Long-Term Outcome of Catheter-Related Arterial Thrombosis in Infants with Congenital Heart Disease

Mattia Rizzi, MD, PhD[1,2], Sabine Kroiss, MD[2,3], Oliver Kretschmar, MD Prof[3,4], Ishilde Forster, MD[5], Barbara Brotschi, MD[3,6], and Manuela Albisetti, MD[2,3]

Objectives To investigate the long-term outcome of catheter-related arterial thrombosis in children.

Study design Data from clinical and radiologic long-term follow-up of infants with congenital heart disease developing arterial thrombosis following femoral catheterization are presented.

Results Ninety-five infants with radiologically proven arterial thrombosis because of cardiac catheter (n = 52; 55%) or indwelling arterial catheter (n = 43; 45%) were followed for a median time of 23.5 months (IQR 13.3-47.3). Overall, radiologic complete thrombus resolution was observed in 64 (67%), partial resolution in 8 (9%), and no resolution in 23 (24%) infants. Complete resolution was significantly more frequent in infants with indwelling arterial catheter-related thrombosis compared with cardiac catheter-related thrombosis ($P = .001$). Patients with complete resolution had a significantly lower blood pressure difference and increased ankle-ankle index compared with patients with partial or no resolution ($P < .0001$). However, symptoms of claudication were present only in 1 case and clinical significant legs growth retardation (≥15 mm) was present in 1%.

Conclusions A significant percentage of persistent occlusion is present in children with arterial catheter-related thrombosis on long-term follow-up. In these children, the magnitude of leg growth retardation is small and possibly not clinically relevant. However, in children with congenital heart disease, the high prevalence of persistent arterial occlusion may hamper future diagnostic and/or interventional catheterization. *(J Pediatr 2016;170:181-7)*.

Femoral catheterization either in form of indwelling arterial catheters (IACs) or cardiac catheter represents frequent procedures in neonatal and pediatric intensive care units. The use of arterial catheters in the pediatric population is associated with several complications, the most frequent of which is thrombosis.[1] We recently reported an overall prevalence of IAC-associated thrombosis of 3.25%. In this study, younger age was independently associated with an increased thrombotic risk.[2] The reported prevalence of thrombosis because of cardiac catheter varies between 0.8% and 40%.[3]

Catheter-related arterial thrombosis may lead to serious acute complications such as skin necrosis, and threatened limb or organ viability. Arterial thrombosis is also thought to cause long-term complications such as limb growth retardation and/or claudication, resulting from chronically impaired blood flow.[4-12] In children with congenital heart disease (CHD), peripheral arterial thrombosis may also jeopardize future diagnostic or interventional cardiac interventions. Reports on the morbidity associated with catheter-related arterial thrombosis in children have been limited to acute complications of thrombosis.[2,13-25] Only a few studies have systematically evaluated long-term sequelae of catheter-related thrombosis. All these studies analyzed data of patients mainly undergoing femoral artery cardiac catheter, and no studies have evaluated complications following IAC-related thrombosis in children.[4-9,11,12]

We aimed to provide data on the long-term outcome of catheter-related arterial thrombosis for both cardiac catheter and IAC, in children with CHD.

Methods

Infants with CHD aged 0-12 months who developed catheter-related arterial thrombosis of the femoral and/or iliac arteries between 2001 and 2012, and

AAI	Ankle/ankle index
BPD	Blood pressure difference
CCD	Calf circumference difference
CHD	Congenital heart disease
DUS	Doppler ultrasonography
IAC	Indwelling arterial catheter
KCD	Knee circumference difference
LLD	Leg length difference
TCD	Thigh circumference difference

From the [1]Division of Hematology/Oncology, The Hospital for Sick Children, Toronto, Ontario, Canada; [2]Division of Hematology, [3]Children's Research Center, [4]Division of Cardiology, [5]Department of Radiology, and [6]Intensive Care Unit, University Children's Hospital, Zurich, Switzerland

M.R. was supported by United Bank of Switzerland by order of a client, and was the recipient of a Baxter BioScience Endowed fellowship in Pediatric Thrombosis and Hemostasis at the Hospital for Sick Children (2011-2013). The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2015.11.024

attending follow-up at the University Children's Hospital in Zurich represent the cohort of this study. Follow-up data were collected during regular scheduled visits and retrospectively reviewed by 3 pediatricians. Infants with bilateral arterial thrombosis, who had died, and for whom no or a too short follow-up (less than 6 weeks after thrombotic event) was available were excluded from the final analysis. This study was approved by the Research Ethics Boards of the University Children's Hospital of Zurich, Zurich, Switzerland.

Data recorded included age at the time of thrombosis, type of CHD (cyanotic vs noncyanotic), type of catheterization (cardiac catheter vs IAC), site of placement (right vs left femoral arteries), degree of thrombus occlusion (nonocclusive vs occlusive), and vessel segment(s) involved (femoral and/or iliac artery).

