Prognosis of Men with Coronary Heart Disease as Related to Blood Pressure

By CHARLES W. FRANK, M.D., D.MED.SCI., EVE WEINBLATT, A.B., SAM SHAPIRO, B.S., AND ROBERT V. SAGER, M.D.

SUMMARY

Hypertension prior to the onset of the initial myocardial infarction in men is associated with an excess early mortality rate: among men with elevated blood pressure the proportion dead within 1 month is more than twice that found among normotensive men with a first infarction. Hypertensives who survive the acute attack show twice the risk of recurrence and more than five times the risk of cardiac death over the next several years in comparison with men with normal blood pressure prior to infarction.

Among men whose first clinical evidence of coronary disease is angina pectoris, those with an elevated blood pressure have two and one half times the likelihood of experiencing a first myocardial infarction and cardiac death within a follow-up period of 30 months.

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

Additional Indexing Words:
Myocardial infarction Angina pectoris Hypertension

SYSTEMIC arterial hypertension has long been recognized as a factor which stresses portions of the cardiovascular system. Studies of different human populations have shown that individuals with relatively high levels of blood pressure are more apt than other individuals to develop cardiovascular disease and to manifest such disease at a relatively young age.¹² This report deals with the prognosis of men from the time of the initial clinical diagnosis of angina pectoris or myocardial infarction and examines the extent to which hypertensives exhibit a less favorable course in comparison with men of the same age who had lower levels of blood pressure.

The data are from the Coronary Heart Disease Study conducted by the Health Insurance Plan (HIP) of Greater New York. The general study population consists of about 110,000 adults, aged 25 to 64 years, who were members of participating HIP medical groups and had been in the Plan for at least 2 years. The study was designed to identify all patients within this population who developed certain clinical manifestations of coronary heart disease over a case finding period of 4 years, starting November 1, 1961.

Methods

The details of the study methodology and criteria have been published.⁵⁶ In brief, patients are invited to attend a special study examination (referred to as the "base line") whenever the medical records suggest the development of coronary heart disease. In addition to the data obtained at this examination, all medical records (in and outpatient) are abstracted. Next of kin interviews, death certificates and autopsy reports are also obtained. Patients satisfying the study's criteria for the development of a new manifestation of coronary heart disease

Circulation, Volume XXXVIII, August 1968
enter one of the several study cohorts that are being followed prospectively.

This report is limited to two groups of men, one with angina and the other with a first myocardial infarction. The angina cohort consists of all men from the entire population at risk who developed angina pectoris without prior myocardial infarction during the study's 4 years of case finding. Excluded from this cohort were those patients who had evidence of aortic valvular disease and those who experienced a definite myocardial infarction after the onset of angina but before the base-line examination. The diagnosis of angina was based entirely upon the characteristics of the pain pattern as recorded by the study's internist at the base-line examination. Those elements which are normally assessed in the clinical diagnosis of angina were weighed in a standardized fashion which has been described. The angina cohort here reported upon is restricted to men in whom this assessment was considered sufficiently characteristic to warrant the designation "definite" angina. The cohort is further limited to men whose symptoms had lasted more than 2 months, in order to permit sufficient time for characterization of the symptom complex, as well as to avoid confusion with "pre-infarction syndrome."

The myocardial infarction (MI) cohort consists of all men who experienced their initial clinical episode of myocardial infarction in the 4 years of case finding. The diagnosis of myocardial infarction was based upon classic ECG abnormalities or upon the combination of characteristic symptoms, clinical and laboratory findings, plus less specific ECG abnormalities. Patients dying prior to clinical evaluation under defined circumstances suggesting that death was due to an initial "new coronary event" are included in this MI cohort.

All surviving patients in both the angina and MI cohorts are reexamined 6 months after the base-line examination and at biennial intervals thereafter. Telephone interviews are conducted in the intervening years.

**Blood Pressure Classification**

**Angina Cohort**

The blood pressure classification for the angina cohort was based on the initial casual blood pressure recorded at the base-line examination. An elevated blood pressure is defined as a systolic reading of 160 mm Hg or greater or a diastolic reading of 95 or greater, or both.

