Randomized Trial of Apneic Oxygenation during Endotracheal Intubation of the Critically Ill

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Abstract

Rationale: Hypoxemia is common during endotracheal intubation of critically ill patients and may predispose to cardiac arrest and death. Administration of supplemental oxygen during laryngoscopy (apneic oxygenation) may prevent hypoxemia.

Objectives: To determine if apneic oxygenation increases the lowest arterial oxygen saturation experienced by patients undergoing endotracheal intubation in the intensive care unit.

Methods: This was a randomized, open-label, pragmatic trial in which 150 adults undergoing endotracheal intubation in a medical intensive care unit were randomized to receive 15 L/min of 100% oxygen via high-flow nasal cannula during laryngoscopy (apneic oxygenation) or no supplemental oxygen during laryngoscopy (usual care). The primary outcome was lowest arterial oxygen saturation between induction and 2 minutes after completion of endotracheal intubation.

Measurements and Main Results: Median lowest arterial oxygen saturation was 92% with apneic oxygenation versus 90% with usual care (95% confidence interval for the difference, −1.6 to 7.4%; $P = 0.16$). There was no difference between apneic oxygenation and usual care in incidence of oxygen saturation less than 90% (44.7 vs. 47.2%; $P = 0.87$), oxygen saturation less than 80% (15.8 vs. 25.0%; $P = 0.22$), or decrease in oxygen saturation greater than 3% (53.9 vs. 55.6%; $P = 0.87$). Duration of mechanical ventilation, intensive care unit length of stay, and in-hospital mortality were similar between study groups.

Conclusions: Apneic oxygenation does not seem to increase lowest arterial oxygen saturation during endotracheal intubation of critically ill patients compared with usual care. These findings do not support routine use of apneic oxygenation during endotracheal intubation of critically ill adults.

Clinical trial registered with www.clinicaltrials.gov (NCT 02051816).

Keywords: intratracheal intubation; airway management; pulmonary ventilation

Hypoxemia is the most common complication of endotracheal intubation in the critically ill (1–4) and the strongest risk factor for periprocedural cardiac arrest and death (5). The traditional approach to avoiding desaturation during intubation is preoxygenation (6–10). However, in critically ill patients, acute physiologic abnormalities render preoxygenation less effective (7) and often insufficient to prevent desaturation during even short periods of apnea (11).

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At a Glance Commentary

Scientific Knowledge on the Subject: Hypoxemia is the most common complication of emergent endotracheal intubation. Provision of supplemental oxygen by nasal cannula during laryngoscopy (apneic oxygenation) has been shown in small randomized trials to prevent desaturation during elective intubation of healthy preoperative patients and has been recommended during intubation of the acutely ill, although it has never been tested in this setting.

What This Study Adds to the Field: This randomized clinical trial found no difference between apneic oxygenation and usual care in the lowest oxygen saturation experienced by critically ill adults undergoing emergent endotracheal intubation.

Apneic oxygenation is the delivery of supplemental oxygen to the nasopharynx in the absence of ventilation (12). Even without lung expansion, alveolar oxygen diffuses into the bloodstream and is consumed into carbon dioxide. Because of the high affinity of carbon dioxide for hemoglobin and effective buffering, the volume of carbon dioxide returned to the alveoli is less than the volume of oxygen removed. As a result, alveolar pressure decreases and gas is drawn down from the nasopharynx (10). By increasing the fraction of oxygen in the gas moving from the nasopharynx to the lungs, apneic oxygenation aims to prevent arterial desaturation.

