Are Specialized Endotracheal Tubes and Heat-and-Moisture Exchangers Cost-Effective in Preventing Ventilator Associated Pneumonia?

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Ventilator-associated pneumonia (VAP) is a common and serious complication of mechanical ventilation via an artificial airway. As with all nosocomial infections, VAP increases costs, morbidity, and mortality in the intensive care unit (ICU). VAP prevention is a multifaceted priority of the intensive care team, and can include the use of specialized artificial airways and heat-and-moisture exchangers (HME). Substantial evidence supports the use of endotracheal tubes (ETTs) that allow subglottic suctioning; silver-coated and antiseptic-impregnated ETTs; ETTs with thin-walled polyurethane cuffs; and HMEs, but these devices also can have adverse effects. Controversy still exists regarding the evidence, cost-effectiveness, and disadvantages and risks of these devices. *Key words: ventilator-associated pneumonia; VAP; heat-and-moisture exchanger; nosocomial pneumonia; subglottic secretion removal; polyurethane cuff; endotracheal tube, silver-coated ; heat-and-moisture exchanger.* [Respir Care 2010;55(2):184–196. © 2010 Daedalus Enterprises]

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Introduction

Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs more than 48–72 hours after endotracheal intubation and the initiation of mechanical ventilation.[1,2] The intubation process itself can contribute to the risk of VAP. While the placement of an endotracheal tube (ETT) is a potentially life-saving procedure and allows for delivery of gas from the mechanical ventilator, it also provides a direct pathway for aspiration of colonized oral, nasal, and gastric secretions, via leakage around the ETT cuff. VAP can therefore more accurately be referred to as ETT-associated pneumonia.[3] VAP is the most common nosocomial infection in intensive care unit (ICU) patients receiving mechanical ventilation.[2-5] The incidence of VAP increases with the duration of mechanical ventilation. VAP causes longer ICU and hospital stay, higher mortality, and higher hospital costs (up to $40,000/case).[2-6] Despite increased awareness of and substantial progress in VAP prevention and treatment, it continues to be a major challenge for clinicians and has been the subject of considerable bench, laboratory, and clinical research. The clinical philosophy regarding VAP has shifted dramatically, from acceptance as an inherent consequence of mechanical ventilation to rigorous implementation of preventive measures and a measured indicator of quality care in the ICU.[6-8]

Accordingly, a great deal of emphasis has been placed on the mechanical ventilator circuit and related appliances such as humidifiers, nebulizers, and suction catheters.[8,9] Several artificial airway devices have been modified with the specific intention of preventing VAP. Specially designed ETTs have been developed to prevent VAP, including ETTs with subglottic suctioning ports (to remove secretions that pool above the cuff); ETTs with thin-walled cuffs (to decrease the size of the folds/channels along the cuff perimeter, which allow secretions to leak past the cuff); and ETTs coated with silver or antiseptic (to reduce accumulation of biofilm). Heat-and-moisture exchangers (HMEs) eliminate ventilator circuit condensate and decrease circuit colonization, which may help prevent VAP development.

Pro: Specialized Endotracheal Tubes and Heat-and-Moisture Exchangers Are Cost-Effective in Preventing Ventilator-Associated Pneumonia

Subglottic Suction Endotracheal Tubes

While a patient is intubated, oropharyngeal secretions accumulate above the ETT cuff and subsequently leak into the lower respiratory tract, thereby becoming a key cause of VAP.[10-12] Efforts have been made to remove these secretions, to reduce aspiration around the ETT cuff and thus
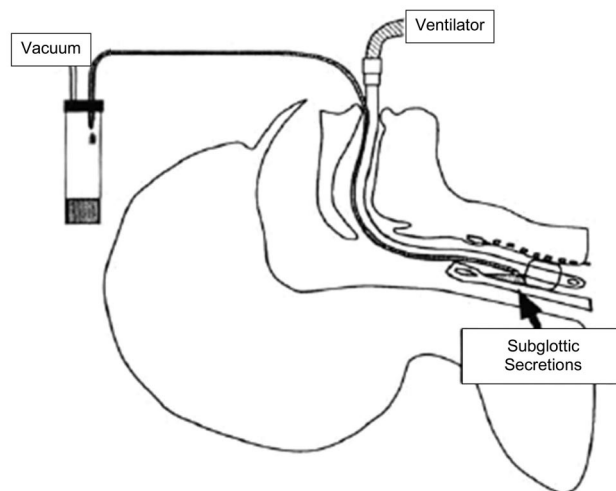

Fig. 1. Subglottic suctioning. The endotracheal tube has a dorsal lumen above the cuff, which is connected to suction to remove the secretions that pool above the cuff in the subglottic space. (Adapted from Reference 14, with permission.)

lower the risk of VAP. A subglottic-suction ETT has a separate dorsal lumen directly above the cuff (Fig. 1 shows the Hi-Lo Evac, Covidien, Boulder, Colorado) that is connected to a dedicated wall suction source, and secretions are intermittently removed with a suction of 70 mm Hg.

Six randomized controlled trials have demonstrated a reduction in the incidence and significant delay in the development of VAP in heterogeneous patient populations.[13-18] A meta-analysis of 5 studies[13-17] that included 896 patients found that subglottic suctioning reduced the incidence of VAP by nearly half (risk ratio 0.51, 95% CI 0.37–0.71) in patients expected to require 72 hours of mechanical ventilation, primarily by reducing early-onset VAP (Fig. 2).[19]

Subglottic-suction ETTs have a higher acquisition cost than conventional ETTs and are more likely to benefit patients who are expected to need prolonged mechanical ventilation. The economic impact of and cost-effectiveness of subglottic-suction ETTs has been evaluated by one study of VAP modeling.[20] With the relative risk reduction at 50% of the base-case estimate model, subglottic suctioning saved $1,924 per case of VAP prevented. Future clinical trials should investigate clinical outcomes and the financial cost/benefit implications of subglottic-suction ETTs.

