Natural History and Classification of Occlusive Thromboaortopathy (Takayasu’s Disease)

Kaichiro Ishikawa, M.D.

SUMMARY Fifty-four Japanese patients with occlusive thromboaortopathy (OTAP), including four males, were classified according to evidence of complications attributed to OTAP at the time when the diagnosis was established: Group I, uncomplicated OTAP; Group II, mono-complicated OTAP; presence of a single complication together with uncomplicated OTAP. Group II was subdivided according to severity into group IIA — mild or moderate form, and group IIB — severe form. Group III, multi-complicated OTAP with two or more complications as well as uncomplicated OTAP. The five-year survival rate after established diagnosis was 83.1%. Seven patients died of OTAP within five years, but all had belonged to group IIB or III.

THE CLASSIFICATION of occlusive thromboaortopathy (OTAP), including the natural history, prognosis and clinical features, has apparently never been documented. Classical Takayasu’s disease, which shows characteristic ocular findings, was renamed often, as it was found that the arterial lesions were far more widespread than originally thought. OTAP or Takayasu’s arteritis indeed may be what is known today as Takayasu’s disease. OTAP is a chronic inflammatory arteriopathy of unknown origin. The site of occurrence is the aorta and/or its main branches and the pulmonary artery is often involved. This pathological condition which is prevalent in females results in occlusive changes in the lumina, often combined with dilatation and secondary thrombus formation.

Although angiographic classifications consisting of arch type, extensive type, and descending thoracic and abdominal type according to the location of arterial lesions were made by several authors for diagnostic and surgical reasons, almost no prognosis can be determined with such classifications. Strachan wrote the only report of the natural history of Takayasu’s arteriopathy and found two distinct phases: the early pre-pulseless phase and the late or fatal pulseless phase.

For a better understanding of the natural history of this chronic disease, a follow-up of many patients, a careful history taking and a collection of past data in the absence of treatment are most important. In general, it has been considered that the prognosis of the disease is either poor or relatively good. It is important that the physician classify the patients correctly in order that the prognosis can be assessed.

In this report a clinical classification of OTAP, with special reference to the natural history and prognosis, is proposed. The course of the disease from the time of the onset of symptoms to the established diagnosis is also analyzed in 54 patients. Finally, a long-term follow-up study is presented.

Patients

During the 18-year period from May 1957 to April 1975, 54 Japanese patients with OTAP cardiovascular disorders were admitted to the Third Department of Internal Medicine, Kyoto University and the diagnosis of OTAP was made. Fifty of the 54 were females. The average age at the time of the established diagnosis was 30.3 years.

In 49 of the 54, angiography and/or autopsy were performed, and in the remaining five the diagnosis was made by clinical manifestations. The pulmonary circulation of 43 patients in this series was studied, 26 by pulmonary arteriography, cardiac catheterization and perfusion lung scanning, and 17 by perfusion lung scanning alone.

Patient Classification

The 54 patients were classified into four groups (groups I, IIA, IIB, III) according to evidence of four complications attributed to OTAP at the time the diagnosis was established.

Group I included seven patients with OTAP with or without the involvement of the pulmonary artery. All group I patients had narrowing or occlusion in some region of the aorta and/or its main branches.

Group II was comprised of 35 patients with OTAP and with one of the following complications: 1) Takayasu’s retinopathy — 14 cases; 2) secondary hypertension — 20 cases; 3) aortic regurgitation — 0; 4) aortic or arterial aneurysm — 1 case. Group IIA patients were the 24 with mild or moderate OTAP; group IIB patients had severe OTAP and numbered 11.

Group III included 12 patients with OTAP with two or more of the complications listed for group II. Four patients with aortic regurgitation were in group III. The complete listing of group III complications is in table 1.

