Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: A systematic review and meta-analysis*

John Muscedere, MD, FRCPC; Oleksa Rewa, MD; Kyle Mckechnie, MD; Xuran Jiang, Msc; Denny Laporta, MD, FRCPC; Daren K. Heyland, MD, FRCPC

Background and Purpose: **Aspiration of secretions containing bacterial pathogens into the lower respiratory tract is the main cause of ventilator-associated pneumonia. Endotracheal tubes with subglottic secretion drainage can potentially reduce this and, therefore, the incidence of ventilator-associated pneumonia. New evidence on subglottic secretion drainage as a preventive measure for ventilator-associated pneumonia has been recently published and to consider the evidence in totality, we conducted an updated systematic review and meta-analysis.**

Design: **We searched computerized databases, reference lists, and personal files. We included randomized clinical trials of mechanically ventilated patients comparing standard endotracheal tubes to those with subglottic secretion drainage and reporting on the occurrence of ventilator-associated pneumonia. Studies were meta-analyzed for the primary outcome of ventilator-associated pneumonia and secondary clinical outcomes.**

Measurements and Main Results: **We identified 13 randomized clinical trials that met the inclusion criteria with a total of 2442 randomized patients. Of the 13 studies, 12 reported a reduction in ventilator-associated pneumonia rates in the subglottic secretion drainage arm; in meta-analysis, the overall risk ratio for ventilator-associated pneumonia was 0.55 (95% confidence interval, 0.46–0.66; $p < .00001$) with no heterogeneity ($I^2 = 0\%$). The use of subglottic secretion drainage was associated with reduced intensive care unit length of stay (−1.52 days; 95% confidence interval, −2.94 to −0.11; $p = .03$); decreased duration of mechanically ventilated (−1.08 days; 95% confidence interval, −2.04 to −0.12; $p = .03$), and increased time to first episode of ventilator-associated pneumonia (2.66 days; 95% confidence interval, 1.06–4.26; $p = .001$). There was no effect on adverse events or on hospital or intensive care unit mortality.**

Conclusions: **In those at risk for ventilator-associated pneumonia, the use of endotracheal tubes with subglottic secretion drainage is effective for the prevention of ventilator-associated pneumonia and may be associated with reduced duration of mechanical ventilation and intensive care unit length of stay. (Crit Care Med 2011; 39:1985–1991)**

Key Words: subglottic secretion drainage; prevention; ventilator-associated pneumonia; meta-analysis

Patients who require invasive mechanical ventilation (MV) are at risk for ventilator-associated pneumonia (VAP) (1). VAP is associated with prolonged duration of MV, intensive care unit (ICU) stay, hospital stay, and increased healthcare costs (2, 3). The attributable mortality of VAP is controversial and is likely small in patients who receive timely, adequate therapy (4), but it may be substantial in those who receive inadequate or inappropriate therapy (5). Given the impact of VAP on patients and scarce healthcare resources, there has been an extensive amount of research on developing effective preventive strategies.

The main cause of VAP is the microscopic aspiration of pathogen-laden secretions into the lower respiratory tract. Intubated patients are at risk for microscopic aspiration because of impairment of laryngeal function by the endotracheal tube (ETT), diminished upper airway reflexes, regurgitation from gastroesophageal sphincter dysfunction, enteral feeding, and nursing in the supine position (6). Exacerbating the significance of microaspiration is that the gastrointestinal tract including the mouth and oropharynx become colonized with pathogenic organisms after ICU admission (7). Although the cuffs on ETTs protect against macroscopic aspiration, they are ineffective at preventing microscopic aspiration around the cuff (8). A technique that may reduce microaspiration is the evacuation of secretions that pool above the ETT cuff or subglottic secretion drainage (9).