Apneic oxygenation has been used to prevent desaturation in patients undergoing brain death examination (13), bronchoscopy (14), endoscopy (15), and even elective endotracheal intubation for general anesthesia (16–19). Although administration of oxygen by nasal cannula (20) during laryngoscopy has been adopted in many emergency departments (21) and intensive care units (ICUs) (22), there are significant differences between intubating electively in the operating room and urgently in out-of-operating room settings. Despite two recent "before-after" studies suggesting benefit for apneic oxygenation in out-of-operating room intubations (22, 23), the effectiveness of apneic oxygenation in this context remains unclear. We conducted a prospective, randomized trial comparing the impact of apneic oxygenation with usual care on lowest arterial oxygen saturation during endotracheal intubation of critically ill adults. We hypothesized that the lowest arterial oxygen saturation during intubation would be higher with apneic oxygenation.

Methods

Study Design

The FELLOW (Facilitating EndotracheaL intubation by Laryngoscopy technique and apneic Oxygenation Within the intensive care unit) Study was a randomized, open-label, parallel-group, pragmatic trial comparing apneic oxygenation with usual care during endotracheal intubation of critically ill adults. The trial was factorialized to also compare direct with video laryngoscopy, the details of which will be reported separately. The study protocol was approved by the institutional review board at Vanderbilt University with waiver of informed consent. The trial was registered online before initiation (NCT02051816), and the statistical analysis plan was made publically available before completion of enrollment (https://starbrite.vanderbilt.edu/rocket/page/FELLOW; available in the online data supplement).

Study Participants

From February 13, 2014 to February 11, 2015 we enrolled patients undergoing endotracheal intubation in the medical ICU at Vanderbilt University Medical Center. All patients 18 years or older being intubated by a pulmonary and critical care medicine fellow were eligible. Patients were excluded if awake intubation was planned, if intubation was required so emergently that randomization could not be achieved, or if the treating clinicians believed a specific approach to intraprocedural oxygenation or a specific laryngoscopy device was mandated for the safe performance of the procedure (Figure 1).

Randomization

Eligible patients were randomly assigned in a 1:1 ratio to receive apneic oxygenation (intervention) or usual care (control). Per the factorial design, patients were also simultaneously randomized to either video or direct laryngoscopy, details of which will be reported separately. The sequence of study group assignments was generated via a computerized algorithm using permuted blocks of 4, 8, and 12. Study group assignments were placed in sequentially numbered opaque envelopes that remained sealed until the decision had been made that a patient required intubation and was enrolled in the study.

Study Treatments

For all patients, study protocol governed only provision of supplemental oxygen during apnea and laryngoscopy device used on the first laryngoscopy attempt. Decisions regarding intubation, approach to preoxygenation, patient positioning, medications for induction and neuromuscular blockade, ventilation between induction and laryngoscopy, choice of laryngoscope blade type and size, and use of additional airway management equipment were made by the clinical team. Intubation practices in the study environment are detailed in the online supplement. Operator compliance with general best-practices in airway management was prospectively collected from a convenience sample of consecutive intubations.

Although preoxygenation was allowed, patients in the usual care group were intubated without supplemental oxygen during laryngoscopy. For patients in the apneic oxygenation group, a high-flow nasal cannula (Comfort Soft Plus; Westmed, Inc., Tucson, AZ) set to 15 L/min flow of 100% oxygen was placed in the patient's nares before induction and kept in place until intubation was complete. Because of the nature of the study intervention, clinicians and study personnel were aware of study group assignments after enrollment.

Data Collection

To minimize observer bias, data collection during intubation was performed by independent observers unaware of the study hypothesis and not involved in the performance of the procedure. To confirm the accuracy of data collected by the independent observers, the primary investigators concurrently assessed the same outcomes for a

