持续口腔吸引对VAP发生的影响

Effect of continuous oral suctioning on the development of ventilator-associated pneumonia: A pilot randomized controlled trial

沙彦春

重症医学科SICU

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摘要（1）

- Background: Both continuous and intermittent aspiration of subglottic secretions by means of specially designed endotracheal tubes containing a separate dorsal lumen that opens into the subglottic region have been shown to be useful in reducing ventilator-associated pneumonia (VAP). However, the high cost of these tubes restricts their use.
- Objective: The aim of this pilot randomized controlled trial was to test the effect of a low- cost device (saliva ejector) for continuous oral suctioning (COS) on the incidence of VAP in patients receiving mechanical ventilation.

- 背景：连续和间歇由门下分泌物误吸含有一个单独的背腔专门设计的气管内导管的装置，其通向门下区已被证明在减少呼吸机是有用的相关性肺炎（VAP）。然而，这些导管的高成本限制了它们的使用。
- 目的：本试验的目的就是采用随机对照试验测试通过使用一个低成本的设备（唾液排出器）持续经口吸痰（英文缩写：COS）对机械通气病人VAP发生率的影响。

摘要（2）

- Methods: The study was conducted in the six-bed medical-surgical ICU of a hospital with over 400 beds that provides comprehensive medical services to the public. The design of this study was a parallel-group randomized controlled trial. While both the experimental and control groups used the conventional endotracheal tube, the saliva ejector was only applied to patients assigned to the experimental group. The device was put between the patient’s cheek and teeth, and then connected to 100 mmHg of suction for the continuous drainage of saliva.

- 方法：这项研究是在一家有超过400张病床为市民提供全面的医疗服务的医院进行的，这家医院的内外科ICU有的6个床位。这项研究的设计是一个平行组随机对照试验。虽然这两个实验与对照组使用常规的气管插管，口水排除器是唯一应用于分配到实验组的患者。该装置被放到病人的脸颊和牙齿之间，然后连接到100毫米汞柱负压的持续吸引口水。

摘要（3）

- Results: Fourteen patients were randomized to receive COS and 13 patients were randomized to the control group. The two groups were similar in demographics, reasons for intubation, co-morbidity, and risk factors for acquiring VAP. VAP was found in 3 patients (23.1%; 71 episodes of VAP per 1000 ventilation days) receiving COS and in 10 patients (83.3%; 141 episodes of VAP per 1000 ventilation days) in the control group (relative risk, 0.28; 95% confidence interval, 0.10–0.77; **p = 0.003**). The duration of mechanical ventilation in the experimental group was 3.2 days(SD1.3),while that in the control group was 5.9 days (SD 2.8) (**p= 0.009**); and the length of ICU stay was 4.8 days (SD 1.6) versus 9.8 days (SD 6.3) for the experimental and control groups, respectively (**p = 0.019**).

- 结果：14例患者被随机分配接受COS和13例随机分到对照组。两组患者的人口统计学相似，气管插管原因、基础疾病、获得VAP的危险因素相似。接受COS的有3例发生VAP（23.1%，每1000待机天有71天发生VAP），而对照组有10例（83.3%，每1000个带机天有141VAP），（相对危险度，0.28；95 %可信区间，0.10-0.77，*P*=0.003）。机械通气时间实验组为3.2天（SD 1.3），对照组为5.9天（SD 2.8）（*P* = 0.009）；而住ICU的时间实验组为4.8天（SD 1.6），对照组为9.8天（SD 6.3）（*P*=0.019）。

摘要（4）

- Conclusion:Continuous clearance of oral secretion by the saliva ejector may have an important role to play in reducing the rate of VAP, decreasing the duration of mechanical ventilation, and shortening the length of stay of patients in the ICU.

- 结论：通过唾液排出器持续清除口腔分泌物可能在降低VAP的发生率中扮演者重要的角色，在减少持续机械通气时间和缩短病人住ICU的时间有着重要作用。

What is already known about the topic?

- Ventilator-associated pneumonia (VAP) is a preventable secondary consequence of intubation and mechanical ventilation. One of the promising preventive measures is aspiration of subglottic secretions.

- 其中一个有用的预防措施是声门下吸引。

What is already known about the topic?

- Both the continuous and intermittent aspiration of subglottic secretions by means of specially designed endotracheal tubes containing a separate dorsal lumen that opens into the subglottic region proved to be useful in reducing VAP. However, the high cost of these tubes restricts their use.

