Hypertensive Crises in Quadriplegic Patients

Changes in Cardiac Output, Blood Volume, Serum Dopamine-β-Hydroxylase Activity, and Arterial Prostaglandin PGE₂

NOSRAT E. NAFTCHI, PH.D., MARGARET DEMENY, PH.D., EDWARD W. LOWMAN, M.D., AND JOHN TUCKMAN, M.D.

SUMMARY The syndrome of autonomic dysreflexia often occurs in quadriplegic subjects and is characterized by paroxysmal hypertension, headache, vasoconstriction below and flushing of the skin above the level of transection, and bradycardia. These attacks may cause hypertensive encephalopathy, cerebral vascular accidents, and death. In five patients during crises, the mean arterial pressure changed from 95 to 154 mm Hg, heart rate 72 to 45 beats/min, cardiac output 4.76 to 4.70 L/min, and peripheral resistance 1650 to 2660 dynes·sec·cm⁻². In eight subjects the control plasma, red cell, and total blood volumes were 19.1, 10.5, and 29.6 ml/cm body height, respectively, and when hypertensive, the plasma protein concentration increased by 9.9% and the hematocrit by 9.5%. Plasma volume was only reduced by an estimated 10–15%. At that time, arterial dopamine-β-hydroxylase (DβH) activity increased 65% and prostaglandin E₂ concentration by 68%. Thus, the augmented DβH activity represented primarily an elevated sympathetic tone and not hemoconcentration of that protein. The rise in prostaglandin may contribute to the severe headaches during hypertensive episodes.

MOST PATIENTS WITH HIGH TRANSVERSE LESIONS of the spinal cord above the origins of the thoracolumbar preganglionic sympathetic neurones eventually develop symptoms of autonomic hyperreflexia or dysreflexia. That is, the stimulation of dermatomes and muscles supplied by nerves from below the injury, and especially, manipulation of the perineum, genitalia and distention of the bladder or rectum evokes a syndrome which includes hypertension, profuse sweating, flushing, piloerection (cutis anserina), and headache. The increase in arterial pressure is often severe and prolonged, and may cause cerebral vascular accidents and death. This syndrome has been mistakenly diagnosed as pheochromocytoma, and during delivery, as toxemia of pregnancy. Also, it becomes a major complication during surgical procedures when it is induced by traction of the viscera.

The hypertensive crises, during episodes of autonomic dysreflexia, are unusual since an increase in sympathetic activity occurs simultaneously with elevated, rather than lowered, parasympathetic tone. The adrenergic activity originates below the level of transection and the cholinergic activity is due to stimulation of the supra-spinally mediated carotid sinus and aortic arch baroreceptor reflexes which produce a dramatic bradycardia. The principle aim of the present investigation was to measure the effect of this anomalous parallel increase in autonomic activity on cardiac output. Another objective was to determine if blood volume decreased during autonomic hyperreflexia, as happens when arterial blood pressure is raised by intravenous infusion of noradrenaline in normotensive subjects. If during the hypertensive episodes in quadriplegic patients, a reduction in plasma volume occurred, it would cause hemoconcentration of high molecular weight plasma proteins including dopamine-β-hydroxylase (DβH) and alter interpretation of the latter’s significance as an index of sympathetic activity. In addition, the existence of such a hypovolemia could be of direct clinical significance, since even a small diminution in blood volume might produce severe hypotension when the hypertensive stimulus, e.g., bladder distension, was abruptly removed.

Severe headache is a characteristic symptom of autonomic hyperreflexia and some experimental data are consistent with the hypothesis that it results from passive dilatation of cerebral vessels in response to the high systemic arterial pressure. However, elevated sympathetic and parasympathetic activity both release prostaglandins, as well as cause rises in blood pressure. Infusions of PGE₁ and PGE₂ in man have been found to cause headache. Therefore, we measured the arterial concentration of PGE₂ to determine if the magnitude of its increase during the hypertensive episodes could help explain the headache.

Materials and Methods

The protocol of this investigation was approved by the Human Studies Committee of the New York University Medical Center. Eleven male quadriplegic subjects participated in the study after they gave their informed consent. The procedures were done before and during the episodes of autonomic hyperreflexia which were associated with routine tests of urinary bladder function carried out in these patients by cystometry.

