

Article Appraisal

**Article: Effect of a fluid bolus on cardiovascular collapse among critically ill adults undergoing tracheal intubation (PrePARE): a randomised controlled trial.**

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**Background and Study Objective(s):**

Background:

* Cardiovascular collapse during the peri-intubation period occurs in ¼ of critically ill patients undergoing intubation. This is associated with a significant risk in mortality.
* 3 primary mechanisms have been proposed: hypotension associated with induction medications, decreased catecholamine reserve leading to decreased venous capacitance and the preload-reduction of positive pressure ventilation.
* One observational study suggested that the use of a pre-intubation fluid bolus decreased the risk of cardiovascular collapse in critically ill patents.
* However, the hypothesis had not been previously assessed in any randomized trial.

Research Question:

 Does administration of 500mL crystalloid bolus prior to induction in critically ill patients aged >18 years undergoing tracheal intubation reduce the risk of cardiovascular collapse?

**Methodology:**

Design: Multicentre, unblinded, randomised-controlled trial.

Population: Critically ill patients >18 years old undergoing tracheal intubation. Nine sites were included in the study including six medical ICUs, one trauma ICU, and one emergency department.

Intervention: 500mL IV bolus of 0.9% saline prior to induction of anesthesia for tracheal intubation. Fluid was infused by both gravity and a pressure bag and it was infused to completion through induction and laryngoscopy.

Comparison: No crystalloid solution between enrolment and 2 minutes after completion of fluid administration

Primary Outcome: Composite outcome of “cardiovascular collapse,” which comprised of:

* New SBP <65 between induction and 2 minutes after intubation
* New or increased vasopressor use between induction and 2 minutes after intubation
* Cardiac arrest or death within 1 hour of intubation

Secondary Outcomes:

* Each individual component of composite primary outcome
* Any additional fluids given
* Lowest SBP
* Change in SBP
* Number of laryngoscopy attempts
* Number of days off the ventilator
* Number of days spent outside of ICU
* In-hospital mortality within 28 days

Safety Outcomes:

* Lowest oxygen saturation in 6-24h after intubation
* Highest fraction of inspired oxygen in 6-24h after intubation
* Highest PEEP in 6-24h after intubation
* Cumulative diuretic dose on day of enrolment to 3 days after enrolment
* Cumulative IV fluid administration from enrolment to 3 days after enrolment

Power: Targeted enrolment of 500 patients to provide 80% power with two-sided alpha level of 0.05 to detect a relative risk reduction of 40%. Enrolment target was not achieved because of early termination of the trial due to futility at interim analysis. Interim analysis performed by the DSMB was planned for after the enrolment of 250 patients.

Randomization: 1:1 block randomisation (blocks of 2, 4, and 6) stratified by study site.

Blinding: No blinding.

Statistics: Unadjusted intention-to-treat. Primary outcome assessed with chi-squared test. Prespecified covariates assess for interaction using a multivariate logistic regression model.

**Results:**

* Total of 337 patients randomised.
* No difference in primary outcome between groups.
* Primary outcome occurred in 20% of bolus group and in 18% in the no bolus group, with an absolute risk difference of 1.3% (95% CI = -7.1 – 9.7).
* No difference in secondary outcomes between groups.
* No difference in safety outcomes between groups.

**Validity of Results:**

Strengths

* Peer reviewed.
* No conflicts of interest.
* Pre-published protocol & registered clinical trial.
* Well-randomized and high adherence to the protocol.
* Having few eligibility criteria increases generalizability.

Limitations

* Groups were not treated equally; the fluid bolus group was more likely to be intubated for hypoxic respiratory failure, was more likely to receive positive-pressure ventilation (either via NIV or BMV), were more likely to be intubated by a non-anesthesia resident and had higher incidence of need for a second operator during intubation. None of these differences reached significance but they could explain why the fluid bolus had little effect (confounders).
* Convenience sample of 38 patients used to assess quality of intervention revealed median value of 200mL of IV infusion completed prior to induction, which begs the question if this was too small a volume to have an effect on outcomes.
* There was no mention of fluid administration prior to enrolment, which could skew the outcome, especially if patients in the fluid bolus group were hypovolemic to begin with.
* Study personnel, providers and patients were unblinded. However, this is unlikely to have a huge effect on therapeutic outcome in this case.
* The trial was underpowered to detect significant differences between the subgroups.
* The study was predominantly carried out in the ICU setting, which limits its generalizability to the ED.

**The Bottom Line:**

Well constructed study assessing clinically relevant outcomes. Successful randomization and appropriate methodology. Underpowered small sample size secondary to early termination due to futility.

Results suggest that there is no benefit to administering a 500mL intravenous saline bolus prior to induction for tracheal intubation. However, these results are rendered essentially un-interpretable based on the substantial limitation in the quality and heterogeneity of the intervention actually provided. I do not believe this trial should impact clinical practice and, at this time, the administration of an IV fluid bolus prior to tracheal intubation should remain a contextual clinical decision made by the provider.