

Continuous Versus Intermittent Subglottic Secretion Drainage to Prevent Ventilator-Associated Pneumonia: A Systematic Review

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BACKGROUND Ventilator-associated pneumonia is associated with high morbidity and mortality in patients receiving mechanical ventilation. Subglottic secretion drainage, which may be performed continuously or intermittently, is believed to be an effective strategy for coping with ventilator-assisted pneumonia. Whether continuous or intermittent subglottic secretion drainage is superior for preventing ventilator-assisted pneumonia remains unknown.

METHODS This study is a comprehensive, systematic meta-analysis of randomized trials comparing continuous and intermittent subglottic secretion drainage in patients receiving mechanical ventilation. Studies in English and Chinese published from January 1970 through November 2015 were identified by searching multiple databases. Summary risk ratios or weighted mean differences with 95% CIs were used to calculate each outcome by means of fixed- or random-effects models.

RESULTS Eight studies enrolling a total of 1071 patients met the inclusion criteria. The summary risk ratio between continuous and intermittent subglottic secretion drainage for incidence of ventilator-assisted pneumonia was 0.83 (95% CI, 0.61-1.13); for time to ventilator-assisted pneumonia occurrence, 2.73 (95% CI, -0.39 to 5.85); for occult blood, 2.34 (95% CI, 0.25-21.88); for duration of mechanical ventilation, -0.89 (95% CI, -2.72 to 0.94); for length of intensive care unit stay, 3.98 (95% CI, -4.44 to 12.41); and for mortality, 0.80 (95% CI, 0.48-1.31).

CONCLUSIONS The results indicate no apparent differences between continuous and intermittent subglottic secretion drainage for the treatment outcomes included in the analysis. Rigorously designed, large-scale randomized controlled trials are warranted to identify the roles of continuous and intermittent subglottic secretion drainage. (*Critical Care Nurse*. 2017;37[5]:e10-e17)

Ventilator-associated pneumonia (VAP) is believed to be the most common hospital-acquired infection in intensive care units (ICUs). Published studies indicate that VAP occurs in 10% to 20% of patients receiving mechanical ventilation for more than 48 hours, 30-day mortality is as high as 23.6%, and VAP may lead to excessive health care costs.¹⁻⁴ Therefore, preventing VAP has been a top research priority for the past few decades.^{3,5} Previous studies have revealed that strategies such as

subglottic secretion drainage (SSD) and the use of oral antiseptics may help prevent VAP.^{6,7} A recent meta-analysis of 17 randomized controlled trials comparing SSD with no SSD in adult patients undergoing mechanical ventilation found that SSD is associated with significant lower VAP rates.⁸

Colonization of upper respiratory tract secretions with potentially pathogenic microorganisms may contribute to VAP. Radiographic studies have revealed that secretions generally accumulate above the cuff of endotracheal tubes (in the subglottic region) before descending to the lower respiratory tract.⁹ Because translocation of these secretions into the pulmonary parenchyma may lead to VAP, SSD has been used in clinical settings to combat VAP. However, SSD may also be associated with risks such as airway mucosal injury and bleeding, detection of which requires testing for occult blood.¹⁰

Although the efficacy of SSD was in question in past decades, previous meta-analyses have consistently concluded that SSD reduces the rate of early-onset VAP,¹¹⁻¹⁵ and the use of SSD for VAP prophylaxis is highly recommended by guidelines and experts.^{16,17} SSD may be performed as continuous SSD (CSSD) or intermittent SSD (ISSD). Both these techniques are used to prevent VAP. Studies have confirmed the benefit of ISSD for reducing the incidence of VAP.¹⁸⁻²⁰ Although many studies have focused on the efficacy of either CSSD or ISSD, to the best of our knowledge few provide insights into the choice between CSSD and ISSD. In addition, guidelines encourage and recommend SSD in general but do not indicate whether CSSD or ISSD should be used.^{17,21,22}

Given the increased number of studies about CSSD and ISSD and the lack of a meta-analysis of randomized controlled trials comparing the efficacy of the 2 techniques, we conducted this systematic review and meta-analysis with the following purposes: (1) to review the current evidence for using CSSD and ISSD, (2) to compare

the complication rates of CSSD and ISSD, and (3) to analyze the choice between CSSD and ISSD.