The patients, 18–25 years of age, all had physiologic transverse lesions of the spinal cord at the level of the sixth to eighth cervical segments. The injuries had occurred at least six months prior to the test and the patients were in an unremarkable chronic stable condition. None had evidence of cardiovascular disease or decreased renal function. Drugs affecting the cardiovascular system were discontinued before the procedures began and the subjects were studied after they had been fasting 10–12 hours.

Blood volume determinations were done in eight of the 11 subjects. Cardiac output studies, without blood volume determinations, were also performed in three of these eight patients on another occasion, and in two other subjects.
Arterial samples for measurements of serum dopamine-β-hydroxylase (DβH) activity and plasma prostaglandin PGE₂ concentration were obtained from the five patients at the time of the cardiac output procedures and from one other subject.

The procedures took place in the morning approximately one hour after the insertion of a Foley catheter coated with lidocaine gel. The control period began after the subjects had been supine for at least 30 min and 15 min after all needles and other catheters were in place. Autonomic dysreflexia was produced by gradually filling the bladder with isotonic saline during cystometry, and terminated by emptying that organ. Brachial arterial pressure was measured by auscultation at least every two minutes. Mean arterial pressure was calculated by adding one third of the pulse pressure to the diastolic pressure.

Direct red cell and plasma volumes were measured simultaneously with chromate-labelled red blood cells (¹⁵⁷Cr-RBC) and iodinated human serum albumin (¹²⁵I-HSA) using multiple venous samples. Microhematocrits of each sample were also determined at 15,000 g, and no correction was made for trapped plasma. The total body/large vessel hematocrits ratios were calculated from the relationship of the direct blood volume measurements and the large vessel hematocrits.

Plasma protein concentrations of the samples were measured by the method of Lowry.

Following the control period, several additional venous samples were obtained during each of the hypertensive episodes to estimate the changes in plasma volume by comparing plasma protein concentrations and hematocrits with the respective control measurements.

Supine cardiac output was measured before and during autonomic hyperreflexia in five patients by the indicator-dilution method using indocyanine green and standard methods of calculations. In each subject, two or three cardiac outputs were determined during the control period, and two or three others, within several minutes, at the height of the hypertension. Peripheral resistance was calculated from the ratio of mean arterial pressure and cardiac output and was expressed in dynes·sec·cm⁻².

The arterial samples for analysis of serum DβH activity and plasma PGE₂ concentration were obtained during the control periods and at the times of greatest elevation of blood pressure. Serum DβH activity was determined by a modification of the sensitive isotopic method of Molinoff et al., and is expressed in n moles of phenylethanolamine/ml serum/hour. The concentration of PGE₂ in plasma was determined by the sensitive radioimmunoassay of Levine et al.

The statistical analysis of the results was by the Student's paired t-test.

### Results

The means for the control supine red cell, plasma and total blood volumes and the total body/large vessel hematocrits ratio are presented in table 1. The volumes are expressed as ml/cm body height. Blood volumes are relatively independent of body height and have been found to be a better reference index for expressing results than weight or surface area in most groups of subjects.

In eight blood volume procedures, the blood pressure was considerably elevated during periods of 9, 9, 13, 16, 21, 22, 26, and 33 min. The average increase of 73% in mean arterial pressure (table 1) was calculated from several measurements obtained in each patient at the end and height of the hypertensive episodes. The average elevations of plasma protein concentration and hematocrit at those times were 9.9 and 9.5%, respectively.

The results from the five hemodynamic investigations are presented in table 2. Blood pressure was significantly elevated in all the procedures during periods of 21, 22, 22, 40, and 55 min. The data in table 2, during autonomic hyperreflexia, represent the means of two or three measurements obtained within several minutes at the end and height of the hypertension. The average increase in blood pressure was 62% which was accompanied by a substantial bradycardia in all patients; heart rate fell by an average of -27 beats/min. A similar bradycardia occurred during the blood volume studies (table 1).

