Journal of Nephrology (2018) 31:249–256
https://doi.org/10.1007/s40620-017-0450-6

ORIGINAL ARTICLE

# Quality of life following hospitalization-associated acute kidney injury in children

**Kelsey L. Richardson[2] · R. Scott Watson[3,4] · Sangeeta Hingorani[1,5]**

Received: 14 April 2017 / Accepted: 21 October 2017 / Published online: 18 November 2017


## Abstract

**Objectives** Acute kidney injury (AKI) is common in hospitalized children. The impact of AKI following hospitalization is not fully understood, particularly the impact on health related quality of life (HRQOL). The goal of this study was to determine the relationship between hospitalization-associated AKI and HRQOL in a pediatric population.

**Study design** We conducted a retrospective cohort study of children with hospitalization-associated AKI. Eligible children were 1–19 years old with AKI defined by kidney disease improving global outcomes (KDIGO) criteria and had at least one completed pediatric quality of life (PedsQL) 4.0 Generic Core Scale survey (N = 139). Participants completed up to three surveys to reflect baseline, admission and follow-up status. We categorized children as having mild AKI (KDIGO stage 1, N = 73) or severe AKI (KDIGO stage 2 or 3, N = 66). Mean PedsQL scores were compared by AKI group. Those with both baseline and follow-up surveys were analyzed to determine the proportion who returned to their baseline level of function within 8 weeks of discharge.

**Results** Children with mild and severe AKI had similar baseline and admission PedsQL scores. Although children with severe AKI had lower follow-up scores, the results were not statistically significant (78.9 vs. 85.8, p = 0.11). Of those with severe AKI, 48% returned to their baseline level of physical functioning by follow-up, compared to 73% with mild AKI (p = 0.05).

**Conclusions** This is the first study of HRQOL following hospitalization-associated AKI. We found that children with severe AKI had depressed physical functioning after discharge when compared to children with mild AKI.

**Keywords** Outcomes · Acute kidney injury (AKI) · Quality of life (QOL) · Pediatric

## Introduction

Acute kidney injury (AKI) is common in hospitalized children, with up to 50% of critically ill children in tertiary medical centers experiencing AKI during their hospitalization [1]. Prior research focused on improving hospital outcomes and reducing AKI-associated mortality. The vast majority (98%) of children with AKI survive their acute hospitalization [2]. However, approximately 50% have longstanding subclinical effects on renal structure or function [3], and survivors have long-term increased risk of hypertension, proteinuria and chronic kidney disease (CKD) [4–6]. With this recognition of long-term renal-related sequelae of AKI, questions have been raised regarding the impact of AKI on health related quality of life (HRQOL).

HRQOL is increasingly recognized as a clinically meaningful outcome. Tools to evaluate HRQOL provide insight into patient or proxy (in the case of young children) perceptions of their own health. Recognition of impairment in HRQOL is the first step to improving quality of life for patients with acute and chronic conditions. The impact of AKI on HRQOL is not well understood and limited to studies of adults. Given what is known about other long-term effects of AKI, we suspect that AKI may lead to decreased quality of life. The few adult studies that evaluated HRQOL

✉ Kelsey L. Richardson
richarke@ohsu.edu

1 Division of Pediatric Nephrology, Department of Pediatrics, University of Washington, Seattle, USA

2 Division of Pediatric Nephrology, Oregon Health & Science University, 707 SW Gaines Street, Portland, OR 97239, USA

3 Division of Pediatric Critical Care Medicine, Department of Pediatrics, University of Washington, Seattle, USA

4 Center for Child Health, Behavior and Development, Seattle Children's Research Institute, Seattle, USA

5 Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, USA

after AKI in critically ill patients requiring renal replacement therapy (RRT) reported varying results [7–16]. To our knowledge, this is the first study of HRQOL in children with AKI. The goal of this study was to determine the relationship between hospitalization-associated AKI and quality of life in a pediatric population. We hypothesized that children with severe AKI would have lower HRQOL following hospitalization and would be less likely to return to their baseline level of HRQOL compared to those with mild AKI.

## Methods

### Study design and participants

Approval for this retrospective cohort study was obtained from the Seattle Children's Hospital institutional review board (IRB). The electronic medical record was used to identify all inpatients admitted between March 2012 and February 2015 who met criteria for AKI based on kidney disease improving global outcomes (KDIGO) criteria [17]. Children 1–19 years of age, admitted for at least 48 h to a medical, surgical or intensive care unit (ICU) were included. Individuals were excluded if they had a prior diagnosis of chronic kidney disease, renal transplantation, congenital anomalies of the kidney or urinary tract or an abnormal baseline creatinine. The cohort for this study was a subset of a larger, IRB-approved research and quality improvement program collecting quality of life data on pediatric inpatients hospitalized at our institution. In this program, collection of pediatric quality of life (PedsQL) survey data was attempted based on program staff availability for all hospitalized children without severe developmental impairment. Participants who had at least one PedsQL survey completed during the hospitalization where AKI occurred were included in this study.

