Calcific Embolization Associated with Valvotomy for Calcific Aortic Stenosis

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EMBOLIZATION by calcified valvular debris from the aortic valve has been reported to occur spontaneously1-3 and in association with aortic valvotomy.4-9

The purpose of the present study was to estimate the approximate incidence of calcific emboli related to operations involving the aortic valve, to document the sites of embolization, and to determine the clinical consequences of the embolic event.

Materials and Methods

The material for this study consisted of 53 adult male and nine adult female patients from the files of the Mayo Clinic between January 1954 and April 1962, inclusive, who had undergone aortic valvular surgery for calcific aortic stenosis. Necropsy was performed in each instance. Information was derived from clinical histories, necropsy protocols, and gross and microscopic examination of the available organs.

The patients were divided into two groups on the basis of the method of valvotomy employed. Group 1 consisted of patients in whom a closed valvotomy (transventricular or transaortic) had been performed. Group 2 consisted of patients in whom a valvotomy (debridement, or excision and prosthetic replacement of one or more cusps, or both; or total excision of valve with prosthetic replacement) had been carried out under direct vision (open valvotomy with the aid of extracorporeal circulation). Group 2 was subdivided into groups 2A and 2B, which consisted of patients in whom the valvotomy had been done prior to (group A) or following (group B) the recognition of the threat and relative frequency of calcific embolization. Certain specific measures were taken for patients in group 2B in an attempt to minimize the occurrence of calcific embolization during valvotomy. Essentially, these measures consisted of occlusion of the coronary ostia during the valvotomy and constant diligence in detecting and removing all bits of valvular debris.

The heart was the only organ uniformly available for study in each patient. The original description of each heart was reviewed, and each heart was re-examined. The methods of examination of the heart and the other available organs, as well as the preparation of tissue for histologic examination, have been previously described.9

The microscopic characteristics of the aortic valve in calcareous aortic stenosis provided some insight into the histologic patterns of calcific emboli derived from such valves (figs. 1-3). Microscopically, the calcified aortic valve contained islands of calcified matrix surrounded and often traversed by collagenous fibers accompanied by a small amount of elastic tissue. The collagenous tissue made up the largest part of the nonealereified tissue of the valve and in certain areas was very dense and relatively avascular, not unlike the outer margins of normal valve cusps. Bone formation, when present, usually occurred in a well-vascularized area near the base of the valve. Most of the elastic tissue of the deformed valve was usually concentrated along the ventricular surface of the valve cusp beneath a layer of collagenous intimal tissue.

Usually the decalcified matrix of the nodular deposits within the deformed valves stained positively with periodic acid-Schiff (PAS) stain and was basophilic with azure-eosin at pH 4.5. At times the basophilia was intense around the periphery of decalcified matrix. Some areas of matrix that were not PAS-positive were often moderately basophilic with azure-eosin at pH 4.5. Significant metachromasia was not seen with either methyl violet or azure-eosin staining of formalin fixed, decalcified valves. All occlusive arterial lesions that were observed histologically were classified as calcific embolic or nonealereified embolic.

A calcific particle was considered to be derived from aortic valvular material and most likely embolic when both the following criteria were fulfilled: (1) the presence, within the lumen of an artery or arteriole, of calcific material with tinctorial characteristics similar to those enumerated above for the aortic valve, and (2) the absence of intimal or medial atheromatous plaques or calcification in the segment of artery containing the embolus.

All calcific embolic events were classified as having been spontaneous or postsurgical. All cal-
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Aortic valve of a 59-year-old man in whom valvular debridement was carried out. Emboli were demonstrated in myocardium. Recent infarct of kidney was also present, but no emboli were found. Death occurred 24 hours after valvotomy.

Aortic valve of 55-year-old man who died 12 hours after valvotomy. Note relationship of connective tissue to foci of decalcified matrix (periodic acid-Schiff; × 5 reduced photographically).

Right middle cerebral artery of a 47-year-old woman in whom a transventricular valvotomy had been carried out for severe calcific aortic stenosis. Following operation, response was slow, and left hemiparesis was noted. Patient died on second postoperative day. A recent calcific embolus containing much collagenous tissue is present within lumen of vessel. Wall of vessel shows minimal atherosclerotic changes (elastic tissue-van Gieson; × 30 reduced photographically).

