Lower extremity ischemia following umbilical artery catheterization: A case study and clinical update

Samuel J. Lin*, Peter F. Koltz, Wellington Davis, Frank Vicari
Division of Pediatric Plastic Surgery, Department of Surgery, Children's Memorial Hospital, Chicago, IL, USA

ABSTRACT
In the neonatal intensive care unit, the use of umbilical artery catheters (UAC) is established. Methods to perform uninterrupted arterial blood gas and pressure monitoring, access for the delivery of fluids and medication, exchange transfusion, cardiac catheterization, and angiography using umbilical artery catheters are used in the care of critically ill neonatal patients. One complication that can develop with the use of UAC's is lower limb ischemia, which can result in catastrophic effects, including limb amputation. In selected cases, conservative management may be an option in patients for limb salvage in the setting of lower limb ischemia.

In this paper, we present a case study of a patient who developed lower limb ischemia during UAC who was treated conservatively. This approach resulted in limb salvage and avoidance of lower extremity amputation. The literature was reviewed for relevant risk factors and treatment options for lower limb ischemia following umbilical artery catheterization.

© 2009 Surgical Associates Ltd. Published by Elsevier Ltd. All rights reserved.

1. Background
Umbilical artery catheters (UAC) are a useful intervention in facilitating care for neonates with cardiopulmonary disease. The most common usages for UAC are blood sampling and infusion of fluids and medications. With an increased use of umbilical artery catheters, there have been notable clinical complications of its use in the literature.1,2 These complications include thrombotic or embolic events, hemorrhage, arterial spasm resulting in ischemia of the lower extremities, sepsis, necrotizing enterocolitis, hypertension, congestive heart failure, visceral gangrene, aortic aneurysm, peritoneal perforation with bleeding, spinal cord infarct and paraplegia, foot drop, osteomyelitis, refractory hypoglycemia, vesicoumbilical fistula, visceral herniation through the umbilical ring, urinary ascites, vascular perforations, and death.3 Wigger suggests that, at one time, catheter associated complications may have been the cause of death in up to 12% of infants with umbilical artery catheters.4 Clinicians may recognize that the visible complications include blanching and/or cyanosis of the distal extremity or buttock area due to vasospasm or thrombosis.

1.1. Risk factors associated with complications from UAC
Both patient and catheter induced factors exist which favor the development of thrombotic complications. Variables related to the patient include low flow states;5 hypoxia, hyperviscous or hypercoaguable states, and sepsis.6 Critically ill neonates often have these clinical conditions favoring these developments. Complications that are associated with the catheter itself may be explained by the method of placement and subsequent manipulation or replacement of the catheter, catheter size, configuration, and composition, placement level in the aorta, use of heparin in the infusate, tonicity and pH of infusates, and the duration of catheter use.5

2. Case study
A neonate was transferred to our NICU following the placement of an umbilical artery catheter who developed a subsequent ischemic limb episode. We review the hospital course of this patient and pertinent literature. This case review was IRB approved for review and no conflicts of interest were identified. The patient was a 2 day old neonate transferred to Children's Memorial Hospital for further management following the insertion of a UAC for monitoring. Within hours following the insertion of the catheter, the patient's right lower
extremity was noted to exhibit signs of ischemia. At the time of external transfer, the patient's entire lower extremity exhibited frank deep and superficial necrosis.

The patient was evaluated by the Plastic Surgery service immediately upon transfer. Duplex ultrasound was used initially to confirm the proximal clot. Based on the senior surgeon's experience with ischemic lower extremity management in the pediatric population, aggressive conservative management was instituted which included bedside debridement and silver sulfadiazine dressing changes. This patient was at extremely high risk for infection and was closely monitored for signs of sepsis and fever. Due to the patient's very high risk for hemorrhage, heparin or thrombolytics were not instituted.

Over the ensuing 6 weeks, the patient's right lower extremity improved remarkably. Figs. 1–4 demonstrate the visible recovery of the lower extremity. There was visible improvement of the skin/soft tissue of the lower extremity and revascularization that was progressive from proximal to distal. In this case, management of this patient with conservative treatment obviated the need for further surgical or alternate intervention. Conservative therapy resulted in successful revascularization of the ischemic limb over several weeks.