Polyurethane Cuff Endotracheal Tubes

High-volume low-pressure ETT cuffs were developed over 30 years ago, and were designed so that the external diameter of a fully inflated cuff exceeds the diameter of the tracheal lumen by 1.5–2 times.[21] A partially inflated cuff with a volume less than the total cuff volume ade-
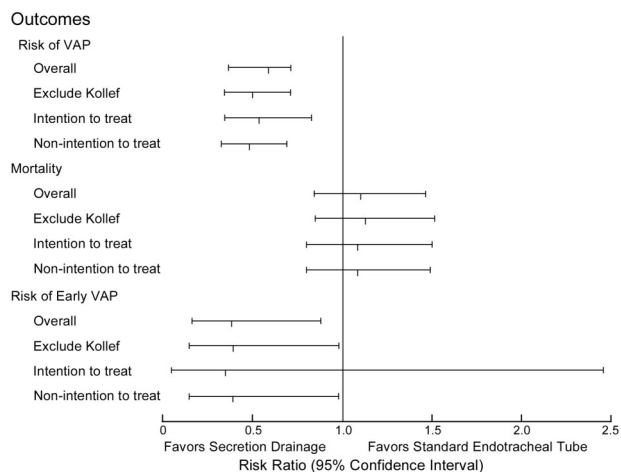
Fig. 2. Summary of risk ratios in the overall meta-analysis and sensitivity analyses. The risk ratios are presented as point estimates. The error bars signify the 95% confidence intervals. A summary risk ratio < 1 favors the use of subglottic suctioning for the outcome displayed. The results of the overall meta-analysis for each outcome appear first, followed by each of the 3 sensitivity analyses for that outcome. VAP = ventilator-associated pneumonia. (Adapted from Reference 19.)
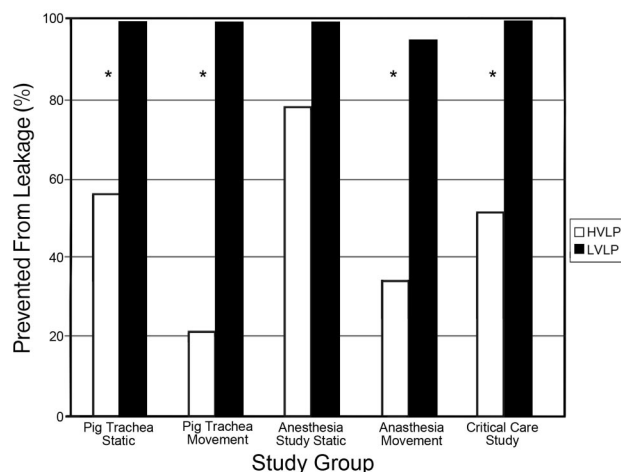

Fig. 3. Summary of studies of high-volume low-pressure (HVLP) versus low-volume low-pressure (LVLP) endotracheal tube cuffs. * $P < .05$. (Adapted from Reference 28.)

quately seals the trachea for ventilation. The internal pressure of the partially inflated high-volume low-pressure cuff therefore reflects the tracheal mucosal pressure, which allows cuff pressure to be measured and adjusted so that tracheal mucosal pressure is minimized and tracheal injury is prevented. Unfortunately, the partial inflation of the cuff causes folds in the cuff material against the trachea wall, and the folds are channels that allow leakage around the cuff, and aspiration.[22] The magnitude of the folds/channels, and therefore the amount of aspiration, increases with the thickness of the cuff material.[21] Folds/channels also increase as the cuff diameter increases in proportion to the tracheal diameter: the more excess cuff material, the more the folds/channels. This may explain the higher risk of late-onset VAP with larger ETTs (> 7.5 mm) (odds ratio 2.06, 95% CI 1.88–3.90, $P = .03$) in non-trauma ICU patients.[23]

A thin-walled polyurethane cuff has a thickness of 7 μm, versus 50–80 μm for a standard high-volume low-pressure cuff,[24] and therefore results in narrower channels, which reduces leakage past the cuff. Polyurethane cuffs reduced leakage around the correctly inflated cuff during in vitro and clinical testing,[24,25] and reduced the frequency of early postoperative pneumonia in cardiac surgery patients.[26]

Altering the shape of the ETT cuff is theorized to reduce the leakage of secretions into the lungs. An ETT (Seal-Guard, Mallinckrodt, Covidien-Nellcor, Boulder, Colorado) with a tapered (as opposed to the standard barrel shaped) cuff was designed to reduce folds/channels and thus decrease aspiration.[27] Redesigned ETT cuffs have been

evaluated in bench[28,29] and clinical studies.[28,30] Young et al compared a high-volume low-pressure cuff to a low-volume low-pressure cuff. The low-volume low-pressure cuff reduced aspiration in the both the bench study and in human subjects[28] (Fig. 3). In a randomized controlled trial, Lorente et al compared the incidence of VAP with a polyurethane-cuff subglottic-suction ETT versus a conventional ETT (polyvinyl cuff, no subglottic suctioning). VAP occurred in 31 (22%) of 140 patients in the conventional ETT group (in 1,558 days of mechanical ventilation), and in 11 (8%) of 140 patients in the intervention group (in 1,463 days of mechanical ventilation) ($P = .001$).[30]

The supply cost of ETTs with specially designed cuffs is many times higher than that of standard ETTs. The financial impact of these new-design tubes has yet to be examined, but can be extrapolated to cost savings due to VAP reduction.

Silver-Coated Endotracheal Tubes

An ETT acts as a reservoir for bacterial accumulation. Microorganisms adhere to the ETT lumen and create a biofilm,[31] which may become the site of antibiotic-resistant pathogens. These pathogens can dislodge and migrate to the lungs, implicating that a contributing factor to VAP is the ETT lumen. Interestingly, coating an ETT with silver is theoretically beneficial because of silver's broad-spectrum antimicrobial activity in vitro, reduction in bacterial adhesion to devices, and elimination of biofilm formation in an animal model.[31]

A recent novel anti-VAP development is a silver-coated ETT (Agento, Bard, Murray Hill, New Jersey), that is designed to prevent biofilm build up on the *inner* lining of the ETT.[31,32] A silver-sulfadiazine-coated ETT prevented

Pseudomonas aeruginosa biofilm formation in a 72-hour in vitro study, and lower-respiratory-tract colonization in sheep mechanically ventilated for 24 hours.[31] Berra et al performed a randomized controlled trial with cardiac surgery patients to compare bacterial colonization in standard versus silver-sulfadiazine-coated ETTs.[32] The silver-coated ETT safely prevented bacterial colonization and narrowing of the ETT in patients who required mechanical ventilation for up to 24 hours.