Critical emboli were considered to have been associated with surgery except when the embolic particle was completely surrounded by collagen or covered by a layer of endothelium and the postoperative survival period was 72 hours or less. It seemed that this degree of mesenchymal reaction to the presence of the embolus probably could not have occurred during a brief postoperative period. It is possible by these criteria that, in patients who survived for long periods postoperatively, an occasional spontaneous embolus was erroneously classified as postsurgical.

Results

Eighty-two instances of embolization were identified in 38 (61 per cent) of the 62 patients studied. In eight of these 38 patients, 16 additional emboli were found which, according to the criteria used, probably occurred prior to valvular surgery. Thirty-five patients (57 per cent) had calcific emboli to the major or minor coronary arteries, or both; in eight patients (13 per cent) emboli were present in the arterial supply of other organs (kidney, five patients; brain, two patients; eye, one patient) (table 1). The general distribution of emboli associated with surgical procedures on the aortic valve was similar to that previously reported for spontaneous embolization.3

Major Coronary Arteries

Major coronary embolization occurred in 10 patients (16 per cent). The left coronary artery was the site of embolization in nine patients (main, one; left anterior descending branch, seven; circumflex branch, one) and

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the right coronary artery was the site in one patient (posterior descending branch). The size of the emboli varied from 1 to 3 mm. Two separate emboli were identified in one patient; one was lodged 3 cm. from the origin of the left anterior descending branch while the other occluded the left circumflex branch 6 cm. from its origin. In several instances elastic and collagenous fibers were seen within and surrounding the calcific particle (fig. 4). Some degree of coronary sclerosis was present in all patients; it was considered grade 1 in three patients, grade 2 in three patients, and grade 3 in four patients. Focal microscopic areas of acute myocardial infarction were present distal to the occluded vessel in two patients. Six of 10 patients had died either directly following operation or during the first postoperative day. Of the four surviving patients one survived 6 weeks, one 14 weeks, one 14 months, and one 4 years.

**Minor Coronary Arteries**

Sixty-one instances of embolization of minor coronary arteries occurred in 33 patients (53 per cent) (figs. 5 and 6). This included seven of 10 patients in whom embolization of a major coronary artery had also occurred. The size of the emboli varied from 0.1 to 0.4 mm. The outline of these emboli was often irregular, with a jagged edge impinging on the wall of the arteriole. The bifurcation of the small arteries was often the site of emboli. The lumen of the vessel was completely occluded in approximately half the patients. The number of emboli found in the 10 samplings of the interventricular and left ventricular portions of the myocardium varied from one to nine (17 cases with one, 13 cases with two, one case with three, one case with six, and one case with nine). In only two pa-

**Table 1**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Arteries</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Major coronary only</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Major and minor coronary</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Minor coronary only</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Large (main renal interlobar)</td>
<td>0</td>
</tr>
<tr>
<td>Kidney</td>
<td>Small (arenate, interlobular, afferent)</td>
<td>5*</td>
</tr>
<tr>
<td>Brain</td>
<td>Large (anterior, middle, posterior)</td>
<td>2*</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>0</td>
</tr>
<tr>
<td>Eye</td>
<td>Central retinal</td>
<td>1*</td>
</tr>
</tbody>
</table>

*Emboli were present in two or more organs.

**Figure 4**

Left circumflex coronary artery 6 cm. from its origin, in a 55-year-old man who died immediately after open valvotomy. Calcific embolus occludes lumen of vessel. An embolus was also present in left anterior descending branch 3 cm. from its origin.

**Figure 5**

Left ventricular myocardium of a 36-year-old man who experienced facial weakness and extensor rigidity soon after a transventricular aortic valvotomy and died 3 days postoperatively. Necropsy was limited to thorax. Calcific particle is present in a myocardial arteriole (hematoxylin and eosin; × 150 reduced photographically).
Patients could acute myocardial infarction be identified distal to or in association with the occluded vessel.

Cerebral Arteries

Cerebral embolization was identified in two patients. In one of these patients, emboli were demonstrated in the right middle and the right anterior cerebral artery (fig. 3). In the other patient, a calcific embolus had occluded the posterior cerebral artery. The size of the embolic particles varied from 1 to 1.5 mm., and in both instances acute cerebral infarction was present distal to the occluded vessel. The cerebral arterial atherosclerosis was considered as grade 1 in both cases. In two additional patients, small cerebral infarcts were noted; however, no emboli could be demonstrated.

