Table 1. Multivariable Model Output with Odds Ratios for Continuous Variables Rescaled to Clinically Relevant Units

Variable	OR	95% CI	*P* Value
Vasopressors	1.14	0.85–1.53	0.37
Fluid bolus	1.19	0.96–1.46	0.11
Use of propofol	1.28	1.05–1.57	0.016
Age (per 10 yr)	**1.24**	**1.17–1.32**	**<0.001**
Adjusted SOFA	1.02	0.99–1.05	0.10
Heart rate (per 20 beats/min)	**1.17**	**1.08–1.27**	**<0.001**
Sp_{O_2}/FI_{O_2} (per 50 unit decrease)	**1.11**	**1.05–1.16**	**<0.001**
sBP (per 20 mm Hg decrease)	**1.41**	**1.30–1.50**	**<0.001**

Definition of abbreviations: CI = confidence interval; OR = odds ratio; sBP = systolic blood pressure; SOFA = Sequential Organ Failure Assessment; Sp_{O_2} = oxygen saturation as measured by pulse oximetry.
ORs for continuous variables from the original Table 3 (highlighted in bold) were rescaled to new base units using the formula: $OR_1 = OR_0^n$, in which OR_1 is the rescaled OR, OR_0 is the originally reported OR, and n is the scaling coefficient. (For example, if converting from 1-yr units to 10-yr units, $n = 10$.) For sBP and the ratio of Sp_{O_2}/FI_{O_2}, we harmonized the directionality of effect sizes to facilitate comparison by rescaling the reciprocal of the original odds ratio using the formula: $OR_1 = (1/OR_0)^n$. Therefore, a higher OR for sBP and the ratio Sp_{O_2}/FI_{O_2} represents the increased risk of instability associated with a decrease in these variables of the indicated quantity.

propensity scores. Association between propofol use and instability may then reflect instances in which peri-intubation cardiovascular risk was misjudged.

We also highlight that propofol was the only induction agent assessed for association with instability.

However, two-thirds of patients in this study received peri-intubation opioids. Opioids are powerful sympatholytics that can independently cause cardiovascular instability and potentiate other sedatives (4). The association of opioids with cardiovascular instability was not assessed, and administered doses of opioids were not reported.

Furthermore, we point out that the prevalence of key patient factors that increase vulnerability to swings in afterload or the introduction of positive-pressure ventilation was not captured: namely, hemorrhage and hypovolemia, severe valvulopathies, and pulmonary hypertension or right ventricular dysfunction.

We hasten to clarify that we do not advocate indiscriminate propofol administration to critically ill patients. An induction strategy should be carefully tailored to individual circumstances.

Rather, we aim to refocus on a crucial implication of the study by Russotto and colleagues: that preinduction vital signs are highly predictive of peri-intubation cardiovascular instability. The finding that "soft" sBP (as distinct from frank systolic hypotension) was robustly associated with instability represents a key result. We similarly stress the strong relationship between tachycardia and instability. Together these results underscore the principle that tachycardia without hypertension should alert clinicians to patients highly likely to decompensate when sympathetic drive is cut at induction, for whom they should tailor their intubation strategy accordingly.

We congratulate the authors on their important contribution to the literature. Insights from their study stand to improve cardiovascular safety for critically ill patients undergoing intubation. ■

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Reply to Leisman and Crowley

From the Authors:

We thank Dr. Leisman and Dr. Crowley for their interest in our study. We absolutely agree that the baseline hemodynamic status may play a major role in the risk of peri-intubation cardiovascular collapse (1). Peri-intubation hemodynamic changes result from a complex interplay of baseline critical illness, volemic status, both left and right ventricular performance, hypoxemia, vasodilatation

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effect of induction drugs, and the transition from spontaneous efforts to positive pressure ventilation (2). We also support the suggestion that critically ill patients may manifest the features of adrenergic activation leading to tachycardia with the maintenance of arterial pressure, which clinicians may falsely interpret as indicating relative cardiovascular stability. Blunting of this adrenergic response by sedatives such as propofol may lead to rapid decompensation and severe hypotension. The authors pointed out the importance of what they call soft hypotension, indicating the condition of roughly normal or only mild systolic hypotension (e.g., 90–100 mm Hg) associated with tachycardia. This profile was associated with a significant risk in our cohort. This observation may trigger two actions:

1. Efforts to optimize preintubation hemodynamic status. Recent evidence has failed to demonstrate the efficacy of a fluid bolus to mitigate the risk of postintubation hypotension, even in patients receiving noninvasive positive pressure ventilation before intubation (3, 4). We advocate personalization of care so that in selected patients, fluids may still be of benefit, whereas others may benefit more from the administration of vasopressors/inotropes.
2. Increased risk awareness with an appropriate selection of sedation agents. We agree with the authors that propofol may be selected under the false perception of the safety in some patients, showing only mild hypotension, normotension, or even hypertension. Our data show that the higher preintubation blood pressure (perhaps reflecting greater activation of adrenergic stress compensatory/adaptive mechanisms), the greater its postintubation drop.

Our emphasis on induction agents, and propofol, in particular, comes from the fact that this is a relatively easily modifiable factor. Many patients' related variables also play an important role, but age is an unmodifiable factor, and preintubation optimization of oxygenation and perfusion may be challenging in the short timeframes before intubation. In contrast, clinicians have the possibility of selecting readily available alternatives to propofol, such as ketamine or etomidate, which, although with their known limitations, have at least a better hemodynamic profile. Given the high frequency of use of propofol in real life (41% of intubation procedures) and the high incidence of peri-intubation cardiovascular collapse (43% of patients) in our cohort, we perceive this association to be clinically important and relevant (5). Propofol is coadministered with different drugs in daily practice. Unfortunately, we were not able to isolate the sole contribution of opioids in the determination of peri-intubation cardiovascular collapse. Indeed, our cohort is representative of the real-life scenario of different drug combinations, which makes understanding the effect of each specific drug rather difficult. We specified this among the limitations of our study (1).

To conclude, we recognize that many pathophysiologic mechanisms may play a role in hemodynamic instability seen during the minutes preceding and after tracheal intubation of a critically ill patient. Their identification and the selection of an appropriate response for any given patient may be challenging, and this represents a core competency for an expert critical care physician. We thank Dr. Leisman and Dr. Crowley for having pointed out the importance of vital parameters and soft hypotension as risk factors for cardiovascular collapse. We agree the presence of borderline hypotension should increase the degree of caution, and that clinicians should adapt their approach to reduce the risk of adverse cardiovascular events in these patients. In adapting their approach, they should strongly consider using alternatives to propofol to induce unconsciousness to facilitate tracheal intubation. ■

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