Most recently, Kollef et al conducted a large multicenter randomized controlled clinical trial of the silver-coated ETT. In 54 centers they studied the incidence of VAP in 2,003 patients expected to require mechanical ventilation for $\geq$ 24 hours.[33] The silver-coated ETT resulted in a 35.9% VAP risk reduction ($P = .03$). Among patients intubated for > 24 hours, the rate of microbiologically confirmed VAP was significantly lower with the silver-coated ETT (4.8% vs 7.5%). The silver-coated ETT was also associated with a significant delay in the occurrence of VAP ($P = .005$).

The cost-effectiveness of silver-coated ETTs was evaluated in a decision model based on a 1,000-patient cohort case-based study, which found financial justification of the cost, compared to a standard uncoated ETT.[34] The concept of a silver-coated ETT is novel and theoretically beneficial. Further investigation should examine the VAP incidence in patients who required mechanical ventilation for longer than 48–72 hours.

Heat-and-Moisture Exchanger

The delivery of cold and dry gas during mechanical ventilation requires humidification, as the nose and upper airway are bypassed. The HME, commonly referred to as an artificial nose, recycles exhaled heat and moisture and thus obviates heated humidification during mechanical ventilation. The low maintenance and cost of HMEs have made them a common entity in the ventilator circuit. An HME eliminates ventilator circuit condensate and decreases circuit colonization, which may impact VAP development. The affect of HME versus heated humidifier on VAP occurrence has been evaluated extensively.[35-45] In a meta-analysis, Hess et al found a lower risk of VAP with HME than with heated humidifier (relative risk 0.65, 95% CI 0.44–0.96, $P = .03$).[39] However, a single trial by Kirton et al, which found a relative risk of 0.41 and a 95% CI of 0.2–0.86,[41] heavily influenced that and subsequent meta-analyses.[45] These results must be taken into account when examining meta-analyses of HME versus heated humidifier influence on VAP.

The cost-effectiveness of HME is at the center of a longstanding argument related to the lower cost of disposable medical devices, versus the higher cost of heated humidification. An HME is a single item that can be used

with any mechanical ventilator circuit, whereas heated humidification requires a heated-wire circuit, a humidifier, and containers of sterile water for inhalation. However, aside from the equipment-acquisition costs is the issue of the frequency of HME replacement. Several studies found no evidence to support routinely replacing the HME, which further decreases the cost of the HME, relative to the heated humidifier.[35-40] According to evidence-based guidelines, the HME does not need to be changed daily for infection control or technical performance.[39] An HME can be safely used for at least 48 hours, and up to 72 hours of mechanical ventilation.[38]

The HME could be considered a cost-saving humidification method, for patients who do not have contraindications, namely, asthma, thick secretions, airway burns, hypothermia, hemoptysis, and bronchopleural fistula.[35,41-46] A rigorous, well designed, randomized controlled trial of HME versus heated humidifier, which incorporates all current evidence regarding mechanical ventilation and VAP prevention, should be conducted to thoroughly answer the remaining questions.

Con: Specialized Endotracheal Tubes and Heat-and-Moisture Exchangers May Be Cost-Effective in Preventing VAP, But Are Associated With Problems, Limitations, and Adverse Effects

Subglottic Suction Endotracheal Tubes: Problems and Adverse Effects

Despite a large body of evidence from prospective randomized trials,[13-18] a systematic review,[46] a meta-analysis,[19] and recommendations in evidence-based practice guidelines,[7,9,47] the use of subglottic-suction ETTs has been infrequent and slow to enter clinical practice.[48-52] Surveys of hospitals in Canada, France, and Spain found a usage rate of 0–4%.[48-50] In the United States, hospital use is around 20%.[51,52] This contradiction between the evidence and practice may be in part due to the conflicting results from prospective studies, disagreement about the strength of the evidence, and problems with and adverse effects of subglottic-suction ETTs.[52] Of the 6 prospective randomized trials to date, 3 found no statistically significant difference in the frequency of VAP between the subglottic-suction group and the control group (via chi-square test, intention-to-treat analysis).[14,15,18] There were also no differences in mortality,[13-15,17,18] ICU stay,[14,15,17,18] hospital stay,[15,17,18] or duration of mechanical ventilation[14,15,17,18] in the studies in which those results were reported.[19] Inconsistencies in the study methods include heterogeneity in the patient populations. The studies and their meta-analyses linked all VAP cases together, but VAP pathogenesis and risk factors differ across patient populations, so it may be illogical to assume that an intervention that

worked for one series of patients or group of organisms will be effective for all.[53]

Lack of a standard diagnostic criteria, and the use of surveillance cultures of the oropharynx and trachea may have resulted in failure to accurately diagnose VAP, which would impact the study results.[54,55] It has been suggested that the positive results of the randomized trials that supported subglottic-suction ETT were more likely an antibiotic effect rather than a suctioning effect, in that more test patients may have received adequate antimicrobial coverage.[56] Microbiological surveillance can distinguish ventilator-associated tracheobronchitis by colonization of the trachea from infection due to VAP. Ventilator-associated tracheobronchitis is recognized as a risk factor and precursor to VAP and therefore may be a better focus for VAP prophylaxis.[57-60] Nseir et al randomized patients to receive targeted antibiotic therapy following serial quantitative surveillance of tracheal aspirate colonization. VAP occurred in 41% of the control group and in none of the patients who received appropriate antibiotics.[58] Michel et al found that appropriate antibiotic coverage in 95% of patients who were eventually diagnosed with VAP could be determined by routine surveillance cultures.[60]

More importantly, patients who received targeted antibiotic therapy based on routine surveillance of microbial colonization had significantly more ventilator-free days ($P < .001$), lower mortality, and fewer hospital days ($P < .005$).[58] This suggests that the early diagnosis and treatment of ventilator-associated tracheobronchitis, rigorous microbial surveillance, and targeted antibiotic treatment may reduce the incidence of VAP, mortality, duration of mechanical ventilation, and hospital stay, which are important outcomes that subglottic suctioning alone has repeatedly failed to impact.

Another important limitation of subglottic-suction ETTs is that, though they decrease early-onset VAP, they do not decrease late-onset VAP.[13-18] The normal flora of endogenous respiratory pathogens (*Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Haemophilus influenzae*) that cause early-onset VAP are generally less virulent, respond easily to treatment, and are therefore less likely to increase mortality or prolong mechanical ventilation or hospital stay.[61] Nosocomial exogenous infections of Gram-negative bacilli and drug-resistant organisms are the more frequent cause of late-onset VAP and are associated with high mortality. Reduction of the volume of bacteria-laden secretions that get past the ETT cuff explains the delayed VAP with subglottic suctioning.