### Measurement of HRQOL

The PedsQL 4.0 Generic Core Scale [18] was used for measurement of HRQOL in children 2–18 years of age, and the PedsQL Infant Scale [19] was used for children less than 2 years of age. These tools have been validated in large pediatric populations [18, 20] and are relatively rapid to complete. Pediatric assessments are separated into physical and psychosocial domains, with the psychosocial domain divided into sub-domains for school, social and emotional functioning. The infant scale does not contain a school domain. These measures provide standardized overall and domain-specific scores on a 0–100 point scale with a higher score indicating higher HRQOL.

Families participating in this program were approached within 72 hours of hospital admission. Not all hospitalized patients were approached due to availability of research staff. Caregivers were asked to complete the survey for all children < 13 years of age. For individuals at least 13 years of age, the child was asked to complete the survey, but the caregiver completed the survey when the child was too ill to participate. Participants were asked to fill out two PedsQL surveys at hospital admission. The first survey asked the family to report on the child's baseline status prior to their acute illness and hospitalization (referred to as "baseline"). The second survey asked for a report on the child's status since hospital admission (referred to as "admission"). Following hospital discharge, families were contacted to fill out a follow-up survey within 8 weeks to assess quality of life in the 7 days prior to filling out the survey (referred to as "follow-up"). Surveys were completed electronically or by telephone interview.

### AKI definitions

AKI was defined using KDIGO criteria [17] for creatinine, with the exception noted below for children with baseline creatinine of < 0.3 mg/dL. Urine output was not available for all participants, so this was not included in the determination of AKI. An increase in serum creatinine of ≥ 0.3 mg/dL or a rise in serum creatinine of at least 1.5 times baseline (if baseline creatinine was ≥ 0.3 mg/dL) was used to identify children with AKI. For children with a baseline creatinine < 0.3 mg/dL, we used only an increase of ≥ 0.3 mg/dL because the change from 0.1 to 0.2 mg/dL or from 0.2 to 0.3 mg/dL has questionable clinical significance.

Many hospitalized children are previously healthy and have never had a baseline creatinine measurement. For these individuals, a baseline creatinine was estimated as a glomerular filtration rate (GFR) of 120 mL/min/1.73 $m^2$ using the bedside Schwartz equation [Creatinine (mg/dL) = 0.413 × height (cm)/120]. This method has been utilized in other pediatric AKI studies [21]. Once a patient was determined to have AKI, AKI stage was determined using KDIGO criteria. Children with a creatinine elevation of 1.5–1.9 times baseline or an increase of ≥ 0.3 mg/dL were considered to have stage 1 AKI. Those with a creatinine elevation of 2.0–2.9 times baseline were considered to have stage 2 AKI. Those with a creatinine elevation of at least 3.0 times baseline, an increase of creatinine to 4.0 mg/dL, or a requirement for renal replacement therapy (RRT) were considered to have stage 3 AKI. Participants were then divided into two groups. Children with AKI stage 1 were categorized as having mild AKI. Children with AKI stage 2 or stage 3 were categorized as having severe AKI. These two groups were used for all analyses.

## Data analysis

Demographic and clinical data were collected from the electronic medical record, including patient age, gender, admitting service, comorbidities, length of stay (in days), requirement of ICU admission, and receipt of surgical procedures or renal replacement therapy. Mean total and domain-specific PedsQL scores were calculated for both groups and compared using a student's t-test. Varni et al. published PedsQL scores for a large number of healthy children to validate the PedsQL as a pediatric population health measure [18]. We compared our total and domain-specific scores to this reference population using two sample t-tests. Given that there is no school domain as part of the PedsQL infant scale, children < 2 years of age were excluded from school domain-specific analyses. Scores were calculated at baseline, admission and follow-up when available. Not all participants had available data at all survey points. For those participants with baseline and follow-up PedsQL data, we assessed if the participant had returned to their baseline level of functioning in each domain by the time of the follow-up survey. A participant was considered to have returned to their baseline level of function if their follow-up score was no more than 4.5 points lower than their baseline score in a particular domain. This cut off was used based on prior studies demonstrating that 4.5 points, on the 100-point standardized scale, is the minimal clinically important difference using the PedsQL tool [18]. The percentage of patients who returned to their baseline level of functioning was then calculated for each group. A chi-squared test was used to compare the frequency between the two groups.

