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A Clinical Score for Quantifying Edema in Mechanically Ventilated Children With Congenital Heart Disease in Intensive Care

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IMPORTANCE: Standardized clinical measurements of edema do not exist.

OBJECTIVES: To describe a 19-point clinical edema score (CES), investigate its interobserver agreement, and compare changes between such CES and body weight.

DESIGN, SETTING, AND PARTICIPANTS: Prospective observational study in a tertiary PICU of mechanically ventilated children with congenital heart disease.

MAIN OUTCOMES AND MEASURES: Differences in the median CES between observer groups.

RESULTS: We studied 61 children, with a median age of 8.0 days (interquartile range, 1.0–14.0 d). A total of 539 CES were performed by three observer groups (medical 1 [reference], medical 2, and bedside nurse) at 0, 24, and 48 hours from enrollment. Overall, there was close agreement between observer groups in mean, median, and upper quartile of CES scores, with least agreement observed in the lower quartile of scores. Across all quartiles of CES, after adjusting for baseline weight, cardiac surgical risk, duration of cardiopulmonary bypass, or peritoneal dialysis during the study, observer groups returned similar mean scores (medical 2: 25th centile +0.1 [95% CI, −0.2 to 0.5], median +0.6 [95% CI, −0.4 to 1.5], 75th centile +0.1 [95% CI, −1.1 to 1.4] and nurse: 25th centile +0.5 [95% CI, 0.0–0.9], median +0.7 [95% CI, 0.0–1.5], 75th centile −0.2 [95% CI, −1.3 to 1.0]) Within a multivariable mixed-effects linear regression model, including adjustment for baseline CES, each 1 point increase in CES was associated with a 12.1 grams (95% CI, 3.2–21 grams) increase in body weight.

CONCLUSIONS AND RELEVANCE: In mechanically ventilated children with congenital heart disease, three groups of observers tended to agree when assessing overall edema using an ordinal clinical score assessed in six body regions, with agreement least at low edema scores. An increase in CES was associated with an increase in body weight, suggesting some validity for quantifying edema. Further exploration of the CES as a rapid clinical tool is indicated.

KEY WORDS: clinical score; edema; fluid overload; pediatric intensive care

Edema is the clinical finding of accumulation of fluid in tissues. Despite considerable advances in the understanding of the mechanisms and pathophysiology underpinning edema (1–4), its measurement in the clinical setting mostly relies on subjective qualitative descriptions. Clinicians determine fluid status in critically ill children using a combination of fluid balance charts and clinical examination. However, far more is understood regarding the adverse outcomes associated with fluid status based on monitoring chart documentation of fluid balance (5–9). This is, because, despite some limitations, fluid balance is easily quantified and readily available to clinicians. In contrast, standardized methods for quantifying edema in critically ill children do not exist, despite their possible utility.

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KEY POINTS

Question: What is the interobserver agreement and validity of a 19 point, ordinal clinical edema score in children in intensive care with congenital heart disease?

Findings: In a prospective observational study, there was close agreement between three observer groups for the median and upper quartile of clinical edema scores, however, less agreement in the lowest quartile of scores.

Meaning: In mechanically ventilated children with congenital heart disease, a new summary edema score showed close agreement between three clinician groups and, a positive relationship to change in body weight, suggesting validity and potential utility.

The present study aimed to develop an ordinal, whole body, edema clinical scoring tool based on the sum of multiple body regions in children in intensive care. Accordingly, we performed a prospective study, in mechanically ventilated children with congenital heart disease, to investigate the interobserver agreement of such a score. A secondary objective was to explore the hypothesis that a positive relationship would exist between changes in clinical edema score (CES) and changes inpatient body weight during the immediate post-operative period.

MATERIALS AND METHODS

A prospective observational study was performed at the Royal Children's Hospital (RCH) PICU between May 2021 and September 2022. Permission to conduct the study was provided by the RCH Human Research Ethics Committee (HREC number HREC/65005/RCHM-2020) and procedures were followed in accordance with the Helsinki Declaration of 1975.

