, and for each pair of indices. The overlap between indices was determined by comparing the amount of information in the single indices to the amount of information in the pair. (Details are given in Appendix II.)

The principle of a stepwise Cox analysis is to select the linear combination of variables that, within the framework of the proportional hazards model, affords the best fit of the model to the observed survival. At step 1 the variable most related to survival is chosen. At subsequent steps all remaining variables are considered for possible inclusion in the model, and the variable most related to survival, when considered in linear combination with variables already in the model, is then added. The process ends when the remaining (unselected) variables do not contribute statistically significant ($P < 0.05$) information to the model. This method was used to compare the eight indices and the left ventricular score. The model constructed by this analysis was also used to generate an overall index, which is a linear combination of single indices. This index, which was a linear combination of left ventricular score, the arterial segments score, the NHCH index, the Friesinger index, and the proximal arterial segments score, was compared with other combination indices that were similarly constructed (Appendix I). The Cox model is used because it allows the survival experience to be related to multiple predictor variables.

The stratified life table approach is used to adjust a survival comparison for other related factors (12). For instance, a comparison of survival among patients with one, two, or three vessels diseased might be adjusted for left ventricular function. Patients are grouped into two or more strata that are homogeneous with respect to ventricular function. The comparison among number of vessels diseased is then made separately within each strata. The individual strata tests are combined in a summary statistic, which may be used to test the difference in survival among patients with one, two, or three vessels diseased after removal of the effect of differing left ventricular function in the three groups. Stratification was used to compare the effect of the number of proximal segments diseased after adjusting for the number of vessels diseased and left ventricular score.

RESULTS

The univariate results of the Cox proportional hazard model and life table analyses for the left ventricular score and the eight arteriographic indices are shown in Table I. The chi-square statistic and the log-rank statistic test the statistical significance of the indices for predicting survival. The arteriographic indices have chi-square and log-rank values of 575 and larger with *P*-values all <0.0001. (The value corresponding with $P = 0.05$ is 3.84 for the chi-square and 9.49 for the log rank when quintiles are compared.) The left ventricular score has the highest chi-square statistic, 1,083, indicating that this score had the most significant prognostic value of the angiographic indices compared.

Figs. 1 and 2 are survival curves for each level of the eight arteriographic indices. Each index separated the patients into a range of distinctly separate survival patterns. Differences among the levels as measured by the log-rank statistic were highly statistically significant. Survival curves for the lowest and highest levels were similar for the eight indices. Survival curves for the two indices involving proximal disease further separated patients into low and high risk groups, rather than showing the continuous gradient across levels as in the other indices.

The most widely used index of severity of coronary artery disease has been the number of vessels involved. The estimated 6-yr survival for percentiles that correspond with the number of vessels diseased are given for each arteriographic index in Table II. 6-yr survival for the percentiles corresponding with patients with less severe but some disease (zero vessel disease) ranged from 86.2 to 94.1; survival for the percentiles corresponding with three vessel disease ranged from 40.0 to 57.8. The difference between survival in the zero vessel group and the three vessel group was of the same order of magnitude for each arteriographic index. Indices four through eight, whose percentiles closely matched the percentiles for number of vessels diseased, differ by no more than 4.6% in estimated 6-yr survival in any risk group.

TABLE I

Univariate Statistical Significance of the Eight Arteriographic Indices and LV Wall Motion Score in Medically Treated Patients with Coronary Artery Disease with the Cox Proportional Hazards Model and the Life Table Methods

Index	Chi-square statistic (Cox model)	Log-rank statistic (life table analysis for quintiles)	*P*-value
No. of vessels diseased	654	682	<0.0001
No. of proximal arterial segments diseased	614	579	<0.0001
Proximal arterial score index	635	575	<0.0001
Friesinger index	580	671	<0.0001
Modified Gensini index	937	735	<0.0001
NHCH index	717	668	<0.0001
Modified NHCH index	707	777	<0.0001
Arterial segment score	859	670	<0.0001
LV wall motion score	1,083	—	<0.0001

The value corresponding to $P = 0.05$ is 3.84 for the chi-square and 9.49 for the log rank when quintiles are compared. LV, left ventricular.

Prognostic information contained in pairs of arteriographic indices and the percentage of this information in each singly is given in Table III. The majority of the prognostic information available jointly from a pair of indices was available from each index alone. The information contained jointly in a pair

