Angina Pectoris in Men

Prognostic Significance of Selected Medical Factors

By Charles W. Frank, M.D., Eve Weinblatt, A.B., and Sam Shapiro, B.S.

SUMMARY

Prognosis of men whose first manifestation of coronary heart disease was angina without antecedent infarction was found to resemble closely that of men followed after an initial MI. Overall mortality over a period of 4.5 years following a baseline examination was the same in the two cohorts: 17.5%.

In both groups of men electrocardiographic abnormalities and blood pressure elevation identified subsets of coronary patients with a relatively poor prognosis, but the course of disease was apparently not influenced by the serum cholesterol level. Among the men with angina no relationship emerged between symptomatic status at time of baseline and risk of mortality in the ensuing observation period.

The findings are from the HIP (Health Insurance Plan of Greater New York) study of the incidence and prognosis of coronary heart disease, a prospective study of a general population of 110,000 men and women aged 25–64 years.

Additional Indexing Words:
Coronary heart disease Hypertension
ECG abnormalities Myocardial infarction
Serum cholesterol

A ngina is commonly the initial clinical manifestation of coronary disease. The prognosis of an individual patient soon after onset of the symptom complex is uncertain, and there is particular concern that myocardial infarction or sudden death may be impending. Information about characteristics which distinguish patients at high risk for these events is important in the clinical management of patients. In addition, the current availability of surgical approaches to myocardial revascularization raises interest in quantitative estimates concerning the prognosis of patients with angina treated nonsurgically.

This report is based on final data from the HIP CHD study, a prospective study of incidence and prognosis of coronary heart disease arising in a large, defined general population. Preliminary data on the prognosis of angina among men, covering a period of 30 months following a baseline examination, have been published. The current report will deal with prognosis of men during the first 5 years after clinical onset of angina, with emphasis on the prognostic significance of selected medical parameters.

Methods

The general population at risk for the development of angina consisted of some 110,000 men and women aged 25–64, enrolled for at least 2 years in the Health Insurance Plan of Greater New York (HIP), a prepaid comprehensive group practice plan. Patients within this population who sought medical care for symptoms suggestive of coronary disease during the 4 case-finding years, 1961–1965, were invited to the study’s baseline examination, and 90% responded. The primary source for identification of such patients was systematic scanning of all service reports routinely received from HIP family physicians and internists for a wide range of cardiovascular terminology. The diagnosis of angina was based entirely upon an assessment of a structured medical history recorded by the study’s internist at the baseline examination. Criteria, summarized in appendix A, were developed to permit a consistent weighting of the various features of the pain syndrome. Descriptions meeting these criteria would usually be considered as convincing histories of definite angina pectoris. Excluded from the angina cohort were patients with aortic valvular disease and those who had suffered a definite myocardial infarction before the baseline examination.
The diagnosis was further restricted to patients who had the syndrome for a minimum of 2 months, in order to provide sufficient time for the characteristics to be well defined and to avoid the inclusion of patients with acute preinfarction angina.

Men first meeting the study's criteria for definite angina in the 4 years of case finding (1961–1965) constitute the cohort whose prognosis is to be presented. During the same time period a myocardial infarction (MI) cohort was also developed—men under age 65 who suffered an initial MI as evidenced by defined highly specific electrocardiographic abnormalities or, alternatively, with characteristic ECG abnormalities associated with a combination of appropriate clinical symptoms and acute phase reactants. Survivors of such first attacks were invited to the study's baseline examination, and their prognosis is used as a frame of reference in presenting the current data.

For men in both the angina and infarction cohorts the baseline examination was conducted, on the average, about 6 months after diagnosis. All patients entering a prognostic cohort were scheduled for study reexamination at 6 months, 2%, and 4½ years after the baseline. Telephone interviews were carried out in the intervening years, and all medical care records were regularly abstracted. Life-table techniques were employed to compute the probabilities of first infarction (for the angina cohort) or first recurrent infarction (for the MI cohort), and of death (from all and cardiac causes) in the 4.5 years following baseline examination, taking into account the varying time periods of follow-up by the final cutoff date for patients entering the cohorts at different times. Data are complete for mortality status. In the angina cohort follow-up for occurrence of a first infarction was complete except for two men for whom this information was not available for some part of the follow-up period; similarly, information on first recurrent MI was missing for part of the follow-up period in three men in the MI cohort.