Methods

Search Strategy

We planned, performed, and reported this meta-analysis in compliance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.²³ We searched PubMed, Embase, Science Direct, the Cochrane Central Register of Controlled Trials, the China National Knowledge Infrastructure, and Wanfang Data for relevant articles published in English or Chinese from January 1, 1970, to November 30, 2015, using the following search terms in both English and Chinese: “subglottic suctioning,” “subglottic drainage,” “subglottic secretion,” “ventilator-associated pneumonia,” “VAP,” “artificial airway,” “ventilation,” and “intubation.” We also reviewed and manually searched the reference lists of the retrieved studies, reviews, and meta-analyses. We made no attempt to identify unpublished reports.

Study Selection

We selected studies first by screening identified titles or abstracts and next by checking full-text articles. Eligible studies met the following criteria: (1) the study was a randomized controlled trial, the study design that provides the strongest evidence; (2) study participants were critically ill patients receiving invasive mechanical ventilation or endotracheal intubation; (3) the comparison groups included CSSD and ISSD; and (4) the outcome data were the incidence of VAP, time from intubation to the diagnosis of VAP, results of tests for occult blood in SSD, duration of mechanical ventilation, length of hospital or ICU stay, and mortality rate.

Both continuous and intermittent subglottic secretion drainage are used to prevent VAP.

Data Extraction

Two reviewers extracted the following data: first author, year of publication, study design, patient population, methods of SSD, concurrent interventions, and main outcomes. The 2 reviewers selected studies and extracted data independently, solving disagreements by discussion. The main outcomes were (1) incidence of VAP, which was identified by clinical, laboratory, or

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imaging findings; (2) time to VAP occurrence; (3) results of tests for occult blood in SSD; (4) duration of mechanical ventilation; (5) length of hospital or ICU stay; and (6) mortality rate.

Assessment of Study Quality

We used the Cochrane Risk of Bias Tool²⁴ to evaluate the methodological quality and risk of bias of the included studies. This tool measures 7 domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other issues. Domains are classified as low risk of bias, high risk of bias, or unclear risk of bias.²⁴

Data Synthesis and Analysis

Extracted data were processed and analyzed with Review Manager (RevMan) version 5.3 (Cochrane). Binary outcomes (such as VAP and mortality) were presented as Mantel-Haenszel-style odds ratios with 95% CIs, and continuous outcomes were reported as inverse-variance-weighted mean differences with 95% CIs. A random-effects model was chosen for data-synthesized

All studies included in the analysis were conducted in China because they directly compared the efficacy of CSSD and ISSD.

analysis regardless of heterogeneity. Publication bias was evaluated by funnel plots, and asymmetry was assessed by means of the Egger regression test ($P < 0.1$ was considered significant funnel plot asymmetry). Sensitivity analyses addressing the influence of a single study on the overall risk estimate were conducted by omitting a study one by one.

Results

Literature Search

The comprehensive search yielded 365 relevant papers, and we reviewed the abstracts of all these citations. We identified 70 potential studies for further full-text review and excluded studies that did not meet the intervention criteria. Eight randomized controlled trials were included in the final analysis.²⁵⁻³²

Study Characteristics

The characteristics of the 8 included studies are presented in the Table. All studies included in the analysis were conducted in China because none of the studies

conducted in other countries directly compared the efficacy of CSSD and ISSD. The 8 included studies involved 1071 patients (512 receiving CSSD, 446 receiving ISSD, and 113 receiving routine care). The main inclusion criteria were based on the duration of mechanical ventilation. The duration of mechanical ventilation was greater than 48 hours in 3 studies,^{26,27,30} greater than 72 hours in 2 studies,^{25,27} and unclear in 2 studies.^{28,31} One study³² did not mention duration of mechanical ventilation. Other interventions, such as use of a rinse after ISSD, were also mentioned in some studies.^{25-27,29,30} The methods used to drain subglottic secretions varied from intermittent aspiration with a syringe to continuous suction with a central negative-pressure suction system.