3. Discussion and review of literature

The literature is replete with numerous potential approaches to management of neonatal ischemic complications of UAC placement. It should be noted that Krueger et al. reported one newborn that developed aortoiliac thrombosis and symptoms for 36 h prior to surgical consultation and died before surgical intervention could take place.5

3.1. Types of injuries from UAC

Iatrogenic arterial injuries account for two thirds of pediatric arterial injuries and have been noted as a common cause of arterial catheterization for diagnostic monitoring purposes.6 The most common conditions requiring catheterization are respiratory distress syndrome, asphyxia, congenital heart disease, pneumothorax, sepsis, hyperbilirubinemia, and meconium aspiration.7 There have been reports regarding post mortem irreversible limb changes, but few cases exhibit clinical reports of limb ischemia in surviving patients. Clinicians have reported clinical complications from UAC usage as less than 5%.8

Cochran reported in 2534 catheterized infants that major thrombotic involvement of the aorta or one of its visceral branches was present in 13% of those autopsied but in only 2.5% of all catheterized.9 Neal et al. performed arteriographic studies and found thrombus formation in 95% of neonates who underwent umbilical artery catheterization, although only 11% presented with clinical sequelae.8 Arterial thrombosis secondary to UAC most often involves branches of the aorta with complete thrombotic occlusion of the aorta extremely rare.8 Catheter induced thrombosis is most likely related to trauma as part of the Virchow’s triad of vascular injury and altered blood flow rather than length of use, but the true nature of thrombosis in survivors is elusive. The timing and setting in which a catheter complication is noted may affect the true incidence of complications and may account for the discrepancy between low clinical incidence of thrombosis and relatively high incidence post mortem. This statistic may be related to thrombosis from poor perfusion in the critically ill neonate resulting from circulatory failure.10

Both patient and catheter induced factors exist which favor the development of thrombotic complications. Variables relating to the
patient include low flow states, hypoxia, hyperviscous or hypercoaguable states, and sepsis. Factors that favor thrombosis related to the catheter itself include method of placement, subsequent manipulation or replacement of the catheter, catheter size, configuration, and composition, placement level in the aorta, use of heparin in the infusate, tonicity and pH of infusates, and the duration of catheter use. Thrombosis due to UAC is thought to occur both on the catheter and along the arterial wall as a result of intimal injury caused by the catheter and infusing hypertonic solutions through the catheter. Improvements have also been made in the catheter material making them more flexible (Silastic) and less likely to contribute to thrombus formation on the catheter. In order to test the effects of thrombogenic construction materials and their effect in resulting in fewer aortic clots, Jackson et al. selected a UA catheter prototype that had heparin bonded to its polyurethane surface (HB-PU). The incidence of either aortic thrombosis or complications associated with use of the HB-PU catheter was found to be no different than in the PVC group. Platelet adhesion is four times greater to Silastic than to polyurethane catheters in vitro, but no difference was found with in vivo thrombus formation after prolonged use if the catheters were of equal stiffness. Thrombogenicity of catheters in prolonged use may be related to damage to the endothelium and subsequent clot formation at the site of intimal injury rather than clot formation on the catheter itself. A high incidence of complications following UAC may be present due to small vessel caliber and the nature of the patient population with many exhibiting decreased cardiac output, polycythemia, and dehydration.

Thrombosis secondary to catheter placement may have both local and humoral manifestations. With respect to humoral factors, ongoing thrombosis and thrombolysis, acid–base imbalance secondary to poor tissue perfusion, and resultant multiple organ failure may be experienced by the patient. Blanching or motting of the lower extremities, difficulty in maintaining a patent catheter, and narrowing of the pulse pressure through the catheter all represent local manifestations of possible thrombosis in the UAC. Decreasing platelet counts and fibrinogen level and elevation of fibrin split products due to localized intravascular coagulation may be seen.

3.3. Catheter placement and thrombosis

Lower catheter tip placement or placement in the internal iliac arteries is favored by Alpert due to fewer long term complications.

Catheter placement may be confirmed by radiography. Careful clinical observation and immediate catheter removal with the institution of heparin therapy if ischemia is present are advocated treatment guidelines. Higher volume and less morbid complications resulting from low catheter tip placement may be due to the differences in blood flow and velocity in the thoracic and abdominal aorta. In three neonatal patients reported by Stringel with major complications the catheter tip was initially in a high position before being changed to a low position. Of the 32 infants with minor complications, five were in the high position, six in the intermediate position, and 21 in the low position.

The management of pediatric arterial trauma may be less defined than in adults, and the pediatric population has inherent unique considerations. Clinicians may be reluctant to recommend surgical intervention due simply to vessel caliber. The growth of the limb must also be taken into consideration. Even in the absence of symptomatic ischemia, limb growth retardation as a result of an uncorrected circulatory impairment is not uncommon and is reported in 14% of patients with circulation problems studied.