**Results**

The overall mortality experience of men in the angina and MI cohorts over the 4.5-year observation period following baseline examination is shown by age in table 1, together with corresponding data for a random sample of age-comparable men from the same population who were free of clinical evidence of heart disease at the start of observation. By the end of 4.5 years after the baseline the two male coronary cohorts exhibited identical cumulated probabilities of death—17.5 per 100 men observed. This approximates an average annual mortality of 4%, and represents an approximately threefold increase in the risk of dying in comparison with the age-comparable men initially free of CHD. The absolute risk of death was similar for the younger (under age 55 years) and older (ages 55–64 years) men with coronary heart disease. The risk relative to the non-CHD population is therefore greater for the younger men: the men under age 55 with MI or angina show about five times the risk of men in the non-CHD cohort over the 4.5 years of observation.

Observations were made uniformly at the baseline examination for all study patients. These

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**Table 1**

*Mortality over 4.5 Years among Men with and without CHD, by Age*

<table>
<thead>
<tr>
<th>Patient</th>
<th>All ages</th>
<th>Under 55 yr</th>
<th>55–64 yr</th>
<th>All ages</th>
<th>Under 55 yr</th>
<th>55–64 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men examined after first CHD manifestation*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>275</td>
<td>120</td>
<td>155</td>
<td>0.175</td>
<td>0.169</td>
<td>0.179</td>
</tr>
<tr>
<td>MI</td>
<td>470</td>
<td>242</td>
<td>228</td>
<td>0.175</td>
<td>0.147</td>
<td>0.204</td>
</tr>
<tr>
<td>Combined CHD cohorts</td>
<td>745</td>
<td>362</td>
<td>383</td>
<td>0.175</td>
<td>0.154</td>
<td>0.194</td>
</tr>
<tr>
<td>Men free of CHD at first observation†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Non-CHD” cohort</td>
<td>2443</td>
<td>1167</td>
<td>1276</td>
<td>0.048</td>
<td>0.026</td>
<td>0.067</td>
</tr>
</tbody>
</table>

*Numbers shown for the CHD cohorts are men who received a baseline examination at an average interval of 6 months after first MI or first diagnosis of angina without prior MI in the years 1961–1965. Follow-up period after the baseline examination ranged from 2.5 to 4.5 years. Of the men in the angina cohort 156 were observed for the full 4.5 years, 79 for 3.5 years, and 40 for 2.5 years; of those in the MI cohort 248 were observed the full 4.5 years, 116 for 3.5 years, and 106 for 2.5 years. Experience of early and late entrants into the cohorts — defined as those observed for the full 4.5 years and those observed for less than that time — was similar during the first 2.5 years of observation. Thus in the angina cohort the cumulative probability of death within 2.5 years of the baseline examination was 0.108 for the early entrants and 0.103 for the late entrants; corresponding probabilities for death from cardiac causes were 0.077 and 0.070, and for first MI 0.129 and 0.106 for the early and late entrants, respectively.*

†The non-CHD cohort consists of a random sample of men enrolled in HIP of ages comparable to the men with CHD. To develop this comparison group a subsample was drawn of men who responded to mail surveys conducted to obtain characteristics of the population at risk for incidence of CHD in April of each of the years 1962, 1963, and 1964. The men in this subsample, free of CHD at initial observation, were resurveyed in October 1966. The resurvey provided information on mortality status for 99% of the men, and a 95% response of those living at the time of resurvey was obtained. Of the men initially free of CHD, 883 were available for a 4.5-year follow-up for mortality, 670 for 3.5 years, and 890 for 2.5 years.

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included a casual blood pressure reading, a 12-lead electrocardiogram (with the patient at rest), and a serum cholesterol determination. Among the men—both in the angina and the MI cohorts—two of these observations provided a basis for classifying the patients into subsets with very different subsequent courses. Both an abnormal electrocardiogram and "elevated blood pressure" defined groups of coronary patients with a relatively poor prognosis, but the prognosis over the 4.5-year observation period was unrelated to the level of serum cholesterol.