Subglottic secretion drainage (SSD) with a specialized ETT incorporating a suction port above the cuff as a method to prevent VAP was first reported in 1992 (10). However, this strategy remains controversial despite substantial investigation. A meta-analysis of five randomized controlled studies (RCTs) published in 2005 by Dezfulian et al (11) concluded that SSD was effective for the prevention of early-onset VAP among patients expected to require >72 hrs of MV and was associated with reduced duration of MV and ICU length of stay (LOS), although there was no effect on mortality. Despite

***See also p. 2015.**

From the Department of Medicine (JM, OR, DKH), Queen's University, Kingston, Ontario; Critical Care Program (JM, KM, DKH) and Department of Clinical Evaluation Research Unit (JM, XJ, DKH), Kingston General Hospital, Kingston, Ontario; Department of Adult Critical Care (DL), Jewish General Hospital, McGill University, Montreal, Quebec, Canada.

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For information regarding this article, E-mail: muscedej@kgh.kari.net

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this evidence, ETTs with SSD have not been uniformly adopted into routine care (12) and are not included in the ventilator bundles recommended by some patient safety organizations (13).

In the interval since the meta-analysis of 2005, new studies evaluating the impact of SSD have been published. Accordingly, we conducted an updated systematic review and meta-analysis of SSD specifically studying the effect of SSD on the incidence of VAP and clinical outcomes including duration of MV, LOS, mortality, and adverse events. Herein we report the results of this meta-analysis.

METHODS

Study Identification. We conducted a systematic review of the published literature to identify all relevant trials. Using text words or MeSH headings containing "subglottic secretion drainage," "ventilator-associated pneumonia," and "endotracheal," we performed computerized searches for relevant articles on MEDLINE (1948–present), EMBASE (1980–present), and Evidence-Based Medicine databases (Cochrane DSR, ACP Journal Club, DARE, and the Cochrane Controlled Trials Register from 1990-present); the search strategy is outlined in SDC Appendix 1 (Supplementary Digital Content 1, http://links.lww.com/CCM/A247). We also searched personal files and reference lists. There were no language restrictions and non-English language articles were translated. For reporting of this meta-analysis, the PRISMA guideline was followed (14).

Study Selection Criteria. All potential studies were retrieved and reviewed in duplicate. We included studies if they: 1) were RCTs; 2) studied adult critically ill patients; 3) included ETTs with SSD in the experimental group compared to standard ETTs in the control group; and 4) reported on the incidence of VAP as defined by the investigators. To select studies with the greatest validity with respect to relative treatment effect, we included only RCTs. To score the methodologic quality of individual studies, we utilized a scoring system (SDC Appendix 2, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247) that we have used in previous studies (15). Data were abstracted in duplicate (J.M. was a data abstractor on all studies) and independently. Disagreement was resolved by consensus. We attempted to contact the authors of included studies for unpublished data.

Data Synthesis. The primary outcome was the occurrence of VAP. Secondary outcomes included ICU and hospital LOS, duration of MV, mortality, time to first episode of VAP, antibiotic utilization, and intermittent vs. continuous for SSD. Safety data and, specifically, reports of airway difficulties were abstracted when reported. When possible, we combined data from relevant studies to obtain pooled estimates of treatment effect. Binary outcomes (i.e., VAP and mortality) are reported as Mantel-Haenszel style risk ratios (RRs), whereas continuous outcomes are reported as inverse variance weighted mean differences. All pooled estimates used the random effects model (16). Heterogeneity was determined using the chi-squared test and interclass correlation (I^2). Risk of bias was assessed by the visual inspection of a funnel plot constructed by plotting effect size vs. standard error. All analyses were performed by Review Manager version 5.0.25 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) (17).

Primary and Secondary Analysis. For the primary outcome of VAP, we included all the studies that met our inclusion criteria. To examine the robustness of the primary analysis, we conducted two sensitivity analyses whereby we first excluded studies that utilized new ETT cuff designs and, second, when there was an imbalance of other VAP-preventive strategies, when reported. Finally, we conducted a subgroup analysis of high-quality studies using the median quality score as the cut-off.