Methodological Quality and Risk of Bias

The methodological quality of the included studies, with bias classifications of low, high, and unclear risk, is shown in Figure 1. Figure 2 illustrates the bias classifications by cross-tabulating the included studies. Although all 8 studies mentioned randomization, only 6 included detailed descriptions of the method used to produce the random sequence; these were classified as having low risk of bias.^{26-28,30-32} In general, sequentially numbered, opaque, sealed envelopes were assigned to each participant to prevent selection bias. Six of the 8 studies described adequate allocation concealment, which reduces ascertainment bias, and were therefore classified as having low risk of bias.^{25,26,28-31} Adequate blinding of personnel, participants, and outcome assessment prevents intentional bias. However, only 1 study reported a blinding design for participants, indicating a low risk of bias.²⁷ The other studies included no details of participant blinding. Six studies reported special training programs regarding outcome assessment and were classified as having a high risk of bias.^{25-27,29,30,32} The other 2 studies did not indicate a blinding design for participants and personnel. Six studies^{25,26,28-30,32} reported complete outcome data, indicating a low risk of bias; 2 were classified as having a high risk of bias because of deficiencies in outcome data.^{26,28} Verifying selective reporting of outcomes is necessary to evaluate the integrity of outcome reporting and to protect against bias. One trial selectively reported the study results and was therefore classified as having a high risk of bias.³¹ Four studies reported the number of patients lost to follow-up during the study period because the patients stopped treatment or were transferred.^{25,28-30}

Table Characteristics of studies included in the meta-analysis

Study	Settings and patients	Exclusion criteria	Types of SSD	Outcomes	Findings
Zeng et al, ³⁰ 2012	ICU patients receiving MV after tracheostomy	Patients expected to receive MV ≤48 h	CSSD vs ISSD, plus intermittent rinse for each group	HR; BP; SpO ₂ ; daily volume of sputum; the volume of drainage secretions; incidence of VAP; time to VAP; occult blood test; mucous injury (bronchoscopy check every 2 d); cough	CSSD plus intermittent rinse improved drainage volume and VAP incidence.
Zhou et al, ³¹ 2009	ICU patients receiving MV with oral intubation		CSSD vs ISSD (performed every 2 h or immediately after vomiting)	Volume of drained secretions; occult blood test	No significant difference was found, but CSSD yielded a higher risk for respiratory mucosa injury.
Fan, ²⁹ 2011	ICU patients receiving MV ≥48 h		CSSD vs ISSD (performed every 2 h, rinsed with 5-10 mL NS after suction)	Incidence of VAP (within and after 6 d); volume of drained secretions; occult blood test	Similar efficacy was found for the 2 methods, but CSSD yielded a higher risk for respiratory mucosa injury.
Yang, ²⁶ 2012	Patients with severe brain injury receiving MV	Patients expected to receive MV ≤48 h; patients with confirmed airway infections or respiratory failure	CSSD vs ISSD (performed every 4 h, rinsed with 5-10 mL NS after suction)	Incidence of VAP; time to VAP occurrence; duration of MV; length of ICU stay	No significant difference was found for the incidence of VAP; ISSD delayed VAP occurrence and reduced the duration of MV and length of ICU stay.
Huang, ²⁷ 2013	ICU patients expected to require MV for ≥72 h		CSSD vs ISSD (performed every 2 h, rinsed with NS after suction)	Incidence of VAP (within a week)	CSSD was associated with a lower incidence of VAP than was ISSD.
Bian, ²⁵ 2008	ICU patients expected to require MV for ≥72 h	Patients expected to require MV for ≤72 h	No SSD vs CSSD vs ISSD (performed every 2 h, rinsed with 10 mL NS after suction)	Incidence of VAP (from 3-7 d); duration of MV; length of ICU stay; mortality rate	SSD effectively prevented VAP; CSSD and ISSD appeared to have similar effects on VAP prophylaxis.
Wang, ²⁸ 2011	Respiratory ICU patients with severe COPD and receiving MV		No SSD vs CSSD vs ISSD	Incidence of VAP (within or after 7 d); time to VAP occurrence; duration of MV; cultures of drained secretions	SSD significantly reduced early onset of VAP. No significant difference was found between the CSSD and ISSD groups.
Tao et al, ³² 2014	Patients receiving endotracheal intubation or MV	Patients with significant respiratory infections before intubation or MV	No SSD vs CSSD vs ISSD (rinsed with 10 mL NS after suction)	Incidence of VAP (<5 d or ≥5 d); mortality; bacteriologic test results	Both CSSD and ISSD prevented early onset of VAP.