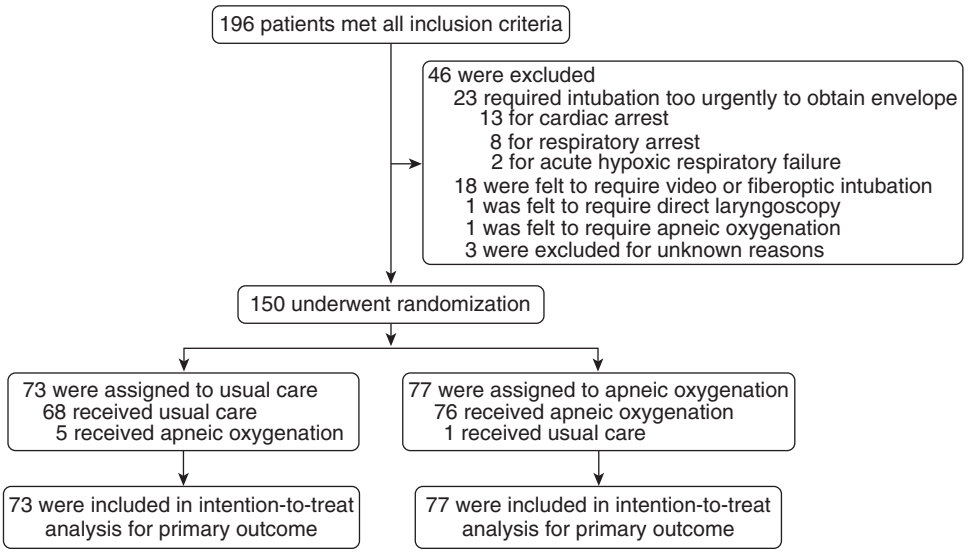

Figure 1. Enrollment, randomization, intervention, and analysis. Of 196 adults intubated by pulmonary and critical care medicine fellows during the study period, 46 were excluded and 150 were randomized, followed, and included in the intention-to-treat analysis.

convenience sample of around 10% of study intubations.

Subjective assessments of Cormack-Lehane grade of view (24), difficulty of intubation, and airway complications during the procedure were self-reported by the operator. All other data on baseline characteristics, prelaryngoscopy and postlaryngoscopy management, and clinical outcomes were collected from the medical record by study personnel. All patients were followed until the first of hospital discharge, death, or 28 days after enrollment.

Study Outcomes

The primary outcome was the lowest arterial oxygen saturation measured by continuous pulse oximetry (Sp_{O_2}) between induction and 2 minutes after successful endotracheal tube placement ("lowest arterial oxygen saturation"). Secondary efficacy outcomes included incidence of hypoxemia (Sp_{O_2} <90%), severe hypoxemia (Sp_{O_2} <80%), desaturation (decrease in Sp_{O_2} >3%), and change in saturation from baseline. Secondary safety outcomes included Cormack-Lehane grade of glottic view (24), incidence of successful intubation on the first laryngoscopy attempt (placement of an endotracheal tube in the trachea during the first insertion of the laryngoscope into the oral cavity without the use of any other devices), number of laryngoscopy attempts, time from induction to intubation, need for additional airway equipment or operators, and incidence of nonhypoxemia complications. Tertiary outcomes included duration of mechanical ventilation, ICU length of stay, and in-hospital mortality.

Statistical Analysis

Anticipating a SD of 10% in lowest arterial oxygen saturation (6), enrollment of 150 patients would provide 80% statistical power (at a two-sided α level of 0.05) to detect a difference between groups in mean lowest arterial oxygen saturation of 4.6%, within the 5% minimum difference considered clinically meaningful in prior studies (*see* online supplement) (6, 9, 17, 18, 22).

Analyses were conducted according to a statistical analysis plan that was publically available before completion of enrollment. Continuous variables were reported as mean ± SD or median and interquartile range (IQR); categorical variables as frequencies and proportions. Between-group differences were analyzed with the Mann-Whitney rank sum test for continuous variables, Fisher exact test for categorical variables, and Spearman rank correlation coefficient for correlation between two continuous variables. The primary analysis was an unadjusted, intention-to-treat comparison of patients randomized to apneic oxygenation versus usual care with regard to the primary outcome of lowest arterial oxygen saturation.