Table 2 presents prognostic data in relation to the baseline ECG findings. ECGs meeting any of the study's defined abnormal categories are here categorized as "abnormal," while normal records or those with nonspecified abnormalities are classified as "not abnormal." Among the men in the angina cohort the abnormalities encountered most frequently were horizontal depressions of the S-T segment of 0.05 mv or greater, or T-wave inversion of 0.1 mv or greater in leads I, II, V₅, or V₆. All patients in the MI cohort had abnormal ECGs at the time of the acute episode. About one fourth of the survivors of their initial MI exhibited a reversion to normal or near-normal tracings by the time of the baseline examination at an average elapsed time of 6 months from the date of diagnosis.

Probability of death—from all causes and from cardiac causes only—within the 4.5 years for men in the angina cohort with an abnormal ECG was twice that of the men without ECG abnormalities as defined. These differentials were even more pronounced among the MI men, where the probability of death from any cause among the men with abnormal ECGs was more than three times that of the other men, and the probability of cardiac death more than six times that of men without abnormal ECGs. In contrast, no important difference in probability of a first MI among the men with angina, or of a first recurrent MI among the men in the MI cohort, is found in relation to the ECG classification at the baseline examination. Since it is technically more difficult to recognize the development of a new infarction when the baseline ECG is abnormal, the failure to find an increased risk of infarction among such men may result from this technical bias.

Hypertension is strongly associated with an unfavorable prognosis for men with angina or recent infarction (table 3). Systolic levels of 160+ or diastolic of 95+ at the baseline examination or documentation from medical records of the patients prior to the baseline of similar levels produced a classification of "elevated blood pressure." These hypertensive men in both the angina and MI cohorts were at higher risk for mortality and for myocardial infarction over the 4.5 years following baseline examination.

Men in the combined CHD cohorts have been cross classified with respect to both ECG findings and blood pressure in table 4. It is seen that the risk of death, especially cardiac death, was higher among men with an abnormal ECG whether the blood pressure was elevated or not. An elevated blood pressure was associated with a higher mortality risk and with a higher risk for MI (first or first recurrence) among men with an abnormal electrocardiogram.

Table 2

<table>
<thead>
<tr>
<th>ECG classification</th>
<th>No. examined at baseline</th>
<th>Cumulative probability in 4.5 years after baseline of</th>
<th>Deaths</th>
<th>Cardiac</th>
<th>First MI or first recur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>275</td>
<td>0.175</td>
<td>0.120</td>
<td>0.188</td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>98</td>
<td>0.271</td>
<td>0.195</td>
<td>0.219</td>
<td></td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>177</td>
<td>0.123</td>
<td>0.060†</td>
<td>0.171</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>470</td>
<td>0.175</td>
<td>0.153</td>
<td>0.243</td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>364</td>
<td>0.208</td>
<td>0.189</td>
<td>0.248</td>
<td></td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>105</td>
<td>0.060†</td>
<td>0.029</td>
<td>0.229</td>
<td></td>
</tr>
<tr>
<td>Combined CHD cohorts</td>
<td>745</td>
<td>0.175</td>
<td>0.141</td>
<td>0.222</td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>462</td>
<td>0.221†</td>
<td>0.190</td>
<td>0.242</td>
<td></td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>282</td>
<td>0.101</td>
<td>0.062†</td>
<td>0.192</td>
<td></td>
</tr>
</tbody>
</table>

*†‡; Confidence levels in tests of statistical significance of the difference between two cumulative probabilities are noted by * for 0.99, † for 0.95, and ‡ for 0.90. All cumulative probabilities in this and subsequent tables are based on observed data; age adjustment produced only trivial changes in the rates.

