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Hypoxemia in Young Children Undergoing One-lung Ventilation: A Retrospective Cohort Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Current approaches to one-lung ventilation in children involve selective endobronchial intubation or use of a bronchial blocker

What This Article Tells Us That Is New

- In a retrospective multisite cohort study in children aged 2 months to 3 yr having one-lung ventilation for thoracic surgery, hypoxemia was common
- Bronchial blocker use as well as left-sided surgeries were associated with a lower risk of hypoxemia during one-lung ventilation

ABSTRACT

Background: One-lung ventilation in children remains a specialized practice with low case numbers even at tertiary centers, preventing an assessment of best practices. The authors hypothesized that certain case factors may be associated with a higher risk of intraprocedural hypoxemia in children undergoing thoracic surgery and one-lung ventilation.

Methods: The Multicenter Perioperative Outcomes database and a local quality improvement database were queried for documentation of one-lung ventilation in children 2 months to 3 yr of age inclusive between 2010 and 2020. Patients undergoing vascular or other cardiac procedures were excluded. All records were reviewed electronically for the presence of hypoxemia, oxygen saturation measured by pulse oximetry (Spo_2) less than 90% for 3 min or more continuously, and severe hypoxemia, Spo_2 less than 90% for 5 min or more continuously during one-lung ventilation. Records were also assessed for hypercarbia, end-tidal CO_2 greater than 60 mmHg for 5 min or more or a $Paco_2$ greater than 60 on arterial blood gas. Covariates assessed for association with these outcomes included age, weight, American Society of Anesthesiologists (Schaumburg, Illinois) Physical Status 3 or greater, duration of one-lung ventilation, preoperative Spo_2 less than 98%, bronchial blocker *versus* endobronchial intubation, left operative side, video-assisted thoracoscopic surgery, lower tidal volume ventilation (tidal volume less than or equal to 6 ml/kg plus positive end expiratory pressure greater than or equal to 4 cm H_2O for more than 80% of the duration of one-lung ventilation), and type of procedure.

Results: Three hundred six cases from 15 institutions were included for analysis. Hypoxemia and severe hypoxemia occurred in 81 of 306 (26%) patients and 56 of 306 (18%), respectively. Hypercarbia occurred in 153 of 306 (50%). Factors associated with lower risk of hypoxemia in multivariable analysis included left operative side (odds ratio, 0.45 [95% CI, 0.251 to 0.78]) and bronchial blocker use (odds ratio, 0.351 [95% CI, 0.177 to 0.67]). Additionally, use of a bronchial blocker was associated with a reduced risk of severe hypoxemia (odds ratio, 0.290 [95% CI, 0.125 to 0.62]).

Conclusions: Use of a bronchial blocker was associated with a lower risk of hypoxemia in young children undergoing one-lung ventilation.

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One-lung ventilation in children undergoing noncardiac surgery presents unique challenges that frequently require specialized equipment and creative solutions to achieve success. At this time, the infrequency of these cases at any one institution has limited our ability to perform prospective trials to compare the efficacy and risks of different devices and approaches. As a result, most of the primary literature on this topic is based on individual experience and single-center case series.[1–4] Further, there are little, if any, multicenter data to guide clinicians in terms of best practices. Current approaches to one-lung ventilation in this age group involve endobronchial intubation or use of a bronchial blocker.[5,6] Currently, there exist almost no data to support the use of one approach or the other in terms of reducing the risk of hypoxemia or other long-term outcomes. In most cases, the approach to one-lung ventilation is based on local preference or technical expertise rather than a choice based on an assessment of the risks and benefits of

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choosing one approach *versus* the other. It is conceivable that technical and physiologic differences in the approach to one-lung ventilation may affect hypoxic vasoconstriction, or incomplete ventilation of the dependent lung may contribute to increased rates of hypoxemia. Additionally, there are little data, and certainly no multicenter data, on what other factors such as age, side of surgery, or lower tidal volume ventilation increase the risk of intraoperative hypoxemia to further stratify risk.

In the modern era, a number of organizations have attempted to create larger multicenter databases to further stratify risk and evaluate best practices. The Multicenter Perioperative Outcomes Group (MPOG) is a national multicenter collaborative that is designed to leverage data, including vital signs, medications, ventilation parameters, and other perioperative information from multiple centers to examine questions of safety, risk, and best practices in anesthesia in ways that were not previously possible.[7–9]

Therefore, the primary aim of this study was to assemble a larger multicenter cohort to assess the incidence of hypoxemia in young children undergoing one-lung ventilation, and whether specific factors including the choice of approach to one-lung ventilation (endobronchial intubation *vs*. use of a bronchial blocker) may be associated with a higher risk of hypoxemia during one-lung ventilation in young children undergoing noncardiac thoracic procedures. Finally, we hypothesize that endobronchial intubation is associated with a higher risk of hypoxemia in children undergoing surgery and one-lung ventilation.

Materials and Methods

Human Subjects Protection

Institutional review board approval was obtained from each organization to contribute a limited dataset to the Multicenter Perioperative Outcomes Group central repository (HUM00024166; University of Michigan, Ann Arbor, Michigan). An additional approval by the institutional review board of Wake Forest University Health Sciences (Winston-Salem, North Carolina) was obtained for the conduct of this retrospective, observational cohort study, utilizing the Multicenter Perioperative Outcomes Group limited dataset (IRB28691) as well as local cases that were performed at Wake Forest University before participation in the Multicenter Perioperative Outcomes Group (IRB66373). Local case data were de-identified before merging with the Multicenter Perioperative Outcomes Group derived dataset. The Strengthening The Reporting of OBservational Studies in Epidemiology checklist was used in preparing this manuscript.

