ANESTHESIOLOGY

Preoperative Fluid Fasting Times and Postinduction Low Blood Pressure in Children

A Retrospective Analysis

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ABSTRACT

Background: Children are required to fast before elective general anesthesia. This study hypothesized that prolonged fasting causes volume depletion that manifests as low blood pressure. This study aimed to assess the association between fluid fasting duration and postinduction low blood pressure.

Methods: A retrospective cohort study was performed of 15,543 anesthetized children without preinduction venous access who underwent elective surgery from 2016 to 2017 at Children's Hospital of Philadelphia. Low blood pressure was defined as systolic blood pressure lower than 2 standard deviations below the mean (approximately the 2.5th percentile) for sex- and age-specific reference values. Two epochs were assessed: epoch 1 was from induction to completion of anesthesia preparation, and epoch 2 was during surgical preparation.

Results: In epoch 1, the incidence of low systolic blood pressure was 5.2% (697 of 13,497), and no association was observed with the fluid fasting time groups: less than 4 h (4.6%, 141 of 3,081), 4 to 8 h (6.0%, 219 of 3,652), 8 to 12 h (4.9%, 124 of 2,526), and more than 12 h (5.0%, 213 of 4,238). In epoch 2, the incidence of low systolic blood pressure was 6.9% (889 of 12,917) and varied across the fasting groups: less than 4 h (5.6%, 162 of 2,918), 4 to 8 h (8.1%, 285 of 3,531), 8 to 12 h (5.9%, 143 of 2,423), and more than 12 h (7.4%, 299 of 4,045); after adjusting for confounders, fasting 4 to 8 h (adjusted odds ratio, 1.33; 95% CI, 1.07 to 1.64; $P = 0.009$) and greater than 12 h (adjusted odds ratio, 1.28; 95% CI, 1.04 to 1.57; $P = 0.018$) were associated with significantly higher odds of low systolic blood pressure compared with the group who fasted less than 4 h, whereas the increased odds of low systolic blood pressure associated with fasting 8 to 12 h (adjusted odds ratio, 1.11; 95% CI, 0.87 to 1.42; $P = 0.391$) was nonsignificant.

Conclusions: Longer durations of clear fluid fasting in anesthetized children were associated with increased risk of postinduction low blood pressure during surgical preparation, although this association appeared nonlinear.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Small studies of focused pediatric surgical patient populations demonstrate that prolonged fasting before surgery is associated with hypotension during anesthesia induction and surgical preparation
- Consensus guidelines regarding the optimal fasting duration lack robust evidence across a broad range of ages and procedures

What This Article Tells Us That Is New

- Among 15,443 pediatric patients undergoing elective surgery with inhalational anesthetic induction, approximately 5% experience hypotension during anesthesia induction and 7% during surgical preparation
- Compared with fasting less than 4 h, fasting between 4 and 8 h or more than 12 h is associated with a 30% increase in the risk of hypotension during surgical preparation
- Hypotension during anesthesia induction is not associated with any specific duration of fasting

Children are required to fast before undergoing elective general anesthesia to ensure elimination of gastric particulate matter, minimize gastric fluid volume, and in turn reduce the risks of regurgitation and pulmonary aspiration of gastric contents.[1] Institutional preanesthetic fasting guidelines may be implemented without regard to the extent to which minimum fasting times are exceeded, resulting in patients experiencing prolonged fasts. Prolonged preoperative fasting that exceeds guidelines by more than 2 h causes hunger, discomfort, headache, dehydration, and

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hypoglycemia.[2] Pediatric hospitals have recently enacted more liberal preoperative clear fluid fasting guidelines.[3,4] Meanwhile, pediatric anesthesia societies in Europe, New Zealand, and Australia have released consensus guidelines allowing shorter minimum clear fluid fasting durations.[5,6]

Quality improvement initiatives designed to shorten fasting duration in clinical practice have been implemented in parallel with research into the prevalence and impact of low blood pressure in anesthetized children.[7–9] A study of traditional and liberal fasting guidelines and post–anesthesia-induction blood pressure readings in children aged 0 to 36 months reported that traditional guidelines were associated with lower blood pressure.[10] However, it remains unclear how fasting duration affects blood pressure among anesthetized children of various ages.

In an earlier study of blood pressure in anesthetized infants, we divided the analysis of blood pressure values in the postinduction, preincision period into two epochs based on disparate clinical conditions.[8] Epoch 1, the anesthesia preparation phase, is typically a dynamic and stimulating period that includes airway management and catheter placement, whereas epoch 2, the surgical preparation phase, is a quiescent period consisting primarily of patient positioning and surgical preparation. In the previous study, we found that the postinduction blood pressure patterns differed markedly between epochs 1 and 2.[8]

Accordingly, we developed a central hypothesis that prolonged clear fluid fasting time before elective anesthesia would be associated with low blood pressure, and this association would differ across the two postinduction epochs. We conducted a retrospective study aimed to (1) report the epoch-specific incidence rate of low blood pressure after induction of anesthesia and (2) determine whether there is an association between clear fluid fasting duration and the incidence of low blood pressure in epoch 1 and epoch 2 separately.

Materials and Methods

Ethics Approval and Reporting Guidelines

The Children's Hospital of Philadelphia Institutional Review Board (Philadelphia, Pennsylvania) approved this study and waived the requirement for written informed consent on October 15, 2018. This article adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[11]

Patient Population

We performed a retrospective cohort study using prospectively collected data from patients receiving elective general anesthesia from January 1, 2016, to September 30, 2017, at Children's Hospital of Philadelphia, an urban, quaternary care pediatric hospital. This was a primary analysis of the data. The study's initial inclusion and exclusion criteria, definitions of low blood pressure, and analysis plan were established before the data was accessed. Patient inclusion criteria were as follows: American Society of Anesthesiologists (ASA) physical status I to IV patients who were less than 18 yr of age and had a recorded time of last clear fluid intake on the day of the anesthetic. Exclusion criteria included hospital inpatients, patients who underwent surgical or interventional procedures or imaging in the cardiothoracic suite, patients who underwent more than one anesthetic during the study period, patients with a known congenital cardiac defect, patients with ASA physical status V or E, patients who received intravenous fluid administration during the preanesthesia fasting period, and patients with any documented venous access in the preoperative area before transport to the operating room.