Circulation, Volume XLVII, March 1973
Table 3

Prognosis of Men following First Diagnosis of Angina or First MI, by Blood Pressure Classification

<table>
<thead>
<tr>
<th>Blood pressure classification</th>
<th>No. examined at baseline</th>
<th>Cumulative probability in 4.5 years after baseline of</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All</td>
<td>Cardiac</td>
<td>First MI or first recur</td>
</tr>
<tr>
<td>Angina</td>
<td>275</td>
<td>0.175</td>
<td>0.120</td>
<td>0.188</td>
</tr>
<tr>
<td>Blood pressure elevated</td>
<td>99</td>
<td>0.271*</td>
<td>0.159</td>
<td>0.263†</td>
</tr>
<tr>
<td>Blood pressure not elevated</td>
<td>176</td>
<td>0.128*</td>
<td>0.098</td>
<td>0.130†</td>
</tr>
<tr>
<td>MI</td>
<td>470</td>
<td>0.175</td>
<td>0.133</td>
<td>0.243</td>
</tr>
<tr>
<td>Blood pressure elevated</td>
<td>157</td>
<td>0.290†</td>
<td>0.263</td>
<td>0.305†</td>
</tr>
<tr>
<td>Blood pressure not elevated</td>
<td>313</td>
<td>0.118*</td>
<td>0.102†</td>
<td>0.214‡</td>
</tr>
<tr>
<td>Combined CHD cohorts</td>
<td>745</td>
<td>0.175</td>
<td>0.141</td>
<td>0.222</td>
</tr>
<tr>
<td>Blood pressure elevated</td>
<td>256</td>
<td>0.287*</td>
<td>0.227*</td>
<td>0.290*</td>
</tr>
<tr>
<td>Blood pressure not elevated</td>
<td>489</td>
<td>0.121*</td>
<td>0.101*</td>
<td>0.191*</td>
</tr>
</tbody>
</table>

*, †, ‡ Confidence levels in tests of statistical significance of the difference between two cumulative probabilities are noted by * for 0.99, † for 0.95, and ‡ for 0.90.

The data in table 5 indicate that the hypercholesterolemic men in neither the angina nor MI cohort were observed to be at increased risk for death or infarction during this observation period. Nor could a disadvantage in relation to serum cholesterol level be demonstrated by using different cutting points for the cholesterol classification or by cross classification with regard to age, blood pressure, or ECG findings.

The possible relationship of symptomatic status to prognosis of men with angina is examined in two ways in table 6. Men who reported their anginal symptoms as occurring relatively more frequently or as induced by relatively less apparent effort (class 1 chest pain) were at no greater risk for mortality or for a first infarction than the other men. Nor was there a difference in risk of death or of first MI over a 4-year observation period between those men who were free of angina in the 6 months following baseline examination and those who reported themselves as symptomatic in this time interval.

Discussion

The overall mortality experience of the men in the HIP angina and MI cohorts is similar to that reported recently by Kannel and Feinleib from the Framingham study. Their analysis of survival, based on 65 men with "uncomplicated" angina and 40 men with "complicated" angina (the latter defined as persons having angina contiguously with a myocardial infarction) produced an estimate of a

Table 4

Prognosis of Men following First Diagnosis of Angina or First MI, by ECG and Blood Pressure Classifications

<table>
<thead>
<tr>
<th>Blood pressure and ECG classification</th>
<th>No. examined at baseline</th>
<th>Cumulative probability in 4.5 years after baseline of</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All</td>
<td>Cardiac</td>
<td>First MI or first recur</td>
</tr>
<tr>
<td>Combined CHD cohorts</td>
<td>745</td>
<td>0.175</td>
<td>0.141</td>
<td>0.222</td>
</tr>
<tr>
<td>Blood pressure elevated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>170</td>
<td>0.360*</td>
<td>0.316*</td>
<td>0.318</td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>86</td>
<td>0.151*</td>
<td>0.063*</td>
<td>0.238</td>
</tr>
<tr>
<td>Blood pressure not elevated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>292</td>
<td>0.149†</td>
<td>0.129†</td>
<td>0.203</td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>196</td>
<td>0.080†</td>
<td>0.060†</td>
<td>0.173</td>
</tr>
<tr>
<td>Blood pressure elevated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>170</td>
<td>0.360*</td>
<td>0.316*</td>
<td>0.318</td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>292</td>
<td>0.149†</td>
<td>0.129†</td>
<td>0.203‡</td>
</tr>
<tr>
<td>Blood pressure not elevated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>86</td>
<td>0.151</td>
<td>0.063</td>
<td>0.238</td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>196</td>
<td>0.080</td>
<td>0.060</td>
<td>0.173</td>
</tr>
</tbody>
</table>