In studies of oropharyngeal and tracheal colonization patterns in animals[62] and humans,[63] continuous subglottic suctioning failed to prevent upper-airway or lung bacterial colonization. In the 72-hour animal study, continuous subglottic suctioning performed per the manufacturer's recommendations only marginally lowered bacterial coloni-
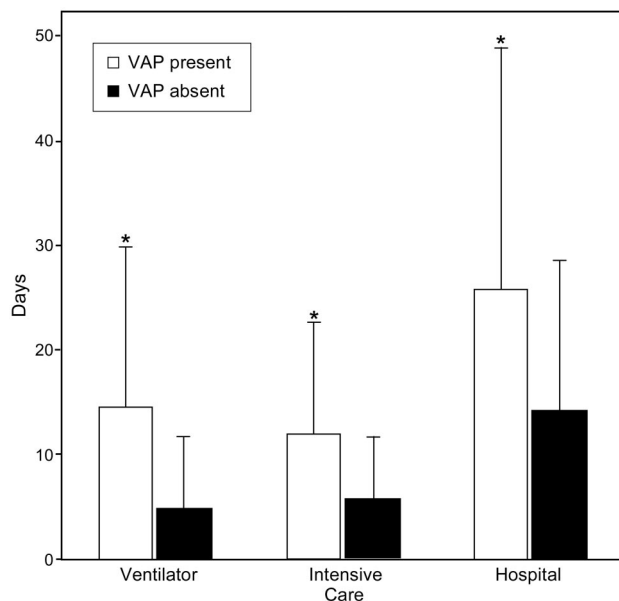

Fig. 4. Health and economic outcomes associated with ventilator-associated pneumonia (VAP), from a large United States database. Patients with VAP had significantly longer mechanical ventilation, intensive-care stay, and hospital stay. * $P < .001$ for all comparisons. (From data in Reference 5.)

zation of the lungs.[62] In mechanically ventilated ICU patients the daily oropharyngeal and tracheal colonization patterns were not modified. Median bacterial counts in patients who received subglottic suctioning were unchanged, and 75% of the subglottic-suction group were colonized in the trachea after 1 day.[63] These results suggest that subglottic suctioning reduces but does not prevent aspiration, which may explain the limited effect on preventing late-onset VAP.

VAP increases ventilator, intensive care, and hospital days (Fig. 4),[5] attributable mortality (Fig. 5),[64] and costs.[20] However, the lower VAP rate with subglottic suctioning has not affected these important outcomes, nor has a cost-of-care difference been directly measured in any randomized study thus far.

Poor clinician acceptance of the subglottic-suction ETT is primarily due to problems and potential adverse effects associated with their use. Frequent failure to suction through the subglottic suction port was first reported in 1996; in that study the failure rate was 34% in 83 intubated patients.[65] A 2007 study reported failure of subglottic suctioning in 19 (48%) of 40 patients.[66] The causes of subglottic suction port obstruction, assessed via bronchoscopy, were: tracheal mucosa suctioned into the suction port (17 patients), thick secretions (1 patient), and undetermined (1 patient). Those findings confirmed the potential for tracheal injury demonstrated in sheep, in which tracheal mucosal damage was found at autopsy in all the animals treated with subglottic suction.[62]
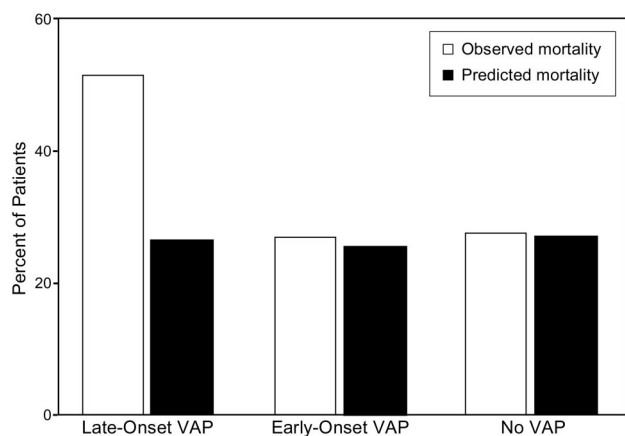
Fig. 5. Predicted and observed mortality in patients treated with endotracheal tubes with subglottic suctioning capability. (From data in Reference 64.)
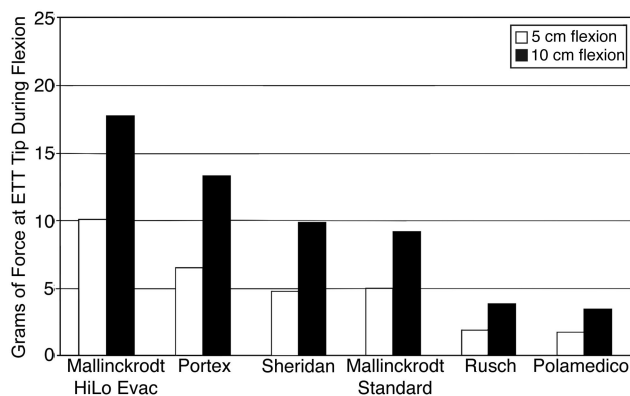

Fig. 6. Endotracheal tube rigidity, measured as force at the tube tip during 2 flexion amounts (5 cm and 10 cm), with 6 endotracheal tube brands. This is aggregate data from 4 of each size tube (6.0, 7.0, 7.5, and 8.0 mm) ($n = 16$ for each brand). The Mallinckrodt Hi-Lo Evac was the most rigid ($P < .05$). (Adapted from Reference 67.)

Fig. 7. Redesigned subglottic suction endotracheal tube showing (A) the repositioned suction port closer to the cuff, to prevent suction (and injury) to the tracheal mucosa, and (B) a larger suction lumen, to prevent occlusion with thick secretions; the latter design change visibly increased the external diameter and probably increased tube rigidity. (From Reference 69.)

