Drug Therapy of Dissecting Aortic Aneurysms

Some Reservations

By Joseph Lindsay, Jr., M.D., and J. Willis Hurst, M.D.

SUMMARY
The records of 56 patients with proved acute aortic dissection were studied for factors bearing on the applicability of vigorous drug therapy to reduce arterial pressure. Fourteen patients had an arterial pressure of 120 mm Hg systolic or less. Fifteen additional patients had evidence of occlusion of a major branch of the aorta. More than half of the 56 patients, therefore, could not have received antihypertensive drugs.

The presence of a contraindication to drug therapy marked a patient for an early death. All 29 died within 2 weeks. Twelve of the 27 in whom no contraindications to drug therapy were observed survived more than 2 weeks and six survived more than a year even though none were placed on a vigorous antihypertensive regimen.

Assessment of the efficacy of drug therapy of dissecting aortic aneurysm should take into account these facets of the natural history.

Additional Indexing Words:
Contraindications to drug therapy

Antihypertensive therapy

THE USE of antihypertensive drugs to decrease the left ventricular "impulse" in patients with acute aortic dissection has aroused considerable enthusiasm. Wheat and Harris and their co-workers have achieved remarkably favorable results with such therapy. These investigators feel that the high risk of emergency surgery may often be avoided.

We have encountered several problems in applying their technique of marked lowering of the arterial pressure. In one patient, we were unable to reduce the arterial pressure sufficiently. In another, treacherous ventricular arrhythmias accompanied drastic reduction of pressure. A third patient developed anuria due to bilateral renal artery obstruction after several days of apparently successful therapy, and surgical intervention was required.

It is not, however, these isolated instances of failure of drug therapy that most detract from its use. We are often prevented from employing such a regimen by the nature of the disease process itself. For this reason, a study of the applicability of drug therapy to a group of unselected patients with this problem was undertaken.

Patients Studied
We have recently reported the clinical features and course of 62 patients with proved dissecting aortic aneurysm. These patients were seen consecutively during the years 1949 to 1965 at a large general hospital. They seem to be a representative sample of the spectrum of the disease. The currently favored regimen of marked reduction of the arterial pressure was not used in this study group.

The onset of the illness could not be dated in four instances, and two patients entered the hospital several weeks after the acute illness. These six patients were excluded. The remaining 56 patients were observed during the early hours of their illness. The records of these 56 were analyzed to determine whether or not vigorous antihypertensive therapy could have been instituted. None actually received this therapy.

From the Department of Medicine, Emory University School of Medicine and the Medical Service, Grady Memorial Hospital, Atlanta, Georgia.
Arterial hypotension or occlusion of a major branch of the aorta seemed to contraindicate vigorous drug therapy in more than half the patients. These factors will be considered separately.

Wheat and his associates\(^1\) endeavored to lower the systolic pressure to 100 mm Hg with intravenous administration of trimetaphan, intramuscular reserpine, and oral guanethidine. A similar, but not identical, drug regimen was suggested by Harris and his coworkers\(^2\) who sought a level of 120 mm Hg systolic. Twelve patients in the present study entered with a systolic pressure of 100 mm Hg or less. The systolic pressure of two additional patients lay between 101 and 120 mm Hg. Antihypertensive therapy would not be applicable in these 14 cases.

Reduction of the arterial pressure in patients with evidence of ischemia of a limb or a vital organ may be expected further to compromise blood flow to the ischemic area. Therefore, evidence of occlusion of a major branch of the aorta is considered a contraindication to the drug regimen.\(^3\) Forty-two patients in the study group had a systolic blood pressure which exceeded 120 mm Hg. Ten of these patients had frankly ischemic limbs, while five of the remainder had hemiplegia or paraplegia due to the aortic dissection. The vigorous drug program was therefore contraindicated in an additional 15 patients. Patients with reduction or loss of a pulse without evidence of ischemia are included among the remaining 27 patients for whom drug therapy was not contraindicated.

Severe aortic regurgitation may occur acutely in patients with dissecting aortic aneurysm, and intractable heart failure may result. In such instances, surgical repair of the root of the aorta must be carried out without delay, and drug therapy is not used.\(^1,2\) The murmur of aortic regurgitation was noted in 20 patients of the present study group including six with no contraindication to drug therapy. In no case was heart failure severe enough to preclude drug therapy.

