Cardiology in the Young

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Neonatal and Paediatric Heart and Renal Outcomes Network: design of a multi-centre retrospective cohort study

Katja M. Gist[1,*], Joshua J. Blinder[2,*], David Bailly[3], Santiago Borasino[4], David J. Askenazi[5], David S. Cooper[6], Catherine D. Krawczeski[7], Michael Gaies[8], David L. S. Morales[9], Kristal M. Hock[4] and Jeffrey Alten[6]

[1]Department of Paediatrics, The Heart Institute, Children's Hospital Colorado, University of Colorado Anschutz Medical Campus, Aurora, CO, USA; [2]Division of Cardiac Critical Care Medicine, Department of Anesthesia/Critical Care, Children's Hospital of Philadelphia, Philadelphia, PA, USA; [3]Division of Critical Care Medicine, Department of Pediatrics, Primary Children's Hospital, University of Utah, Salt Lake City, UT, USA; [4]Division of Critical Care Medicine, Department of Paediatrics, Alabama Children's Hospital, University of Alabama, Birmingham, AL, USA; [5]Division of Paediatric Nephrology, Department of Paediatrics, Alabama Children's Hospital, University of Alabama, Birmingham, AL, USA; [6]Department of Paediatrics, University of Cincinnati College of Medicine and Division of Cardiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; [7]Division of Cardiology, Department of Paediatrics, College of Medicine, Nationwide Children's Hospital, The Ohio State University, Columbus, OH, USA; [8]Division of Cardiology, Department of Paediatrics, University of Michigan Medical School, Ann Arbor, MI, USA and [9]Department of Paediatrics Surgery, The Heart Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Abstract

Background: Cardiac surgery-associated acute kidney injury is common. In order to improve our understanding of acute kidney injury, we formed the multi-centre Neonatal and Pediatric Heart and Renal Outcomes Network. Our main goals are to describe neonatal kidney injury epidemiology, evaluate variability in diagnosis and management, identify risk factors, investigate the impact of fluid overload, and explore associations with outcomes. *Methods:* The Neonatal and Pediatric Heart and Renal Outcomes Network collaborative includes representatives from paediatric cardiac critical care, cardiology, nephrology, and cardiac surgery. The collaborative sites and infrastructure are part of the Pediatric Cardiac Critical Care Consortium. An acute kidney injury module was developed and merged into the existing infrastructure. A total of twenty-two participating centres provided data on 100–150 consecutive neonates who underwent cardiac surgery within the first 30 post-natal days. Additional acute kidney injury variables were abstracted by chart review and merged with the corresponding record in the quality improvement database. Exclusion criteria included >1 operation in the 7-day study period, pre-operative renal replacement therapy, pre-operative serum creatinine >1.5 mg/dl, and need for extracorporeal support in the operating room or within 24 hours after the index operation. *Results:* A total of 2240 neonatal patients were enrolled across 22 centres. The incidence of acute kidney injury was 54% (stage 1 = 31%, stage 2 = 13%, and stage 3 = 9%). *Conclusions:* Neonatal and Pediatric Heart and Renal Outcomes Network represents the largest multi-centre study of neonatal kidney injury. This new network will enhance our understanding of kidney injury and its complications.

Advancements in paediatric cardiac surgical techniques and post-operative intensive care have led to marked improvements in clinical outcomes after neonatal cardiac surgery.[1–4] In-hospital mortality rates after cardiac surgery are approaching <5% for even the most complex operations, including the Norwood operation.[1–4] In an effort to further improve perioperative care for this population, investigators seek to identify modifiable pre-operative, intraoperative, and post-operative risk factors associated with clinically significant outcomes. Post-operative complications, including hospital-acquired infection, seizures, and cardiac arrest, are associated with increased intensive care unit and hospital length of stay and other morbidity, including neuro-development delays and nutritional failure.[3–10] Post-operative end-organ injury, specifically acute kidney injury, is associated with increased morbidity and mortality.[11–13]