RESULTS

From our search strategy, we identified 1209 references and 14 were selected for secondary review; 13 met the inclusion criteria and were included in the meta-analysis (10, 18–29). The excluded study used SSD in both the control and experimental groups and was therefore ineligible (30). The included studies, randomizing a total of 2442 patients, are summarized in Table 1. The main inclusion criterion was predicated on the duration of expected MV in 11 of the 13 studies: one study with an expected duration of MV >24 hrs, four studies with an expected duration of MV >48 hrs, five studies with an expected duration of MV >72 hrs; and one study with an expected duration of MV >5 days. In all studies, ETTs with SSD were placed at time of original intubation. The definitions of VAP always included radiologic criteria (new or persistent infiltrates on a chest radiograph), along with clinical and microbiological criteria; three studies did not require microbiological confirmation, six utilized quantitative cultures via broncho-alveolar lavage or protected specimen brush, two used quantitative endotracheal aspirates, and two used usual endotracheal aspirates. Other VAP-preventive measures were variably described (SDC Table 1, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247) and in two studies SSD was combined with semirecumbency in the experimental group, although the achieved elevation of head of the bed was not described in both (23, 24). Scoring of methodologic rigor varied and ranged from six to 13, with a median of nine (SDC Table 2, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247); four studies met our *a priori* definition of methodologic rigor with a score greater than the median (20, 25, 26, 29). Of the 13 studies, 12 of them reported reduced VAP rates in the SSD arm. There was no evidence of bias on visual inspection of the funnel plot (SDC Fig. 1, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247).

In the meta-analysis for the primary outcome, the overall risk ratio for VAP was 0.55 (95% confidence interval, 0.46–0.66; $p < .00001$) with no heterogeneity ($I^2 = 0\%$) (Fig. 1). The number needed to treat or to receive an ETT with SSD to prevent one case of VAP was 11. In sensitivity analysis, we identified one trial by Lorente et al (25) that utilized a new cuff design and, on exclusion, a similar reduction in VAP was still observed (RR, 0.57; 95% confidence interval, 0.48–0.69; $p < .0001$) (SDC Fig. 2, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247). In further sensitivity analysis, when we excluded the two studies that combined semirecumbency with SSD (23, 24), a similar reduction in VAP was observed (RR, 0.54; 95% confidence interval, 0.44–0.65; $p < .0001$). On subgroup analysis of high-quality methodologic studies (20, 25, 26, 29), there was still a highly significant reduction in VAP (RR, 0.54; 95% confidence interval, 0.4–0.73; $p < .0001$), with no heterogeneity ($I^2 = 0$) (Fig. 2). VAP was also similarly reduced in the remaining nine studies of low methodologic quality (RR, 0.56; 95% confidence interval, 0.45–0.70; $p < .0001$; $I^2 = 0$). Of the 13 studies, five utilized intermittent suction SSD (10, 19, 22, 25, 29), whereas the rest utilized continuous SSD; reduction in VAP was similar between continuous suction (RR, 0.50; 95% confidence interval, 0.37–0.66; $p < .00001$) and intermittent SSD (RR, 0.59; 95% confidence interval, 0.47–0.74; $p < .00001$).

Clinical outcomes, including mortality, LOS (hospital and ICU), and duration of MV, were variably reported (SDC Table 3, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247). Ten studies reported on mortality (either ICU or hospital), eight reported on ICU LOS,

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Table 1. Summary of studies included in the meta-analysis