- 声门下分泌物吸引有连续和间歇两种，通过专门设计的包含一个单独的背腔气管插管打开到声门下被证明对减少VAP是有用的。然而，这些插管的高成本限制其使用。

What this paper adds

- Continuous clearance of oral secretion by the saliva ejector, which was designed with five holes for effective suctioning, resulted in a significant reduction in the rate of VAP, duration of mechanical ventilation, and length of ICU stay.
- The results of this pilot study can be used as a guide in the design and implementation of a full-scale, definitive randomized controlled clinical trial (RCT).

- 通过有5个小孔的唾液排出器，持续有效的排出口腔分泌物，显著降低VAP发生、机械通气时间和住ICU时间的比率。

- 这项试验研究结果可以作为一个全面的、明确的随机对照临床试验（RCT）的设计和实施的指南。

1. Introduction

- VAP的定义
- VAP与经济
- VAP的诱因
- 声门下吸引对预防VAP的意义
- 引出COS

2. Methods

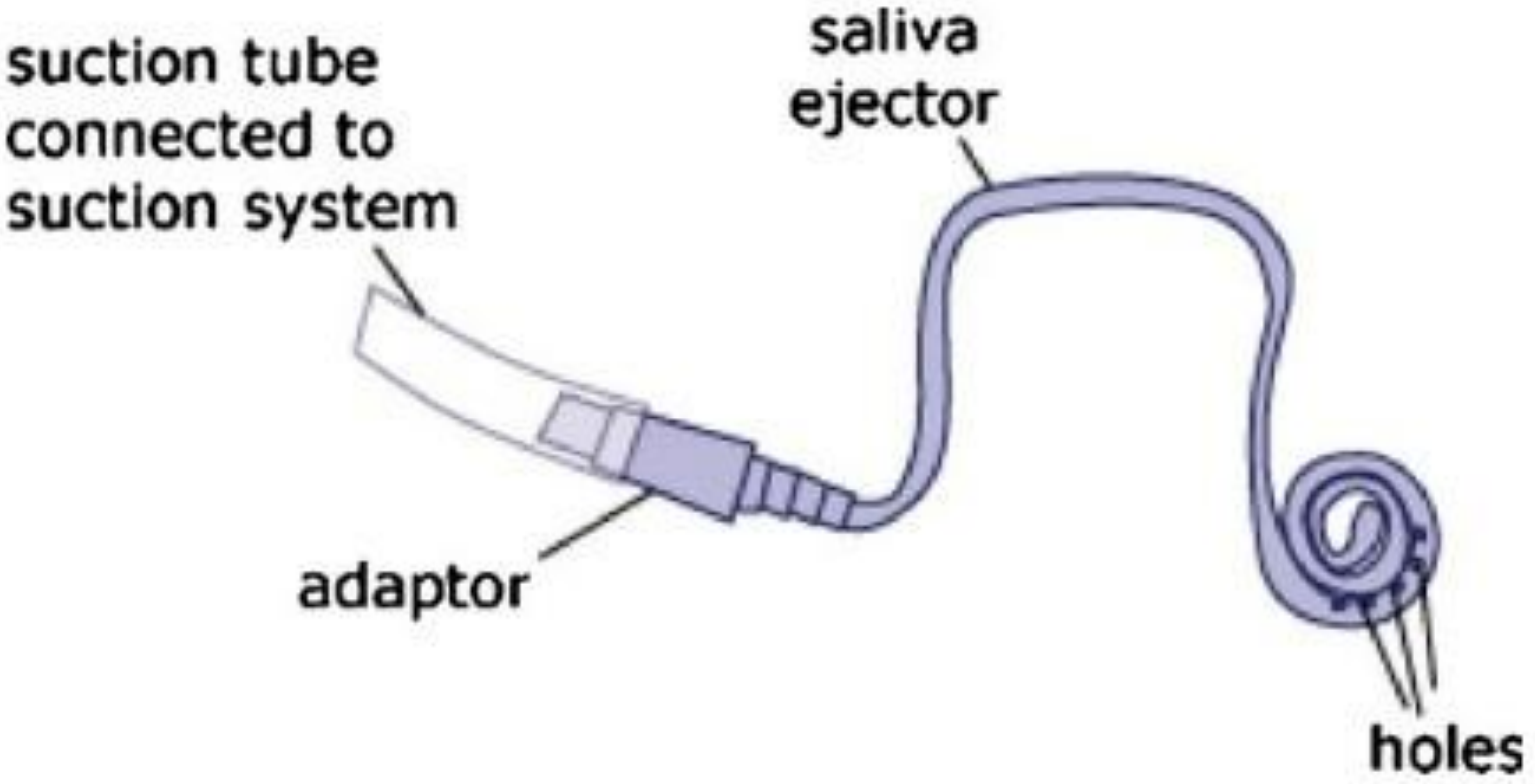


Fig. 1. Orsing Hygoformic Saliva Ejector (Adult Universal).