Data Source

The central Multicenter Perioperative Outcomes Group database and our local electronic health record system were queried initially. All manual reviews were performed using the Multicenter Perioperative Outcomes Group Case Reviewer Module for cases identified from the Multicenter Perioperative Outcomes Group dataset. Local cases not included in the dataset were manually reviewed using our local electronic health record case viewer.

Patients

Patients 2 months to 3 yr of chronologic age inclusive undergoing noncardiovascular thoracic surgery with one-lung ventilation were included. Surgical or anesthetic current procedural terminology codes were used initially to query the Multicenter Perioperative Outcomes Group databases for cases likely to meet criteria for inclusion. These included 32601, 32661, 32662, 32663, 32652, 32650, 32666, 32667, and 32100. Additionally, all cases with documentation of one-lung ventilation using either a free-text note or one-lung ventilation start or stop were also included.

Exclusions

Children less than 2 months of age were excluded to avoid selection bias as a number of neonatal surgical repairs including trachea-esophageal repairs as well as congenital diaphragmatic hernia repairs are typically performed in this time period and represent a subset of patients distinct in many ways from patients undergoing more routine thoracic procedures. Patients 4 yr of age or older as well as those who were American Society of Anesthesiologists (ASA; Schaumburg, Illinois) Physical Status V or VI were excluded. Premature infants 2 months of age and older were included if their chronologic age was at least 2 months of age at the time of surgery. Patients undergoing any thoracic cardiovascular procedure such as patent ductus arteriosus ligation, coarctation repair, or repair of vascular ring were excluded. Patients with cyanotic congenital heart disease and any patient with an initial room air oxygen saturation measured by pulse oximetry (Spo_2) less than 94% were excluded. Patients who had one-lung ventilation for less than 10 min were also excluded.

All cases were evaluated for the presence of the following data: Spo_2 every 1 min, end-tidal carbon dioxide ($ETco_2$) at least every 15 min, and arterial blood gas data during one-lung ventilation. Cases missing more than 20% of the oxygen saturation data were excluded. In cases where less than 20% of the Spo_2 or $ETco_2$ values were missing, the values were imputed using the last value carried forward approach.

Outcome Measures

The primary outcome was the occurrence of at least one episode of hypoxemia, which was defined as a continuous oxygen desaturation less than 90% for 3 min or more during the period of one-lung ventilation. The primary outcome of oxygen desaturation less than 90% was determined before analysis during project development *via* a poll and general consensus of all members of the Multicenter

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Perioperative Outcomes Group research committee as being sufficiently clinically relevant to warrant concern or possible intervention. While any threshold will be arbitrary to an extent, many studies looking at perioperative respiratory adverse events have defined hypoxemia much more liberally.[10–13] Secondary outcomes included the occurrence of severe hypoxemia and hypercarbia. Severe hypoxemia was defined as a continuous oxygen desaturation less than 90% for 5 min or more during one-lung ventilation. Hypercarbia was defined as an $ETCO_2$ greater than 60 mmHg for 5 min or more or $PaCO_2$ greater than 60 mmHg on arterial blood gas during one-lung ventilation.

Covariates

All records were reviewed for the following covariates: preoperative room air oxygen saturation less than 98%, age, weight, endobronchial intubation *versus* bronchial blocker, type of procedure, open *versus* video-assisted thoracoscopic surgery, weight, ASA Physical Status classification III or greater, left- *versus* right-sided procedure, the presence of lower tidal volume ventilation defined as tidal volume 6 ml/kg or less, and at least 4 cm H_2O of positive end-expiratory pressure for at least 80% of the duration of one-lung ventilation, and the overall duration of one-lung ventilation in hours. The procedures were broken down into four classes: resection of pulmonary lesion, decortication and pleurodesis, mediastinal procedures, and other. Variables of age, weight, and one-lung ventilation duration were treated as continuous independent variables.

Many of these covariates were selected as possible predictors as a result of previous work demonstrating their relevance to pulmonary outcomes in pediatric patients. Accordingly, they may be relevant in the setting of one-lung ventilation. Age was selected because younger patients have higher oxygen requirement and less pulmonary reserve and therefore may be at increased risk of hypoxemia.[14] Low tidal volume ventilation was selected because of recent research in adults and a study by Lee *et al.* in children in which lower tidal volume ventilation was associated with lower rates of hypoxemia and better pulmonary outcomes in patients undergoing one-lung ventilation.[15–17] Use of a bronchial blocker *versus* endobronchial intubation was selected as a covariate because these two techniques represent vastly different approaches to one-lung ventilation that may have different risk profiles.[18] Other covariates such as type of procedure, surgical side, and open *versus* video-assisted thoracoscopic surgery were selected as intuitively these may also have an impact on the risk of intraprocedural hypoxemia.

Out of concern that institution might play a larger confounding role than initially anticipated, an anonymous center code for each institution contributing cases was also collected. To be considered as a case in which a bronchial blocker was used, explicit documentation of bronchial blocker placement or mention of the use of a bronchial blocker was deemed necessary. All other cases with documented one-lung ventilation that did not specifically mention endobronchial or mainstem intubation were considered cases of endobronchial intubation. In cases where individual covariates could not be determined *via* electronic review of the case record, cases were manually reviewed to determine if the missing covariate could be deciphered. Cases in which one or more covariates were missing and could not be determined after manual review were excluded from the analysis.