Multiple risk factors for cardiac surgery-associated acute kidney injury have been reported. These include deleterious intra- and post-operative hemodynamics, more complex surgery, pre-operative acute kidney injury, prolonged cardiac support times, nephrotoxins, and cyanosis.[12,14] Neonates represent the highest risk cohort with rates ranging from 40 to 60%.[12] Outside of the neonatal population, the incidence ranges from 15 to 45% with inconsistent impact on post-operative outcomes.[11,12,14] Cardiac surgery-associated acute kidney injury is associated with poor short-term and long-term outcomes, including hospital mortality, prolonged intensive

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Author for correspondence: Katja M. Gist, University of Colorado Anschutz Medical Campus, Department of Paediatrics, The Heart Institute, Children's Hospital Colorado, 13123 E 16th Ave, B100, Aurora CO 80045, USA. Tel: 720-777-3614; Fax: 720-777-7290; E-mail: Katja.gist@childrenscolorado.org
*Both authors contributed equally

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care unit and hospital length of stay, and prolonged mechanical ventilation.[11–17] Many of the published acute kidney injury studies are limited due to small sample size, disparate definitions, variations in case ascertainment, heterogeneous subject populations, and limited covariate exploration.[11–14,19] To highlight the complexities of acute kidney injury diagnosis and outcome attribution, a secondary analysis from the two-site randomised Safe Pediatric Euglycemia after Cardiac Surgery trial found significantly different cardiac surgery-associated acute kidney injury rates between the two sites. These findings were despite using the same acute kidney injury definition. In addition, this study noted differing effects of cardiac surgery-associated acute kidney injury on outcomes, including time to extubation and intensive care unit and hospital length of stay.[18] Furthermore, detailed analysis of independent modifiable risk factors that may impact neonatal acute kidney injury development has not been possible. As a result, we remain more or less where we were 10 years ago. At this time, investigators identified cardiac surgery-associated acute kidney injury as an important perioperative complication. Efforts aimed at reducing the clinical burden of cardiac surgery-associated acute kidney injury remain elusive.

Through multi-institutional collaborative discussion, investigators formed what would become the Neonatal and Pediatric Heart and Renal Outcomes Network steering committee. This group identified five principal specific aims that seek to foster advancements in cardiac surgery-associated acute kidney injury understanding, that is, to describe the multi-centre epidemiology of neonatal cardiac surgery-associated acute kidney injury utilizing the current consensus modified kidney disease improving global outcomes criteria[19]; to describe neonatal acute kidney injury rate variability across institutions and create a risk adjustment model to benchmark institutional performance against the Pediatric Cardiac Critical Care Consortium cohort; to determine the epidemiology and risk factors associated with post-operative fluid overload, its relationship with cardiac surgery-associated acute kidney injury and identify independent associations with clinically relevant post-operative outcomes; to explore the performance of different cardiac surgery-associated acute kidney injury definitions on relevant post-operative outcomes, including mortality, hospital and intensive care unit length of stay, and duration of mechanical ventilation; and to test whether post-operative diuretic responsiveness affords earlier cardiac surgery-associated acute kidney injury detection when compared with current acute kidney injury detection methods.

Table 1. Modified neonatal kidney disease: improving global outcomes criteria

Stage	Serum creatinine	Urine output (ml/kg/hour)
0	No change from baseline *or* < 0.3 mg/dl	≥0.5
1	≥0.3 mg/dl within 48 h *or* ≥ 1.5–1.9 baseline* within 7 days	0.5–1.0
2	≥2.0–2.9 baseline*	0.3–0.5
3	≥3 baseline* *or* Receipt of dialysis for AKI or FO	<0.3

AKI = acute kidney injury; FO = fluid overload; mg/dl = milligrams per decilitre
Adapted from Selewski et al[25]
*Baseline serum creatinine was defined as the last available serum creatinine value prior to operation. Urine output averaged over each post-operative day to determine daily urine output stage

Materials and methods

Neonatal and Pediatric Heart and Renal Outcomes Network development and infrastructure

