



# Peritoneal catheters in neonates undergoing complex cardiac surgery: a multi-centre descriptive study

## Original Article

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### Abstract

**Background:** The use of peritoneal catheters for prophylactic dialysis or drainage to prevent fluid overload after neonatal cardiac surgery is common in some centres; however, the multi-centre variability and details of peritoneal catheter use are not well described. **Methods:** Twenty-two-centre NEonatal and Pediatric Heart Renal Outcomes Network (NEPHRON) study to describe multi-centre peritoneal catheter use after STAT category 3–5 neonatal cardiac surgery using cardiopulmonary bypass. Patient characteristics and acute kidney injury/fluid outcomes for six post-operative days are described among three cohorts: peritoneal catheter with dialysis, peritoneal catheter with passive drainage, and no peritoneal catheter. **Results:** Of 1490 neonates, 471 (32%) had an intraoperative peritoneal catheter placed; 177 (12%) received prophylactic dialysis and 294 (20%) received passive drainage. Sixteen (73%) centres used peritoneal catheter at some frequency, including six centres in >50% of neonates. Four centres utilised prophylactic peritoneal dialysis. Time to post-operative dialysis initiation was 3 hours [1, 5] with the duration of 56 hours [37, 90]; passive drainage cohort drained for 92 hours [64, 163]. Peritoneal catheter were more common among patients receiving pre-operative mechanical ventilation, single ventricle physiology, and higher complexity surgery. There was no association with adverse events. Serum creatinine and daily fluid balance were not clinically different on any post-operative day. Mortality was similar. **Conclusions:** In neonates undergoing complex cardiac surgery, peritoneal catheter use is not rare, with substantial variability among centres. Peritoneal catheters are used more commonly with higher surgical complexity. Adverse event rates, including mortality, are not different with peritoneal catheter use. Fluid overload and creatinine-based acute kidney injury rates are not different in peritoneal catheter cohorts.

### Background

Neonates undergoing surgery for CHD are at high risk for disorders of fluid balance and developing fluid overload.<sup>1</sup> Severe fluid overload occurs commonly and is independently associated with adverse outcomes including duration of mechanical ventilation, cardiac ICU length of stay, and mortality.<sup>2–5</sup> Preventing and/or treating fluid overload may be a strategy to improve post-operative recovery. A method some centres use to prevent post-operative fluid overload in neonates is the placement of an intraoperative peritoneal catheter for prophylactic peritoneal dialysis or passive peritoneal drainage.<sup>6–10</sup>

Several single-centre retrospective and prospective studies have investigated the use of prophylactic peritoneal dialysis or passive peritoneal drainage to prevent neonatal post-operative fluid overload.<sup>7,9–13</sup> These studies have demonstrated to varying degrees that peritoneal dialysis or drainage is safe and associated with improved fluid balance and better post-operative outcomes.<sup>7,9–13</sup> However, these single-centre reports offer an incomplete understanding of the multi-centre epidemiology of peritoneal catheter use across hospitals.

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A 22-centre collaborative, the NEONatal and Pediatric Heart Renal Outcomes Network (NEPHRON), was established to improve the understanding of fluid overload and acute kidney injury after neonatal cardiac surgery.<sup>2,14–17</sup> In this planned NEPHRON secondary study, we sought to fill a knowledge gap of the epidemiology of contemporary peritoneal catheter use at both the centre and patient level by describing variability in use of peritoneal catheters among centres, patient characteristics for those who undergo placement of peritoneal catheters, impact on fluid balance and acute kidney injury metrics, and associated adverse events. It was our goal that the data generated from this report would be hypotheses generated for future studies aimed at determining the utility of post-operative peritoneal catheter.

## Methods

This is a multi-centre observational study of a subset of the NEPHRON dataset with the goal of describing peritoneal catheter use in neonates undergoing high complexity CHD.

### Data source

Data were collected from the NEPHRON supplemental module within the Pediatric Cardiac Critical Care Consortium (PC<sup>4</sup>) registry. This supplemental module included renal-specific information on all consecutive neonates (age  $\leq 30$  days) undergoing an cardiac index surgery between September 2015 and January 2018 at 22 paediatric cardiac centres with a maximum enrollment of 150 patients per centre. Full details of the dataset have been previously published.<sup>14</sup> Non-renal study data were utilised from the peritoneal catheter<sup>4</sup> registry. Peritoneal catheter<sup>4</sup> is a quality improvement collaborative that collects data on all patients with cardiac disease admitted to the cardiac ICU at participating hospitals and currently has over 70 participating centres.<sup>18</sup> The peritoneal catheter<sup>4</sup> dataset has high integrity with comprehensive site education and data validation established through regular audits.<sup>19,20</sup> The University of Michigan Institutional Review Board provided oversight for the PC<sup>4</sup> Data Coordinating Center and has reviewed and approved this study for waived consent, given the retrospective nature of the study.

### Population and data variables

The NEPHRON dataset includes data on neonates undergoing cardiac surgery with and without cardiopulmonary bypass. In order to study a population with high risk of fluid overload, only neonates in the dataset undergoing Society of Thoracic Surgeons–European Association for Cardio-Thoracic Surgery (STAT) category 3–5 surgery<sup>21</sup> with cardiopulmonary bypass who were admitted to the cardiac ICU receiving mechanical ventilation were included.