Children with congenital heart disease were eligible if they were admitted to the ICU within the previous 72 hours and were mechanically ventilated and expected to remain so for at least 48 hours. Only infants nursed in Atom Infant warmer cots (Parker Healthcare, Mitcham, VIC, Australia) were eligible because they could be accurately weighed using built-in scales (10). Children were excluded if they had other reasons for facial edema (such as caval or cerebral venous obstruction, facial injuries, or prolonged prone positioning) or were previously enrolled in the study. Following parental consent, children had weight measurements (performed by the principal investigator or trained investigators S.K.K./V.M.) and concurrent CES performed at baseline, 24 hours, and 48 hours after recruitment. The weighing procedure is shown in **Supplementary Digital Content Table 1** (http://links.lww.com/CCX/B198) and the methodology and precision of weight measurements, in children in intensive care, has been described previously (11) Data were entered into a case report form and subsequently, to a database managed using Research Electronic Data Capture tools (12).

Demographic and clinical characteristics were recorded from the PICU database, including age, sex, admission diagnosis (based on Australian and New Zealand Paediatric Intensive Care Registry diagnostic codes) (13), Risk Adjustment for Congenital Heart Surgery (RACHS) risk of death (14), Pediatric Index of Mortality score (15), duration of invasive mechanical ventilation (MV), use of extracorporeal membrane oxygenation and renal replacement therapy, and intensive care length of stay and intensive care mortality.

Clinical Edema Score

The 19-point CES was defined as the sum of grades of edema in six body regions including the periorbital region, upper limb, hand, torso, lower limb, and foot. Each region was assessed as having either none (score = 0), mild (1), moderate (2), or severe (3) edema based on descriptive criteria. The CES is shown in **Figure 1**. Scores were performed at baseline (time 0), 24 hours, and at 48 hours from enrollment. At each timepoint, the CES was performed by the primary investigator (B.G.) or either of two trained doctors (V.M./S.K.K.), a second intensive care doctor who was not directly caring for the infant, and the bedside nurse. Each observer was trained in the use of the scoring tool prior to performing a score. Education consisted of description of each level of edema severity for each body region and a tabular guide on the scoring report form. When observers were not available for all three assessments, an observer with equivalent experience was chosen as

Case Report Form - Clinician Assessment	Med 1/med 2/ nurse
Date/Time	
Patient	
UR	
Edema Score	
Eyelid	
none	0
mild	1
mod	2
severe	3
Upper Limb	
none	0
mild	1
mod	2
severe	3
Hands	
none	*0*
mild	1
mod	2
severe	3
Torso	
none	*0*
mild	1
mod	2
severe	3
Lower Limb	
none	*0*
mild	1
mod	2
severe	3
Feet	
none	*0*
mild	1
mod	2
severe	3
total score out of 18	

Figure 1. Clinical edema score case report form. Circumferences: upper arm and leg. Eyelid: 0—none (preserved eyelid creases/normal eyelids); 1—mild (loss of normal eyelid creases can easily open eye complete iris visible); 2—moderate (some restricted eye opening, moderate retraction to visualize whole iris); and 3—severe (very restricted eye opening, unable to visualize complete iris). Limbs: 0—none (no edema); 1—mild (loss of normal skin creases); 2—moderate (fullness of tissues, some pitting); 3—severe (significant pitting). Med 1 = medical 1, Med 2 = medical 2.

a replacement. Clinicians were blinded to each other's score and to other measurements.

Outcomes

The primary outcome was the difference between the median (quantile 0.5) total CES for each group of observers. Secondary outcomes included the difference between observer groups for the CES at the 25th and 75th centile of scores (quantiles 0.25 and 0.75), and separately for the overall mean CES. The relationship between body weight compared with CES was also explored over the three times of observation.