The following is the criteria for severity of each of the four complications. Estimation of the severity of Takayasu’s retinopathy was made according to Uyama and Asayama’s classification: stage 1, dilatation of small vessels; stage 2, microaneurysm formation; stage 3, arterio-venous anastomoses; stage 4, ocular complications. In this report, the mild and moderate forms are identical with stages 1 and 2, respectively. The severe form is equivalent to stages 3 and 4. The findings in the ocular fundi of all patients in this series were those of an ophthalmologist, who also handled all the measurements of retinal artery pressure. Blood pressure

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TABLE 1. Clinical Classification of 54 Cases of Occlusive Thromboangiopathy (Takayasu’s Disease)

<table>
<thead>
<tr>
<th>Classification at the time of diagnosis</th>
<th>Number of cases</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I, Uncomplicated</td>
<td>7</td>
<td>13.0</td>
</tr>
<tr>
<td>Group II, Mono-complicated</td>
<td>35</td>
<td>64.8</td>
</tr>
<tr>
<td>Takayasu’s retinopathy</td>
<td>14</td>
<td>25.9</td>
</tr>
<tr>
<td>Not severe: (IIa)</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Severe: (IIb)</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Secondary hypertension</td>
<td>20</td>
<td>37.0</td>
</tr>
<tr>
<td>Not severe: (IIa)</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Severe: (IIb)</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Aneurysm (IIa)</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>Group III, Multi-complicated</td>
<td>12</td>
<td>22.2</td>
</tr>
<tr>
<td>AR, SH</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>AN, SH</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>TR, SH</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>AN, TR</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>AR, SH, TR</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AR = aortic regurgitation; SH = secondary hypertension; AN = aneurysm; TR = Takayasu’s retinopathy.

values were graded according to: mild form — 140 to 159 mm Hg brachial systolic and/or 90 to 94 mm Hg diastolic, or 160 to 179 mm Hg popliteal systolic and/or 90 to 94 mm Hg diastolic; severe form — 200 mm Hg or over brachial systolic and/or 110 mm Hg or over diastolic, or 230 mm Hg or over popliteal systolic and/or 110 mm Hg or over diastolic; moderate form — between the mild and severe forms. For the measurement of blood pressure in the thighs, an 18 cm width cuff was used. There were some patients in whom it was impossible to obtain the “correct” blood pressure in any extremity because of occlusion or marked narrowing of the aorta or its main branches. In these patients the blood pressure was evaluated on the basis of retinal artery pressure in ophthalmodynamometric measurements or blood pressure in the ascending aorta by means of direct measurement. Severity of aneurysm of the aorta and its main branches was assessed by angiography. Severe aneurysm was defined as a diameter more than twice that of normal vessels. Severity of aortic regurgitation was estimated angiographically or clinically.

A scrupulous history was taken of each patient. All past records and roentgenograms were collected and each patient has been followed-up for observation periods ranging from 6 months to 18.4 years, the average being 6.4 years, from May 1957 through October 1975. The 5-year survival rate after established diagnosis of OTAP for the 54 patients was calculated using the life table method.

Results

Classification

Distribution of Cases

Group I included only seven of the 54 patients, group II 35 cases, in which groups IIA and IIB included 24 and 11 cases, respectively, and group III 12 cases. Four patients with aortic regurgitation complications belonged to group III. Takayasu’s retinopathy was found in 20 cases (37%), 14

Figure 1. The percentages of patients with involvement of the pulmonary artery are shown by group. Nineteen of the 43 patients examined (44.2%) had pulmonary involvement.

Figure 2. Thoracic aortogram (A) and pulmonary arteriogram (B) at age 26 in case 38. A) Occlusion of the left subclavian artery and slight narrowing of the proximal portion of the ipsilateral common carotid artery. B) Occlusion at the orifice of the ascending branch of the left pulmonary artery, moderate generalized narrowing of the descending branch and occlusion of the posterior basal branch.
An example in group I

Major results of the examination of a case in group I at the time of established diagnosis are presented. S.K. (case 38), a 26-year-old female, was admitted with a pulselessness of the left radial artery, episodes of transient blurring of vision, and transient, mild, easy fatigability of the left arm of three years' duration. Her physical activity was not restricted by her symptoms. Complete occlusion of the left subclavian artery and slight narrowing of the proximal portion of the ipsilateral common carotid artery were evident (fig. 2A). Nearly normal appearance of the abdominal aorta and its main branches was revealed by abdominal aortography. There was a moderate involvement of the pulmonary artery with occlusion and narrowing of the branches of the left pulmonary artery (fig. 2B). The ESR showed 61 mm/hr.