*, †, ‡ Confidence levels in tests of statistical significance of the difference between two cumulated probabilities are noted by * for 0.99, † for 0.95, and ‡ for 0.90.
4% mortality per year, whether the angina arose de novo or in conjunction with a myocardial infarction. Both the Framingham and HIP studies were designed to identify all cases arising in a general population, and similarities in the findings have previously been noted with respect to incidence of specified CHD manifestations. Earlier reports on angina from the Mayo clinic and the 25-year follow-up of Richards, Bland, and White noted a somewhat less favorable prognosis. A higher mortality in a hospital-based series might reasonably be related to the conditions which led to hospitalization; since patients are rarely hospitalized for angina, such a series is likely to be unrepresentative of angina as it arises in a general population. In comparison with the HIP angina cohort, these earlier studies also included older patients, patients who had been symptomatic for longer periods of time before coming under observation, and patients whose angina was associated with prior myocardial infarctions, cardiac enlargement, and congestive heart failure.

There is a well-established association between increased risk for incidence of coronary heart disease in general populations and elevated serum cholesterol levels. However, convincing evidence to prove hypotheses assuming a parallel relationship of lipid levels to prognosis among men with clinically manifest coronary disease is still not available. Among observational and intervention studies both negative and positive results have been reported on the issue of whether relatively low levels of serum lipids are associated with improved prognosis of patients with atherosclerotic disease.

### Table 5

**Prognosis of Men following First Diagnosis of Angina or First MI, by Serum Cholesterol Classification**

<table>
<thead>
<tr>
<th>Cholesterol level*</th>
<th>No. examined at baseline</th>
<th>Cumulated probability in 4.5 years after baseline of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All</td>
<td>Cardiac</td>
</tr>
<tr>
<td>Angina</td>
<td>275</td>
<td>0.175</td>
<td>0.120</td>
</tr>
<tr>
<td>Cholesterol 270+</td>
<td>59</td>
<td>0.157</td>
<td>0.137</td>
</tr>
<tr>
<td>Cholesterol under 270</td>
<td>204</td>
<td>0.182</td>
<td>0.114</td>
</tr>
<tr>
<td>MI</td>
<td>470</td>
<td>0.175</td>
<td>0.153</td>
</tr>
<tr>
<td>Cholesterol 270+</td>
<td>108</td>
<td>0.142</td>
<td>0.115</td>
</tr>
<tr>
<td>Cholesterol under 270</td>
<td>329</td>
<td>0.170</td>
<td>0.152</td>
</tr>
<tr>
<td>Combined CHD cohorts</td>
<td>745</td>
<td>0.175</td>
<td>0.141</td>
</tr>
<tr>
<td>Cholesterol 270+</td>
<td>167</td>
<td>0.147</td>
<td>0.122</td>
</tr>
<tr>
<td>Cholesterol under 270</td>
<td>533</td>
<td>0.175</td>
<td>0.137</td>
</tr>
</tbody>
</table>

*Cholesterol measured in mg/ml. Tests of statistical significance of the difference between cumulative probabilities for the two cholesterol classes in no case reached a confidence level of 0.90.

### Table 6

**Prognosis of Men following First Diagnosis of Angina, by Symptomatic Classifications**

<table>
<thead>
<tr>
<th>Symptomatic status</th>
<th>No. examined at baseline</th>
<th>Cumulated probability in 4.5 years after baseline of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All</td>
<td>Cardiac</td>
</tr>
<tr>
<td>“Class 1” chest pain*</td>
<td>155</td>
<td>0.165</td>
<td>0.108</td>
</tr>
<tr>
<td>All other classified chest pain</td>
<td>119</td>
<td>0.188</td>
<td>0.134</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptomatic status</th>
<th>No. examined at first follow-up</th>
<th>Cumulated probability in 4.5 years from 6 mo postbaseline of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>All</td>
<td>Cardiac</td>
</tr>
<tr>
<td>Angina reported in 6 mo following baseline</td>
<td>164</td>
<td>0.133</td>
<td>0.092</td>
</tr>
<tr>
<td>No angina in 6 mo following baseline</td>
<td>94</td>
<td>0.190</td>
<td>0.127</td>
</tr>
</tbody>
</table>

