The Effects of Ergonovine Maleate on Coronary Arterial Size

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SUMMARY Changes in coronary arterial size due to ergonovine maleate are described and quantitated in 90 patients — 18 with typical angina pectoris, 56 with atypical chest pain, nine with variant angina pectoris, and seven heart transplant (allograft) recipients. We observed two angiographic changes in the diameter of coronary arteries: 1) spasm, which was characterized by occlusion or marked (>85%) focal or diffuse vessel narrowing, or 2) relatively mild and diffuse vessel narrowing, which was interpreted as the normal pharmacologic response to the drug. Serial bolus injections of 0.05 mg, 0.10 mg and 0.25 mg of ergonovine maleate produced diffuse narrowing of the diameter of coronary arteries of 10 ± 1.5%, 16 ± 1.4% and 20 ± 1.3% (mean ± SEM), respectively, in the 72 patients with anginal syndromes who did not develop coronary spasm. The degree of coronary arterial narrowing was the same in heart transplant recipients and in patients with normally innervated hearts who did not develop coronary spasm. We believe the normal pharmacologic response to ergonovine maleate was due to a direct vasoconstrictor action of the drug; this action was independent of neural control extrinsic to the heart.

CORONARY ARTERIAL SPASM is recognized as a cause of angina pectoris. In attempts to identify patients with this condition, various pharmacologic agents, including methacholine,1, 2 epinephrine,2 propranolol,2 and ergonovine maleate (EM),3-7 have been used to provoke coronary vasospasm during coronary arteriography. EM has been shown to induce coronary artery spasm at sites where spontaneous spasm was observed,5, 8 and vasospastic coronary artery disease has been demonstrated during coronary angiography by administering this drug. In this study we describe and quantify the changes in coronary arterial diameter produced by EM when given to patients with various anginal syndromes. In addition, EM was given to heart transplant (allograft) recipients in an attempt to define the mechanism by which this drug affects coronary arterial size.

Materials and Methods

We studied 90 patients who received EM (Ergotrate Maleate, Eli Lilly & Co) after left ventriculography and coronary arteriography, using the Judkins technique, at Stanford University Hospital during 1975–1977. The administration of EM to induce coronary artery spasm has been approved by the Stanford Medical Committee on the Use of Human Subjects in Research. Patients with chest pain were selected for study if coronary artery spasm was a consideration clinically or if coronary angiography demonstrated arterial narrowing which was thought to be insufficient to account for their pain. They were told that they would be given a drug that produced marked coronary artery narrowing which appeared to explain the cause of chest pain in some patients. Patients were told that we expected the results of the study to yield information that would be helpful in their medical treatment.

The 90 patients studied included 47 men and 43 women ranging in age from 25–75 years (mean age 48 years). Eighty-three patients were given EM to determine if their anginal syndromes were related to coronary artery spasm. Eighteen of these 83 had typical angina pectoris produced by exercise and relieved by rest or nitrates. Fifty-six patients had chest pain that was not predictably related to stress or relieved by rest or nitrates, and at the time of study we did not know if their pain was cardiac in origin. Nine patients had variant angina pectoris, characterized by nonexertional chest pain that frequently occurred at night and was accompanied by ST-segment elevation. EM was also given to seven clinically stable heart transplant (allograft) recipients who were studied at the time of yearly coronary arteriography.

The 83 patients with anginal syndromes had coronary arterial narrowing of varying degrees demonstrated before the administration of EM. Forty-five patients, seven with typical angina pectoris and 38 with atypical chest pain, had no coronary arterial narrowing. Ten patients, including two with typical angina pectoris, five with atypical chest pain, and three with variant angina pectoris, had >0 and <50% narrowing of the diameter of the left anterior descending, circumflex and/or right coronary artery. Twenty-eight patients, nine with typical angina pectoris, 13 with atypical chest pain, and six with variant angina pectoris, had >50% narrowing of the diameter of one or more of these major coronary arteries. None of the heart transplant recipients had coronary arterial narrowing.