Measurements and Data Handling

The anesthesia information management system database (Epic Systems Corporation, USA) was queried to obtain each patient's perioperative data including age, weight, sex, date of birth, surgery date, ASA physical status, race, time of last fluid intake, noninvasive blood pressure values, medications, and anesthesia information management system event timestamps. We used anesthesia information management system event timestamps to define the two post–anesthesia-induction epochs: epoch 1, from induction of anesthesia to completion of anesthesia preparation (based on the Induction and Anesthesia Ready event timestamps); and epoch 2, after the end of anesthesia preparation to completion of surgical preparation (based on the Anesthesia Ready and Procedure Start event timestamps).

The primary outcome of our study was low systolic blood pressure (SBP). The primary outcome changed during the revision process. In the initial version of this study, the primary outcome was defined as an SBP value more than 20% below baseline SBP. Based on editor and reviewer feedback, we changed to a definition based on reference normograms, which may be more appropriate when defining pediatric low blood pressure.[12] Thus, low SBP was ascertained in the two epochs separately if any measured SBP was lower than sex- and age-specific values from reference normograms for noninvasive blood pressures in anesthetized children: approximately the 2.5th percentile, which is the 50th percentile minus 2 standard deviations.[12] Noninvasive SBP measurements were recorded by the anesthesia information management system every 3 min. At our institution, blood pressure cuffs are typically placed on the patient's upper arm; the cuff size is selected so that the edge of the cuff falls within the range markings on the other side of the cuff and the width does not extend over a joint. SBP data filtering and validation were performed to identify and exclude from analysis any blood pressure artifact values that were blank, zero, negative, or greater than 200 mmHg. We excluded from analysis the patients who met the low SBP criterion before induction of anesthesia.

Clear fluid fasting duration was the primary exposure of interest. Fasting duration was calculated for each patient as the amount of time between the time of last preanesthesia fluid intake and the induction event. The time of last fluid intake was documented by nurses according to patient's or guardian's self-report. We categorized fasting duration into four exposure groups based on the approximate quartiles of fasting duration. The quartiles of fasting duration were rounded down to the nearest whole integer for clinical simplicity, and therefore the four exposure groups consisted of less than 4 h, 4 to 8 h, 8 to 12 h, and greater than 12 h, which aligns with the definition of Dennhardt *et al.*[2] for prolonged fasting: 2 h longer than our hospital's clear fluid fasting guideline of 2 h (*i.e.*, 4 h or greater).

Baseline blood pressure was defined as the final blood pressure recorded in the preanesthesia holding area, and patients without records of baseline blood pressure were excluded from the analysis. Age was classified into six groups based on National Institute of Child Health and Human Development standard age groups for pediatric trials: less than 6 months, 6 months to 1 yr, 1 to 2 yr, 2 to 5 yr, 6 to 11 yr, and 12 to 18 yr.[13] Other covariates include sex, race/ethnicity, body mass index, ASA physical status, anesthesia time, and medications (propofol, opioids, neuraxial anesthesia, and neuromuscular blocking agent). The covariate "medications" was the presence or absence of that medication class during epoch 1 or 2. If a medication was given in epoch 1 but not epoch 2, it was coded as "received" in both epochs 1 and 2. If a medication was given in epoch 2 but not epoch 1, it was coded as "received" only in epoch 2. The classes were defined as follows: (1) propofol: a bolus or infusion of propofol; (2) opioids: any opioid, such as fentanyl, morphine, hydromorphone, or methadone, administered *via* any route; (3) neuraxial anesthesia: any local anesthetic given *via* either spinal or epidural route; and (4) neuromuscular blocking agent: rocuronium, vecuronium, cisatracurium, or succinylcholine.

Statistical Analysis

There was no statistical power analysis conducted before the study, and the sample size was based on our experience with annual patient volume. A statistical analysis plan was developed before assessing the data; *post hoc* analysis was performed per the editor's and reviewers' suggestions. Descriptive statistics were used to present demographic and clinical characteristics of 15,543 patients across exposure groups: categorical and numeric variables were described as counts with percentages and medians with interquartile ranges, respectively. Chi-square and Kruskal–Wallis tests were conducted to assess crude differences as appropriate. Our primary analyses were used to build the multivariable logistic regression models to assess the association between fasting time and low SBP in epochs 1 and 2, separately. The key assumptions of logistic regression were evaluated: neither influential outliers nor multicollinearity were detected, whereas the assumption of linearity between continuously scaled fasting time and the log odds (natural logarithm of odds) of outcome was violated. To address the nonlinearity issue, we used a multivariable fractional polynomial approach to search for a suitable transformation of fasting time. Categorized fasting time was also analyzed in the multivariable models. The final model adjusted for covariates such as age, sex, race/ethnicity, ASA physical status, anesthesia time, medications (propofol, opioids, neuraxial anesthesia, or neuromuscular blocking agent), and baseline SBP. The selection of these covariates was primarily based on the conceptual causal model, preliminary data analysis, and logistic regression model diagnostics. Adjusted odds ratio and 95% CI were reported. Model diagnostics were also reported, including the Hosmer–Lemeshow goodness-of-fit test, c-statistic, and the area under the precision–recall curve.