3.4. Diagnosing thrombosis from UAC

The diagnosis of aortic thrombosis should be confirmed in a noninvasive manner whenever possible. Signs of aortic thrombosis may not be present until removal of the catheter in many cases, and so utilizing the catheter for contrast aortography is likely not the best option. Congenital heart disease, coarctation, or an interrupted aortic arch should be included as part of the differential diagnosis, and the actual malady may not be discovered until the time of cardiac catheterization and aortography. Radionuclide scanning and sonography are usually sufficient to confirm the diagnosis and for follow-up.

3.5. Alternatives to UAC

When analyzing the risks of UAC, Stringel notes that the safest means of sampling blood should be used. Percutaneous catheters available in small sizes in which cannulization of the radial and posterior tibial arteries, the dorsalis pedis artery, and small branches of the temporal arteries are all possible to use. While these interventions are not without complications and may be technically more difficult to use, Stringel argues that they should be used instead of UAC when possible. In situations when a complication is suspected, it is imperative that the catheter be removed immediately. Stringel does not advocate the use of heparin, noting it has not been shown to affect incidence of thrombosis or embolism. It is stated that angiography should be performed through the UAC before it is removed when thrombosis is suspected and surgical consult sought. Peripheral venous cutdowns are safer than UAC for infusion of medications or intravenous solutions. When peripheral hyperalimentation is impossible, a central venous line may be inserted. When arterial blood gases cannot be measured percutaneously or through a capillary vessel, a peripheral arterial cutdown may be performed.

Heparin and percutaneous cannulation should be used routinely, according to Flanigan, during catheterization when possible. Since injuries are often detected with Doppler pressure measurements, it is likely that complication rates are actually higher than often reported; pressure measurements would only be expected to detect injuries causing stenosis greater than 70%. While there appears to be some uncertainty whether duration of catheter use increases the risk of thrombosis, it is important to remove any catheter not required. Five of the six limb length discrepancies that were seen were in the nonsurgical group. In attempts at late revascularization, increased growth of soft tissue was seen but no

Fig. 4. At 6 weeks, the patient's lower limb has nearly completely healed up to the distal aspect of the metatarsal region.
Ischemic lesions on the buttocks and lower limbs in two cases reported by Krueger required only local wound care and healed within several weeks. Treatment for nerve palsy subsequent to UAC induced vasospasm includes physiotherapy (massage, electrotherapy, and strengthening exercises) and night splinting.

3.8. Diagnostic testing and management for thrombosis from UAC

Because of the known risk of impaired limb growth, any patient with an ischemic extremity for longer than 30 days may be studied with serial orthorhoentgenograms to assess limb growth. Flanigan et al. established general guidelines regarding management for these patients. Any patient whose lower extremity pulses remained absent subsequent to cardiac or UAC removal or any patient having loss of pulses for any other iatrogenic reason should be immediately heparinized (1 mg/kg), if not contraindicated, and observed for 6 h. If femoral pulses remain absent after 6 h of observation, the patient is a candidate for surgery unless otherwise contraindicated. All the surgical patients are heparinized immediately in order to decrease their likelihood of proximal and distal clot propagation. Heparin therapy is generally continued for 24 h after surgery. Patients with palpable femoral pulses but absent distal pulses and Doppler evidence of the impaired distal perfusion are recommended to continue heparin therapy unless anticoagulation therapy is contraindicated. In patients with femoral pulse but distal ischemia it is believed that noninvasive imaging techniques may be useful to identify patients with common femoral artery thrombi. Vascular surgery may be beneficial in patients with common femoral artery occlusion. Distal occlusions should probably be treated nonoperatively with continued heparin therapy. It is imperative to weigh patient risk against risk of limb loss or limb growth retardation and feasibility of good repair.

Infants with mild and transient ischemia apparent by blanching and cyanosis which resolve with catheter removal, protective wrappings of the extremity, limb dependency, reflex warming, and observation may have no need for further intervention. Therapeutic intravenous heparin (1 mg/kg per 24 h) should not be started until a vascular surgery consult is obtained. The interval between catheterization and ischemia is about 6 h, and so it is imperative that if signs of ischemia do not resolve in this time, alternative, usually surgical, approaches be taken to spare the limb and often the life of the child. Amputation may often be required to spare the life of the child subsequent to gangrenous development even after the administration of heparin. The removal of the catheter may aggravate ischemia and early gangrene can project a fatal prognosis. If limb ischemia appears early, it is imperative that the UAC is removed, and if placed elsewhere, done so with heparin administration.

