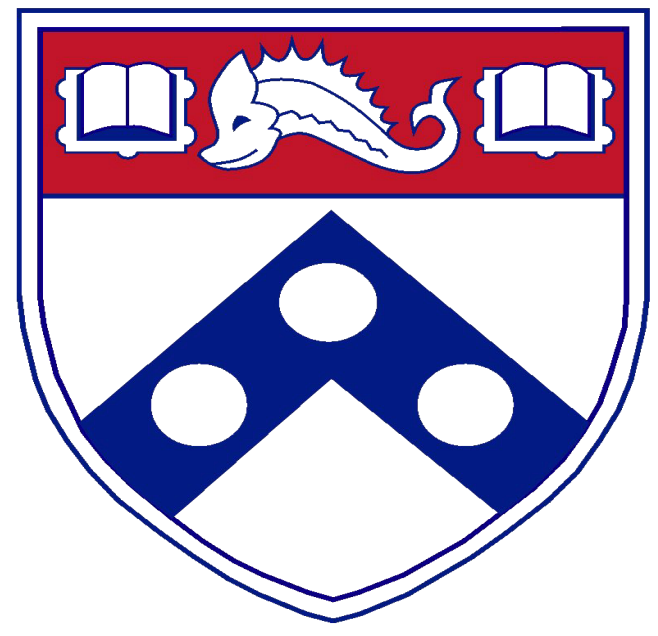




Risk Factors and Biomarker Profiles Associated with Pediatric Arterial Catheter- Associated Proximal Ischemic Injuries



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Background

- Critically ill patients frequently require arterial access for hemodynamic management and blood sampling
- Some patients who require arterial access may exhibit dysregulation of their microvascular circulation
- Dysregulation combined with the presence of an arterial catheter can put the surrounding tissues at risk for injury
- Arterial Catheter Associated Proximal Ischemic Injury (ACAPII) can present with various degrees of injury
- Previous institutional work has defined mild ACAPII as exhibiting blanching, erythema and ecchymosis
- Severe ACAPII includes the progression to an open wound or severe diminished distal pulses

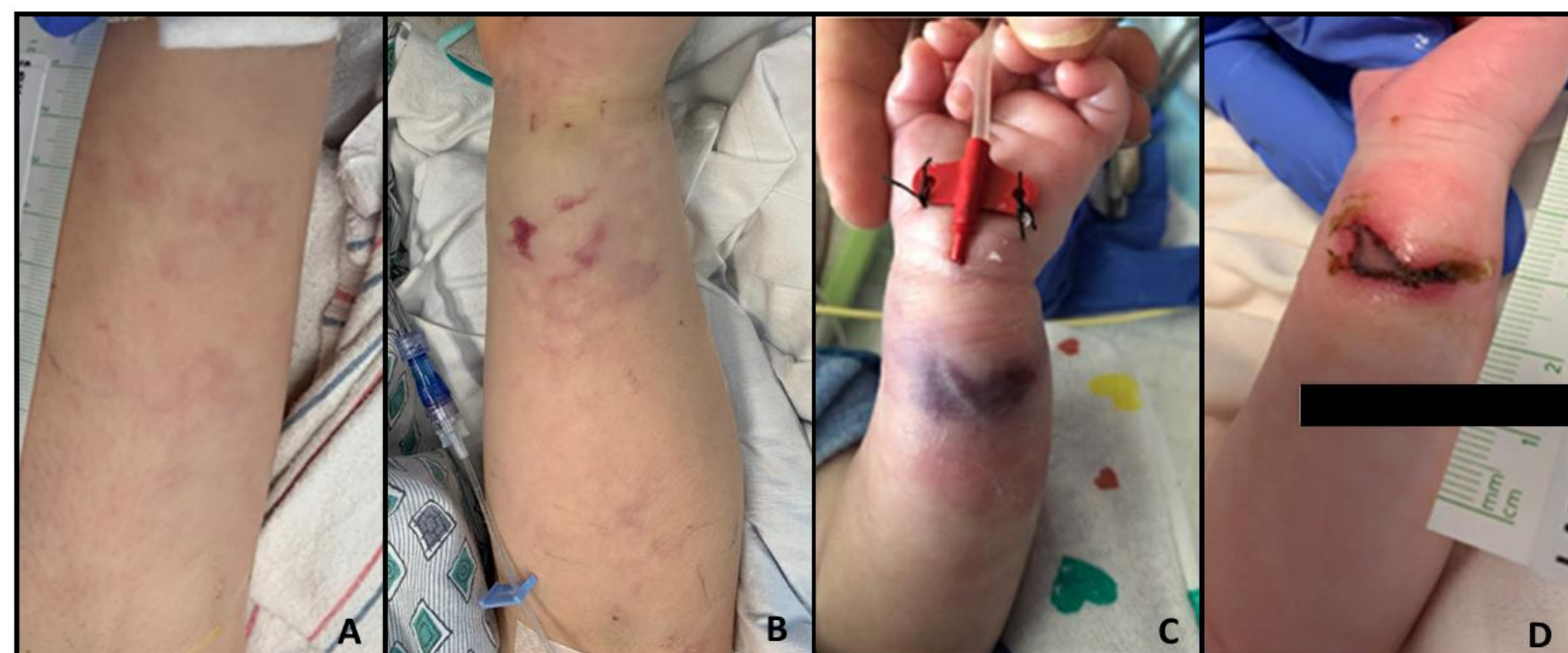
Methods

- Retrospective analysis of arterial catheters placed in children > 1 month and < 18 years from January 2020 to December 2022 in a single center pediatric intensive care unit
- Assessment of patient, provider and device related factors
- Additional assessment using a biomarker repository data comparing a subset of patients with ACAPII with control patients