Nitrates and atropine were withheld before coronary angiography. There was continuous electrocardiographic monitoring and standard 12-lead ECGs were obtained at appropriate times during the
procedure. Sublingual and intravenous nitroglycerin (0.40 mg) was available for administration. EM was given in intravenous bolus injections after left ventriculography and coronary angiography. A total of 0.40 mg of EM was given in incremental doses of 0.05, 0.10 and 0.25 mg. We gave an additional bolus injection of 0.40 mg of EM (for a total dose of 0.80 mg EM) to five patients who did not develop coronary artery spasm after the initial 0.40 mg of EM. Four of these patients had atypical chest pain with no coronary artery narrowing, and one patient had variant angina pectoris with 50% diameter narrowing of the mid-left anterior descending and 60% diameter narrowing of the mid-right coronary artery. If electrocardiographic ST-segment shifts suggestive of myocardial ischemia were observed during spontaneous angina pectoris before coronary arteriography, the coronary arterial circulation (i.e., left or right coronary artery) which supplied the ischemic region of the myocardium was studied during the initial administration of the drug. Coronary arteriography was performed immediately if the patient developed chest pain or electrocardiographic changes of myocardial ischemia caused by the administration of EM. Sublingual nitroglycerin was given once coronary spasm was demonstrated by angiography; therefore, with the Judkins technique, we were unaware of simultaneous changes in the diameter of the opposite coronary artery. In the absence of symptoms or electrocardiographic changes of myocardial ischemia, coronary arteriography was routinely done 3 minutes after each injection of the drug. After the total dose of EM was given and one coronary arterial system had been studied, arteriography of the other coronary arterial system was performed without giving more EM.

The diameters of the proximal, middle and distal third of the right, left anterior descending, and circumflex coronary arteries were measured with calipers from 35 mm coronary cineangiograms which were projected on a 9" × 12" screen. Serial measurements were made at one site in each of these coronary artery segments. The measurements were made at enddiastole and in the same projection, before giving EM and after each injection of the drug. Anatomic features such as branch arteries and irregularities in the lumen of vessels served as references which allowed serial measurements of coronary artery diameters to be made at the same site. Segments of vessels that appeared to be normal angiographically were measured; measurements were not made at the origins of branch arteries or at sites of atherosclerotic narrowing. Reproducible measurements at 0.5 mm intervals could be obtained using this technique. The diameter of the coronary artery catheter was used as a standard of reference for determining the true size of coronary arteries, and alterations in coronary artery diameter size were calculated in millimeters and percent change in the size of the vessel before the administration of EM.

The data were analyzed to assess changes in the diameter of the proximal, middle and distal third of the right, left anterior descending, and circumflex coronary arteries after each injection of EM in patients with anginal syndromes who did not develop coronary arterial spasm. The following model for the analysis of variance gave a good fit for the data from these 72 patients:

\[
y_{ijk1} = \mu + \alpha_i + \beta_j + \gamma_k + \delta_i + \phi_{jk} + \eta_{ki} + \text{error}_{ijk1}\]

The dependent variable in this model is \(y_{ijk1}\), in which \(i\) indexes patients, \(j\) indexes EM doses, \(k\) indexes coronary artery segments and \(l\) indexes coronary arteries. Measurements of coronary artery diameters from coronary angiograms were converted to the true size of these vessels by dividing the diameter of the coronary artery by the diameter of the coronary artery catheter.

For the statistical analysis of variance, the measurements were converted to their natural logarithm. Therefore, in this model, \(y\) is the natural logarithm of the true size of the diameter of the coronary artery. We were primarily interested in determining the effects of doses of EM upon changes in coronary arterial diameter; however, it was important to consider factors which accounted for some of the variability within the data that was not related to EM.