In an effort to better understand cardiac surgery-associated acute kidney injury, stakeholders consisting of paediatric cardiac intensivists, cardiologists, nephrologists, and cardiac surgeons joined to form the Neonatal and Pediatric Heart and Renal Outcomes Network collaborative to investigate neonatal and paediatric acute kidney injury. The Neonatal and Paediatric Heart and Renal Outcomes Network collaborative was developed from the recently established Pediatric Cardiac Critical Care Consortium, a large multi-institutional registry aimed at fostering collaboration, quality improvement efforts, and clinical investigation across all cardiac critical care domains.[20,21]

Existing information within the Paediatric Cardiac Critical Care Consortium registry includes demographics, granular pre-, intra-, and post-operative clinical data and outcomes and complications for each cardiac intensive care unit patient encounter at all participating centres. Important cardiac surgery-associated acute kidney injury-related variables, including frequent serum creatinine measurements, urine output information, and details of fluid status were lacking. By coupling the already existing Paediatric Cardiac Critical Care Consortium infrastructure with additional cardiac surgery-associated acute kidney injury-related variables, the Neonatal and Paediatric Heart and Renal Outcomes Network collaborative seeks to further understand variables impacting acute kidney injury development and the deleterious effects of acute kidney injury on post-operative outcome in this vulnerable population. The overarching goal is to develop a multi-disciplinary, multi-institutional network with the expertise and resources to foster advancements in cardiac surgery-associated acute kidney injury understanding which can be leveraged to prospectively identify measures to mitigate the consequences associated with this important post-operative complication.

The Neonatal and Paediatric Heart and Renal Outcomes Network infrastructure consists of a project manager and a nine-member steering committee led by an executive director (Supplementary Table 1). All steering committee members collaborate on project development and execution, formal scientific review of both primary and ancillary protocols, and oversight of all data analyses and manuscript preparation. The Neonatal and Paediatric Heart and Renal Outcomes Network encourages inclusivity and multi-centre participation in development of all study protocols, analyses, presentations, and manuscript preparation.

Neonatal cardiac surgery-associated acute kidney injury data module

Initial Neonatal and Paediatric Heart and Renal Outcomes Network efforts sought to develop a multi-institutional infrastructure incorporating granular cardiac surgery-associated acute kidney injury data elements, not previously collected as part of the Paediatric Cardiac Critical Care Consortium dataset. Each participating site (Supplementary Table 2) was requested to contribute 100–150 individual consecutive eligible neonatal subjects to the cohort, starting with their most recent Paediatric Cardiac Critical Care Consortium case and proceeding backwards. This number was determined to limit the effect of large contributors on the overall sample. Moreover, investigators felt that data collection on this number of institutional subjects was feasible for each centre and would not be unduly burdensome. Steering committee

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Table 2. Inclusion and exclusion criteria

Inclusion	Exclusion
PC[4] neonatal (<30 days) surgical encounter	>1 index operation in the first 7-day study period
Index operation with or without CPB at <30 days	Preoperative renal replacement therapy
Discharged from the hospital or died	Preoperative serum creatinine >1.5 mg/dl
Completed PC[4] core data set	Intraoperative ECMO
At least one **post-operative serum creatinine**	ECMO during first 24 hours after the index operation

CPB = cardiopulmonary bypass; ECMO = extracorporeal membrane oxygenation; mg/dl = milligrams per decilitre; PC[4] = Paediatric Cardiac Critical Care Consortium

members met to generate a list of candidate pre-, intra-, and post-operative variables using expert consensus. Specifically, the cardiac surgery-associated acute kidney injury data module includes daily serum creatinine measurements, detailed fluid balance measurements, and urine output (Supplementary Table 3). The study period was *a priori* defined from the time of post-operative intensive care unit admission through post-operative day 6. This was chosen in order to relate the AKI episode to cardiac surgery versus some other etiology. ArborMetrix Inc. (Ann Arbor, Michigan, United States of America) created a web-based data entry platform linked to each patient's eligible cardiac intensive care unit encounter. Data definitions were available to data abstractors (Supplementary Table 4). Ongoing database operations and management as well as training of individual abstractors are managed by ArborMetrix Inc. and funded by private donation.