One-lung Ventilation Time

The period of one-lung ventilation for the purposes of analysis was considered as the period of time from the start of one-lung ventilation to the end of one-lung ventilation. In cases where the initial start time was documented but a specific end time was not, the records were manually reviewed to determine a plausible one-lung ventilation end time. In all these cases, the one-lung ventilation end time was determined, looking for significant and consistent changes in three different parameters: fraction of inspired oxygen (FIO_2), $ETCO_2$, and tidal volume. In many cases, FIO_2 was typically greater than 90% during one-lung ventilation but was frequently reduced toward the end of the procedure, presumably upon the reinitiation of two-lung ventilation, and then increased again at the point of extubation. $ETCO_2$ data were also reviewed, and frequently an elevated $ETCO_2$ would fall fairly precipitously toward the end of the procedure to a more consistent level closer to 40 mmHg. Finally, tidal volume data were also examined for abrupt and consistent increases toward the end of a given procedure. In all cases, the anticipated change was present in at least one of these parameters, and in many cases, it was present in more than one, further corroborating the likelihood that a reasonable estimate of the end of one-lung ventilation had been made. The total number of cases where an end time was manually derived was 82, and a sensitivity analysis based on the exclusion of these cases for the primary outcome was performed.

In cases where there was an end time for one-lung ventilation but no documented start time, each case was manually reviewed for rapid increases in FIO_2 to greater than 90% or abrupt and consistent reductions in tidal volume in proximity to surgical incision or a note indicating endobronchial intubation. In cases where we could not confidently establish a start time based on these parameters, the procedure start time was used as the one-lung ventilation start time. The total number of cases where a start time was manually derived was four.

In cases where there was more than one period of one-lung ventilation, the case was reviewed manually to determine the primary period of one-lung ventilation, which was frequently the longest as well as the first period of one-lung ventilation, although this was not universally true. If there were two lengthy but separate periods of one-lung ventilation documented separated by a short time period,

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typically less than 5 min, these periods were collapsed into a single time epoch. If the two epochs were separated by a longer period of time, only the first epoch was used for analysis. This occurred in a very small minority of patients.

Conversion to Open Thoracotomies or Open Surgeries

In four instances, a video-assisted thoracoscopic surgery case was converted to open thoracotomy or open surgery. In these situations, the case was considered video-assisted thoracoscopic surgery for the purposes of the analysis, and one-lung ventilation was considered to have ended at the point of conversion to open.

Missing Data, Artifact, and Dataset Validation

In cases where less than 20% of the physiologic data such as Spo_2 or ventilator parameters were missing, we first attempted to manually review the record to determine if the data could be retrieved or further clarified. *A priori*, in cases in which these data could not be retrieved, the last value carried forward approach to imputation was planned, recognizing that this might lead to an overestimate of the number of cases with the chosen outcomes. After electronic and manual review of cases, we found 65 of 306 (21.2%) cases with at least one gap in the Spo_2 data greater than 1 min during one-lung ventilation. One of these cases had an instance of an Spo_2 less than 90% followed by a gap in data that led to a hypoxic event. Overall, more than 99% of the Spo_2 data during one-lung ventilation were available when examining the entire dataset. In 15 cases, $ETco_2$ was only recorded at 15-min intervals. These values during one-lung ventilation were again imputed using the last value carried forward approach. Weight was missing in seven cases and was imputed using the 50th percentile weight for age and gender based on the Centers for Disease Control and Prevention (Atlanta, Georgia) growth charts. Extreme or implausible physiologic or ventilator data values were rare during one-lung ventilation and were manually or electronically reviewed. Any Spo_2 greater than 100% was adjusted to 100%. Tidal volumes in excess of 14 ml/kg were excluded. All tidal volumes less than 14 ml/kg were included in the analysis. $ETco_2$ values greater than 150 mmHg or less than 15 mmHg during one-lung ventilation were excluded as implausible. Overall data validity and fidelity within the Multicenter Perioperative Outcomes Group limited dataset have been previously demonstrated in a number of other previously published reports.[7–9] Additionally, *post hoc*, a random sampling of 20% of records were re-reviewed manually against the actual case record to further validate the accuracy of both covariates and outcomes used for analysis.

Practice Trends

Given a lack of standard practice guidelines in these less frequent cases, the dataset was evaluated for current trends in terms of ventilation parameters during one-lung ventilation. These included the following: Fio_2, tidal volume, positive end-expiratory pressure, peak inspiratory pressure, and $ETco_2$.

A Priori Sample Size Analysis

Given the rarity of these cases, we planned to use all available cases meeting inclusion criteria within our local registry and the Multicenter Perioperative Outcomes Group database. An initial query at the time of project development indicated there might be between 250 and 350 cases available, generating between 60 and 120 events based on analysis of local data. Assuming a 30% event rate, a sample size of 300 would give us an 80% power at the 0.05 significance level to detect a minimal odds ratio of 2.01 or larger using chi-square analysis.

Statistical Analysis

A data analysis and statistical plan was written and filed with the Multicenter Perioperative Outcomes Group perioperative clinical research committee before the data were accessed. The frequency as well as 95% CI of hypoxemia, significant hypoxemia, and hypercarbia, and other planned observational outcomes were tabulated. All categorical covariates were evaluated initially using the chi-square test to determine their association with the outcome of hypoxemia at a univariate level. In any case where the cell count was less than 5, a Fisher exact test was used. Normal data distribution was evaluated using the Shapiro–Wilk normality test and Kolmogorov–Smirnov goodness-of-fit test. Normally distributed data are presented as mean ± SD, and nonnormally distributed data are presented as median and interquartile range. Normally distributed continuous covariates were compared at the univariate level using an independent, two-sample, two-tailed *t* test. If they were not found to be normally distributed, a Mann–Whitney U test was used for comparison of nonparametric data. We did not correct for multiple hypothesis testing in the univariate analysis because we have fewer than four dependent outcome variables and because we had decided *a priori* to create a multivariable logistic regression model to ultimately assess the effect size associated with each covariate. Significance for the univariate analysis was established at $P < 0.05$.