The control mean cardiac output of 4.76 L/min remained essentially unchanged during the hypertensive episodes (table 2). The individual changes were modest and included reductions of 0.18, 0.57, and 0.79, and elevations of 0.50 and 0.73 L/min. There were also small changes when expressed as percentages in four of the subjects and varied between -3 and +13%. In the fifth patient (subject 4), there was a 25% increase in cardiac output, but this larger relative rise was due to a low control measurement (2.95 L/min) rather than
a large absolute change (+0.73 L/min). In all subjects, mean peripheral resistance rose considerably (61%) between 32% to 85%.

Serum D\(\beta\)H activity and plasma PGE\(_2\) concentration in arterial blood samples increased in all patients during autonomic hyperreflexia and the average changes were +65% and +68%, respectively (table 3).

Hyperhidrosis, piloerection, and flushing were present in various degrees over the face, neck, and upper trunk during all the episodes of autonomic hyperreflexia. A half of the patients also experienced headache. No attempt was made, however, to correlate the severity of this symptom with the rises in arterial plasma PGE\(_2\) concentration.

**Discussion**

Patients with high spinal cord lesions become inordinately responsive to many types of stimulations below the level of the transaction from approximately three months after their injury. Thus, the afferent stimuli can produce widespread activation of preganglionic sympathetic neurones in the intermediolateral cell columns of the distal cord stump which results in episodes of autonomic hyperreflexia (dysreflexia). A generalized increase in sympathetic tone could alter hemodynamics and raise arterial pressure by a) reducing the distensibility of postarteriolar capacity vessels, b) directly increasing myocardial contractility, and c) elevating arteriolar resistance. But analysis of the hypertension in autonomic hyperreflexia is more complex since it also involves a parallel increase in parasympathetic tone. The latter causes a striking bradycardia which depends presumably on excessive stimulation of the carotid sinus and aortic-arch baroreceptor reflexes, that is, elevated afferent IX and X and efferent X cranial nerve activity.

In fact, there have been relatively few hemodynamic investigations of autonomic dysreflexia. The blood flow has been measured in fingers and toes by calorimetry,\(^{11}\) in the calf by venous occlusion plethysmography,\(^{31, 36, 37}\) and in plantar, thigh, chest, forearm and palmar surfaces the cutaneous blood flow has been "assessed" by photoelectric plethysmography.\(^{38}\) In all of these studies, the blood flow was found to be diminished and since it occurred simultaneously with considerable elevations in arterial pressures, this indicated that there were large increases in arteriolar vascular resistance in those regions. Other investigations of blood flow in the forearm and kidney have been too few to permit adequate analysis of the data.\(^{36, 39}\) Further, results of venous tone determinations have not been sufficient\(^{36, 37}\) to indicate whether venous tone was changed during autonomic hyperreflexia.

Several groups of workers have measured cardiac output and total peripheral resistance. Agrest and Roncoroni, 1960,\(^{40}\) used the direct Fick and indicator-dilution methods in two patients in whom the syndrome was evoked by bladder distension. They found that the cardiac output varied between -21% and +7% and peripheral resistance between +9% and +58%. It is difficult to draw general conclusions from only two patients. In addition, the patients did not become hypertensive during the episodes of dysreflexia; the highest pressures were only 116/88 and 112/78 mm Hg. Other investigators have used methods of doubtful validity to measure cardiac output\(^{40}\) or did not publish adequate details of their methods or results.\(^{41, 42}\)

In the present hemodynamic studies, bladder distension induced considerable increases in mean arterial pressure in all five subjects (from +36 to +119%). Heart rate also decreased in all the procedures (from 17 to -46 beats/min, table 2). These large changes in mean arterial pressure and heart rate were associated with an insignificant and very small fall in cardiac output of 0.06 L/minute. The total peripheral resistance increases ranged from +32 to +85% and the average change was +61% (table 2). Hypertensive episodes of autonomic hyperreflexia are, therefore, accompanied by a significant degree of "overall" arteriolar vasocostriction. This conclusion could not be drawn from previous studies which measured cardiac output\(^{40, 44}\) or from the relatively few hemodynamic investigations of local circulations.

