

Noninvasive monitoring of physiologic compromise in acute appendicitis: New insight into an old disease

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ABSTRACT

Introduction: Physiologic compromise in children with acute appendicitis has heretofore been difficult to measure. We hypothesized that the Compensatory Reserve Index (CRI), a novel adjunctive cardiovascular status indicator, would be low for children presenting with acute appendicitis in proportion to their physiological compromise, and that CRI would rise with fluid resuscitation and surgical management of their disease.

Methods: Ninety-four children diagnosed with acute appendicitis were monitored with a CipherOx CRI™ M1 pulse oximeter (Flashback Technologies Inc., Boulder, CO). For clarity, CRI = 1 indicates supine normovolemia, CRI = 0 indicates hemodynamic decompensation (systolic blood pressure < 80 mmHg), and CRI values between 1 and 0 indicate the proportion of volume reserve remaining before collapse. Results are presented as counts with proportion (%), or mean with 95% confidence interval (CI).

Results: Mean age was 11 years old (95% CI: 10–12), and 49 (52%) of the children were male. Fifty-four (57%) had nonperforated appendicitis and 40 (43%) had perforated appendicitis. Mean initial CRI was significantly higher in those with nonperforated appendicitis compared to those with perforated appendicitis (0.57, 95% CI: 0.52–0.63 vs. 0.36, 95% CI: 0.29–0.43; $P < 0.001$). The significant differences in mean CRI values between the two groups remained throughout the course of treatment, but lost its significance at 2 h after surgery (0.63, 95% CI: 0.57–0.70 vs. 0.53, 95% CI: 0.46–0.61; $P = 0.05$).

Conclusion: Low CRI values in children with perforated appendicitis are indicative of their lower reserve capacity owing to peritonitis and hypovolemia. CRI offers a real-time, noninvasive adjunctive tool to monitor tolerance to volume loss in children.

Level of evidence: Study of diagnostic test; Level of evidence: Level III.

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Children presenting with acute appendicitis experience varying degrees of hypovolemia owing to a combination of intraabdominal infection and third space fluid losses, reduced oral intake and vomiting [1]. Initial management of these children includes prompt initiation of intravenous (IV) fluids and early antibiotic therapy [2]. Perforated appendicitis with extensive peritoneal contamination requires administration of larger volumes of resuscitative fluids owing to the greater inflammatory response. Detection of hypovolemia, fluid resuscitation and

monitoring of fluid responsiveness rely on clinical assessment and traditional vital signs such as blood pressure and heart rate, which are dynamic and highly variable in children [3–8].

The Compensatory Reserve Index (CRI) is a new adjunctive cardiovascular status indicator. It uses signals from continuous noninvasive sensors and was designed to estimate the proportion of additional volume loss a patient can tolerate before reaching the point of hemodynamic decompensation [systolic blood pressure (SBP) < 80 mmHg]. CRI is a proprietary technology of Flashback Technologies Inc. [9]. It is based on advanced signal processing and data analytics, applied to a large raw signal database from a human simulated hemorrhage (LBNP) model, where subjects were taken from normovolemia to cardiovascular collapse. The intent was to develop a noninvasive method to quickly identify those at risk of cardiovascular collapse. CRI values range between 1 and 0, where CRI = 1 indicates supine normovolemia, and CRI = 0 indicates the point of decompensation. CRI values between

Abbreviations: CRI, Compensatory Reserve Index; CI, Confidence interval; DBP, Diastolic blood pressure; DSS, Disease Severity Score; HR, Heart rate; ICU, Intensive care unit; IV, Intravenous; SBP, Systolic blood pressure.

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1 and 0 indicate the proportion of volume reserve remaining before the sudden onset of decompensation.

CRI has proven to be a sensitive and specific, noninvasive method for monitoring acute volume loss in adults [9–12]. Although the algorithm was developed based on sensor data from adults [9,10,12–20], it has been shown to correlate with fluid requirements and the extent of burn injury in children [21]. CRI has also been shown to identify hypovolemia and trend fluid resuscitation in children with dengue shock syndrome [22]. We therefore hypothesized that children presenting with acute appendicitis would have low CRI values in proportion to their physiological compromise, and that these values would rise with fluid resuscitation and surgical management of their disease. Thus, the aims of this study were: 1) to determine whether the CRI algorithm is sensitive to the greater physiological compromise in children with perforated appendicitis, 2) to evaluate changes in CRI during treatment for acute appendicitis, and 3) to evaluate the effects of IV fluid administration on CRI.

1. Methods

1.1. Study population

This study was approved by the Colorado Multi-Institutional Review Board. Informed consent was obtained from all subjects prior to data collection. Children ages 1–17 years old who presented to Children's Hospital Colorado with signs and symptoms of acute appendicitis and underwent surgical consultation were eligible for the study.