*“Class 1” refers to patients with angina reported as occurring more frequently than once a week in the month before baseline and/or usually induced by less than two flights of stairs or walking less than four blocks at normal pace.
The 4.5-year follow-up data here presented confirm previously reported findings from the HIP study showing no apparent disadvantage associated with elevated serum cholesterol levels among men with either first MI or angina without antecedent MI. The Canadian studies by Shanoff et al. of male MI survivors followed over a 10-year period have similarly found no relationship between survival and serum lipid level. Several clinical trials of lipid-lowering drugs have reported the experience of men treated only with placebos in relation to their initial serum cholesterol level. In the Scottish clofibrate trial almost identical rates of “events” over a 6-year period were experienced by men with a high serum cholesterol (over 260 mg/ml) and those with lower values (260 or less) both among the men who had had a first MI and those who had presented with angina. In the similar clofibrate trial in Newcastle-upon-Tyne, however, the placebo-treated men with initial cholesterol exceeding 260 mg/ml showed somewhat higher rates of “events” over the 5-year observation period than the comparable men with initial cholesterol levels of 260 or less. In both these studies it was pointed out by the authors that the protective action of the clofibrate against new infarcts and death bore no apparent relation to the cholesterol- and triglyceride-reducing properties of the drug. But recently presented data for placebo-treated men from the Coronary Drug Project show a somewhat lower mortality over an average follow-up period of 3 years among men with initial cholesterol less than 250 mg/ml (11.5%) than among those with higher levels (14.7%).

It is plausible to suggest that the level of serum cholesterol in a general population reflects the amount of arterial fatty streaking and atheroma formation which leads ultimately to fibrous plaque formation. The continued growth of these plaques—with formation of excess fibromuscular scar, calcification, cracking of the intima, extrusion of contents, subintimal hemorrhage, platelet aggregation, and intraluminal thrombosis—may lead to progressive coronary artery occlusion without relation to the general or local lipid metabolism or serum cholesterol level. Hyperlipidemia undoubtedly favors the initiating steps leading to vascular atheromatosis and fibrous plaques, but other factors may become more relevant to the subsequent progression of these lesions.

Hypertension may represent one type of vascular stress that accelerates degenerative processes in the arteriosclerotic plaques of men with coronary disease. Hypertension also represents an increased “afterload” to the left ventricle and leads to myocardial hypertrophy. Both these circumstances contribute to an increased requirement for coronary blood flow. The necessity for increased coronary flow, coupled with accelerated disease of the coronary arteries, may explain in part the relatively poor prognosis of hypertensive men with CHD, noted here and previously from the HIP study. It must be emphasized that the findings here reported on prognosis with respect to serum cholesterol and elevated blood pressure are for men surviving a first MI or diagnosis of angina. The prognosis of women with such newly diagnosed coronary heart disease in relation to blood pressure and cholesterol levels is quite different. Neither is it possible to draw any conclusions from these observations about any potential benefits which might result from the treatment of elevated blood pressure in men with coronary disease.

Electrocardiographic findings at the baseline examination were of great prognostic significance. Both in the angina and MI cohorts the men with specified ECG abnormalities showed three times the risk of cardiac death found among the other men over the 4.5 years of observation. It is likely that the presence of an abnormal ECG in a coronary population identifies patients with relatively more extensive pathology. Horizontal depressions of the S-T segment may imply persisting ischemia, presumably from more extensive obstruction to coronary blood flow. Other abnormalities, such as T-wave inversions, may reflect myocardial damage not specific enough for a diagnosis of infarction but sufficiently important to influence prognosis. In this connection it is of interest that a recent analysis of the men in the placebo group of the Coronary Drug Project noted among these 2789 MI survivors followed for an average period of 30 months that of 100 baseline variables the one showing the largest independent association with total mortality was S-T-segment depression. In the HIP experience here presented (table 2) mortality risk among men with abnormal ECGs was more than twice that of the other men in the angina cohort and more than three times that of men without abnormal ECGs in the MI cohort. The HIP angina cohort excluded patients with a history of or with definite ECG evidence of myocardial infarction. The S-T and T-wave abnormalities in this population were nevertheless associated with a
distinctly adverse prognosis whether or not hypertension was present. The combination of elevated blood pressure and an abnormal ECG was associated with a particularly poor prognosis.