2.1. Research design and setting

- The device used for COS in this study was a dental device, the Orsing Hygoformic Saliva Ejector (Adult Universal) (Fig. 1), which was originally designed for use in dental surgery for the purpose of suction. The tube of the saliva ejector is arranged spirally and equipped with five holes at the inner rim of the spiral head for suction.
- This design enables the user to avoid placing the suction ports in direct contact with the patients' oral mucosa, thus minimizing the chances of mucosal injury. To ensure comfort, the device can also be adjusted to fit cheeks of different shapes and sizes.

- 本研究中的COS的装置是牙科装置，这个Orsing Hygoformic唾液排出器（成人通用型）（图1），最初是用于牙科手术中抽吸。
- 这设计能够避免将吸入口与患者的口腔黏膜直接接触，从而减少粘膜损伤的机会。

2.1. Research design and setting

- The saliva ejector is made from a non-toxic and non-polluting mixture of polyethylene and polypropylene. To ensure that the material composing the device is safe for long-term placement in the oral cavity, a migration test was undertaken in accordance with the European Commission Directive 2007/72/EC and its amendment 2007/19/EC.
- The result of the test revealed that the overall migration of the material making up the device was very low, indicating that the device is safe for continuous usage.
- In this study, the saliva ejector was changed every 24h and whenever necessary to ensure that it was continuing to effectively drain secretions.

- 唾液排出器是由无毒的和无污染的聚乙烯和聚丙烯的混合物制成的。
- 试验结果表明，构成该装置的材料总的降解是非常低，这表明该装置连续使用是安全的。
- 在这项研究中，唾液排出器每24小时或必要时更换，以确保它能持续有效地排出分泌物。

2.1. Research design and setting

- The design of this study was a parallel-group randomized controlled trial. While both the experimental and control groups used the conventional endotracheal tube, the saliva ejector was only applied to patients assigned to the experimental group. The device was put between the patient's cheek and teeth, and then connected to 100 mmHg of suction for the continuous drainage of saliva. When the patient changed position, the device had to be adjusted to the dependent side to ensure the effective clearance of secretions (Fig. 2).

- 这项研究的设计是一个平行组随机对照试验。实验组和对照组都使用常规的气管导管，唾液排出器只适用于分配到实验组的病人。
- 该装置被放入病人的脸颊和牙齿之间，然后连接到100毫米汞柱负压以持续抽吸唾液。
- 当病人改变位置时，该设备的位置必须要进行调整，以确保有效吸引分泌物（图2）。

