



## Original Contribution

## Apneic oxygenation to prevent oxyhemoglobin desaturation during rapid sequence intubation in a pediatric emergency department

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## ABSTRACT

**Background:** Apneic oxygenation is the delivery of oxygen to the nasopharynx during intubation. It may mitigate the risk of oxyhemoglobin desaturation but has not been well-studied in children.

**Methods:** We conducted a retrospective, observational study of patients undergoing rapid sequence intubation (RSI) in a pediatric emergency department. We compared patients who received apneic oxygenation, delivered via simple nasal cannula at age-specific flow rates, to patients who did not receive apneic oxygenation. The main outcome was occurrence of oxyhemoglobin desaturation during RSI, defined as oxyhemoglobin saturation dropping to <90% at any time after the administration of paralytic medication and before the endotracheal tube was secured. Data were analyzed using logistic regression, with groups as a fixed effect and patients' age and number of attempts as covariates.

**Results:** Data were collected for 305 of 323 patients who underwent RSI over a 49 month period. Oxyhemoglobin desaturation occurred for 50 patients when apneic oxygenation was used (22%, 95% CI 17% to 28%) and 11 patients without apneic oxygenation (14%, 95% CI 7% to 24%;  $p > 0.05$ ). There was no difference in the median duration of desaturation or depth of desaturation for the apneic oxygenation group (52 s, 71%) compared to the group without apneic oxygenation (65 s, 79%;  $p > 0.05$ ). Controlling for covariates, apneic oxygenation was not associated with a lower risk of oxyhemoglobin desaturation, time to desaturation, or depth/duration of desaturation episodes.

**Conclusions:** In an observational, video-based study of pediatric patients, apneic oxygenation was not associated with a lower risk of oxyhemoglobin desaturation during RSI.

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## 1. Introduction

Rapid sequence intubation (RSI) is the standard method for definitive airway management in the emergency department (ED). Paralytic-induced apnea during RSI increases the risk of adverse events, including oxyhemoglobin (SpO<sub>2</sub>) desaturation and hypercarbia. Hypoxemia increases the risk of primary and secondary hypoxic brain injury, bradycardia and cardiac arrest [1]. Children are at increased risk of desaturation during RSI due to differences in airway anatomy and greater risk of failed attempts, decreased total lung volume and increased metabolic demand. These factors are compounded by concurrent critical illness or injury [2–5].

Numerous approaches to improving the safety of emergent intubation have been studied [2], and apneic oxygenation has a prominent place in the recent literature. First described in 1959, apneic oxygenation is the provision of a high percentage of oxygen to the pharynx during laryngoscopy to maintain a positive diffusion gradient towards the alveoli. Multiple methods of oxygen delivery have been studied, including simple nasal cannula, high-flow nasal cannula, and various face masks. Apneic oxygenation theoretically provides additional oxygen for alveolar diffusion and global metabolic needs during apnea and prolongs the time available for laryngoscopy and tracheal intubation [6,7]. In operating rooms and intensive care units, apneic oxygenation has been associated with delayed onset of desaturation using various methods of oxygen delivery. Continuous positive airway pressure and high-flow nasal cannula have been shown to prolong safe apnea time in adults [8–12]. In the ED, the benefits of apneic oxygenation remain unclear. Multiple trials and systematic reviews suggest that apneic oxygenation prolongs the safe apnea period and is associated with decreased desaturation in adults [13–20]. However, two recent and prominent randomized controlled trials failed to demonstrate any benefit [21,22]. The published literature on apneic oxygenation

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for children during emergency intubation is especially limited [23–25]. In addition to the few studies published in children and the conflicting results from adult studies, the current literature is limited in several other ways. Most existing studies were based on chart review or self-report, which have been demonstrated to be unreliable approaches to data collection during critical care [26–31]. Moreover, the use of chart review or self-report makes measuring time-based outcomes difficult to impossible, and apneic oxygenation is specifically designed to delay the onset of desaturation.