Author, Year	Population (n)	Inclusion Criteria	Clinical Suspicion of VAP[a]	VAP[b]	Cointerventions[c]	Score[d]	Rate of VAP a. Cases/1000 Ventilator-Days b. Cases/Patients		
							SSD	Control	*p*
Mahul, 1992	145	Expected duration of MV >3 days	Chest radiograph	BAL	None specified	6	a. 8/1000 b. 9/70	a. 17.5/1000 b. 21/75	a. <.05 b. NR
Valles, 1995	153	Expected duration of MV >3 days	Chest radiograph plus temp >38.5°C, WBC >12 or <4, purulent secretions	BAL or PSB	None specified	9	a. 19.9/1000 b. 14/76	a. 39.6/1000 b. 25/77	a. NR b. NR
Metz, 1998	24	Expected duration of MV >3 days	Chest radiograph, temp > 38.5°C, WBC >12 or <3, purulent secretions	ETA or BAL	None specified	7	a. NA/1000 b. 5/10	a. NA/1000 b. 10/14	a. NA b. NS
Kollef, 1999	343	Need for MV after cardiac Surgery	Chest radiograph plus pulmonary abscess or histology or positive blood or pleural cultures or 2 of 3 of the following: fever, leukocytosis, purulent sputum	ETA or no micro	None specified	11	a. 34.5/1000 b. 8/160	a. 43.2/1000 b. 15/183	a. NR b. 0.24
Bo, 2000	68	Expected duration of MV >72 hrs	Chest radiograph + temp ≥38.3°C or WBC >12 or <4 or purulent sputum	BAL or PSB	None specified	8	a. NA/1000 b. 8/35	a. NA/1000 b. 15/33	a. NA b. <.05
Smulders, 2002	150	Expected duration of MV >72 hrs	Chest radiograph ± evidence for cavitation, histology, positive blood culture, a positive pleural fluid culture, or any of the 2 following symptoms/signs: fever (rectal >38°C), WBC <3 or >10, purulent tracheal aspirate (>25 WBC per field)	ETA	None specified	9	a. 9.2/1000 b. 3/75	a. 22.5 b. 12/75	a. NR b. .01
Girou, 2004	18	Expected duration of MV >5 days	Chest radiograph, temp ≥38.3°C or WBC >12, or purulent sputum	PSB or BAL	Elevation of head of bed in SSD group	9	a. NA/1000 b. 5/8	a. NA/1000 b. 6/10	a. NA b. NS
Liu, 2006	86	Age older than 60 yrs, expected MV >48 hrs	Chest radiograph and 3 of 4: temp >38.0°C or <35.5°C, WBC >10 or <3, >10 WBC high-power field in ETA, or a positive ETA culture	PSB or BAL or positive blood or pleural fluid culture	Elevation of head of bed, gastrointestinal agents in SSD group	9	a. NA/1000 b. 14/41	a. NA/1000 b. 30/45	a. NA b. <.01
Lorente, 2007	280	Expected MV >24 hrs	Chest radiograph, purulent secretions, temp >38°C or <35.5°C, WBC >10 or <4	Quantitative ETA	Polyurethane cuff in addition to SSD	13	a. 7.5/1000 b. 11/140	a. 19.9/1000 b. 31/140	a. .001 b. .003
Bouza, 2008	714	Major heart surgery	Chest radiograph and 2 of: temp >38.5°C or <36°C, WBC > 12, purulent secretions, reduction in PF >15% or CPIS >6	Quantitative ETA or PSB	None specified	12	a. 17.9/1000 b. 12/359	a. 27.6 b. 19/331	a. .2 b. .18
Yang, 2008	91	MV >48 hrs	Chest radiograph and 2 of: temp >38.3°C, WBC >12, WBC <4.0, purulent secretions	No micro or ETA or positive blood culture	None specified	9	a. NA/1000 b. 12/48	a. NA/1000 b. 20/43	a. NA b. .03

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Table 1.—*Continued*

Author, Year	Population (n)	Inclusion Criteria	Clinical Suspicion of VAP[a]	VAP[b]	Cointerventions[c]	Score[d]	Rate of VAP a. Cases/1000 Ventilator-Days b. Cases/Patients SSD	Control	*p*
Zheng, 2008	61	MV >48 hrs	Chest radiograph + temp >38°C or WBC >12 or <4.0 or altered mental status + 2 of purulent sputum, cough, abnormal physical examination, or worsening gas exchange	No micro	None specified	7	a. NA/1000 b. 9/30	a. NA/1000 b. 16/31	a. NA b. <.05
Lacherade, 2010	333	Expected MV >48 hrs	Chest radiograph and 2 of: temp >38.3°C or <36°C, WBC >10 or <4 and purulent tracheal secretions	PSB or BAL	None specified	12	a. 17/1000 b. 25 cases	a. 34/1000 b. 42 cases	a. .002 b. .02

BAL, broncho-alveolar lavage; *CPIS*, clinical pulmonary infection score; *ETA*, endotracheal aspirate; *MV*, mechanical ventilation; *NA*, not applicable; *No micro*, microbiological; *NR*, not reported; *NS*, not significant; *PF*, PaO_2/FIO_2 ratio; *PSB*, protected specimen brush; *SSD*, subglottic secretion drainage; *temp*, temperature; *VAP*, ventilator-associated pneumonia; *WBC*, white blood cell count.