Due to the expected small sample size and infrequency of the primary outcome, we expected fewer than 100 patients demonstrating the primary outcome. This number appeared to be conservative given the 11 covariates being evaluated at 10 events per predictor. As a result, *a priori*, all covariates were placed into a least absolute shrinkage and selection operator logistic regression model with hypoxemia, as defined in Outcome Measures, as the primary outcome.[19,20] Model overfitting and smaller sample size relative to the number of covariates were also addressed using the least absolute shrinkage and selection operator approach for regularization. The lambda values used for analysis

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ranged from 0.00001 to 0.05. The optimal lambda value is stated in the individual analyses. Additionally, we internally validated the least absolute shrinkage and selection operator model using 10-fold cross-validation to ensure that the model performed well across randomly selected validation samples from the dataset. Covariates were also evaluated using the least absolute shrinkage and selection operator approach to create a multivariable model insofar as they had the ability to predict secondary outcomes, including severe hypoxemia and hypercarbia as defined in Outcome Measures. Similar procedures for internal validation were upheld. Collinearity was evaluated by calculating a variance inflation factor for each covariate in the model. If a variance inflation factor in excess of 10 was found, one of the colinear covariates was removed. Age and weight were the only covariates found to be colinear; therefore, weight was removed from the analysis. A *post hoc* Kaplan–Meier analysis of the timing of hypoxemia was also performed to further assess the timing of hypoxemic events in patients undergoing one-lung ventilation with a bronchial blocker *versus* endobronchial intubation.

Additionally, two sensitivity analyses were performed to evaluate whether institution or manually derived one-lung ventilation start and stop time would affect the results. In the case of institution, another model using least absolute shrinkage and selection operator regression including institution as a covariate with the other previously mentioned covariates was created to assess its association with hypoxemia as previously defined to reduce selection bias. In another separate least absolute shrinkage and selection operator regression analysis, cases with manually derived start and stop times were removed from the analysis to determine if this also would affect the results with regard to the primary outcome, hypoxemia, to reduce information bias. Finally, a *post hoc* analysis of model calibration for the outcome, hypoxemia, was also performed.

Statistical analyses were performed in R v3.6.1 (R Foundation for Statistical Computing, Austria) using RStudio environment v1.1.456 (RStudio, USA).

Results

Patients

An initial query of the Multicenter Perioperative Outcomes Group database using current procedural terminology codes and concept identifiers and age restrictions returned 499 patients from 15 different institutions. Additionally, a query of a local registry of one-lung ventilation cases meeting inclusion criteria from 2012 to 2017, and not uploaded to the Multicenter Perioperative Outcomes Group database, yielded an additional 25 cases for analysis. The 499 cases returned from the Multicenter Perioperative Outcomes Group database were then reviewed, yielding 338 cases meeting inclusion criteria. Fourteen cases were then excluded for one or more missing covariates, while 18 were excluded for lack of Spo_2 or ventilatory data. This yielded 306 cases for analysis when combined with the 25 additional cases from our local registry. This is summarized in figure 1.

Outcomes

The prevalence of hypoxemia was 81 of 306 (26% [95% CI, 21 to 31%]). The presence of severe hypoxemia was 56 of 306 (18% [95% CI, 14 to 22%]). The prevalence of hypercarbia was 153 of 306 (50% [95% CI, 44 to 56%]). The majority of hypoxemic events occurred within the first 90 min of one-lung ventilation (Supplemental Digital Content 1, http://links.lww.com/ALN/C681). Additionally, the median number of hypoxemic events per case in which at least one hypoxemic event occurred was three (range, one to eight).

Univariate Analysis

Increasing one-lung ventilation duration was associated with a 23% increase per hour in the risk of hypoxemia. Other factors associated with hypoxemia included right-sided cases and the use of endobronchial intubation as the lung isolation technique. Younger age was associated with an increased risk of hypoxemia. These results are summarized in table 1.

Multivariable Analysis of Hypoxemia and Severe Hypoxemia

The multivariable analysis included all covariates from the univariate analysis, although several beta coefficients were reduced to 0 by the least absolute shrinkage and selection operator regression. This analysis echoed in many ways the results found at the univariate level, although there were a few notable differences. These findings are summarized in table 2. Right-sided surgeries and endobronchial intubation continued to be significantly associated with the outcome of hypoxemia, while the use of a bronchial blocker and left-sided cases appears to be protective. Lower tidal volume ventilation, type of surgery, lower preoperative Spo_2, and younger age were not associated with an increased risk of hypoxemia or severe hypoxemia. Additionally, the use of a bronchial blocker was associated with a lower risk of severe hypoxemia. Figure 2A summarizes these findings in relation to severe hypoxemia.

Two different sensitivity analyses, including institution as a covariate for the primary outcome of hypoxemia and another excluding cases for which the start or end times were manually derived, did not substantially change the results. The association of left-sided cases with a lower risk of hypoxemia did not achieve statistical significance in the analysis, which excluded cases with manually derived start and stop times. However, the use of a bronchial blocker continued to achieve significance and be associated with a lower risk of hypoxemia in both analyses. These results are presented in Supplemental Digital Content 2 (http://links.lww.com/ALN/C682) and 3 (http://links.lww.com/ALN/C683). Finally, a *post hoc* analysis of model calibration across all institutions for hypoxemia demonstrated

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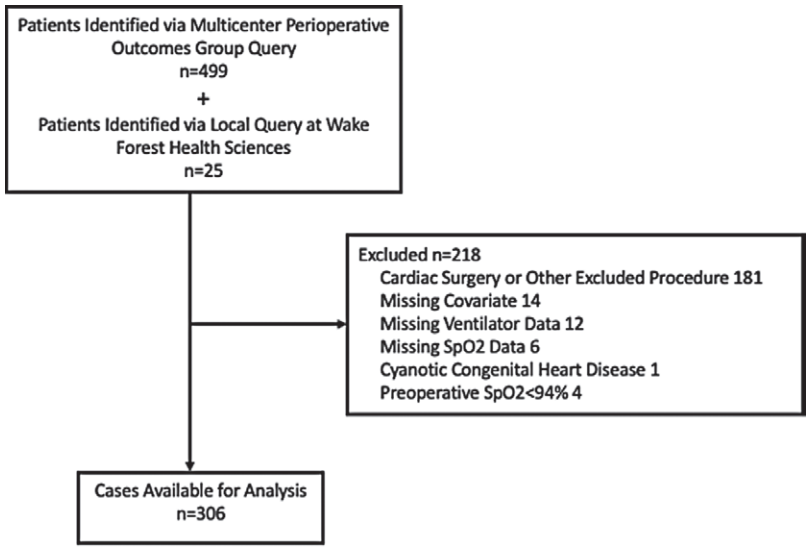