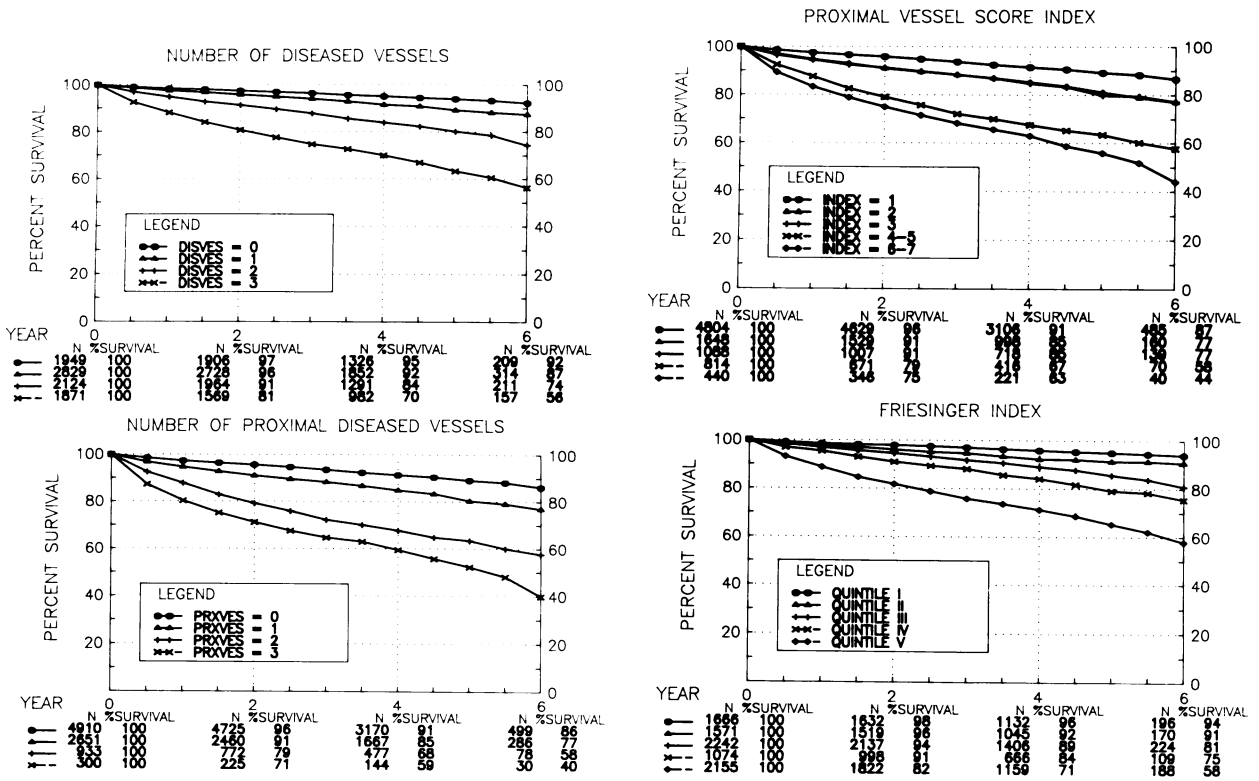

FIGURE 1 6-yr medical survival for four arteriographic indices: the number of diseased vessels ($P < 0.0001$; log-rank statistic = 681.536), the number of proximal arterial segments diseased ($P < 0.0001$; log-rank statistic = 578.764), the proximal arterial segments score ($P < 0.001$; log-rank statistic = 575.432), and the Friesinger index ($P < 0.0001$; log-rank statistic = 670.992). See text for details.

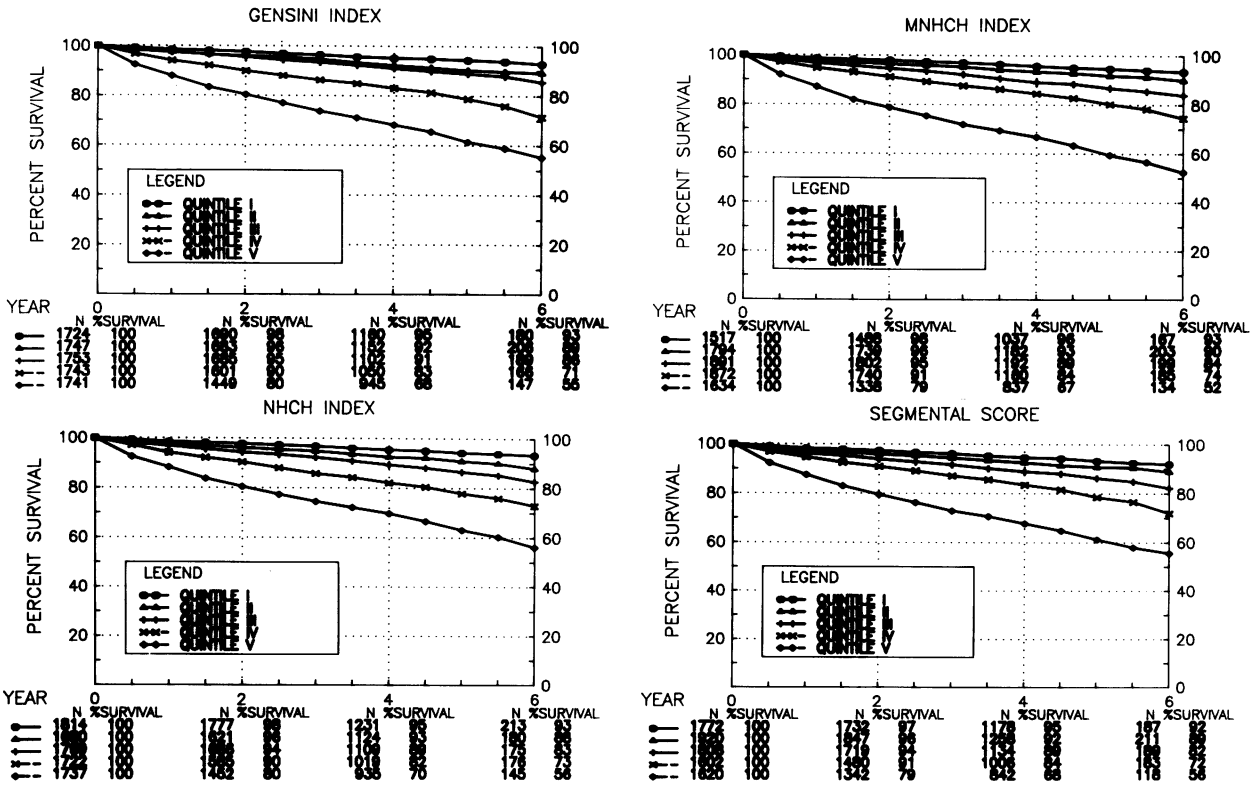

FIGURE 2 6-yr medical survival for four arteriographic indices: the Gensini index ($P < 0.0001$; log-rank statistic = 735.363), the NHCH index ($P < 0.0001$; log-rank statistic = 668.349), the modified NHCH (MNHCH; $P < 0.0001$; log-rank statistic = 777.051), and the arterial segments score ($P < 0.0001$; log-rank statistic = 669.703). See text for details.

ranged from 42%, for number of proximal segments diseased paired with the Friesinger index, to 97% for number of proximal segments diseased paired with the proximal segments score. The percentage of information one index contained of the joint information ranged from 54 to 98% with an average value of 83%.

TABLE II
Estimated Percentage 6-yr Survival for Eight Arteriographic Indices by Percentiles Corresponding to Number of Vessels Diseased

Index	Percentile group (vessels)			
	Zero	One	Two	Three
Number of vessels diseased	92.4	87.5	74.4	56.3
Number of proximal arterial segments diseased	86.2	77.0	57.8	40.0
Proximal arterial segment score	86.6	77.1	77.3	52.6
Friesinger index	94.1	87.2	76.6	57.8
Modified Gensini index	92.3	87.9	74.3	56.2
NHCH index	93.7	86.2	74.1	56.3
Modified NHCH index	92.7	86.7	76.2	52.4
Arterial segment score	92.0	87.2	75.9	57.0

The results of the comparison by stepwise Cox analysis are shown in Table IV. Five indices were selected by the stepwise procedure. Each of the five indices gives additional statistically significant predictive information in the presence of the other four. When left ventricular score was included it was selected first by the stepwise procedure as being most predictive. Ventricular score was followed by the arterial segment score, the NHCH index, the Friesinger index, and the proximal segments score.