We performed four prespecified secondary analyses: (*1*) the effect of the intervention on secondary and tertiary outcomes, (*2*) the effect of the intervention on the primary outcome in prespecified patient and procedural subgroups, (*3*) "per-protocol" analyses comparing lowest arterial oxygen saturation between patients who received apneic oxygenation with those who did not, and (*4*) linear regression for the outcome of lowest arterial oxygen saturation in which the exposure variable of randomized group assignment was accompanied first by just the covariate of oxygen saturation at induction and then by potential baseline confounders. Subgroup analyses were performed using logistic regression with heterogeneity of treatment effect determined on the basis of statistical test for interaction between treatment assignment and subgrouping variable. A two-sided *P* value less than 0.05 was used to determine significance. All analyses were performed using SPSS Statistics v.22 (IBM Corp., Armonk, NY) or R version 3.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Enrollment and Baseline Characteristics

Of 196 medical ICU patients intubated by fellows during the study period,

Table 1. Patient and Operator Characteristics at Baseline

	Usual Care (*n* = 73)	Apneic Oxygenation (*n* = 77)
Patient characteristics		
Age, median (IQR), yr	60 (50–67)	60 (51–68)
Male, n (%)	46 (63.0)	45 (58.4)
White, n (%)	62 (84.9)	63 (82.9)
BMI, median (IQR), kg/m^2	28.6 (23.4–32.8)	28.6 (23.3–32.8)
APACHE II score, median (IQR)	22 (17–27)	22 (16–27)
Vasopressors, n (%)	9 (12.3)	11 (14.3)
Lowest MAP in prior 6 h, median (IQR), mm Hg	68 (57–80)	65 (57–79)
Lowest oxygen saturation in prior 6 h, median (IQR), %	91 (88–93)	92 (88–95)
Highest F_{IO_2} in prior 6 h, median (IQR)	0.40 (0.30–0.80)	0.40 (0.27–0.60)
BiPAP use in prior 6 h, n (%)	31 (42.5)	26 (33.5)
Reintubation within 24 h of extubation, n (%)	11 (15.1)	9 (11.7)
Intensive care unit diagnoses, n (%)		
Sepsis	50 (68.5)	49 (63.6)
Septic shock	14 (19.2)	20 (26.0)
Hemorrhagic shock	3 (4.1)	6 (7.8)
Cardiogenic shock	1 (1.4)	2 (2.6)
Myocardial infarction	9 (12.3)	4 (5.2)
COPD exacerbation	8 (11.0)	4 (5.2)
Hepatic encephalopathy	10 (13.7)	10 (13.0)
Delirium	35 (50.0)	33 (43.4)
Indication for intubation, n (%)		
Hypoxic or hypercarbic respiratory failure	42 (57.5)	43 (55.8)
Altered mental status or encephalopathy	18 (24.7)	21 (27.3)
Other	13 (17.8)	13 (16.8)
Comorbidities complicating intubation, n (%)		
BMI >30 kg/m^2	23 (31.5)	25 (32.5)
Upper gastrointestinal bleeding	7 (9.6)	6 (7.8)
Limited mouth opening*	3 (4.1)	3 (3.9)
Limited neck mobility*	3 (4.1)	2 (2.6)
Head or neck radiation	1 (1.4)	0 (0.0)
Airway mass or infection	0 (0.0)	1 (1.3)
Witnessed aspiration	1 (1.4)	0 (0.0)
Epistaxis or oral bleeding	0 (0.0)	0 (0.0)
Preoxygenation,† n (%)		
Nonrebreather mask	32 (43.8)	25 (32.5)
BiPAP	23 (31.5)	23 (29.9)
Bag-valve-mask ventilation‡	31 (42.5)	33 (42.9)
Standard nasal cannula§	2 (2.7)	6 (7.8)
Other	1 (1.4)	0 (0.0)
Oxygen saturation at induction, median (IQR), %	98 (94–99)	99 (96–100)
Operator characteristics		
Total number of prior intubations, median (IQR)	56 (40–69)	68 (52–69)
Months of fellowship training, median (IQR)	21.5 (14.4–29.5)	22.9 (15.4–31.6)

Definition of abbreviations: APACHE II = Acute Physiology and Chronic Health Evaluation II, ranging from 0 to 71 with higher scores indicating higher severity of illness; BiPAP = bilevel positive airway pressure; BMI = body mass index; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; MAP = mean arterial pressure; shock = MAP less than 65 mm Hg or vasopressor use.