In the above model \(\mu\) is the grand mean or the average coronary artery diameter for these 72 patients; \(\alpha_i\) is the main effect for patient \(i\) or a factor which accounts for individual variation in average coronary arterial size; \(\beta_j\) is the main effect for dose \(j\) (and the primary variable of interest) or the change in coronary arterial size that is due to the dose of EM; the \(\gamma\) and \(\delta\) are main effects for factors that are accounted for by variations within the different coronary arteries (right, left anterior descending or circumflex) and coronary artery segments (proximal, mid or distal). The \(\phi\) and \(\eta\) are interaction terms which account for a relationship between dose of EM and coronary artery \(\phi\) and dose of EM and coronary artery segment \(\eta\), since it was possible that different coronary arteries or coronary arterial segments might react differently to EM. The "error" term in the model is equivalent to the unexplained variability in the data which has not been accounted for by the other parts of the model. This term would include errors in measurement and factors which were not considered.

Differences in response to EM between groups of patients were analyzed in an expanded model. The change in diameter of coronary arteries to cumulative doses of 0.05 mg, 0.15 mg and 0.40 mg of EM was determined for the groups of patients with typical angina pectoris and atypical chest pain in whom EM did not provoke coronary spasm, and the group of heart transplant recipients. To test for differences in response to EM among these three groups of patients, extra terms were added to the above model:

\[
y_{ijk1} = \mu + \alpha_i + \beta_j + \gamma_k + \delta_i + \phi_{jk} + \eta_j + \xi_{ij} + \text{error}_{ijk1}\]

Here the model has been expanded to include \(\xi_{ij}\), which is a difference in dose response at the \(j^{th}\) dose
level in patient group I when I indexes a group of patients. \( \xi_{ij} \) represents an interaction term to account for the possibility that groups of patients with typical angina pectoris and atypical chest pain or heart transplant recipients might react differently to EM. The null hypothesis of no difference between pairs of these groups of patients, that is, \( \xi_{ij} = 0 \), was tested using standard F tests.

Results

We observed two angiographic changes in the diameter of coronary arteries resulting from EM. One change, which we call coronary arterial spasm, was characterized by either focal or diffuse narrowing of 85–100% of the diameter of a vessel (fig. 1). Eleven of the 83 patients who had an anginal syndrome had coronary spasm. The other basic angiographic change was relatively mild and diffuse narrowing of all coronary arteries. We interpreted this change as the normal pharmacologic response to the drug, and it occurred in all of the remaining 72 patients with anginal syndromes (fig. 2) and in the seven heart transplant recipients (fig. 3).

The clinical and angiographic features of the 11 patients who developed coronary arterial spasm are summarized in table 1. Two of these 11 patients (1 and 11) had typical angina pectoris. Patient 1 had the onset of angina pectoris 10 months before being studied with EM. Coronary arteriography done at that time was normal; however, angina pectoris recurred with increasing frequency. Before being studied with EM, a treadmill exercise ECG showed 6 mm ST-segment elevations in leads II, III, and aVf with chest pain and Mobitz type I atrioventricular heart block. These changes occurred 2–3 minutes into the recovery period of the stress test, and they were promptly reversed by sublingual nitroglycerin. Patient 11 had the onset of angina pectoris 1 year before he was studied with EM. In the month before study, pain began to occur with less exertion and he was hospitalized for possible myocardial infarction which was not confirmed by electrocardiographic changes or abnormal cardiac enzymes. This patient did not have an exercise treadmill ECG. One (patient 7) had atypical chest pain and eight patients (2–6 and 8–10) had variant angina pectoris. Coronary spasm occurred after 0.05 mg and 0.40 mg of EM. It occurred in the right coronary artery of five patients (1–3, 8 and 10) and in the left anterior descending coronary artery of six patients (4–7, 9 and 11). Spasm occurred at sites where there was no coronary arterial narrowing in three patients (1, 5 and 7), 0–50% coronary arterial narrowing in three patients (2, 8 and 11), and >50% coronary arterial narrowing in five patients (3, 4, 6, 9 and 10). Nine patients (1–7, 8 and 11) experienced their usual chest pain after EM administration, one (patient 10) could not characterize the pain, and one (patient 8) did not have chest pain when spasm was demonstrated. Electrocardiographic ST-segment shifts caused by ischemia were present over the myocardium, which was supplied by the artery in spasm in each patient, except patient 8, who also did not experience chest pain. Sublingual nitroglycerin (0.40–0.80 mg) promptly reversed coronary spasm induced by EM in each patient. Frequently, patients had nausea and/or tightness in the neck after EM; however, these symptoms were unlike their usual
Anginal pain. No complications resulted from the administration of EM.