### Table 2. Cardiac Output and Peripheral Resistance during Autonomic Hyperreflexia in Five Quadriplegic Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>MAP (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>Cardiac output (L/min)</th>
<th>Peripheral resistance (dynes-sec-cm(^{-2}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>A.H.*</td>
<td>C</td>
<td>A.H.*</td>
</tr>
<tr>
<td>1</td>
<td>108</td>
<td>147</td>
<td>84</td>
<td>38</td>
</tr>
<tr>
<td>2</td>
<td>112</td>
<td>179</td>
<td>79</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>102</td>
<td>132</td>
<td>72</td>
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<td>4</td>
<td>67</td>
<td>147</td>
<td>80</td>
<td>43</td>
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<tr>
<td>5</td>
<td>88</td>
<td>144</td>
<td>64</td>
<td>43</td>
</tr>
<tr>
<td>Mean</td>
<td>95</td>
<td>154</td>
<td>72</td>
<td>45</td>
</tr>
<tr>
<td>SEM</td>
<td>8.2</td>
<td>6.4</td>
<td>4.5</td>
<td>3.1</td>
</tr>
<tr>
<td>P % change</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*Measurements obtained at the height of the hypertensive period.

**Abbreviations:** C = control; A.H. = autonomic hyperreflexia; MAP = supine mean arterial pressure (diastolic + 1/3 pulse pressure).

### Table 3. Changes in Arterial Prostaglandin and Dopamine-\(\beta\)-Hydroxylase Levels During Hypertension in Quadriplegics

<table>
<thead>
<tr>
<th>Pt</th>
<th>ng PGE(_2)/ml plasma Before</th>
<th>After</th>
<th>Arterial Serum D(\beta)H* Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.45</td>
<td>0.56</td>
<td>695</td>
<td>1580</td>
</tr>
<tr>
<td>2</td>
<td>0.31</td>
<td>0.49</td>
<td>1145</td>
<td>1418</td>
</tr>
<tr>
<td>3</td>
<td>0.40</td>
<td>0.64</td>
<td>702</td>
<td>1106</td>
</tr>
<tr>
<td>4</td>
<td>0.10</td>
<td>0.36</td>
<td>905</td>
<td>1456</td>
</tr>
<tr>
<td>5</td>
<td>0.37</td>
<td>0.69</td>
<td>794</td>
<td>1235</td>
</tr>
<tr>
<td>6</td>
<td>0.44</td>
<td>0.75</td>
<td>640</td>
<td>1270</td>
</tr>
<tr>
<td>Mean</td>
<td>0.34</td>
<td>0.57</td>
<td>814</td>
<td>1344</td>
</tr>
<tr>
<td>SEM</td>
<td>0.05</td>
<td>0.06</td>
<td>76</td>
<td>70</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*units = nmoles phenylethanolamine/ml serum/hour.
Another objective of this study was to determine if the increased sympathetic activity and circulating noradrenalin levels during dysreflexia reduced plasma volume as occurs during intravenous infusions of noradrenalin in man. Finnerty et al. and Cohn reported that infusions which raised mean arterial pressures by 56% and 36% decreased plasma volumes by 15% and 9.6%, respectively. These losses were most likely caused by the drug-induced elevation of capillary hydrostatic pressure, and not unexpectedly, they were associated with increases in plasma protein concentrations and large vessel hematocrits. Only Finnerty et al. measured the plasma protein concentration, by a relatively crude method; it rose by 6%. However, both studies followed the changes in hematocrit which increased by 8% in one and 2.7% in the other. Partly, this difference could have reflected dissimilar potencies of the infusions, but even when an adjustment simply based on the discrepancy between the decreases in plasma volumes is made, the rise of hematocrit in Cohn's study would be altered to only slightly above 4%. Although it would be surprising if the changes in plasma protein concentrations and hematocrits exactly corresponded to these reductions in plasma volumes for several reasons, among which are increased diffusion of the proteins from the capillaries and shifts of blood volumes between vascular beds with different hematocrits, there can be little doubt that noradrenalin infusions in man cause hemoconcentration and significant elevations of those two measurements.

In the eight procedures done here (table 1), there were considerable elevations of mean arterial pressures for periods of 9 to 33 min, and during the final five to ten minutes the average increases in blood pressure, plasma protein concentration and hematocrit were 73%, 9.9% and 9.5%, respectively. When these data are compared with those observed by Finnerty et al. and Cohn, and consideration is taken of their plasma volume measurements, it is likely that plasma volume decreased during the episodes of autonomic hyperreflexia, and to estimate that the reduction was between 10–15%.