Statistical Analyses

Demographic and clinical characteristics were summarized as frequencies with proportions if categorical, mean (SD) if approximately normally distributed and, otherwise median (interquartile range) (full range). The relationship between total CES from clinicians was initially summarized within a correlation matrix, reporting Pearson correlation coefficient for continuous covariates. Subsequently, to investigate the agreement over a range of scores, a multivariable quantile linear regression (τ: 0.25, 0.5, 0.75) was applied, accounting for repeated measures within children. Explanatory variables, incorporated as fixed effects, included observer class (medical 1 [reference], medical 2, nurse), time (zero [reference], 24 hr, 48 hr), body weight at enrollment (in kg), RACHS (risk of death as a percentage), duration of cardiopulmonary bypass (hr), and whether peritoneal dialysis was provided within 48 hours of enrollment. The model accounted for repeated measurements within individuals by applying cluster robust SEs derived from 10,000 bootstrap procedures (16). The CES was subsequently explored within a similar multivariable linear mixed model, incorporating all the above fixed covariates and a random intercept to account for repeated observations within individual children. Finally, the relationship across timepoints between the CES and body weight, was displayed graphically and explored within a similar multivariable, linear mixed model. Similarly, the relationship between the CES and body weight, within body regions, were displayed graphically. Analyses were performed within R software, Version 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) using the various statistical packages listed in the **Supplemental Digital Content** (http://links.lww.com/CCX/B198). The Strengthening the Reporting of Observational Studies in Epidemiology checklist for cohort studies was completed and is found in the **Supplemental Digital Content File** (http://links.lww.com/CCX/B198).

RESULTS

Sixty-one children were enrolled between May 2021 and September 2022. The demographic and clinical characteristics of all children are shown in **Table 1**. Fifty-nine had complete data for each time point. Consent was withdrawn by two families: one following baseline measurements and, another, after 24 hours. All remaining observational data were incorporated into the analyses reported in this study.

Clinical Edema Score

A total of 539 CES were available for analysis. The mean total CES at each time point, for each observer group are shown in **Figure 2** and the distribution of all CES for each observer are shown in **Supplementary Digital Content Figure 1** (http://links.lww.com/CCX/B198). The summarized CES are shown in **Supplementary Digital Content Table 2** (http://links.lww.com/CCX/B198). The median CES of all observers, for each body region, show that higher scores were returned for the eye region and the torso compared with other assessed anatomical locations (**Supplementary Digital Content Fig. 2**, http://links.lww.com/CCX/B198).

Interobserver Comparisons of the Total Clinical Edema Score

A correlation matrix of the total CES and selected continuous clinical covariates is shown in **Supplementary Digital Content Figure 3** (http://links.lww.com/CCX/B198). It displays graphically the distribution of the CES (by observer groups), the distribution of continuous covariates and the observed correlation (with 95% confidence bands) between such covariates. In the linear quantile regression analyses, the CES showed the greatest apparent difference between observer groups for the lowest quartile (25th percentile) of CES, with much closer estimates for the median and highest quartile (75th percentile); with, however, no strong evidence of disagreement across these quartiles when accounting for clinical covariates (**Table 2**). In the separate