Relatively mild and diffuse coronary arterial narrowing was observed after the serial injection of 0.05 mg, 0.10 mg and 0.25 mg of EM in the 72 patients with anginal syndromes who did not develop coronary spasm. These patients did not have their usual chest pain or electrocardiographic changes of myocardial ischemia after the administration of EM. A dose-response curve (fig. 4) shows that the serial injection of EM, in 0.05 mg, 0.10 mg and 0.25 mg amounts, produced corresponding decreases in the diameter of coronary arteries of 10 ± 1.5%, 16 ± 1.4%, and 20 ± 1.3% (mean ± SEM). Although coronary arteries usually narrowed as indicated by the dose-response curve, occasionally we observed either no change in the diameter of the vessels or mild coronary dilatation after injection of EM. An additional 0.40 mg bolus of EM, in four patients with atypical chest pain and one patient with variant angina pectoris, produced either no further measurable change or a small amount of coronary artery narrowing without clinical or electrocardiographic changes of myocardial ischemia. There was no statistically significant difference in the changes in diameter of the right, left anterior descending and circumflex coronary arteries or the corresponding coronary arterial segments when comparing patients with typical angina pectoris and atypical chest pain (F = 0.88) or patients with atypical chest pain and heart transplant recipients (F = 0.47). Table 2 presents the mean values of coronary arterial diameter narrowing which occurred in
patients who did not develop spasm after the cumulative injection of 0.40 mg EM. In the absence of coronary arterial spasm, coronary arteries appeared to narrow relatively uniformly throughout their length. However, statistical analysis of the changes indicated small differences in the dose response of proximal (P), mid (M), and distal (D) coronary arterial segments as follows: M > D > P (table 2). The F test for differences in these three segments of the vessel was only of borderline significance with an estimated significance level (p value) of approximately 0.15.

### Table 1. Clinical Features and Coronary Angiographic Findings in 11 Patients with Coronary Spasm Induced by Ergonovine Maleate

<table>
<thead>
<tr>
<th>Pt no.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Angina</th>
<th>Total ERG dose (mg)</th>
<th>Typical chest pain induced</th>
<th>ECG changes</th>
<th>Site of CA spasm</th>
<th>Diameter CA narrowing at site of spasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>M</td>
<td>T</td>
<td>0.40</td>
<td>+</td>
<td>ST^\II</td>
<td>RCA</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>M</td>
<td>V</td>
<td>0.40</td>
<td>+</td>
<td>ST^\II,III,F</td>
<td>RCA</td>
<td>20% 85%</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>F</td>
<td>V</td>
<td>0.40</td>
<td>+</td>
<td>ST^\II,III,F</td>
<td>RCA</td>
<td>80% 100%</td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>M</td>
<td>V</td>
<td>0.05</td>
<td>+</td>
<td>ST^\V_1,4</td>
<td>LAD</td>
<td>80% 99%</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>F</td>
<td>V</td>
<td>0.05</td>
<td>+</td>
<td>ST^\V_1,6</td>
<td>LAD</td>
<td>None 99%</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>F</td>
<td>V</td>
<td>0.40</td>
<td>+</td>
<td>ST^\V_1,4</td>
<td>LAD</td>
<td>70% 99%</td>
</tr>
<tr>
<td>7</td>
<td>57</td>
<td>F</td>
<td>A</td>
<td>0.40</td>
<td>+</td>
<td>ST^\II</td>
<td>LAD</td>
<td>None 85%</td>
</tr>
<tr>
<td>8</td>
<td>57</td>
<td>F</td>
<td>V</td>
<td>0.05</td>
<td>0</td>
<td>None in II</td>
<td>RCA</td>
<td>20% 90%</td>
</tr>
<tr>
<td>9</td>
<td>58</td>
<td>M</td>
<td>V</td>
<td>0.40</td>
<td>+</td>
<td>ST^\V_3,4</td>
<td>LAD</td>
<td>60% 100%</td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>F</td>
<td>V</td>
<td>0.05</td>
<td>?</td>
<td>ST^\II,III,F</td>
<td>RCA</td>
<td>50% 95%</td>
</tr>
<tr>
<td>11</td>
<td>66</td>
<td>M</td>
<td>T</td>
<td>0.40</td>
<td>+</td>
<td>ST^\V_1,4</td>
<td>LAD</td>
<td>10% 90%</td>
</tr>
</tbody>
</table>