**Myocardial Infarction Cohort**

To characterize the blood pressure level of men prior to their first myocardial infarction, a combination of medical record information and patient history was utilized. Patients for whom three or more casual blood pressure determinations were recorded in the HIP medical charts (not during any hospitalization) with systolic levels of 160 mm Hg or greater, or diastolic levels of 95 or greater, or both, were classified as having elevated blood pressure. If only one or two elevated readings were noted, the blood pressure was classified as elevated only if in addition a diagnosis of hypertension was indicated on the medical record or if left ventricular hypertrophy was in evidence on the ECG.

Patients were classified as normal with respect to blood pressure if the systolic pressure was recorded as under 140 mm Hg and the diastolic as under 90 on one or more occasions, provided no higher levels of blood pressure were recorded, and no history of hypertension was noted in the chart. For patients with no blood pressure readings recorded prior to the MI, a classification of normal blood pressure was made if there was a denial of hypertension by history and the base-line reading was under 160 mm Hg systolic and under 95 diastolic.

Patients with blood pressure findings not meeting the definition of "elevated" or "normal" were classified as borderline.

**Results**

**Angina Pectoris**

In the 4 years of case finding, ending October 31, 1965, 275 men were identified as having developed angina pectoris in the apparent absence of myocardial infarction or valvular heart disease. These men reached the base-line examination relatively early in the course of disease. Nearly half had been symptomatic for 6 months or less, and four out of five for 12 months or less.

The prognosis for this group of men in the 2.5 years following the base-line examination is presented in Table 1 in terms of the probability of experiencing an initial myocardial infarction and cardiac death. The probability

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*These probabilities, cumulated over three time intervals, were computed by standard life table techniques. At the cut-off date for the observations included in this report (May 1, 1967), the men in the angina cohort had been followed for differing periods of time. Information on the first interval of 6 months following the base line was available on the entire cohort; 87% were under observation during the next interval of 12 months; the final 12-month interval was applicable to 60% of the cohort. Observations on mortality and on the occurrence of a first MI were complete in all men due to a given examination or interview.
Table 1
Probability of First Myocardial Infarction and of Cardiac Death Within 30 Months of Base-line Examination, by Age and Blood Pressure Category: Men Followed for Prognosis of Angina

<table>
<thead>
<tr>
<th>Blood pressure category at base line</th>
<th>No. examined at base line</th>
<th>No. experiencing given event within 30 months per 100 examined</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>First MI</td>
</tr>
<tr>
<td>Total cohort</td>
<td>275</td>
<td>12.5</td>
</tr>
<tr>
<td>Age at base line</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 55 yr</td>
<td>120</td>
<td>10.0</td>
</tr>
<tr>
<td>55 yr and over</td>
<td>155</td>
<td>14.4</td>
</tr>
<tr>
<td>Blood pressure at base line*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated</td>
<td>73</td>
<td>24.0)†</td>
</tr>
<tr>
<td>Not elevated</td>
<td>202</td>
<td>8.7†</td>
</tr>
<tr>
<td>Age-adjusted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated</td>
<td>73</td>
<td>21.6)†</td>
</tr>
<tr>
<td>Not elevated</td>
<td>202</td>
<td>8.7)†</td>
</tr>
</tbody>
</table>

*An elevated blood pressure at the base-line examination is defined as a casual reading of 160+ mm Hg systolic or 95+ mm Hg diastolic.

Note: Confidence levels in tests of statistical significance between two rates are noted by † for 0.95 and ‡ for 0.90.

Table 2
Mortality among Men in the Month Following First Myocardial Infarction, by Age and Blood Pressure Category: Men Followed from Diagnosis of First Myocardial Infarction

<table>
<thead>
<tr>
<th>Blood pressure category</th>
<th>No. of patients</th>
<th>% Dead in 1 month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All ages</td>
<td>Age at diagnosis (yr)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 45</td>
</tr>
<tr>
<td>Total</td>
<td>881</td>
<td>99</td>
</tr>
<tr>
<td>Blood pressure*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated</td>
<td>223</td>
<td>13</td>
</tr>
<tr>
<td>Other known</td>
<td>551</td>
<td>73</td>
</tr>
<tr>
<td>Borderline</td>
<td>268</td>
<td>26</td>
</tr>
<tr>
<td>Normal</td>
<td>283</td>
<td>47</td>
</tr>
</tbody>
</table>

*The blood pressure classification is described under “Methods.” Omitted from the table are 107 men with first MI for whom there was insufficient information to categorize blood pressure as of date of MI. The most common situation in which the blood pressure could not be classified arose from men who died suddenly under circumstances meeting the study criteria for “new coronary events leading to death” for whom no prior medical records containing blood pressure information could be located. Thus 67 of the 107 men were dead within 1 month of their first MI.

