




Prophylactic Peritoneal Dialysis in Pediatric Cardiac Surgery

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Abstract

Purpose of review This review examines the role of prophylactic peritoneal dialysis in pediatric patients after cardiac surgery. We identify benefits and risks of the intervention while highlighting gaps in current knowledge.

Recent findings The usage of peritoneal dialysis to manage and acute kidney injury (AKI) and fluid overload (FO) after pediatric cardiac surgery may demonstrate advantages over conventional diuresis and more invasive forms of renal replacement therapies (RRT) in some patients. Outcomes vary by population in limited single and multicenter studies but suggest decreased mechanical ventilation time, earlier time to net negative fluid balance, and shorter ICU stays when compared to conventional therapies.

Summary Prophylactic peritoneal dialysis use in the pediatric cardiac population varies widely across pediatric cardiac centers but is increasingly being demonstrated as a safe, effective treatment of AKI and FO, both of which are common and associated with deleterious outcomes in this population. Clinical decision support tools have been developed to assist in identifying patients most likely to benefit from RRT outside of the cardiac population, but further work is needed to determine if they can be applied to postoperative

cardiac patients. Complications are relatively infrequent but may indicate benefits for center-specific peritoneal dialysis management protocols.

Introduction

Acute kidney injury (AKI) and fluid overload (FO) are common and associated with poor outcomes in heterogeneous populations of critically ill children [1–3]. A detailed discussion of the epidemiology of cardiac surgery-associated AKI and FO are beyond the scope of this review. Briefly, recent epidemiologic data from the Neonatal and Pediatric Heart and Renal Outcomes Network (NEPHRON) demonstrated highly variable rates of AKI across centers when using the modified neonatal Kidney Disease Improving Global Outcomes serum creatinine and urine output criteria [1]. Unlike prior studies, where AKI was associated with increased resources utilization and mortality [4–6], in the NEPHRON study by Alten and colleagues, only stage 3 AKI was associated with mortality, but not other clinically relevant outcomes. Bailly and colleagues also used the NEPHRON data for evaluation of the impact of FO on outcomes [7]. In this study, the degree of FO was much lower than has previously reported in children undergoing cardiac surgery [5, 8] measuring approximately 4.9% [7]. Peak FO and postoperative day 1 FO were not associated with clinically relevant outcomes; however, hospital resource utilization, characterized by longer duration of ventilation and ICU length of stay, was increased on each successive day of not achieving a negative fluid balance [7]. This lower peak FO suggests that clinicians may be more aware and mindful of the deleterious effects of FO limiting excessive fluid accumulation in their patients. Thus, it is imperative

that focus now be shifted to actionable targets such as earlier achievement of negative fluid balance to minimize hospital resource utilization.

The etiology of AKI after pediatric cardiac surgery is multifactorial. Intra- and post-operative factors that are associated with AKI include hemolysis, blood product transfusion, systemic inflammatory response from deep hypothermic circulatory arrest, long cardiopulmonary bypass (CPB) duration, and nephrotoxic medication exposures [9]. These mechanistic factors may lead to exacerbation of either AKI and FO, or both. Indeed, there is a bidirectional risk associated with the presence of AKI and FO and in critically ill children, and they appear to have a synergistic effect in negatively impacting outcomes [10]. In the most severe form of both AKI and FO, renal replacement therapy (RRT) is used as supportive therapy when there is oliguria, electrolyte disturbances, and uremia present. Peritoneal dialysis has been shown to be an effective alternative method of RRT for AKI and fluid management in infants undergoing cardiac surgery and is the modality of choice in some centers in the immediate postoperative period to prevent AKI and FO. Peritoneal dialysis has demonstrated comparable morbidity and mortality outcomes to extracorporeal therapies in both cardiac and non-cardiac pediatric populations. The purpose of this review is to discuss utilization of peritoneal drains and peritoneal dialysis in children undergoing cardiac surgery.