Baseline characteristics, demographic, pre-operative, and intra-operative variables were collected. Post-operative variables included detailed data for the first six post-operative days of urine output, fluid balance, creatinine, and dialysis or peritoneal drain use. Adverse events reported to peritoneal catheter<sup>4</sup> and potentially related to a peritoneal catheter were collected, including acute kidney injury, necrotising enterocolitis, unplanned gastrointestinal surgery, sternal site infection, and deep surgical site infection. Data were not captured on post-operative placement of a peritoneal catheter for drainage.

### Study cohorts

Patients were assigned to one of three cohorts: (1) prophylactic peritoneal dialysis: neonates with intraoperative peritoneal catheter placement undergoing peritoneal dialysis initiated during the first 24 post-operative hours, (2) passive peritoneal drainage: neonates with intraoperative peritoneal catheter placement undergoing passive peritoneal drainage initiated during the first 24 post-operative hours and (3) neonates without the use of an intraoperative placed peritoneal catheter.

Any patient that received prophylactic peritoneal dialysis in the first 24 hours was classified as dialysis even if the catheter was later used for passive drainage, as dialysis was the original intent of therapy. These patients do not have data on time allocated to drainage. Patients who had intraoperative placement of a peritoneal catheter that was not used were included in the cohort without placement of an peritoneal catheter. While peritoneal dialysis protocols differ among centres, they all share the general practice of low volume dextrose containing dialysate (10 ml/kg) with hourly cycles.<sup>10,22</sup>

### Definitions

The post-operative day fluid balance (daily percent fluid overload) was calculated as:  $100 \times \text{cumulative net daily post-operative fluid balance/pre-operative weight}$  and represents the daily change in fluid balance adjusted to weight on that individual post-operative day.<sup>14</sup> Acute kidney injury was defined using the modified neonatal kidney diseases: Improving Global Outcomes (KDIGO) criteria.<sup>23,24</sup> Urine output criteria were determined using each day's mean hourly urine rate (ml/kg/hour).

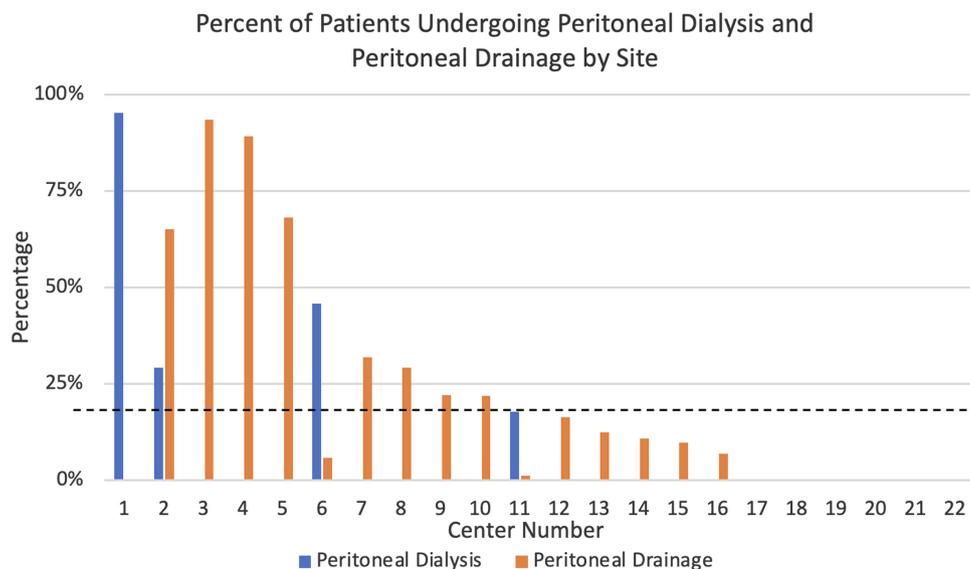
### Analysis

Descriptive data are presented as frequency (%) and median [interquartile range (IQR)] for categorical and continuous variables, respectively. Univariate analyses assessed associations between patient demographic, pre-operative, and intraoperative clinical variables and catheter placement using Chi-square, Fisher exact, or Kruskal–Wallis testing as appropriate. To determine if earlier initiation of prophylactic dialysis differed from later prophylactic dialysis, characteristics and outcomes of patients initiated within 4 hours of cardiac ICU admission were compared to those initiated between 4 and 24 hours. In post hoc analysis, linear mixed effects modelling was used to determine the association of peritoneal catheter use with post-operative creatinine using clinically relevant variables demonstrating a statistically significant association ( $p < 0.1$ ). Analyses were performed using SAS Version 9.4 (SAS Institute, Cary, NC) or SPSS Version 21 (IBM SPSS Statistics for Windows, Armonk, NY), with statistical significance at a  $p$ -value of less than 0.05. These analyses are purely hypothesis generating so correction for multiple comparisons was not performed.

## Results

### Patient characteristics

Among the 2,240 neonates in the NEPHRON module, this study included 1,490 patients (Consort Figure); 269 patients were STAT 3, 843 were STAT 4, and 378 were STAT 5 surgeries. The median age at surgery was 6 days [4,10] with a weight of 3.2 kg [2.9, 3.6]. Prior to surgery, 447 (30%) patients were mechanically ventilated.