[a]Chest radiograph. Requirement for new or persistent pulmonary infiltrate on a chest radiograph for suspicion of VAP. WBC per 10^6 mL; [b]microbiological criteria for VAP. This refers to the minimum microbiological criteria for the diagnosis of VAP. BAL or PSB = quantitative invasive cultures. No micro = microbiological culture not required for VAP diagnosis; [c]cointerventions. When described, this refers to imbalances between SSD group and control in measures that may have an effect on VAP; [d]methodological score. Refer to SDC Table 1 (see Supplemental Digital Content 1, http://links.lww.com/CCM/A247) for components.

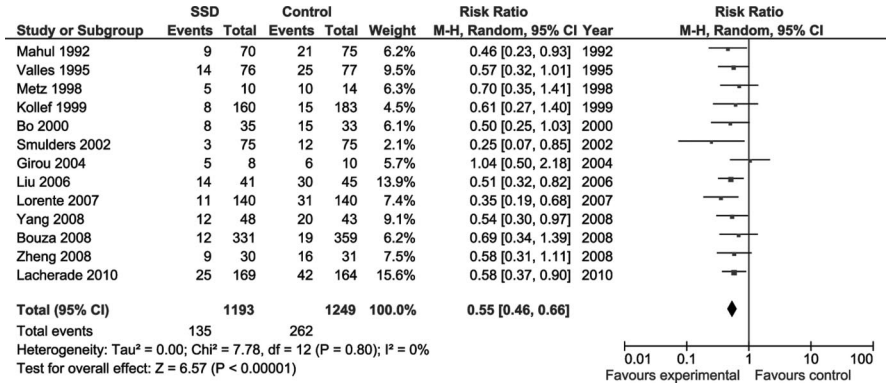

Figure 1. Rate of ventilator-associated pneumonia between groups with subglottic secretion and without subglottic secretion. *M-H*, Mantel-Henszel; *SSD*, subglottic secretion drainage; *CI*, confidence interval.

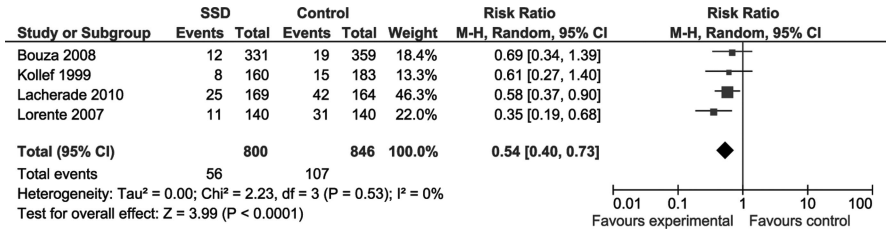

Figure 2. Rate of ventilator-associated pneumonia between groups with subglottic secretion and without subglottic secretion in studies of high methodologic quality. *M-H*, Mantel-Henszel; *SSD*, subglottic secretion drainage; *CI*, confidence interval.

four reported on hospital LOS, and ten reported on duration of MV. There was no effect of mortality in either ICU (RR, 1.01; 95% confidence interval, 0.85–1.20; p = .95) or hospital (RR, 0.97; 95% confidence interval, 0.83–1.13; p = .65) (Figs. 3 and 4, respectively). There was a significant reduction in the duration of ICU LOS of 1.52 days (95% confidence interval, −2.9 to −0.11; p = .03), although there was significant heterogeneity (I^2 = 77%) (Fig. 5). For hospital LOS, data that could be aggregated were available for only three studies (20, 22, 26) and this was not performed. Seven studies reporting on MV duration could be aggregated and in these, MV was reduced (1.08 days; 95%confidence interval, 2.04–0.12; p = .03), although there was significant heterogeneity (I^2 = 86%) (Fig. 6).