Peritoneal drains and dialysis

Peritoneal dialysis is a commonly employed technique in children in the acute and chronic setting, particularly in neonates and infants, and is the primary therapy in low resource settings [11, 12]. The utility of peritoneal dialysis has been extended to children undergoing cardiac surgery in the absence of standard indications. In this setting, peritoneal drains are used either for passive peritoneal drainage or prophylactic peritoneal dialysis [13,

14]. Cardiac surgery, particularly with CPB and circulatory arrest, can result in activation of pro- and anti-inflammatory cytokines with a resultant significant inflammatory response, capillary leak, and low cardiac output syndrome [15]. These factors are often associated with the development of AKI and FO. For this reason, preoperative decision making has been employed in some centers for placement of peritoneal catheters for either postoperative passive drainage or prophylactic peritoneal dialysis to mitigate the deleterious inflammatory response by augmenting cytokine and fluid removal and perhaps reduce the burden of AKI [16–20]. Table 1 summarizes considerations for identifying high- and medium risk patients in whom peritoneal dialysis catheter (PDC) placement would most likely be beneficial following cardiac surgery.

Peritoneal catheter placement and dialysis prescription.

Peritoneal drain catheters (PDC) can either be placed in the operating room or at bedside in the intensive care unit (ICU) as the need arises. The single or double cuffed pediatric sized Tenckhoff pediatric PD catheter is the most used catheter in children after cardiac surgery. The standard approach in the operating room is performed after cardiac surgery and prior to chest closure, where a small incision is made into the peritoneum at the inferior portion of the sternotomy incision and the catheter tunneled into the peritoneal cavity under direct visualization. This is followed by closing the peritoneal incision and fixing the catheter to the skin with a stay suture. In the ICU, drain placement can be performed with or without ultrasound guidance. The most common approach involves making an incision either inferior to the umbilicus or at the midpoint between the umbilicus and anterior inferior iliac spine to avoid the inferior epigastric artery that traverses along the lateral aspect of the rectus abdominis sheath [11, 21]. The PDC is then placed into the peritoneum and secured in a similar fashion. For both operating room and ICU placement, the catheter is then connected to a standard collection bag, which can be exchanged for a closed system to allow flushes for patency and passive drainage, or regular cycles of peritoneal dialysis. The only catheter-related interventions that have been shown by meta-analysis to be successful at preventing catheter-associated peritonitis is the usage of disconnect (twin-bag and Y-set) systems as opposed to conventional spike systems [22]. Prophylactic perioperative antibiotics should be administered 60 min prior to PDC insertion to prevent early-onset peritonitis [23, 24].

Once placed, the peritoneal catheter may be used either for passive drainage or dialysis depending on the clinical status of the patient and clinician discretion. Passive drainage is often used but when augmented fluid removal is necessary, prophylactic peritoneal dialysis can instead be implemented at any time during the patient's post-operative recovery. The most common

Table 1. Moderate and high-risk considerations for peritoneal dialysis catheter placement

Moderate risk	High risk
<ul style="list-style-type: none"> • Infants >3 months undergoing cardiac surgery with cardiopulmonary bypass • Cardiopulmonary bypass > 150 min 	<ul style="list-style-type: none"> • Single ventricle patients undergoing stage 1 palliation • Neonates and infants with restrictive right ventricular physiology