Natural History

**Erythrocyte Sedimentation Rate**

Markedly accelerated ESR at the time of the established diagnosis of OTAP was usually seen in the young patients. The average interval from the time of onset of symptoms to diagnosis was relatively short. The ESR value tended to decelerate with aging (fig. 3, table 2). The occurrences of death and acute events during the follow-up period were not always dependent on the severity of the ESR at the time of diagnosis (table 2).

**Interval from Onset to Diagnosis**

In 54 patients, the average age at the time of onset of symptoms of OTAP and of the established diagnosis was 22.1 (9 to 43) and 30.3 years (16 to 63), respectively (table 3). The onset commonly occurred in those of 10 to 24 years of age (64.8%). In only six of the 54 did the onset occur after 30 years of age. The distribution according to age at the time of diagnosis is presented in figure 3. During the average interval from the onset to the diagnosis, 8.2 years (less than 1 to 35), complications developed. The interval in group III was obviously longer than that of the other groups (table 3).

**Number of Deaths and Patients with Acute Events**

Nine of the 54 patients died during the follow-up period, seven of them within five years after the established diagnosis. These seven patients comprised 30.4% of groups IIb and III. Of the remaining two patients, the one in group IIa died of OTAP and the one in group I died of a uterine cervix carcinoma. Among five other patients in whom acute events occurred during the follow-up period, three belonged to groups IIb and III and the remaining two to group IIa (table 3).

During the follow-up period, steroid and anticoagulant therapy was given to 19 and 41 patients, respectively. These drugs were given concomitantly to most patients. Among the 19 treated with corticosteroids, five were on the drugs for over four years. As adjuvant drugs, acetylsalicylic acid and vasodilators were employed. For symptomatic therapy, digitalis, antihypertensive agents, and antibiotics were frequently used. Surgical treatment consisted of patch-graft reconstruction of the abdominal aorta in one patient, bypass graft of the thoracic aorta in one, and right nephrectomy in one.

**Deaths and Acute Events**

Eight patients died of OTAP during the follow-up period. In these patients the average interval from onset to diagnosis usually was relatively long (10.5 years) and the time from

### Table 2. Relation between ESR at Diagnosis and Interval from Onset to Diagnosis, Death and Acute Event after Diagnosis

<table>
<thead>
<tr>
<th>ESR at the time of diagnosis (mm/hr)</th>
<th>Number of cases</th>
<th>Average years</th>
<th>Interval from onset to diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deaths</td>
<td>Acute events after diagnosis</td>
<td>Acute events nil after diagnosis</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>--------</td>
<td>-----------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>0-19</td>
<td>5 (1)*</td>
<td>3</td>
<td>17 (1)</td>
</tr>
<tr>
<td>20-39</td>
<td>2 (1)</td>
<td>2</td>
<td>14 (1)</td>
</tr>
<tr>
<td>40-60</td>
<td>2</td>
<td>0</td>
<td>9 (3)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses indicate those on steroid therapy.
Table 3. *Number of Deaths and Patients with Acute Events after Diagnosis*

<table>
<thead>
<tr>
<th>Classification at the time of diagnosis</th>
<th>Number of cases</th>
<th>Average years</th>
<th>Interval; onset to diagnosis</th>
<th>Length of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deaths</td>
<td>Acute events after diagnosis</td>
<td>Acute events nil after diagnosis</td>
<td>Total</td>
</tr>
<tr>
<td>Group I, Uncomplicated</td>
<td>1*</td>
<td>0</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Group II, Mono-complicated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not severe: (IIa)</td>
<td>1</td>
<td>2</td>
<td>21</td>
<td>24</td>
</tr>
<tr>
<td>Severe: (IIb)</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Group III, Multi-complicated</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>5</td>
<td>40</td>
<td>54</td>
</tr>
</tbody>
</table>