Eight studies reported time to first VAP. SSD was associated with a delay to the occurrence of VAP of 2.66 days (95% confidence interval, 1.06–4.26; p = .001) (SDC Fig. 3, see Supplementary Digital Content 1, http://links.lww.com/CCM/A247). Two studies reported on antibiotic utilization. Bouza et al (26) reported a reduction in the number of defined daily doses of antibiotics with SSD (1213 vs. 1932; p < .001), whereas Lacherade et al (29) did not find any difference in antibiotic utilization. Re-intubation rates were available in three studies: Kollef et al (20) reported re-intubation rates of five of 160 (3.1%) in the SSD group and six of 183 (3.3%) in the control group, Bouza et al (26) reported 12 of 331 (3.6%) vs. 14 of 359 (3.9%), and Lacherade et al (29) reported 21 of 169 (1.2%) vs. 20 of 164 (1.2%), respectively. Two studies reported the incidence of stridor after extubation. Girou et al (23) reported stridor in two of five SSD patients but did not report on stridor in the control group, whereas Lacherade et al (29) reported

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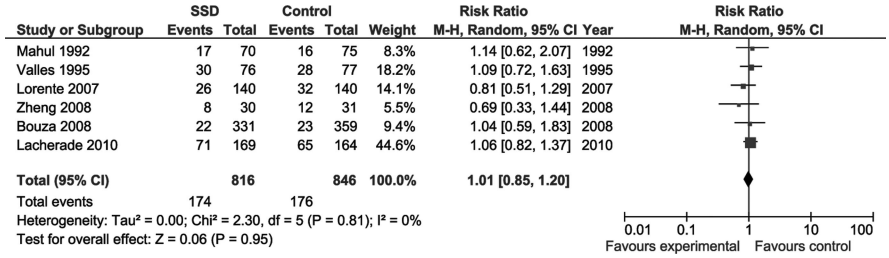

Figure 3. Intensive care unit mortality compared between patients receiving endotracheal tubes with subglottic secretion drainage and standard endotracheal tubes. *CI*, confidence interval; *M-H*, Mantel-Henszel; *SSD*, subglottic secretion drainage.

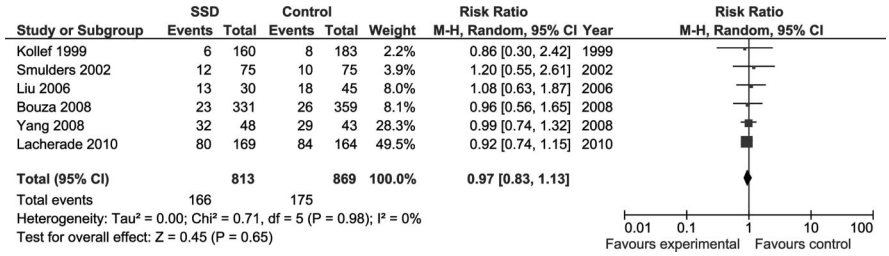

Figure 4. Hospital mortality compared between patients receiving endotracheal tubes with subglottic secretion drainage and standard endotracheal tubes. *CI*, confidence interval; *M-H*, Mantel- Henszel; *SSD*, subglottic secretion drainage.

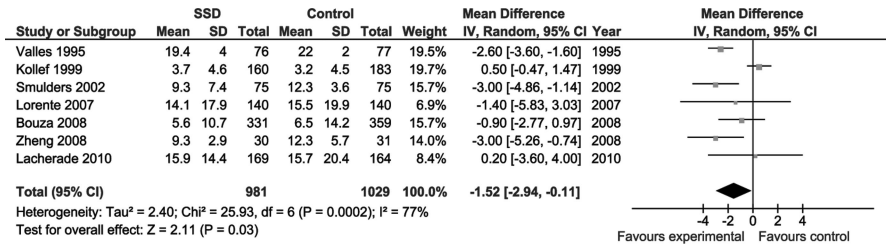

Figure 5. Intensive care unit length of stay compared between patients receiving endotracheal tubes with subglottic secretion drainage and standard endotracheal tubes. *IV*, inverse variance; *CI*, confidence interval; *M-H*, Mantel-Henszel; *SSD*, subglottic secretion drainage.