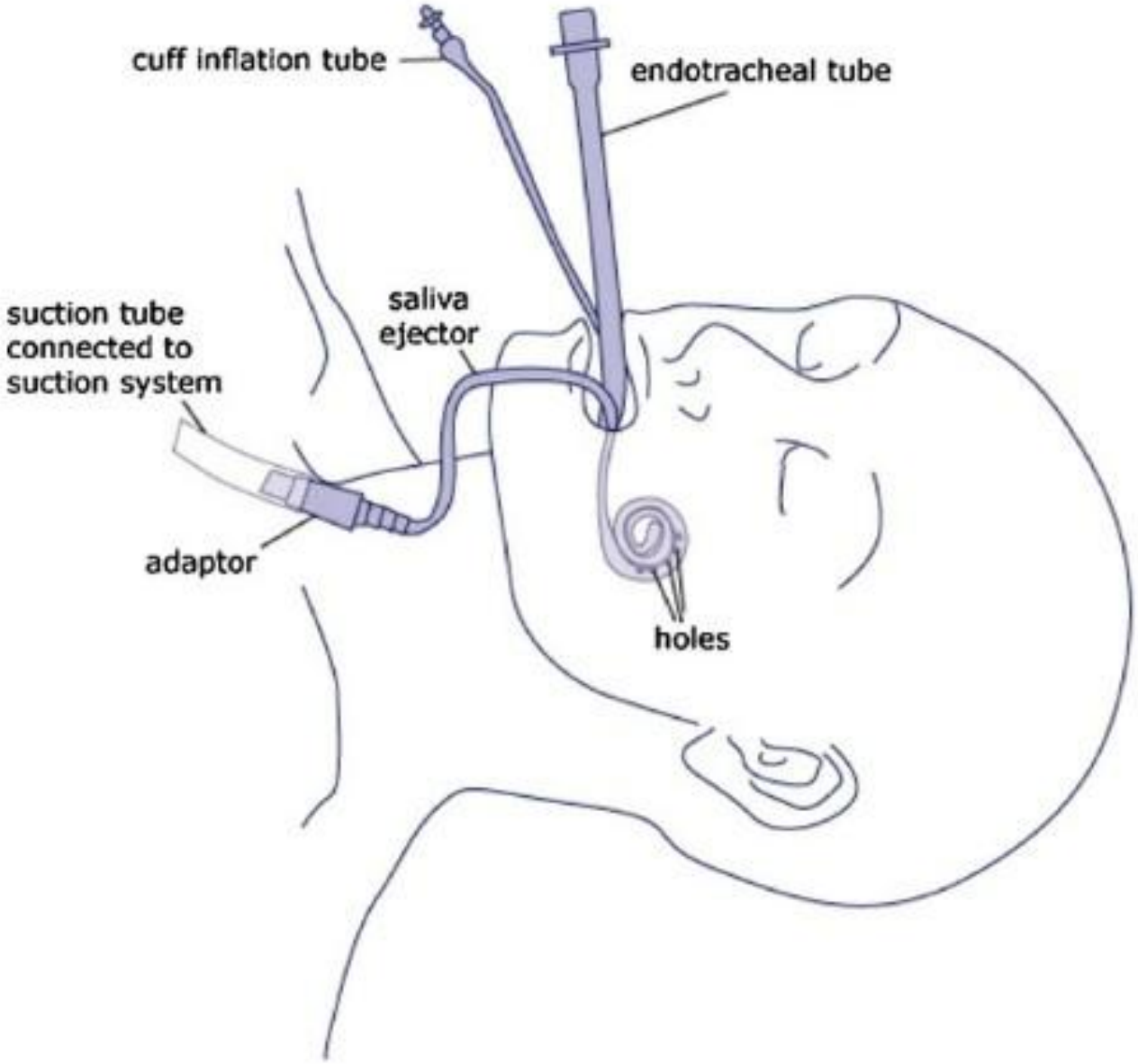


Fig. 2. Diagram of continuous oral suctioning of secretions with saliva ejector.

2.1. Research design and setting

- Before the first patient was enrolled, all ICU bedside nurses participated in at least one orientation session, in which they learned about the rationale for the study, became familiar with the saliva ejector, and had their questions answered. After demonstration of the application of the saliva ejector, each nurse was asked to perform a return demonstration of the procedure to ensure that they had mastered the required skill. An audit trail was done during the study period and it was noted that the device had been properly applied to the subjects.

- 在第一个病人入院前，ICU所有护士至少要参加一次介绍会，主要是让他们了解该研究的理论基础，熟悉唾液排出器的使用，并回答他们的问题。
- 唾液排出器的应用示范后，每个护士被要求有一个操作的反馈，以确保他们掌握了所需的技能。
- 索引跟踪已经在研究期间完成，该设备已被适当地应用到项目。

2.1. Research design and setting

- The study was conducted in the six-bed medical-surgical ICU of a hospital with over 400 beds that provides comprehensive medical services to the public.
- The study was reviewed and approved by the Ethics Committee of the hospital and the Human Subjects Ethics Sub-committee of the university with which the research team was affiliated, and was carried out in accordance with the ethical standards set forth in the Helsinki Declaration of 1975.

- 该研究已经通过了该医院隶属的伦理委员会和大学的人体试验伦理委员会根据1975年通过的赫尔辛基宣言关于伦理标准中规定的审查和批准。

2.2.Sample

- Considering the popularity of pilot studies, there is little discussion in the medical literature of how to determine appropriate sample sizes for pilot studies. However, some articles have raised the issue. For example, in a discussion on pilot testing an instrument, Treece and Treece (1982) contended that for a project with 100 people as the sample, a pilot study with 10 participants should be a reasonable number.

