Results of nonoperative management of acute limb ischemia in infants

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ABSTRACT

Objective: Acute limb ischemia (ALI) in infants poses a challenge to the clinician secondary to poor operative outcomes, limb loss risk, and lifelong morbidity. This retrospective study reviewed a 10-year institutional experience with the nonoperative management of ALI in infants.

Methods: Infants (aged ≤12 months) diagnosed with ALI by duplex ultrasound and treated with initial nonoperative management at a tertiary care children's hospital were identified through vascular laboratory arterial duplex ultrasound records and *International Classification of Diseases* and *Current Procedural Terminology* codes associated with ALI. Demographics of the patients, injury characteristics, treatment administered, and outcomes were abstracted by chart review and presented using descriptive statistics.

Results: During the study period, a total of 25 (28% female) infant patients were diagnosed with ALI. The average age for this cohort was 3.5 ± 3.2 months (standard deviation). Most cases were secondary to iatrogenic injury (88%) from arterial cannulation. Injury sites were more concentrated to the lower extremities (84%) compared with the upper. Absence of Doppler signals was noted in 64% of infants, whereas limb cyanosis was observed in 60% at the time of presentation. Infants were initially treated with anticoagulation (80%) when possible. Two patients failed to respond to nonoperative management and required thrombolysis secondary to progression of thrombus burden while anticoagulated. There were no major (above-ankle) amputations at 30 days. Three deaths occurred within 30 days; all were unrelated to limb ischemia. In the 30-day survivors, overall duration of follow-up was 53.5 ± 38.5 months. One infant required above-knee amputation 6 weeks after diagnosis, resulting in an overall limb salvage rate of 96% on follow-up. Long-term morbidity included two patients with a chronic wound of the affected limb and one patient with limb length discrepancy. No subjects reported claudication at the latest follow-up appointment. In addition, all patients were independently ambulatory except for one adolescent girl who was using a walker with leg braces.

Conclusions: In contrast to the adult population, ALI in infants can be managed with anticoagulation alone with good results. Long-term follow-up continues to demonstrate excellent functional results and minimal disability. (J Vasc Surg 2018;67:1480-3.)

Acute limb ischemia (ALI) is a devastating consequence of a sudden loss of blood flow that can progress to irreversible ischemia of nerve and muscle tissue within 4 to 6 hours if it is not revascularized.[1] Because of the relative scarcity of this disease in the pediatric population, little is known about the optimal management algorithm for limb salvage and morbidity prevention. In infants, the complete cessation of limb blood flow represents a minority of the clinical presentations. In these cases, collateral flow through pre-existing healthy small branch vessels or through early collateralization may prove adequate for limb perfusion. Therefore, a trial of anticoagulation or observation may be the optimal first treatment modality, given the historically abysmal outcomes of early surgical revascularization.[2,3] We have previously published our experience describing excellent short-term results with the nonoperative management of ALI in infants. In this study, we extend follow-up to report the long-term morbidity associated with infants who develop ALI and are not offered initial surgical intervention.

METHODS

This retrospective analysis was approved by the Indiana University Institutional Review Board (No. 1707534935); consent of the patients was not required for this study. The data presented herein were obtained in accordance with the latest Declaration of Helsinki.[4] Medical records of infants (aged ≤12 months) diagnosed with ALI between 2004 and 2014 (upper and lower extremities) were identified at Riley Hospital for Children (Indianapolis, Indiana), a tertiary referral center, through review of *International Classification of Diseases* and *Current Procedural Terminology* codes corresponding to a diagnosis of ALI and vascular laboratory arterial duplex

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ultrasound records. Identified charts were reviewed to confirm ALI diagnosis and to abstract demographics of the patients, sites of injury, etiology, treatment, and outcomes. All patients initially treated with surgical intervention or intravenous or catheter-directed thrombolysis within 24 hours of ALI diagnosis were classified as infants receiving initial operative intervention and excluded from further analysis. Descriptive statistics were performed in GraphPad Prism (GraphPad Software Inc, La Jolla, Calif).