Cardiac surgery-associated acute kidney injury definitions

Current acute kidney injury definitions use changes in serum creatinine and oligo-anuria.[19] It is well known that serum creatinine is an imperfect measure of renal function, particularly in neonates, as it is affected by factors unrelated to renal disease including muscle mass, fluid status, medications, and gender.[23,24] Moreover, many neonates undergo cardiac surgery within the first several days of life, which makes determination of the baseline value difficult to ascertain because serum creatinine in the first few days of life represents both maternal serum creatinine and neonatal kidney function. Additionally, the delayed elevation of serum creatinine in response to renal injury limits its utility as a real time and/or early indicator of acute kidney injury. Most recently, investigators have been using the modified Kidney Disease Improving Global Outcomes criteria to define neonatal acute kidney injury. Each serum creatinine value is compared with the previous lowest value which serves as a changing baseline level.[22] A recent National Institute of Health neonatal acute kidney injury workshop stressed that this definition should be used (to allow for comparisons between studies) but stressed the need for evaluation of its performance using large multi-centre studies.[25] Whether this definition can be applied to neonates undergoing cardiac surgery is unknown.

For the initial set of studies, cardiac surgery-associated acute kidney injury will be defined according to a modification of the neonatal kidney disease improving global outcome criteria (Table 1).[24] We modified the urine output criteria by averaging total urine output over the total number of post-operative hours for each post-operative day to determine maximum urine output.

Table 3. Neonatal and Pediatric Heart and Renal Outcomes Network patient demographics, and operative and post-operative characteristics

	All patients
Demographics	
Age at surgery (days)	7 (5, 11)
Weight at surgery (kilograms)	3.2 (2.80, 3.56)
Sex (male)	1358 (61)
Prematurity (yes)	291 (13)
Chromosomal anomaly/syndrome	382 (17)
Extracardiac anomaly	378 (17)
Pre-operative clinical factors	
Prostaglandin infusion	1609 (72)
Pre-operative feeding (yes)	914 (41)
Lowest pre-operative serum creatinine (mg/dl)	0.43 (0.35, 0.53)
Serum creatinine prior to surgery (mg/dl)	0.47 (0.38, 0.60)
Umbilical arterial catheter	719 (32)
Pre-operative necrotizing enterocolitis	13 (0.6)
Single ventricle (yes)	559 (25)
Pre-operative cardiac catheterization	255 (11)
Balloon atrial septostomy	178 (8)
Operative characteristics	
STAT category	
1	83 (4)
2	307 (14)
3	285 (13)
4	1158 (52)
5	403 (18)
Inotropes at surgery	329 (15)
Vasoactive inotrope score at surgery	5 (4, 8)
Use of cardiopulmonary bypass	1657 (74)
Cardiopulmonary bypass duration (minutes)	131 (91, 166)
Cross clamp duration (minutes)	58 (35, 90)
Deep hypothermic circulatory arrest (yes)	626 (28)
Modified ultrafiltration in the operating room	993 (60)
Furosemide in the operating room	560 (25)
Delayed sternal closure	709 (32)
Bleeding requiring reoperation (first 24 hours)	48 (2)
Unplanned reoperation/intervention (first 24 hours)	36 (2)

mg/dl = milligrams per decilitre
Continuous variables are reported as median with interquartile range. Categorical variables are reported as number with percent

The urine output criteria were modified due to the availability of data. Specifically, hourly urine output was only collected from arrival to the intensive care unit until the first post-operative morning. Total urine output per day was then collected for each subsequent 6 post-operative days. Moreover, we defined baseline serum creatinine *a priori* as the last measurement before surgery in order to measure the effect that the surgical encounter had on cardiac surgery-associated acute kidney injury development. An expected and accepted limitation of this approach is that this

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Table 4. Incidence of acute kidney injury in the neonatal cohort of the Neonatal and Paediatric Heart and Renal Outcomes Network

	All (n = 2240)	CPB (n = 1657)	Non-CPB (n = 583)
Any AKI	1207 (54)	983 (59)	224 (38)
Stage 1	702 (31)	569 (34)	133 (23)
Stage 2	302 (13)	253 (15)	49 (8)
Stage 3	203 (9)	161 (10)	42 (7)
Severe AKI	505 (22)	414 (25)	91 (15)