In another study, published in 2004, Girou et al reported a high rate of laryngeal edema and upper-airway obstruction that required re-intubation in 2 of 5 patients following the use of the subglottic-suction ETT.[63] Laryngeal edema in those patients can be explained by the greater stiffness and larger external diameter of the subglottic-suction ETT. The addition of the suction lumen in the subglottic-suction ETT increased the wall thickness and the overall external diameter by 0.7–0.8 mm, compared to a standard ETT of the same internal diameter.[67] The effect on the rigidity of the subglottic-suction ETT was quantified in a laboratory experiment (Fig. 6). Larger external diameter ETTs are associated with laryngeal and vocal cord injury[68] and a higher incidence of late-onset VAP because of more fluid leakage through bigger cuff folds/channels.[23] The greater rigidity and external diameter of the subglottic-suction ETT increase pressure on soft tissue at the points of contact in

the upper airway and may increase the incidence and severity of laryngeal and vocal cord injury.

To address the problems of tracheal injury and suction lumen obstruction with thick secretions, the manufacturer introduced a design change in 2005. The suction port was moved closer to the cuff to prevent tracheal mucosa occlusion of the suction port, and the suction port and lumen were enlarged to prevent obstruction with thick secretions (Fig. 7).[69] The redesigned tube has an even larger outer diameter (0.8–1.0 mm) than a standard ETT, and is therefore probably more ridged. The manufacturer recommends compensating for the larger external diameter by using a half-size smaller ETT.[51] The effects of these design changes on the rate of subglottic suctioning failure or tracheal/laryngeal injury has not been assessed.[51]

Additional problems associated with subglottic suction ETTs include the higher cost and the time required for tube manipulation and maintenance of suction lumen pa-

Table 1. Bundled Interventions and Hospital Policies Implemented for the Prevention of Ventilator-Associated Pneumonia

1. Maintain endotracheal tube cuff pressure at 20–30 mm Hg.
2. Place patient semi-recumbent (30° head-elevated).
3. Provide frequent oral hygiene with an antiseptic agent.
4. Use a protocol to facilitate weaning from mechanical ventilation.
5. Avoid frequent changing of ventilator circuit and in-line suction catheter.
6. Avoid opening or manipulating the ventilator circuit for routine care.
7. Implement policies to reduce accidental extubation.
8. Avoid insertion of nasal endotracheal or gastric tubes, to prevent sinusitis.
9. Use noninvasive ventilation when possible.
10. Promptly re-intubate patients who fail extubation.
11. Provide adequate humidification and prevent aspiration of ventilator condensate.
12. Suction only when necessary, to avoid airway contamination and trauma.
13. Avoid gastric distension and monitor gastric residual volume.
14. Adopt strict guidelines on and avoid overuse of antibiotics.
15. Implement strict hand hygiene with waterless antiseptic agents.
16. Adopt strict policies on use of barrier measures to prevent cross-colonization.
17. Improve sedation methods
18. Avoid use of paralytic agents.
19. Provide immunizations for clinicians.
20. Ensure adequate intensive care unit staffing.

(Adapted from References 72-75.)

Fig. 8. Endotracheal tube with a tapered thin-walled polyurethane cuff and subglottic suction port. (Courtesy of Mallinckrodt.)

tency. Because of their history of frequent suctioning failure, subglottic-suction ETTs are perceived to be unreliable and labor intensive. Subglottic suctioning techniques used in clinical studies have included manual hourly syringe aspiration,[13] continuous low[14,16] and high (100–150 mm Hg)[18] wall suction, intermittent low[15] and high (100 mm Hg) wall suction,[17,18] and air[13,18] or saline[14,18] boluses through the suction lumen. Some of these practices are not recommended by the manufacturer,[70] which imposes liability risk on clinicians.

Reducing VAP rate and incidence can be achieved by other means besides subglottic-suction ETT. Simple interventions, such as suctioning of oral secretions prior to position changes, significantly impact the VAP rate.[71] Comprehensive staff education and bundled interventions also reduce VAP (Table 1).[72-75] There have been many reports of VAP reduction without subglottic-suction ETT,[76-84] which minimizes the importance of subglottic-suction ETT in VAP prevention.

An alternative method to clear subglottic secretions is described in respiratory care and anesthesia textbooks.[85,86] After suctioning the oropharynx, a positive-pressure lung hyperinflation with an inspiratory hold is applied, then the cuff is rapidly deflated and the gas flows upward past the

deflated cuff and propels secretions toward the oropharynx, where they can be cleared with repeated oropharyngeal suctioning. This maneuver purges the subglottic space during extubation[87-89] and could be used to periodically clear subglottic secretions as a VAP-prevention measure. This maneuver warrants clinical investigation as an alternative to subglottic-suction ETT.

Redesigned Cuffs and Endotracheal Tubes: Limitations, Safety, and Costs

Thin-walled polyurethane cuffs have narrower folds/channels, when properly inflated,[24,25] but this improved cuff design only slows cuff leakage and aspiration: it does not prevent it. Secretions remain pooled above the cuff unless removed, and deep oropharyngeal suctioning alone is inadequate to clear the subglottic area above the cuff. A randomized controlled trial of a polyurethane-cuff ETT with cardiac surgery patients found reduced frequency of early postoperative pneumonia and less antibiotic prescription, but no effect on mortality, ICU stay, or hospital stay.[26] However, study limitations included lack of microbiological confirmation of clinically suspected pneumonia in 65% of the patients, use of effective empirical antibiotics in all
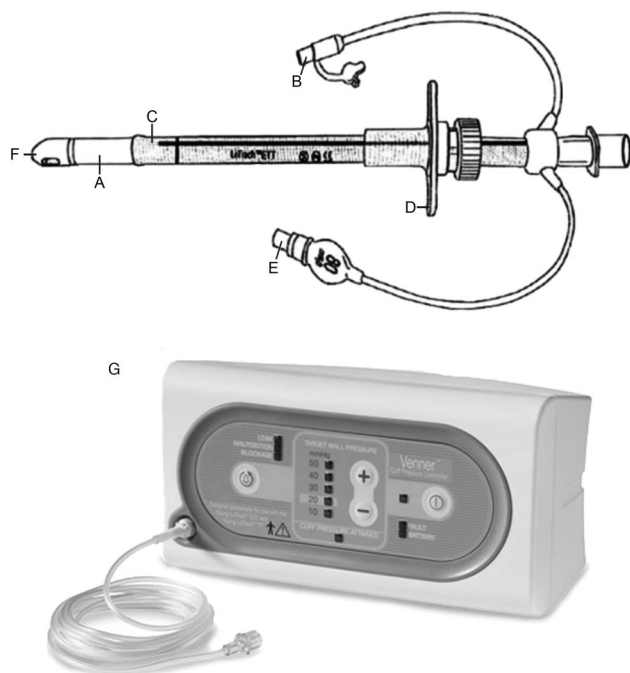
Fig. 9. The LoTrach endotracheal tube system is designed to reduce the risk of ventilator-associated pneumonia. A: Low-volume low-pressure cuff, to eliminate folds/channels in the cuff material and thus prevent leakage past the cuff. B: Subglottic suction and irrigation channel. C: Three subglottic suction ports, to reduce the risk of tracheal injury from subglottic suctioning and allow irrigation of the subglottic space without risk of aspiration. D: Combination integrated bite block and adjustable flange securing system to prevent tube movement and accidental extubation. E: Inflation tube. F: Atraumatic tip. G: Electronic cuff-inflation device maintains a constant cuff pressure. The inner lumen of this tube has a non-stick coating that inhibits secretion accumulation and biofilm adhesion. (Courtesy of LoTrach, Venner Medical, Kiel, Germany)