TABLE 1.
Demographic and Clinical Characteristics of All Children

Characteristic	*n* = 61
Age (d)	8.0 (1.0–14.0)
Sex (male), *n* (%)	37 (60.7)
Pediatric Index of Mortality III	2.1 (1.4–5.7)
Risk Adjustment for Congenital Heart Surgery–Risk of Death (%)	20.9 (14.3–32.4)
Diagnosis, *n* (%)	
Aortic insufficiency	1 (1.6)
Aortic stenosis	1 (1.6)
Atrioventricular septal defect	4 (6.6)
Coarctation	1 (1.6)
Double outlet right ventricle	1 (1.6)
Hypoplastic left heart syndrome	
Hypoplastic left ventricle (not hypoplastic left heart syndrome)	2 (3.3)
Interrupted or hypoplastic aortic arch	5 (8.2)
Levo-transposition of great arteries	2 (3.3)
Pulmonary atresia or stenosis	8 (13.1)
Total anomalous pulmonary venous drainage	5 (8.2)
Dextro-transposition of great arteries	18 (29.5)
Tricuspid atresia or stenosis	2 (3.3)
Truncus arteriosus	1 (1.6)
Ventricular septal defect	7 (11.5)
Cardiopulmonary bypass, *n* (%)	49 (80.3)
Time from surgery to first clinical edema score (hr), *n* = 60	26.9 (23.6–29.7)
Mechanical ventilation duration (hr)	93.0 (67.0–163.8)
Peritoneal dialysis, *n* (%)	29 (47.5)
Extracorporeal membrane oxygenation, *n* (%)	4 (6.6)
Intensive care length of stay (hr)	164.8 (117.2–302.5)
Survival to intensive care discharge, *n* (%)	61 (100.0)

Data are median (interquartile range) unless stated.

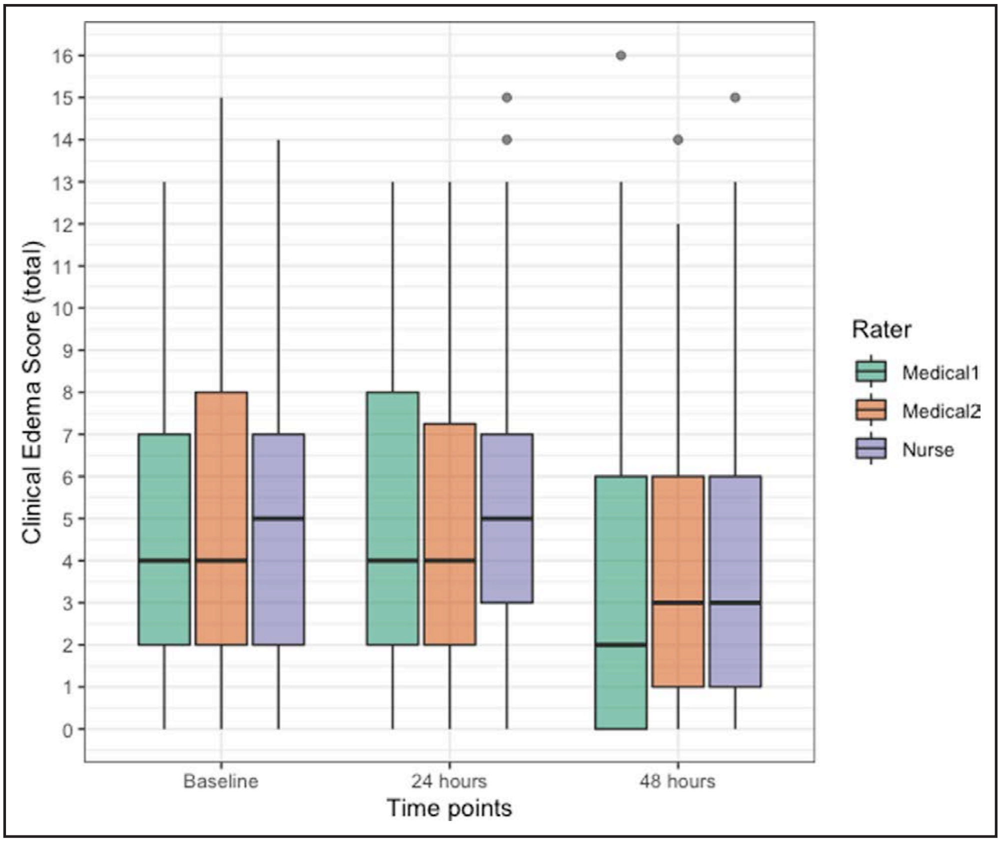

Figure 2. Total clinical edema scores at each time point for each observer group. *Dark line* indicates the median value, and the *box hinges* represent the 25th and 75th centiles. *Lower* and *upper whiskers* contain values that extend 1.5 times the interquartile range from the 25th and 75th centiles, respectively.