RESULTS

Demographics. Our query identified 27 individuals with potential for study inclusion. Two infants were excluded secondary to revascularization within 24 hours; one subject underwent immediate systemic thrombolysis, and one infant underwent emergent lower extremity thrombectomy with concurrent four-compartment fasciotomy. Therefore, 25 patients were identified to have met clinical criteria for nonoperative management and were included in our study; 28% of patients were female (Table I). The mean age at presentation in our cohort was 3.5 ± 3.2 months; 54% of the patients had at least one major congenital comorbidity, of which a congenital heart malformation was the most common. There was an additional 16% incidence of prematurity (gestational age of ≤37 weeks). No hypercoagulable disorders were identified in any of the patients.

Injury characteristics. The most common cause of ALI was iatrogenic injury secondary to vessel cannulation (88%). In these iatrogenic injuries, the device inserted was either an appropriately sized arterial blood pressure line (n = 20) or an extracorporeal membrane oxygenation cannula (n = 2). The remainder of the injuries were idiopathic (Table II). The noniatrogenic cases consisted of one patient with a distal aortic thrombosis on day 2 of life, one patient with bilateral femoral occlusions, and one patient with a spontaneous radial artery occlusion; 84% of vessel occlusions occurred in the lower extremities, with the femoral artery (76%) being the most common vessel affected. On initial duplex ultrasound examination, 88% of affected arteries were identified as completely occluded. Other findings noted on duplex ultrasound examination included one pseudoaneurysm with associated arteriovenous fistula and two cases of severe, hemodynamically significant arterial stenosis. At presentation, 64% of infants had no signals identified on ankle-level Doppler evaluation, and 60% demonstrated limb cyanosis. All affected extremities were cool compared with the contralateral side.

Treatment. Intravenous anticoagulation with heparin was started in 80% of the patients immediately at the time of diagnosis and universally managed by the hematology team after recommendations were made by the vascular surgery consulting team. Patients were transitioned to enoxaparin or warfarin for 4 weeks, at which time duplex ultrasound examination was repeated, or until documentation of occlusion resolution. If resolution was not documented at 4-week follow-up, anticoagulation was continued for an additional 8 weeks, when duplex ultrasound examination was repeated. No infants were continued on anticoagulation past the 3-month mark. The mean length of therapeutic anticoagulation in our cohort was 3.0 ± 2.4 weeks. However, 40% of infants treated with anticoagulation had treatment durations in excess of 4 weeks. Aspirin was initiated empirically after anticoagulation (32%) if duplex ultrasound demonstrated incomplete thrombus resolution or some hypercoagulability was suspected by the individual clinician. Five patients were observed without anticoagulation secondary to a prohibitively high risk of bleeding. Those patients had hand ischemia in the setting of prematurity (n = 2), were postoperative after congenital heart surgery (n = 2), and had a major neurologic malformation (n = 1) with concern for intraventricular hemorrhage.

One patient required open surgical intervention during observation. This was a child who developed a proximal radial artery pseudoaneurysm and arteriovenous fistula after instrumentation and underwent ligation, resection, and native artery reanastomosis under a dissecting microscope using 9-0 Prolene on a 70-μm needle by the pediatric plastic surgery team. Only two patients required thrombolysis (both systemic). The first was a 2-day old infant girl with an aortic thrombus that had progressed to occlude the iliac arteries bilaterally on anticoagulation. Thrombolysis was successfully performed, and anticoagulation was continued before transitioning to aspirin. The second patient developed worsening cyanosis in the setting of an enlarging iliofemoral

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, single-center cohort study
- **Take Home Message:** Nonoperative management with an anticoagulation protocol in 25 infants (mean age, 3.5 months) with acute limb ischemia (88% due to arterial cannulation) resulted in two failures requiring thrombolysis and one major amputation during a mean follow-up of 53.5 months. One chronic wound, one limb length discrepancy, and no claudication were reported; one patient walks with braces.
- **Recommendation:** This study suggests that treatment of acute limb ischemia in infants with anticoagulation will frequently result in excellent outcome, preventing midterm to long-term morbidity and disability.