Fig. 10. In vitro test of 3 brands of endotracheal tube cuff. At the normal inflation pressure, liquid passes through the folds in the cuff. A: Standard high-volume low-pressure cuff. B: Ultra-thin polyurethane high-volume low-pressure cuff. C: Low-volume low-pressure cuff (LoTrach, Venner Medical, Kiel, Germany). (From Reference 89a, with permission.)

patients for 5–7 days, a mean duration of ICU care of 3 days in each group, and the clinical diagnosis of pneumonia was made after most of the patients were already extubated.[26] Further study of thin-walled cuffs is required to establish their utility in VAP prevention.

The SealGuard ETT has a tapered polyurethane cuff and subglottic suction capability, and the manufacturer claims that this ETT reduces aspiration by 95% (Fig. 8). A randomized clinical trial found significantly less early-onset and late-onset VAP, but the trends toward shorter duration of mechanical ventilation, fewer ICU days, and lower mortality were not significant.[30] Although these results look promising and no complications or problems were reported, the study did not report or assess the subglottic suctioning failure rate nor the impact of previous design changes on the risk of tracheal mucosal injury.

A completely redesigned ETT (LoTrach, Venner Medical, Kiel, Germany)[28] (Figs. 9 and 10)[89a] attempts to minimize multiple ETT-related VAP risk factors.[90,91] The

LoTrach is currently available only in Europe and Asia, has had limited laboratory and clinical testing,[28] and is probably cost prohibitive.

Silver-Coated Endotracheal Tubes: Limitations of the Evidence

The silver-coated ETT delays biofilm formation and thus decreases the bacterial burden in tracheal aspirates,[92] but all the studied ETTs were colonized within the 7-day study period.[93] Animal studies had similar results. Silver coating delayed bacterial colonization of the ETT lumen up to 3.2 ± 0.8 days in dogs,[94] and reduced tracheal colonization, eliminated or reduced bacterial colonization of the ETT and ventilator circuit, and prevented lung bacterial colonization for 24 hours in sheep.[31]

Reason for controversy regarding the North American Silver-Coated Endotracheal Tube randomized trial[33] has been expressed.[95,96] The bacteriologic culture threshold of 10^4 colony-forming units/mL for defining VAP in that study has historically had low sensitivity and specificity for diagnosing histological VAP or clinically important

First Author	Treatment n/N	Control n/N	Odds Ratio (random) (95%CI)	Odds Ratio	95% CI
Branson[14]	3/49	3/54		1.11	0.21–5.77
Dreyfuss[13]	6/61	8/70		0.85	0.28–2.59
Hurni[28]	5/59	7/56		0.65	0.19–2.18
Kirton[15]	9/140	22/140		0.37	0.16–0.83
Kollef[10]	15/163	15/147		0.89	0.42–1.89
Lacherade[21]	47/185	53/184		0.84	0.53–1.33
Lorente[23]	21/53	8/51		3.53	1.39–8.98
Martin[11]	2/31	8/42		0.29	0.06–1.49
Mernish[19]	14/123	19/120		0.68	0.33–1.43
Roustan[12]	5/55	9/61		0.58	0.18–1.84
Boots[18]	14/75	7/41		1.11	0.41–3.03
Boots[22]	24/190	23/191		1.06	0.57–1.95
Total (95% CI)	1,184	1,157		0.85	0.62–1.16

Total events: 165 Treatment, 182 Control
Test for heterogeneity: chi-square = 16.44, degrees of freedom = 11, P = .13, I^2 = 33.1%
Test for overall effect: Z = 1.03, P = .30

0.1   0.2   0.5   1   2   5   10
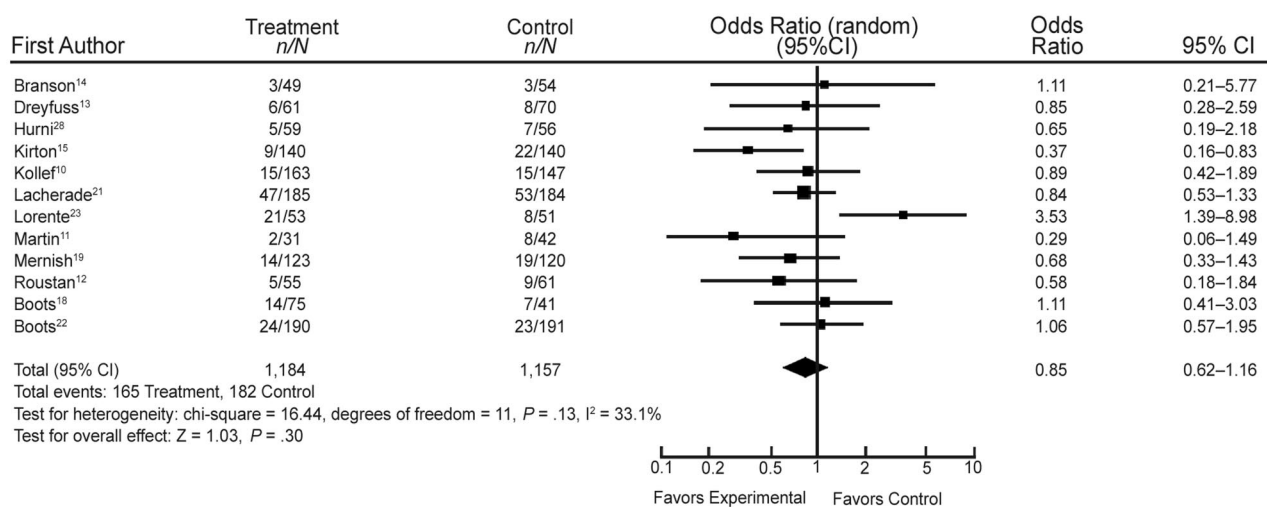Favors Experimental   Favors Control