starting prescription for prophylactic peritoneal dialysis is Dianeal with 2.5% dextrose with a fill volume of 10 mL/kg to prevent peritoneal fluid leakage. Per the International Society for Peritoneal Dialysis, fill volumes may be gradually increased to 30–40 mL/kg if higher prescriptions are needed to achieve optimal fluid status [11]. The near-physiologic dialysate infusion then facilitates diffusion of fluid, metabolites, and molecules between blood and peritoneal fluid through the semi-permeable peritoneal membrane. Higher dialysate dextrose concentrations can be used to enhance fluid removal by increasing the osmotic gradient for ultrafiltration. Diffusion of molecules such as potassium, creatinine, and urea across the peritoneal membrane are dependent on concentrations in the dialysate, which allows for targeted ultrafiltration and removal of toxic metabolites in the setting of AKI. The resultant ultrafiltrate is drained from the peritoneal cavity to achieve improved metabolic and hemodynamic status [11, 25]. The prescription usually allows for a 5–10-min fill time, a 30–45-min dwell time and drainage of 10 min. Both the fill volume and dwell time can be increased to optimize dialysis.

Peritoneal dialysis complications

Despite the known benefits of peritoneal dialysis in this cohort, risk–benefit analysis should be individualized for each potential candidate as there is always risk for complications. A potentially life-threatening complication of peritoneal dialysis is peritonitis. Leakage of peritoneal fluid through the dialysis catheter can increase the risk of infection. Advancements in PDC insertion techniques and antibiotic usage have reduced rates of peritonitis in patients. Numerous studies have reported on PD catheter related complications after pediatric cardiac surgery. Flores et al. demonstrated no increase in peritonitis among those with PDC [26]. Another study identified peritonitis in 2 out of 23 patients treated with peritoneal dialysis [13]. In an older study at a single institution from 1993 to 2002, only 2 patients transitioned to hemodialysis as a result of peritonitis. Risk factors associated with peritoneal dialysis complications included longer duration of peritoneal dialysis, higher Risk Adjusted Classification for Congenital heart Surgery (RACHS-1) score and hyperkalemia at time of peritoneal dialysis initiation [20].

Metabolic derangements are an additional potential complication that necessitates routine lab monitoring. The semi-permeable quality of the peritoneal membrane is bi-directional, permitting diffusion of dextrose from the high concentration dialysate into the blood stream which can cause hyperglycemia. Potassium may diffuse across the peritoneal membrane from the blood into the low concentration dialysate, resulting in hypokalemia. Up to one-third of patients have been reported to have hypokalemia, and increased morbidity and mortality have been associated with persistent hypokalemia [27–29]. To mitigate the risk of peritoneal dialysis-associated hypokalemia, potassium should be added to dialysate solutions once serum potassium drops below 4 mmol/L. In addition, a bicarbonate buffer is recommended for patients exhibiting significant metabolic acidosis, hemodynamic instability,

and hepatic dysfunction during peritoneal dialysis. Small solute clearance can be assessed as a measure of PD efficacy. Residual kidney function, if present, would contribute to total clearance. Routine monitoring of electrolytes, albumin, and bicarbonate is recommended to prevent electrolyte derangement and identify nutritional deficiencies associated with peritoneal dialysis [11, 21].

Another potential complication of peritoneal dialysis includes intra-abdominal organ damage from the indwelling catheter [30]. In addition, long-term use of high concentration dextrose solutions may lead to sclerosis of the peritoneal membrane rendering dialysis ineffective. Fortunately, this is uncommon with prophylactic peritoneal dialysis after cardiac surgery as it is most often used only for the first few postoperative days. The PDC can also communicate with the pleural space, which can lead to numerous complications and negates the ability to use the PDC for prophylactic dialysis. Removal of catheters in awake children with an acute increase in intraabdominal pressure, such as during cough, can increase the risk of omental herniation [31]. Finally, the development of an abdominal hernia during catheter removal is a relatively common complication that has been identified in certain patient populations [32].