To visualize the association between fasting time and low SBP, (1) probability density curves were made displaying the distributions of fasting time by low *versus* normal SBP, and (2) a scatterplot was drawn in which the log odds of low SBP was plotted against fasting hours and a smooth curve with 95% CI was fitted using locally estimated scatterplot smoothing regression algorithm.

Post hoc sensitivity analyses were conducted: (1) we built a mixed effect logistic regression model (*i.e.*, generalized linear mixed model) to account for the influence of the attending anesthesiologist, in which the anesthesiology attending at induction was fitted as a random intercept; and (2) we assessed the impact of a different categorization of the exposure, and fluid fasting time was classified into seven categories including less than 4 h, 4 to 6 h, 6 to 8 h, 8 to 10 h, 10 to 12 h, 12 to 14 h, and greater than 14 h.

All analyses were performed using R 3.4.2 (R Foundation for Statistical Computing, Austria). The R packages stats, lme4, mfp, and ggplot2 were used for logistic regression, mixed effect logistic regression, fractional polynomial transformation, and data visualization, respectively. A two-sided P value less than 0.05 was used as the criterion for statistical significance.

Results

Study Population

The study population included 15,543 anesthetized patients with a median age of 6.8 yr (interquartile range, 3.7, 11.8) and a median body mass index of 17.2 kg/m^2 (interquartile range, 15.6, 20.2). The flowchart of the study population and sample size for the analysis is shown in figure 1; 116 patients were excluded because of low SBP before induction of anesthesia, and 2,597 patients were excluded because of a lack of recorded clear fluid fasting time. Patient characteristics by total study cohort and the four fasting time groups are shown in table 1.

Low SBP during Anesthesia and Surgical Preparation

Of all 15,543 study patients, 1,290 (8.3%) experienced low SBP during either one epoch or both epochs. In epoch 1, there were 13,497 patients who had valid SBP

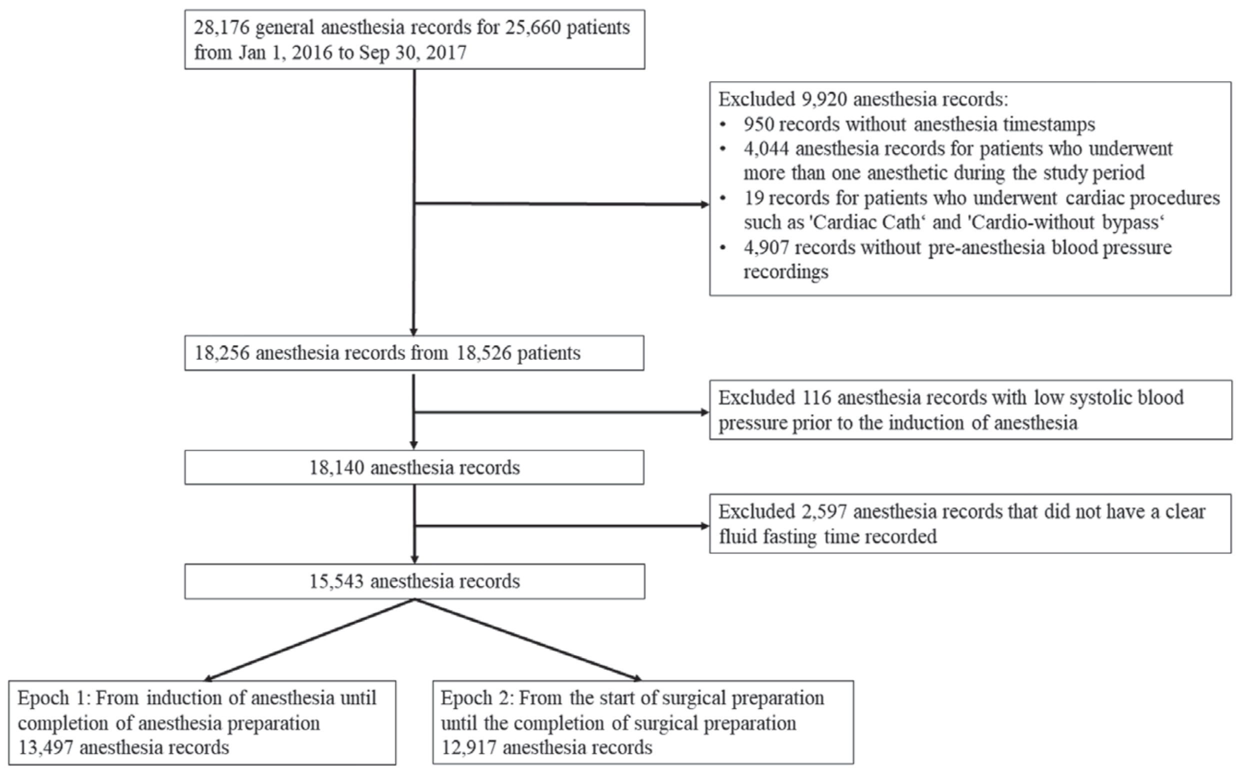

Fig. 1. Flowchart of the study population and sample size.

measurements, where 697 (5.2%) had at least one episode of low SBP. During epoch 2, 889 (6.9%) of 12,917 patients had SBP measurements that were considered low SBP. There were 67 attending anesthesiologists included in the study, and the average number of anesthesia cases per anesthesiologist was 232 (median, 215 cases; interquartile range, 108 to 306; range, 1 to 802).

When assessing baseline preanesthesia SBP and SBP in both epochs, there were statistically significant differences across the four fasting time groups (all $P < 0.0001$). In epoch 2, the incidence rate of low SBP significantly differed with increasing fasting duration, with the lowest rate in the group of less than 4h (5.6%, 162 of 2,918) and higher rates in the other three groups of 4 to 8h (8.1%, 285 of 3,531), 8 to 12h (5.9%, 143 of 2,423), and more than 12h (7.4%, 299 of 4,045; $P < 0.0001$). This pattern was also observed in epoch 1 ($P = 0.049$).