Fig. 1. Flow chart of cases from initial query using current procedural terminology codes and Multicenter Perioperative Outcomes Group concept identifiers for one-lung ventilation to those available for analysis. Spo_2, oxygen saturation measured by pulse oximetry.

reasonable predictive accuracy. A composite line of calibration curves for all centers is presented in Supplemental Digital Content 4 (http://links.lww.com/ALN/C684).

Multivariable Analysis of Hypercarbia

Lower tidal volume ventilation, preoperative Spo_2 less than 98%, video-assisted thoracoscopic surgery, and increasing one-lung ventilation duration were associated with hypercarbia. The use of a bronchial blocker was also associated with a lower risk of hypercarbia. Age and laterality were not associated with a higher risk of hypercarbia. These findings are summarized in figure 2B.

Bronchial Blocker *versus* Endobronchial Intubation

Consistently, the use of a bronchial blocker as the lung isolation technique appears to be associated with a lower risk of both hypoxemia and severe hypoxemia. There were six institutions that did not use bronchial blockers in any case. The distribution of left- or right-sided cases, age, and weight appear to be fairly equivalent between patients in whom a bronchial blocker was used and those that employed endobronchial intubation. Additionally, 23 of 64 (36%) and 7 of 17 (41%) hypoxic events for endobronchial intubation and bronchial blocker, respectively, occurred in left-sided surgeries. Interestingly, patients in whom a bronchial blocker was used for lung isolation appear overall to have an increased proportion of ASA Physical Status III or greater than those who underwent endobronchial intubation. Endobronchial intubation was also used with greater frequency in video-assisted thoracoscopic surgery cases. A comparison of various case and procedure characteristics by isolation approach (bronchial blocker *vs.* endobronchial intubation) is summarized in table 3. Additionally, a *post hoc* Kaplan–Meier analysis of hypoxemia demonstrated that hypoxemia occurred earlier and more often in patients in whom endobronchial intubation was used (fig. 3).

Additional Clinical Observations in One-lung Ventilation in Young Children

Overall, cases using a bronchial blocker utilized a lower median Fio_2 when compared to cases in which endobronchial intubation was used. Tidal volume and other ventilatory parameters do not appear to differ significantly based on side or approach to lung isolation. These findings are summarized in table 4. Finally, there was one documented instance of the use of continuous positive airway pressure *via* a bronchial blocker to the nonventilated lung in response to hypoxemia.

Discussion

In this retrospective cohort analysis, there were several important findings. The first was that hypoxemia and severe hypoxemia were relatively common in children undergoing one-lung ventilation. Additionally, the use of a bronchial blocker as well as left-sided surgeries were associated with a lower risk of hypoxemia during one-lung ventilation. Finally, the risk of hypoxemia did not appear to be associated with lower tidal volume ventilation, younger age, lower preoperative Spo_2, or increased duration of one-lung ventilation after controlling for other factors.

The risk of hypoxemia in adults undergoing one-lung ventilation and surgery has been reported to be around 4%.[21] Clearly, the risk of hypoxemia and severe hypoxemia

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Table 1. Univariate Analysis of Risk Factors for Hypoxemia (Spo_2 Less than 90% for 3 Min or More Continuously) in Young Children Undergoing Thoracic Surgery and One-lung Ventilation

	No Hypoxemia, n = 225	Hypoxemia, n = 81	Odds Ratio	95% CI	*P* Value
Age, yr, median [interquartile range]	0.75 [0.50–1.67]	0.67 [0.42–1.17]	0.64	0.43–0.94	0.027
Weight, kg, median [interquartile range]	9.0 [7.5–11.5]	8.5 [7.1–10.5]	0.92	0.83–1.01	0.082
ASA Physical Status III or IV, n (%)	98 (43.6)	27 (33.3)	0.65	0.377–1.10	0.110
Left-sided cases, n (%)	119 (52.9)	30 (37.0)	0.52	0.309–0.88	0.015
One-lung ventilation duration, h, median [interquartile range]	2.67 [1.80–3.75]	3.42 [2.32–4.43]	1.23	1.04–1.45	0.013
Bronchial blocker, n (%)	90 (40.0)	17 (21.0)	0.398	0.214–0.71	0.003
Preoperative Spo_2 < 98% n (%)	32 (14.2)	16 (19.8)	1.485	0.75–2.85	0.243
Lower tidal volume ventilation, n (%)	39 (17.3)	20 (24.7)	1.564	0.84–2.86	0.152
Video-assisted thoracoscopic surgery, n (%)	164 (72.9)	56 (69.1)	0.833	0.48–1.47	0.519
Type of surgery*					
1	163 (72.4)	73 (90.1)			
2	3 (1.3)	0 (0.0)	Unable to calculate odds ratio because there were no instances of hypoxemia in surgical type 2	Unable to calculate odds ratio because there were no instances of hypoxemia in surgical type 2	Unable to calculate odds ratio because there were no instances of hypoxemia in surgical type 2
3	28 (12.4)	3 (3.7)	0.239	0.056–0.70	0.022
4	31 (13.8)	5 (6.2)	0.36	0.119–0.89	0.042

*Type of surgery: 1, pulmonary wedge or lobe resection; 2, pleurodesis or decortication; 3, mediastinal surgery; 4, other. Surgery type 1 used as reference to estimate other odds ratios.
ASA, American Society of Anesthesiologists; Spo_2, oxygen saturation measured by pulse oximetry.

appear to be significantly higher in young children. The etiology of this is likely multifactorial. In the lateral position, the smaller hydrostatic gradient present in children reduces preferential perfusion of the ventilated lung in comparison to adults leading to additional shunt.[22,23] Additionally, the increased compliance of the rib cage leads to reduced dependent lung volume.[5] These factors, combined with the increased rate of oxygen consumption and technical issues associated with lung isolation in small children, likely contribute to this increased risk of hypoxemia.