The information content of the overall index constructed from the stepwise Cox analysis of all the angiographic indices is compared with several other indices in Table V. The overall index, which was selected as the most predictive linear combination of the single indices, is computed from the left ventricular score, arterial segments score, NHCH index, Friesinger Index, and proximal segments score. The other combination indices were constructed by Cox analyses restricted to subgroups of indices. The left ventricular score alone had 63% of the information joint with the

TABLE III

Overlap in Predictive Information for Pairs of Indices

Pair of indices	Percentage of joint information: In common	In first variable	In second variable
1-2	50	90	60
1-3	48	87	60
1-4	85	89	96
1-5	66	79	87
1-6	80	88	92
1-7	79	84	95
1-8	75	89	86
2-3	97	98	98
2-4	42	54	88
2-5	47	54	93
2-6	53	62	92
2-7	51	56	95
2-8	55	63	92
3-4	45	58	87
3-5	46	55	91
3-6	51	63	88
3-7	52	59	93
3-8	55	65	90
4-5	69	84	85
4-6	77	91	86
4-7	78	87	91
4-8	76	93	82
5-6	70	90	80
5-7	71	86	86
5-8	72	90	81
6-7	83	84	98
6-8	79	92	87
7-8	79	93	86
Average	65	83	
Minimum	42	54	
Maximum	97	98	

Indices: 1, number of vessels diseased; 2, number of proximal arterial segments diseased; 3, proximal arterial segment score; 4, Friesinger index; 5, modified Gensini index; 6, NHCH index; 7, modified NHCH index; 8, arterial segment score.

overall index, but to obtain most of the joint information, 83–88%, both ventriculographic and arteriographic information must be used.

Estimated 6-yr survival for subgroups classified by number of vessels diseased, number of proximal segments diseased, and left ventricular score are shown in Table VI. 6-yr survival percentages for 30 separate categories are given. Approximately 95%-confidence intervals for the survival percents are obtained by adding and subtracting 1.96 SE (given in parentheses) from each figure. Within each of the 10 categories defined by number of vessels diseased and number of proximal segments diseased there was a statistically

TABLE IV

Stepwise Cox Survival of Analyses of Prognostic Value of Nine Angiographic Indices of Coronary Artery Disease

Index	Without LV score: Final *P*-value	Entry step	With LV score: Final *P*-value	Entry step
No. of vessels diseased	0.14	•	0.45	•
No. of proximal segments diseased	0.91	•	0.36	•
Proximal arterial segment score	0.0002	3	0.04	5
Friesinger index	0.0004	4	0.0007	4
Modified Gensini index	<0.0001	1	0.20	•
NHCH index	0.47	•	0.0008	3
Modified NHCH index	<0.0001	2	0.26	•
Arterial segments score	0.06	•	0.0003	2
LV wall motion score	—	—	<0.0001	1

• Variable was not selected by the stepwise procedure.
P-values were determined by the distribution of the chi-square with one degree of freedom. LV, left ventricular.

significant reduced 6-yr survival with decreasing left ventricular score ($P < 0.0001$).

For patients with normal or mildly impaired ventricular function (score 5–11), there were no statistically significant differences in 6-yr survival percentage between zero and one proximal segments diseased in the one, two, and three vessel diseased categories. Pa-

TABLE V

Percentage of Predictive Information That Is Joint with the Overall Index for Selected Angiographic Indices of Coronary Artery Disease*

Index	Percent of joint information
Number of vessels diseased	57
Number of proximal arterial segments diseased	37
Number of vessels diseased plus number of proximal arterial segments diseased	60
Arterial segment score	61
LV wall motion score	63
LV wall motion score plus number of vessels diseased	83
LV wall motion score plus number of vessels diseased plus number of proximal arterial segments diseased	84
LV wall motion score plus arterial segment score	88

* The overall index, selected by a stepwise Cox survival analysis to be the most predictive linear combination of the single indices, is computed from the LV score, arterial segment score, NHCH index, Friesinger index, and proximal arterial segment score. LV, left ventricular.

TABLE VI

6-yr Survival Percents±1.96 SE by Number of Vessels Diseased, Number of Proximal Arterial Segments Diseased, and Left Ventricular Wall Motion Score (Number of Patients in Cell at Enrollment)

No. diseased vessels	No. proximal segments diseased	Left ventricular score			
		5-11	12-16	17-30	Total
0	0	93±2	76±13	78±27	
		(1,836)	(45)	(9)	(1,890)
1	0	92±2	81±8	65±20	
		(1,430)	(219)	(36)	(1,685)
1	1	90±3	76±9	55±19	
		(796)	(204)	(65)	(1,065)
2	0	81±6	49±22	52±18	
		(652)	(128)	(37)	(817)
2	1	86±4	67±10	54±14	
		(617)	(188)	(71)	(876)
2	2	72±9	51±14	43±20	
		(234)	(102)	(39)	(375)
3	0	76±10	53±12	25±36	
		(238)	(96)	(29)	(363)
3	1	74±7	43±12	47±13	
		(371)	(191)	(71)	(633)
3	2	66±8	47±9	24±13	
		(297)	(165)	(74)	(536)
3	3	57±13	29±14	16±14	
		(156)	(93)	(46)	(295)
					(8,535)

tients with two and three proximal segments diseased had a reduced estimated survival relative to patients with zero and one proximal segments diseased in both the two and three vessel disease categories ($P < 0.0001$).

The survival percentage decreases with increasing number of proximal arterial segments diseased ($P < 0.0001$ overall) after adjustment for the number of vessels diseased and the left ventricular score. However, survival for zero and one proximal segments is similar ($P = 0.12$) and survival for two and three proximal segments diseased differ only marginally ($P = 0.01$) under similar adjustments.

The figures in Table VI were recalculated after eliminating patients with 50% or greater left main stenosis. The 6-yr estimates of survival changed by <2% in all cases. In another analysis, after adjustment was made for the number of vessels diseased, number of proximal segments diseased, and left ventricular score, there was no statistically significant difference in survival between patients with and without 50% or greater left main stenosis. Only 302 patients with left main stenosis > 50% were available for this analysis since most left main patients received early coronary artery bypass surgery. For this reason this paper has little bearing upon nonoperative survival in left main coronary artery disease patients.