We compared the mean total and domain specific scores for the group of participants with both baseline and follow-up data available to those without follow-up data to evaluate for participation bias. We used simple linear regression to evaluate if there was a relationship between follow-up survey score and timing of follow-up survey (days since hospital discharge) to assess for confounding by timing of follow-up survey administration.

To evaluate the impact of disease severity, we used length of stay (in days) as a crude disease severity measure. We calculated mean length of stay for each AKI severity group. We performed linear regression to evaluate the relationship between total follow-up PedsQL scores and length of stay. To evaluate for the impact of comorbidities, we conducted a subgroup analysis based on the presence or absence of comorbidities identified by chart review. Stratified by subgroup we compared mean total and domain-specific scores with a two sample t-test. We did a similar subgroup analysis of children without baseline creatinine measurements available, under the assumption that this subgroup represents a healthier patient population, as children with significant comorbid conditions require routine lab monitoring which would include renal function assessment.

## Results

Of the 888 children identified with AKI during the study period, 37 were excluded due to chronic kidney disease or elevated baseline creatinine. Of the 851 remaining children with AKI, 139 had at least 1 completed PedsQL survey during their hospitalization and were included in this analysis (Fig. 1). The 139 participants were compared to the 712 children without PedsQL data, and no differences were found in age, gender, length of hospital stay or requirement of ICU admission.

Of the 139 participating children, 73 had mild AKI and 66 had severe AKI. Age, gender, length of stay and admitting service were similar between the two groups (Table 1). The most common admitting services were cardiology, oncology and endocrinology. Frequency of ICU admission was similar between the two groups (47% in the mild AKI group vs. 44% in the severe AKI group, p = 0.76). Only 6 (9%) of the children in the severe AKI group required RRT, and all were RRT-independent by time of hospital discharge.

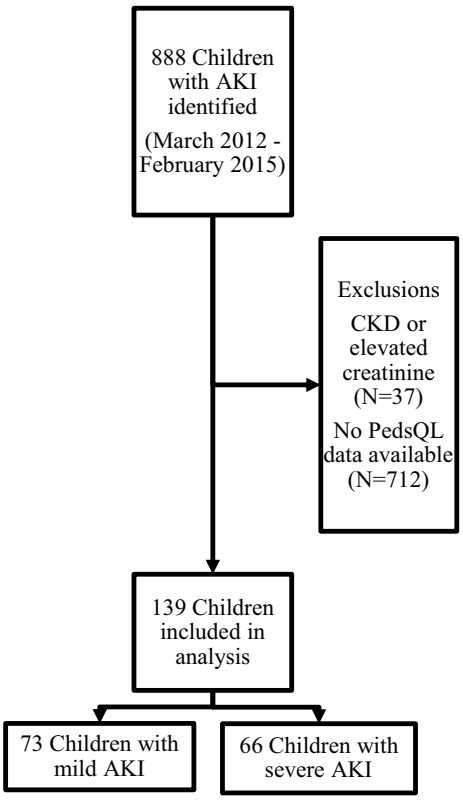


**Fig. 1** Flow diagram of participant selection and exclusion indications

**Table 1** Descriptive characteristics of participants, separated by AKI severity group

| | Mild AKI (N = 73) | | Severe AKI (N = 66) | |
|---|---|---|---|---|
| | n | (%) | n | (%) |
| Age (years) | | | | |
| 1–5 | 18 | (25) | 16 | (24) |
| 6–10 | 17 | (23) | 14 | (21) |
| 11–15 | 23 | (32) | 26 | (39) |
| ≥ 16 | 15 | (21) | 10 | (15) |
| Gender | | | | |
| Female | 28 | (39) | 26 | (39) |
| Admitting service | | | | |
| Cardiology | 16 | (22) | 13 | (20) |
| Oncology | 10 | (14) | 10 | (15) |
| Endocrinology | 11 | (15) | 8 | (12) |
| General surgery | 7 | (10) | 3 | (5) |
| Neurology | 5 | (7) | 3 | (5) |
| Gastroenterology | 4 | (5) | 3 | (5) |
| Pulmonology | 5 | (7) | 1 | (2) |
| Other | 15 | (20) | 25 | (38) |
| Length of stay (days) | | | | |
| Mean (SD) | 15 | (16) | 15 | (25) |
| ICU admission[a] | | | | |
| Yes | 34 | (47) | 29 | (44) |
| Surgical procedure[b] | | | | |
| Yes | 23 | (32) | 16 | (25) |
| Received RRT | | | | |
| Yes | 0 | (0) | 6 | (9) |