multivariable linear regression analysis, accounting for clinical covariates at baseline and, peritoneal dialysis during the study period, there was no strong evidence of overall disagreement between observer groups in mean CES scores (**Supplementary Digital Content Table 3**, http://links.lww.com/CCX/B198). The model diagnostics are provided in **Supplementary Digital Content Figure 4** (http://links.lww.com/CCX/B198).

Change in a Clinical Edema Score Over Time

The changes in CES between time intervals for observer groups, are summarized in Figure 2 and **Supplementary Digital Content Figure 5** (http://links.lww.com/CCX/B198) and the distribution of changes in **Supplementary Digital Content Figure 6** (http://links.lww.com/CCX/B198). The largest change in mean CES compared with baseline was observed at 48 hours rather than 24 hours (coefficient, –1.16 [95% CI, –1.63 to –0.68]) (Supplementary Digital Content Table 3, http://links.lww.com/CCX/B198). However, this difference was not sufficient in that there was no evidence of an interaction between observer group, CES and time (Supplementary Digital Content Table 3, http://links.lww.com/CCX/B198, footnotes).

Relationship Between the Clinical Edema Score and Body Weight

The observed time course of body weight and CES is shown in a scatterplot in **Figure 3**. In a multivariable, linear mixed-effects model, accounting for the CES at baseline, each 1 point increase in CES was associated with a 12 grams (95% CI, 3.2–21 grams) increase in mean body weight (**Table 3**). Within body regions, the relationship between individual CES and body weight for the eye, the torso, the foot, and the hand are shown in **Supplementary Digital Content Figure 7** (http://links.lww.com/CCX/B198).

DISCUSSION

Key Findings

In this prospective study investigating the performance of a CES in mechanically ventilated infants with congenital heart disease, the overall CES results were very similar between three clinical observer groups. Analyses using unadjusted linear quantile models suggested that total scores may diverge between observer groups only in children with the least amount of edema. However, across all three quantiles (25%, 50%, and 75% of total CES), after accounting for potentially influential clinical covariates, there was no strong evidence of large differences in CES estimates from experienced clinicians. Likewise, in similar linear mixed-effects regression analyses, there was no

TABLE 2.
Quantile Regression Analyses With Cluster Robust Inference for the Difference in Clinical Edema Scores Between Observer Groups