Associations between Fasting and Low SBP

There was a significant association between longer fasting duration and increased odds of low SBP in epoch 2 after controlling for multiple confounders (table 2). Compared with the group who fasted less than 4h, the groups with fasting durations of 4 to 8h (adjusted odds ratio, 1.33; 95% CI, 1.07 to 1.64; $P = 0.009$) and greater than 12h (adjusted odds ratio, 1.28; 95% CI, 1.04 to 1.57; $P = 0.018$) were associated with significantly higher rates of low SBP, whereas the increased rate of low SBP associated with fasting 8 to 12h (adjusted odds ratio, 1.11; 95% CI, 0.87 to 1.42; $P = 0.391$) was nonsignificant. Such associations remained when accounting for anesthesiology attending at induction as a random effect (table 3 and Supplemental Digital Content, supplemental table 1, http://links.lww.com/ALN/C376). The adjusted associations between fasting and low SBP in epoch 1 were not significant (table 2). Model diagnostics were summarized in tables 2 and 3.

The increased odds of low SBP associated with prolonged fluid fasting in epoch 2 was visualized in figure 2. As shown in the scatterplot, there was an upward trend in the log odds of low SBP with prolonged fasting time, but this trend appeared to be nonlinear. This relationship can be illustrated by comparing the probability density curves of fasting duration among patients with low SBP *versus* normal SBP; the group of patients with low SBP appear collectively to have longer fasting durations than those with normal SBP.

Further, the associations between fasting duration and low SBP in epoch 2 were examined by assessing the effect of fasting in 2-h increments (table 3 and Supplemental Digital Content, supplemental table 2, http://links.lww.com/ALN/C376). Compared with patients fasting less than 4h, those fasting 4 to 6h (adjusted odds ratio, 1.27; 95% CI,

Table 1. Demographics and Clinical Features of 15,543 Anesthetized Children, Total and Grouped by Four Fasting Time Categories Based on Quartiles

		Clear Fluid Fasting Time			
	Total (n = 15,543)	Up to 4 h (n = 3,560)	4 to 8 h (n = 4,068)	8 to 12 h (n = 2,941)	More than 12 h (n = 4,974)
Demographics					
Age, yr (median, interquartile range)	6.8 (3.7–11.8)	6.9 (4.1–11.1)	7.2 (3.7–12.1)	5.8 (2.9–11.9)	6.9 (4.1–11.9)
Age groups, n (%)					
< 6 months	55 (0.4)	9 (0.3)	38 (0.9)	7 (0.2)	1 (0.0)
6 months to 1 yr	691 (4.4)	180 (5.1)	271 (6.7)	153 (5.2)	87 (1.7)
1 to 2 yr	1,427 (9.2)	254 (7.1)	358 (8.8)	378 (12.9)	437 (8.8)
2 to 5 yr	4,675 (30.1)	1,059 (29.7)	1,015 (25.0)	963 (32.7)	1,638 (32.9)
6 to 11 yr	4,947 (31.8)	1,288 (36.2)	1,347 (33.1)	722 (24.5)	1,590 (32.0)
12 to 18 yr	3,748 (24.1)	770 (21.6)	1,039 (25.5)	718 (24.4)	1,221 (24.5)
Male, n (%)	9,319 (60.0)	2,138 (60.1)	2,490 (61.2)	1,727 (58.7)	2,964 (59.6)
Race/ethnicity, n (%)					
Black	2,518 (16.2)	376 (10.6)	631 (15.5)	582 (19.8)	929 (18.7)
White	9,321 (60.0)	2,306 (64.8)	2,452 (60.3)	1,691 (57.5)	2,872 (57.7)
Hispanic	1,187 (7.6)	234 (6.6)	314 (7.7)	223 (7.6)	416 (8.4)
Asian and Pacific Islander	588 (3.8)	133 (3.7)	171 (4.2)	119 (4.0)	165 (3.3)
Others	1,705 (11.0)	453 (12.7)	446 (11.0)	294 (10.0)	512 (10.3)
Race/ethnicity unknown, n (%)	224 (1.4)				
Clinical features					
Body mass index, kg/m² (median, interquartile range)	17.2 (15.6–20.2)	17.2 (15.6–20.0)	17.5 (15.7–20.6)	17.2 (15.6–20.0)	17.1 (15.5–20.2)
Body mass index unknown, n (%)	168 (1.1)				
ASA physical status					
I	4,887 (31.4)	1,194 (33.5)	1,117 (27.5)	987 (33.6)	1,589 (31.9)
II	9,223 (59.3)	2,103 (59.1)	2,371 (58.3)	1,725 (58.7)	3,024 (60.8)
III and IV	1,433 (9.2)	263 (7.4)	580 (14.3)	229 (7.8)	361 (7.3)
Anesthesia induction time					
7:00 AM to 12:00 PM	11,194 (72.0)	2,707 (76.0)	1,907 (46.9)	2,812 (95.6)	3,768 (75.8)
12:00 to 6:00 PM	4,321 (27.8)	849 (23.8)	2,152 (52.9)	117 (4.0)	1,203 (24.2)
Medication					
Propofol, n (%)	9,005 (57.9)	2,023 (56.8)	2,509 (61.7)	1,652 (56.2)	2,821 (56.7)
Opioids, n (%)	10,782 (69.4)	2,566 (72.1)	2,776 (68.2)	1,887 (64.2)	3,553 (71.4)
Neuraxial anesthesia, n (%)	1,921 (12.4)	427 (12.0)	570 (14.0)	418 (14.2)	506 (10.2)
Neuromuscular blocker, n (%)	1,017 (6.5)	177 (5.0)	386 (9.5)	224 (7.6)	230 (4.6)
Baseline SBP (mmHg)	109 (100–118)	108 (99–117)	110 (101–119)	109 (101–119)	109 (100–118)
SBP in epoch 1 (n = *13*,497)					
SBP (mmHg), median (interquartile range)	88 (79–99)	90 (80–100)	86 (77–97)	88 (78–98)	89 (80–100)
Low SBP, n (%)	697 (5.2)	141 (4.6)	219 (6.0)	124 (4.9)	213 (5.0)
SBP in epoch 2 (n = *12*,917)					
SBP (mmHg), median (interquartile range)	84 (77–93)	85 (77–94)	83 (75–92)	84 (77–93)	85 (77–94)
Low SBP, n (%)	889 (6.9)	162 (5.6)	285 (8.1)	143 (5.9)	299 (7.4)