No missing data. No statistically significant differences between AKI severity groups, however, those requiring RRT by definition are all categorized as severe AKI

*RRT* renal replacement therapy, *AKI* acute kidney injury, *ICU* intensive care unit

[a]ICU admission includes all children admitted to the ICU at some point during hospitalization

[b]Surgical procedures exclude minor procedures such as central line placement, lumbar punctures and bone marrow aspirates

Presence of comorbidity was identified in 63% (n = 46) of children in the mild AKI group and in 62% (n = 41) of children in the severe AKI group. The most common comorbidities were congenital heart disease (n = 26), type 1 diabetes mellitus (n = 18) and leukemia (n = 14). Other comorbidities included, but were not limited to, inflammatory bowel disease, seizure disorder, cystic fibrosis and liver failure. At baseline, admission and follow-up, 75, 77 and 85% of surveys were completed by parent proxy report respectively. There were no differences in the proportion of child self-reports vs. parent proxy-reports based on AKI group. The number of completed surveys in each domain is reported by AKI severity group in Table 2.

**Table 2** Number of participants with a completed survey at each survey time point, by AKI severity group

| | Mild AKI (N = 73) | | Severe AKI (N = 66) | |
|---|---|---|---|---|
| | n | (%) | n | (%) |
| Baseline | | | | |
| Physical | 55 | (75) | 49 | (74) |
| School | 43 | (59) | 38 | (58) |
| Social | 53 | (73) | 45 | (68) |
| Emotional | 53 | (73) | 45 | (68) |
| Admission | | | | |
| Physical | 54 | (74) | 48 | (73) |
| School | 29 | (40) | 21 | (32) |
| Social | 50 | (68) | 36 | (55) |
| Emotional | 52 | (71) | 45 | (68) |
| Follow-up | | | | |
| Physical | 34 | (47) | 30 | (45) |
| School | 28 | (38) | 26 | (39) |
| Social | 33 | (45) | 33 | (50) |
| Emotional | 40 | (55) | 33 | (50) |

Not all surveys were completed in each domain at each survey time point

There were no statistically significant differences in baseline, admission or follow-up HRQOL scores between AKI groups (Table 3). Although the mean total PedsQL

**Table 3** Mean PedsQL scores for mild and severe AKI groups at baseline, admission and follow up

| | Mild AKI | | Severe AKI | | P-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Baseline | | | | | |
| Total | 76.5 | 17.6 | 76.8 | 16.5 | 0.94 |
| Physical | 71.8 | 25.4 | 77.6 | 23.17 | 0.23 |
| Psychosocial | 77.2 | 16.8 | 76.5 | 16.5 | 0.72 |
| Admission | | | | | |
| Total | 50.6 | 22.5 | 53.0 | 18.6 | 0.71 |
| Physical | 29.6 | 25.9 | 31.3 | 31.8 | 0.76 |
| Psychosocial | 59.2 | 24.9 | 60.8 | 16.0 | 0.82 |
| Follow up | | | | | |
| Total | 85.8 | 13.2 | 78.9 | 15.9 | 0.11 |
| Physical | 83.7 | 18.7 | 74.1 | 24.7 | 0.08 |
| Psychosocial | 84.4 | 13.4 | 81.8 | 15.0 | 0.43 |

Baseline survey done at hospital admission to reflect quality of life before acute illness leading to hospitalization

Admission survey done within 72 h of hospital admission to reflect quality of life since admissionFollow-up survey done 2–8 weeks after hospital discharge to reflect post-hospitalization quality of life

*AKI* acute kidney injury, *SD* standard deviation

score was lower at follow-up in the severe AKI group, 78.9 compared to 85.8 in the mild AKI group, the difference was not statistically significant (p = 0.11). In the physical domain, there was also a suggestion of lower scores in the severe AKI group at follow-up, with a mean score of 74.1 compared to 83.7 in the mild AKI group (p = 0.08). There were no differences between mild AKI follow-up scores and reference population scores published by Varni et al. [18]. There was a statistically significant difference between severe AKI physical domain follow-up scores and published physical domain scores (83.3 vs. 74.1, p < 0.001). Total and psychosocial domain scores were not statistically significant between the reference population and severe AKI mean scores at follow-up.