**Figure 1.** Bar chart demonstrating the percent of patients undergoing prophylactic peritoneal dialysis or passive peritoneal drainage by site. Dashed line demonstrates median peritoneal catheter placement across all centers of 18%.

The median serum creatinine was 0.49 [0.40, 0.60] mg/dl. There were 420 (28%) patients with single ventricle physiology.

#### Peritoneal dialysis catheter placement

Peritoneal catheters were placed in the operating room in 471 (32%) patients, including almost 40% of STAT 5 patients. Seven patients had peritoneal catheters placed after post-operative cardiac ICU admission for the treatment of acute kidney injury or fluid overload and were excluded from study analysis. While 16 of 22 (73%) centres placed peritoneal catheter, there was significant centre variation with respect to frequency of peritoneal catheter placement in the operating room (Fig 1). In 6 of 22 (27%) centres, peritoneal catheters were used on greater than 50% of neonates whereas in six centres surgeons did not place a peritoneal catheter in any patient. Patients with peritoneal catheters were of similar demographics to those without a catheter (Table 1). Patients who underwent catheter placement were more likely to have pre-operative mechanical ventilation, longer cardiopulmonary bypass and cross-clamp times, undergone deep hypothermic circulatory arrest, had a STAT 5 surgery, and more likely to have single ventricle physiology.

#### Post-operative peritoneal catheter use

There was also important variability in how peritoneal catheters were managed post-operatively. Overall, 177 (12%) patients underwent prophylactic peritoneal dialysis, and 294 (20%) patients underwent passive peritoneal drainage only (Fig 1). Four (18%) institutions utilised prophylactic dialysis and 15 (68%) used passive drainage. Patients who underwent prophylactic dialysis were less likely to have undergone modified ultrafiltration (Table 1). Patients undergoing peritoneal drainage had statistically lower, but clinically similar, pre-operative serum creatinine (Table 1).

#### Prophylactic peritoneal dialysis

The median time from cardiac ICU post-operative admission until the initiation of prophylactic peritoneal dialysis was 3 hours [1, 5] with a median duration of 56 hours [37, 90] (Supplemental Figure 1). Duration of dialysis was less than 2 days in 46% (81/177). The median ultrafiltration volume was highest during

post-operative day 1 (Fig 2a); which was greater than three times more fluid removed from the peritoneum than the passive drainage cohort on post-operative day 1: 38 [18, 54] versus 13 ml/kg [3, 27]. Less than half of the patients in the dialysis cohort were administered diuretics on the first two post-operative days, and this increased on each post-operative day (Table 2).

Among the four centres using prophylactic peritoneal dialysis, there was variation in the timing of initiation, with 49, 73, 88, and 97% of patients initiated within 4 hours of arrival in the cardiac ICU at respective centres ( $p < 0.001$ ). Those with earlier initiation were more likely to have use of aortic cross clamp and underwent higher STAT category surgery but otherwise had similar baseline and operative characteristics (Supplemental Table 1). Patients with later initiation of peritoneal dialysis had similar urine output, fluid balance, and acute kidney injury metrics but had statistically lower creatinine (0.35 mg/dl vs. 0.40 mg/dl;  $p = 0.02$ ) on post-operative day 6. Those with later initiation of peritoneal dialysis were more likely to receive a diuretic dose during the first post-operative day (63% vs. 34%;  $p < 0.001$ ).

#### Passive peritoneal drainage

Almost all patients (86%,  $n = 254$ ) undergoing passive peritoneal drainage had initiation during the first hour of arrival to the cardiac ICU and the median duration of drainage was 92 hours [64, 163]. The volume drained was the highest on the day of operation (17 ml/kg [6, 34]) and decreased each day thereafter. Most had stopped drainage before post-operative day 4 (Fig 2b). Almost half were administered diuretics starting on the day of surgery, and 86% of patients by the first post-operative day (Table 2).

#### Association of peritoneal catheters with urine output

There was significant reduction in daily UOP in the dialysis cohort on post-operative days 0–3 compared to the other two cohorts (Table 2, Fig 3a). The largest difference was on post-operative day 1, during which there was a threefold reduction compared to the drainage cohort and a fourfold reduction compared to the cohort without a peritoneal catheter. Urine output was similar among all cohorts by post-operative days 4–5. At least 1 day of urine output  $< 0.3$  ml/kg/hr occurred in 4% of patients without peritoneal catheters compared to 13% of dialysis patients and