Abbreviations: BP, blood pressure; COPD, chronic obstructive pulmonary diseases; CSSD, continuous subglottic drainage; HR, heart rate; ICU, intensive care unit; ISSD, intermittent subglottic secretion drainage; MV, mechanical ventilation; NS, normal saline; SpO₂, oxygen saturation as measured by pulse oximetry; SSD, subglottic secretion drainage; VAP, ventilator-associated pneumonia.

Main Analysis

Incidence of VAP. Seven studies reported the incidence of VAP.^{25-30,32} The reported incidence of VAP was similar in 4 studies, most of which found no obvious

differences between CSSD and ISSD.^{25,26,28,29} However, in 2 studies, CSSD was associated with a low incidence of VAP.^{27,30} The summary odds ratio for the incidence of VAP between CSSD and ISSD was 0.83

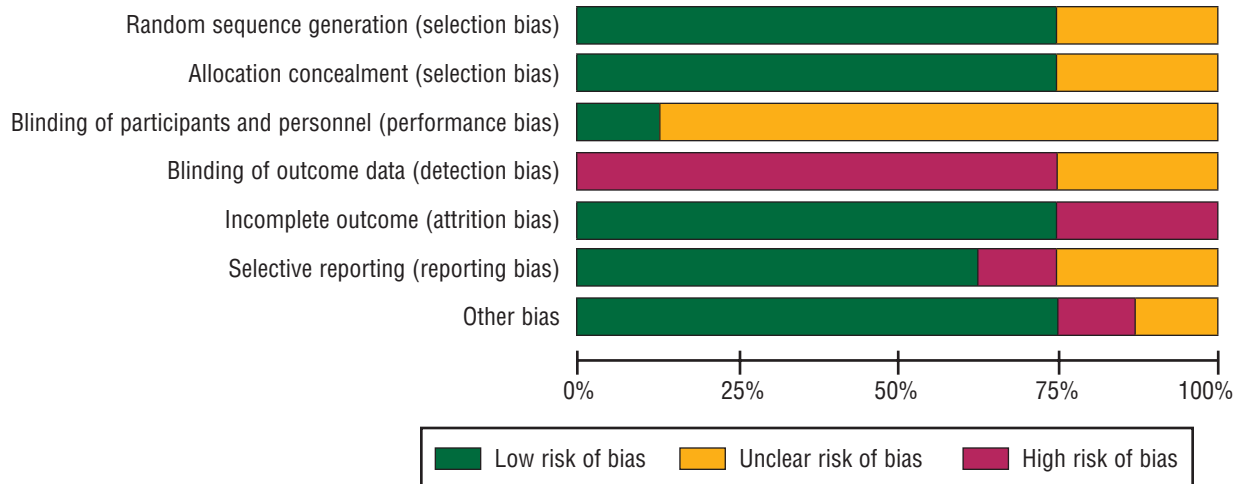


Figure 1 Bias classification low, high, and unclear risk in the included studies.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bian et al, ²⁵ 2008	?	+	?	-	+	+	+
Fan, ²⁹ 2011	?	+	?	-	+	+	?
Huang, ²⁷ 2013	+	?	+	-	-	?	-
Tao et al, ³² 2014	+	?	?	-	+	+	+
Wang, ²⁸ 2011	+	+	?	?	+	+	+
Yang, ²⁶ 2012	+	+	?	-	+	?	+
Zeng et al, ³⁰ 2012	+	+	?	-	+	+	+
Zhou et al, ³¹ 2009	+	+	?	?	-	-	+

Figure 2 Cross tabulation of bias classification.