AKI = Acute kidney injury; CPB = cardiopulmonary bypass
AKI was defined using either serum creatinine or urine output criteria according to the modified Kidney Disease Improving Global Outcomes Criteria. Severe AKI is classified as stage 2 and 3 disease. Data are presented as number with percent

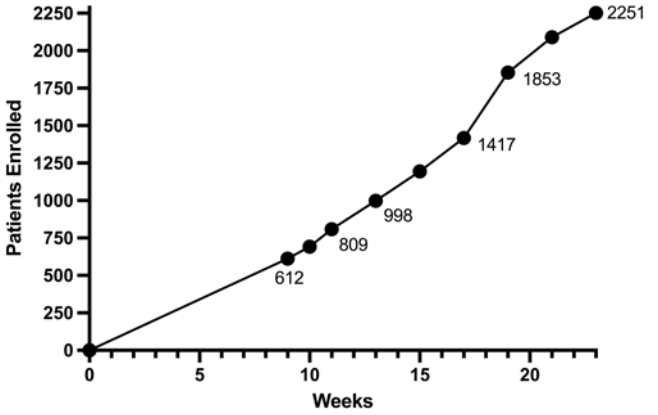

Figure 1. Temporal enrolment progress across all centres. Between August 2017 and January 2018, 2251 neonates were enrolled across all centres, and 11 subjects were then excluded due to meeting exclusion criteria.

pre-operative "baseline" may not accurately reflect the neonates' true steady-state serum creatinine for reasons previously described. Additionally, serum creatinine at time of surgery may not be the lowest measured pre-operative value; however, we were precisely interested in measuring the impact of the cardiac surgery episode on the patient's immediate pre-operative kidney function. We will assess both the daily maximum acute kidney injury stage and the duration of acute kidney injury. Daily maximum acute kidney injury stage will be determined by either urine output or serum creatinine criteria or need for renal replacement therapy. Automatic renal replacement therapy stage 3 criteria only pertains to those started on peritoneal dialysis for acute kidney injury or fluid overload after the first 24 post-operative hours. We defined "prophylactic" peritoneal dialysis as that starting in the first 24 post-operative hours. Fluid overload will be calculated using both weight-based and fluid balance-based measurements using the following equations:

$$\text{Weight-based \% fluid overload} = \frac{(\text{Daily weight} - \text{Dry weight})}{\text{Dry weight}} \times 100$$

$$\text{Fluid balance-based \% fluid overload} = \frac{(\text{Total fluid intake} - \text{Total fluid output})}{\text{Total fluid output}} \times 100$$

Site recruitment and data collection

A total of twenty-two United States Pediatric Cardiac Critical Care Consortium centres were recruited to participate; and contributed data (Supplementary Table 2). Patient inclusion and exclusion criteria are summarised in Table 2. Consecutively eligible neonatal subjects were obtained from the Pediatric Cardiac Critical Care Consortium registry with an enrolment target of 100–150 subjects at each site. Retrospective data were entered into each subject's linked cardiac intensive care unit encounter via the web-based data module. Collaborators continue to meet regularly to discuss study and protocol development and statistical results and plans for presentation at national and international meetings.

Neonatal cardiac surgery-associated acute kidney injury study

In parallel to data module development, steering committee members met to develop the specific aims noted earlier. Each protocol to address these specific aims will be led by steering committee members and enrolled site principal investigators. After completion of the initial specific aims, the steering committee will accept ancillary protocols submitted by site principal investigators; these protocols will be adjudicated by the steering committee.

Data analysis

A sample size of approximately 2200 subjects was determined to have adequate statistical power to describe neonatal cardiac surgery-associated acute kidney injury epidemiology, identify previously unmeasured covariates, challenge existing acute kidney injury definitions and explore the relationship between fluid overload and acute kidney injury. The analyses for these specific outcomes have not yet been performed and will be detailed in the specific manuscripts to follow. All data management and analyses will be executed by the Paediatric Cardiac Critical Care Consortium data coordinating centre. All research protocols addressing the primary specific aims and any ancillary studies require a detailed analytic plan approved by the Neonatal and Paediatric heart and Renal Outcomes Network steering committee prior to starting the analysis. Data analysis will be performed in collaboration with the data coordinating centre and project leads.