Alpert et al. found a 1% incidence of clinically recognized significant ischemia, which supports the low clinical incidence reported by others. Krueger reports that seven patients of approximately 5200 infants who had UAC in the neonatal intensive care unit over a 10 year period were surgically managed. Diagnosis was made by contrast aortography in three patients and radionuclide flow scanning and/or sonography in the remaining patients. Flanigan et al. report the first attempt at surgical correction of umbilical artery catheter induced aortic occlusion with successful results. One case illustrates several treatment regimens that should be considered with a variety of pathologies. In Flanigan’s report, an infant had a UAC placed after which the infant began feeding poorly. Mottling of the lower half of the body developed along with tachypnea, and hepatomegaly, and upper extremity hypertension. Laboratory results showed evidence of consumptive coagulopathy with thrombocytopenia, prolonged prothrombin and partial thromboplastin times, and the presence of fibrin split

3.6. Other complications of UAC use

Acute-onset neonatal paraplegia with minimal neurologic recovery associated with the development of progressive lower limb deformities is another complication of UAC. These cases represent a challenging situation and may require intervention to treat contractures of joints of the lower extremity. Anterior spinal cord infarct in neonates associated with UAC are caused by hypotension, high catheter tip placement, and injection of hypertonic solutions or blood. The areas of spinal cord infarction (anteri thoracolumbar) correspond to the distribution of the artery of Adamkiewicz, with sensory sparing findings. Ischemic, atraumatic neonatal paraplegia is a relatively rare condition and is usually associated with prematurity, perinatal asphyxia, or hypotension and hypothesized to be due to absence or failure of spinal cord blood flow autoregulation as a result of prematurity and systemic hypotension. This failure of autoregulation is also consistent with skin manifestations with a similar defect in the spinal cord vascular supply. An ischemic event associated with a generalized vascular spasms of the vessels of the lower limbs may release thromboxanes and other potent vasoactive substances into the spinal cord leading to the progressive neurologic damage first noted several days later.

Incidence of an insulin dependent mother with poor blood glucose control whose infant developed a peroneal nerve palsy after ischemic necrosis of the gluteal region subsequent to UAC has been reported. Three of the seven infants reported by Krueger were also born to diabetic mothers. Although no specific abnormalities have been associated with maternal disabilities, abnormalities of the cardiovascular system, including the development and normal branching patterns of the umbilical vessels, frequently are seen due to exposure of the fetus to hyperglycemia. This anatomic finding leads to incorrect placement of the catheter which requires removal and often replacement. Necrotic gluteal region has been reported several days following replacement, which requires surgical debridement.

3.7. Lower extremity ischemia

The lower extremity ischemia due to acute thrombosis of an abdominal aortic aneurysm (AAA) in the neonatal population. AAA is rare, and the recommended management of thrombosis is in situ placement of a prosthetic graft or an extra anatomical bypass in those patients that are at high risk. Mortality of thrombosis of an AAA may be related to delay in diagnosis. Diagnosis is made by careful examination with high level of suspicion. A CT scan of the abdominal aorta with intravenous contrast is adequate for confirming the diagnosis. Arteriogram may not be implemented due to potential for distal embolization. Collateral vascular development in neonates is potentially great, and occlusion may not cause irreversible ischemia. Fibrinolytic therapy for acute aortic occlusion in infancy may lead to delays in treatment. A history of UAC with acute congestive heart failure and upper extremity hypertension is also indicative of a possible aortic thrombosis. The differential diagnosis should include embolism, thrombosis, and aortic coarctation with dissection. The diagnosis can be made with Doppler ultrasound, real time B-mode ultrasound scans, radioisotope aortography, or contrast arteriography via umbilical artery. None of these should delay the beginning of surgical intervention.

3.8. Diagnostic testing and management for thrombosis from UAC

Because of the known risk of impaired limb growth, any patient with an ischemic extremity for longer than 30 days may be studied with serial orthorhoentgenograms to assess limb growth. Flanigan et al. established general guidelines regarding management for these patients. Any patient whose lower extremity pulses remained absent subsequent to cardiac or UAC removal or any patient having loss of pulses for any other iatrogenic reason should be immediately heparinized (1 mg/kg), if not contraindicated, and observed for 6 h. If femoral pulses remain absent after 6 h of observation, the patient is a candidate for surgery unless otherwise contraindicated. All the surgical patients are heparinized immediately in order to decrease their likelihood of proximal and distal clot propagation. Heparin therapy is generally continued for 24 h after surgery. Patients with palpable femoral pulses but absent distal pulses and Doppler evidence of the impaired distal perfusion are recommended to continue heparin therapy unless anticoagulation therapy is contraindicated. In patients with femoral pulse but distal ischemia it is believed that noninvasive imaging techniques may be useful to identify patients with common femoral artery thrombi. Vascular surgery may be beneficial in patients with common femoral artery occlusion. Distal occlusions should probably be treated nonoperatively with continued heparin therapy. It is imperative to weigh patient risk against risk of limb loss or limb growth retardation and feasibility of good repair.