†Confidence level in test of statistical significance between the two rates is 0.99.

of initial infarction for the entire cohort within this 30-month period is 12.5%, and that of cardiac death 7.5%. Men aged 55 years and over appear to be at somewhat higher risk for these events than those under 55, but at this stage of the study the difference is not statistically significant.

The blood pressure classification, adjusted for age, bore a striking relationship to the prognosis. Approximately one fourth of the men in the angina cohort had a systolic level of 160 mm Hg or greater or a diastolic level of 95 or greater, or both, on casual examination. Over the next 30 months these men have two and one half times the probability of a first MI or cardiac death shown by the men with lower levels of blood pressure. (See age-adjusted rates in table 1.)

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Table 3
Probability of First Recurrent Myocardial Infarction and of Cardiac Death within 4.5 Years of Initial Infarction, by Age and Blood Pressure Category: Men Followed from 1 Month after First Myocardial Infarction

<table>
<thead>
<tr>
<th></th>
<th>No. alive 1 month post MI</th>
<th>No. experiencing given event 1 month after 1st MI</th>
<th>Age-adjusted rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>within 4.5 yr/100 men alive</td>
<td></td>
</tr>
<tr>
<td>Total cohort</td>
<td>564</td>
<td>25.0</td>
<td>15.9</td>
</tr>
<tr>
<td>Age at 1st MI (yr)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 45</td>
<td>74</td>
<td>19.6</td>
<td>11.7</td>
</tr>
<tr>
<td>45-54</td>
<td>231</td>
<td>23.1</td>
<td>15.5</td>
</tr>
<tr>
<td>55-64</td>
<td>259</td>
<td>28.2</td>
<td>17.4</td>
</tr>
<tr>
<td>Blood pressure as of time of MI*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated</td>
<td>126</td>
<td>44.2†</td>
<td>35.9†</td>
</tr>
<tr>
<td>Other‡</td>
<td>438</td>
<td>19.7†</td>
<td>10.5†</td>
</tr>
<tr>
<td>Borderline</td>
<td>171</td>
<td>20.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Normal</td>
<td>227</td>
<td>19.1</td>
<td>6.5</td>
</tr>
</tbody>
</table>

*The blood pressure classification is described under “Methods.”
†Confidence level in test of statistical significance between the two rates is 0.99.
‡Included are 40 men whose blood pressure as of time of MI was unclassified.

Myocardial Infarction
Early Mortality

Of the 881 men who experienced a first MI in the 4 years of case finding, 36% were dead within 1 month of onset. This early mortality rate is similar to that found in other population studies which use periodic examinations of the entire population to locate new cases.5, 6 The early mortality increased with age, from 25% among men under age 45 to 42% of those aged 55 to 64 years (table 2). Among the 601 men who were hospitalized with their first infarction, early mortality was about half that shown for the entire cohort (17%). A parallel increase with age also appeared among the hospitalized men, from 10% among men under 45 years of age to 23% of those aged 55 to 64 years.

Hypertension prior to the onset of a first MI is associated with substantially increased risk of death with the acute episode (table 2). The disadvantage for the hypertensive men is exhibited within each age group, and is especially pronounced among men under 55 years of age. When the data are compared following adjustment for age, the early mortality rate for men with elevated blood pressure is twice that for men considered to have had normal blood pressure prior to infarction (43 and 21%, respectively).