Results

Data submission occurred from August, 2017 to January, 2018 after several training data collection Webinars. Multi-institutional enrolment updates and correspondence were provided at least monthly. Temporal enrolment progress is summarised in Figure 1. A total of 2251 subjects were enrolled. Eleven patients were removed from the analysis after subsequently being discovered to have met exclusion criteria. The final sample size to be analysed includes 2240 neonatal patients of whom 1657 patients underwent cardiopulmonary bypass and 583 did not. A summary of patient demographics and pre-operative and operative characteristics are summarised in Table 3.

Cardiac surgery-associated acute kidney injury occurred in 54% of patients, of whom 59% (n = 983) patients underwent cardiopulmonary bypass and 23% (n = 133) did not. The highest proportion of patients had stage 1 acute kidney injury, and severe acute kidney injury (classified as stages 2 and 3) occurred in 22% of all subjects (25% cardiopulmonary bypass and 15% without cardiopulmonary bypass). A summary of the incidence of cardiac surgery-associated

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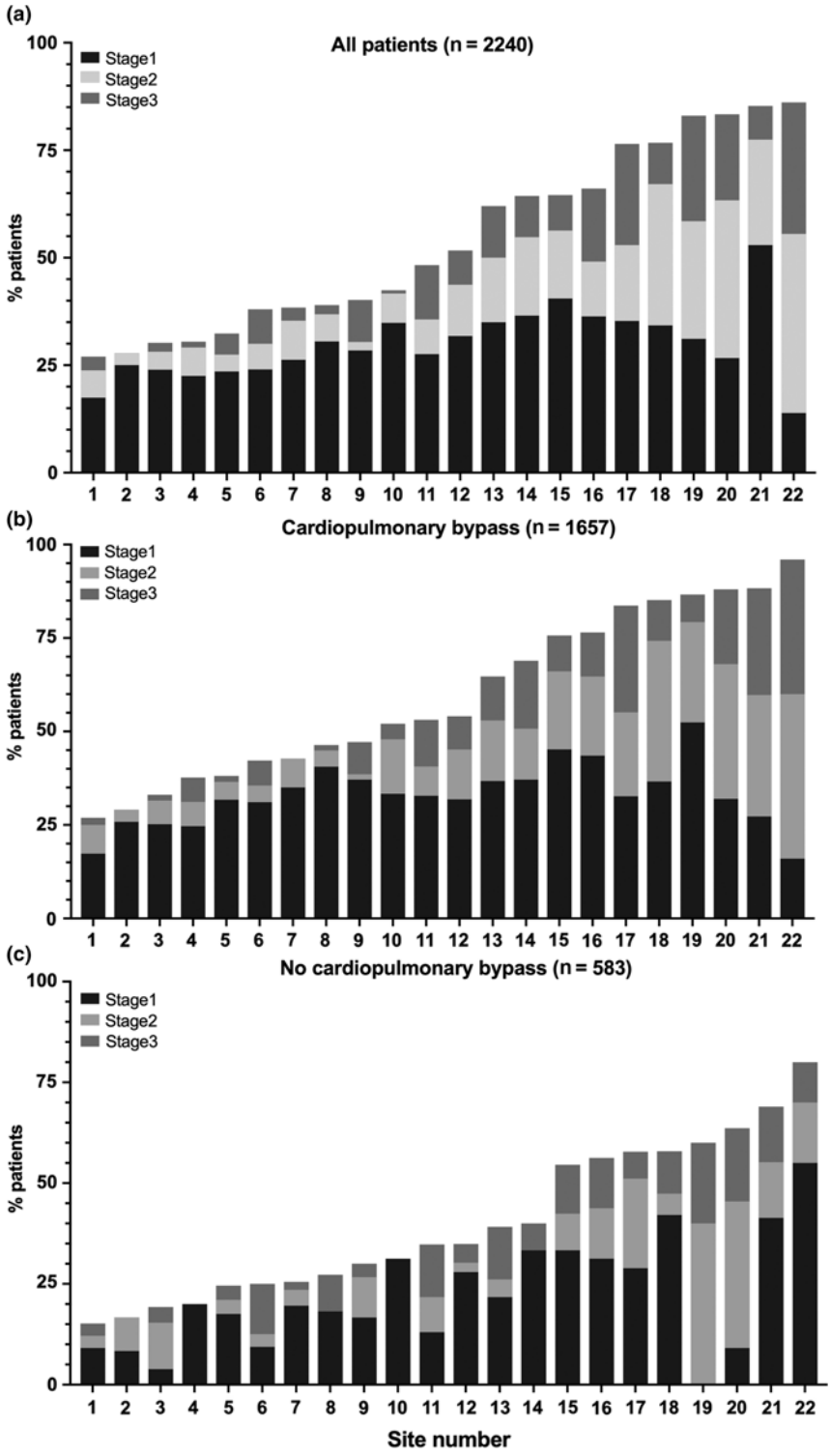