The above gap in the current literature on apneic oxygenation suggests a critical need for additional studies, especially in children, based on methods of data collection that permit reliable data collection during critical care, especially time-based outcomes. The purpose of the current study was to begin to address this gap by completing an observational, video-based study of apneic oxygenation during RSI in children. We hypothesized that apneic oxygenation will be associated with both decreased frequency and delayed onset of desaturation compared to patients undergoing RSI without apneic oxygenation.

## 2. Methods

### 2.1. Design and setting

This was an observational, retrospectively planned study of data collected during and after a quality improvement initiative, the aim of which was to improve the safety of RSI in our PED. Our institutional review board approved the protocol prior to study commencement.

The study setting was the resuscitation suite of an academic PED, with an annual patient volume of approximately 90,000 visits. RSI is only performed in a dedicated resuscitation area, where patients are managed by pre-defined, multidisciplinary teams, led in most cases by a faculty physician who is board-certified or eligible for pediatric emergency medicine (PEM). Laryngoscopy attempts are performed by PEM fellows or faculty physicians or emergency medicine residents. Pediatric residents are not generally permitted to attempt intubation. Anesthesiology fellows or faculty physicians are present for all intubations performed during trauma team activations and are otherwise available on a consultative basis.

### 2.2. Subjects and enrollment

All patients undergoing RSI in the resuscitation area were eligible for study inclusion. RSI was defined as the administration in rapid succession of a sedating and paralyzing agent to facilitate tracheal intubation. To identify eligible patients, we used the same daily electronic medical record report used for ongoing quality assurance efforts [32].

### 2.3. Quality improvement initiative

The RSI quality improvement initiative began in July 2012. The intervention bundle, designed to standardize procedural and patient preparation and limit the duration of failing attempts, consisted of: [1] a procedural checklist, [2] a second PEM faculty physician to execute the checklist, [3] use of a video laryngoscope for all initial attempts, and [4] exclusion of pediatric residents from intubation attempts. Following introduction of the bundle, the rate of desaturation during RSI dropped from 33% to 16% [33]. These improvements have been sustained since the end of active improvement efforts in December 2013; current performance of key RSI processes remains above 90% and the rate of desaturation is approximately 17%.

### 2.4. Apneic oxygenation

After initial improvements were detected in early 2013, the RSI improvement team began refining the intervention bundle and considering additional interventions. Apneic oxygenation was added to the

intervention bundle in November 2013 and was the final change made to the bundle before it was operationalized in December 2013; no other major changes were made concurrent with or after the addition of apneic oxygenation. RSI medications were selected by the attending PEM physician from those available on the RSI checklist. The sedative options were etomidate, ketamine or fentanyl, and the neuromuscular blocking agents were rocuronium or succinylcholine. Two pre-medications, atropine and lidocaine, were also routinely administered.

The respiratory therapist for a given patient was responsible for starting apneic oxygenation, and the RSI checklist was modified to include an apneic oxygenation item. Apneic oxygenation was performed using age-based flow rates (2 lpm (liters per minute) for <3 years, 4 lpm 3–8 years, and 6 lpm > 8 years); flow rates were selected based on commonly used rates for age/weight and were delivered via simple nasal cannula. All ED providers, including respiratory therapists, were provided education on apneic oxygenation, including staff meetings, shift reports, and emails.

### 2.5. Data collection

We abstracted data for the current study from existing records. The primary data source was the database maintained for ongoing RSI quality improvement activities. Full methodology for the quality improvement initiative and the reliability of video review for RSI data have been reported previously [26,27]. The main source of data for the RSI database is video review. Each “bay” in our resuscitation area is equipped with a ceiling-mounted, digital camera and microphone, both of which record continuously. The patient monitor is also recorded. For patients undergoing RSI, videos were reviewed using a proprietary software program (B-line Medical, Live Capture, Washington, D.C.). After a patient is identified in the medical record, a trained research associate reviews the corresponding video and records all pertinent RSI data on a standard form. We then enter a subset of these data into a Microsoft Excel database (Release 2010, Microsoft Corporation, Redmond, WA). For the current study, we developed a separate study form and abstracted data from either the original RSI quality improvement form or the RSI database. KO, SB, and BK drafted and refined the data abstraction form, and KO abstracted all data.

