Risk factors in relation to prognosis

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To advise the patient concerning the relative merits of coronary artery surgery, the physician must know those factors that are prognostically important. It is generally accepted that the rubric, coronary heart disease, includes a number of subgroups, not all of which can be expected to increase longevity with surgical management. The ability to determine this prognosis from a noninvasive clinical evaluation would allow the primary care physician to identify those patients requiring subsequent arteriographic studies. The purpose of this report is to relate the utility of various demographic, biochemical, and clinical variables in estimating the severity of coronary artery disease and the risk of subsequent death. Such estimates can be compared with findings from known data on survival in relation to angiographic findings to determine when and to what extent prognostic evaluation is improved with coronary arteriography.

The reference population consisted of all patients referred to the University of Alabama Medical Center in Birmingham between February 1967 and June 1975 for evaluation and treatment of ischemic heart disease on whom coronary arteriography was performed. Perti-

nent clinical data were collected during the admission for coronary arteriography. Baseline traits were used to determine the likelihood of survival 2 years from the date of the arteriogram. In addition to demographic data, these baseline traits included major risk factors, the symptom complex relating to angina and congestive heart failure, drug usage, risk factors, heart size, electrocardiographic variables, and extensive clinical data. All patients were followed for a period of at least 2 years.

The first manifestations of ischemic heart disease may be angina pectoris (38%), myocardial infarction (42%), preinfarctional syndrome (7%), or death (13%), more than one half is sudden death.[1] The prognosis for each of these has been reported many times. Generally, the mortality for individuals with coronary disease is approximately five times that for the general population, about 4% to 5% per year, with angina pectoris, classic myocardial infarction, and unrecognized myocardial infarction sharing this common mortality rate. Although there seems to be no difference in prognosis among the clinical subgroups, it is obvious that ischemic heart disease contains at least several subgroups with widely varying prognosis. Numerous arteriographic studies demonstrate a range of annual mortality from about 2% to 20% or more, depending upon the number of vessels diseased and the status of the left ventricle.[2, 3]

There is a need for evaluating risk of subsequent death prior to the use of invasive techniques with their attendant costs and risks. Basically, there are two different questions: (1) Can risk factors be used to predict the extent of coronary artery disease? (2) Can the prognosis for various subgroups be accurately estimated with risk indicators? Data from several large-scale studies on the association of risk factors with subsequent mortality have revealed significant factors, but the strength of the association is of relatively low magnitude. Frank et al[4] examined men after angina and myocardial infarction were first diagnosed and estimated subsequent mortality. They found a high risk group composed of men with abnormal electrocardiograms and blood pressure had five times the probability of coronary death within 4.5 years after baseline as those with neither abnormal electrocardiograms nor elevated blood pressure. Humphries et al[5] also found that S-T segment in combination with the arteriogram improved the prediction of subsequent mortality. The Coronary Drug Project, a nationwide collaborative study to determine the efficacy of drugs influencing lipid metabolism among men surviving one or more episodes of infarction, also provided the opportunity to study the natural history of coronary heart disease.[6] Of 40 factors evaluated in that study, it was evident that 10 variables satisfactorily classified the patients according to risk of death within 3 years. These factors were S-T segment depression, cardiomegaly, functional class, ventricular conduction defect, diuretics, intermittent claudication, cholesterol, ectopic beat, inactivity and Q-wave findings. Thirty-one percent of the deaths occurred among those patients in the upper 10% of estimated risk as judged by these variables in a logistic risk function.

The logical step is to relate these risk factors and symptoms to coro-

nary artery lesions. Even though patients will be misclassified on the basis of history of angina alone, angina is predictive of coronary disease.[7] Recently, Salel et al[8] related coronary risk profile to coronary artery disease. The index of risk increased with the number of coronary arteries diseased and the presence of congestive heart failure.

We attempted to relate specific factors comparable to those used in the Coronary Drug Project to prediction of the presence or absence of coronary artery stenosis in the major coronary vessels. The vessel was considered diseased if there was 50% or more stenosis. Two vessels were considered diseased if the left main coronary artery was diseased. *Table 1* shows a number of clinical variables were important in predicting the diseased vessels. Coefficients of determination were approximately 0.25 except for left main coronary artery disease, 0.11. The highest R^2, 0.35, was for estimating the number of vessels diseased.

In order to determine the role of the clinical risk indicators, we "forced" 21 risk factors into the discriminant function analysis to predict death at 2 years, achieving a total R^2 of 0.156 (*Table 2*). The p values for the partial coefficients are listed also. We then added the coronary arterial segments to determine whether these contributed significantly to the prediction of death over and above the multitude of risk factors. An additional 5% of the variance was explained by adding arteriographic variables. This was a significant ($p < 0.01$) improvement in the coefficient of determination. It is of note that these significant risk indicators for prediction of death were those previously identified, the S-T segment, the history of myocardial infarction, heart size, ventricular conduction defects, and antihypertensive therapy. In summary, clinical factors alone are rather weak prognostic tools and are substantially improved by knowledge of coronary artery lesions. However, a number of clinical indicators can be used to gauge the extent of coronary artery disease. These variables potentiate other risk factors to demonstrate convincingly the possibility for identifying high risk subgroups, namely those with previous myocardial infarction, congestive heart failure, cardiomegaly, and various electro-

Table 1. Discriminant function analysis; prediction of death (2 yr, N = 417)

Variables	p value
S-T segment	0.003
Cholesterol	0.895
Age	0.788
Angina	0.598
Unstable angina	0.173
History of myocardial infarction	0.019
Congestive heart failure	0.984
Intermittent claudication	0.746
Diastolic blood pressure	0.516
Cigarette smoking	0.564
Alcohol	0.779
Inotropic	0.871
Diuretics	0.633
Heart rate	0.213
Antiarrhythmics	0.558
Heart size	0.037
Ectopic beats	0.169
Q-waves	0.520
T-waves	0.582
Ventricular conduction defects	0.016
Antihypertensive ($R^2 = 0.156$)	0.012
LAD-mid	0.004
LAD-proximal	0.021
LAD-distal	0.038
RCA-distal *($R^2 = 0.204$)	0.075

LAD = left anterior descending artery; RCA = right coronary artery.
* Additional arteriographic variables ($p < 0.01$).

Table 2. Clinical factors relating to diseased vessels (N = 435)

	Coronary arteries—maximal stenosis ≥50%				
	Left main	LAD	Cir	Rt	Vessel disease
R^2 (coefficient determinant)	0.11	0.25	0.22	0.25	0.35
Age		XXX	XXX	X	XXX
Angina	XXX	XXX	XX	XXX	XXX
Myocardial infarction				XXX	
Congestive heart failure	XX	XX	XX	X	XX
Intermittent claudication			X		
Diuretics		X	XX		XX
Antiarrhythmics	XX				
Cholesterol			XXX	XX	XXX
Q-wave		XXX	XXX	XXX	XXX
S-T T wave		XXX	X	X	XXX
Ectopic beats	X		X		
Heart size	XX				

$p \leq 0.05$, X; $p \leq 0.01$, XX; $p \leq 0.001$, XXX.

cardiographic abnormalities. It appears that such indexes can be used to advantage for evaluating the need for coronary arteriography and subsequent surgery.

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