*Died with uterine cervix carcinoma.*

Table 4. *Duration, Grouping and Major Factors Related to Death in Eight Cases*

<table>
<thead>
<tr>
<th>Case no</th>
<th>Onset</th>
<th>Diagnosis</th>
<th>Death</th>
<th>Classification at the time of diagnosis</th>
<th>Major factors related to death</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>16</td>
<td>21</td>
<td>23</td>
<td>G IIIb: SH</td>
<td>Aortic reconstruction</td>
</tr>
<tr>
<td>10</td>
<td>39</td>
<td>42</td>
<td>43</td>
<td>G IIIb: SH</td>
<td>CHF</td>
</tr>
<tr>
<td>11</td>
<td>21</td>
<td>21</td>
<td>31</td>
<td>G IIa: SH</td>
<td>Cerebrovascular accident</td>
</tr>
<tr>
<td>20</td>
<td>27</td>
<td>62</td>
<td>67</td>
<td>G III: SH, AR</td>
<td>Cerebral thrombosis</td>
</tr>
<tr>
<td>22</td>
<td>13</td>
<td>19</td>
<td>21</td>
<td>G III: SH, AR</td>
<td>Sudden death, CHF</td>
</tr>
<tr>
<td>28</td>
<td>14</td>
<td>23</td>
<td>25</td>
<td>G III: SH, AN</td>
<td>CHF</td>
</tr>
<tr>
<td>32</td>
<td>28</td>
<td>46</td>
<td>50</td>
<td>G IIIb: TR</td>
<td>Steroid withdrawal shock</td>
</tr>
<tr>
<td>45</td>
<td>23</td>
<td>31</td>
<td>34</td>
<td>G III: SH, TR</td>
<td>Cerebral embolism</td>
</tr>
<tr>
<td>Av.</td>
<td>22.6</td>
<td>33.1</td>
<td>36.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: SH = secondary hypertension; AR = aortic regurgitation; AN = aneurysm; TR = Takayasu's retinopathy; CHF = congestive heart failure.

diagnosis to death usually was short (3.7 years in average). In most patients, death stemmed from congestive heart failure and cerebrovascular accidents (table 4). Various acute events due to OTAP occurred in five other patients who survived (table 5).

*Five-year Survival Rate after Diagnosis*

The 5-year survival rate after the established diagnosis for 54 patients was 83.1%; such estimations assisted in determining the prognosis (table 6, fig. 4).

*Two Typical Patients with a Progressive Long Course*

In M.S. (case 45), the onset occurred at age 23 when all her left fingers frequently looked transiently pale; however, her physical activity was hardly restricted. Only after eight years was the diagnosis established. At that time, there had been considerable improvement in the ESR, but narrowing of the main branches from the arch of the aorta had gradually increased and extended. Takayasu's retinopathy and mild hypertension developed but a small integral dose of corticosteroid was the only prescription she had received until that time. While under treatment she died at age 34 of a cerebral embolism following blindness (fig. 5). The photograph of her left ocular fundus shows retinal arteriovenous anastomoses on and around the optic disc (fig. 6). Total permanent visual loss occurred in this eye approximately one month after this photograph was taken.

In C.M. (case 39), the symptoms of onset included dizziness and easy fatigability of the upper extremities at age 24. While the disease ran a course of approximately 16 years, including an almost asymptomatic interval of about seven years, aortic regurgitation, marked narrowing of the right renal artery and hypertension developed and the pattern of symptoms changed from those of aortic arch syndromes into cardiac complaints. At age 40, she developed acute pulmonary edema. She had had scarcely any treatment until that time (fig. 7). Retrograde thoracic arteriography and pulmonary arteriography revealed extensive involvement of the aorta and its main branches and of the pulmonary artery, respectively. Marked narrowing of the right renal artery and normal appearance of the left were