Variable	Unadjusted			Adjusted[b]		
Quartile (τ)	First (0.25)	Second (0.5)	Third (0.75)	First (0.25)	Second (0.5)	Third (0.75)
		Coefficient (95% CI[a])			Coefficient (95% CI[a])	
Observer						
Medical 1	Reference	Reference	Reference	Reference	Reference	Reference
Medical 2[c]	1.0 (0.2–1.8)[f]	0 (−1.0 to 1.0)	0 (−1.2 to 1.2)	0.1 (−0.4 to 0.6)	0.6 (−0.2 to 1.4)	0.1 (−1.2 to 1.4)
Nurse	1.0 (0.2–1.8)[f]	0 (−1.2 to 1.2)	0 (−1.4 to 1.4)	0.5 (−0.0 to 1.0)	0.7 (−0.1 to 1.5)	−0.2 (−1.6 to 1.2)
Time						
Baseline (time 0)	Reference	Reference	Reference	Reference	Reference	Reference
24 hr	0 (−0.8 to 0.8)	0 (−1.2 to 1.2)	0 (−1.3 to 1.3)	0.3 (−0.2 to 0.8)	0.2 (−0.6 to 1.0)	0.5 (−0.6 to 1.6)
48 hr	−1 (−1.8 to −0.2)[f]	−1 (−2.2 to 0.2)	−1 (−2.7 to 0.7)	−1.1 (−1.8 to −0.4)[f]	−1.6 (−2.5 to −0.7)[f]	−1.6 (−3.0 to −0.2)[f]
Weight (time 0) (kg)	0 (−0.6 to 0.6)	0 (−1.5 to 1.5)	1.2 (−2.6 to 2.6)	0.4 (−0.3 to 1.1)	0.6 (−0.9 to 2.1)	1.2 (−1.3 to 3.7)
Risk Adjustment for Congenital Heart Surgery[d]	0.3 (−0.1 to 0.7)	0.5 (−0.0 to 1.0)[f]	0.7 (0.1–1.3)[f]	0.3 (0.0–0.5)[f]	0.4 (−0.2 to 1.0)	0.9 (0.2–1.6)[f]
Cardiopulmonary bypass (hr)	0 (−0.5 to 0.5)	0 (−0.8 to 0.8)	0.3 (−0.3 to 0.9)	−0.3 (−0.6 to −0.0)[f]	−0.4 (−1.1 to 0.3)	−0.4 (−1.0 to 0.3)
Peritoneal dialysis[e]	2.0 (0.6–3.4)[f]	2.0 (0.1–3.9)[f]	2.0 (−0.6 to 4.6)	1.5 (0.5–2.5)[f]	1.9 (0.1–3.7)[f]	2.3 (−0.1 to 4.7)

[a]CIs are derived from cluster robust SEs and calculated using 10,000 bootstrap replicates within the quantile regression model.
[b]Effect estimate is adjusted for all other variables in this table.
[c]Reference for each user group is the observer medical 1.
[d]Risk Adjustment for Congenital Heart Surgery (RACHS) percentage risk of death—effect estimate for each 10% change in RACHS.
[e]Peritoneal dialysis within 48 hr from enrollment.
[f]$p < 0.05$.
Interactive terms were explored within the multivariable model (not reported). However, no evidence of interaction of importance was found and, therefore, only the main effects were reported.