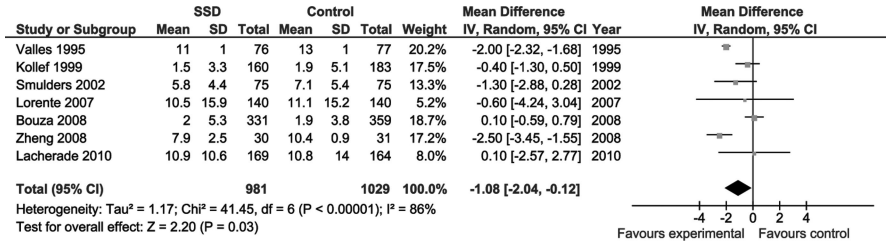

Figure 6. Duration of mechanical ventilation compared between patients receiving endotracheal tubes with subglottic secretion drainage and standard endotracheal tubes. *IV*, inverse variance; *CI*, confidence interval; *SSD*, subglottic secretion drainage.

stridor in eight of 79 (10.1%) SSD patients vs. four of 89 (4.5%) control patients ($p = .25$).

The amount of secretions suctioned daily with SSD was reported in three studies. Lacherade et al (29) reported a median of 14 mL (interquartile range, 8–28 mL), whereas both Bo et al (21) and Zheng et al (28) reported that patients who had VAP develop had lower amounts of secretions drained daily as compared to those who did not (24 ± 17 vs. 54 ± 27 mL; $p < .05$; and 13.3 ± 3.3 vs. 37.8 ± 11.2 mL; $p < .01$, respectively).

DISCUSSION

In our systematic review and meta-analysis of ETTs with SSD, there was a highly significant reduction in VAP of approximately 50% in MV patients who received this intervention. Although the number of RCTs has increased to 13 with more than 2400 randomized patients, our findings confirm those of a previous smaller meta-analysis of five RCTs that also found a 50% reduction in VAP (11). Similarly, we were also able to demonstrate a reduction in ICU LOS and duration of MV, although the strength of this association is weakened in that these outcomes were variably reported and there was significant heterogeneity on meta-analysis. Furthermore, in the patients receiving SSD in whom VAP occurred, there was a delay to its occurrence as compared to that in patients without SSD. We were not able to demonstrate a reduction in mortality with the use of SSD, although this may not be surprising given that adequately treated VAP may have little or no attributable mortality (4).

Endotracheal tubes with SSD are not widely utilized (12); however, given these findings, further efforts to implement them into routine clinical practice may be warranted. Two perceived barriers to implementation are the incremental cost and the identification, before intubation, of patients who are likely to need MV long enough to be at risk for VAP. Regarding the incremental costs, using conservative assumptions, Shorr et al (31) demonstrated the potential cost-effectiveness of SSD. In our study, the number needed to treat for an ETT with SSD to prevent one case of VAP was 11 contrasted with the low acquisition cost of these ETTs and the large amount of costs associated with VAP (2). Number needed to treat will vary depending on the underlying incidence of VAP and further up-to-date cost analyses and modeling are required. Regarding patient identification, ETTs with SSD should be made available in areas where patients could potentially require emergent intubation, such as the ICU, medical wards, and the emergency department. In the operating room, an approach such as that by Bouza et al (26) could be utilized when every patient requiring postoperative MV receives an ETT with SSD. Patients who arrive in the ICU with standard ETTs and who require ongoing MV are problematic. Two approaches are possible. The first is to continue with other VAP-preventive measures and leave the standard ETT in place, and the second is to potentially conduct a tube exchange to an ETT with SSD. There is little evidence

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in this regard and further study is required.