ACAPII Criteria and Management

Mild ACAPII Criteria	Mild ACAPII Management	Severe ACAPII Criteria	Severe ACAPII Management
Decreased distal perfusion (delayed capillary refill) or cool extremity	Monitor	Presence of open wound or necrotic tissue	Remove catheter Nitroglycerin ointment on intact skin
Proximal blanching with flushing	Add papaverine if not previously started	Severe decreased distal or proximal perfusion (prolonged delay or absent capillary refill)	
Continuous blanching, proximal mottling or ecchymosis	Add nitroglycerin ointment and papaverine if not previously started	Diminished or absent pulse	

Progression of ACAPII Over Time



A) Initial mild injury with proximal mottling, B) Progression of proximal mottling to ecchymosis, C) Further progression of ecchymosis, D) Progression severe injury with open wound.

Treatment Outcomes with Topical NTG and Papaverine

(Line days/Arterial Catheter; 95% CI)

	Mild Injury With TNG	Mild Injury Without TNG	p-value (IRD [95% CI])
Baseline	NA	3.50 (21/6; 2.28, 5.37)	NA
Phase I	7.20 (36/5; 5.19, 9.98)	3.14 (69/22; 2.48, 3.97)	NA*
Phase II	6.58 (158/24; 5.63, 7.69)	3.27 (108/33; 2.71, 3.95)	p<0.01 (3.31 [2.11, 4.51])
	Mild Injury With Papaverine	Mild Injury Without Papaverine	p-value (IRD [95% CI])
Baseline	3.80 (19/5; 2.42, 5.96)	2.00 (2/1; 0.50, 8.00)	0.28 [1.8 (-1.46, 5.06)]
Phase I	4.95 (99/20; 4.06, 6.03)	0.86 (6/7; 0.39, 1.91)	<0.01 [4.09 (2.90, 5.28)]
Phase II	4.90 (255/52; 4.34, 5.54)	2.20 (11/5; 1.22, 3.97)	<0.01 [2.7 (1.27, 4.14)]

IRD: Incidence rate difference; CI Confidence Interval

Results

2111 index arterial catheters were evaluated (45% female)

Incidence of ACAPII

72 patients had an episode of ACAPII, 12 of which has severe ACAPII

Patient Related Factors Seen in ACAPII

-----> *sicker and smaller patients*

Younger age (5.2 (0.9, 12.2) vs 8.5 (2.8, 14.6)

Higher vasopressor usage (62% vs. 40%; p<0.01)

Higher PIM3 ROM (3 [1,5] vs. 1 [0,3]; p<0.01).

Provider Related Factors

No significance related to vessel accessed or insertion attempts

Device Related Factors Seen in ACAPII

-----> *more frequent in smaller patient*

Smaller catheters 24g (39% vs. 11%; p<0.01)

Shorter Catheters < 2.5 cm (31% vs. 12%)

Biomarker Data Seen in ACAPII

-----> *mimics thrombotic microangiopathies*

Lower platelets (168 [57,230] vs. 199 [133,267]; p=0.01),

Elevated D- Dimer dimer (20 [6,31] vs. 4 [1,12]; p=0.03),

Decreased Albumin (2.5 [2.3,3.18] vs. 2.8 [2.3,3.5] p=0.04)

Lower pH (pH 7.23 (7.15,7.33) vs. 7.31 (7.24,7.38); p<0.01)

Plasma Protein Expression Seen in ACAPII

-----> *genetic predilection to microthrombi during illness*

(biobank data of 5 patients with ACAPII compared to 66 without)

Increased expression of TSLP, LIF, and IL24, proinflammatory factors related to endothelial dysfunction

These three factors lead to signaling of the Stat3 pathway

Stat3 signaling leads to a protein scaffold encouraging platelet activation

The platelet activation can lead to increased microthrombi in certain critically ill children

Conclusions

- We identified candidate pathways of immune dysregulation and endothelial dysfunction at MODS onset which are associated with the development of arterial catheter associated proximal ischemic injury.

- These injuries likely develop in the setting of hyperinflammation, endothelial dysfunction, and platelet aggregation.

- Further studies linking these dysregulated pathways to platelet aggregation and thrombosis could suggest new therapeutic targets for pediatric patients at risk for ACAPII

- Increased use of Papaverine may limit occurrence of severe ACAPII

- Further validation of the grading scales with inter-rater reliability would improve diagnostic accuracy

Objectives

- Identify risk factors, including biomarker profiles, associated with AC-associated ischemic injuries in critically children