(95% CI, 0.61-1.13), with no evidence of heterogeneity ($P = .56$, $I^2 = 0\%$).

Time to VAP Occurrence. The time to VAP occurrence was reported in only 3 studies.^{26,28,30} Of these, one study found that ISSD delayed the onset of VAP²⁶; the other 2 found that the onset of VAP was the same for CSSD and ISSD. The summary weighted mean difference in the time to VAP occurrence (in days) between CSSD and ISSD was 2.73 (95% CI, -0.39 to 5.85), with evidence of heterogeneity ($P < .001$, $I^2 = 91\%$).

Testing for Occult Blood. Results of testing for occult blood were reported in only 3 studies.²⁹⁻³¹ The summary odds ratio for occult blood testing between CSSD and ISSD was 2.34 (95% CI, 0.25-21.88), with evidence of heterogeneity ($P < .001$, $I^2 = 91\%$).

Duration of Mechanical Ventilation. The duration of mechanical ventilation was reported in only 3 studies.^{25,26,28} The summary weighted mean difference for the duration of mechanical ventilation (days) between CSSD and ISSD was -0.89 (95% CI, -2.72 to 0.94), with evidence of heterogeneity ($P = .004$, $I^2 = 70\%$).

Length of ICU Stay. The length of ICU stay was reported in only 2 studies.^{25,26} Yang concluded that ISSD was more beneficial than CSSD for the length of ICU stay,²⁶ whereas Bian et al²⁵ found no significant difference between CSSD and ISSD in the length of ICU stay. The summary weighted mean difference for the length of ICU stay (days) between CSSD and ISSD was 3.98 (95% CI, -4.44 to 12.41), with evidence of heterogeneity ($P < .001$, $I^2 = 97\%$).

Mortality. Two studies reported mortality in the CSSD and ISSD groups.^{25,32} The summary odds ratio for mortality between CSSD and ISSD was 0.80 (95% CI, 0.48-1.31), with no evidence of heterogeneity ($P = .99$, $I^2 = 0\%$).

Publication Bias and Subgroup and Sensitivity Analyses

A funnel plot indicates the intervention effect estimates from each study plotted against a measure of study size or precision.²⁴ Because funnel plots require 10 or more studies to provide significant evidence, we did not perform funnel plot analysis. Similarly, because of the limitation of the study data, we did not perform subgroup analyses. Our sensitivity analysis suggested that the overall risk estimates were not substantially changed by any single study.

Discussion

The evidence from previously published randomized controlled trials regarding CSSD and ISSD is not conclusive. Our meta-analysis indicated that CSSD and ISSD may have similar effects on the incidence of VAP, time to VAP occurrence, presence of occult blood in SSD, duration of mechanical ventilation, length of ICU stay, and mortality rate. To the best of our knowledge, this is the first meta-analysis comparing CSSD and ISSD for VAP prophylaxis.

The value of SSD for VAP prophylaxis is unclear, although numerous studies of SSD have been published on this topic. Lorente et al³³ examined costs of care and found that using an endotracheal tube with a lumen to accommodate SSD together with a system providing continuous cuff pressure control can reduce health care costs. Several meta-analyses and guidelines have also highly recommended using SSD for VAP prophylaxis.^{5,7,11-14,16} However, a recent meta-analysis concluded that although SSD may significantly lower the incidence of VAP, it did not reduce the duration of mechanical ventilation, length of hospital stay, ventilator-associated events, mortality rate, or antibiotic use, raising concerns about the usefulness of SSD.⁸ We conducted our study under the assumption that SSD is beneficial, but because the efficacy of SSD remains unclear, our results should be interpreted with caution. Whether CSSD and ISSD prevent VAP to a similar degree also remains unknown. Surprisingly, our literature review yielded few studies

comparing the efficacy and appropriateness of CSSD and ISSD, and all of them were from China.