- 考虑研究样本的普及,医学文献中几乎没有讨论如何确定合适的试验研究样本大小。然而，一些文章已经提出了这个问题。例如，在讨论试验测试工具，Treece and Treece（1982）争辩说，一个项目有100人的样本，初步研究纳入10名参与者应该是一个合理的数值。

2.2.Sample

- In the medical field, Julious (2005) observed that for small sample sizes there is a marked gain in precision for each increase of 1 in the sample size per group. However, the gains are less distinct after the sample size has reached 12. He then recommended 12 per group for pilot studies as being an appropriate sample size. This is equivalent to n = 24 for a traditional two-group study.

- 在医疗领域，Julious（2005）观察到对于小样本中有一个精确的增益显着在每组样本量每增加1。然而，样本量达到12后增加都不太明显。他建议每组12个作为一个试点研究合适的样本大小。这是相当于N=24为传统的两组研究。

2.2.Sample

- Similar calculations were made by van Belle (2002), who also suggested a sample size of at least 12 per group to construct a confidence interval. In this pilot randomized controlled trial, we anticipated recruiting a total sample size of approximately 27 to accommodate a potential attrition rate of 10% among the participants.

- 类似的计算是由van Belle在2002年提出来的，他建议的每组至少12个的样本大小，以构造一个可信区间。在这个随机对照试验，我们预计招募总样本约27个，以容纳一个潜在10%的参与者的损耗率。

2.3. Procedure

- Patients entering the ICU were screened for inclusion and exclusion criteria. If a patient met the inclusion criteria and informed consent was obtained, he or she would be randomized into the experimental or control group.
- A randomization list was generated from a computer, and treatment allocation was concealed using sequentially numbered opaque sealed envelopes.
- All patients hospitalized in the ICU, aged 18 or above, and requiring mechanical ventilation through an oro-endotracheal tube for 48h or more **were included in the study.**

- 进入ICU患者筛选纳入和排除标准。如果患者符合纳入标准和知情同意了,他将被随机分为实验或对照组。
- 从计算机生成一个随机化列表,和治疗分配隐藏使用顺序编号不透明的密封信封。
- 纳入标准：所有在ICU住院的患者,18岁或以上,并需要经口气管插管进行机械通气48小时以上。

2.3. Procedure

- **Exclusion** criteria were being HIV positive or contraindicated to the use of a continuous oral suctioning device (e.g., suffering from oral trauma or having undergone oral surgery),
- receiving immunosuppressive therapy (including COPD patients receiving ≥0.8 mg/kg/day of prednisone equivalent),
- having a blood leukocyte count of less than 1000 cells/mm3, or having been diagnosed with solid or hematological tumors.

- 排除标准：HIV阳性或禁忌使用持续口腔吸引装置。（如：患有口腔外伤或经过口腔外科手术）
- 接受免疫抑制治疗（包括接受≥0.8mg/kg/day 的强的松治疗的COPD病人）
- 白细胞计数≦1000/mm^3，或者被诊断为实体或血液肿瘤。

2.3. Procedure

- Identical measures for the prevention of nosocomial pneumonia were applied in both groups, e.g., no routine change of ventilator circuit, a closed tracheal suction system, a semi-recumbent body position, oral care, and hand hygiene. Enteric nutrition would also be started as soon as possible, and periodic verification of the residual gastric volume would be performed.

- 两组均采用相同的措施预防院内的肺炎，例如，不改变常规的呼吸机回路，一个封闭的气管吸引系统，半卧位体位，口腔护理以及手卫生。同时也将尽早开始进行肠内营养，并将定期测定残余胃容量。

2.3. Procedure

- In both groups of patients, tracheal aspirate would be collected for culture at the time of endotracheal intubation and repeated when there was any sign of pneumonia:

1、two or more serial chest radiographs with new or progressive and persistent infiltrate or consolidation or cavitation or pneumatoceles;

2、fever >38.8℃ with no other recognized cause;

- 在两个组中患者，当有任何肺炎迹象时（以下几点），在气管插管期间，气管内分泌物会被收集和重复收集进行培养：

1、两个或两个以上的胸部X光片与新的或渐进性和持续性浸润或合并或气蚀或肺囊肿；

2、发热> 38.8℃，没有其他公认的原因；

2.3. Procedure

3、leukopenia (<4000 WBC/mm^3) or leukocytosis (≥2000 WBC/mm^3);

4、a new onset of purulent sputum or a change in the character of the sputum or increased respiratory secretions or increased suctioning requirements;

5、rales or bronchial breath sounds;

6、and worsening gas exchange (e.g., O_2 desaturations [e.g., PaO2/FiO2<240], increased oxygen requirements, or increased ventilator demand) (Horan et al., 2008).