In the subgroup of children without identified comorbidities, the trends in HRQoL were similar to the entire cohort (Table 4). There were no statistically significant differences in HRQoL scores at baseline or admission by AKI severity group. Total follow-up scores were lower in the severe AKI group, 83.4 compared to 90.8 in the mild AKI group (p = 0.12). Physical domain scores were also lower in the severe AKI group at follow-up, 71.9 compared to 87.3 in the mild AKI group, but did not reach statistical significance (p = 0.07). In the group of children with identified comorbidities, all PedsQL scores were lower than scores for children without comorbidities, with the exception of physical domain admission scores. Although total and physical domain follow-up scores were lower in the severe AKI group in the subgroup with comorbidities, the differences were less notable (Table 4). The mean PedsQL scores demonstrated a similar pattern in the subgroup of children without a baseline creatinine measurement (Table 5). In this subgroup, baseline and admission scores were similar across AKI severity groups, however, significant differences were appreciated in follow-up scores. Total follow-up scores were lower in the severe AKI group, 79.7 compared to 88.6 in the mild AKI group (p = 0.04). Physical domain scores were also lower in the severe AKI group at follow-up, 70.9 compared to 88.6 in the mild AKI group (p = 0.005).

Follow-up surveys were obtained between 2 and 8 weeks following discharge. The mean number of days between discharge and follow-up survey differed by 7 days between the two groups, with a mean of 37 days (standard deviation [SD] 21.4 days) in the mild AKI group and 44 days (SD 27.1 days) in the severe AKI group, but this difference was not statistically significant (p = 0.15). There was no statistically significant relationship between days since discharge and follow-up score (p = 0.70). For every one day increase in time from discharge to follow-up survey, the total mean follow-up score increased by 0.07 points (95% Confidence Interval [CI] −0.29, 0.42). We used linear regression to evaluate the relationship between follow-up score and length of hospital stay. There was no statistical association between total follow-up score and length of hospital stay (p = 0.75).

**Table 4** Mean PedsQL scores by AKI severity at baseline, admission and follow up in participants with and without a comorbid condition

| | Mild AKI | | Severe AKI | | P-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Comorbidities present[a] | | | | | |
| Baseline | | | | | |
| Total | 71.2 | 17.3 | 73.1 | 18.1 | 0.72 |
| Physical | 63.7 | 23.5 | 72.7 | 24.6 | 0.15 |
| Psychosocial | 74.3 | 16.5 | 73.8 | 19.1 | 0.93 |
| Admission | | | | | |
| Total | 47.8 | 23.3 | 47.3 | 11.8 | 0.95 |
| Physical | 35.1 | 26.2 | 35.1 | 31.6 | 1.0 |
| Psychosocial | 54.6 | 24.7 | 56.9 | 13.9 | 0.82 |
| Follow up | | | | | |
| Total | 80.4 | 12.8 | 74.5 | 19.2 | 0.38 |
| Physical | 80.5 | 17.9 | 76.0 | 25.3 | 0.55 |
| Psychosocial | 78.3 | 13.6 | 76.8 | 20.5 | 0.83 |
| No comorbidities | | | | | |
| Baseline | | | | | |
| Total | 82.5 | 16.2 | 80.4 | 14.3 | 0.67 |
| Physical | 83.9 | 23.7 | 83.6 | 20.2 | 0.96 |
| Psychosocial | 81.9 | 16.7 | 79.2 | 13.3 | 0.59 |
| Admission | | | | | |
| Total | 54.3 | 21.9 | 57.1 | 21.8 | 0.77 |
| Physical | 21.0 | 23.7 | 26.5 | 32.2 | 0.53 |
| Psychosocial | 65.4 | 25.0 | 63.5 | 17.8 | 0.84 |
| Follow up | | | | | |
| Total | 90.8 | 11.9 | 83.4 | 10.9 | 0.12 |
| Physical | 87.3 | 19.6 | 71.9 | 24.7 | 0.07 |
| Psychosocial | 90.5 | 10.4 | 85.4 | 10.8 | 0.23 |

Baseline survey done at hospital admission to reflect quality of life before acute illness leading to hospitalization. Admission survey done within 72 h of hospital admission to reflect quality of life since admission. Follow-up survey done 2–8 weeks after hospital discharge to reflect post-hospitalization quality of life

*AKI* acute kidney injury, *SD* standard deviation

[a]Comorbidities include: congenital heart disease, heart failure, cardiac transplantation, leukemia, Wilm's tumor, brain tumor, inflammatory bowel disease, cystic fibrosis, diabetes mellitus, trisomy 21, cyclic vomiting, encephalopathy, cleft palate, seizure disorder, immunodeficiency, vasculitis, cerebral palsy, psychiatric disorders, liver failure, short gut syndrome

Baseline and follow-up physical functioning data were available for 33 participants with mild AKI and 29 participants with severe AKI. Of those with mild AKI, 73% returned to their baseline level of physical functioning, compared to 48% of the severe AKI group (p = 0.05). The percentage of children who returned to their baseline level of functioning was lower in the severe AKI group across all domains; however, the physical domain was the only domain