Table 5. *Duration, Grouping and Acute Events in Five Cases*

<table>
<thead>
<tr>
<th>Case no</th>
<th>Onset</th>
<th>Diagnosis</th>
<th>Occurrence of acute events</th>
<th>Classification at the time of diagnosis</th>
<th>Acute events after diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>17</td>
<td>19</td>
<td>28</td>
<td>G IIa: TR</td>
<td>Cerebral hemorrhage at the 2nd stage of delivery</td>
</tr>
<tr>
<td>21</td>
<td>40</td>
<td>44</td>
<td>48</td>
<td>G IIa: AN</td>
<td>Dissecting aneurysm</td>
</tr>
<tr>
<td>26</td>
<td>26</td>
<td>40</td>
<td>48</td>
<td>G IIb: SH</td>
<td>Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>39</td>
<td>24</td>
<td>40</td>
<td>40</td>
<td>G III: SH, AR</td>
<td>Acute pulmonary edema</td>
</tr>
<tr>
<td>41</td>
<td>28</td>
<td>35</td>
<td>36</td>
<td>G IIIb: TR</td>
<td>Unilateral blindness</td>
</tr>
<tr>
<td>Av.</td>
<td>27.0</td>
<td>35.6</td>
<td>40.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
revealed by abdominal aortography and selective right renal arteriography at age 41 (fig. 8A and B). The renal venous plasma renin activity from the right and the left sides was 14.0 and 7.6 ng/ml/hr, respectively. Right nephrectomy was done approximately nine months after aortography. The markedly elevated blood pressure decreased considerably but incompletely (fig. 7).

Discussion

The natural history and clinical classification of OTAP is shown in figure 9. The nature of OTAP gives rise to four main complications. These established complications may influence the subsequent course of OTAP even when the accelerated ESR, which well reflects the activity of the disease, tends to decelerate (table 2). According to Nasu’s reports of autopsy series,7, 17 most commonly viewed lesions in the arterial wall were not those of an inflammatory cell reaction but rather a fibrosis. In the present series, approximately one-third of all patients who belonged to groups IIb and III at the time of established diagnosis died of OTAP within five years, despite treatment. Other patients also developed acute events which resulted in a marked restriction of their physical activity. On the other hand, the prognosis was excellent or fairly good in the well treated patients in groups I and IIa (tables 3, 4, 5). This clinical classification well represents the natural history and the key manifestations influencing the prognosis elicited from protein clinical features of OTAP. Strachan19 stressed the importance of an early diagnosis on the basis of his own three cases and reviews of the literature. It was clearly evident in the experience with the 54 patients herein that any delay in diagnosis and commencement of medical treatment necessarily meant a poor prognosis, except for a few patients with spontaneous healing and mild circulatory sequelae. In the advanced stage, the results of surgical treatment are not always good.18

Such a long interval as described above between the onset and the established diagnosis may be due to the following: 1) failure to diagnose a simple but important early sign of bruits over the stenosing aorta and/or its main branches, 2) failure to detect diminished or unpalpable pulses and the accelerated ESR, 3) emphasis put on related symptoms rather than on intense research of the pertinent etiology, 4) mild complaints without limitation of physical activity in most patients in the early phase, and particularly the presence of an asymptomatic state during some period in the course thereafter.

Takayasu’s Retinopathy

The stage of retinal arteriovenous anastomoses like Takayasu’s original finding1 corresponds to the advanced stage, stage three in the Uyama and Asayama classification.18 We had encountered no such patient with a late sign when we published our previous data;11 however, four cases are included in the present series. Aortography in these four revealed that a normal lumen was never apparent in any artery of the four vessels (bilateral common carotid and vertebral arteries) in each case, but rather occlusion and marked narrowing were present. Of the four, one improved from stage three to two during the follow-up period while treatment was being continued. One patient developed unilateral blindness. Progression was halted in the remaining two patients. One other case belonging to group III at the time of diagnosis progressed from stage two to three despite treatment (fig. 6). In a previously reported case,19 only the left common carotid artery was opacified by means of aortography but the ocular fundi showed no findings of Takayasu’s retinopathy. Palpatory, auscultatory and retinal findings, including values of retinal artery pressures, before aortography should serve to assess the degree of involvement of the vessels.

Secondary Hypertension

The occurrence of systemic hypertension in OTAP has been reported by many authors.11, 18, 20, 21 Ask-Upmark21 found that almost 50% of the 60 patients reported in the literature, including his own four cases, had hypertension. The reduced elasticity of the wall of the arterial “wind-kettle” and the renal origin were emphasized in the pathophysiology of this hypertension. Renovascular hypertension16, 18, 23-28 and proximal hypertension due to an atypical coarctation of the disease16, 18, 24, 29, 30 have been reported. Recently, Kulkarni et al.31 reported an impressive case in which amelioration of stenotic lesions affecting the abdominal aorta and the renal arteries and reversal of hypertension occurred with corticosteroid therapy.