Epoch 1 is anesthesia preparation after induction of anesthesia, whereas epoch 2 is the surgical preparation phase.
ASA, American Society of Anesthesiologists; SBP, systolic blood pressure.

1.01 to 1.59; *P* = 0.038), 6 to 8 h (adjusted odds ratio, 1.55; 95% CI, 1.13 to 2.13; *P* = 0.007), 12 to 14 h (adjusted odds ratio, 1.33; 95% CI, 1.04 to 1.71; *P* = 0.026), and greater than 14 h (adjusted odds ratio, 1.28; 95% CI, 1.01 to 1.62; *P* = 0.043) were more likely to experience low SBP, whereas those fasting 8 to 10 h (adjusted odds ratio; 0.99, 95% CI, 0.69 to 1.42; *P* = 0.952) and 10 to 12 h (adjusted odds ratio, 1.16; 95% CI, 0.88 to 1.52; *P* = 0.287) did not show a significant increase in the odds of low SBP.

Transformations of continuously scaled fasting time were attempted. Although a first-degree fractional polynomial with a power of −0.5 worked best statistically, the model diagnostics were not improved. More importantly, the transformation neither adequately reflected the complex nonlinear relationship shown in figure 2 nor provided a straightforward clinical interpretation. Accordingly, we have reported the findings based on the categorized fasting time instead of the fractional polynomial transformation.

Discussion

Our study found prolonged clear fluid fasting duration was associated with increased odds of low blood pressure during the surgical preparation phase in anesthetized children, but

Table 2. Adjusted Associations between Risk Factors and Low SBP during Postinduction, Preincision Anesthesia, and Surgical Preparation Epochs in Anesthetized Infants and Children

	Epoch 1: Anesthesia Preparation		Epoch 2: Surgical Preparation	
Independent Variables	**Adjusted Odds Ratio (95% CI)**	***P* Value**	**Adjusted Odds Ratio (95% CI)**	***P* Value**
Fluid fasting time				
< 4 h	Reference		Reference	
4 to 8 h	1.17 (0.93–1.48)	0.177	1.33 (1.07–1.64)	0.009
8 to 12 h	1.07 (0.83–1.39)	0.584	1.11 (0.87–1.42)	0.391
> 12 h	1.06 (0.85–1.33)	0.621	1.28 (1.04–1.57)	0.018
Age groups				
< 6 months	0.46 (0.06–3.49)	0.455	1.91 (0.56–6.6)	0.305
6 months to 1 yr	1.13 (0.64–1.99)	0.680	1.10 (0.61–1.98)	0.749
1 yr to 2 yr	Reference		Reference	
2 to 5 yr	1.05 (0.69–1.59)	0.820	1.11 (0.73–1.67)	0.631
6 to 11 yr	1.36 (0.91–2.05)	0.139	1.89 (1.27–2.81)	0.002
12 to 18 yr	3.70 (2.47–5.55)	< 0.0001	5.1 (3.40–7.6)	< 0.0001
Sex				
Male *vs.* female	0.93 (0.79–1.09)	0.354	1.07 (0.93–1.24)	0.361
Race/ethnicity				
Black	Reference		Reference	
White	0.79 (0.65–0.97)	0.026	0.91 (0.75–1.10)	0.329
Hispanic	0.96 (0.70–1.32)	0.817	1.23 (0.93–1.63)	0.146
Asian and Pacific Islander	0.84 (0.55–1.30)	0.438	0.86 (0.58–1.28)	0.462
Others	0.80 (0.59–1.09)	0.159	1.00 (0.76–1.31)	0.982
ASA physical status				
I	0.50 (0.385–0.64)	< 0.0001	0.48 (0.383–0.61)	< 0.0001
II	0.55 (0.44–0.69)	< 0.0001	0.57 (0.47–0.70)	< 0.0001
III and IV	Reference		Reference	
Anesthesia induction time				
7:00 AM to 12:00 PM *vs.* 12:00 PM to 6:00 PM	1.11 (0.93–1.33)	0.264	1.17 (0.99–1.37)	0.052
Medication				
Propofol	1.22 (1.02–1.46)	0.033	1.18 (1.01–1.39)	0.047
Opioids	1.03 (0.86–1.22)	0.755	1.25 (1.06–1.47)	0.008
Neuraxial anesthesia	1.18 (0.94–1.49)	0.147	1.12 (0.91–1.37)	0.291
Neuromuscular blockade	1.50 (1.16–1.94)	0.002	0.91 (0.69–1.18)	0.466
Baseline SBP, mmHg	0.98 (0.97–0.99)	< 0.0001	0.98 (0.98–0.99)	< 0.0001

Two multiple logistic regression models were fitted separately for epochs 1 and 2. Each model regressed log odds of low SBP on multiple variables including fluid fasting time groups, age groups, sex, race/ethnicity, ASA Physical Status, anesthesia time, medications (propofol, opioids, neuraxial anesthesia, or muscle relaxant), and baseline SBP. Model diagnostics for epoch 1: *P* value of Hosmer–Lemeshow goodness-of-fit test = 0.774, c-statistic = 0.68, and area under precision recall curve = 0.11; for epoch 2: *P* value of Hosmer–Lemeshow goodness-of-fit test = 0.815, c-statistic = 0.70, and area under precision recall curve = 0.14.