**Table 1.** Baseline characteristics and operative variables

| Variable                                     | No peritoneal catheter<br>(n = 1,019) | Prophylactic peritoneal dialysis<br>(n = 177) | Passive peritoneal drainage<br>(n = 294) | p-Value |
|--|---------------------------------------|---|--|---------|
| Age at surgery (days)                        | 6 [4, 10]                             | 7 [5, 10]                                     | 7 [4, 10]                                | 0.16    |
| Weight at surgery (kg)                       | 3.22 [2.90, 3.60]                     | 3.21 [2.85, 3.51]                             | 3.22 [2.90, 3.50]                        | 0.59    |
| Sex (Female)                                 | 397 (39.0)                            | 68 (38.4)                                     | 118 (40.1)                               | 0.54    |
| Race   |                                       |   |  | 0.41    |
| Non-Hispanic Caucasian                       | 586 (57.5)                            | 97 (54.8)                                     | 171 (58.2)                               |         |
| Black/African American                       | 137 (13.4)                            | 27 (15.3)                                     | 31 (10.5)                                |         |
| Hispanic                                     | 172 (16.9)                            | 35 (19.8)                                     | 47 (16.0)                                |         |
| Other  | 124 (12.2)                            | 18 (10.2)                                     | 45 (15.3)                                |         |
| Preterm (<37 weeks)                          | 103 (10.1)                            | 22 (12.4)                                     | 26 (8.8)                                 | 0.22    |
| Chromosomal abnormality                      | 169 (16.6)                            | 33 (18.6)                                     | 43 (14.6)                                | 0.63    |
| Extra-cardiac anomaly                        | 164 (16.1)                            | 35 (19.8)                                     | 44 (15.0)                                | 0.37    |
| Preoperative mechanical ventilation          | 265 (26.0)                            | 66 (37.3)                                     | 116 (39.5)                               | <0.001  |
| Baseline serum creatinine (mg/dL)            | 0.50 [0.40, 0.60]                     | 0.50 [0.40, 0.60]                             | 0.45 [0.40, 0.52]                        | 0.004   |
| STAT category                                |                                       |   |  | <0.001  |
| 3  | 207 (20.1)                            | 13 (7.3)                                      | 49 (16.7)                                |         |
| 4  | 579 (56.8)                            | 111 (62.7)                                    | 153 (52.0)                               |         |
| 5  | 233 (22.9)                            | 53 (29.9)                                     | 92 (31.3)                                |         |
| Single ventricle                             | 262 (25.7)                            | 64 (36.2)                                     | 94 (32.0)                                | 0.005   |
| Modified ultrafiltration                     | 650 (63.8)                            | 63 (35.6)                                     | 187 (63.6)                               | <0.001  |
| Cardiopulmonary bypass time (minutes)        | 130 [91, 164]                         | 152 [123, 211]                                | 141 [106, 176]                           | <0.001  |
| Cross clamp (yes/no)                         | 930 (91.3)                            | 171 (96.6)                                    | 275 (93.5)                               | 0.033   |
| Cross clamp time (minutes; if applicable)    | 64 [43, 92]                           | 87 [56, 125]                                  | 66 [45, 103]                             | <0.001  |
| Deep hypothermic circulatory arrest (yes/no) | 386 (37.9)                            | 85 (48.0)                                     | 132 (44.9)                               | 0.009   |

All data presented as n (%) or median [interquartile range]; p-value comparing all three cohorts.

9% of drainage patients. The incidence of anuria was 2% (4/177 vs. 5/295) in the dialysis and drainage cohorts, respectively. On post-operative day 1, fewer than half of the dialysis cohort received diuretics compared to >85% of the other two cohorts. Starting on post-operative day 3, all three cohorts had similar incidence of diuretic utilisation.

#### Association of peritoneal catheters with creatinine and fluid balance

Serum creatinine peaked most commonly on post-operative day 1 in all cohorts (53% no peritoneal catheter, 64% dialysis and 55% drainage) and trended down daily thereafter through post-operative day 6. The median serum creatinine is displayed in Fig 3b. Both cohorts with catheters had a statistically significant lower serum creatinine compared to those without catheters on post-operative days 4–6.

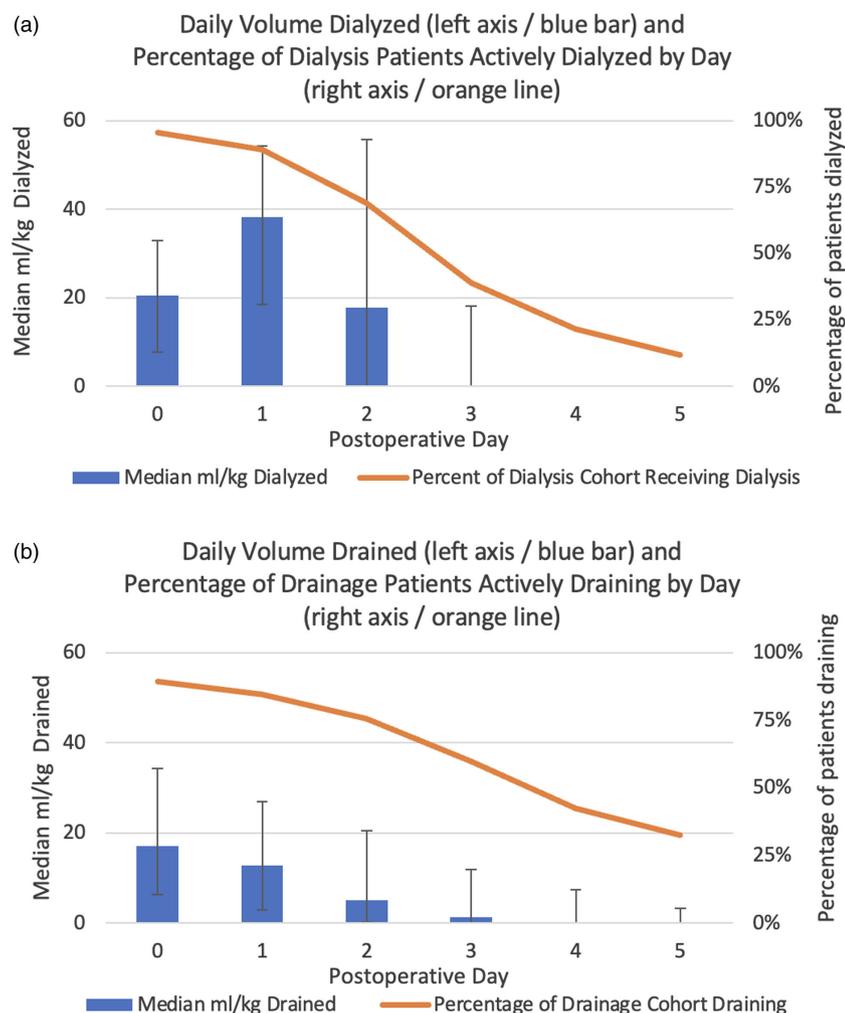
The difference in fluid balance between groups was negligible. Daily net fluid balance was only clinically different on post-operative day 1 (Fig 3c). While there were statistically significant differences in net daily fluid balance on post-operative days 3 and 5, balances were within 1% and thus likely of little clinical importance. All groups had a negative median daily fluid balance on post-operative days 1 and 2.

