Reply to: "Predicting Peri-intubation Cardiovascular Instability: Pre-Intubation Vital Signs are Vital"

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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 for 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 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 maintenance of arterial pressure, which clinicians may falsely 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 mmHg) associated with tachycardia. This profile was associated with a significant risk in our cohort. This observation may trigger two actions:

1. Effort to optimize pre-intubation hemodynamic status. Recent evidence has failed to demonstrate the efficacy of a fluid bolus to mitigate the risk of post-intubation 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 be still of benefit while others may benefit more from administration of vasopressors/inotropes.
2. Increased risk awareness, with appropriate selection of sedation agents. We agree with authors that propofol may be selected under the false perception of safety of some patients, showing only *mild hypotension*, normotension, or even hypertension. Our data

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show that the higher pre-intubation blood pressure (perhaps reflecting greater activation of adrenergic stress compensatory/adaptive mechanisms), the greater its post-intubation 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 pre-intubation optimization of oxygenation and perfusion may be challenging 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 co-administered with different drugs in daily practice. Unfortunately, we were not able to isolate the sole contribution of opioids in determination of peri-intubation cardiovascular collapse. Indeed, out cohort is representative of the real-life scenario of different drugs combinations, which makes understanding the effect of each specific drug rather difficult. We specified this among limitations of our study (1).

To conclude, we recognize that many pathophysiologic mechanisms may play a role during the minutes preceding and following tracheal intubation of a critically ill patient. Their identification and the selection of an appropriated response in 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 level of caution and clinicians adapt their

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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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