### 2.6. Outcomes and measures

The main outcome was oxyhemoglobin desaturation during RSI. Desaturation was defined as the peripherally measured pulse oximetry reading dropping below 90% at any time after the administration of the paralytic medication and before the endotracheal tube was secured. Outcomes were determined by direct observation of the patient monitor on video review. The supervising physician was expected to stop all laryngoscopy attempts at 45 s or if the SpO<sub>2</sub> dropped to <95%. A timer with an audible alarm was used to reinforce limiting attempts to 45 s. Including the study period, historical compliance with this practice in our ED is better than 95%. The main outcome measure was the proportion of patients with at least one episode of desaturation during RSI. For patients with at least one episode of desaturation, additional outcomes of interest were the time to the onset of desaturation, the total duration of each desaturation episode, and the oxyhemoglobin saturation nadir. The time to desaturation was defined as the time in seconds from the flush of the first neuromuscular blocker until the SpO<sub>2</sub> first dropped below 90%. The duration of desaturation the time from the initial drop below 90% until the SpO<sub>2</sub> rose above 90% again.

### 2.7. Analysis

All data were tabulated and standard descriptive statistics generated. Baseline and demographic characteristics were summarized using means and standard deviations for continuous variables that were normally distributed, medians and inter-quantile range for non-normally distributed variables, and proportions for categorical

variables. The association between outcomes of interest and desaturation was first assessed at the bi-variable level, using the *t*-test for normally distributed data, Wilcoxon rank sum test for nonparametric data, and Chi-square or Fisher's exact test to evaluate proportions in dichotomous variables.

The association between apneic oxygenation and the main outcome (desaturation yes/no) was then modeled using multivariate logistic regression with several possible covariates: age, sex, comorbidities, indication for intubation, number of attempts, and month, year, and time of day of intubation. Covariates ( $p > 0.05$ ) were manually excluded from the model in a backward fashion. Model strengths were compared with the Akaike Information Criteria, Receiver Operating Characteristic Curve, and Hosmer-Lemeshow goodness-of-fit test.

For each of the secondary outcomes (time to desaturation, length of desaturation, and saturation nadir), we performed Wilcoxon rank sum tests to evaluate for significant differences between exposure groups, i.e., with and without apneic oxygenation. Additionally, we conducted analysis of covariance by adjusting for potential covariates (age, sex, comorbidities, indication for intubation, number of attempts, month, year and time of day of intubation). *P* values of  $<0.05$  were considered statistically significant. All statistical analyses were conducted using SAS 9.4.

### 3. Results

#### 3.1. Enrollment and data quality

We collected complete data for 305 of 323 eligible intubations (94%) over a 49-month period (September 2013 to October 2017). The few patients not captured were due to either technical failure of the video recording system or inadequate visualization of critical events during RSI (Fig. 1).

#### 3.2. Description of study sample

Table 1 presents patient and procedural characteristics by main exposure of interest (apneic oxygenation). Apneic oxygenation was applied more often when the intubating provider was a PEM attending or fellow and for medical (non-trauma) patients.

**Table 1**

Patient and procedural characteristics for patients with and without apneic oxygenation during rapid sequence intubation in a pediatric emergency department.

Characteristic	Apneic oxygenation (n = 227)	No apneic oxygenation (n = 78)
<b>Patient</b>		
Age, median years [Q1, Q3]	2.21 [0.38, 8.49]	2.91 [0.54, 12.03]
Sex (male)	146 (64.3%)	49 (62.8%)
Co-morbidity <sup>a</sup>	146 (64.3%)	54 (69.2%)
<b>Procedural</b>		
Indication for intubation		
Neurologic <sup>b</sup>	105 (46.3%)	22 (28.2%)
Trauma <sup>c</sup>	35 (15.4%)	36 (46.2%)
Shock	12 (5.3%)	6 (7.7%)
Respiratory failure	75 (33.0%)	14 (17.9%)
Intubating provider		
PEM fellow/attending	180 (79.3%)	49 (62.8%)
Anesthesiologist	16 (7.0%)	21 (26.9%)
Resident <sup>d</sup>	26 (11.5%)	4 (5.1%)
Other <sup>e</sup>	5 (2.2%)	4 (5.1%)
Number of attempts		
1	147 (64.8%)	51 (65.4%)
2	45 (19.8%)	17 (21.8%)
3	13 (5.7%)	5 (6.4%)
4	15 (6.6%)	4 (5.1%)
5	5 (2.2%)	1 (1.3%)
>5	2 (0.9%)	0
<b>Main outcome</b>		
Oxyhemoglobin desaturation <sup>f</sup>	50 (22.0%)	11 (14.1%)

PEM: pediatric emergency medicine.