**Table 5** Mean PedsQL scores for mild and severe AKI groups at baseline, admission and follow up for subgroup of participants without baseline creatinine measurement

| | Mild AKI | | Severe AKI | | P-value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Baseline | | | | | |
| Total | 77.6 | 18.2 | 76.5 | 16.5 | 0.80 |
| Physical | 74.8 | 25.7 | 77.7 | 21.2 | 0.59 |
| Psychosocial | 78.9 | 17.6 | 76.1 | 16.4 | 0.52 |
| Admission | | | | | |
| Total | 49.1 | 22.3 | 53.6 | 20.5 | 0.57 |
| Physical | 25.1 | 23.8 | 21.3 | 32.1 | 0.35 |
| Psychosocial | 57.9 | 25.9 | 60.5 | 17.0 | 0.75 |
| Follow up | | | | | |
| Total | 88.6 | 11.3 | 79.7 | 13.8 | 0.04 |
| Physical | 88.6 | 12.3 | 70.9 | 25.5 | 0.005 |
| Psychosocial | 86.8 | 12.5 | 82.1 | 14.4 | 0.28 |

Baseline survey done at hospital admission to reflect quality of life before acute illness leading to hospitalization. Admission survey done within 72 h of hospital admission to reflect quality of life since admission. Follow-up survey done 2–8 weeks after hospital discharge to reflect post-hospitalization quality of life

*AKI* acute kidney injury, *SD* standard deviation

**Table 6** Percentage of participants with baseline and follow-up data who returned to baseline level of function at time of follow-up in each PedsQL domain, by AKI group

| PedsQL domain | Mild AKI | | Severe AKI | | P-value[a] |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Physical | 33 | 73 | 29 | 48 | 0.05 |
| School | 25 | 64 | 25 | 56 | 0.57 |
| Social | 38 | 84 | 32 | 66 | 0.07 |
| Emotional | 38 | 66 | 32 | 53 | 0.29 |

Number of participants with survey data in each domain differs due to incomplete completion of PedsQL surveys by participants at baseline and/or follow-up

*AKI* acute kidney injury

[a]P-value comparing mild vs. severe AKI groups

showing a statistically significant difference between groups (Table 6). To evaluate for participation bias, participants with both baseline and follow-up surveys were compared to those without follow-up data. Overall, those with both baseline and follow-up data had higher total scores (79.5 vs. 71.9, $p=0.05$) and higher physical domain scores at baseline (79.3 vs. 67.2, $p=0.01$). Although 6 children received RRT, only two contributed survey data at all three survey time points (baseline, admission and follow-up). No differences in mean total or domain-specific scores were detected between RRT-requiring participants and those who did not require RRT.

## Discussion

To our knowledge, this is the first study describing HRQOL in pediatric patients with AKI. We found that the physical domain is affected in children following severe AKI, which is demonstrated by lower mean PedsQL physical domain scores at follow-up, although not reaching statistical significance in our main analysis. Additionally, our study found a reduction in the percentage of children with severe AKI who returned to their baseline level of physical functioning compared to those with mild AKI. This is important knowledge for nephrologists and primary care providers caring for children after hospitalizations complicated by AKI, so providers can counsel families that children may experience prolonged impairments in activities of daily living following severe AKI.

It is helpful to interpret these results in the context of the PedsQL 4.5 point minimal clinically important difference established by Varni et al. [18]. Mean physical domain follow-up scores in our study population were $>4.5$ points lower than physical domain scores published in healthy children. Mean total and physical domain scores in the severe AKI group were also $>4.5$ points lower than the mild AKI group mean scores. These differences exceed the minimal clinically important difference, suggesting children with severe AKI have a clinically meaningful prolonged reduction in HRQOL after hospitalization compared to those with mild AKI and compared to healthy controls.

There were no differences in baseline or admission scores in either the physical or psychosocial domains by AKI group. The mean PedsQL physical scores were actually higher in the severe AKI group at baseline and admission in our main analysis and in the subgroup of participants without comorbidities. This suggests that the lower scores seen at follow-up in the severe AKI group are not just a reflection of more severe illness at hospital admission. Given that the scores for participants with baseline and follow-up data were higher than the scores for those individuals without follow-up data, it is likely that this study does not fully capture the impairment in HRQOL experienced by all children. Adjustment for disease severity is difficult in a population of children who are not all critically ill. There are many disease severity scores available, but they are intended for ICU level patients. We used length of stay (in days) as a marker of illness severity and did not find an association between lengths of stay and total PedsQL follow-up scores, suggesting that lower follow-up scores in the severe AKI group are not simply a representation of overall illness severity. We recognize further studies are needed with improved ability to adjust for disease severity to better interpret the impact of AKI on HRQOL.

