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EDITORIAL

Beware the siren's song of novel endotracheal tube designs

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Ventilator-associated pneumonia (VAP) remains a common and morbid complication of mechanical ventilation. Notwithstanding hospitals' and device manufacturers' extensive efforts to prevent this condition, clinical audits suggest VAP rates have changed little over the past decade [1]. VAP's persistence compels us to redouble our efforts to find better ways to prevent this condition. Prevention efforts to date can be divided into two major domains: (1) technical innovations to reduce biofilm accumulation and passage of secretions around the endotracheal tube cuff, and (2) adaptive work to minimize duration of mechanical ventilation and thus time at risk for VAP. Examples of technical innovations include antiseptic-coatings, subglottic secretion drainage, tracheal cuff pressure maintenance systems, and novel endotracheal tube cuff designs. Examples of adaptive efforts include minimizing sedation, increasing the use of spontaneous awakening and spontaneous breathing trials, and early mobilization programs.

Technical innovations have followed a familiar pattern. Initially promising bench studies have given way to disappointing clinical trials [2]. Antiseptic coating decreased endotracheal tube colonization rates in sheep but did not decrease duration of mechanical ventilation or mortality rates in humans [3, 4]. Subglottic secretion drainage (SSD) reduces VAP diagnoses but does not reduce time to extubation or mortality rates [5]. Persistently low tracheal cuff pressures are a risk factor for VAP but automated cuff pressure control devices have yielded conflicting results [6, 7]. Tapered and polyurethane cuffs decrease (but do not eliminate) leakage around the cuff in bench studies but have not reduced VAP rates in randomized controlled trials [8, 9].

A recent article by Jaillette and colleagues in *Intensive Care Medicine* continues this disappointing pattern [10]. The investigators compared conical polyvinylchloride cuffs to standard-shaped cuffs on aspiration rates, VAP, and ventilator-associated events (VAE), and assayed endotracheal tube aspirates for pepsin and alpha-amylase. Pepsin was considered a surrogate marker for aspirating gastric fluids and alpha-amylase a surrogate marker for aspirating oropharyngeal fluids. The investigators found no difference in the frequency of positive pepsin assays (54% of tapered cuff samples vs 51% of standard cuff samples) or positive alpha-amylase assays (77 vs 69%). Likewise, there were no differences in VAP or VAE rates, ventilator-free days, ICU length-of-stay, or ICU mortality.

This multicenter, cluster, randomized cross-over trial has a number of strengths. The primary outcome was positive pepsin assays, but to their credit the authors also reported on VAP, VAE, ventilator-free days, ICU length-of-stay, and ICU mortality. Including these secondary outcomes provides useful clinical context to interpret the pepsin and alpha-amylase assays, especially since they are imperfect markers for aspiration [11].

A number of important observations and questions arise from the study. First, it is apparent that the correlation between aspiration and VAP is imperfect. Almost 80% of the study population had positive pepsin or alpha-amylase assays but only 22% developed VAP and only 11% had VAEs. This mirrors prior work showing that microaspiration is a near constant event for humans in general and intubated humans in particular, but only a fraction of microaspirations lead to clinically meaningful lung infections. Second, one might wonder whether the limited correlation between aspiration and infection means that ongoing efforts to improve endotracheal

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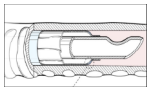
Table 1 Comparison of cuff modifications that have been successful at preventing aspiration in bench studies that have not yet been studied in clinical trials