It seems that hypertension in this disease is secondary to marked narrowing of the aorta, renovascular origin, reduced
Aortic Regurgitation

Jervell\textsuperscript{32} was apparently the first to detect, on auscultation, aortic regurgitation in this disease. Since then, such has been determined by auscultation\textsuperscript{10, 25, 34} and aortography.\textsuperscript{18, 23, 35, 36} Pathologically, dilatation of the involved ascending aorta, separation of the aortic commissures and thickening of the valve cusps themselves are described as the lesions responsible for aortic regurgitation in this disease.\textsuperscript{5, 37, 38} It is often difficult to differentiate aortic regurgitation OTAP from that due to aortitis in giant cell arteritis.\textsuperscript{29, 40}

Aortic or Arterial Aneurysm

OTAP has been considered essentially one of the occlusive arterial diseases of the aorta, its main branches and the pulmonary artery. It has, however, been reported by several authors\textsuperscript{19, 25, 27, 30, 41-43} that narrowing and/or occlusion are sometimes combined with aneurysm as well as dilatation. Grollman and Hanafee\textsuperscript{44} described an aneurysm formation with atypical manifestations as seen in this disease. Vinichchaikul\textsuperscript{45} reported aneurysmal dilatations in seven of eight cases. Case 1 in his report had an isolated aneurysm and no narrowing. In this disease process, occlusive lesions may be first produced and in some cases aneurysmal changes follow at any other portion of the aorta and its main branches. A clinical differential diagnosis between aneurysm due to this disease and that due to aortitis of giant cell arteritis may be difficult.\textsuperscript{40}

Pulmonary Arterial Involvement

Ota\textsuperscript{46} first described autopsy findings in a patient with this disease where the pulmonary artery was involved. Since elasticity of the aortic wall, aortic regurgitation, and some overlapping. Hypertension due to abnormal function of the carotid sinuses and to cerebral ischemia has not been established. An example of some overlapping of the causes for hypertension is shown in figures 7 and 8.

then, pulmonary arterial involvement has been confirmed not only by autopsy\textsuperscript{47, 50, 46} but also by plain chest roentgenography,\textsuperscript{47-49} pulmonary arteriography,\textsuperscript{5, 19, 47, 50-52} measurement of pulmonary arterial pressure,\textsuperscript{19, 40, 56} and pulmonary perfusion scanning.\textsuperscript{56-58} Association with pulmonary arterial involvement has been found in 50% or more of patients with this disease. In this series, 19 of the 43 patients in whom pulmonary involvement was appraised had pulmonary arterial involvement and there was no relation between systemic and pulmonary arterial systems regarding extent and severity of the involvement (fig. 1).

We previously reported a case of OTAP with pulmonary hypertension.\textsuperscript{19} Later, pulmonary hypertension (mean pulmonary arterial pressure above 20 mm Hg) was found in

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure5}
\caption{A natural history of one case of occlusive thromboaortopathy (case 45): death following blindness.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure6}
\caption{Fundus photograph of the left eye at age 32 in case 45. Arteriovenous anastomoses on and around the disc and preretal hemorrhages (Takayasu’s retinopathy stage 3). (By courtesy of Dr. M. Uyama.)}
\end{figure}
eight of 22 and in seven of 26. According to the latter report, there were three types of secondary pulmonary hypertension: pulmonary arterial origin in which it is generally mild, left ventricular origin and combined pulmonary arterial and left ventricular origin.

Lupi et al. suggested that pulmonary arterial involvement should be included in the classification of this disease and they separated it as Type IV from the previously described three types. In this series, it is emphasized as pulmonary Takayasu's disease (fig. 1).

**Erythrocyte Sedimentation Rate**

ESR is an excellent index for the activity of this disease and patients in the active stage respond remarkably to corticosteroids. Not only are patients' complaints reduced but progression of arterial involvement during the active period of the disease is prevented.