Serum D/ßH activity rose by 65% (table 3) during autonomic hyperreflexia in the present study. This confirmed previous findings from this laboratory. However, since the protein has a molecular weight of 290,000 daltons, it seemed logical to consider how much of this elevated activity reflected true release with noradrenalin by exocytosis and how much reflected hemoconcentration. Using the "maximal" possible decrease of plasma volume estimated in this investigation, we believe hemoconcentration could only have accounted for, at most, one quarter of the 65% rise in serum D/ßH activity.

A 5–9% reduction in total blood volume, which corresponds to a 10–15% decrease in plasma volume in subjects with hematocrits of 41% (table 1) would not significantly reduce arterial blood pressure in those who had normal control volumes and intact compensatory sympathetic cardiovascular reflexes. Since quadriplegic patients, in general, have a diminished muscle mass, it was considered necessary for this study to determine if they were hypovolemic. The results in table 1 show that the total blood volume was normal in these male patients. However, in subjects without quadriplegia receiving drugs which reduce resting vascular tone and reflex sympathetic activity, this small degree of blood loss can cause severe hypotension and syncope, even when supine. This did not occur here when the hypertensive episodes were quickly ended by allowing the bladder to empty, despite the inability of the carotid sinus and aortic arch baroreceptors, and receptors in the low-pressure vascular compartment to mediate a compensatory excitation of the preganglionic sympathetic neurones below the spinal cord transection. This indicated that the quadriplegic patients had essentially normal levels of adrenergic cardiovascular tone when not in a state of autonomic hyperreflexia and/or that they had the ability to compensate for minor blood volume disturbances. The compensatory mechanisms could include cardio-cardiac and cardioarterial excitatory spinal sympathetic reflexes which have been demonstrated in animals and reduction of efferent vagal tone regulated above the spine.

In any event, these subjects should not be placed in a seated or head-up "tilt" position immediately after a dysreflexic attack because of the peripheral venous pooling of blood. Furthermore, conditions which reduce resting blood volume, arteriolar and venous tone, or depress the myocardium, should be avoided; these include excessively hot rooms, fever and infection in patients, and administration of cardioactive drugs. Such considerations will assume greater clinical relevance as quadriplegic subjects continue to live longer. The incidence of coronary heart disease and hypertension should increase and drug regimes which importantly affect the heart and blood vessels may be considered.

Headache is a characteristic symptom of autonomic hyperreflexia and can be severe. Although headache is a frequent complaint, it does not always occur during the episodes of dysreflexia, and its presence, absence, or degree or severity, has not been correlated with the level of hypertension. One-half of the subjects in the present study volunteered that they had the symptom during the hypertensive episode.

Many investigators have hypothesized that passive vasodilatation of cerebral vessels during the systemic hypertension causes the headache, and there is some evidence to support this conclusion. For example, intravenous infusion of angiotensin II, in man, sometimes produces elevations of blood pressure which break through the cerebral auto-regulatory mechanism and increase blood flow to the brain. It is noted, in this regard, that angiotensin II has no direct vasoconstricting effect on the cerebral arterioles. Also, initial analysis of results reported by Schumacher and Guthrie in 1951 provide strong support for this hypothesis of the cause of the headache. In six subjects, during attacks of autonomic hyperreflexia, the investigators increased the lumbar subarachnoidal spinal fluid pressure by forced saline infusions. This procedure eliminated headache in the four patients who had an open communication between the lumbar and cranial subarachnoidal spaces, despite continued systemic hypertension, but not in the other two subjects in whom the spinal canal was blocked. Moreover, in two of the patients, the internal carotid arterial pulsations were repeatedly obliterated by bilateral manual compression during 10–20 second periods, and these maneuvers, in the majority of attempts, temporarily stopped or diminished the headaches.

