Variables predictive of survival in patients with coronary disease

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Seattle Heart Watch is a cooperative, community-wide registry that closely observes patients with known or suspected coronary heart disease with the intent of identifying those at risk for sudden cardiac death. It is the purpose of this report to define the variables from the clinical, electrocardiographic, exercise, arteriographic, and quantitative angiographic evaluations that are univariately and multivariately predictive of cardiac death. This analysis is based on 1836 and 730 patients who initially received medical treatment for coronary disease, all of whom were entered into the Seattle Heart Watch at the time of coronary arteriography between 1969 and 1974. Average follow-up for this analysis is 42 months (range, 30 to 78 months). The surgical cohort is unique in that it represents most (94%, 1870/1985) patients undergoing direct myocardial revascularization in Seattle during this time. The medical cohort is an approximate 40% sample of patients undergoing arteriography during this 5-year period and initially treated medically. Follow-up is by mailed questionnaire at 6-month intervals. In the medical cohort, 70 of the 85 deaths were of cardiac causes (82%); in the surgical cohort, 151 of the 173 deaths (87%) were of cardiac causes.

Baseline characterization of these patients is complete and includes more than 300 data items from

the history, physical examination, resting electrocardiogram, chest roentgenogram, exercise electrocardiogram, and cardiac catheterization. Left ventricular function was assessed by measuring left ventricular volumes and ejection fraction from the left ventricular angiogram. The goal of our analyses was to select from this large number of variables the smallest number that contained all or most of the prognostic information available to us at the time of baseline characterization of these patients.

First, two types of univariate analyses were applied to some 46 variables selected on the basis of previous studies and clinical judgment. The significance of the difference of the means or the distribution of two variables between the survivors and the nonsurvivors was tested. Also, mortality rates were calculated with patients classified according to the presence or absence of a dichotomous variable or subgrouped according to several levels of a continuous variable. With these two univariate techniques, 35 variables were found to be significantly predictive of survival.

Next, stepwise discriminant analysis based on death within 2 years of follow-up was applied to three groups of variables: (1) Those from the history, physical examination, electrocardiogram, x-ray; (2) those from the exercise test; (3) those from the cardiac catheterization. A second stepwise discriminant analysis was performed on those variables with significant predictive value in the previous step. Finally, Cox's regression analysis (which has the advantage over stepwise discriminant analysis of including time to death or time to follow-up) was used to test the significant variables from the previous step.

As a result of this somewhat complex series of statistical analyses, seven variables were found to contain all of the significant prognostic information (*Table*). Among medically treated patients, ejection fraction was by far the most important variable predictive of survival, followed by age, number of stenotic vessels, and ventricular arrhythmia on the resting electrocardiogram. In the surgical cohort, the presence of any ventricular arrhythmia on the resting electrocardiogram was the most important variable, followed closely by ejection fraction, and then heart murmur, left main coronary artery stenosis, and use of diuretics.

These data are clinically relevant because they emphasize the singular importance of left ventricular performance in predicting survival in medically treated patients with angiographically proved coronary disease. The lesser predictive value of ejection fraction among surgically treated patients could be due to the fact that a much smaller proportion of surgically treated patients had abnormal ejection fractions than medically treated patients. We emphasized that the quantitative assessment of left ventricular function by ejection fraction

Table Stepwise selection of covariates with Cox's regression model for survival analysis

Cohort	Step	Variable entered	X_i^2
Medical		N = 550	
	1	Ejection fraction	48.54
	2	Age	17.16
	3	Number of vessels with stenosis(es) ≥ 70%	7.36
	4	Ventricular arrhythmia	4.46
Surgical		N = 913	
	1	Ventricular arrhythmia	19.4
	2	Ejection fraction	13.22
	3	Heart murmur	10.96
	4	Left main coronary artery stenosis	7.94
	5	Use of diuretics	5.38

is more important in predicting outcome than the number of diseased coronary vessels.

Also of interest is the predictive significance of any ventricular arrhythmia seen on a single resting electrocardiogram. Since these are multivariate analyses, the predictive value of the ventricular arrhythmia is independent of other variables, particularly those related to left ventricular function and extent of coronary disease. This finding is particularly encouraging in regard to current attempts to study the effect of antiarrhythmic agents for preventing sudden death.

If the ventricular arrhythmia was caused by poor left ventricular function, as has been hypothesized, then it would not have been an independent predictive variable in our scheme. Also, one would predict that attempts to control the arrhythmia with drugs would not necessarily lead to a reduction in sudden death, since the primary problem is abnormal left ventricular function and this would not be altered by antiarrhythmic therapy.

Finally, these data are helpful in comparing survival between nonrandomized groups of medically and surgically treated patients with coronary disease. Subsequent to this analysis, we matched one medically treated patient with one surgically treated patient according to each of the seven variables. Actuarial survival analyses indicated improved survival for the 287 surgically treated patients in comparison with the 387 medically treated matched pairs. Subgroup analysis indicated that this difference in survival was seen primarily in the subgroup with two-vessel disease. There was no significant difference in survival among the 140 pairs with single-vessel disease. In the small group (50 pairs) with three-vessel disease the operative mortality was unusually high (10%), negating any potential difference in survival in favor of surgical therapy.