Table 2. Multivariable Least Absolute Shrinkage and Selection Operator Regression Analysis of Risk Factors for Hypoxemia (Spo_2 Less than 90% for 3 Min or More Continuously) in Young Children Undergoing Thoracic Surgery and One-lung Ventilation

	Odds Ratio	95% CI	*P* Value
Age, yr	0.78	0.49–1.21	0.278
ASA Physical Status III or IV	*	—	—
Left-sided cases	0.45	0.251–0.78	0.005
One-lung ventilation duration, h	1.17	0.98–1.41	0.085
Bronchial blocker	0.351	0.177–0.67	0.002
Preoperative Spo_2 < 98	1.78	0.81–3.85	0.143
Lower tidal volume ventilation	1.91	0.96–3.78	0.062
Video-assisted thoracoscopic surgery	0.68	0.358–1.32	0.249
Type of surgery			
1	2.23	0.80–7.3	0.148
2	*	—	—
3	0.295	0.064–0.97	0.986
4	0.45	0.137–1.25	0.986

Type of surgery: 1, lung wedge or lobe resection; 2, pleurodesis or decortication; 3, mediastinal surgery; 4, other. The optimal lambda value was determined to be $\lambda = 0.0167$ with an alpha value of 1.

*Covariate beta coefficient reduced to 0 by least absolute shrinkage and selection operator regression method.

ASA, American Society of Anesthesiologists; Spo_2, oxygen saturation measured by pulse oximetry.

At the outset, it is not immediately obvious why use of a bronchial blocker would be associated with a lower risk of hypoxemia, although this is consistent with the randomized trial by Yan *et al.* in which they compared the use of a bronchial blocker to endobronchial intubation in young children.[18] Not surprisingly, endobronchial intubation was used almost twice as often as bronchial blockers to institute one-lung ventilation in this cohort of patients from both private and academic centers. We speculate that this is likely related to greater technical ease in terms of execution, but this may come at a cost. Precise depth of placement of an endotracheal tube can be challenging in young children and infants, even with the use of a flexible fiberoptic bronchoscope. In right-sided endobronchial intubations, frequently the right upper lobe takeoff is less than 1 cm from the carina, making the margin of error for correct placement very small and the chance of excluding the entire right upper lobe fairly high.[24] Additionally, sometimes there is an incomplete seal at the level of the bronchus in the setting of endobronchial intubation, which may lead to the leakage of serosanguineous debris and secretions from the operative side to the dependent lung. These secretions can cause partial and sometimes complete obstruction of the endotracheal tube.[5] Bronchial blockers, when used correctly, should completely occlude

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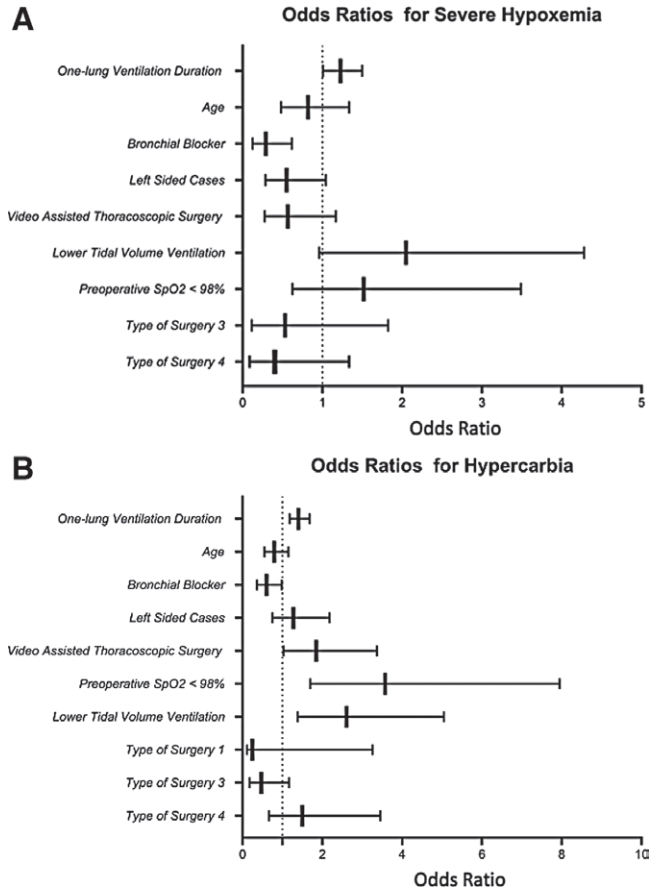

Fig. 2. Odds ratios from least absolute shrinkage and selection operator regression analysis for severe hypoxemia and hypercarbia. (*A*) Beta coefficients for American Society of Anesthesiologists Physical Status greater than or equal to III and surgery types 1 and 2 were set to 0 by least absolute shrinkage and selection operator regression for severe hypoxemia. (*B*) American Society of Anesthesiologists Physical Status greater than or equal to III and surgery type 2 were eliminated in least absolute shrinkage and selection operator regression for hypercarbia. Type of surgery: 1, lung wedge or lobe resection; 2, pleurodesis or decortication; 3, mediastinal surgery; 4, other. Spo_2, oxygen saturation measured by pulse oximetry.

the mainstem bronchus as the balloon cuff conforms to the shape of the bronchus, preventing leakage of debris into the ventilated side. Also, complete occlusion of the operative lung *via* the occlusive balloon of the bronchial blocker may enhance hypoxic vasoconstriction as no air is entering the operative lung, thus improving ventilation/perfusion matching overall. Finally, although it was not documented, it is possible that some clinicians insufflated oxygen through the central lumen present in some bronchial blockers, which may have reduced the risk of hypoxemia in these patients.