One-Month Survivors

Among men still alive 1 month after their initial MI, the probabilities of experiencing a second infarction and of cardiac death within the period ending 4.5 years from initial MI were computed* (table 3). Twenty-five per cent of the 1-month survivors can be expected to experience a second MI, and 16% can be expected to die of cardiac disease within this time period. These probabilities are lower for men under 45 years of age at the time of initial infarction than for older men, and the data with respect to hypertension have therefore been age-adjusted.

The blood pressure classification, which was based upon information recorded prior to the onset of the initial MI, showed a striking relationship to these probabilities. Men classified as having elevated blood pressure had twice the likelihood of experiencing

*All observations, which were due on these men before May 1, 1968, are included in the analysis. Over the course of the observation period, extending up to 4.5 years from date of MI, five men were lost to follow-up for mortality and seven men for recurrence status.
a second infarction and more than five times the likelihood of cardiac death shown by men with normal blood pressure.

The data in table 3 were obtained by cumulating the entire experience gained in a total of 4.5 years of observation after the initial event. To determine whether the disadvantage of the hypertensive men was concentrated in a particular segment of this follow-up period, the 4.5 years after onset were divided into three consecutive time intervals; the probabilities of first recurrence and cardiac death were computed separately for each interval and are presented as annualized age-adjusted rates in table 4. In each of these time intervals the men with elevated blood pressure prior to their initial MI showed distinctly higher rates of recurrence and cardiac death than the men with lower levels of blood pressure.

**Discussion**

This study provides data on the extent to which the arterial blood pressure is related to the prognosis of men following the clinical onset of coronary heart disease. Cases are obtained from a study based on 55,000 men aged 25 to 64 years enrolled in the Health Insurance Plan. Among men whose disease begins as angina pectoris, the "hypertensives" are two and one half times as likely to suffer an infarction and cardiac death in comparison with the "normotensives" of the same age, in a period of 30 months of observation following the diagnosis.

In this population a myocardial infarction was by far the commoner initial clinical manifestation of coronary heart disease. Over the 4 years of case findings 881 men experienced a first MI, while 275 men sustained a diagnosis of angina without prior MI. The habitual blood pressures recorded prior to the initial clinical MI permitted definition of groups of men who differed greatly in their immediate and longer-term response to this event. The early mortality was twice as high in the hypertensives as in normotensives after taking age differences into account. This relative disadvantage continued long after the period of early mortality. Men classified as hypertensives on the basis of their pre-infarction blood pressure exhibited a much higher recurrence rate throughout the 4.5 year period of observation following their initial MI. Their relative disadvantage was even greater with respect to the risk of cardiac death.

It is probable that hypertension exerts a number of influences which might account for these findings. Arterial hypertension represents an increased impedance to left ventricular ejection, requiring an increase in the left ventricular work load and an increase in the left ventricular myocardial oxygen consumption. This is normally provided by an increase in coronary blood flow per unit

**Table 4**

<table>
<thead>
<tr>
<th>No. alive at start of time interval*</th>
<th>% with 1st recurrence per year in time interval*</th>
<th>% dying cardiac death per year in time interval*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood pressure†</strong></td>
<td><strong>I</strong> (5 mo)</td>
<td><strong>II</strong> (24 mo)</td>
</tr>
<tr>
<td>Elevated</td>
<td>126</td>
<td>117</td>
</tr>
<tr>
<td>Other‡</td>
<td>438</td>
<td>426</td>
</tr>
</tbody>
</table>

*Definition of time intervals: I = from 2nd month post MI through 6th month post MI (5 months); II = from 7th month post MI through 30th month post MI (24 months); III = from 31st month post MI through 54th month post MI (24 months).
†The blood pressure classification is described under "Methods."
‡See corresponding footnote, table 3.
of muscle mass. In addition, systemic hypertension induces left ventricular hypertrophy. This increase in muscle mass creates an increase in the total coronary blood flow requirement.

There is also evidence to indicate that arterial hypertension accelerates the rate of atheroma formation in experimental animals on an atherogenic diet. In all likelihood the same effect occurs in humans. Data from the Framingham study suggest that for any given level of serum cholesterol the incidence of myocardial infarction increases with the level of blood pressure.