In linear mixed model analysis, controlling for baseline serum creatinine, STAT score, and use of MUF, peritoneal catheter placement was associated with a daily post-operative decrease in serum creatinine of 0.11 mg/dL ((95%CI 0.04–0.18);  $p = 0.003$ ). When looking at specific interventions, passive drainage was associated with a daily post-operative decrease in serum creatinine of 0.04 mg/dl ((95%CI 0.02–0.05);  $p < 0.001$ ). Peritoneal dialysis was not associated with a difference.

#### Adverse events

Lower urine output in the dialysis cohort resulted in a significant increase in acute kidney injury diagnosis by urine output criteria: 77% dialysis versus 39% drainage versus 33% no catheter ( $p < 0.001$ ). However, there was no difference in acute kidney injury diagnosis by serum creatinine criteria. Stage 2 or worse creatinine-based acute kidney injury (severe acute kidney injury) was seen in 25/177 (14%) of dialysis patients and 33/294 (11%) of drainage patients, which was similar to the 159/1,019 (16%) in neonates without catheters.

The incidence of necrotising enterocolitis was 3 of 177 (1.7%) in patients undergoing prophylactic dialysis and 10 of 294 (3.4%) among those undergoing passive drainage, which was not different than those without a catheter (26/1019; 2.6%). No patients in either peritoneal catheter group developed a deep sternal site infection



**Figure 2.** Bar charts demonstrating median [IQR] volume (ml/kg) of fluid removed per day with overlapping line graph showing percentage with active peritoneal dialysis in the Prophylactic Peritoneal Dialysis cohort (A), and percentage undergoing drainage in the Passive Peritoneal Drainage cohort (B). In patients in the Dialysis cohort who also underwent drainage, only net ultrafiltered volume is reported.

and no patients undergoing dialysis had any surgical site infection. Surgical site infection was reported among 2.4% of those with drainage. No patient in any group underwent reintervention for unplanned gastrointestinal surgery. There was no difference in in-hospital mortality between groups (3.4% no PD, 2.8% dialysis, 5.8% drainage).

## Discussion

This study fills a critical gap in knowledge regarding the epidemiology of contemporary use of prophylactic peritoneal dialysis and drainage in neonates after complex cardiac surgery with findings that are not well demonstrated by previous publications. Overall, most of the centres in this study placed intraoperative peritoneal catheter at some frequency, more commonly among patients with higher pre-operative acuity and surgical risk. We found substantial practice variability: while some centres used a peritoneal catheter in most patients, others placed no catheters. Furthermore, only a few centres use peritoneal catheter for prophylactic dialysis, with most using them primarily for drainage. The concept behind prophylactic dialysis or drainage is to prevent fluid accumulation rather than waiting to treat fluid overload. This is driven by the belief that this practice allows earlier nutrition and liberal use of medications without developing extravascular fluid accumulations that may cause worsening organ

function (including AKI) which may subsequently cause worse fluid balance. Additionally, peritoneal catheter has the potential to remove deleterious inflammatory cytokines which are associated with kidney and other organ injuries after neonatal cardiac surgery.<sup>22,25</sup> However, there is no consensus for which patients would benefit from this therapy, which therapy is optimal, and if patients should demonstrate clinical evidence of renal insufficiency before initiating therapy. Therefore, there remains great variation in practice. Even among centres using prophylactic dialysis there is variation in timing, as some centres start dialysis early on arrival and others may await poor diuretic responsiveness. These data reflect the importance of investigating multi-centre practices regarding peritoneal catheter use, as clinical experience and preference drives practice variation. Overall, there was no clinically important difference in daily fluid balance or creatinine-based acute kidney injury in patients with peritoneal catheter, while our non-risk adjusted analysis identified no increase in the rate of adverse events in those with a peritoneal catheter.