Sealing system	Picture	Materials	Design	Principle by which leakage is avoided	Relationship between cuff pressure and intra-trachael wall pressure	Bench studies
Doublelayer cuff		Outer cuff: Guayule latex Inner cuff: polivinylchloride	The outer cuff is a thin, 13 mm diameter and 50–60 µm thick, lowprotein guayule latex rubber cuff mounted on a standard polivinyl-chloride cuff (inner cuff). Between cuffs 0.5 ml sterile gel is introduced	Guayule latex rubber cuff is highly compliant, tear resistant, requires low pressure to be stretched, and relies on the mechanical support of the internal high-flow low-pressure cuff to be uniformly expanded facilitated by the presence of the gel. Thus, the cuff creates a tight seal and prevents fluid leakage even at low pressures	Intracuff pressure is trasmitted almost entirely to the tracheal wall. It has been calculated that guayule latex cuff exerts on average a wall pressure 7.0 ± 1.9 cmH_20 lower than the intracuff pressure	Absence of folds on the outer cuff and fluid leakage
Lycra cuff		Lycra polyurethane cuff	This is a ultra-thin 10 µm walled, cylindrical lycra polyurethane cuff	The super-elastic lycra has a maximum elongation of ~500% avoiding formation of folds and leakage of secretions are prevented	Though lycra is highly distensible, it needs some pressure to be inflated and stretched; part of the intracuff pressure is spent to keep the cuff inflated and part is spent on the tracheal wall, depending on the size of the trachea	Absence of folds and fluid leakage
Silicone cuff		Silicone cuff	This is a pressure limited cuff with a thick silicone cuff which determines a high-volume high-intracuff pressure but low-tracheal wall pressure	Silicone cuff avoids formation of folds by inflating the cuff with fixed pressure and relying upon the plateauing of the shape of the pressure–volume curve beyond a certain pressure value	Intracuff pressure is mostly spent to inflate the silicone material. It requires 80 cmH_20 of intracuff pressure to generate 27.4 ± 2.4 cmH_20 of tracheal wall pressure	Absence of folds and fluid leakage
Gills		Polyurethane "gills" substitute for the cuff	The cuff is replaced with a 15–20 toroidal layers of 25–75 µm thick polyurethane films ("gills") in the laryngeal portion of the tracheal tube	Following surface tension the multiple layers of thin gills adhere to the tracheal mucosa. The surface tension will be proportional to the number of gills and the surface of adhesion between the gill and tracheal mucosa	This is a cufless design. This is the only cuff design that does not apply pressure to the tracheal wall	Absence of leakage

[a] Large human trial: we consider only trials in critically ill patients ventilated for more than 72 h

[b] CPIS: Clinical Pulmonary Infection Score as described by Hilbert P and Stuttmann R in Intensivmed (2011), 48:43–47

tube design are misplaced? We believe that Jaillette and colleagues' work affirms that further innovations in endotracheal tube design are desperately needed. Aspiration around the cuff appears to be a near universal event in intubated patients and if only a fraction develop into pneumonia these are still important to prevent.

At present, polyvinylchloride and polyurethane are the most commonly used materials to produce endotracheal tube cuffs. Polyvinylchloride or polyurethane are relatively inelastic thus cuffs made with these materials are designed to be larger than the trachea to ensure that they obstruct the entire trachea. The large size of the cuffs, however, means that it is inevitable that they will form micro-folds against the trachea that allow fluids to flow into the lungs regardless of cuff shape [12].

Various solutions have been proposed. Adding a layer of water-soluble lubricant on the ETT cuff can decrease the amount of fluid that flows across the cuff but this effect only lasts about 24-h in clinical practice [13]. Another approach is to make the cuff out of highly distensible Lycra instead of polyvinylchloride or polyurethane [14]. A third option is to drape a highly elastic latex rubber cuff over a polyvinylchloride cuff with a layer of gel between the two cuffs [15]. This dual-cuff technology allows the rubber outer cuff to adhere firmly to the tracheal wall while avoiding compression of the mucosa. A fourth option is to replace the standard cuff with several ring-shaped disks ("gills") made of thin polyurethane film (0.025–0.075 mm thick) [16]. This cuffless endotracheal tube conforms to the opening of the glottis and prevents leakage of secretions in intubated sheep. A final option is to replace standard cuff materials with a thick silicon cuff [12]. These cuffs require high intra-cuff pressure in order to overcome silicone elasticity but still transmit low tracheal wall pressures.

The latter four options (Table 1) are the only cuff designs that block all leakage across the cuff in laboratory studies, but none of these technologies have been tested in large randomized controlled trials. Translating promising technologies from the lab into clinical practice is challenging: endotracheal cuffs in clinical practice need to preserve the correct level of inflation for prolonged periods, accommodate continual changes in ventilation parameters, and maintain the seal between trachea and cuff even when patients get agitated, moved, or ambulate. Nonetheless, these promising technologies merit comprehensive clinical trials.

In the interim, we advise clinicians to focus their energies on adaptive strategies to prevent VAP and VAE. In contrast to the endotracheal tube design literature, most studies on minimizing sedation, encouraging spontaneous awakening and breathing trials, and ambulating patients have been able to demonstrate meaningful improvements in patient-centered outcomes in "real-world" populations, including less time to extubation and sometimes lower mortality rates [17]. These strategies are less sexy than innovative tube designs and much harder to implement, but experience has repeatedly shown that they can reliably help patients whereas the siren's song of new tube design has yet to prove itself.

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