ASA, American Society of Anesthesiologists; SBP, systolic blood pressure.

this relationship was nonlinear. Unnecessarily long fasting intervals in children are currently undergoing widespread scrutiny, and our study adds to the international discourse on efforts to reduce prolonged fluid fasting.[14] Prolonged fasting times subject children to considerable discomfort and may be a risk factor for emergence delirium.[2,15] Encouraging fluid intake until premedication decreases fasting times, but this practice must be weighed against the risk of increased gastric residual volumes if fasting times are 30 min or shorter.[16,17]

Our findings complement earlier studies that examined the effects of prolonged fasting in anesthetized children. Higher mean arterial pressures were observed after induction of anesthesia in a cohort of "optimized fasting management" children with fasting times that were significantly shorter than a preoptimization group.[10] Although a threshold effect with preoperative fasting and hemodynamics has been reported in infants who experienced greater drops in blood pressure when the infants had fasting durations over 8 h, we observed a nonlinear association between clear fluid fasting duration and rates of systolic low blood pressure.[18] There are several possible reasons for the observed nonlinearity in the clear fluid fasting duration and incidence of low blood pressure. First, blood pressure in children tends to be highest in the morning and then fall as the day progresses.[19] The majority of patients (95.6%) in the 8 to 12 h fasting duration group underwent induction of anesthesia in the morning (7:00 AM to 12:00 PM), whereas the 4 to 8 h fasting duration group had a greater proportion of patients who underwent induction of anesthesia in the afternoon and evening. Although table 1 shows a similar baseline SBP across the fasting time groups, perhaps the mechanisms underlying circadian blood pressure changes

Table 3. Associations between Clear Fluid Fasting Time and Low Systolic Blood Pressure during Surgical Preparation (Epoch 2) in Infants and Children: *Post Hoc* Sensitivity Analyses Comparing Different Exposure Categorizations and Logistic Regression Modeling

Categorized Fluid Fasting Time and Selected Logistic Regression Models	Epoch 2: Surgical Preparation Adjusted Odds Ratio (95% CI)	*P* Value
Model I: mixed effects logistic regression		
< 4 h	Reference	
4 to 8 h	1.30 (1.05–1.61)	0.015
8 to 12 h	1.10 (0.86–1.40)	0.450
> 12 h	1.28 (1.05–1.58)	0.017
Model II: mixed effects logistic regression		
< 4 h	Reference	
4 to 6 h	1.27 (1.01–1.59)	0.038
6 to 8 h	1.55 (1.13–2.13)	0.007
8 to 10 h	0.99 (0.69–1.42)	0.952
10 to 12 h	1.16 (0.88–1.52)	0.287
12 to 14 h	1.33 (1.04–1.71)	0.026
> 14 h	1.28 (1.01–1.62)	0.043

Models I and II were adjusted for age, sex, race/ethnicity, American Society of Anesthesiologists physical status, anesthesia time, medications (propofol, opioids, neuraxial anesthesia, or muscle relaxant), and baseline systolic blood pressure. Mixed effects logistic regression was used to account for the influence of attending anesthesiologists' behavior, and the attending anesthesiologist at induction was fitted as a random effect in the model. Model diagnostics for model I: *P* value of Hosmer–Lemeshow goodness-of-fit test = 0.299, c-statistic = 0.73, and area under precision recall curve = 0.17; and for model II: *P* value of Hosmer–Lemeshow goodness-of-fit test = 0.353, c-statistic = 0.73, and area under precision recall curve = 0.17.

also influence blood pressure responsiveness to anesthesia and impacted postinduction SBP in the 8 to 12 h group. Second, fasting duration was calculated based on the self- or parent-reported time of last clear fluid intake, which is a potential source of error and recall bias. Third, missing data could have impacted our results. As shown in the sample size flowchart, 2,597 patients were excluded from analysis because of a lack of a clear fluid fasting time, which might have contributed to inconsistent associations and selection bias. Although the records of fasting time were likely missing at random, the loss of approximately 15% (2,597 of 15,543) of fasting records could impact statistical power, particularly when performing multiple fasting group comparisons of an outcome with approximately 5% incidence.

Although other studies have described postinduction blood pressure in anesthetized children, our study incorporated clear fluid fasting duration, two clinically distinct epochs in the preincision period, and the use of multicenter reference values that may be more appropriate when defining pediatric low blood pressure.[20,21] Our observed low blood pressure rates are similar to the 6.1% rate that Pasma *et al.*[22] reported in a study that also used multicenter reference values to define their primary outcome of low blood pressure. In contrast, in a study of 6,737 pediatric surgical patients that used a relative definition of hypotension based on baseline blood pressure, a 60% incidence of hypotension was reported.[23] Our group reported relative hypotension in over 70% of infants who underwent pyloromyotomy.[8] A multicenter study of infant and neonatal anesthesia found mild, moderate, and severe hypotension in 62, 36, and 13% of infants and neonates, respectively.[24] This disparity highlights the importance of definition in studies of low blood pressure under anesthesia.[25] The actual long-term impact of low blood pressure during anesthesia remains unclear. Some researchers have emphasized the importance of optimizing organ perfusion and not merely maintaining a particular blood pressure value.[26] Although clinically relevant outcomes after low blood pressure in anesthetized children have not been identified, the potential risk of end organ hypoperfusion in anesthetized children is real and in need of further research.[27]