In our meta-analysis, we found that CSSD had no advantage over ISSD in the incidence of VAP, time to VAP occurrence, presence of occult blood, duration of mechanical ventilation, length of ICU stay, or mortality rate. One potential explanation is that differences in methodology, end points, and study groups among the included studies prevented us from being able to find differences between CSSD and ISSD.

Opinions on the appropriateness and superiority of CSSD versus ISSD vary. CSSD may work because continuous pressure control combats the downward movement of contaminated secretions. However, the continuous negative pressure of CSSD may lead to mucosal injury.^{29,31} Animal studies have revealed that continuous control could give rise to ischemic tracheal lesions.³⁴ Dragoumanis et al³⁵ reported that aspiration failure might occur because of herniation of tracheal mucosa into the suction port, and Girou et al³⁶ found a higher-than-expected rate of laryngeal edema in patients receiving CSSD at a pressure of -30 mm Hg, possibly necessitating reintubation. The timing and choice of pressure for CSSD therefore warrants further investigation.

Compared with CSSD, ISSD is less likely to cause mucosal injury; its intermittent interruption of mucosal blood flow may allow time for temporary recovery. However, Suys et al³⁷ revealed that ISSD might cause tracheal damage in patients with scant oropharyngeal secretions, so oropharyngeal secretions should be evaluated before performing SSD.

Compared with CSSD, ISSD is less likely to cause mucosal injury; its intermittent interruption of mucosal blood flow may allow time for recovery.

The lack of standardization of ISSD technique could have affected our results. Confounding factors such as differences in suction pressure could have introduced bias. Most ISSD procedures in studies included in our meta-analysis were performed with 5- or 10-mL syringes, but in some studies, ISSD was performed with wall-mounted suctioning systems or automated vacuum suctioning devices.¹⁸ These devices may be useful clinically, although standardization of parameters such as the strength and frequency of suctioning is necessary.

Factors such as secretion viscosity, suction pressure, and secretion volume may affect SSD efficacy. Patients

requiring more-intensive nursing care may have subglottic secretions of disproportionately higher viscosity. O'Neal et al³⁸ demonstrated that secretions of higher viscosity were easier to remove than those of lower viscosity. Kollef et al³⁹ suggested that for patients with higher Acute Physiology and Chronic Health Evaluation II scores, increasing the suction pressure from 20 mm Hg to 30 mm Hg may optimize suction efficiency. Establishing appropriate SSD pressure will ensure safe and effective practice, and further investigation of how these factors interact with SSD is needed.

Limitations

Several limitations of this study should be considered. First, all of the included studies are from China; therefore, population factors and study bias may have affected the results. Second, the included studies have significant heterogeneity, including different CSSD and ISSD techniques, VAP definitions, concurrent interventions, and patient populations (such as patients with severe cerebral injuries and chronic obstructive pulmonary disease). The extreme heterogeneity in this small number of studies may reflect different SSD effects in different populations. More homogeneous studies are warranted. Third, we did not perform subgroup or funnel plot analysis because of data limitations, potentially introducing publication bias. Finally, the small number of studies in this meta-analysis was a limitation. Only 2 or 3 studies were included in some of the outcome analyses, which warrants further validation.

Conclusions

Our meta-analysis suggests that the incidence of VAP, time to VAP occurrence, presence of occult blood, duration of mechanical ventilation, length of ICU stay, and mortality rate are the same for CSSD and ISSD. The evidence is not sufficient to confirm that CSSD is more beneficial than ISSD. Although the role of SSD remains unclear, SSD is in wide clinical use. Because evidence of the efficacy of CSSD and ISSD for VAP prophylaxis remains weak, large and rigorous randomized controlled trials are warranted.

CSSD and ISSD may have similar effects on the incidence of VAP, time to VAP occurrence, mucosal bleeding, duration of mechanical ventilation, length of ICU stay, and mortality rate. However, CSSD and ISSD should be performed with caution. Future studies focusing on the

role of CSSD and ISSD and standardization of CSSD and ISSD techniques are needed. **CCN**

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None reported.

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