The analysis for Table VI was also repeated using an alternate method of survival analysis wherein patients were included in the analysis up until the time of bypass surgery, then removed from further calculations. Changes in the survival percentage were minimal in most cases. The difference in estimated survival exceeded 2% in only 7 of the 30 cells.

DISCUSSION

Data from several studies relating severity of coronary artery disease to survival have indicated that prognosis worsens as the number of vessels diseased increases. Most studies have used the subdivision of one, two, and three coronary arteries diseased (1, 2, 7, 8). More complex indices have been constructed (3–5) to characterize arteriographic findings more precisely and increase the prognostic value of the measurement. In this study eight arteriographic indices including previously published indices and the empirically constructed indices from CASS were compared. A wide

spectrum of disease ranging from minimal stenosis to extensive diffuse involvement of the coronary arteries was present in this large study, affording a unique opportunity to study the prognostic value of different angiographic indices with regard to survival. Although the CASS sites varied in attitudes and practices of surgical and medical therapy, we believe that in the aggregate they were representative of clinical practice in the United States during this period.

All eight of the indices evaluated are highly significant statistically in predicting survival. Differences in rank of the evaluations when the chi-square statistics from the Cox survival model and the log-rank statistics from the life table analyses are compared illustrate the dependence upon the method of analysis used. Although the modified Gensini index seems a little better than the other indices, the data demonstrate that all the arteriographic indices are very predictive and have roughly the same magnitude of predictive power. It is noteworthy that left ventricular performance is more predictive of prognosis than any of the arteriographic indices. Other studies have also shown that left ventricular function is an important predictor of subsequent survival in patients with cardiovascular disease (6–8).

When the range of survival experience is compared with the most widely used index, the number of vessels diseased, the spread between the zero vessel and three vessel groups is similar for all of the arteriographic indices (35–46%). The low survival in the three vessel group for the number of proximal segments diseased arises because the upper percentile for this group, which corresponds to three proximal segments diseased, has only 7% of the cases. This is not a close match to the three vessel group, which has 34%. Again one concludes the indices have roughly the same predictive power.

Although the indices have about the same predictive power, in many instances the indices contain much independent predictive information as shown in Table III. For example, in considering the number of vessels diseased and the number of proximal segments diseased (the 1–2 pair), 90% of the joint information is available if the categorization is based only on the number of vessels diseased. On the average, 17% of the predictive information for 6-yr survival available in a pair of indices is lost if only one index is used.

Stepwise Cox analysis of the eight indices reveals that the majority of the predictive ability is contained in a linear combination of five indices. This observation suggests that several of the indices measure different characteristics affecting the prognosis. However, the number of indices chosen by the stepwise procedure is large in part because of the statistical power afforded by the large number of patients in CASS.

To obtain maximum predictive information, both the performance of the left ventricle and the extent of coronary artery disease need to be characterized, as illustrated in Table V. Characterization by ventricular function alone or arterial disease alone is inadequate for good prediction. Subsets can be identified for which patients with one vessel diseased have a worse prognosis than those with three vessel disease. Measures of both ventricular function and extent of arterial disease are needed to obtain 88% of the predictive information.

For practical clinical use, simple indices of severity are preferable to the more complex indices if the predictive power is similar. We suggest that three simple angiographic indices: the left ventricular score, the number of vessels diseased, and the number of proximal segments diseased are together powerful predictors of prognosis. The combination of the number of vessels diseased and left ventricular score has a high joint predictive power for survival but each of the indices has independent information. The number of proximal segments diseased, previously shown to predict survival (13), is easily obtained at the time of angiographic interpretation and has independent information in addition to that revealed by the number of vessels diseased and ventricular score. In combination, the three indices may be used to adjust for the effect of left main stenosis of 50% or more.

The use of the three indices combined is suggested even though the data in Table V indicate that left ventricular score and number of vessels diseased together give nearly as much information. The comparisons in the table result from linear combinations of the indices involved, while the effect of the combination is not precisely linear (in the log hazard). Further, the contribution is small for subsets with a small proportion of the cases. Nevertheless, information regarding patients in the smaller categories may be especially useful to the clinician. The information regarding survival added by using the number of proximal arterial segments diseased was shown to be important in most of the subsets.

It is important to note that no consideration was taken of the influence of anthropometric, clinical, or laboratory variables. Such data were not considered in the development of the predictive angiographic indices. It has recently been shown that in patients with coronary artery disease, subgroups with low, middle, and high risk can be delineated using only clinical variables (14).

In summary, analysis of mortality in nonsurgically treated patients in the CASS registry using life table analysis and the stepwise Cox proportional hazards survival model has shown that: (*a*) Several commonly used indices of the extent of arterial disease have

roughly the same amount of prognostic information for nonoperative survival. (*b*) The various prognostic indices do have differences and contain independent information. Often 20% or more of the joint prognostic information in a pair of variables is lost by using only one variable. (*c*) To characterize survival optimally it is important to include a measure of left ventricular function together with arteriographic findings. (*d*) We suggest that a simple useful set of prognostic indices that are easily obtained from the angiography consists of left ventricular wall motion score, the number of vessels diseased, and the number of proximal arterial segments diseased. These indices provide good discrimination of patients with coronary artery disease who are at high and low risk.

APPENDIX I

Computation of the arteriographic indices

This appendix defines the eight arteriographic indices studied. The 27 possible segments with associated numbers, mnemonics, and brief descriptions are described first:

1. *PRXRCA (proximal right coronary artery).* Main stem of RCA from the ostium to one half the distance to the acute margin of the heart.
2. *MIDRCA (middle RCA).* Main stem of RCA from end of above segment to acute margin of the heart.
3. *DSTRCA (distal RCA).* Main stem of RCA usually running along the posterior right atrioventricular groove, from the acute margin of the heart to the origin of the posterior descending artery (PDA).
4. *RPDA (right PDA).* Artery of the posterior interventricular groove, which gives off septal perforators and is supplied by the distal right (90%).
5. *RPLS (right posterolateral segment).* Continuation of the distal right beyond the origin of the posterior descending artery. This segment is situated in the posterior atrioventricular groove, in the region of the crux of the heart, and may have an inverted U-shaped configuration. It usually gives off the A-V node artery and a variable number of branches, which run parallel to the PDA, on the posterolateral surface (or inferior surface) of the left ventricle.
6. *RPL1 (first RPLS branch).* First branch off the RPLS and often the only branch; synonym, left ventricular branch.
7. *RPL2 (second RPLS branch).* Usually not present.
8. *RPL3 (third RPLS branch).* Usually not present.
9. *Inf Septal (inferior septal).* Posterior descending septal arteries are the septal perforator arteries originating from the PDA then extending into the inferior septum.
10. *AC MARG (acute marginal vessels).* A large branch or branches supplying the acute marginal wall of the right ventricle. The origin of the largest of these vessels may be variable, but usually coincides with the acute margin of the heart. These vessels are often an important source of collateral circulation.
11. *LMCA (left main coronary artery).* Aortic ostium to bifurcation.
12. *PRXLAD (proximal left anterior descending).* Extends from its origin off the left coronary artery to the first visible septal no matter how small this vessel is. In some cases there will be a major septal proceeded by one or more small septals. In this instance, the definition should still be rigidly adhered to and the first visible septal, no matter what size, should be used to indicate the end of the proximal segment of the LAD.
13. *MIDLAD (middle LAD).* LAD immediately distal to the origin of the first major septal branch and extending to a point where the LAD forms an angle (Right anterior oblique [RAO] view), often, but not always, coinciding or close to the origin of the second diagonal branch. If said angle or branch is not identifiable, the segment ends one half the distance from the first major septal to the apex of the heart.
14. *DSTLAD (distal LAD).* Terminal segment of the LAD running along the interventricular sulcus, beginning with the end of the previous segment, and usually extending beyond the apex.
15. *1st DIAG (first diagonal; D-1).* The largest, and usually the first, diagonal branch having its origin from the proximal segment of the LAD and supplying the anterior wall. Occasionally, a separate branch of the main left coronary artery. If there is no diagonal with its origin from the proximal LAD, then D-1 should be coded with a "5" under morphology of distal vessel to signify anatomically not present.
16. *2nd DIAG (second diagonal; D-2).* The second diagonal branch, which often has its origin at the angle of the anterior descending when visualized in the RAO projection. Origin is usually near junction of middle and distal thirds of LAD, but may come off higher, from MIDLAD.
17. *1st Ant Septal (first anterior septal).* This vessel is designated as the first large branch of the LAD to penetrate into the anterior interventricular septum.
18. *PRXCX (proximal circumflex).* That portion of the circumflex artery from its origin off the main left coronary artery to and including the origin of the first obtuse marginal branch (No. 20). The distal circumflex (No. 19) may originate before the first marginal but the proximal circumflex continues until the origin of the first marginal.
19. *DSTCX (distal circumflex).* Begins from the proximal portion of the circumflex as the circumflex runs along or close to the posterior left atrioventricular groove. In right dominant circulation, the distal circumflex may be very small or absent.

Marginal circumflex branches that are very small or "twigs" are not to be counted as marginals or described. The first marginal branch (No. 20) may sometimes be a very large branch with the second marginal (No. 21) appearing as a division of the first marginal. All branches that come off the distal circumflex will be labeled marginals (Nos. 20, 21, and 22 below), and all branches that come off the left atrioventricular artery will be labeled left posterolateral branches (No. 24, 25, and 26 below).

20. *1st OB MARG (first obtuse marginal).* The first major branch of the circumflex artery supplying the lateral left ventricular wall, in the general area of the obtuse margin of the heart.
21. *2nd OB MARG (second obtuse marginal).* The second branch of the circumflex distributing to the lateral surface of the ventricle. Sometimes smaller in caliber than the first obtuse marginal. May be absent or may be a division of the first obtuse marginal branch.
22. *3rd OB MARG (third obtuse marginal).* The third branch of the circumflex supplying the posterolateral left ventricular wall (often absent). Runs parallel to the LPDA in the left predominant pattern.
23. *LAV (left atrial ventricular artery).* The left atrial ventricular artery is present only in a left dominant or balanced circulation. This artery is a continuation of the distal circumflex and has been arbitrarily defined as the distal half of the remainder of the circumflex after the take-off of the first marginal. The proximal half of the circumflex after the take-off of the first marginal will be defined as the distal circumflex (No. 19). Note that this definition is appropriate only for left dominant or balanced circulation.

Left posterolateral branches that are very small or "twigs" are not to be counted as branches or described. The first left posterolateral branch (No. 24) may sometimes be a very large branch with the second left posterolateral branch (No. 25) appearing as a division of the first branch. All branches that come off the distal circumflex will be labeled marginals (No. 20, 21, and 22), and all branches that come off the left atrioventricular artery will be labeled left posterolateral branches (Nos. 24, 25, and 26).

24. *1st LPL (first left posterolateral branch).* First branch off the LPL segment and often the only branch; synonym, left ventricular branch.
25. *2nd LPL (second left posterolateral branch).* Second branch off the LPL segment.
26. *3rd LPL (third left posterolateral branch).* Third branch off the LPL segment. Usually not present.
27. *LPDA (left PDA).* Posterior descending when present as a branch of the circumflex in the predominant left coronary artery.

The pattern of dominance in the circulatory system is defined as follows.

1. *Left.* The left atrioventricular and posterior descending arteries originate from the left circumflex coronary artery. Thus, segments Nos. 23 and 27 must be present and segments Nos. 4 and 5 should not be present.
2. *Right.* The posterior descending and the right posterolateral segments originate from the right coronary artery. Thus, segment Nos. 4 and 5 must be present and segment Nos. 23 and 27 should not be present.
3. *Balanced.* The right coronary artery gives a posterior descending artery, which does not extend beyond the crux. The left circumflex gives the posterolateral branches and rarely a second posterior descending as well. Thus, segment Nos. 4 and 23 will always be present, segment No. 27 may rarely be present, but segment No. 5 should not be present.

The eight indices and their computation follow.

1. Number of Vessels Diseased

The number of diseased vessels is a measure of the extent of disease in the three major branches of the coronary arteries. The three major vessels referred to by single, double, and triple vessel disease are determined by dominance. In a right dominant, balanced, or unknown system, these three branches include the RCA, the LAD, and the left circumflex arteries. In a left dominant circulation, they include the left anterior descending artery, the proximal left circumflex and its marginal branches, and the distal left circumflex and its posterolateral branches. The LMCA is equivalent to three vessels in a left dominant circulation and two vessels in a right dominant, balanced, or unknown circulation.