<sup>a</sup> Comorbidities: Chronic lung disease, heart disease, facial abnormalities, genetic disorder, prematurity  $<37$  weeks gestation.

<sup>b</sup> Status epilepticus, obtundation.

<sup>c</sup> Traumatic arrest, Glasgow Coma Scale  $<8$  or declining, airway protection.

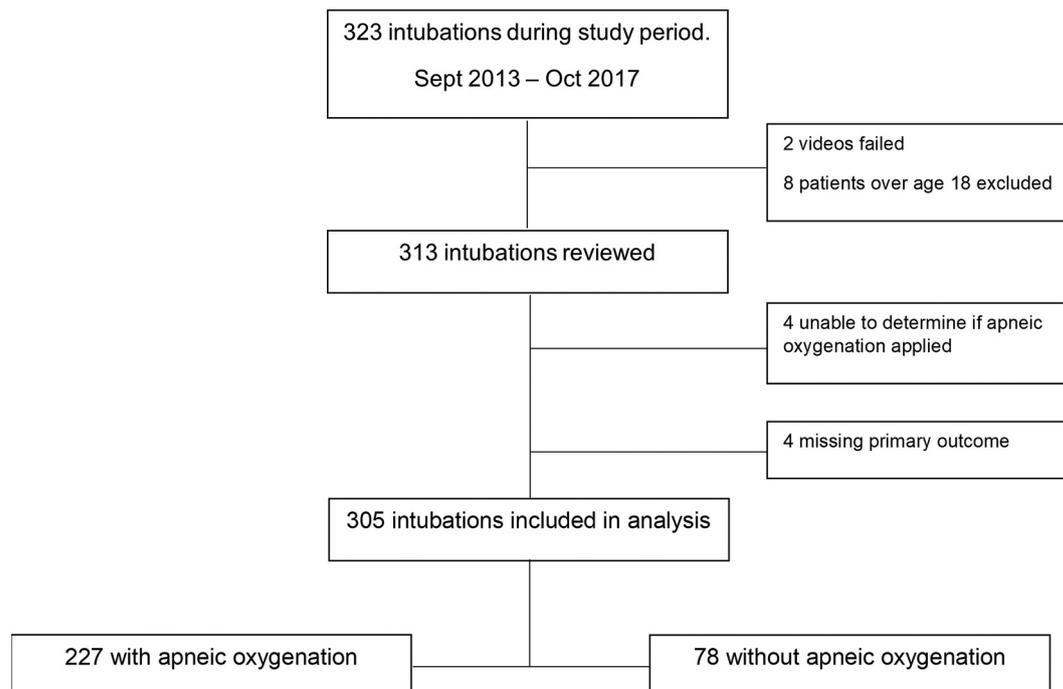
<sup>d</sup> Emergency medicine residents and pediatric residents.

<sup>e</sup> Cardiology faculty and otolaryngology residents.

<sup>f</sup> SpO<sub>2</sub> dropping to  $<90\%$ .

#### 3.3. Main outcome

Apneic oxygenation was applied for 227 of 305 study patients (74%). Fifty patients in the apneic oxygenation group had at least one episode of desaturation (22.0%, 95% CI 16.8%, 28.0%) compared with eleven of 78



**Fig. 1.** Flow diagram of patient inclusion and exclusion.

patients (14.1%, 95% CI 7.3%, 23.8%) in the group that did not receive apneic oxygenation (absolute difference 7.9%;  $p > 0.05$ ). Patient age and number of attempts were the only potential covariates with statistically significant bi-variable associations with desaturation. While controlling for age and attempt number, there remained no statistically significant association between apneic oxygenation and desaturation ( $p = 0.29$ ). We also controlled for sex, year, month, time of day, indication for intubation, and patient co-morbidity; there remained no association between apneic oxygenation and desaturation.

