Critical Review Form
Therapy

PGY-1

Bohman JK, Kashyap R, Lee A, He Z, Soundar S, Bolling LL, Kor DJ. A pilot randomized clinical trial assessing the effect of cricoid pressure on risk of aspiration. Clin Respir J. 2018 Jan;12(1):175-182.

Objectives: **"to evaluate the effectiveness of cricoid pressure as an intervention to prevent gastric-to-pulmonary aspiration during elective induction of anesthesia and intubation." (p. 176).**

Methods: **This parallel design, single-center, randomized controlled trial was conducted at a single academic center in the US between August 5 and October 3, 2014. Patients undergoing elective surgical procedures who were over 18 years of age, were planned to undergo endotracheal intervention, and had either obesity (BMI > 30), diabetes mellitus, or gastroesophageal reflux disease (GERD) were eligible for enrollment. Patients were randomized in a 1:1 fashion to receive cricoid pressure from the commencement of general anesthesia until endotracheal intubation had been confirmed or to receive no cricoid pressure during intubation.**

Following intubation, all patients had 5 mL of sterile saline infused into the endotracheal tube, followed by aspiration via a sterile suction catheter. Pepsin A testing was then performed on the aspirate. A pepsin A concentration > 0.1 ng/mL was considered positive for microaspiration, while a concentration less than this was considered negative.

The primary outcome was the rate of microaspiration based on pepsin A testing. Secondary outcomes included the rates of difficult mask ventilation and difficulty laryngoscopy, as well as rates of development of ARDS and HAP (determined by chart review for a period of 7 days following intubation).

During the study period, a total of 103 patients were enrolled, with 8 excluded for various reasons. Of the remaining 95 patients, 3 were excluded from primary outcome analysis (2 for initial esophageal intubation and 1 for failure to collect an adequate aspiration sample). This left 92 patients in the final analysis, with a median age of 68. Sixty-eight percent of patients were male.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	Yes. Patients were randomized in a 1:1 fashion to either receive or not receive cricoid pressure during intubation.
2.	Was allocation concealed? In other	Likely yes. "We obtained the randomization log

	words, was it possible to subvert the randomization process to ensure that a patient would be “randomized” to a particular group?	from out collaborating statistician (DS)." (p. 177) Unfortunately, there are no details regarding how this was prepared, who had access to the log, or how it was used to randomize patients. Overall, it seems unlikely that the randomization process could have been subverted (allocation concealment).
3.	Were patients analyzed in the groups to which they were randomized?	Yes. "Unless otherwise specified, analyses were performed using an intention-to-treat approach whereby subjects are analyzed according to their randomly allocated treatment arm." (p. 177) There were 7 patients in the cricoid pressure arm (7.4%) who did not receive cricoid pressure. No patients in the no cricoid pressure arm received cricoid pressure.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, gender, median BMI, history of GERD, and history of diabetes. More patients in the no cricoid group underwent video laryngoscopy compared to the cricoid group (8 vs. 4).
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	No. While patients were not specifically blinded, they would have been under general anesthesia at the time of the intervention and hence would not have been aware of which treatment they were receiving. There is no way performance bias on the part of the patients could have influenced the outcomes.
2.	Were clinicians aware of group allocation?	Yes. Clinicians were not blinded to group allocation and no sham cricoid pressure was used in the control group. While this could have influence outcomes (i.e. the performance of aspiration), this seems unlikely.
3.	Were outcome assessors aware of group allocation?	No. "The laboratory personnel [performing pepsin A testing] were blinded to the study participant's randomization arm." (p. 176)
4.	Was follow-up complete?	Mostly yes. For the primary outcome, pepsin A levels were missing for only 3 of 95 patients (3.2%). Outcome data appears to have been available for all patients for the secondary outcomes.
II.	**What are the results ?**	
1.	How large was the treatment effect?	• For the primary outcome, microaspiration rates (based on elevated pepsin A levels) were similar between the no cricoid [pressure and

		cricoid pressure groups: 17.0% vs. 22.2% , RR 0.77 (95% CI 0.33 to 1.8). • There were no macroaspiration events in either group. • There was no difference in the incidence of difficult mask ventilation between the no cricoid pressure and cricoid pressure groups (36.7% and 37%, respectively), nor was there any difference in the incidence of difficulty with laryngoscopy (7.3% vs. 11.9%). • The incidence of HAP and ARDS were both low and were similar between the two groups.
2.	How precise was the estimate of the treatment effect?	See above. This was a very small study and hence the 95% confidence intervals were quite wide.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	No. This study was conducted in the operating room with patients undergoing elective procedures using general (presumably inhaled) anesthetics. The overall incidence of aspiration in this group would likely be much lower than among patients being emergently intubated in the ED using rapid sequence intubation (RSI). Additionally, the authors only included patients with specific risk factors for aspiration (obesity, diabetes, GERD) rather than a general population of patients being intubated (external validity).
2.	Were all clinically important outcomes considered?	No. The primary outcome of this study (elevated pepsin A levels in endotracheal aspirate) was a surrogate outcome of very uncertain clinical significance. The authors did consider the additional patient-oriented outcomes of HAP and ARDS development, but this study was vastly underpowered to detect a clinically significant difference in these outcomes given the very low incidence of both.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. This study suggests no benefit to the use of cricoid pressure during elective intubation in the operating room among patients felt to be at higher risk of aspiration. Unfortunately, the primary outcome evaluated is of very uncertain clinical significance and the study was vastly underpowered to detect a clinically important difference in more meaningful outcomes. Additionally, the risks of aspiration and potential benefits of cricoid pressure may be very different

		in ED patients being emergently intubated using RSI, and these results cannot be generalized to our patient population.

Limitations:

1. **This was an unblinded study, and hence is subject to significant bias.**

2. **The primary outcome in this study was a surrogate outcome of very uncertain clinical significance. While additional patient-oriented outcomes were considered, the study was vastly underpowered to detect a clinically significant difference in these outcomes.**

3. **The patients and setting in this study are very different from our practice environment, and it is unclear if these results would be externally valid when considering emergent intubation using RSI in the ED.**

4. **Despite the performance of a sample size analysis, the authors chose to perform this study as a pilot trial. There has been significant concern about the ethics of performing such underpowered studies (Halpern 2002).**

Bottom Line:

This small, pilot study conducted with patients undergoing intubation for elective surgery found no difference in rates of microaspiration, HAP, or ARDS between patients receiving cricoid pressure during intubation and those not receiving cricoid pressure. This study unfortunately used a surrogate outcome of very uncertain clinical significance in a practice setting very different from ours. It is impossible to generalize these results to patients undergoing emergent intubation in the ED using RSI.