1.2. Data collection

Continuous CRI measurements were collected using CIPHEROX CRI™ M1 monitors (Flashback Technologies Inc., Boulder, CO), from the time of enrollment until after interventions were performed and subjects were considered stable. Caregivers and clinicians were unaware of the CRI values since they were not visible on the investigational device screen. A CIPHEROX CRI™ M1 device was placed on one of three middle fingers of the hand without an indwelling intravenous catheter or blood pressure cuff whenever possible. Clinical information, such as the amount of fluid administered and operative findings, was collected from electronic medical records. Vital signs (temperature, heart rate, and blood pressure) were recorded upon admission. Mean CRI values averaged over 30 min at each time point were used for the final analysis.

Disease Severity Score (DSS), a descriptive grading system for acute appendicitis developed by Garst et al. [23], was used to grade the

severity of acute appendicitis for subjects who underwent appendectomy. The scores were assigned after two researchers (YMC, DL) separately reviewed each patient's electronic medical record, including the brief operative note, dictated operative report and the final pathology report.

1.3. Statistical methods

Length of stay was log transformed and presented as a geometric mean. Two-sample t-tests were used to analyze associations between continuous variables and appendicitis perforation status. Fisher's Exact or chi-square tests were used to test for associations between categorical variables and appendicitis perforation status. Linear regression was used to analyze the association between CRI and vital signs and the amount of fluid received. All tests used a significance level of 0.05 and were two-sided. Results are presented as counts with proportion (%), or mean with 95% confidence interval (CI). R version 3.2.5 software (R Foundation for Statistical Computing, Vienna, Austria, <http://www.R-project.org/>) was utilized.

2. Results

2.1. Demographics and clinical information

A total of 108 subjects were enrolled over a six-month period in 2016. Eight subjects who underwent appendectomy had final pathology that had no pathological evidence of appendicitis, and six subjects were found to have a diagnosis other than appendicitis prior to any intervention and therefore excluded from the final analysis (Fig. 1). Data were analyzed for 94 subjects who had confirmed appendicitis and underwent appropriate interventions, which included appendectomy in 83 children, radiographic-guided drainage of abscesses together with IV antibiotics in six children and IV antibiotics alone in five children (Fig. 1).

Demographics and clinical information are presented in Table 1. Fifty-four children (57%) had nonperforated appendicitis and 40 (43%) had perforated appendicitis. Children with nonperforated appendicitis were significantly older than those with perforation (11 years, 95% CI: 10–12 vs. 10 years, 95% CI: 9–11; $P = 0.03$). They also had significantly lower initial heart rate (96, 95% CI: 91–101 vs. 110, 95% CI: 104–116; $P < 0.001$) and lower temperature (98.9, 95% CI: 98.5–99.4 vs. 100.4, 95% CI: 99.9–100.9; $P < 0.001$).

Of those who were transferred from another facility ($n = 59$), children with nonperforated appendicitis received significantly less fluid prior to transfer (10 ml/kg, 95% CI: 5–15 vs. 19 ml/kg, 95% CI: 13–25;

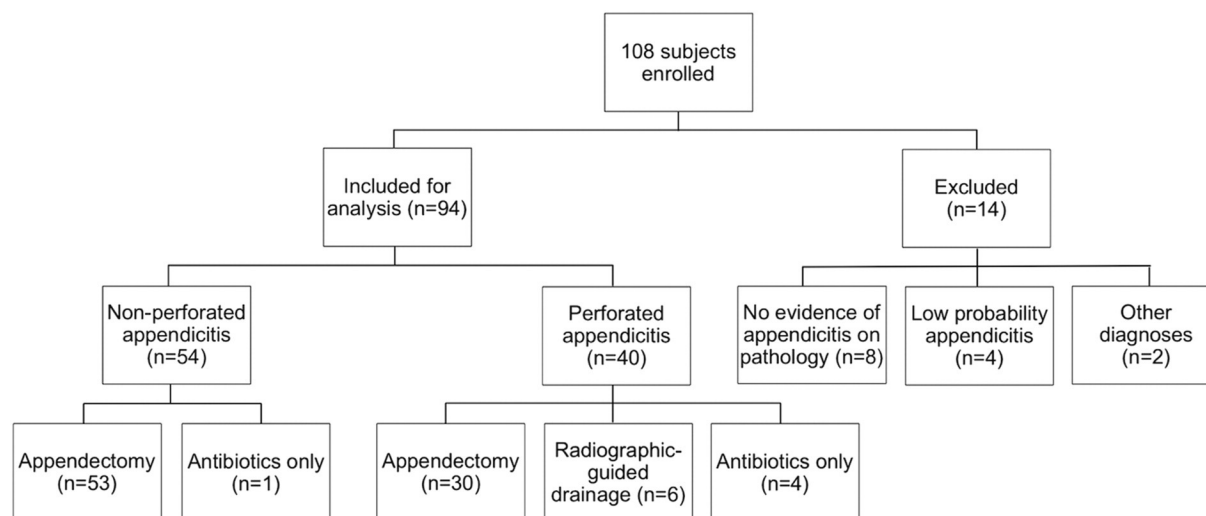


Fig. 1. Enrollment of eligible patients to the study.

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