3.4. Additional outcomes

Table 2 shows the secondary, time-based outcomes for the 61 patients with at least one episode of desaturation, by apneic oxygenation group. Fig. 2 shows the distribution of time to each outcome across groups. None of the differences were statistically significant, in bi-variable analysis or when controlling for patient age and attempt number.

4. Discussion

In an observational, single center study of apneic oxygenation during RSI in a PED, we found no association with the prevention or delay of oxyhemoglobin desaturation. Study strengths include a large sample size for a single center, video-based data collection, standardized approach to apneic oxygenation, and a relatively standardized process of care for patients undergoing RSI, mitigating some of the risks of confounding by process variation.

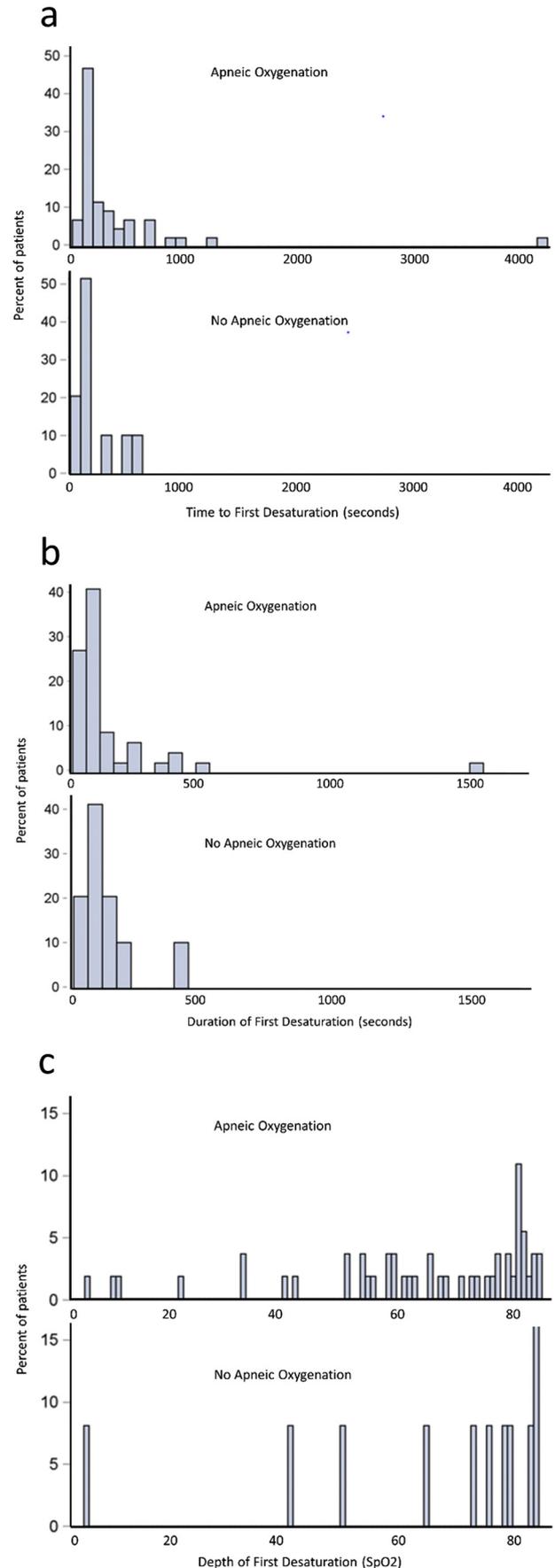
The benefits of apneic oxygenation during emergency intubation remain unclear. Early studies from the anesthesiology literature reported that apneic oxygenation considerably prolonged safe apnea time in healthy volunteers [34,35], and multiple systematic reviews of apneic oxygenation outside the operating room have generally found a small but significant reduction in the risk of desaturation. Oliveira et al. found apneic oxygenation to be associated with increased oxygenation, decreased incidence of desaturation episodes, and improved first attempt success [17], and White et al. concluded that apneic oxygenation was beneficial for patients undergoing elective surgery, obese patients, and emergent intubations for patients without respiratory failure [15]. The systematic reviews, however, were based largely on studies using chart review or self-report for data collection, less reliable methods for data collection during emergent intubation.