There remains a lack of consensus on what constitutes hypotension in children under elective general anesthesia and what the best measure of hypotension is in anesthetized children.[26,27] This study was not designed to measure end organ perfusion or define hypotension in children. We chose SBP as an outcome because it remains the criterion by which hypotension is defined in pediatric advanced life support and in pediatric and neonatal septic shock.[27,28] SBP was analyzed and reported in the multicenter reference blood pressure normograms and other recent studies of blood pressure in anesthetized infants and children.[12,24,29–31]

Our study's bimodal distribution of clear fluid fasting times is similar to other studies of clear fluid fasting in pediatric patients.[32,33] Most pediatric patients report their last clear liquid intake as occurring either in the evening before their surgery or in the morning of surgery before arrival at the hospital. Because clear fluid fasting duration was calculated using the last reported clear liquid intake time in our study, the bimodal fluid fasting distribution is likely conditional on the bimodal nature of reported times of last fluid intake (Supplemental Digital Content, supplemental fig. 1, http://links.lww.com/ALN/C375). Some other, unidentified confounder may have also contributed to the bimodal distribution of the clear fluid fasting durations.

Our study had several limitations. First, as with any retrospective study, our study is limited by confounders and cannot establish causation. We selected the time period between induction of anesthesia and the start of a procedure to minimize the impact of intravenous fluid administration on blood pressure readings. However, each patient's initial hydration status was unknown, because neither gastric volumes nor the volumes of liquid consumed before fasting were recorded. Second, our analysis included only four categories of medications because of the prohibitively complex heterogeneity in administered drugs, timing of drug administration, and patients' weights and ages. We did not include induction type as a covariate because the standard practice at our hospital is to induce anesthesia using sevoflurane unless the patient has venous access before induction. Although the proportion of intravenous

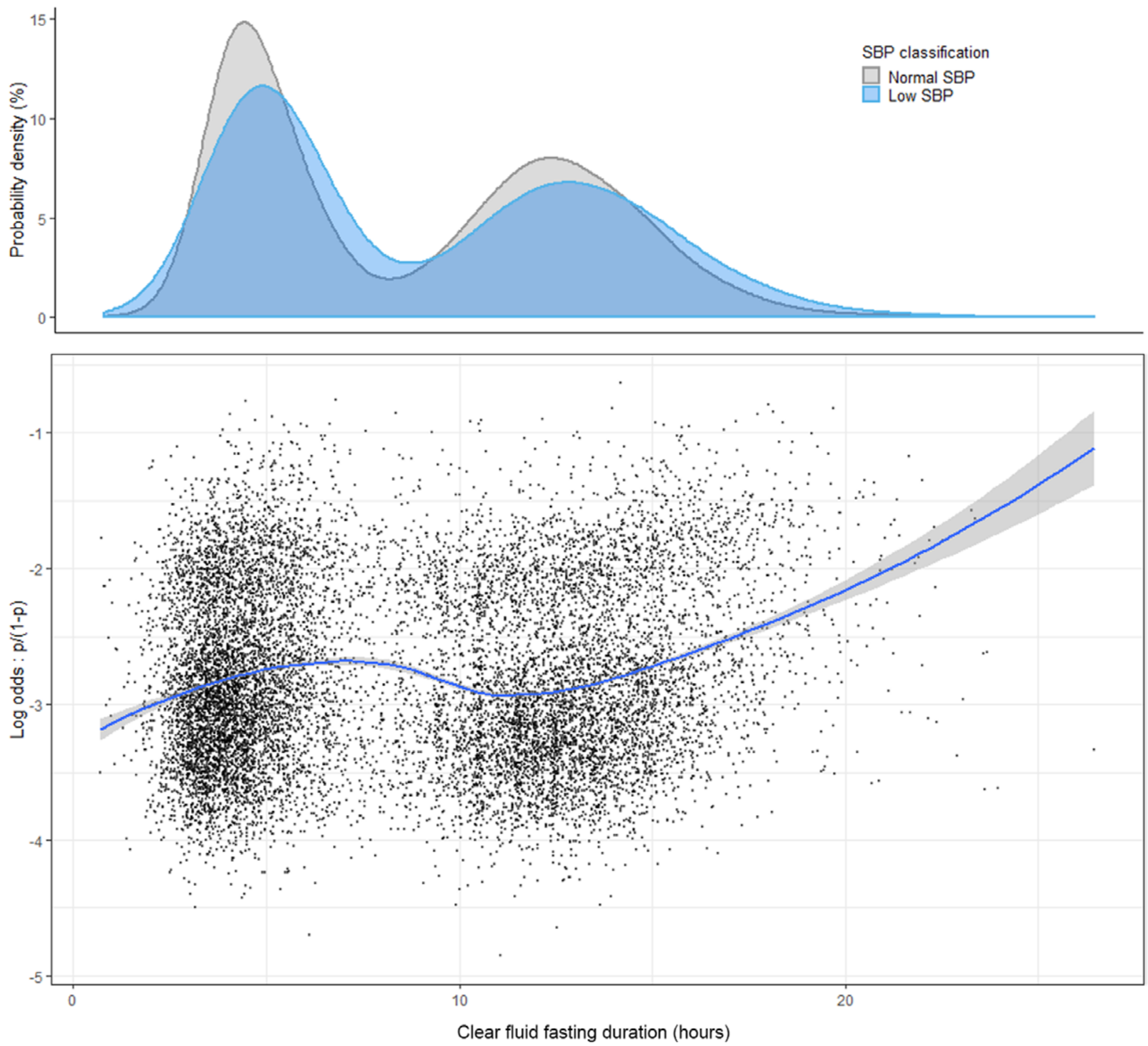

Fig. 2. Clear fluid fasting time and low systolic blood pressure (SBP) during the surgical preparation phase (epoch 2). Two probability density curves display the distributions of clear fluid fasting time by low and normal SBP. The scatterplot with a locally estimated scatterplot smoothing curve and 95% CI displays the trend between fasting time and the odds of low SBP. The odds of low SBP equals $p/(1-p)$, where p denotes the probability of low SBP. The natural logarithm was taken for the odds necessary to build a logistic regression model.