Figure 2. Cardiac surgery-associated acute kidney injury by site. (***a***) All patients (n = 2240), (***b***) Cardiopulmonary bypass patients only (n = 1657), and (***c***) Non-cardiopulmonary bypass patients (n = 583).

acute kidney injury is summarised in Table 4. The incidence of acute kidney injury was quite variable between the 22 sites. A summary of the incidence by site is summarised in Figure 2a (all patients), 2b (cardiopulmonary bypass), and 2c (no cardiopulmonary bypass). Cardiac surgery-associated acute kidney injury occurred most commonly on day 1 (32%) with the incidence decreasing from post-operative days 2–6 (data not shown).

Discussion

The Neonatal and Paediatric Heart and Renal Outcomes Network neonatal acute kidney injury project has yielded a robust dataset of 2240 neonatal cardiac surgical patients across 22 centres and is poised to improve our understanding of neonatal acute kidney injury and fluid overload. Cardiac surgery-associated acute kidney

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injury incidence in this cohort was highly variable among centres ranging from 27 to 86%. Based on these data, this large, multi-centre cohort will allow the collaborative to develop a risk-adjustment model to benchmark cardiac surgery-associated acute kidney injury prevention performance. Uniquely, our dataset will provide a detailed evaluation of the epidemiology and impact of acute kidney injury in patients not requiring cardiopulmonary bypass (n = 583). Together this project promises to fill existing knowledge gaps to inform prospective multi-centre initiatives aimed at acute kidney injury and fluid overload prevention and mitigation after neonatal cardiac surgery. In order to improve our understanding of cardiac surgery-associated acute kidney injury for future prospective studies, we have outlined each of the planned retrospective studies.

Cardiac surgery-associated acute kidney injury epidemiology

While two existing multi-centre collaboratives describe acute kidney injury epidemiology in critically ill neonates and children, neither study included subjects undergoing cardiac surgery.[26,27] The Neonatal and Paediatric Heart and Renal Outcomes Network collaborative will describe cardiac surgery-associated acute kidney injury rates and severity across participating centres stratified according to cardiopulmonary bypass exposure and other pre-, intra-, and post-operative patient characteristics. We have shown that cardiac surgery-associated acute kidney injury occurs in approximately 58% of subjects with significant variability of both the incidence and severity across institutions. The clinical outcomes to be explored will include in-hospital mortality, duration of mechanical ventilation, hospital length of stay, and other resource utilization. Importantly, we will be able to adjust for potential confounders that could mitigate the impact between acute kidney injury and outcomes, including fluid balance indices, modified ultrafiltration, blood product exposure, perioperative inotrope exposure, and peritoneal dialysis utilization, among others.

Fluid overload

The Neonatal and Pediatric Heart and Renal Outcomes Network aims to evaluate the independent role of post-operative fluid overload on clinical outcomes and to determine interactions between fluid overload and acute kidney injury. The role of post-operative fluid overload on outcomes has been poorly characterised. Prior studies have separated fluid overload into ordinal severity categories (>10, 10–20, or >20 ml/kg).[28] Fluid overload is a ubiquitous clinical entity that has been associated with prolonged mechanical ventilation, length of stay, and mortality.[29–36] However, the timing, degree, and association with acute kidney injury and other risk factors are poorly understood. Certainly, acute kidney injury contributes to fluid overload but not all neonates with acute kidney injury have fluid overload and not all neonates with fluid overload have acute kidney injury or oligo-anuria. In addition, we will be able to evaluate the impact of prophylactic peritoneal dialysis on post-operative acute kidney injury and fluid overload mitigation across multiple centres.[35,37]