These findings may be relevant to current concerns about selection of patients for surgical therapy of coronary heart disease. Table 7 presents a prognostic classification of the total 745 male coronary patients based upon the ECG and blood pressure findings. Almost one fourth (23%) of the men had both an abnormal ECG and an elevated blood pressure; the probability of cardiac death over the 4.5 years of observation for these men was 32 of 100. In contrast, slightly over one fourth (26%) of the men with coronary heart disease of recent origin were free of hypertension and did not show an abnormal ECG at baseline. For them the 4.5-year probability of cardiac death was only six of 100. Thus half of this study population—readily identified by simple, noninvasive technics—could be classified into groups with very different prognosis. Since the total 4.5-year mortality of the “low-risk” group approximates that to be expected as an immediate operative mortality during coronary bypass surgery, and since any reduction in mortality risk associated with successful surgery of this type has yet to be demonstrated, it is not reasonable to attempt to prove surgical benefit in patients of this type. It is of importance also that the overall mortality experience of the “low-risk” men in the coronary cohorts (ECG not abnormal and blood pressure not elevated) is only moderately higher than that of an age-comparable random sample of men from the same general population who were initially free of recognized heart disease at the start of the 4.5-year observation period (eight of 100 compared with five of 100).

In contrast, the fourth of the patients defined as at “high risk”—with an estimated probability of cardiac death in 32 of 100 over the 4.5 years—might well constitute an appropriate group for further clinical investigation and intervention trials. The mortality experience is high enough to justify offering newer, promising though unproven, therapeutic approaches irrespective of the symptomatic status of such patients. It is most disappointing to clinicians to note (table 6) that patients who might appear to be “doing well” in regard to their angina symptoms are not necessarily “doing well” in regard to their risk of infarction and death, and that patients with relatively frequent anginal attacks (or attacks produced by relatively little effort) are not found to be at higher mortality risk than less symptomatic patients. If patients with “stable” angina are referred for angiographic studies and surgical intervention primarily to reduce their risk of infarction and death, the initial screening to select such patients might more justifiably be related to risk categories defined in terms of ECG and blood pressure findings rather than to symptomatic status.

Appendix A

Criteria for Diagnosis of Angina

All persons who had never met the study criteria for MI and who were free of aortic valvular disease were considered to be at risk for a first diagnosis of angina. A diagnosis of angina was made only for patients who had the baseline examination, during which the study’s examining physician recorded the details of any complaint of chest pain on a highly structured form. To achieve the greatest possible consistency in deciding on borderline histories a scoring system, described in table A, was applied to all evaluated patients. A net score exceeding 10 was required for a diagnosis of definite angina, and only such patients are included in this report. Only those symptom patterns

Table 7

<table>
<thead>
<tr>
<th>ECG and blood pressure classification</th>
<th>No. of men</th>
<th>% of total</th>
<th>Cumulated probability of cardiac death within 4.5 yr after baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined CHD cohorts</td>
<td>745</td>
<td>100.0</td>
<td>0.141</td>
</tr>
<tr>
<td>“High risk”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG abnormal</td>
<td>462</td>
<td>62.0</td>
<td>0.190</td>
</tr>
<tr>
<td>Blood pressure elevated</td>
<td>256</td>
<td>34.4</td>
<td>0.227</td>
</tr>
<tr>
<td>Both ECG abnormal and BP elevated</td>
<td>170</td>
<td>22.8</td>
<td>0.316</td>
</tr>
<tr>
<td>“Low risk”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG not abnormal</td>
<td>282</td>
<td>37.9</td>
<td>0.062</td>
</tr>
<tr>
<td>Blood pressure not elevated</td>
<td>489</td>
<td>65.6</td>
<td>0.101</td>
</tr>
<tr>
<td>Neither abnormal ECG nor elevated BP</td>
<td>196</td>
<td>26.3</td>
<td>0.060</td>
</tr>
</tbody>
</table>