Two recent and prominent randomized controlled trials of apneic oxygenation in adult patients undergoing emergent intubation have called into question the benefits of apneic oxygenation. Semler et al. found no difference in desaturation for adults intubated in the ICU [22], and Caputo et al. found no benefit for adults undergoing RSI in the ED [21].

The literature on apneic oxygenation for children undergoing emergency intubation is very limited. Unique characteristics of pediatric airways and pulmonary function, as well as increased metabolic demand during critical illness and injury, make children a high-risk group for study [36,37]. Intubation of young children is known to be more difficult, requiring repeated and prolonged attempts, in turn increasing the amount of apneic time [4,38]. Apneic oxygenation may, therefore, be of special interest in pediatric patients. Vukovic et al. reported a

**Table 2**  
Secondary, time-based outcomes of interest for patients with oxyhemoglobin desaturation while undergoing rapid sequence intubation in a pediatric emergency department. Median seconds/SpO2 percentage [interquartile range] shown.

Characteristic	Apneic oxygenation	No apneic oxygenation	P-value
Time to desaturation	140 [108, 382]	125 [83, 272]	0.25
Duration of desaturation	52 [19, 115]	65 [30, 82]	0.53
Depth of desaturation (SpO2)	71 [56, 85]	79 [51, 87]	0.66



**Fig. 2.** Distribution of the time from initiation of the first attempt to desaturation event, duration of desaturation events, and depth of first desaturation event, each by main exposure (apneic oxygenation).

significant benefit of apneic oxygenation in the pediatric ED setting [25]. However, this study relied upon less optimal data collection methods and results may be biased by significant confounding factors between groups. Our study has limitations but utilizes video review and robust procedural RSI standards to evaluate the use of apneic oxygenation for pediatric patients undergoing emergent intubation in a PED.

#### 4.1. Limitations

Our study also has several important limitations. First, given its retrospective and observational nature, the selection of patients who received apneic oxygenation could not random and therefore significant bias was likely. For example, we found that presence of a non-PEM provider was associated with reduced use of apneic oxygenation, specifically for trauma patients. Trauma patients are generally older and have less acute and chronic lung disease, lowering their risk of desaturation. We conducted multivariable analyses to control for several known or potential covariates and found no association between apneic oxygenation and desaturation. We also considered the use of propensity scoring to further control for unmeasured confounders, but our sample size was not large enough.

Second, although our use of video review likely resulted in a more valid determination of whether apneic was used, we did not record the actual flow rate. Moreover, our selection of age-based flow rates was somewhat arbitrary, and we may have “under-dosed” flow rates to the point that we could not detect any treatment effect.

Finally, despite a relatively large sample size, our study was single center and conducted during an intense quality improvement initiative. It is possible that apneic oxygenation may be beneficial in the context of a less controlled RSI process, as our RSI improvement bundle likely reduced much of the procedural variation that leads to desaturation episodes.

#### 4.2. Future directions

If apneic oxygenation has any benefit for patients undergoing RSI, the available evidence suggests the effect size is small. Our study, given the risk of bias especially, is insufficient to support any clinical decision-making. What our study should make clear is that future studies of apneic oxygenation in children undergoing RSI should meet several criteria: [1] randomized and controlled, [2] multicenter to provide adequate power, [3] video-based data collection to maximize validity, especially for determining the use of apneic oxygenation and the occurrence and timing of desaturation events, and [4] sufficiently high flow rates to eliminate any chance that the “dosing” of oxygen was insufficient.

#### 4.3. Conclusion

In a video-based, observational study in an academic PED, the use of apneic oxygenation during RSI was not associated with a decrease in the incidence, duration, or depth of desaturation. Given the vulnerability of this patient group and the limited evidence base, a multicenter randomized trial, based on the most valid methods of data collection and focused on the most relevant outcomes, is critically needed.

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The authors have no conflicts of interest to disclose.

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