The Use of Heparinization to Prevent Arterial Thrombosis after Percutaneous Cardiac Catheterization In Children

By Michael D. Freed, M.D., John F. Keane, M.D., and Amnon Rosenthal, M.D.

SUMMARY

Thrombosis at the site of arterial puncture is a common and serious complication of percutaneous cardiac catheterization in children. A double-blind study was therefore designed to test the efficacy of heparin administered during catheterization in reducing this complication. One hundred and sixty-one unselected children over one year of age were studied. Prior to catheterization, the pulse amplitudes were measured in both legs using a Pulse Volume Recorder (a standardized oscillometer). Immediately after arterial cannulation, heparin, 1 mg/kg, or a placebo was administered. On the morning following catheterization, the pulse amplitude in both legs was remeasured and a pulse volume index calculated using the uncatheterized leg as a control. Patients in whom the catheterized leg was cold, with poor capillary filling and absent arterial pulses four hours after the completion of catheterization, were started on intravenous infusion of heparin. If no improvement occurred within 48 hours, embolectomy was performed.

There was no evidence of arterial compromise to the catheterized extremity to any patient older than 10 years. Of 77 children ten years of age or younger, systemic heparinization postcatheterization was required for a pulseless extremity in 40% (15/37) of those in the placebo group and 8% (3/40) in the heparin group (P = 0.003). Only 5% (2/40) of children in the heparinized group had a pulse volume index of less than 50%, compared to 27% (10/37) in the placebo group (P = 0.003). Embolectomy was performed in seven of the 37 children in the placebo group and none of 40 in the heparin group (P = 0.01). No complications related to the use of heparin were found. We conclude that heparin administered during percutaneous catheterization is effective in preventing arterial thrombosis in children ten years of age or younger and should be routinely administered unless a specific contraindication to its use exists.

Additional Indexing Words:
Anticoagulation
Embolectomy
Arterial spasm
Pulse volume recorder
Arteriography

Retrograde Arterial Catheterization is often essential in the diagnosis of complex congenital heart disease. Although the incidence of postcatheterization thrombosis at the site of arteriotomy has been reduced by the percutaneous approach, as compared to open surgical exposure, arterial thrombosis remains the most common serious complication of cardiac catheterization in children. Its incidence in large series of cases is between 2 and 3%, with greater frequency encountered in young children compared to older children or young adults.

Systemic heparinization during transfemoral percutaneous coronary arteriography in adults has significantly reduced the incidence of thromboembolism. In the study by Walker et al., there was also a reduction in the incidence of femoral artery thrombosis. This complication, however, was so rare that the differences between the heparinized and placebo group were not statistically significant. Furthermore, neither random allocation nor a double-blind technique was utilized.

Some centers have routinely used systemic heparinization during cardiac catheterization in children, but in a survey of 121 pediatric cardiologists (H. Ruttenberg, personal communication), only 11% of those using the percutaneous method used total body heparinization. This study was, therefore, designed to test the efficacy of heparinization in preventing arterial thrombosis after percutaneous catheterization in a pediatric population by the use of random allocation and a double-blind technique.

Material and Methods

One hundred and sixty-one unselected patients ages 1–34 years (median = 11) and weighing more than 10 kg undergoing elective cardiac catheterization at the Children’s Hospital Medical Center between April 15, 1973, and
November 30, 1973, were admitted to the study. On the evening prior to cardiac catheterization, the amplitude of the pulses in both calves was evaluated using a Pulse Volume Recorder, a quantitative oscillometer developed at the peripheral vascular laboratory at the Massachusetts General Hospital. This instrument was standardized by inflating the cuff to a set pressure, usually just below diastolic blood pressure, with a known volume of air. The recordings obtained, via an ECG recorder, were approximately the same from both calves at any given time, although the amplitude varied from hour to hour with changes in the heart rate, cardiac output, blood pressure, etc. (fig. 1). In addition, the dorsalis pedal and posterior tibial pulses were graded on a 1 to 4 scale by the clinical cardiac fellow.