3、白细胞减少症（<4000WBC/mm^3）或白细胞增多（≥2000 WBC/mm^3）；

4、一个新发脓性痰或性质发生变化的痰或呼吸道分泌物增多或吸痰的需求增加；

5、罗音或支气管呼吸音；

6、以及日益恶化的气体交换（例如，O_2 去饱和作用[例如PaO2/FiO2<240]，O_2需求增加，或通气需求增加）（Horan的等人，2008）。

2.3. Procedure

- The following data were prospectively recorded for all study patients: demographics, the Acute Physiology and Chronic Health Evaluation (APACHE) II score, the reason for intubation, and co-morbidities. Several risk factors for VAP were recorded, such as a history of COPD, a failure to achieve a semi-recumbent position of 30°, and the use of intravenous sedation, a paralytic agent, stress ulcer prophylaxis, antibiotic therapy, and corticosteroid. In addition to the occurrence of VAP, we assessed secondary outcomes, including VAP-free time, the duration of mechanical ventilation, tracheostomy, the length of the ICU stay, the length of the hospital stay, and mortality in the ICU.

- 我们希望记录的所有研究患者的以下数据：人口统计特征，急性生理和慢性健康评估（APACHE）Ⅱ评分，插管原因，还有基础疾病。记录几个VAP发生的危险因素，如慢性阻塞性肺病的历史，未能达到30°的半卧位，并进行静脉镇静，肌松剂，应激性溃疡预防，抗生素治疗，皮质类固醇。除了VAP的发生，我们也要评估次要的结果，包括VAP-free time，持续机械通气时间，气管切开，住ICU的时间，住院时间和ICU死亡率。

2.3. Procedure

- All of the participants were screened daily for the occurrence of VAP by ICU physicians who were not members of the research team.
- Episodes of pneumonia diagnosed within 48 h of ventilation were not considered to be associated with the ventilator. Screening for VAP was maintained until the first episode of VAP, or 48 h after weaning from the ventilator or death.
- In the event of unsuccessful weaning, which was taken to mean that ventilator support was needed again less than 48 h after extubation, patients were kept in the study. After extubation, all patients would be followed up for the occurrence of pneumonia after 48 h.

- 该研究小组的ICU医师每天对所有受试者进行VAP发生的筛选。
- 在通气48小时内确诊肺炎并不需考虑与呼吸机有关。维持筛查直到筛查出第一例VAP，或脱机48小时候或死亡。
- 脱机不成功，是指拔管后不到48小时再次给予呼吸机支持的病人，这类病人则留在研究中。拔管48小时后，所有患者将随访肺炎的发生。

2.3. Procedure

- The diagnostic criteria of VAP in this study were adapted from Horan et al. (2008).
- Owing to safety and feasibility, instead of obtaining bronchial secretions using a bronchoscope and a protected specimen brush, tracheal aspirate was collected as a specimen for establishing the microbiological diagnosis of pneumonia (Chawla, 2008).
- The criteria were as follows:

(i) Radiological

(ii) Sign and symptom （I、 II）

(iii) Laboratory

- VAP的诊断标准在Horan等人的研究中进行了调整。（2008年）。
- 由于安全性和可行性，避免利用支气管镜和保护支气管分泌物样本毛刷获得痰标本，而是收集气管吸出物作为标本，建立诊断肺炎的微生物学（Chawla，2008）。
- 该标准如下：

（i）影像学检查

（ii）症状和体征（I、 II）

（iii）实验室检查

2.4. Data analysis

- Quantitative variables were reported as the mean standard deviation, and were compared using the T test.
- Qualitative variables were reported as percentages, and were compared using the chi-square test or the Fisher's exact test as appropriate.
- The probability of remaining free of VAP was calculated using the Kaplan–Meier method, and a comparison between the two groups was performed with the log-rank test. For statistical analyses, the Statistical Package for the Social Sciences (SPSS) version 18.0 for Windows was used throughout this study.