Prior to this study, the only multi-centre analysis of peritoneal catheter incidence and associated outcomes had been reviews of large administrative datasets. One study examining paediatric cardiac surgical patients within the Kid's Inpatient Database (KID) between 2006 and 2009 found a 2% incidence of post-operative peritoneal catheter placement (3.3% among neonates).<sup>26</sup> A second study evaluating all paediatric cardiac surgical patients in the KID

**Table 2.** Urine output, fluid balance, and creatinine data

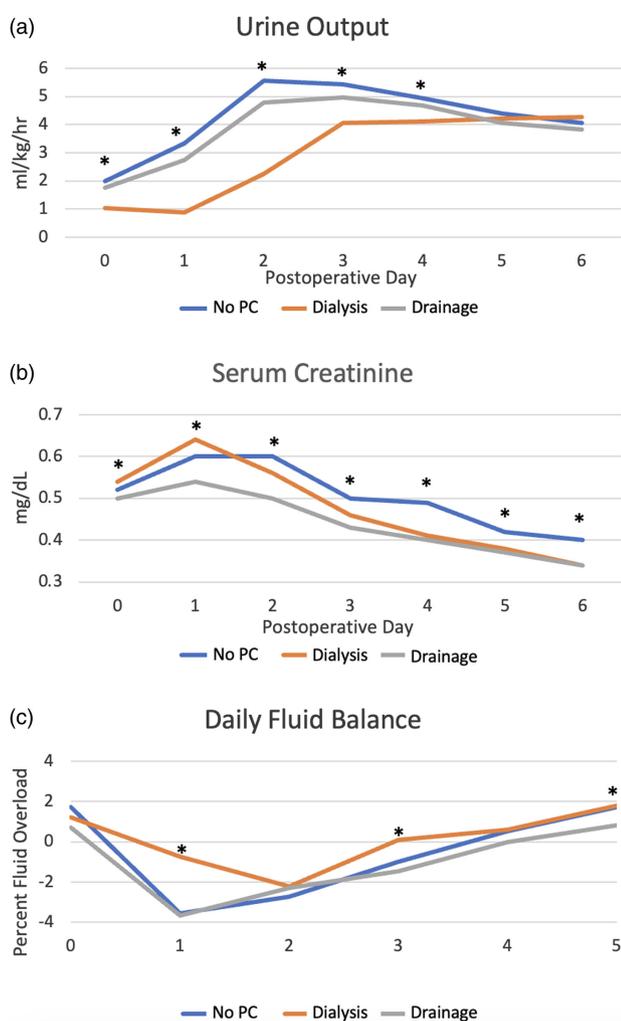
| Variable  | No peritoneal catheter<br>n = 1,019 | Prophylactic peritoneal dialysis<br>n = 177 | Passive peritoneal drainage<br>n = 294 | p-Value |
|---|-------------------------------------|---|--|---------|
| <b>Diuretic Use (y/n)</b>                       |                                     |   |  |         |
| POD 0   | 577 (56.6)                          | 76 (42.9)                                   | 129 (45.1)                             | <0.001  |
| POD 1   | 965 (95.3)                          | 85 (48.0)                                   | 252 (85.7)                             | <0.001  |
| POD 2   | 978 (96.5)                          | 129 (72.9)                                  | 266 (90.5)                             | <0.001  |
| POD 3   | 964 (95.3)                          | 149 (84.2)                                  | 264 (89.8)                             | <0.001  |
| POD 4   | 956 (94.7)                          | 150 (84.7)                                  | 266 (90.5)                             | <0.001  |
| POD 5   | 936 (94.3)                          | 154 (87.0)                                  | 265 (90.8)                             | <0.001  |
| POD 6   | 900 (92.2)                          | 147 (84.0)                                  | 251 (87.8)                             | <0.001  |
| <b>AKI Maximum Stage</b>                        |                                     |   |  |         |
| 0   | 439 (43.1)                          | 32 (18.1)                                   | 122 (41.5)                             | <0.001  |
| 1   | 341 (33.5)                          | 77 (43.5)                                   | 99 (33.7)                              |         |
| 2   | 152 (14.9)                          | 43 (24.3)                                   | 36 (12.2)                              |         |
| 3   | 87 (8.5)                            | 25 (14.1)                                   | 37 (12.6)                              |         |
| <b>Serum Creatinine based AKI Maximum Stage</b> |                                     |   |  |         |
| 0   | 611 (60.3)                          | 108 (61.7)                                  | 187 (63.8)                             | 0.32    |
| 1   | 243 (24.0)                          | 42 (24.0)                                   | 73 (24.9)                              |         |
| 2   | 111 (11.0)                          | 21 (12.0)                                   | 27 (9.2)                               |         |
| 3   | 48 (4.7)                            | 4 (2.3)                                     | 6 (2.0)                                |         |
| <b>Urine Output based AKI Maximum Stage</b>     |                                     |   |  |         |
| 0   | 685 (67.6)                          | 41 (23.2)                                   | 178 (61.0)                             | <0.001  |
| 1   | 229 (22.6)                          | 79 (44.6)                                   | 67 (22.9)                              |         |
| 2   | 57 (5.6)                            | 34 (19.2)                                   | 20 (6.8)                               |         |
| 3   | 43 (4.2)                            | 23 (13.0)                                   | 27 (9.2)                               |         |
| <b>Urine Output (ml/kg/hr)</b>                  |                                     |   |  |         |
| POD 0   | 2 [1.2, 3.2]                        | 1 [0.7, 1.4]                                | 1.8 [1.2, 3]                           | <0.001  |
| POD 1   | 3.3 [1.7, 5.4]                      | 0.9 [0.6, 1.5]                              | 2.7 [1.3, 4.6]                         | <0.001  |
| POD 2   | 5.6 [3.9, 7.2]                      | 2.3 [1.1, 3.9]                              | 4.8 [3.4, 6.4]                         | <0.001  |
| POD 3   | 5.4 [4, 6.8]                        | 4.2 [2.6, 5.5]                              | 5 [3.4, 6.5]                           | <0.001  |
| POD 4   | 5 [3.4, 6.2]                        | 4.1 [3.1, 5.3]                              | 4.7 [3, 6.1]                           | <0.001  |
| POD 5   | 4.4 [3.1, 5.6]                      | 4.2 [3.1, 5.1]                              | 4.1 [2.6, 5.6]                         | 0.12    |
| POD 6   | 4.1 [2.7, 5.3]                      | 4.3 [3, 5.4]                                | 3.8 [2.4, 5.4]                         | 0.22    |
| <b>Serum Creatinine (mg/dL)</b>                 |                                     |   |  |         |
| POD 0   | 0.52 [0.45, 0.60]                   | 0.54 [0.46, 0.60]                           | 0.50 [0.40, 0.60]                      | <0.001  |
| POD 1   | 0.60 [0.50, 0.71]                   | 0.64 [0.52, 0.78]                           | 0.54 [0.45, 0.68]                      | <0.001  |
| POD 2   | 0.60 [0.46, 0.72]                   | 0.56 [0.44, 0.70]                           | 0.50 [0.40, 0.67]                      | <0.001  |
| POD 3   | 0.50 [0.40, 0.70]                   | 0.46 [0.39, 0.60]                           | 0.43 [0.36, 0.60]                      | <0.001  |
| POD 4   | 0.49 [0.38, 0.60]                   | 0.41 [0.33, 0.54]                           | 0.40 [0.30, 0.51]                      | <0.001  |
| POD 5   | 0.42 [0.34, 0.54]                   | 0.38 [0.30, 0.50]                           | 0.37 [0.30, 0.49]                      | <0.001  |
| POD 6   | 0.40 [0.30, 0.50]                   | 0.34 [0.30, 0.40]                           | 0.34 [0.29, 0.45]                      | <0.001  |