Catheterization was performed by a cardiac fellow using the Seldinger technique as modified by Lurie. Sheaths were not used in the artery. The catheters were made of woven dacron (Gensini) and were inserted using stainless steel spring guide wires. During catheterization both venous and arterial catheters were intermittently flushed with 200–300 cc of a solution of 5% dextrose in ¼ normal saline to which heparin had been added to achieve a concentration of two units per milliliter. Numbered syringes were prepared by the senior author (M.D.F.) using a random number table and contained sodium heparin, 10 mg or 1000 units/ml, Liquaemin sodium 5% or 5% dextrose in ¼ normal saline (placebo).

Immediately after inserting the arterial catheter into the common femoral artery, the children were given 0.1 ml/kg from a numbered syringe containing a placebo or heparin.

During catheterization, the presence of a distal pulse in the femoral, dorsalis pedal, or posterior tibial arteries was ascertained while the largest catheter was in place. At the conclusion of the catheterization, the arterial catheter was removed and the presence or absence of visible thrombus material on the tip of the catheter noted. Hemostasis was achieved by digital pressure, and the children were returned to the ward with an Elastoplast pressure dressing.

If both posterior tibial and dorsalis pedal pulse were absent four hours after catheterization and the leg was cold with poor capillary filling, heparin, 1 mg/kg, was given intravenously and repeated every 4–6 hours, depending on clotting time. Amplitude of the pulses in both legs was remeasured using the Pulse Volume Recorder the morning following catheterization by the same technician using the same pressure and volume to inflate the cuff. If the distal pulses were not palpable 48 hours after catheterization, and the extremity remained cold with poor capillary filling, surgical embolectomy under general anesthesia was performed.

Postcatheterization bleeding was evaluated the morning following catheterization upon changing the dressing. Bleeding was graded as none, mild (not requiring a change of the dressing), moderate (requiring a change of dressing), or severe (requiring protamine to reverse anticoagulation).

A pulse volume index (PVI) was calculated using the noncatheterized leg as a control by the equation:

\[
\text{PVI (\%) = } 100 \times \frac{\text{pulse amplitude in catheterized leg postcath}}{\text{pulse amplitude in control leg postcath}}
\]

3. Organon, Sodium Heparin from porcine intestinal mucosa, West Orange, New Jersey.

**Figure 1**

Pulse volume recordings on L.P., an 11-year-old boy catheterized from the right groin. Pulse amplitude before cardiac catheterization (pre cath) is shown on the left and post catheterization (post cath) on the right. Although the magnitude of the recorded pulse is less after catheterization, the changes on the right and left are the same. Pulse volume index (PVI) is 98% (see text). Systolic blood pressure (BP) measured by sphygmomanometry is essentially unchanged. This boy therefore showed no compromise of the circulation in the catheterised extremity.

\[
\text{PVI} = \frac{\text{pulse amplitude in control leg postcath}}{\text{pulse amplitude in catheterized leg postcath}} \times 100
\]

When the PVI was less than 50%, the pulse was considered diminished.

Data was analyzed by an IBM 370 at the Harvard-MIT computer center using the Statistical Package for the Social Sciences. Significance testing was done by the Chi square test using the Yates correction and a two-tailed t-test.

**Results**

Heparin reduced the incidence of arterial spasm and thrombosis as measured by a) the need to institute postcatheterization systemic heparinization, b) the pulse volume index, and c) the need for surgical exploration and embolectomy.

The occurrence of postcatheterization arterial spasm and thrombosis was directly related to the age of the patient on whom the procedure was performed. Children under five years of age were at greatest risk. Systemic heparinization postcatheterization was required in 38% (11/29) of children five years of age or less, and in 15% (7/48) of those six to ten years old. Embolectomy was required in 14% (4/29) of children at or under five years of age and in 6% (3/48) of those between six and ten years old. No one 11 years of age or older (84 children or 52% of our total group) required systemic heparinization (P = 0.001) or embolectomy (P = 0.01).