Nakao et al. demonstrated that the elevated ESR during the early and active stages of the disease was generally followed by a gradual return to normal. The present study shows that the accelerated ESR tends to spontaneously decelerate with aging, although there were young patients with a normal ESR (fig. 3). Factors influencing susceptibility to occurrence of OTAP are not well defined. Etiology and pathogenesis of OTAP remain unknown and can only be speculative. Group A streptococcal infection, tuberculosis and hormonal imbalance have been suggested as factors relating to the pathogenesis. Concerning circulating

**FIGURE 7.** A natural history of one case of occlusive thromboaortopathy (case 39): changing pattern of symptoms.

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**FIGURE 8.** Abdominal aortogram (A) and selective right renal arteriogram (B) at age 41 in case 39. Marked narrowing of the right renal artery at its orifice (arrow, A), followed by marked generalized narrowing (B). Note the irregular contour of the aorta; the distal portion of the superior mesenteric artery is not visible and there is formation of the meandering artery of the inferior mesenteric artery (A).
antibodies against antigens of the arterial wall, there have been both positive \(^1\), \(^2\), \(^6\), \(^4\) and negative results. \(^1\), \(^6\), \(^7\)

**Prognosis**

In several studies, death occurred in 12 of 69 patients, \(^1\) in 17 of 67 during observation which ranged from one to 21 years, \(^4\) in 13 of 64 during an average follow-up period of 6.6 years, \(^8\) and in 16 of 107. \(^9\) In the present series, death occurred in nine of 54 during the follow-up period. In most of these patients, death followed congestive heart failure and cerebrovascular accidents, although there also were deaths related to surgery. The prognosis, however, should be assessed not as a whole but rather group by group as there are marked differences in the outcome among the groups. As is the case in most clinical pathologies, the sooner the diagnosis is established and adequate therapy initiated, the better is the prognosis.

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**References**

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Evaluation of Methods for the Quantification of Experimental Myocardial Infarction

ARTHUR J. ROBERTS, M.D., PAUL R. CIPRIANO, M.D., DANIEL R. ALONSO, M.D., JEROME G. JACOBSTEIN, M.D., JOHN R. COMBES, AND WILLIAM A. GAY, JR., M.D.

SUMMARY Several invasive and noninvasive techniques used in determining the size of experimental myocardial infarction were evaluated after acute ligation of the left anterior descending (LAD) coronary artery in ten dogs. Systemic blood pressure, left ventricular end-diastolic pressure (LVEDP), and heart rate did not change significantly for up to 24 hours after coronary occlusion. Left ventricular wall motion abnormalities were detected by left ventriculography in the distribution of the LAD but these changes did not correlate well with the infarct weight determined at autopsy.

THE DEVELOPMENT OF A TECHNIQUE which rapidly and accurately determines the presence and extent of myocardial injury after coronary artery occlusion has been an elusive, but important goal.1,2 Immediate and long term disability in patients with myocardial infarction depends in large part on the degree of myocardial damage. Mortality from cardiogenic shock,3 ventricular dysrhythmia,4 and left ventricular dysfunction5 following acute myocardial infarction appears to be directly related to the extent of myocardial necrosis. Furthermore, the selection of patients for coronary artery bypass surgery might be influenced by the detection of recent myocardial necrosis if the latter could be reliably measured.

In recent years, it has been demonstrated that infarct size can be modified by pharmacologic and hemodynamic interventions in acute experimental preparations6 and perhaps in man as well.7 An accurate means of determining infarct size could provide information that would be potentially useful for evaluating the effectiveness of interventions used to protect ischemic myocardium. Serial measurements of infarct size might also provide information about the natural history of infarcts and allow correlations between infarct size and ultimate left ventricular functional impairment.

Acute myocardial injury has been assessed in the past in the experimental animal by various techniques including ventriculography,8 epicardial electrocardiography,9 radionuclide imaging,10 histochemical staining,11 histologic

On the other hand, the number of epicardial sites with ST-segment elevation of ≥2mm (mean 15.1 sites ± 6.6 SEM) and the infarct area as measured by 99mTc-glucophonate (TeCGH) myocardial imaging (15.7 sq cm ± 6.0) did correlate strongly with the infarct weight (16.8 g ± 0.7) determined by the nitroblue tetrazolium (NBT) technique (r = 0.91).

TeCGH myocardial scintigraphy and epicardial ST-segment mapping allowed early and accurate quantification of experimental myocardial infarcts ranging from <1 g to 28 g.

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K Ishikawa

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