Identifying new cardiac surgery-associated acute kidney injury definitions

There are many limitations to the current consensus modified kidney disease improving global outcomes acute kidney injury definitions.[22] It is unknown whether the kidney disease improving global outcomes criteria alone or with the neonatal modification are the relevant definitions for paediatric cardiac surgery-associated acute kidney injury. We plan to challenge the current acute kidney injury definition (using serum creatinine versus urine output versus renal replacement therapy), acute kidney injury severity (stages 0, 1, 2, and 3), and timing/duration of cardiac surgery-associated acute kidney injury (first 2 days versus after 2 days) with respect to impact on clinical outcomes. In addition, using part of the inception cohort, we will propose alternative neonatal acute kidney injury definitions and then internally validate these definitions using the remaining cohort. We will explore multiple serum creatinine, urine output, and fluid balance metrics to determine whether the existing definition or alternative definitions provide better acute kidney injury diagnostic uniformity and prognostication for poor clinical outcomes. If established, this new definition can be used as a consistent endpoint to improve the reproducibility and external validity of cardiac surgery-associated acute kidney injury research.

Exploring earlier acute kidney injury detection

We will construct a novel cardiac surgery-associated acute kidney injury risk prediction model for earlier, bedside identification of at-risk patients. Earlier identification enables clinicians to employ strategies aimed at acute kidney injury prevention or mitigation (such as early fluid restriction or prophylactic peritoneal dialysis) to reduce the clinical impact of cardiac surgery-associated acute kidney injury.

Diuretic responsiveness predict post-operative cardiac surgery-associated acute kidney injury

Several studies have examined whether lack of post-operative diuretic responsiveness has utility as an early acute kidney injury predictor according to modified kidney disease improving global outcomes criteria.[38,39] The Neonatal and Paediatric Heart and Renal Outcomes Network collects hourly urine output for the first 8 hours after initial diuretic administration. This will permit a more detailed examination of diuretic responsiveness and acute kidney prediction among the 1162 subjects receiving furosemide within the first 24 post-operative hours.

Prevention of chronic kidney disease

Existing data demonstrated an increased risk for chronic kidney disease after acute kidney injury[40] and that subsequent cardiac surgical procedures are fraught with increased acute kidney injury risk.[41] With this inception acute kidney injury cohort, we anticipate identifying a subset of patients who are at risk for developing chronic kidney disease from the index acute kidney injury exposure as well as multiple subsequent acute kidney injury exposures (including subsequent surgical encounters and interventions), setting the stage for the development of additional longitudinal studies.

In summary, through multi-centre collaboration and a granular acute kidney injury dataset, the Neonatal and Paediatric Heart and Renal Outcomes Network is uniquely positioned to describe the epidemiology of neonatal cardiac surgery-associated acute kidney injury using the current consensus definition, define and validate the definition of neonatal acute kidney injury specific to cardiac patients, identify risk factors for acute kidney injury, investigate the independent contribution of fluid overload to cardiac surgery-associated acute kidney injury diagnosis and short- and long-term

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outcomes, and validate the furosemide stress test in a large multicentre cohort.

In the future, the Neonatal and Paediatric Heart and Renal Outcomes Network collaborative and the results of this neonatal cardiac surgery-associated acute kidney injury study will become the backbone to trial acute kidney injury prevention strategies, and through collaboration with the Paediatric Cardiac Critical Care Consortium and presentation of acute kidney injury outcomes metrics on the Paediatric Cardiac Critical Care Consortium quality dashboard, stimulate shared multi-centre learning and improvement initiatives.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951119000210

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Conflicts of Interest. K.M.G. is a consultant for BioPorto. No funds were received from Bioporto to conduct the methods/studies discussed herein.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on research in children and with the Helsinki Declaration of 1975 as revised in 2008, and has been approved by the institutional review board at each participating site.

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