At follow-up visits, clinical and radiologic investigations were performed and whenever possible combined. Clinical follow-up included history of symptoms such as pain, cool or pale limb, and claudication. Clinical examinations included: (1) palpation of femoral, popliteal, and ankle pulses; (2) Doppler derived systolic blood pressure of the upper (brachial) and lower extremities (ankle); (3) leg length measured in the supine position with a tape from the anterior superior iliac spine to the lateral malleolus; and (4) leg circumferences by tape measuring the mid of the thigh and calf, and of the knee by circumventing the knee at the level of the patella.

From the age of 4 years and in collaborating children, assessment of leg length was also performed in the standing position. Leg circumference was measured. Measurements were performed by 3 experienced pediatricians. An interrater reliability testing was not performed.

Clinically suspected thrombosis was confirmed by Doppler ultrasonography (DUS). Ultrasonography screening of all patients following cardiac catheter or IAC is not performed in our institution. Radiologic diagnosis of thrombosis included the site and the extension of the clot. Radiologic outcome of arterial thrombosis was also performed using DUS and included resolution of thrombosis defined as: (1) complete: the thrombus was no longer detected and/or the blood flow had returned to normal; (2) partial: reduction of the thrombus and/or still reduced blood flow; and (3) no resolution: no changes in size or volume of the thrombus and/or no changes in blood flow. DUS was always performed by experienced pediatric radiologists.

In our institution, antithrombotic prophylaxis during cardiac catheter is performed using unfractionated heparin at a bolus dose of 100 IU/kg administered intravenously after arterial puncture and repeated at a dose of 50 IU/kg after 1 hour, targeting an activated clotting time of 250 seconds. In infants, IAC are flushed by a continuous infusion of a saline solution containing 1 U/mL unfractionated heparin at a rate of 1 mL/h.

Statistical Analyses

Data are expressed as percentage, median with IQR or mean with SD and/or 95% CI.

The difference of the Doppler-derived blood pressure (blood pressure difference [BPD]) was calculated by subtracting the blood pressure of the unaffected leg from the blood pressure of the affected leg.[11,26,27] The ratio of Doppler blood pressures of the affected and unaffected ankle (ankle/ankle index [AAI]) was also calculated. A Doppler index ≤ 0.9 is considered to reflect arterial stenosis or occlusion.[12] Doppler-derived ankle blood pressure to brachial pressure is used to indicate the degree of superficial femoral artery compromise.[6] The use of the blood pressure measurements of the unaffected leg other than that of the upper extremity (brachial) for calculation allows removing the potential error occurring in certain patients with cardiac condition affecting the aortic arch, such as coarctation that may result in BPD values not caused by arterial occlusion.[12] Leg length difference (LLD) was calculated by subtracting the length (in cm) of the unaffected leg from the length of the affected leg. Differences of the circumference of the thigh (thigh circumference difference [TCD]), the knee (knee circumference difference [KCD]), and the calf (calf circumference difference [CCD]) were calculated by subtracting the measurement (in cm) of the unaffected leg from the value obtained from the affected leg.

Contingency tables, χ^2, and Fisher exact tests were used to discern differences in the patient characteristics or outcomes as appropriate. Between-group comparisons were performed using 1-way ANOVAs for normally distributed variables and using Mann-Whitney or Kruskal-Wallis test for variables that were categorical, ordinal, or not normally distributed. Estimation of thrombus resolutions over time monitored by DUS was performed using life curve/table. Time 0 was defined as the time of thrombosis diagnosis after which patient were followed until thrombus complete resolved (=event) or censored at the time of latest available DUS data. The period of observation into smaller time intervals of 1 month (30 days) and the probability from each of the intervals are estimated. To assess predictors of thrombus resolution, logistic regression were used and expressed in OR with 95% CI. Variables analyzed included age at thrombosis, sex, type of catheter (IAC vs cardiac catheter), type of cardiac disease (cyanotic vs noncyanotic), degree of vessels occlusion (partial vs complete occlusion) at diagnosis, and the type of cardiac catheter procedure (diagnostic vs interventional). The level of statistical significance was set at $P < .05$. Statistical analyses were performed with the IBM SPSS statistics v 21.0-23.0 (SPSS Inc, Chicago, Illinois).

Results

Infants with CHD (n = 159) developed catheter-related arterial thrombosis of the lower limb during the study period. Of these, 64 were excluded from the analysis. Reasons for exclusion included death because of the underlying disease prior to follow-up (15 patients), lost to follow-up (33 patients), failure to confirm clinical suspected thrombosis by DUS (4 patients), no patient consent (2 patients), bilateral arterial