We conducted subgroup analyses of children with and without comorbidities as well as those without baseline creatinine data available. The evaluation of individuals without baseline creatinine data was done to isolate participants who were healthier at baseline, suggested by the lack of routine outpatient laboratory monitoring. Similar trends in PedsQL scores were seen in these subgroup analyses. Baseline and admission scores were the same regardless of AKI severity group, whereas follow-up scores continued to be lower in the severe AKI group. This was less apparent in the subgroup of children with comorbidities which is likely due to the heterogeneous population. However, in the subgroup without comorbidities, as well as the subgroup without baseline creatinine data, lower total and physical domain scores at follow-up continued to be present in those with severe AKI. These healthier participants provide a less confounded evaluation of the relationship between AKI and quality of life, suggesting impairment following hospital discharge.

Previous studies of adults found that the physical domain is most affected following AKI, which is reflected in our results. Adult studies have focused on critically ill patients receiving renal replacement therapy. Results have been varied, with some studies demonstrating a reduction in HRQOL [7, 11] while others do not demonstrate a difference in HRQOL following AKI [10, 22–24]. Nisula et al. did evaluate critically ill adults with varying AKI stages, not just those requiring RRT, and did not find differences in quality of life scores among that cohort [24]. These adult studies are difficult to apply to pediatric patients given the differences in admission indications and associated comorbidities. Additionally, varying HRQOL measurement tools have been used in the adult literature and varying follow-up intervals evaluated, making comparisons difficult.

A strength of our study is the evaluation of a pediatric population with a broad range of AKI severity. Only six children in our study received RRT, therefore, we were unable to conduct any subgroup analyses on this subset of children. Our study was limited by a small sample size and larger scale studies are needed. Additionally, the time between hospitalization and follow-up in our population was short. Longer follow-up would help determine persistence of the effects on HRQOL following AKI. Our ability to account for disease severity and comorbidities were also limited, which should be a focus of future studies in this area.

The current study describes HRQOL in pediatric patients with AKI. The results suggest that the physical domain of the PedsQL is depressed in children following stage 2 or stage 3 AKI and that they are less likely to return to their baseline level of functioning within 8 weeks of hospital discharge. This preliminary study should be repeated on a larger scale to better understand the impact of AKI on pediatric quality of life.

**Acknowledgements** This study was supported by the National Institutes of Health T32 research training Grant (T32 DK007662). The authors would like to acknowledge Dr. Rita Mangione-Smith, MD, MPH for supplying the PedsQL data for this manuscript.

## Compliance with ethical standards

**Funding** This study was supported by the National Institutes of Health T32 research training Grant (T32 DK007662).

**Conflict of interest** Kelsey Richardson is supported by the National Institutes of Health T32 research training grant (T32 DK007662). Sangeeta Hingorani is the principal investigator of this grant (T32 DK007662). The funding agency had no part in design, manuscript preparation or the decision to submit this manuscript. The authors declare that they have no other conflicts of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

**Informed consent** For this type of study formal consent is not required.

## References

1. Volpon LC, Sugo EK, Consulin JC, Tavares TLG, Aragon DC, Carlotti APCP (2016) Epidemiology and outcome of acute kidney injury according to pediatric risk, injury, failure, loss, end-stage renal disease and kidney disease: improving global outcomes criteria in critically ill children-a prospective study. Pediatr Crit Care Med 17:e229–38. doi:10.1097/PCC.0000000000000685
2. Sutherland SM, Byrnes JJ, Kothari M et al (2015) AKI in hospitalized children: comparing the pRIFLE, AKIN, and KDIGO definitions. Clin J Am Soc Nephrol 10:554–561. doi:10.2215/CJN.01900214
3. Brady HR, Singer GG (1995) Acute renal failure. The Lancet 346:1533–1540
4. Mammen C, Al Abbas A, Skippen P et al (2012) Long-term risk of CKD in children surviving episodes of acute kidney injury in the intensive care unit: a prospective cohort study. Am J Kidney Dis 59:523–530. doi:10.1053/j.ajkd.2011.10.048
5. Goldstein SL, Devarajan P (2011) Acute kidney injury in childhood: should we be worried about progression to CKD? Pediatr Nephrol 26:509–522. doi:10.1007/s00467-010-1653-4
6. Chawla LS, Eggers PW, Star RA, Kimmel PL (2014) Acute kidney injury and chronic kidney disease as interconnected syndromes. N Engl J Med 371:58–66. doi:10.1056/NEJMra1214243
7. Wang AY, Bellomo R, Cass A et al (2015) Health-related quality of life in survivors of acute kidney injury: the prolonged outcomes study of the randomized evaluation of normal versus augmented level replacement therapy study outcomes. Nephrology (Carlton) 20:492–498. doi:10.1111/nep.12488
8. Villeneuve P-M, Clark EG, Sikora L, Sood MM, Bagshaw SM (2016) Health-related quality-of-life among survivors of acute kidney injury in the intensive care unit: a systematic review. Intensive Care Med 42:137–146. doi:10.1007/s00134-015-4151-0
9. Delannoy B, Floccard B, Thiolliere F et al (2009) Six-month outcome in acute kidney injury requiring renal replacement therapy