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### Table A

**Scoring of Elements of the Angina History**

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td></td>
</tr>
<tr>
<td>Subternal</td>
<td>+3</td>
</tr>
<tr>
<td>Precordial</td>
<td>+2</td>
</tr>
<tr>
<td>Left chest, base of neck, lower jaw, epigastrium</td>
<td>+1</td>
</tr>
<tr>
<td><strong>Radiation</strong></td>
<td></td>
</tr>
<tr>
<td>Either arm</td>
<td>+2</td>
</tr>
<tr>
<td>Shoulder, back, neck, lower jaw (arm not mentioned)</td>
<td>+1</td>
</tr>
<tr>
<td><strong>Character</strong></td>
<td></td>
</tr>
<tr>
<td>Crushing, pressing, squeezing</td>
<td>+3</td>
</tr>
<tr>
<td>Heaviness or tightness</td>
<td>+2</td>
</tr>
<tr>
<td><strong>Severity</strong></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>+2*</td>
</tr>
<tr>
<td>Moderate</td>
<td>+1*</td>
</tr>
<tr>
<td><strong>Relationship to effort</strong></td>
<td></td>
</tr>
<tr>
<td>Precipitated by effort and response is consistent</td>
<td>+3</td>
</tr>
<tr>
<td>Usually but not always related to effort</td>
<td>+1</td>
</tr>
<tr>
<td><strong>Other precipitants</strong></td>
<td></td>
</tr>
<tr>
<td>Emotion</td>
<td>+1</td>
</tr>
<tr>
<td>Cold weather</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Usual duration</strong></td>
<td></td>
</tr>
<tr>
<td>1–4 min</td>
<td>+3†</td>
</tr>
<tr>
<td>5–10 min</td>
<td>+2</td>
</tr>
<tr>
<td><strong>Relief by rest</strong></td>
<td></td>
</tr>
<tr>
<td>Yes, in 5 min or less</td>
<td>+2</td>
</tr>
<tr>
<td>No, no further information</td>
<td></td>
</tr>
<tr>
<td><strong>Relief by NTG</strong></td>
<td></td>
</tr>
<tr>
<td>Yes, in less than 5 min</td>
<td>+5</td>
</tr>
<tr>
<td>Yes, in 5–10 min</td>
<td>+3</td>
</tr>
<tr>
<td><strong>Relief by other</strong></td>
<td></td>
</tr>
<tr>
<td>Improved with long-acting nitrates</td>
<td>+1</td>
</tr>
<tr>
<td>Relieved by antacids</td>
<td></td>
</tr>
</tbody>
</table>

*Score is entered for severity only if some positive score has been entered for location, radiation, or character.
†Fleeting pain, characterized as lasting only for seconds, produces no score.
‡Only the single highest negative score from these items is tallied.
§If "no relief by rest" seems clearly related to the fact that the patient always takes NTG, no negative score is applied here.
described as occurring over a period of 2 months or more were classified as angina, provided the scoring requirements were met. The 2-month requirement was adopted in order for a reasonable time to have elapsed to establish the usual precipitants, duration, and pattern of response to rest and drugs, and in order to avoid including in the angina cohort both patients with preinfarction prodromes and those with spontaneous remissions after one or two episodes. It is to be noted that the final decision to classify a patient as new angina was made centrally by the study's medical director on the basis of the scored chest pain history recorded at the baseline examination; the decision was made solely from the evaluation of the history, without relation to the ECG findings at rest or after exercise, to the coexistence of any other evidence of CHD, or to the expressed opinion of the examining physician.

Through the cooperation of Dr. Thomas Dawber and Dr. Joseph Doyle, the investigators examining patients in the Framingham and Albany studies of cardiovascular disease completed HIP angina history forms on a series of their patients with chest pain. Application of the HIP scoring system to these histories produced a high concordance of classification: 17 of 18 patients with scores in the "definite" range were considered to have definite angina by these examining physicians. Conversely, 17 of the 18 patients considered to have definite angina by these investigators scored for definite angina with the HIP classification device.

References