Abbreviations: + = yes; 0 = no; ? = indeterminate; A = atypical; CA = coronary artery; ERG = ergonovine maleate; LAD = left anterior descending coronary artery; RCA = right coronary artery; T = typical; V = variant; ↑ = elevation; ↓ = depression.

### Discussion

Recently, coronary angiography has shown that EM can provoke coronary arterial spasm in some patients who have angina pectoris resulting from spontaneous coronary artery narrowing.3,6 We observed that EM produced two distinct angiographic changes in coronary arterial diameter in patients with various anginal syndromes. One change was coronary spasm with marked narrowing (85–100% of the diameter) or occlusion of a vessel, which was nearly always accompanied by the patient’s usual chest pain.
The angiographic change of relatively mild and diffuse vessel narrowing as a normal pharmacologic response to EM.

It has not been determined whether coronary arterial spasm that has been provoked by EM is a sensitive indicator of spontaneous coronary artery narrowing. Occasionally, EM induces coronary arterial spasm in patients who do not have the diagnosis of variant angina pectoris,\(^3\) as it did in three of our patients. Two of these three, (table 2, patients 1 and 11) had exertional chest pain for approximately 1 year, and they were thought to have typical angina pectoris before they were studied with EM. Coronary angiograms of these patients demonstrated no or mild coronary arterial narrowing. One patient (1) had a 6-mm ST-segment elevation in leads II, III, aVF, during both the recovery phase of an exercise treadmill ECG and when coronary arterial spasm was later induced by EM. Patient 7 (table 1), who had a diagnosis of atypical chest pain had chest pain on exertion for 3 years, and the recent onset of nonexertional chest pain was difficult to characterize. This patient had no coronary arterial narrowing demonstrated before administration of EM. The angiographic changes in coronary arterial diameter which we observed in response to EM lead us to conclude that these three patients, and similar patients who have been studied with EM by other investigators,\(^3\) are representative of the clinical spectrum of spontaneous coronary artery narrowing that has recently been demonstrated.\(^7\)

EM was first used as a stress test by Stein\(^9,11\) to diagnose atherosclerotic coronary artery disease by inducing angina pectoris and/or electrocardiographic changes of myocardial ischemia. This drug might be expected to produce myocardial ischemia in patients with moderate (>60% vessel diameter narrowing) or marked (>85% vessel diameter narrowing) atherosclerotic coronary artery disease if the relatively mild and diffuse narrowing of epicardial coronary arteries and mild rise in systemic blood pressure that it produces\(^3\) adversely affected the myocardial oxygen supply and demand relationship by reducing coronary blood flow and increasing myocardial work. The usefulness of giving EM to identify patients with vasospastic coronary artery disease would be