Our previously published data suggested that hypotension, absent pulses, and neurological signs (all contraindications to drug treatment) were frequent in patients in whom aortic dissection involved the ascending aorta, but were unusual when the process began distal to the arch vessels.\(^3\) Furthermore, patients in the former group were far less likely to survive the acute illness. Table 1 classifies the study patients according to the extent of the dissection and enumerates the contraindications for those in each group.

Of the 29 patients for whom drug therapy was contraindicated, 28 were known to have involvement of the ascending aorta. None of the 29 survived more than 2 weeks. On the other hand, 17 of the 27 patients who could have been offered drug therapy were of the more favorable group whose dissection began distal to the arch vessels. Twelve of the 27 patients (44%), who had no contraindication to drug therapy, survived more than 2 weeks, and six (22%) for more than a year. In figure 1, the survival of patients who had no contraindication to drug therapy is

<table>
<thead>
<tr>
<th>Contraindication</th>
<th>Ascending aorta involved</th>
<th>Ascending aorta spared</th>
<th>Extent uncertain</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mm Hg</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>or less</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>100-120 mm Hg</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Ischemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Limb</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>No contraindication</td>
<td>9</td>
<td>17</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>17</td>
<td>2</td>
<td>56</td>
</tr>
</tbody>
</table>

*Table 1: Contraindications to Drug Therapy to Lower the Arterial Pressure*

Circulation, Volume XXXVII, February 1968
compared with that of those in whom contraindications were observed. We should re-emphasize that no patient received vigorous drug therapy.

Rupture of the aorta into the pericardium, mediastinum, pleural space, or peritoneal space is the major cause of death during acute stages of aortic dissection.3 The use of drugs to reduce the hydraulic stresses on the aortic wall early in the course of the disorder is intended to diminish the danger of external rupture of that vessel. Of the present series 37 (66%) patients died of external rupture. Unfortunately, only 13 were among the group to whom drug therapy could have been given. Noteworthy, however, is the fact that 12 of 15 of the “treatable” patients who died in the first 14 days of illness did so from external rupture.

**Discussion**

It is often difficult to assess new therapy. This is especially true if the natural history of the disease under study is incompletely understood. Several features of the natural history of aortic dissection are pertinent to the assessment of vigorous antihypertensive therapy.

The data presented suggest that contraindications to marked reduction in the arterial pressure exist in approximately half of the patients seen with acute aortic dissection. Furthermore, the factors which contraindicate drug therapy mark the patient for an early demise. Conversely, the very fact that a patient is suitable for drug therapy marks him for a select group more likely to have a favorable outcome.

We have pointed out previously the fallacy of comparing patients treated surgically with a “control population” made up of all untreated patients with this condition.3 The same fallacies may arise when individuals treated with antihypertensive agents are contrasted with those not so treated. We believe that vigorous drug therapy may be extremely beneficial in the treatment of some patients during the acute episode. Its superiority over no drug treatment or over less vigorous antihypertensive therapy in comparable pa-
tients has not been conclusively demonstrated. It is not our intention to discourage the use of vigorous medical therapy for aortic dissection but to urge a critical analysis of its place in the spectrum of this disease.

We presently recognize four therapeutic groups among patients with aortic dissection: (1) A few patients are beyond the help of either surgical or drug therapy when first seen. By definition, we have nothing to offer them at present. (2) There are others with advanced age or complicating illnesses which preclude surgical intervention. These we treat with vigorous antihypertensive therapy if no contraindication exists. (3) There is a large group who may be subjected to surgery but in whom drug therapy is contraindicated. These should be operated on. (4) Finally, there are those suitable for surgery, for drug therapy, or for drug therapy followed by surgery. This group must be studied in a carefully planned manner. To do otherwise will not resolve the dilemma.

References
Drug Therapy of Dissecting Aortic Aneurysms: Some Reservations
JOSEPH LINDSAY, JR. and J. WILLIS HURST

Circulation. 1968;37:216-219
doi: 10.1161/01.CIR.37.2.216

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1968 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/37/2/216

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/