Another finding in this study was the reduced risk of hypoxemia in left-sided surgeries. This reduced risk in left-sided procedures appeared to be independent of the approach to isolation and one-lung ventilation. In fact, the lower rates of hypoxemia in left-sided procedures were similar: 41% *versus* 36% in patients who received a bronchial blocker and those that underwent endobronchial intubation, respectively. Thus, left-sided endobronchial intubation appears to be associated with a higher risk of hypoxemia when compared to right-sided endobronchial intubation. This is somewhat counterintuitive. Given the small margin of correct placement when performing a right-sided endobronchial intubation, it seems intuitive that it would be easier to exclude the right upper lobe from gas exchange as previously stated, leading to an increased risk of hypoxemia.[24] Alternatively, perhaps deep positioning of the endotracheal tube within the left mainstem bronchus leads to exclusion of the left upper lobe, and the smaller amount of lung tissue in the left lower lobe is not able to adequately compensate when compared to the right middle and lower lobes when the right upper lobe is excluded.

Finally, there are several descriptive practice observations worth noting. Interestingly, the median Fio_2 used in cases

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Table 3. Direct Comparison between Endobronchial Intubation and Bronchial Blocker in Children Undergoing Thoracic Surgery and One-lung Ventilation

	Endobronchial Intubation, n = 199	Bronchial Blocker, n = 107	*P* Value
Age, yr, median [interquartile range]	0.67 [0.50–1.33]	0.75 [0.46–1.67]	0.447
Weight, kg, median [interquartile range]	8.9 [7.4–11.2]	8.8 [7.3–11.3]	0.757
ASA Physical Status III or IV, n (%)	68 (34.2)	57 (53.3)	0.002
Left-sided surgeries, n (%)	99 (49.7)	50 (46.7)	0.701
One-lung ventilation duration, h, median [interquartile range]	2.99 [2.03–4.09]	2.65 [1.64–3.69]	0.039
Preoperative Spo_2, median [interquartile range]	100 [98–100]	99 [98–100]	0.022
Preoperative Spo_2 < 98%, n (%)	27 (13.6)	21 (19.6)	0.221
Lower tidal volume ventilation, n (%)	36 (18.1)	23 (21.5)	0.570
Video-assisted thoracoscopic surgery, n (%)	158 (79.4)	62 (57.9)	< 0.001
Type of surgery, n (%)			
1	161 (80.9)	75 (70.1)	
2	2 (1.0)	1 (0.9)	
3	15 (7.5)	16 (15.0)	
4	21 (10.6)	15 (14.0)	
Institutional identifier, n (% of cases at institution)			
10	4 (2.0)	14 (13.1)	
13	5 (2.5)	0 (0.0)	
15	4 (2.0)	3 (2.8)	
16	1 (0.5)	0 (0.0)	
18	25 (12.6)	1 (0.9)	
19	45 (22.6)	31 (29.0)	
27	7 (3.5)	31 (29.0)	
39	21 (10.6)	1 (0.9)	
42	10 (5.0)	0 (0.0)	
46	8 (4.0)	0 (0.0)	
47	1 (0.5)	0 (0.0)	
48	14 (7.0)	23 (21.5)	
5	4 (2.0)	0 (0.0)	
53	48 (24.1)	0 (0.0)	
7	2 (1.0)	3 (2.8)	
Outcomes, n (%)			
Hypoxemia	64 (32.2)	17 (15.9)	0.003
Severe hypoxemia	46 (23.1)	10 (9.3)	0.005
Hypercarbia	99 (49.7)	54 (50.5)	0.932

Comparisons made using chi-square or Mann–Whitney U test.

ASA, American Society of Anesthesiologists; Spo_2, oxygen saturation measured by pulse oximetry.

employing endobronchial intubation was higher than that observed in cases where a bronchial blocker was used. This aligns with the above finding that the use of a bronchial blocker appears to be associated with a lower incidence of hypoxemia. In terms of mechanical ventilation practices, median tidal volumes and peak inspiratory pressures appeared to be fairly equivalent across operative side and approach to one-lung ventilation. Type of surgery, generally, does not appear to affect the risk of hypoxemia.

Limitations

The major limitation of this study was that, despite the size of the Multicenter Perioperative Outcomes Group database, these cases still remain relatively rare; therefore, the sample size still remains fairly small. There were, however, clinically relevant findings that achieved significance at the multivariable level. Another limitation of this study was its retrospective nature, which led to some cases being excluded for missing data, creating a risk of selection bias. However, there is no reason to suspect that missing data were not missing at random. Additionally, while some centers did not use bronchial blockers at all, the institutional effect did not achieve significance in terms of the outcome of hypoxemia *via* our sensitivity analysis (Supplemental Digital Content 2, http://links.lww.com/ALN/C682). This is further amplified by the fact that there were actually only three centers where bronchial blockers were used in a majority of cases. Finally, while specific centers may have contributed larger volumes of cases when compared to others, and therefore may theoretically have increased expertise as a result of this increased frequency, this did not appear to have a large enough effect on the outcome of hypoxemia to be detected. Finally, our categorization of cases where the use of a bronchial blocker was not accurately documented may