In a right dominant, balanced, or unknown circulation, the number of diseased vessels is determined in the following manner. The right coronary artery is considered diseased if there is a ≥70% stenosis in the proximal, mid, or distal right coronary arteries, or the RPDA; this constitutes one diseased vessel. If the LMCA has a 50% or greater stenosis, this constitutes an additional two diseased vessels. If the LMCA is not diseased or has <50% stenosis and there exists a stenosis of 70% or greater in the proximal, mid, or distal LAD or the first or second diagonal, there is one diseased vessel. If there is a stenosis of 70% or greater in the PRX or DSTCX, or in one of the three OB MARG, then the left circumflex is diseased; this constitutes one diseased vessel.

In left dominance, the number of diseased vessels is determined in the following fashion. If the left main coronary artery has a stenosis ≥ 50%, this constitutes three vessel disease. The remaining arteries are considered only if the LMCA has <50% stenosis. The criteria for defining disease in the LAD are the same as in a right dominant circulation. If there is a stenosis of 70% or greater in the proximal or distal circumflex arteries, this counts as two vessel disease. The remaining arteries are considered only if the PRX or DSTCX arteries are not diseased. If there is a stenosis of 70% or greater in the first, second, or third OB MARG, there is one diseased vessel. Finally, if there is a stenosis of 70% or greater in the left atrial ventricular artery, the first, second, or third posterolateral branches, or the LPDA, this constitutes an additional diseased vessel.

2. Number of Proximal Arterial Segments Diseased

In a right, balanced, or unknown dominance system, a LMCA that is ≥70% counts as two proximal segments diseased. If in addition the PRXRCA is ≥70% there are three proximal segments diseased. If LMCA is <70%, the number of proximal segments diseased is the number of the PRXRCA, PRXLAD, and PRXCX with ≥70% stenosis.

In a left dominant system, LMCA that are ≥70% count as three proximal segments diseased. If the LMCA is <70%, PRXLAD that are ≥70% count as one diseased proximal segment; if the PRXCX is ≥70% two diseased proximal segments are counted. If PRXCX is <70%, then one proximal segment diseased is counted if DSTCX is ≥70%.

3. Proximal Arterial Segment Score

The score ranges from 1-7. The criteria for reduction of the internal diameters were the same as for the number of vessels diseased (Index 1). The definitions of the proximal segments of the coronary arteries were the same as for number of proximal vessel segments diseased.

Score 1. No proximal segment diseased.

Score 2. One proximal segment diseased, either the circumflex coronary artery, CX, or RCA.

Score 3. Proximal segment of LAD diseased.

Score 4. Proximal segments diseased in both the CX and RCA.

Score 5. Proximal segment diseased in LAD and in CX or RCA.

Score 6. LMCA diseased.

Score 7. Three proximal segments diseased with or without a diseased LMCA.

4. Friesinger Index

The Friesinger Index is a score ranging from 0 to 15. Each of the three main arteries of the heart is scored separately receiving a score from zero to five.

0: An artery will obtain a score of 0 if there are no arteriographic abnormalities seen.

RCA. For the RCA to obtain this score, segments PRXRCA, MIDRCA, DSTRCA, and RPDA must all have 0% stenosis.

LAD. For the LAD to obtain this score, segments LMCA, PRXLAD, MIDLAD, DSTLAD, DIAG1, and DIAG2 must all have 0% stenosis.

CX. For the CX to obtain this score, segments LMCA, PRXCX, DISTCX, OBMRG1, OBMRG2, and OBMRG3 must all have 0% stenosis.

1: Trivial irregularity(ies) in luminal diameter.

RCA. At least one of segments PRXRCA, MIDRCA, DSTRCA, or RPDA has stenosis 1-29%, all have <30% stenosis.

LAD. At least one of segments LMCA, PRXLAD, MIDLAD, DSTLAD, DIAG1, or DIAG2 has stenosis 1-29%, all have <30% stenosis.

CX. At least one of segments LMCA, PRXCX, DISTCX, OBMRG1, OBMRG2, or OBMRG3 has stenosis 1-29%, all have <30% stenosis.

2: Localized narrowing estimated to be >50% but <90% of the luminal (cross-sectional) area (i.e., stenosis 30-68%).

RCA. At least one of segments PRXRCA, MIDRCA, DSTRCA, or RPDA has stenosis 30-68%, all have <69% stenosis.

LAD. At least one of segments LMCA, PRXLAD, MIDLAD, DSTLAD, DIAG1, or DIAG2 has stenosis 30-68%, all have <69% stenosis.

CX. At least one of segments LMCA, PRXCX, DISTCX, OBMRG1, OBMRG2, or OBMRG3 has stenosis 30-68%, all have <69% stenosis.

3: Multiple narrowing in the same vessel estimated to be >50% and <90% in cross-sectional area. The segment has a lesion with morphology coded as multiple, diffuse, or tubular lesion(s); or two segments with stenosis 30-68%.

RCA. The algorithm looks at segments PRXRCA, MIDRCA, DSTRCA, and RPDA to see if the above conditions are met.

LAD. The algorithm looks at segments LMCA, PRXLAD, MIDLAD, DSTLAD, DIAG1, and DIAG2.

CX. The algorithm looks at segments LMCA, PRXCX, DISTCX, OBMRG1, OBMRG2, and OBMRG3.

4: Narrowing or narrowings estimated to be >90% of the luminal cross section area.

RCA. At least one of segments PRXRCA, MIDRCA, DSTRCA, or RPDA has stenosis 69-100% and PRXRCA <100%.

LAD. At least one of segments LMCA, PRXLAD, MIDLAD, DSTLAD, DIAG1, or DIAG2 has stenosis 69-100% and LMCA <100% and PRXLAD <100%.

CX. At least one of segments LMCA, PRXCX, DISTCX, OBMRG1, OBMRG2, or OBMRG3 has stenosis 69-100% and LMCA <100% and PRXCX <100%.

5: Total obstruction of a vessel without any filling of the distal segment from the proximal portion.

RCA. Segment PRXRCA = 100%.

LAD. Segment LMCA or PRXLAD = 100%.

CX. Segment LMCA or PRXCX = 100%.

Note: In 5 above only the proximal segments were used, unlike 0-4 which use the whole vessel.