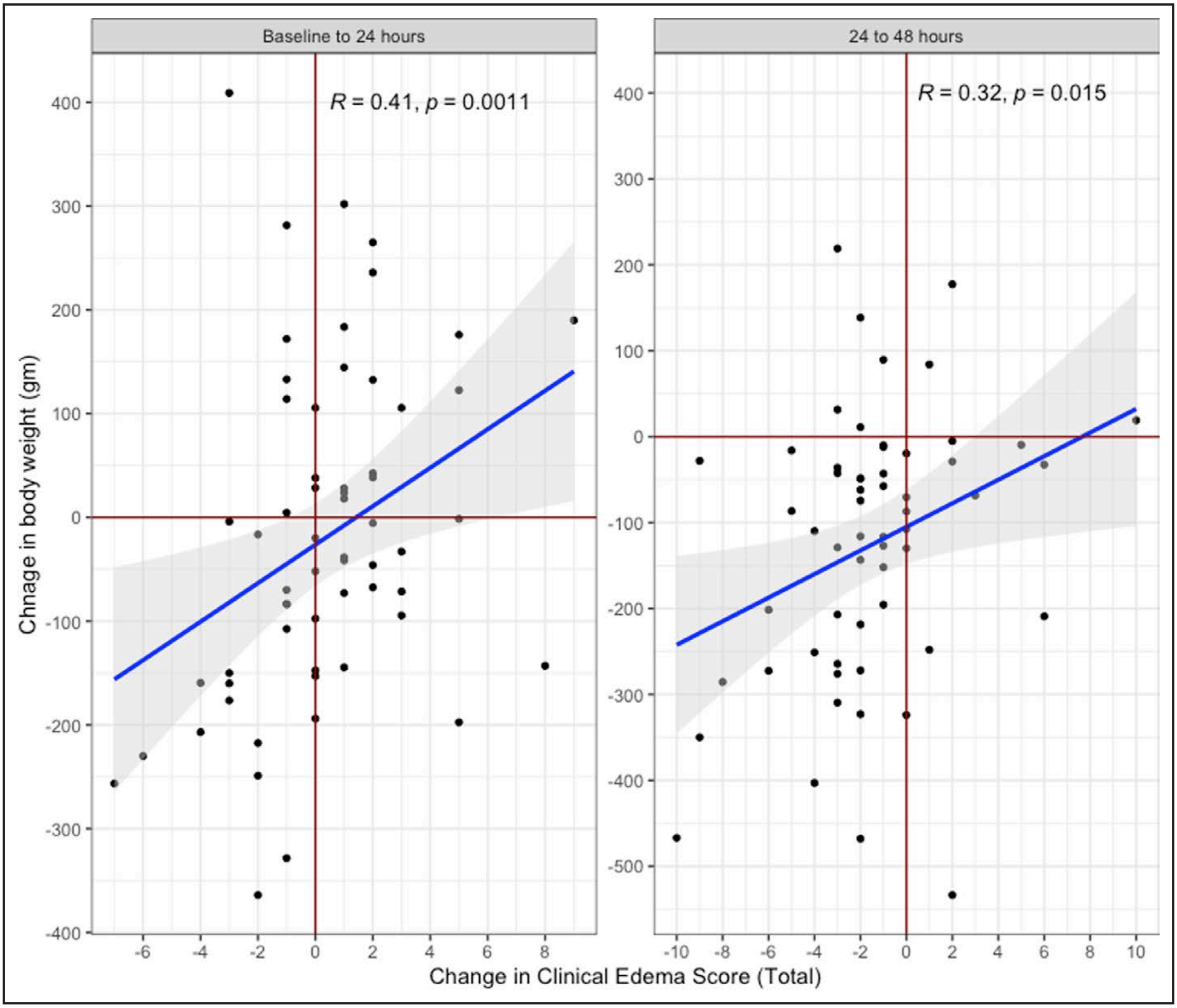

Figure 3. Relationship between change in clinical edema score and change in body weight. *Bivariate plot* showing unadjusted change in the clinical edema score against body weight. The unadjusted relationship displayed in these graphs may include an influence of regression to the mean. Adjustment for individual patient baseline clinical edema scores was included in a multivariable linear mixed-effects model of which the results are displayed in Table 3 (17).

evidence of substantial differences between observer groups for mean scores overall. Importantly from the perspective of clinical utility, there was strong evidence that an increase in CES was associated with an increase in body weight.

Relationship to Previous Studies

There are few studies that report methods for clinically quantifying edema in critically ill children. Some approaches have been described in ambulatory patients with lymphedema by measuring the displacement of water of an edematous limb (18, 19) or using CT imaging to measure water-specific radiation attenuation (20). Such methods have limited applicability in intensive care. A retrospective study, of 85 children post-cardiac surgery, reported a relationship between fluid accumulation, edema, and duration of MV (21); however, edema was measured by a radiologist's assessment of chest wall thickness rather than by clinical assessment of the patient. Pediatric intensivists consider edema to be an important factor in fluid management (22) despite a lack of clinical tools to quantify it.

TABLE 3.
Mixed Linear Effects Regression Analysis for the Association Between Changes in Clinical Edema Score and Body Weight