The question of where SSD fits in with other VAP-preventive measures is unclear because there are no direct comparisons. RCT evidence for VAP prevention can be categorized as interventions that aim to decrease the time at risk for VAP, such as reduction in duration of MV and interventions that aim to reduce the quantity of bacteria aspirated. Reduction in time at risk or MV by earlier extubation is a worthwhile goal regardless of the type of ETT used and SSD is associated with reduced duration of MV. Strategies that aim to reduce the quantity of bacteria aspirated are semirecumbency positioning (32) and those that reduce the inoculums of bacteria in aspirated secretions, such as decontamination of the oral cavity with chlorhexidine (33) or selective decontamination of the digestive tract (34). Semirecumbency positioning was used in both the control and SSD groups in four studies (25, 27–29), although the degree achieved was only reported by Lacherade et al (29). In all of these studies, SSD was associated with an additive reduction in VAP. SSD may be complementary with semirecumbency positioning because, as a sole VAP-preventive strategy, it is difficult to implement in practice, is contraindicated in some patients, cannot be performed continuously, and is only modestly effective (35).

For selective decontamination of the digestive tract, concern exists over long-term effects on microbial resistance, it is expensive, and it is unknown if it is effective for VAP prevention in patients receiving SSD. Chlorhexidine decreases bacterial burden but does not completely sterilize upper airway secretions, does not completely prevent VAP (36), and it is likely that reducing the amount of secretions that access the lower airway would still be beneficial. Thus, SSD and chlorhexidine may be potentially complementary, as was found in two of the studies included in our meta-analysis (25, 27); however, further study in this regard is required. Last, there is evidence for the effectiveness of silver-coated endotracheal tubes. A recent study by Kollef et al (37) demonstrated a relative risk reduction for VAP of 36% (95% confidence interval, 3.6%–69%), with no effect on LOS or duration of MV. Again, direct comparisons have not been published and further study is required. Given the potential complementary effects of chlorhexidine, semirecumbency, and SSD, these interventions should be implemented together until further evidence emerges.

Only two studies reported on the association between the volume of secretions aspirated and VAP; those in whom VAP developed had less secretion drainage than those who did not. This may account for the incomplete effect of SSD on VAP prevention; secretion drainage may fail because of secretion properties or malposition of the suction port (38, 39). The combination of new cuff designs that reduce microaspiration with SSD (8) could potentially be beneficial in this regard, but further study is required because there is only one published study reporting clinical outcomes (25).

The strengths of this study are that we included only RCTs, utilized conservative analytical methods including random effects aggregation, and conducted sensitivity analyses. The effect on VAP prevention was maintained in sensitivity analyses. The inherent weaknesses in any meta-analysis are varying inclusion and exclusion criteria and different populations in the underlying studies. In our study, there was little heterogeneity across the studies in regard to the primary outcome. There was variable reporting of clinical outcomes and, despite our efforts, we were unable to obtain all the additional data. Only three of the 13 studies reported on the incidence of post-extubation stridor and re-intubation and, in these, no adverse effects were noted. However, given the minimal data reported on the occurrence of airway difficulties, an increase in these associated with SSD may have been missed. Airway pathology associated with SSD has been reported in animal models (40) and there have been case reports of tracheal injury after prolonged use of ETTs with SSD (41), although increased incidence of airway difficulties has not been reported in large populations in which SSD has been utilized (42). Further systematic study, including long-term follow-up, of airway complications associated with SSD is required. An additional potential weakness of this meta-analysis is that the majority of the studies were conducted with one type of ETT tube and the generalizability to other ETTs with SSD is unclear and deserves further study (43).

CONCLUSION

In a systematic review and meta-analysis, we have found that the utilization of ETTs with SSD reduces the occurrence of VAP and may improve clinical outcomes. Given the morbidity and healthcare cost of VAP in comparison with the minimal incremental costs of ETTs with SSD, an ETT with SSD should be considered for patients potentially requiring MV of sufficient duration to put them at risk for VAP. Further research on cuff designs, methods to implement ETTs with SSD into practice, and the role of SSD when combined with other VAP prevention measures is required.

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