![Figure 4](image_url)  
**Figure 4.** Dose-response curve which demonstrates progressive narrowing of coronary arteries, of 10 ± 1.5%, 16 ± 1.4% and 20 ± 1.3% (mean ± SEM), after serial intravenous injections of 0.05 mg, 0.10 mg, and 0.25 mg ergonovine maleate (EM). The increment of narrowing of coronary arteries decreases with successive injections of larger amounts of EM.

and electrocardiographic ST-segment shifts caused by myocardial ischemia. EM induced coronary spasm in eight of our nine patients with variant angina pectoris. The patient who did not develop coronary arterial spasm had spontaneous coronary spasm documented by angiography 5 years earlier, and it was our clinical impression that his coronary vasospastic disease was inactive when he was studied with EM. The high sensitivity with which EM provokes coronary arterial spasm in patients who have variant angina pectoris has now been confirmed by several investigators.\(^3\)

EM produced relatively mild and diffuse coronary arterial diameter narrowing in patients who did not develop coronary artery spasm. It involved all epicardial coronary arteries uniformly, and it was not accompanied by angina pectoris or electrocardiographic changes of myocardial ischemia. A dose-

response relationship was demonstrated among patients with anginal syndromes who did not develop coronary spasm when EM was given. We interpreted the angiographic change of relatively mild and diffuse vessel narrowing as a normal pharmacologic response to EM.

### Table 2. Coronary Arterial Diameter Narrowing after 0.40 mg Ergonovine Maleate

<table>
<thead>
<tr>
<th>Angina</th>
<th>Reduction in vessel diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Proximal</td>
</tr>
<tr>
<td></td>
<td>(mm)</td>
</tr>
<tr>
<td>Typical (n = 16)</td>
<td>0.50 (0.14)</td>
</tr>
<tr>
<td>Atypical (n = 55)</td>
<td>0.68 (0.06)</td>
</tr>
<tr>
<td>Heart transplant (n = 7)</td>
<td>0.94 (0.18)</td>
</tr>
</tbody>
</table>

Values are mean (± SEM).
diminished if angina pectoris, electrocardiographic changes of myocardial ischemia, or changes of marked coronary arterial narrowing were produced in patients with moderate or marked coronary artery disease in whom coronary vasospasm was not the cause of chest pain. In fact, patients with and without coronary artery disease demonstrated by coronary angiography have had their usual chest pain provoked by EM in the absence of coronary arterial spasm. However, EM does not produce shifts in ST segments in patients without marked triple-vessel coronary artery disease in the absence of coronary arterial spasm, and coronary arteriographic examinations have not substantiated the validity of electrocardiographic criteria which Stein used to identify atherosclerotic coronary artery disease. EM did not produce angina pectoris or electrocardiographic changes that were suggestive of myocardial ischemia in our patients who did not develop coronary artery spasm, even though several of these patients had moderate (>60%) or marked (>85%) narrowing of one or two major coronary arteries. Thus, the angiographic changes in coronary artery size resulting from the administration of EM may be specific as well as sensitive indicators of spontaneous coronary artery narrowing.

The major pharmacologic actions of ergot alkaloids are smooth muscle contraction, adrenergic blockade and central nervous system effects. EM, an amine ergot alkaloid, is thought to affect predominantly the cardiovascular system by stimulating contraction of smooth muscle; it also has effects on the central nervous system, such as blocking the response to baroreceptors, but it does not produce adrenergic blockade. In experimental animals, EM stimulates vascular smooth muscle to contract by acting upon adrenergic receptors which are present in large epicardial coronary arteries. Stimulation of smooth muscle contraction has been presumed to be the mechanism of coronary arterial narrowing in human subjects which occurs after the administration of EM, although the potential effect of a central nervous system action of the drug upon coronary arterial narrowing has not been determined. Direct effects vs neurally mediated effects of EM upon the size of coronary arteries may be studied by examining changes in coronary arterial diameter that are produced in heart transplant recipients since the hearts of these patients lack extrinsic neural control. The similar degree of coronary arterial narrowing in heart transplant recipients and in patients with normally innervated hearts who did not develop coronary arterial spasm due to the administration of EM indicates that cardiac denervation neither diminished nor augmented the action of EM. The effect of EM was independent of extrinsic neural control. The increments of coronary arterial narrowing caused by serial injections of increasing amounts of EM to patients who did not develop coronary arterial spasm is similar to the diminished pressor response and smooth muscle contraction which have been observed in experimental animals after repeated injections of the drug.