	Unadjusted		Adjusted[a]	
Variable	Coefficient (95% CI	*p*	Coefficient (95% CI)	*p*
Change in clinical edema score	19.0 (10.4–27.6)	< 0.001	12.1 (3.2–21.0)	0.008
Covariates				
Clinical edema score (time 0)	−6.8 (−15.4 to 1.8)	0.12	−5.2 (−14.0 to 3.6)	0.24
Time (reference baseline to 24 hr)	−106.9 (−166.2 to −47.7)	< 0.001	−86.0 (−142.7 to −29.3)	0.003
Weight (time 0) (kg)	−70.1 (−119.1 to −22.1)	0.005	−43.9 (−93.6 to 5.8)	0.08
Risk Adjustment for Congenital Heart Surgery[b] (% Risk of Death)	10.2 (−4.9 to 25.3)	0.18	14.4 (−0.6 to 29.3)	0.06
Cardiopulmonary bypass (hr)	−1.4 (−19.0 to 16.2)	0.88	−9.8 (−28.2 to 8.7)	0.29
Peritoneal dialysis[c]	62.5 (0.32–124.6)	0.05	43.0 (−3.7 to 118.8)	0.06

[a]Effect estimate is adjusted for all other variables in this table.
[b]Risk Adjustment for Congenital Heart Surgery—each unit represents 10 percentage points.
[c]Peritoneal dialysis within 48 hr from enrollment.
Effect estimates represent the mean change in body weight (g) for each point change in clinical edema score.

Interpretation of Findings

This study shows that a clinical assessment of tissue edema using an ordinal clinical score based on six anatomical sites is feasible, and there was relatively close overall agreement on the magnitude of the score between clinical observer groups comprising experienced PICU nursing and medical staff. For each observer group, higher scores were returned in the eye region and the torso, compared with other regions, suggesting that these regions may be more susceptible to edema or more easily recognized by clinicians, or both. Agreement in total CES was least at the lowest total edema scores, which might be important in distinguishing between "none" or "any" edema. The positive relationship between changes in CES and body weight (a surrogate for total body water) provides some evidence of its validity as a rapid clinical assessment tool. Importantly, this relationship may be stronger in central body regions compared with peripheral. However, the changes in CES between time intervals, and the accompanying absolute changes on body weight, were small. Quantifying edema in children in intensive care is important because it is a common component of the management of fluid status and clinicians need to recognize its presence, measure the response to fluid removal therapies and modify them accordingly. Fluid accumulation is widely reported to be harmful based on research where it is measured using fluid-balance charts. However, the independent effects of edema on clinical outcomes are unknown. Objective methods to quantify edema could improve its assessment and therefore, overall management of fluid status during critical illness. This study has shown preliminary evidence of agreement between clinician groups when using a scoring tool based on subjective clinical assessment.

Strength and Limitations

The strengths of this study are the prospective design and the investigation of a sample of critically ill mechanically ventilated children in intensive care for whom edema is common. The CES is a pragmatic, clinical scoring tool assessing six body regions. Scores were performed at equivalent times by three observer groups who were trained in the use of the scoring tool and who were blinded to fluid balance charts, body weight measurements, and each other's scores. Modeling techniques used to assess differences controlled for repeated measurements within individual children. We acknowledge some limitations. This study was a single-center study and therefore the external validity of findings requires further investigation. Furthermore, the study sample comprised infants with congenital heart disease making the findings of the present study not generalizable to older children with potentially alternate pathophysiological processes such as lung disease or sepsis. The CES was defined arbitrarily based on the sum of simple ordinal scores from six body regions using a very simple clinical grading. However, this pragmatic scale was based on commonly used clinical descriptions, and observers were provided with a written guide to improve standardization of scores. Not all observers were available at each time point and therefore, replacements were required, particularly for nursing staff. Therefore, the similarity of scores were reported between observer groups rather than between individual clinical observers. We did not record the variability in pediatric intensive care clinical experience of observers but note that a CES will likely be most useful if accessible to all user groups across a wide level of clinical experience. Whether it can be implemented in clinical practice, outside the conditions of a study, requires further investigation.

CONCLUSIONS

A simple CES grading multiple body regions in mechanically ventilated children with congenital heart disease, returned similar estimates across three clinical observer group, overall, with least agreement at lower edema scores. Changes in the proposed CES between time intervals were small, however, a positive association between the CES and body weight was observed, suggesting some further exploration of the utility of the CES in quantifying edema in critically ill children.

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