Hypertension thus may promote the development of obstructive coronary artery disease by accelerating atherogenesis while simultaneously increasing the requirement for coronary blood flow by increasing the left ventricular work load and muscle mass. This combination of circumstances might be expected to lead to myocardial ischemia, angina pectoris, myocardial infarction, and sudden death. An hypertrophied heart, supplied by atheromatous coronary arteries, might be less capable of adapting to an acute myocardial infarction than the nonhypertrophied heart of a normotensive subject. Thus, the higher early mortality experience of hypertensives is not unexpected. The continuation of these processes might account for the relatively poor longer-term prognosis of the hypertensive survivors of a first myocardial infarction.

These data cannot be interpreted to indicate whether lowering of the blood pressure would reduce these adverse influences and, if so, how soon and how effectively. They do add support to the suggestion that the level of arterial blood pressure is a major factor which determines the rate of development of generalized and coronary atherosclerosis in American men. The prevalence of hypertension among men with no clinical evidence of coronary heart disease is substantial, and hypertensives who develop clinical manifestations of coronary heart disease have a subsequent prognosis which is demonstrably worse than that of men with lower levels of blood pressure. These observations add urgency to the desirability of suitable clinical trials designed to test the hypothesis that reduction of elevated blood pressure levels in men apparently free of coronary heart disease will reduce their risk of incurring this disease and dying from it.

Acknowledgment

Thanks are due to the examining physicians in the participating medical groups for their contribution to this project through the detailed medical observations they make at the special examination sessions structured for this project. These physicians are:

Dr. Hector Battaglia, Jamaica Medical Group
Dr. Anthony Bianco, Astoria Medical Group
Dr. Murray Burns, Bay Ridge Medical Group
Dr. Morris Drazin, Queens Boulevard and Queensboro Medical Groups
Dr. Theodore R. Fink, New York Medical Group
Dr. Arthur Gaynor, Montefiore Hospital Medical Group
Dr. Laurence Horowitz, Kings Highway Medical Group
Dr. Jawad S. Idriss, Clinton Medical Group
Dr. Kurt E. Lauer, Washington Heights Medical Group
Dr. Gerald Mirrer, Queensboro Medical Group
Dr. John Ohmysty, Jamaica Medical Group
Dr. Harold B. Orenstein, Central Medical Group of Brooklyn
Dr. Gilberto Ramirez, Central Manhattan Medical Group
Dr. Alvin A. Schaye, Metropolitan-Hudson Medical Group
Dr. Israel A. Schiller, Kings Highway Medical Group
Dr. Joseph H. Schwab, Jamaica Medical Group
Dr. Norman Shaftel, Flatbush Medical Group
Dr. Stanley L. Slater, Bay Ridge Medical Group
Dr. Stephen Wagner, Brooklyn Medical Group
Dr. Lothar Wertheimer, Montefiore Hospital Medical Group

Credit is also due to the field staff responsible for the high response rate of patients and the efficient conduct of the examining sessions: Mrs. Sylvia Chromow, Mrs. Nettie Cohen, Mrs. Florence Katz, Mrs. Lucille Siegel, and Mrs. Lenore Silberman. Significant contributions to the processing of the material used in this paper were made by Mrs. Gay Greene, Mrs. Regina Friedlander, and Mrs. Leanor Sherman of the central study staff.

Thanks are due also to Dr. George E. Seiden, the study's electrocardiographer.
References

Related Publications from This Study Not Referred to Directly in Text

Parry’s Concluding Remarks
Angina Pectoris
End of the Eighteenth Century

I have thus endeavoured to ascertain the symptoms, and establish the pathology, of the Syncope Anginosa. It is painful to me, that the most important part, that which respects the cure or relief, should have been so defective; and that the nature of the disorder itself should promise so little success to any further enquirers. It may be hoped, however, that the investigation has not been without its value in a philosophical view; and that he, who, by throwing any light on an obscure subject, had prevented disappointment, and consequent censure or self-accusation, had contributed in some degree to the welfare of mankind.—Caleb Hillier Parry: An Inquiry into the Symptoms and Causes of the Syncope Anginosa, Commonly Called Angina Pectoris. London, Cadell and Davies, 1799, p. 167.
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Circulation. 1968;38:432-438
doi: 10.1161/01.CIR.38.2.432

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