Retinal Arteries

A calcific embolus was identified in the central retinal artery in one patient (previously reported by Edwards)\(^9\) (fig. 7). The embolus had been demonstrated funduscopically on the seventh postoperative day, appearing similar to the “white body” previously described by Hollenhorst.\(^10\) Associated with the embolus was early degeneration of the nerve fibers of the retina. Clinical evidence of embolization had occurred in an additional patient following aortic valvotomy 2 years prior to death; however, the eyes were not examined at necropsy.

Renal Arteries

Calcific emboli were observed within renal arcuate and interlobular arteries of five patients (fig. 8). In two of these patients, emboli were also identified in an afferent arteriole. Acute infarction of the renal cortex was present in one patient distal to an occluded interlobular artery. In the remaining four patients, no renal infarcts were observed. The renal arteries and their branches showed minimal arteriosclerotic changes and did not have any evidence of medial calcification. Acute renal cortical infarction was present in two additional patients in whom no emboli could be demonstrated.

Relationship of Emboli to Cause of Death

The relationship of the incidence of emboli to the postoperative interval and to the cause of death was investigated. Calcific emboli occurred in about half the patients who died...
either on the day of operation (first postoperative day) or after the first postoperative week. Approximately three quarters of the patients who died between the second and seventh postoperative days experienced calcific embolization. In only six cases were the calcific emboli thought to be the immediate cause of death (four to major coronary arteries, two to cerebral arteries). Postoperatively, myocardial infarction was associated more frequently with coronary atherosclerosis than with coronary embolization. Postoperative hemorrhage was a serious problem in nine patients. In eight of these nine patients, calcific emboli were demonstrated in minor coronary arteries.

**Frequency of Embolization by Groups**

The frequency of major and minor coronary embolization is recorded in table 2. Both major and minor coronary embolization were more frequent in group 2 (patients in whom valvotomy had been performed under direct vision) than in group 1 (patients in whom a transventricular or transaortic valvotomy had been performed). The frequency of major coronary embolization was less in group 2B (patients whose aortic valvotomy had been carried out following the recognition of the present incidence of calcific embolization) than in group 2A (patients whose valvotomy had been performed prior to the recognition of the present incidence of calcific embolization), but the same high frequency of minor coronary embolization occurred throughout group 2.

### Table 2

**Comparison of Surgical Procedure with Incidence of Calcific Embolization in 62 Patients Undergoing Surgery for Calcific Aortic Stenosis**

<table>
<thead>
<tr>
<th>Group</th>
<th>Surgical procedure</th>
<th>Total patients</th>
<th>Patients with coronary artery embolization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Major</td>
</tr>
<tr>
<td>1</td>
<td>Closed*</td>
<td>11</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>2</td>
<td>Open†</td>
<td>39</td>
<td>9 (23%)</td>
</tr>
<tr>
<td></td>
<td>Open†</td>
<td>12</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Transventricular or transaortic valvotomy.
†Debridement or partial valve replacement under direct vision with the aid of extracorporeal circulation, or both; or total prosthetic valve replacement.

**Figure 8**

Right kidney of a 45-year-old man who died 2 days after open valvotomy. Small calcific particle occludes lumen of a glomerular afferent arteriole. In addition, an interlobular artery was occluded with a calcific embolus and an acute cortical infarction was present distal to occlusion (hematoxylin and eosin; × 275 reduced photographically).

**Discussion**

In a previous study, evidence of spontaneous calcific embolization was found in almost one fifth of patients who had calcific aortic stenosis. In the present study, postsurgical calcific embolization was observed in more than half of the patients who died at various intervals following surgical procedures for the relief of calcific aortic stenosis.

The true incidence of arterial embolization of an organ can most reliably be determined by complete examination of the entire vasculature of that organ. In our studies the heart was the only organ that was extensively ex-
Examined in all patients. Cross sections of the subepicardial portions of the major coronary arteries were made at intervals that were sufficiently close to allow visualization of the entire lumen, and thus probably to detect all emboli of major coronary arteries.