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Because there was no evidence that the arterial circulation of the catheterized leg was compromised in children over ten, the data on the efficacy of heparin vs placebo has been analyzed for only the 77 children ten years of age or younger (Table 1). Forty received heparin at catheterization and 37 were in the placebo group.

Systemic heparinization four hours after catheterization was required because of the development of a cool, pulseless extremity in 40% (15/37) of the children in the placebo group compared to 8% (3/40) of the group receiving heparin during catheterization (P = 0.003). Twenty-seven percent of the children in the placebo group (10/37) had a pulse volume index less than 50% compared to 5% (2/40) of children in the heparinized group (P = 0.003) (Fig. 2). In 19% (7/37) of the children in the placebo group, the catheterized leg remained cold 48 hours after catheterization and surgical exploration was performed. At surgery, a clot was noted at the puncture site in all seven and an embolectomy was performed without complications. Embolectomy was not necessary in any of the 40 children in the heparin group (P = 0.01).

A notation on the presence or absence of distal pulses was made during catheterization in 121 children. Systemic heparinization after catheterization was required in 38% (5/13) of those who had no palpable pulsations during the procedure compared to 6% (7/108) of those who had a palpable pulse during catheterization (P = 0.002).

Inspection of the catheter after its removal from the artery in 144 children revealed a very high incidence of thrombi within the lumen of the catheter in the placebo group (21/77 or 27%) compared to the group receiving heparin (2/67 or 3%) (P = 0.002), although there was no gross evidence of systemic arterial embolization in either group.

No correlation between postcatheterization heparinization, PVI, or embolectomy was found with respect to sex, duration of arteriography, size of the catheter used, thrombi in the arterial catheter, hematocrit, diagnosis, or postcatheterization bleeding.

Table 1

<table>
<thead>
<tr>
<th>The Effect of Heparinization During Catheterization on Arterial Thrombosis Postcatheterization (Children ≤ 10 Years of Age)</th>
<th>Placebo</th>
<th>Heparin</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic heparinization (4 hours postcatheterization)</td>
<td>N = 37</td>
<td>N = 40</td>
<td>P = 0.003</td>
</tr>
<tr>
<td>Pulse Volume Index &lt; 50%</td>
<td>10</td>
<td>2</td>
<td>P = 0.003</td>
</tr>
<tr>
<td>Embolectomy</td>
<td>7</td>
<td>0</td>
<td>P = 0.01</td>
</tr>
</tbody>
</table>

No complications related to heparin were noted during this study, and the incidence of postcatheterization bleeding was not significantly different between the heparin and the placebo group (P = 0.70). Our clinical impression, however, was that a longer period of pressure over the artery to obtain hemostasis was needed in those who were anti-coagulated. Protamine to correct a prolonged clotting time was not required in any patient.

Discussion

Our study demonstrates that heparin administered during cardiac catheterization is effective in preventing arterial spasm and thrombosis in children ten years of age and under.

While the exact mechanism of postcatheterization thrombus formation is still incompletely understood, Nejad et al.11 in dogs and Siegelman et al.12 and later Formanek et al.13 in humans have shown in elegant studies that one mechanism of thrombosis is stripping off of fibrinous material that has accumulated on the catheter surface when the catheter is being withdrawn through the small hole in the artery. Although some materials seem more thrombogenic than others,11,13 no material now in use is entirely devoid of this hazard. Systemic heparinization in animals prevents or retards the formation of these fibrin deposits,11,14,15 and in humans, decreases the incidence of thromboembolism.4,6

We also demonstrated a significantly lower in-

![Figure 2](http://circ.ahajournals.org/)

Pulse volume recordings on M.B., a three-year-old girl catheterized from the left groin. Pulse amplitude, contour and decreased systolic blood pressure (BP) in the left calf postcatheterization (post cath) suggests significant compromise in the arterial circulation. Pulse volume index (PVI) is 10%. Surgical exploration was carried out and a clot was removed from the left common femoral artery.
cidence of catheter clots in the heparinized group. It is likely, therefore, that heparinization during catheterization may prevent or retard the formation of thrombus on the catheter and the subsequent propagation in the vessel lumen, and thus prevent arterial occlusion by thrombus.