(Continued)

**Table 2.** (Continued)

| Variable  | No peritoneal catheter<br>n = 1,019 | Prophylactic peritoneal dialysis<br>n = 177 | Passive peritoneal drainage<br>n = 294 | p-Value |
|---|-------------------------------------|---|--|---------|
| Daily Fluid Balance<br>(Percent fluid overload) |                                     |   |  |         |
| POD 0   | 1.7% [-2.3, 5.9]                    | 1.2% [-0.8, 3.6]                            | 0.7% [-2.8, 4.6]                       | 0.05    |
| POD 1   | -3.6% [-7.2, 0.4]                   | -0.7% [-3.5, 1.6]                           | -3.7% [-6.7, 0.1]                      | <0.001  |
| POD 2   | -2.7% [-6.4, 0.6]                   | -2.2% [-4.6, 0.9]                           | -2.3% [-6.1, 0.4]                      | 0.1     |
| POD 3   | -1% [-4.3, 2]                       | 0.1% [-3.1, 2.6]                            | -1.5% [-5.2, 1.5]                      | 0.013   |
| POD 4   | 0.5% [-2.4, 3.1]                    | 0.6% [-2, 3]                                | 0 [-2.9, 2.6]                          | 0.1     |
| POD 5   | 1.7% [-1.2, 4.1]                    | 1.8% [-0.7, 4]                              | 0.8% [-2.2, 3.3]                       | 0.003   |

All data presented as n (%) or median [interquartile range]; p-value comparing all three cohorts. AKI – acute kidney injury, POD – post-operative day.



**Figure 3.** Line graphs demonstrating urine output (A), serum creatinine (B) and daily fluid balance (C) by day for patients with no peritoneal catheter (No PC) and those undergoing prophylactic peritoneal dialysis, and passive peritoneal drainage.

database from 1997 to 2012 found an even lower peritoneal catheter incidence (0.4%).<sup>8</sup> These studies are both subject to coding limitations, as the intraoperative placement of peritoneal catheter may not be identified separately from the cardiac surgical

procedure. Furthermore, these studies lack granularity to identify timing and indication for placement, details of peritoneal catheter use, or whether patient-related factors informed peritoneal catheter placement. In our contemporary cohort of moderate to large cardiac surgical programmes, peritoneal catheter use was almost 10-fold higher. It is unknown if more frequent use is due to an increase in practice, sampling biases, or more complete reporting. Contrary to the administrative database studies, we noted no difference in creatinine-defined acute kidney injury or mortality in neonates with a peritoneal catheter.