- 计量资料用平均值的标准差表示,采用t检验进行比较。
- 计数资料用百分比表示,采用卡方检验或确切概率法进行比较。
- 可能与VAP有关的其他资料使用Kaplan-Meier方法统计和他们每两组之间用log-rank检验。本研究的所有数据均使用SPSS18.0版本进行分析。

3. Results

- During the study period, 197 patients were admitted to the ICU. Forty patients met the criteria for inclusion in the study. Of the 40 eligible patients, 15 were excluded from the study because 4 of them had hematological tumors, 2 were on immunosuppressive therapy, and 7 declined to participate. A total of 27 patients were enrolled into the study. Among them, 14 were randomly assigned to the experimental group and 13 to the control group. Of these, 2 were lost to follow-up because they had received mechanical ventilation for less than 48 h (Fig. 3).

- 在研究期间，197例患者被送往ICU。40例符合纳入研究的标准。40例符合条件的患者中，15例排除研究，其中4例有血液系统肿瘤，2例接受免疫抑制治疗，7拒绝参加。共有27例患者入组研究。其中，14例被随机分配到实验组及13例被分到对照组。其中，2人失去随访，因为他们接受机械通气时间少于48小时（图3）。

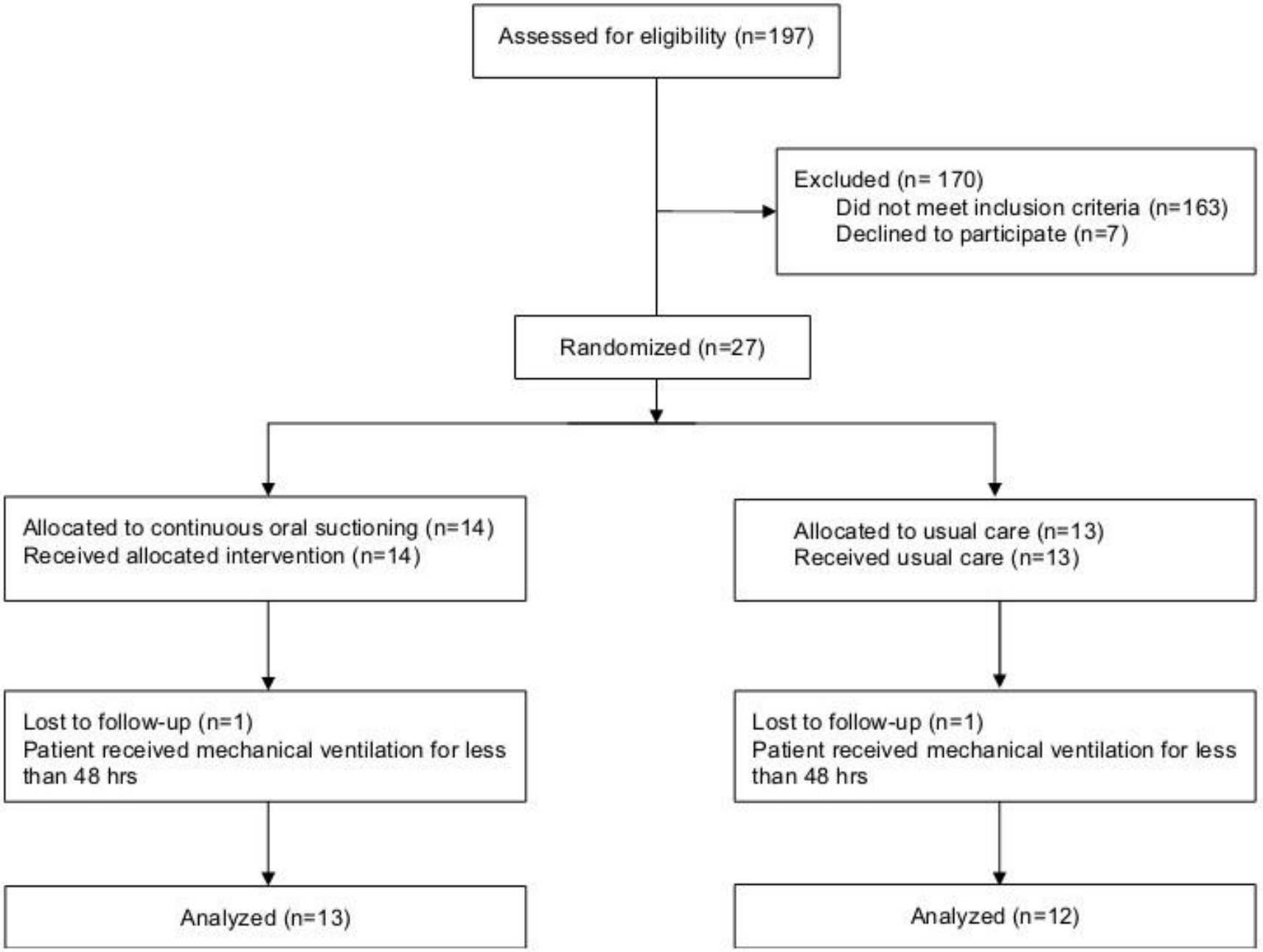


Fig. 3. Flow of participants through trial.