Note: In 3 above, segments with stenosis of 30-49% were considered to have a single lesion only. This was necessary because the morphology variable is not filled out for this group in the CASS study.

5. Modified Gensini Index

Each arterial segment is weighted by a value from 0.5 to 5.0. (The weight for segments 1 through 4 is changed to 0.5 if the system is left dominant.) The stenosis is weighted from 2 to 64. The product of these two weights is the total weight for each arterial segment. The modified Gensini index is the sum of the total weights for each segment.

The segment weights are (segment, weight): 1 PRXRCA, 1.0; 2 MIDRCA, 1.0; 3 DSTRCA, 1.0; 4 RPDA, 1.0; 5 RPLS, 0.5; 6 RPL1, 0.5; 7 RPL2, 0.5; 9 8 RPL3, 0.5; 10 AC MARG, 0.5; 11 LMCA, 5.0; 12 PRXLAD, 2.5; 13 MIDLAD, 1.5; 14 DSTLAD, 1.0; 15 1st DIAG, 1.0; 16 2nd DIAG, 0.5; 17 1st Ant Septal, 0.5; 18 PRXCX, 2.5; 19 DSTCX, 1.0; 20 1st OB Marg, 1.0; 21 2nd OB Marg, 0.5; 22 3rd OB Marg, 0.5; 23 LAV, 0.5; 24 1st LPL, 0.5; 25 2nd LPL, 0.5; 26 3rd LPL, 0.5; 27 LPDA, 1.0.

The stenosis weights are (percentage stenosis, weight): 0-25, 2; 26-50, 4; 51-75, 8; 76-90, 16; 91-99, 32; 100, 64.

6. NHCH INDEX

The NHCH index uses a diagram of the coronary artery tree. The diagram for balanced and right dominant circulation is given in Fig. 3.

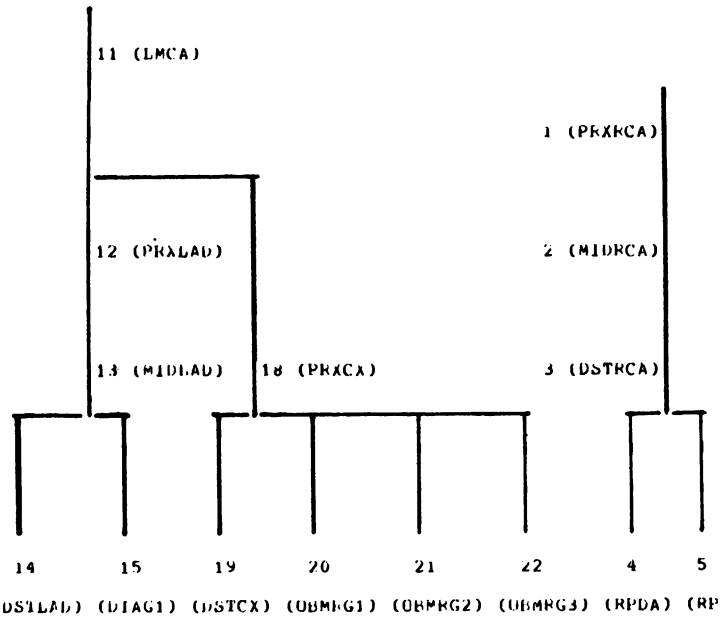

FIGURE 3 Diagram of the coronary arteries used in calculating the NHCH index for balanced and right dominant systems.

Let W_i be the fraction of the luminal diameter that is open for segment i; that is, $W_i = 1 - (s_i/100)$, where s_i is the percentage stenosis for segment i. For each path in the diagram, calculate the product of the W_i and sum the products for each path. The sum is then multiplied by a constant to normalize the values to fall between 0 and 100. The index is:

$$NHCH = \frac{100}{n}\{W_{11}[W_{12}W_{13}(W_{14} + W_{15}) + W_{18}(W_{19} + W_{20} + W_{21} + W_{22})] + W_1W_2W_3(2W_4 + W_5)\},$$

where n is the number of segments among (4, 5, 14, 15, 19, 20, 21, and 22) with known percentage stenosis or a proximal 100% occlusion (plus 1 if segment number 4 is known).

For left dominant systems, the diagram and function are given in Fig. 4.

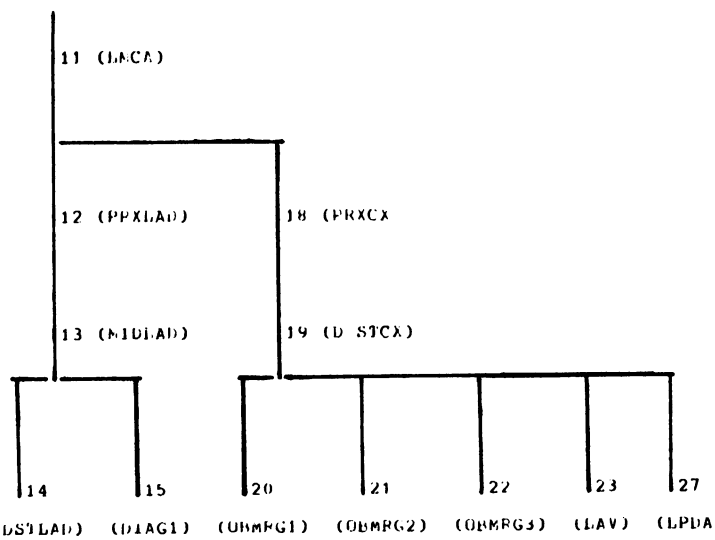

FIGURE 4 Diagram of the coronary arteries use in calculating the NHCH index for left dominant systems.

$$NHCH = \frac{100}{n}\{W_{11}[W_{12}W_{13}(W_{14} + W_{15}) + W_{18}W_{19}(W_{20} + W_{21} + W_{22} + W_{23} + W_{27})]\}.$$

In this case n is the number of known segments among 14, 15, 20, 21, 22, 23, and 27.