Peritoneal dialysis utilization in the pediatric cardiac population

There is significant heterogeneity in utilization of peritoneal drains for passive drainage or prophylactic dialysis across pediatric cardiac surgery centers. In the large epidemiology study, prophylactic dialysis was used in 13.8% of patients within the first 24 h [1]. A more detailed report on the impact and outcomes of patients receiving prophylactic dialysis from NEPHRON is forthcoming. There are several perceived benefits to using peritoneal drains in children after cardiac surgery: [1] relative ease in catheter placement, [2] lack of requirement for a large intravenous dialysis catheter and anticoagulation (regional or systemic), [3] cytokine removal that occurs with passive drainage and is enhanced by prophylactic dialysis, [4] less need for electrolyte replacements with prophylactic dialysis, and [5] small amount of supplemental nutrition from the dextrose-containing dialysis solution [14, 18–20, 33–36].

Peritoneal dialysis has been shown to effectively mitigate FO and promote diuresis with improved outcomes following cardiac surgery. Among patients who do undergo PDC placement, Sasser et al. evaluated the use of prophylactic peritoneal dialysis in comparison with passive drainage plus diuretic therapy in 52 high-risk neonates and infants undergoing cardiac surgery with similar intraoperative variables [37]. The dialysis group had a more negative median net fluid balance 24 h after surgery. The dialysis group was also found to have earlier time to sternal closure, lower mean inotrope scores, and lower serum concentrations of inflammatory markers (interleukin-6 and interleukin-8) 24-h after surgery [37]. Kwiatkowski et al. published a retrospective study which found that in 42 high-risk infants with planned

PDC placement at time of cardiac surgery, there was a faster time to negative fluid balance when compared to age and procedure-matched infants. Notably, time to extubation, inotropy scores, and frequency of medications administered for electrolyte correction were also reduced in the cohort with planned PDC placement [19]. In a subsequent single center randomized controlled trial of infants undergoing cardiac surgery who were either randomized to a standard regimen of furosemide or prophylactic peritoneal dialysis within 6 h of arrival to the ICU, those who received prophylactic dialysis had lower % FO, shorter ventilation time, shorter inotropic medication use, and fewer electrolyte replacements [18]. In a single-center retrospective study of neonates undergoing arterial switch operation, fluid accumulation was reduced among those receiving prophylactic peritoneal dialysis [38]. In addition, there was a 42% reduction in mechanical ventilation and 34% reduction in ICU length of stay among patients who received peritoneal dialysis [38]. Whether the benefits of prophylactic peritoneal dialysis translate across multiple centers is unknown, especially given the recent reports of heterogeneous rates of AKI and FO across centers included in the NEPHRON study [1, 7]. A recent meta-analysis evaluated the efficacy, safety and outcomes (duration of ventilation, length of stay, and mortality) of using diuretics compared to prophylactic peritoneal dialysis across 8 studies including 507 pediatric patients after cardiac surgery. Patients who received prophylactic peritoneal dialysis had longer cardiopulmonary bypass. There was also a notable reduction in duration of mechanical ventilation among those who received prophylactic dialysis. This study found no significant difference in length of ICU or hospital stay between those who did and did not receive prophylactic peritoneal dialysis. However, there was insufficient power to determine differences between negative fluid balance on postoperative day 1 and time to negative fluid balance between the groups [26]. Two of the eight studies were from the same center and randomized in their approach, two were prospective and observational, and the remaining studies were retrospective. This highlights the potential bias in perceived benefits of PD in the small number of studies which included centers that were already routinely performing prophylactic peritoneal dialysis in their patients. A more recent meta-analysis demonstrated some benefits in select patients but the authors recommended prospective studies [39]. Additionally, further investigation is needed to assess if a standardized approach can be feasibly applied to all patients or if it should be implemented using a clinical decision support tool after appropriate risk stratification. Indeed, it is likely not a one size fits all approach, and therapy should be individually considered and tailored based on pre-, peri-, and postoperative factors.