in the ICU: a multicentre prospective study. Intensive Care Med 35:1907–1915. doi:10.1007/s00134-009-1588-z
10. Hofhuis JGM, van Stel HF, Schrijvers AJP, Rommes JH, Spronk PE (2013) The effect of acute kidney injury on long-term health-related quality of life: a prospective follow-up study. Crit Care 17:R17. doi:10.1186/cc12491
11. Abelha FJ, Botelho M, Fernandes V, Barros H (2009) Outcome and quality of life of patients with acute kidney injury after major surgery. Nefrol publicación Of la Soc Española Nefrol 29:404–414. doi:10.3265/Nefrologia.2009.29.5.5456.en.full
12. Korkeila M, Ruokonen E, Takala J (2000) Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. Intensive Care Med 26:1824–1831
13. Morgera S, Kraft AK, Siebert G, Luft FC, Neumayer H-H (2002) Long-term outcomes in acute renal failure patients treated with continuous renal replacement therapies. Am J Kidney Dis 40:275–279. doi:10.1053/ajkd.2002.34505
14. Gopal I, Bhonagiri S, Ronco C, Bellomo R (1997) Out of hospital outcome and quality of life in survivors of combined acute multiple organ and renal failure treated with continuous venovenous hemofiltration/hemodiafiltration. Intensive Care Med 23:766–772
15. Ahlström A, Tallgren M, Peltonen S, Räsänen P, Pettilä V (2005) Survival and quality of life of patients requiring acute renal replacement therapy. Intensive Care Med 31:1222–1228. doi:10.1007/s00134-005-2681-6
16. Vaara ST, Pettilä V, Reinikainen M, Kaukonen K-M, Finnish Intensive Care Consortium (2012) Population-based incidence, mortality and quality of life in critically ill patients treated with renal replacement therapy: a nationwide retrospective cohort study in Finnish intensive care units. Crit Care. 16:R13. doi:10.1186/cc11158
17. Kellum JA, Lameire N, KDIGO AKI Guideline Work Group (2013) Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (part 1). Crit Care. 17:204. doi:10.1186/cc11454
18. Varni JW, Burwinkle TM, Seid M, Skarr D (2003) The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr 3:329–341
19. Varni JW, Limbers CA, Neighbors K et al (2011) The PedsQL™ Infant scales: feasibility, internal consistency reliability, and validity in healthy and ill infants. Qual Life Res 20:45–55. doi:10.1007/s11136-010-9730-5
20. Desai AD, Zhou C, Stanford S, Haaland W, Varni JW, Mangione-Smith RM (2014) Validity and responsiveness of the pediatric quality of life inventory (PedsQL) 4.0 generic core scales in the pediatric inpatient setting. JAMA Pediatr 168:1114–1121. doi:10.1001/jamapediatrics.2014.1600
21. Zappitelli M, Parikh CR, Akcan-Arikan A, Washburn KK, Moffett BS, Goldstein SL (2008) Ascertainment and epidemiology of acute kidney injury varies with definition interpretation. Clin J Am Soc Nephrol 3:948–954. doi:10.2215/CJN.05431207
22. Faulhaber-Walter R, Scholz S, Haller H, Kielstein JT, Hafer C (2016) Health status, renal function, and quality of life after multiorgan failure and acute kidney injury requiring renal replacement therapy. Int J Nephrol Renovasc Dis 9:119–128. doi:10.2147/IJNRD.S89128
23. Oeyen S, De Corte W, Benoit D et al (2015) Long-term quality of life in critically ill patients with acute kidney injury treated with renal replacement therapy: a matched cohort study. Crit Care 19:289. doi:10.1186/s13054-015-1004-8
24. Nisula S, Vaara ST, Kaukonen K-M et al (2013) Six-month survival and quality of life of intensive care patients with acute kidney injury. Crit Care 17:R250. doi:10.1186/cc13076