Our observations are compatible with the concept that EM, and/or circulating factors which result from EM, act upon local receptors (possibly α-adrenergic receptors) within the walls of coronary arteries. EM also may provoke coronary arterial spasm by a direct action upon abnormally reactive segments of coronary arteries of both normally innervated hearts and denervated transplanted hearts. The causes of such an abnormal reactivity have not been determined.

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Relationship of Cardiothoracic Ratio and Plain Film Heart Volume to Late Survival

K. E. HAMMERMEISTER, M.D., PAUL M. CHIKOS, M.D., LLOYD FISHER, PH.D., AND HAROLD T. DODGE, M.D.

SUMMARY We assessed the prognostic value of cardiothoracic ratio and plain film heart volume in relation to other clinical, exercise, hemodynamic and quantitative angiographic variables. Both cardiothoracic ratio and plain film heart volume are highly sensitive, but nonspecific, indicators of abnormal left ventricular end-diastolic volume and ejection fraction. Both variables are univariately important predictors of survival in cohorts of medically and surgically treated heart disease patients. Plain film heart volume significantly adds to the multivariate prediction of prognosis obtained from groups of clinical, exercise, hemodynamic and quantitative angiographic variables. These measurements from the routine chest roentgenogram are sensitive detectors of abnormal left ventricular function or volume and important predictors of long-term survival. The fact that they contribute prognostic information in addition to left ventricular volume and ejection fraction suggests that other cardiac chamber volumes are of prognostic importance.

PREVIOUSLY, WE HAVE DEMONSTRATED the significance of left ventricular end-diastolic volume and related variables such as ejection fraction in the prediction of survival of patients with heart disease.1, 2 Chikos et al.3 showed a high correlation between total heart volume measured from the standard chest roentgenogram (plain film heart volume) and left ventricular end-diastolic volume measured angiographically in patients with aortic valve disease. In this study we examined the prognostic value of plain film heart volume and cardiothoracic ratio with respect to late survival and compared the prognostic value of these noninvasive parameters with other clinical, exercise, hemodynamic and quantitative angiographic variables frequently obtained in the evaluation of the patient with heart disease.

Methods

Patient Population

We have previously reported analyses of late survival in all adult patients and the subgroup with mitral valve disease who had quantitative angiography at the Veterans Administration and University Hospitals, Seattle, Washington, from 1960–1970.1, 4 In this report, we analyzed all available chest roentgenograms taken in standard fashion (posterior-anterior and lateral at 6 feet) at the time of cardiac catheterization in these 831 patients. Suitable chest roentgenograms could be found on 320 of the 831 patients. The remaining patients did not have appropriate films available due to non-standard views, film in a single projection, or disposal of inactive film files. These 320 patients, who have quantitative angiographic measurement of left ventricular volume and long-term follow-up of up to 13.5 years (mean 4.1 years), are reported here. Distribution of patients by diagnosis, age, sex, therapy and functional class are given in table 1. Valvular heart disease was the principal diagnosis in 73% (233 of 320) of the patients. Heart surgery was performed in 64% (205 of 320); 45% (93) had valve replacement. 42% (87) had valvuloplasty, and 7% (15) had coronary artery surgery.

Laboratory Analyses

Maximal treadmill exercise stress tests were performed using the multistage protocol described by


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