Considerations for risk stratification for passive peritoneal drains or prophylactic PD

Recent work by the 26th acute disease quality initiative (ADQI) working group suggested that risk stratification tools be developed and implemented to identify those most likely to develop AKI and FO [40]. This working group also suggested that there are multiple different AKI phenotypes exists. Perhaps the reason we have identified variable benefit of prophylactic peritoneal dialysis across pediatric studies is because it is currently applied to patients who clinicians perceived to be at high risk for AKI and FO based on experience rather than real-time clinical decision support [40]. The renal angina index (RAI), a calculable bedside clinical risk score has been used in the pediatric intensive care unit within 12 h of admission to identify those at highest risk for day 2–4 severe AKI [41]. The performance of the RAI was enhanced by integration of a urinary biomarker (neutrophil gelatinase associated lipocalin – NGAL) [42]. At Cincinnati Children’s Hospital, the RAI is now automatically calculated for patients within 12 h of admission to the pediatric ICU and if the score is greater than or equal to 8, a urine NGAL is sent. Clinical decision support is then provided to clinicians to either fluid restrict or consider early implementation of renal replacement therapy among those with very elevated urine NGAL or who fail to respond to diuretics [43]. Results of the implementation of this clinical decision support tool for mitigation of FO in those at risk for severe day 2–4 AKI are forthcoming. Unfortunately, the RAI, in its current form is not applicable for use in children following cardiac surgery. However, a cardiac modification of the RAI was recently published (44) and could certainly be optimized by studying the integration of biomarkers as well as developing a clinical decision support tool for which prophylactic peritoneal dialysis could be used as the fluid removal modality of choice. We have proposed a clinical decision support tool for use of peritoneal dialysis in this population (Fig. 1). This would need to be tested prospectively, preferably in a multi-center fashion to determine whether it improves AKI and FO related outcomes in children undergoing cardiac surgery.

In summary, peritoneal drains are used with variable frequency after cardiac surgery, but most commonly in neonates and infants. The benefits of prophylactic peritoneal dialysis also vary across institutions and patient populations, and to date, no multicenter trials exist. Risk stratification and clinical decision support can aid in identification of who should receive prophylactic dialysis to improve outcomes.

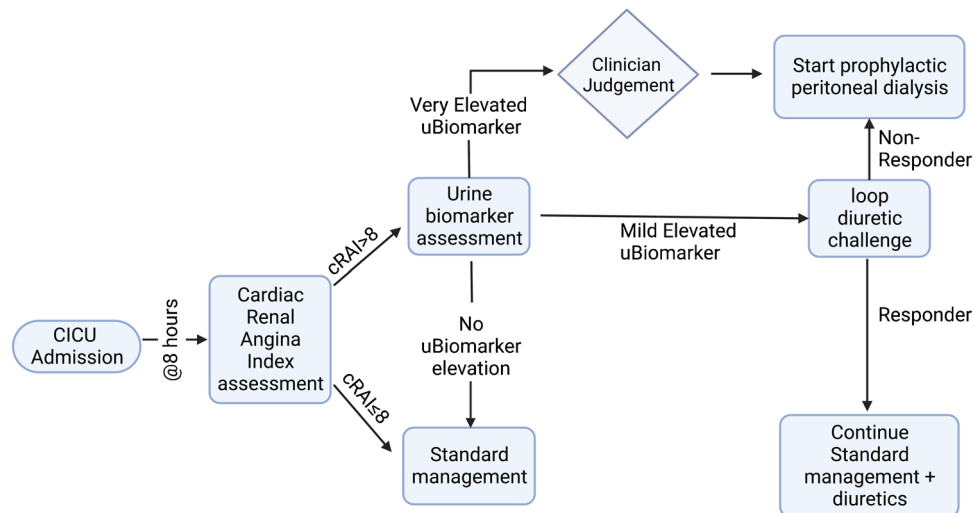


Fig. 1 Proposed clinical decision support tool for delineating risk and consideration of initiating prophylactic peritoneal dialysis for augmented fluid removal

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Declarations

Conflict of Interest

Katie Brandewie, Katherine Melink and Katja M Gist DO each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent

The article does not contain any studies with human or animal subjects performed by any of the authors.

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