Noninvasively measured oxygen saturation at the time of induction was higher in the apneic oxygenation arm ($P = 0.03$).

*As reported by the fellow performing the intubation.

†Patients could receive more than one method of preoxygenation.

‡Bag-valve-mask ventilation was routinely accompanied by use of a positive end-expiratory pressure valve set to 5–10 cm H_2O.

§Standard nasal cannula delivered <6 L/min of nonhumidified oxygen.

150 met no exclusion criteria and were enrolled (Figure 1). Patients randomized to receive apneic oxygenation (n = 77) and usual care (n = 73) were similar at baseline (Table 1). There was no difference between the two arms in the prior airway management experience of the fellow performing the intubation (Table 1). There were no differences in method of preoxygenation (Table 1), choice of induction agent or neuromuscular blocker, ventilation between induction and laryngoscopy, or laryngoscope type, except for higher propofol use for induction in the usual care arm (13.7 vs. 2.5%; $P = 0.02$) (*see* Table E1 in the online supplement). Oxygen saturation at the time of induction was 99% (IQR, 96–100%) with apneic oxygenation compared with 98% (IQR, 94–99%) with usual care ($P = 0.03$).

Airway Management

Five patients (6.8%) in the usual care arm received apneic oxygenation during intubation, and two patients (2.6%) in the

Table 2. Study Outcomes

	Usual Care (*n* = 73)	Apneic Oxygenation (*n* = 77)	*P* Value
Oxygenation outcomes			
Lowest oxygen saturation, median (IQR), %	90 (80–96)	92 (84–99)	0.16
Lowest oxygen saturation <90%, n (%)	34 (47.2)	34 (44.7)	0.87
Lowest oxygen saturation <80%,* n (%)	18 (25.0)	12 (15.8)	0.22
Decrease in oxygen saturation, median (IQR), %	4.5 (1–14)	4.0 (0–12)	0.60
Decrease in oxygen saturation >3%, n (%)	40 (55.6)	41 (53.9)	0.87
Procedural outcomes			
Intubation on the first laryngoscopy attempt, n (%)	49 (67.1)	52 (67.5)	0.96
Number of laryngoscopy attempts, median (IQR)	1 (1–2)	1 (1–1)	0.60
Time from induction to secured airway, median (IQR), s	150 (102–245)	132 (88–205)	0.31
Clinical outcomes			
Duration of mechanical ventilation, median (IQR), d	3 (2–7)	3 (1–10)	0.73
Intensive care unit length of stay, median (IQR), d	7 (3–10)	4 (2–9)	0.24
Died within 1 h of intubation, n (%)	1 (2.8)	0 (0.0)	>0.99
Died before hospital discharge, n (%)	36 (49.3)	27 (35.1)	0.10

Definition of abbreviation: IQR = interquartile range.
There were no differences between the study groups in the primary outcome of lowest arterial oxygen saturation between induction and 2 minutes after completion of the procedure, secondary procedural outcomes, or clinical outcomes.
*Lowest oxygen saturation <80% was added to the analysis *post hoc*.

apneic oxygenation arm did not (Figure 1). There was no difference between those randomized to apneic oxygenation and usual care in the rate of successful intubation on the first laryngoscopy attempt (67.5 vs. 67.1%; $P = 0.96$), time from induction to secured airway (132 vs. 150 s; $P = 0.31$), or any other recorded aspect of the performance of the procedure (Table 2; *see* Table E2).