Infants with mild and transient ischemia apparent by blanching and cyanosis which resolve with catheter removal, protective wrappings of the extremity, limb dependency, reflex warming, and observation may have no need for further intervention. Therapeutic intravenous heparin (1 mg/kg per 24 h) should not be started until a vascular surgery consult is obtained. The interval between catheterization and ischemia is about 6 h, and so it is imperative that if signs of ischemia do not resolve in this time, alternative, usually surgical, approaches be taken to spare the limb and often the life of the child. Amputation may often be required to spare the life of the child subsequent to gangrenous development even after the administration of heparin. The removal of the catheter may aggravate ischemia and early gangrene can project a fatal prognosis. If limb ischemia appears early, it is imperative that the UAC is removed, and if placed elsewhere, done so with heparin administration.

Alpert et al. found a 1% incidence of clinically recognized significant ischemia, which supports the low clinical incidence reported by others. Krueger reports that seven patients of approximately 5200 infants who had UAC in the neonatal intensive care unit over a 10 year period were surgically managed. Diagnosis was made by contrast aortography in three patients and radionuclide flow scanning and/or sonography in the remaining patients. Flanigan et al. report the first attempt at surgical correction of umbilical artery catheter induced aortic occlusion with successful results. One case illustrates several treatment regimens that should be considered with a variety of pathologies. In Flanigan’s report, an infant had a UAC placed after which the infant began feeding poorly. Mottling of the lower half of the body developed along with tachypnea, and hepatomegaly, and upper extremity hypertension. Laboratory results showed evidence of consumptive coagulopathy with thrombocytopenia, prolonged prothrombin and partial thromboplastin times, and the presence of fibrin split
products. Coarctation of the thoracic aorta was ruled out by two-dimensional echoaortography; however, a large mass was seen in the abdominal aorta just below the renal arteries and extending into the iliac arteries. The neonate was treated with a urokinase infusion at a rate of 4000 units/kg per h for 24 h with no improvement in clinical status, Doppler flow measurements, or echoaortographic findings. As the status worsened, surgical thrombectomy was decided upon. After surgery, the congestive heart failure resolved, but hypertension persisted.²

In surgical therapy for thrombus, infants typically are heparinized (100 u/kg). Using a transabdominal approach, a vertical or transverse infrarenal aortotomy is made, Fogarty catheters inserted, and thrombectomy carried out both proximally and distally. When significant aortic wall injury has occurred, systemic utilization of heparin may be beneficial. However, due to the fact that many newborns who are utilizing UAC also have intracranial hemorrhage, it is imperative to weigh the risks versus the benefits of anticoagulation.

3.9. Other ischemic complications

Patients experiencing severe persistent hypertension have thrombus involving the renal arteries. Persistent hypertension is managed with diuretics and fluid restriction to diurese the excess volume in the extracellular space. To acutely reduce blood pressure and/or as a second line of defense, vasodilators can be used along with or independently from beta-blockers: hyperrenninemia should be ruled out.³ Long term follow-up is imperative with these patients.

Arterial occlusion can occur in children due to a variety of sources. Nontraumatic etiologies include embolization from cardiac sources and spontaneous arterial thrombosis secondary to dehydration, polycythemia, infection, and congestive heart failure. Traumatic arterial occlusions may be more common.

4. Conclusions

The use of the UAC for monitoring and blood sampling has benefit for the neonatal critically ill patient. However, the use of the UAC is not without complications. Proper selection of patients in applying invasive monitoring and diagnostics is imperative. A threat of thrombotic induced limb ischemia can result in limb amputation. While limb loss or even death do not occur often, economic and emotional costs to these patients and a limb length discrepancy in 14% of patients relate to a need for relevant indications for invasive monitoring techniques. In our case study, we described a patient who was treated for limb ischemia using a conservative approach. The result in this patient was favorable.

Conflict of interest

There are no conflicts of interest to report with the authors or institution involved in this study.

Funding

None.

Ethical approval

The authors received approval from the Children’s Memorial Hospital Institutional Review Board before writing this manuscript.

References