Careful consideration of the above data, however, suggests that the hypothesis may not hold up. In most subjects, if the initial rate of intravenous infusions of angiotensin or noradrenalin is gradually increased over several
minutes, attendant quite high arterial blood pressure can be maintained during prolonged periods without causing headache.\(^7\)\(^8\) Noradrenalin as well as angiotensin does not have a direct vasoconstricting effect on cerebral arterioles.\(^5\)\(^1\) Furthermore, the levels of spinal pressure which successfully ended headache during autonomic dysreflexia were not higher than 50 cm H\(_2\)O and were at least as low as 30 cm H\(_2\)O.\(^7\) Increasing cerebrospinal fluid pressure within this range, and even to 100 mm Hg, did not reduce blood flow in dogs, probably because the decrease in the cerebral artery-venous pressure gradient was compensated for by the normal autoregulatory mechanism and consequent arteriolar vasodilatation.\(^5\)\(^4\) Thus, at present there is no single direct explanation for the mechanism of the headache which is associated with hyperreflexia. In this study, the arterial concentration of PGE\(_2\) rose by 68\% (from 0.34 to 0.57 ng/ml plasma, table 3) and infusions of PGE, or PGE\(_2\), in man, at sufficiently high rates, typically produce flushing in the face, neck and upper trunk, and headache.\(^7\)\(^8\)\(^1\)\(^9\)\(^-\)\(^2\)\(^1\) These substances cause vasodilatation in many vascular beds and a reduction in total peripheral resistance,\(^4\)\(^5\)\(^6\)\(^7\) but their action on cerebral vessels is not clear.\(^6\)\(^8\)\(^-\)\(^9\) Nonetheless, intravenous infusions of PGE\(_2\) at rates of 5-20 \(\mu\)g/min would cause headache,\(^2\)\(^0\)\(^2\)\(^1\) and assuming 90\% destruction during each pulmonary transit,\(^2\)\(^0\)\(^2\)\(^1\) produce arterial concentrations similar to those measured here at the time of autonomic hyperreflexia. It seems reasonable then to hypothesize that the headache in this syndrome may be caused by increased concentrations of the prostaglandins. The symptoms could be the result of a direct biochemical effect or of relaxation of vascular smooth muscles which would reduce the autoregulatory control of cerebral blood flow.\(^6\)\(^8\) In the latter circumstance, the headache might then, indeed, be due to the “passive” vasodilatation of cerebral vessels during the hypertensive episodes.

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Prediction of Late Survival in Patients with Mitral Valve Disease From Clinical, Hemodynamic, and Quantitative Angiographic Variables

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SUMMARY Late follow-up (average = 7.2 years) has been obtained in 249 patients with mitral valve disease who had quantitative angiographic assessment of left ventricular function at the time of initial catheterization in the 1960s. Surgically treated patients with mitral valve disease had significantly improved survival as compared to medically treated patients with mitral disease. The subgroup with mixed mitral stenosis and regurgitation and the subgroup with moderate impairment of ejection fraction account for this improved survival in surgically treated patients, which occurred despite greater functional and hemodynamic impairment in the surgical cohorts.

Using univariate life table survival analysis, ten variables were found to be predictive of survival in the medical cohort, and three in the surgical cohort. With multivariate Cox's regression analysis, end-diastolic volume and arteriovenous oxygen difference were significantly predictive of survival in the medical cohort; age was predictive of survival in the surgical cohort.

KNOWLEDGE OF PROGNOSIS in patients with valvular heart disease and, in particular, knowledge of how prognosis is altered by therapy are vital to making rational therapeutic decisions regarding these patients. Intuitively, left ventricular function would seem to be an important prognostic factor. Indeed, several studies have demonstrated that qualitative variables relating to ventricular performance such as radiographic heart size and/or left atrial size are predictive of late prognosis. Quantitative angiographic measurement of left ventricular volumes provides a more precise estimate of ventricular performance and may improve ability to predict survival.

Since the development of the technique of quantitative angiography at this institution over 15 years ago, measurement of left ventricular volumes and ejection fraction has been routine in most patients undergoing cardiac catheterization. This report details the analysis of potential prognostic indicators (including clinical, exercise, hemodynamic and angiographic variables) in 249 patients with mitral valve disease who had quantitative angiographic assessment of left ventricular performance between 1960 and 1970, and who have been followed for three to 14 years.

Methods

Patient Population

The medical records and catheterization files of all 831 adult patients having quantitative angiographic measure-

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