Main Outcomes

There was no significant difference between apneic oxygenation and usual care with regard to the primary outcome of median lowest arterial oxygen saturation during the procedure: 92% (IQR, 84–99%) versus 90% (IQR, 80–96%), respectively ($P = 0.16$) (Figure 2). Apneic oxygenation did not impact the proportion of patients who experienced an oxygen saturation less than 90%, less than 80%, or a desaturation greater than 3% during the procedure (Table 2). There were no differences in duration of mechanical ventilation, ICU length of stay, or in-hospital mortality (Table 2).

In multivariable linear regression adjusting for saturation at induction alone or with age, body mass index, Acute Physiology and Chronic Health Evaluation II score, shock, prior noninvasive ventilation, highest fraction of inspired oxygen in the prior 6 hours, laryngoscope choice, and operator experience, apneic oxygenation did not impact the lowest arterial oxygen saturation during the procedure (*see* Table E3).

Secondary Analyses

There was no difference in lowest arterial oxygen saturation between apneic oxygenation and usual care in any of the subgroups examined (Figure 3). Specifically, apneic oxygenation was not significantly more effective for patients at potentially greater risk for hypoxemia based on higher $F_{I_{O_2}}$ requirement, lower oxygen saturation at induction, lower ratio of oxygen saturation to $F_{I_{O_2}}$ ($Sp_{O_2}/F_{I_{O_2}}$ ratio [25]) in the prior 6 hours, higher body mass index, more difficult intubation, or longer duration of laryngoscopy (*see* Figure E1). The type of laryngoscopy device assigned did not modify the effect of apneic oxygenation on lowest arterial oxygen saturation (*P* value for the interaction = 0.15) (*see* Figure E2).

One patient in each arm of the study was missing a value for lowest arterial oxygen saturation. In sensitivity analyses imputing both values (by carrying forward the saturation at induction or by assigning apneic oxygenation the highest possible saturation and usual care the lowest), there remained no difference between apneic oxygenation and usual care.

In an *a priori* defined per-protocol analysis comparing patients who received apneic oxygenation (n = 80) with those who did not (n = 68), there was no difference in lowest arterial oxygen saturation (92% [IQR, 84–98%] vs. 90% [IQR, 80–96%], respectively; $P = 0.21$) or in any other clinical outcome (*see* Tables E4 and E5 and Figure E3).

The values for lowest arterial oxygen saturation recorded concurrently by independent observers and the primary investigators were strongly correlated (Spearmen $R^2 = 0.893$; $P < 0.001$). Operators were frequently compliant with general best-practices in airway management including preoxygenation, equipment preparation, end-tidal carbon dioxide detector availability, and presence of a second operator (*see* Table E6).

Discussion

This randomized trial comparing apneic oxygenation with usual care during endotracheal intubation of critically ill adults found that apneic oxygenation did not increase the lowest arterial oxygen saturation. There were no significant differences between apneic oxygenation and usual care in any primary or secondary outcome, overall or in any subgroup.

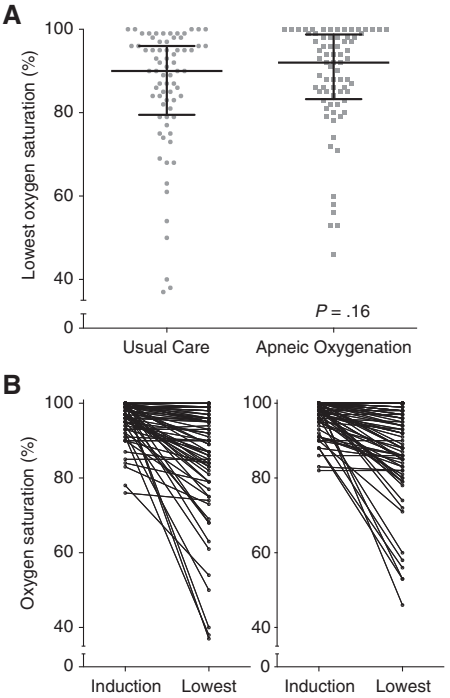

Figure 2. Lowest arterial oxygen saturation by study group. (*A*) The primary outcome of lowest arterial oxygen saturation between induction and 2 minutes after completion of endotracheal intubation (lowest oxygen saturation) is displayed for patients randomized to apneic oxygenation (*squares*) and usual care (*circles*). *Horizontal bars* represent median and interquartile range. (*B*) The relationship between oxygen saturation at induction and lowest oxygen saturation is displayed for each patient in the usual care (*left*) and apneic oxygenation (*right*) groups.