inductions in our cohort was negligible, we added four variables related to medications to the multivariable modeling (propofol, opioids, neuraxial anesthesia, and muscle relaxant) that were treated as binary variables indicating whether a medication was given during the anesthesia or surgical preparation epochs (epochs 1 and 2, respectively). Although we excluded patients with preoperative venous access, we did not specifically exclude "mixed" inductions with nitrous oxide for venous access and intravenous induction, and patients with undocumented preinduction venous access certainly may have been included in our analysis. As suggested by reviewers, we built a mixed-effect logistic regression model that included anesthesiology attending as a random effect to account for their influence on medications and dosing. Third, excluding patients who underwent multiple anesthetics during the study period might have skewed the cohort to healthier patients who were less susceptible to low blood pressure. Fourth, because studies have shown little difference in gastric emptying across various types of liquids, we did not analyze the type of liquid administered to our patients before the *non per os* period.[34] Fifth, although we identified and excluded vital sign artifacts, artifacts could have remained that impacted our findings.[35] Sixth, we were unable to assess clinicians' awareness of fluid fasting time at the time of anesthesia induction and thus did not include it in our analysis as a potential confounder. Seventh, our institution intentionally schedules younger children in the morning and older children in the afternoon, so there are fewer infants in the afternoon undergoing anesthesia, which could have impacted our analysis of morning *versus* afternoon induction times. Eighth, because we only included patients who had a valid preoperative blood pressure reading, our study population only had a small number of patients less than 6 months of age because patients in this age group are typically inpatients, designated as emergency procedures, or do not have preoperative blood pressures taken and were thereby excluded from this study. Finally, the duration of fluid fasting was based on the time of last fluid intake and did not account for the amount of fluid ingested, which could have influenced our findings.

Conclusions

Prolonged clear fluid fasting duration was associated with increased odds of low blood pressure after induction of anesthesia in anesthetized children, but this relationship was nonlinear. Further study is needed to elucidate the relationship between clear fluid fasting and blood pressure in anesthetized children.

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Competing Interests

The authors declare no competing interests.

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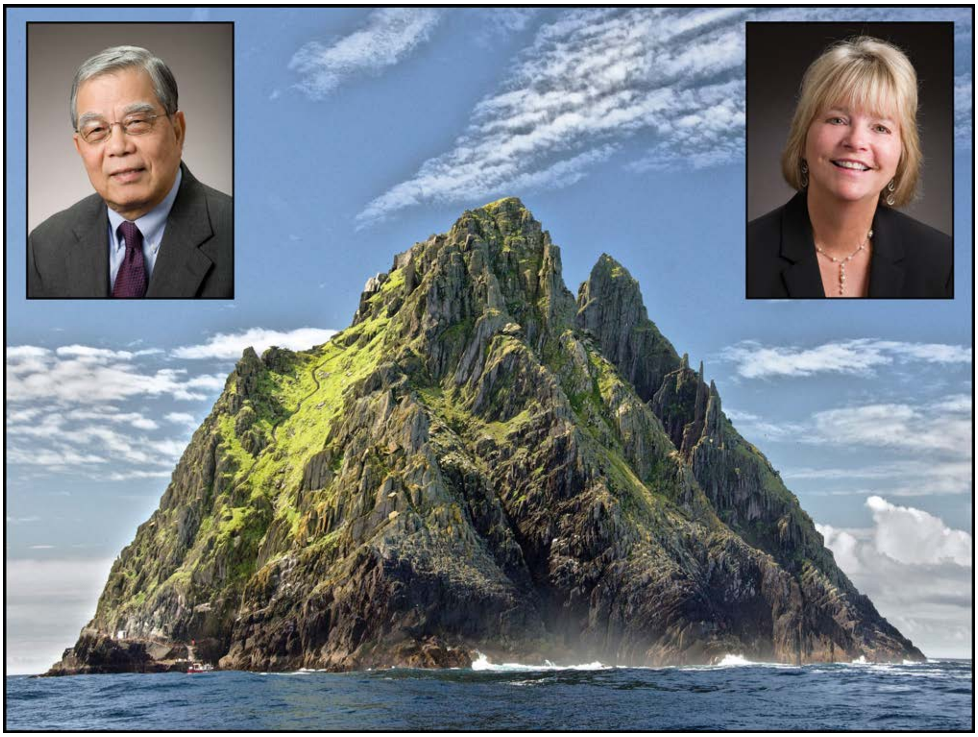
ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

"The Force" Gently Guiding Historical Researchers at the Wood Library-Museum



As a long-distance curator since 1987, I marveled at the deftness with which Wood Library-Museum (WLM) Librarian Patrick Sim, M.L.S. (1936 to 2010, *upper left*), could assist historical researchers. Sadly, by early 2010, Patrick was diagnosed with terminal cancer. After moderating a conference in Ireland, I ferried eight miles off County Kerry's coast to the island of Skellig Michael, years before Star War's Mark Hamill would do so to film *The Force Awakens* and *The Last Jedi*. Atop this 714-foot pyramid (*backdrop*) of Old Red Sandstone—treasured by bibliophiles like Patrick—Irish monks had dodged Viking raiders to keep the flame of knowledge burning during the Dark Ages. I ascended 600-plus rocky steps to pray for Patrick at a stony shrine, an emailed image of which helped him rally, briefly, ten years ago this month. Years after Patrick's passing, his brilliant successor, Karen Bieterman, M.L.I.S. (WLM Manager then Director, 2011 to 2019; *upper right*), and I continued to feel that Patrick's "force was with" us among the galleries and library stacks he so treasured at the WLM. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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