Fig. 11. Odds ratio of incidence of ventilator-associated pneumonia (VAP) in the randomized controlled trials that have compared heat-and-moisture exchanger (treatment) and heated humidifier (control) for patients undergoing mechanical ventilation and pooled analysis. There was no heterogeneity among the identified comparisons (P = .13, I^2 = 0.33, 95% confidence interval [CI] 0–0.66). There was no difference in the incidence of VAP between the patients managed with HME and those managed with heated humidifier (odds ratio 0.85, 95% CI 0.62–1.16, P = .30, 2,341 patients). The vertical line represents the no-difference point between the 2 treatments. The squares indicate the odds ratios, and the size of each square denotes the proportion of information given by that trial. The diamond indicates the pooled odds ratios for all the included trials. (Adapted from Reference 45.)

disease. When we exclude non-pathogenic colonizing organisms from the study analysis, the difference in VAP rate between the treated (30/968, 3.1%) and untreated (45/964, 4.7%) groups loses statistical significance (P = .08).[95] This changes the absolute risk reduction to 1.6%, which may be achievable by means other than the silver-coated ETT. Additionally, there were no differences in the important clinical variables of duration of mechanical ventilation, ICU stay, hospital stay, or mortality, based on findings from 1,932 patients enrolled. There was also a statistically significant difference in the proportion of patients with chronic obstructive pulmonary disease, which was lower in the group that received the silver-coated ETT. Chronic lung disease is a recognized risk factor for VAP and may have biased the study results.[96]

Given these important study limitations, silver-coated ETTs should not be viewed as the definitive answer for VAP prevention. Until additional data confirm clinical effectiveness and cost benefit, these tubes might be considered in high-risk patients in whom the incidence of VAP remains above the benchmarked rates and institutional goals. A comprehensive, multifaceted, multidisciplinary VAP-prevention program should be considered first.[96]

Heat-and-Moisture Exchangers: Cheaper But Ineffective in VAP Prevention

HMEs are cheaper than heated humidification. The HME eliminates circuit condensate and bacterial colonization,

which are a potential source of VAP. However, studies of HMEs have not consistently shown a lower incidence of VAP. A recent meta-analysis by Siempos et al[45] examined 12 randomized controlled trials that included 2,580 patients,[42-44,97-105] and found that HME and heated humidifier had a similar VAP rate (relative risk 0.85, 95% CI 0.62–1.16) (Fig. 11). A subgroup analysis examined only trials in which the mean duration of mechanical ventilation was > 7 days, and found no difference in VAP incidence between heated humidifier and HME (odds ratio 0.81, 95% CI 0.54–1.21, 1,812 patients). The available evidence does not support a preference for either the HME or heated humidifier with regard to VAP incidence, morbidity, or mortality.[45]

Furthermore, the HME is associated with unfavorable mechanical effects, and can alter mucus viscosity and CO_2 clearance. The cumulative episodes of airway occlusion that required re-intubation during HME use in 11 studies were 22/1,038 (2.1%) in the HME group, versus 8/1,012 (0.8%) in the heated humidifier group: a relative risk difference of 62%.[45] One of those studies was terminated early after a patient death in the HME group, from complete airway occlusion.[99] Mucus clearance via cough was found to diminish after 72 hours of HME use.[106] Air flow resistance through the HME can increase after 24 hours of use, in excess of the manufacturer's specifications,[42] which increases the imposed work of breathing.[107] Also, the additional volume of the HME increases mechanical dead space and reduces CO_2 clearance.[108-111]

Summary

The cost-effectiveness of VAP-prevention devices has been estimated with various methods, but has not been directly measured in randomized controlled trials. VAP prevention may be best achieved with a multifaceted, multidisciplinary bundle of simple interventions, such as stringent hand hygiene, semi-recumbent positioning, and improved oral hygiene, which can effectively reduce VAP without the use of special devices. Studies of VAP-prevention devices have thus far been under-powered to show outcome benefits in mortality or duration of care. Future studies should include cost/benefit analysis and risk assessment. Questions of safety, potential for injury, and device failure rate need to be addressed. Several new ETT design changes look promising but need further rigorous study. The current evidence is inconclusive on the effects of HME on VAP; HMEs are associated with adverse effects but are a cost-saving alternative to the heated humidifier.

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Discussion

MacIntyre: So we have a strategy that reduces mortality by 10% and it doesn't cost you a dime, because all it requires is to turn down the tidal volume slightly, and it's still taken 9 years to get many places to even drop the tidal volume a little. Now we hear from Mike and Mark about these new ETTs that are several-fold more expensive but may have nowhere near that effect on mortality. I think it'll take much longer for these ETTs to be adopted in widespread use. When the cost is that high and the benefit is that marginal, I'm not sure these things will really "take off."

I'm always confused by these studies that talk about reducing the VAP rate, because VAP is so poorly defined. At CMS [Centers for Medicare and Medicaid Services] I represented an organization I'm a member of, and there was a discussion of whether CMS should set VAP targets to meet or else be penalized. But it became obvious that the various definitions of VAP rate are all over the map. Some people cited studies that VAP occurred 150 times per 1,000 patient days. Other studies said it happened once or twice.

In anticipation of a CMS penalty for VAP, some hospitals have already altered their definitions so that VAP has gone away. It just doesn't exist anymore in some ICUs—not because we're better at treating or preventing it, but because we played with the definition to get within the bounds. So I'm a bit concerned when people tell me there's a new gadget that's going to reduce such an ill-defined entity as VAP. It disturbs me and makes it difficult to sort through this literature.

Hess: Just to follow up on the point you just made, one of the things that impressed me the most about Marin Kollef's[1] study with the silver-coated ETT was how low the VAP rate was in the control group.