Hypoxemia is the most common complication of endotracheal intubation (1–3) and the most closely linked to cardiac arrest and death (5). Preoxygenation is often insufficient to prevent desaturation during intubation (3, 11) and the provision of supplemental oxygen during apnea has been advocated as a safe and inexpensive intervention to improve periintubation oxygenation (10, 26, 27). The use of apneic oxygenation has been reported in four small randomized trials in the operating room (16–19) and two "before-after" studies of emergent intubation (22, 23). Trials of apneic oxygenation during elective anesthesia ranged in size from 12 to 34 patients, all without acute pulmonary dysfunction (16–19). Provision of 3–5 L/min of oxygen nasally significantly prolonged the duration of apnea without desaturation (16–19). Outside the operating room, Miguel-Montanes and coworkers (22) observed higher oxygen saturation during intubation after their ICU switched from apneic oxygenation at 6 L/min to 60 L/min and Wimalasena and coworkers (23) reported a 6% decrease in the incidence of desaturation after their helicopter emergency medical service adopted apneic oxygenation at 15 L/min by nasal cannula.

In contrast to prior studies, our trial showed no difference between apneic oxygenation and usual care. There are several potential explanations for this discordance. Prior reports of apneic oxygenation's use outside the operating room were "before-after" designs in which other changes over time may have confounded the perceived impact of apneic oxygenation. Self-reported outcomes in prior studies may have predisposed to observer bias. In contrast to healthy patients undergoing elective anesthesia (16–19) and patients intubated primarily for traumatic, hemodynamic, or neurologic conditions (22, 23), most patients in our study were intubated for respiratory failure. For patients with pulmonary function so abnormal that provision of oxygen by mask or noninvasive ventilation was insufficient to avert intubation, providing 15 L/min by nasal cannula during intubation might be expected to be similarly ineffective. Although our analyses did not suggest efficacy for apneic oxygenation in any subgroup, whether apneic oxygenation could be effective in patients with normal pulmonary function being intubated for other reasons requires further study.

Finally, whether the dose of apneic oxygenation delivered was adequate is important. Our use of 15 L/min via high-flow nasal cannula was based on expert recommendation (10) and is a higher flow rate than prior trials in the operating room (16–19) but lower than the 60 L/min delivered in a recent observational study (22). It seems unlikely that a higher flow rate would improve results, however, based on the recent PREOXYFLOW trial (9). Although the PREOXYFLOW trial focused on preoxygenation with high-flow nasal cannula versus face mask, saturation at induction was the same in both arms and the high-flow nasal cannula continued to deliver 60 L/min of oxygen during laryngoscopy compared with no oxygen delivery in the control arm. Median lowest arterial oxygen saturations for those receiving 60 L/min apneic oxygenation versus none were identical to our study at 92 and 90%, respectively.

Our study has several strengths. It is the first randomized trial specifically comparing apneic oxygenation with usual care during intubations outside the operating room and is five times larger than any prior trial. The primary outcome, lowest arterial oxygen saturation during intubation, is of interest to clinicians; has been used in prior airway management trials; and is linked to patient-centered outcomes, such as cardiac arrest and death. Collection of study endpoints by an independent observer and contemporaneous validation of these data by the primary investigators reduces potential for observer bias. The limited exclusion criteria and relatively small number excluded promote generalizability.