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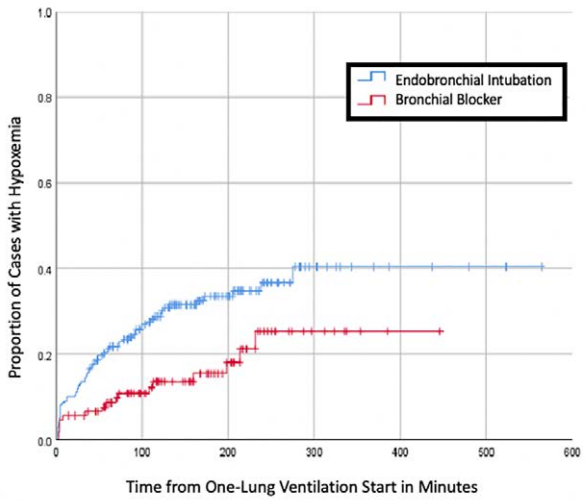

Fig. 3. Kaplan–Meier analysis of hypoxemia. The occurrence of the first episode of the primary outcome of hypoxemia defined as an episode of oxygen desaturation less than 90% for 3 min or more is presented with respect to time from the point of initiation of one-lung ventilation for bronchial blocker (*red*) and endobronchial intubation (*blue*). Hypoxemia occurred earlier and in a larger proportion of patients who underwent endobronchial intubation.

have led to a misclassification of a minority of cases that could have affected our results. However, all cases included for analysis were manually and electronically reviewed for the use of a bronchial blocker, and in all cases, an airway note or some other documentation of airway management was present. Given the investment in time, equipment, and effort to use a bronchial blocker in a young child, it seems unlikely that the use of a bronchial blocker would simply have been omitted in this documentation, although this remains possible.

Conclusions

In summary, children appear to be at higher risk of hypoxemia than adults when undergoing one-lung ventilation. Additionally, the use of a bronchial blocker appears to be associated with a lower risk of hypoxemia and severe hypoxemia despite being used in a minority of cases in this cohort. Clinicians must, however, exercise extreme caution and strongly consider the risks and benefits of changing their practice based on these findings as this association should not be taken as evidence of causation.[25] More prospective studies in the form of a trial comparing rates of hypoxemia in patients in whom a bronchial blocker is used compared to those in whom endobronchial intubation is employed should likely be performed to further clarify possible causation and potentially guide future practice.

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Competing Interests

The authors declare no competing interests.

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Table 4. Observational Ventilatory and Respiratory Data by Side and Device

	Operative Side	$ETco_2$, mmHg	Tidal Volume, ml/kg	Peak Inspiratory Pressure, cm H_2O	PEEP, cm H_2O	Fio_2, %
Bronchial blocker	Left, n = 50	48 (40–55)	6.5 (4.9–8.3)	21 (17–26)	4 (3–5)	72 (68–95)
	Right, n = 57	48 (41–57)	6.7 (4.9–8.7)	22 (17–28)	4 (2–6)	80 (50–94)
Endobronchial intubation	Left, n = 99	47 (40–56)	6.1 (4.3–8.1)	22 (17–28)	5 (4–5)	80 (56–100)
	Right, n = 100	45 (39–53)	6.4 (4.6–8.3)	24 (18–30)	4 (2–5)	96 (92–99)

All values are presented as median (25th to 75th interquartile range).

$ETco_2$, end tidal carbon dioxide; Fio_2 %, fraction of inspired oxygen × 100; PEEP, positive end expiratory pressure.

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Appendix: Multicenter Perioperative Outcomes Group Investigators

The following collaborators attest to their substantial role in research protocol revisions or data collection/validation efforts as part of the Multicenter Perioperative Outcomes Group (MPOG) Perioperative Clinical Research Committee: Mark Neuman, M.D., M.Sc., University of Pennsylvania, Philadelphia, Pennsylvania; Michelle T. Vaughn, M.P.H., Michigan Medicine; Roy Soto, M.D., Beaumont Health, Belleville, Michigan; Surendrasingh Chhabada, M.D., Cleveland Clinic, Cleveland, Ohio; Robert E. Freundlich, M.D., M.S., M.S.C.I., Vanderbilt University Medical Center, Nashville, Tennessee; Michael F. Aziz, M.D., Oregon Health and Science University, Portland, Oregon; Shital Vachhani, M.D., University of Texas, M.D. Anderson Cancer Center, Houston, Texas; Robert B. Schonberger, M.D., M.H.S., Yale School of Medicine, New Haven, Connecticut; Karen B. Domino, M.D., M.P.H., University of Washington, Seattle, Washington; Catherine L. Chen, M.D., M.P.H., University of California, San Francisco, San Francisco, California.

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One fateful morning in 1962, a community hospital pathologist telephoned John Bunker, M.D., Chair of Anesthesia at Stanford. A 16-year-old girl had died of liver failure two weeks after receiving halothane (branded "Fluothane," *left*) anesthesia for a wrist-laceration repair. Her case, along with others, sparked the National Halothane Study (*right*), a large-scale comparison of halothane with other anesthetics in relation to the incidence of fatal hepatic necrosis. Within the first month, randomization was halted on ethical grounds following a new case of lethal hepatitis. In the end, a retrospective cohort design found 82 unexplained cases of massive hepatic necrosis out of 856,000 general anesthetics given at 34 hospitals over 4 years (1959 to 1962). Most occurred after high-risk surgery. There were too few cases to establish "halothane hepatitis" as a clinical syndrome, but the rare occurrence of halothane-induced liver failure could not be ruled out. Overall mortality was shown to be lower with halothane than with other agents. Although inconclusive with respect to its primary objective, the National Halothane Study was a revolution in modern data processing. By revealing a surprisingly large difference in surgical outcomes between institutions, it ushered in a new era of quality improvement. (Copyright © the American Society of Anesthesiologists' Wood Library-Museum of Anesthesiology.)

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