7. Modified NHCH index

The Modified NHCH index uses empirically derived weights. The products associated with different paths in Figs. 3 and 4 were used as potential covariates in a stepwise Cox survival analysis. Cases with left dominant coronary systems were analyzed separately from the cases with right, balanced, or unknown dominance. Using the notation of the NHCH index, for right, balanced and unknown dominance the resulting index is:

$$\textit{Modified NHCH} = 0.096(W_1W_2W_3W_4) + 0.134(W_{11}W_{12}W_{13}W_{14}) + 0.045(W_{11}W_{18}W_{19}) + 0.031(W_{11}W_{18}W_{20}) + 0.022(W_{11}W_{18}W_{21}).$$

For left dominance,

$$\textit{Modified NHCH} = 0.109(W_{11}W_{12}W_{13}W_{14}) + 0.120(W_{11}W_{18}W_{19}W_{23}).$$

8. Arterial segment score

The percent stenoses in each segment 1–27 were used as potential covariates in a stepwise Cox survival analysis. The cases with left dominant coronary systems were analyzed separately from the cases with right, balanced, or unknown dominance. The segments selected by the stepwise procedure and their estimated coefficients are given below. For right, balanced and unknown dominance,

$$\textit{Score} = 0.086(\%\ \text{LMCA}) + 0.090(\%\ \text{PRXLAD}) + 0.060(\%\ \text{PRXRCA}) + 0.044(\%\ \text{PRXCX}) + 0.046(\%\ \text{MIDLAD}) + 0.039(\%\ \text{DSTCX}) + 0.019(\%\ \text{MIDRCA}) + 0.034(\%\ \text{OBMRG1}) + 0.019(\%\ \text{OBMARG2}) + 0.030(\%\ \text{OBMARG3}).$$

For left dominance,

$$\textit{Score} = 0.071(\%\ \text{PRXLAD}) + 0.094(\%\ \text{PRXCX}) + 0.066(\%\ \text{DISTCX}).$$

APPENDIX II

Quantification of the predictive information (13)

If each patient can belong to one of two populations (in this case, alive or dead), let X and Y be discrete variables related to the two populations. Let $P_r(i, j)$ be the proportion or probability of dead ($r = 1$) or alive ($r = 2$) cases with $X = i$ and $Y = j$. The joint information in X and Y for distinguishing between populations 1 and 2 is:

$$I_{xy} = \sum_{i,j} \ln\,(P_1(i, j)/P_2(i, j))(P_1(i, j) - P_2(i, j)).$$

(In this expression ln is the natural logarithm.) The information in X alone for distinguishing between dead or alive is given by:

$$I_x = \sum_{i} \ln\,(P_1(i)/P_2(i)(P_1(i) - P_2(i)),$$

where $P_r(i)$ is the proportion of population r cases with $X = i$. A similar expression gives I_y, the Y information. The percentage of the joint XY information contained in variable X is defined to be $100(I_x/I_{xy})$.

To estimate the probabilities P from the data, each of two indices was used to group the cases into approximate quintiles of risk. (Instead of quintiles, categories for number of vessels diseased, number of proximal vessel segments diseased, and the proximal vessel segment score were simply formed by the different values of the index.) The life table method was used to estimate 6-y survival in each cell. Let $S(i, j)$ be the estimated 6-yr survival in cell i, j. Let $n_{i,j}$ be the number of individuals in the i, j cell at time zero. The probabilities $P_1(i, j)$ and $P_2(i, j)$ are estimated by

$$P_1(i, j) = n_{i,j}(1 - S(i, j))/\sum_{k,m} n_{k,m}(1 - S(k, m))$$

$$P_2(i, j) = n_{i,j}S(i, j)/\sum_{k,m} n_{k,m}S(k, m),$$

where the summation is over all cells k, m. Only cells with 100 or more cases initially were included in the estimate of the $P_r(i, j)$. In each comparison <3% of the cases were in cells deleted from the comparison.

ACKNOWLEDGMENTS

The following people are acknowledged for their help in this study.

Cooperating clinical sites: University of Alabama in Birmingham: Drs. William J. Rogers,* Richard O. Russell, Jr., Albert Oberman, and Nicholas T. Kouchoukos. Albany Medical College: Drs. Julio A. Sosa,* Eric K. Foster, Joseph MacIlduff, and Thomas Older. Boston University: Dr. Thomas Ryan,* Dr. David Faxon, Dr. Laura Wexler, Dr. Robert L. Berger, and Carolyn H. McCabe. Loma Linda University: Drs. Melvin P. Judkins,* and Joan Coggin.* Marshfield Medical Foundation, Inc. and Marshfield Clinic: Drs. William Myers,* Richard D. Sautter,* John N. Browell, Dieter M. Voss, and Robert D. Carlson. Massachusetts General Hospital: Drs. J. Warren Harthorne,* W. Gerald Austen,* Robert Dinsmore, Frederick Levine, and John McDermott. Mayo Clinic and Mayo Foundation: Drs. Robert L. Frye,* Hugh C. Smith, Ronald E. Vlietstra, Michael B. Mock, David R. Holmes, and Richard Fulton. Miami Heart Institute: Drs. Arthur J. Gosselin,* Parry B. Larsen, and Paul Swaye. Montreal Heart Institute: Drs. Martial G. Bourassa,* Bernard R. Chaitman, Claude Goulet, and Jacques Lesperance. New York University: Drs. Ephraim Glassman,* and Michael Schloss. St. Louis University: Drs. George Kaiser,* J. Gerald Mudd,* Robert D. Wiens, Hendrick B. Barner, John E. Codd, Denis H. Tyras, and Vallee L. Willman. St. Luke's Hospital Center: Drs. Harvey G. Kemp, Jr.,* and Airlie Cameron. Stanford University: Drs. Edwin Alderman,* Francis H. Koch,* Paul R. Cipriano,* James F. Silverman,* and Edward B. Stinson.* Medical College of Wisconsin: Drs. Felix Tristani,* Harold L. Brooks,* and Robert J. Flemma. Yale University: Drs. Lawrence S. Cohen,* Rene Langou, Alexander S. Geha, Graeme L. Hammond, and Richard K. Shaw.

Central Electrocardiographic Laboratory University of Alabama: Dr. L. Thomas Sheffield,* Dr. David Roitman, and Carol Troxell.

Coordinating Center, University of Washington: Dr. Lloyd Fisher,* Mary Jo Gillespie, Dr. Kathryn Davis, Dr. J. Ward Kennedy, and Dr. Richard Kronmal.

Chairman of Steering Committee: Dr. Thomas Killip, Henry Ford Hospital.

National Heart, Lung, and Blood Institute: Dr. Eugene R. Passamani, Dr. Peter L. Frommer, Suzanne M. Mullin, Dr. Kent Bailey, and Dr. David DeMets.

* Principal Investigator

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