Our study also has limitations. Conduct in one medical ICU at a single academic center may limit generalizability. High compliance with preoxygenation (including noninvasive ventilation for patients with hypoxemia), patient positioning, and equipment preparation best-practices may have reduced the potential additive impact of apneic oxygenation (6, 28, 29). Had we used a standardized intubation protocol (6) or a highly uniform group of operators (7), we might have reduced practice-related variation in lowest arterial oxygen saturation, making any effect of apneic oxygenation easier to detect. Comparing apneic oxygenation with a nasal cannula delivering ambient air (placebo) could have allowed blinding, but would have inaccurately represented usual care, obscured complications related to the delivery of the intervention (e.g., disruption of mask seal for bag-valve-mask ventilation by the nasal cannula itself), and created a safety hazard by providing a false source of oxygen to teams conducting emergent intubation. Our study was powered to detect the 5% difference in lowest arterial oxygen saturation that has been considered clinically meaningful in prior trials (6, 9, 17, 18), but a smaller difference might have been missed. Exclusion of patients clinically determined to require video laryngoscopy may limit applicability of our results to patients with abnormal upper airway anatomy at risk for prolonged

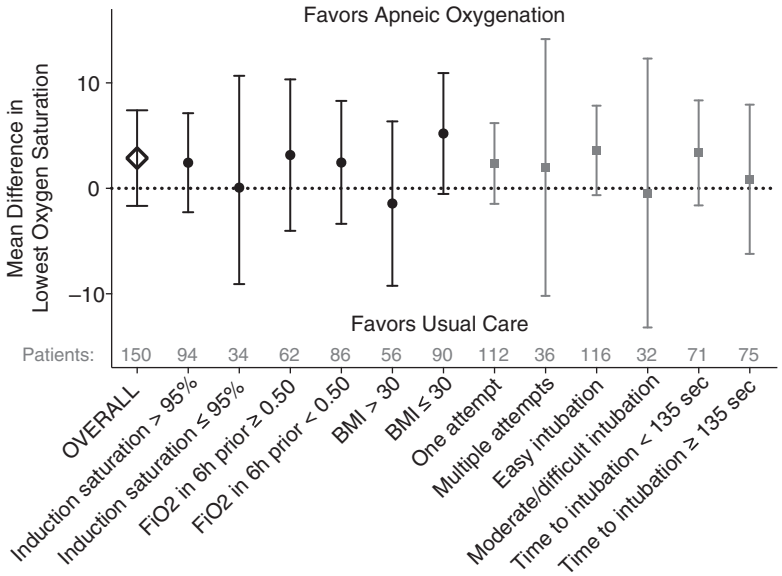

Figure 3. Subgroup analyses. The mean difference in lowest arterial oxygen saturation (%) between apneic oxygenation and usual care is given for patients in prespecified subgroups present at the time of induction (*circles*) and arising after procedure initiation (*squares*). *Vertical bars* represent the 95% confidence interval around the mean difference. BMI = body mass index in kg/m^2; F_{IO_2} in 6 hours prior = the highest fraction of inspired oxygen in the 6 hours before the intubation; time to intubation = time from induction until successful endotracheal intubation.

intubation times. Although not observed in our analyses, benefit in specific subgroups of patients (e.g., severe hypoxic respiratory failure, preserved pulmonary function) cannot be excluded.

The results of our trial suggest that, for patients being intubated in the medical ICU, routine use of apneic oxygenation is safe but ineffective. Safety without efficacy is insufficient in the high-stakes, time-sensitive world of emergent endotracheal intubation and clinicians should focus their resources on interventions that prevent complications (e.g., effective preoxygenation [6]). Future research should use rigorously designed trials either to identify populations who do benefit from apneic oxygenation or shift focus to other aspects of airway management with potential to improve patient outcomes.

In summary, the results of this clinical trial suggest that apneic oxygenation during endotracheal intubation of critically ill adults does not increase lowest arterial oxygen saturation compared with usual care. Routine use of apneic oxygenation during emergent intubation cannot be recommended. ■

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