1. Kollef MH, Afezza B, Anzueto A, Veremakis C, Kerr KM, Margolis BD, et al; NASCENT Investigation Group. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. JAMA 2008; 300(7):805-813.

MacIntyre: Yes, it makes it hard to justify adopting an expensive technology to protect against something that doesn't occur that often.

Siobal: In a recent paper[1] on subglottic-suction ETTs, the control group had 50 cases and the group treated with the subglottic-suction ETT had 30 cases per 1,000 ventilator days. So they need to do something else besides use those tubes to reduce their VAP rates.

1. Bouza E, Pérez MJ, Muñoz P, Rincón C, Barrio JM, Hortal J. Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. Chest 2008;134(5):938-946.

Gay: That said, VAP is coming back. The CMS group decided initially that they could either say, yes, VAP is present or no, it is not present, since they could only track it that way. So they initially decided that incidence tracking of VAP was impractical. The new commission is going to look at hospital-acquired infection and try to do it the right way—come up with a definition and then track the incidence rate in various areas of the country. I think it'll be better defined and a much more real thing in the future.

MacIntyre: But one person's congestive heart failure and low-grade fever from tracheal bronchitis is somebody else's florid VAP. It's going to be very difficult to come up with a really solid definition that is trackable by third parties.

Durbin: I think most of us agree that aspiration of secretions that get past the cuff is the primary etiology of VAP, and if that's so, it would explain why, in the early days, the first anti-VAP intervention that improved outcomes in neurosurgical patients was to recover them in the prone position, because the secretions would drain out rather than into the lungs. That probably explains the lower incidence of infections and the better survival back in the 1930s, before ETTs, mechanical ventilators, and critical care units existed. Is there any evidence that proning reduces VAP?

Hess: I think it was the Guerin study[1] of proning; there was a lower VAP rate in the prone group.

1. Guerin C, Gaillard S, Lemasson S, Ayzac L, Girard R, Beuret P, et al. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. JAMA 2004;292(19): 2379-2387.

Moores: We've been talking about these things we can do that cost little or nothing, and in the ventilator bundle I think that keeping the head of the bed at 30 degrees and washing your hands probably have the biggest impact. Those are the things we can target more directly, with signs everywhere and red lines that mean "don't go in there." Our nurses will grab you if you go in there without washing your hands. Our data indicated that we were really good at writing the order and keeping the head of the bed elevated at 30 degrees, but the patient just slides down in the bed.

MacIntyre: Their neck was at 30 degrees!

Moores: Yeah. And I can't get the nurses to watch that and bring them back up. Has anyone figured out how to keep the patient up and not sliding down?

Epstein: Van Nieuwenhoven et al[1] also observed that patients don't stay semi-recumbent. And 30 degrees is inadequate. It was 45 degrees that was shown to be of benefit in a recent meta-analysis.[2] So on that the VAP bundle is not fully evidence-based.

1. van Nieuwenhoven CA, Vandenbroucke-Grauls C, van Tiel FH, Joore HC, van Schijndel RJ, van der Tweel I, et al. Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: a randomized study. Crit Care Med 2006;34(2):396-402
2. Alexiou VG, Ierodiakonou V, Dimopoulos G, Falagas ME. Impact of patient position on the incidence of ventilator-associated pneumonia: a meta-analysis of randomized controlled trials. J Crit Care 2009;24(4):515-522.

Moores: We tried 45 degrees, and it was even worse, so we went back to 30 degrees, thinking maybe they'd stay semi-recumbent.

MacIntyre: And the steeper the angle, the greater the risk of pressure ulcers on their rear ends, so you go from one CMS violation to another.

Epstein: What about the impact of HMEs on weaning? An HME increases work of breathing and the dead space, and that additional work might be enough to keep a marginal patient from coming off the ventilator.

Gentile: Yes, I agree, but in the VAP literature there's no difference, so it fueled the fire for the HME supporters saying, "See, it doesn't make a difference in VAP." But, yes, HME increases the work of breathing and minute volume, so HME increases P_{aCO_2}.

Epstein: I want to follow up on Mark's crazy idea about delivering a large-volume inflation, then deflating the ETT cuff during the exhalation to clear secretions.

MacIntyre: To blow the pipes clean.

Epstein: We wondered whether subglottic secretions contribute to extubation failure. Those secretions may not be appreciated until you deflate the cuff and they drip down. There is no established method for how to remove an ETT, and the guidelines[1] don't tell exactly how to properly remove the tube. So in a pilot randomized controlled trial[2] we randomized the 2 techniques: one arm was similar to what Mark mentioned: a large inflation, then deflate the cuff and remove the tube. The other group had a suction catheter placed through the ETT, the cuff was deflated, and continuous suction was applied as the ETT was removed. Because the study was small we didn't find a statistically significant difference, but the extubation failure rate tended to be higher in the

continuous-suction group, which is interesting. I don't know if the technique was beneficial or if the continuous suctioning is a bad thing that produced atelectasis as the tube was removed.

1. American Association for Respiratory Care. Clinical Practice Guideline. Removal of the endotracheal tube, 2007 revision and update. Respir Care 2007;52(1):81-93.
2. Bahhady I, Howard W, Rothaar R, Epstein SK. Extubation outcome: a randomized controlled trial to evaluate outcomes using 2 different extubation techniques in mechanically ventilated patients (abstract). 2004 International Conference of the American Thoracic Society.

Siobal: I think if you apply suction and deflate the cuff, you may be sucking the secretions down the airway past the deflated cuff, and then you only suction some of it out while you're pulling the tube out. That could explain it.

Gentile: When you deliver that big breath, how many mL/kg is the volume?

Siobal: I don't know. You can limit it by pressure.

MacIntyre: Pressure-targeted ventilation!

Siobal: It would be nice to have a button that would deliver 30 cm H_2O and maintain that as you deflate the cuff, so it blows gas up past the deflated cuff. That flow would blow secretions up out of the subglottic space. You can also do an inspiratory hold, maybe with a stacked breath, to increase FRC [functional residual capacity] a little bit, then deflate the cuff, and as the gas flows out of the lung, it purges the secretions from the subglottic space. The maneuver causes lung stretch, but it's only for one breath.

MacIntyre: Say, 40 cm H_2O for 40 seconds, like a recruitment maneuver.