There was transiently decreased urine output in patients undergoing prophylactic peritoneal dialysis that resolved when patients in this cohort typically stopped dialysis and increased diuretic administration. As a result, peritoneal catheter patients may appear to have important oliguria (and meet acute kidney injury criteria), however increased rate of acute kidney injury was not identified using serum creatinine criteria. This suggests that oliguria in the presence of a peritoneal drain is likely not related to kidney tubular injury, but rather a physiologic response to an alternative source of fluid removal as effective ultrafiltration via the peritoneal membrane decreases intravascular volume, which would serve to decrease glomerular filtration. Similar trends in urine output have been described in a single-centre neonatal peritoneal catheter study on patients undergoing the arterial switch operation.<sup>7</sup> A contributing factor to the lower urine output in peritoneal catheter patients is that urine output may be more dependent on diuretic use, and those without peritoneal catheters were more likely to receive diuretics, especially in the early post-operative periods. The finding of short-term oliguria without creatinine-based acute kidney injury calls into question the validity of urinary-based acute kidney injury diagnoses in the presence of peritoneal catheter and may impact how we define acute kidney injury in the future.

There was no difference in the rates of serum creatinine-based acute kidney injury among the three cohorts, in the context of the peritoneal catheter cohorts comprising patients with greater surgical acuity, in which acute kidney injury rates are typically significantly higher.<sup>17</sup> Despite similar fluid balances, the median serum creatinine was actually lower in both peritoneal catheter cohorts during the study period. Mixed effects modelling demonstrated that peritoneal catheter use was associated with lower creatinine, even after control of multiple risk factors. Although dialysis allows active clearance of creatinine, this trend persisted after almost all patients discontinued dialysis. This

suggests peritoneal catheter may allow more renal protective strategies to occur while maintaining stable fluid balances. Peritoneal catheter use may also protect glomerular filtration by decompressing the abdomen and preventing relative renal tamponade.<sup>27</sup> Additionally, peritoneal catheter use may allow avoidance of excessive diuretic use, which may be detrimental to renal health.<sup>28</sup> It may appear these results are at odds with single-centre studies that show significantly more negative fluid balance with peritoneal catheter use. This could result from analysing aggregate data across multiple centres in which FB is quite variable, but we point out again that this cohort was comprised of higher risk patients, which are shown to have a more fluid overload.<sup>2</sup> We hypothesise that maintenance of similar fluid balance to a lower risk non-peritoneal catheter cohort is a potential clinical benefit of peritoneal catheter with or without dialysis.

This study adds to existing evidence that peritoneal catheter placement and use is not associated with major adverse events. Low adverse event rates are demonstrated in multiple single-centre studies on peritoneal catheter use in infants after cardiac surgery, particularly those with intraoperative placement.<sup>6,10,11,13,22,29</sup> In this relatively large study using a dataset with well-demonstrated fidelity,<sup>19</sup> there was not an increase in adverse events including necrotising enterocolitis, infection, and unplanned gastrointestinal surgical interventions in the peritoneal catheter cohort.

The purpose of this manuscript was to understand the details of intraoperative peritoneal catheter placement - to lay the foundation for future outcome studies. Knowledge gained from this study has made it clear there is important patient and centre variation with respect to frequency of peritoneal catheter use. Inherent biases with regards to which treatment a patient receives (based on provider preference, institutional patterns, and/or patient acuity/risk factors) will make outcome associations challenging to determine in multi-centre study. These are important considerations for our next steps of study aimed at determining if early use of peritoneal catheter has utility after neonatal cardiac surgery.

While this study represents one of the largest reports of neonatal post-cardiac surgery peritoneal catheter use, this study has several limitations associated with retrospective data analyses. As highlighted, there is significant variation in frequency of peritoneal catheter placement and method of management across centres, thus the results are subject to biases of centre-specific practice. Furthermore, little can be inferred about patient outcomes, as the cohorts are not matched, and the outcomes are unadjusted. That said, because peritoneal catheter patients are higher risk and underwent more complex procedures, this heterogeneity would bias towards making outcomes worse among the peritoneal catheter group. Unfortunately, intraoperative fluid balance and modified ultrafiltration management could not be well-described and likely differed among centres. This may be one of the larger influences on post-operative fluid balance and haemodynamics and should be better controlled in a prospective evaluation. It is possible that this study may underestimate the true incidence of peritoneal catheter use, as it does not include patients with post-operative placement of a catheter for reasons other than acute kidney injury or FO. Additionally, while this study utilises a reliable dataset, there is the potential for incomplete reporting of adverse events, including peritonitis, omental hernia, or catheter leakage which are not events identified in peritoneal catheter<sup>4</sup>.

In conclusion, these data show that peritoneal catheter use is frequent, with substantial variability in placement and application among centres. Although short-term oliguria may be seen with

prophylactic pancreatic duct, it likely does not reflect true renal injury, which may cast doubt on the use of oliguria in the definition of acute kidney injury in this population. Although we are not able to conclude on clinical benefit of prophylactic peritoneal dialysis or passive peritoneal drainage, our data suggests non-inferiority with respect to acute kidney injury and fluid overload metrics, despite a higher risk cohort. We do not demonstrate an association with reported adverse events. We believe that findings of this study will establish the foundation for future study aimed at understanding the multi-centre association of peritoneal catheter use with clinical outcomes and resource utilisation, which will ultimately determine whether a multi-centre trial is indicated to evaluate for the benefit of peritoneal catheter use in this high-risk population.

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