The frequency of compromise of the arterial circulation in our series is considerably higher than that quoted in the literature but similar to our previous experience. We feel that the reason for the discrepancy may be that many cardiologists have been inadvertently anticoagulating their patients by using high concentrations of heparin in the flush solutions. The description of the percutaneous catheterization method as adapted to children by Lurie suggests wiping the catheters with a solution of 50 mg of heparin in 100 ml of saline and using a flush solution of 20 mg heparin in 50 ml saline. This dose is adequate to anticoagulate most children under 25 to 30 kg, i.e., those shown in our study to be at highest risk. Many pediatric cardiologists use a flush solution containing 100 mg of heparin per liter (H. Ruttenberg, personal communication). This also is a significant dose and probably sufficient to anticoagulate most young children undergoing catheterization. This inadvertent anticoagulation by heparin in the flush solution has previously been reported in adults and is postulated as the reason for the reduced incidence of thrombembolism with the Sones technique of coronary arteriography vs the Judkins method.

In most of the children in whom there was significant compromise of the arterial circulation four hours after catheterization, pulses returned spontaneously. It is likely that in these cases circulatory changes were due to arterial spasm. Although the value of heparin in this situation has not been clearly established, it is probable that in vessels with intimal disruption from the catheter and low flow or stasis from spasm around the catheter, heparinization could be very helpful by reducing the likelihood of late thrombosis. Contrary to observations that adequate pulses may return as long as two weeks after catheterization, our experience in children has been that if the extremity is cold with poor capillary filling and absent pulses 48 hours after catheterization, the vessel is occluded by thrombus and embolectomy is indicated. All seven patients in this study operated on 48 hours after catheterization had complete femoral artery occlusion by clot.

This and other studies clearly indicate that the incidence of postcatheterization thrombosis is inversely related to age, with the younger patients at higher risk. This finding has caused some pediatric cardiologists to abandon the percutaneous approach in infants weighing less than ten kg. Why smaller children are at higher risk is unknown, but it is likely that in the small child the ratio of the catheter size to arterial lumen is larger than in older children and adults. Therefore, the fibrin accumulation on the catheter surface is relatively larger and more likely to obstruct the lumen of the artery upon catheter removal. Heparin was just as effective in preventing thrombosis in our study in the younger children and this suggests that the size for percutaneous approach may be safely lowered below ten kg.

We noted no serious side effects from heparinization during catheterization although eight months prior to the inception of the study a serious complication occurred that may have been aggravated by anticoagulation and points out one potential hazard. A myocardial stain with perforation and extravasation of contrast material during a left ventricular angiocardiogram of a two-year-old boy with a ventricular septal defect occurred. Tamponade developed despite the immediate administration of protamine. When fluid reaccumulated after two pericardiocenteses the child was taken to the operating room where the bleeding was finally controlled. The possibility that heparinization aggravated the perforation by allowing continued bleeding into the pericardium exists but is impossible to prove or disprove.

No similar complication has been reported in over two thousand adults in other studies and we did not note this complication during the seven months of the study. The use of continuous heparinization during and for several days after the procedure, however, has been reported to result in excessive late bleeding. Reversal of heparin anticoagulation with protamine sulfate was not necessary in any of the patients in our study but is always available in emergency.

While we have not demonstrated the efficacy of heparin in preventing compromise to the arterial circulation in children over ten years of age, others have suggested its usefulness. Several studies have demonstrated that heparinization during catheterization will drastically reduce the incidence of thromboembolism. For these reasons we recommend that all children undergoing percutaneous cardiac catheterization be given 1 mg/kg of heparin intravenously immediately after arterial cannulation unless a specific contraindication to the use of heparin exists. If within 4–6 hours after catheterization, the arterial pulse has not returned, the child should be maintained on systemic heparinization (1 mg/kg i.v. every 4–6 hours depending on clotting time). If the pulses in the catheterized extremity have not returned within 48 hours, even without other evidence of arterial compromise of the circulation, surgical embolectomy is probably indicated.
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