Estimation of the incidence of embolization of minor coronary arteries was a more difficult problem. The myocardium of the left ventricle and ventricular septum was examined by taking 10 blocks of tissue, each block weighing about 1 Gm. Collectively, these blocks represented approximately 2 to 3 per cent of the mass of the left ventricle and the septal musculature. From each block two paraffin sections were prepared, each measuring 2 by 1.5 cm. with a thickness of 10 μ. Thus, from each block approximately 1/200 of the tissue contained within the block was examined histologically. Even this laborious routine resulted in inspection of only a small fraction of the total myocardial mass. If more extensive sampling had been undertaken, an appreciably greater incidence of minor coronary artery embolization might have been observed.

Comparison of the frequency of calcific embolization in groups 1 and 2 suggests that calcific embolization is a particular hazard of those surgical procedures of the aortic valve made possible by open-heart technics. Most calcific emboli to the major coronary arteries in this series occurred to the left coronary artery and its branches. Open-heart surgery of the aortic valve is usually performed with the patient supine, the surgeon working through a median sternotomy. In this position the orifice of the coronary artery, particularly the left, is dependent, so that calcific fragments may fall into it during manipulations upon the valve. These considerations suggest that the time of greatest jeopardy of embolism to the major coronary arteries may be during the period of valvotomy itself, rather than after reestablishment of circulation. Obviously, myocardial, cerebral, renal, and other embolization will occur after resumption of blood flow.

Recognition of the high incidence of calcific embolization required that measures be taken by the cardiac surgeon to minimize this hazard. The following precautions are presently being followed:

1. Surgical repair of the calcified aortic valve, whether it be incision of the commissures, sculpturing away of calcium deposits, or even excision of leaflets, is never allowed to proceed when the orifice of the left coronary artery is not protectively occluded. This occlusion is provided by cannulas for perfusion of the coronary arteries; these are inserted immediately after the aorta is incised and are left in position until the aortic incision is nearly closed.

2. Fragments of loose calcium and all free bits of valvular debris are removed from the operative field the instant they are seen. Constant, vigilant inspection of the aortic wall, sinuses of Valsalva, valve surfaces, and even subvalvular areas is maintained to detect any free foreign fragments. Manipulations of the valve are interrupted immediately in favor of removal of any discovered debris before the particle can slip from sight.

3. At the completion of the valve repair, and just prior to closure of the aortotomy incision, the valve surfaces are carefully inspected for fragments of calcium still attached to the valve, where they may be dislodged by the force of ventricular ejection. These are picked away or rubbed off with a dry gauze sponge.

4. Suction is applied to a vent placed in the left ventricle, allowing aspiration and subsequent entrapment in a filter of any valvular debris falling into the left ventricle. Comparison of groups 2A and 2B (table 2) indicates that institution of the above-mentioned measures seemed to reduce the occurrence of major coronary embolization. However, no decrease was observed in the incidence of embolization to the smaller coronary arteries.

The clinical significance of the microscopic emboli to the myocardium and other organs is not clear. Glotzer and associates demonstrated...
strated focal myocardial infarcts in three of
five patients who had undergone aortic valvotomy
for calcific aortic stenosis, and in all
three they had resulted from calcific emboli
to minor coronary arteries. In the present
study, myocardial necrosis caused by calcific emboli
occurred only twice in the series of
61 emboli to the myocardium. The remaining
emboli, however, may have had untoward ef-
facts on an already compromised or failing
myocardium without causing actual death of
the myocardial fibers.8

Summary
Calcific emboli were observed in 38 of 62
patients (61 per cent) who died at varying
intervals following aortic valvotomy for
calcific aortic stenosis. Major coronary emboli-
ization occurred in 10 patients (16 per cent)
and was considered to be a major cause of
death of four patients. Minor coronary em-
bolization occurred in 33 patients (53 per
cent) and was not directly implicated as a
cause of death in any patient. Calcific emboli
occurred to other organs in eight patients (13
per cent). The techniques instituted for reduc-
ing the incidence of embolization—occlusion
of coronary ostia, diligence in detection
and removal of any debris, and final aspiration
of the left ventricle—appeared to have had a
favorable effect.

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Head and Hand in Experimental Medicine
To be worthy of the name, an experimenter must be at once theorist and practitioner.
While he must completely master the art of establishing experimental facts, which are
the materials of science, he must also clearly understand the scientific principles which
guide his reasoning through the varied experimental study of natural phenomena. We
cannot separate these two things: head and hand. An able hand, without a head to
direct it, is a blind tool; the head is powerless without its executive hand.—CLAUDE
BERNARD, M.D. An Introduction to the Study of Experimental Medicine. New York,
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