3. Results

- There were no significant differences between the groups with respect to demographics, reasons for intubation, co-morbidity, and risk factors for VAP (Table 1).
- Thirteen patients (52%) developed VAP: three (23.1%; 71 episodes of VAP per 1000 ventilation days) in the experimental group and 10 (83.3%; 141 episodes of VAP per 1000 ventilation days) in the control group (relative risk, 0.28; 95% confidence interval, 0.10–0.77; p = 0.003).

- 两组之间没有显著差异在人口结构，插原因管，基础疾病和VAP的危险因素等方面（表1）

- 本研究中13例患者（52%）发生VAP：实验组三名（23.1%；每1000通气天有71天VAP），而对照组10例（83.3%，每1000个通气天有141天VAP）（相对风险，0.28；95%可信区间为0.10-0.77，*P*=0.003）。

病人的基本信息
的统计学分析

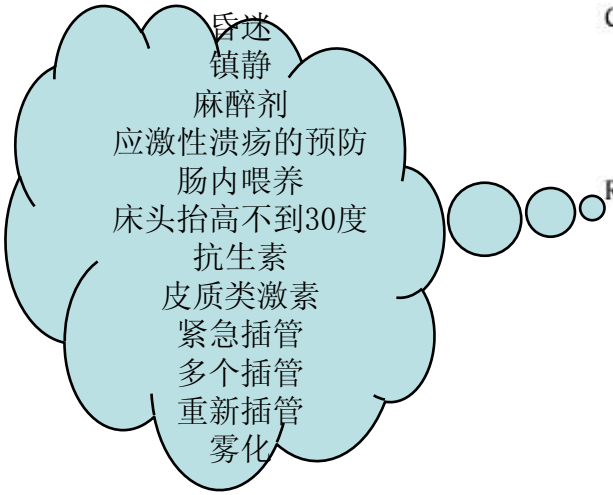


Table 1
Demographics and characteristics of patients.

	Experimental group (N = 13) Mean (SD)	Control group (N = 12) Mean (SD)	p value
Age (year)	70.3 (14.3)	79.4 (12.5)	0.104
APACHE II score	21.5 (7.3)	23.0 (6.4)	0.601

	Experimental group N (%)	Control group N (%)	p value
Gender			
Male	7 (53.8%)	7 (53.8%)	0.821
Female	6 (46.2%)	5 (41.7%)	
Reason for intubation			
Acute respiratory failure	7 (53.8%)	7 (53.8%)	0.821
Shock	2 (15.4%)	0 (0%)	0.157
Cardiac failure	2 (15.4%)	2 (16.7%)	0.930
Neurological disease	2 (15.4%)	1 (8.3%)	0.588
Miscellaneous	0 (0%)	2 (16.7%)	0.125
Co-morbidity			
COPD	3 (23.1%)	5 (41.7%)	0.319
Cardiovascular disease	7 (53.8%)	4 (33.3%)	0.302
Chronic renal disease	5 (38.5%)	2 (16.7%)	0.225
Diabetes mellitus	6 (46.2%)	5 (41.7%)	0.821
Risk factors			
Coma	9 (69.2%)	9 (75.0%)	0.748
Sedation	5 (38.5%)	6 (50.0%)	0.561
Paralytic agent	1 (7.7%)	2 (16.7%)	0.490
Stress ulcer prophylaxis	12 (92.3%)	10 (83.3%)	0.490
Enteric feeding	9 (69.2%)	5 (41.7%)	0.165
Head of bed less than 30°	1 (7.7%)	0 (0%)	0.327
Antibiotics	12 (92.3%)	12 (100%)	0.327
Corticosteroid	0 (0%)	1 (8.3%)	0.288
Urgent intubation	8 (61.5%)	7 (58.3%)	0.870
Multiple intubation	4 (30.8%)	4 (33.3%)	0.891
Reintubation	0 (0%)	1 (8.3%)	0.288
Nebulization	8 (61.5%)	9 (75%)	0.471

3. Results

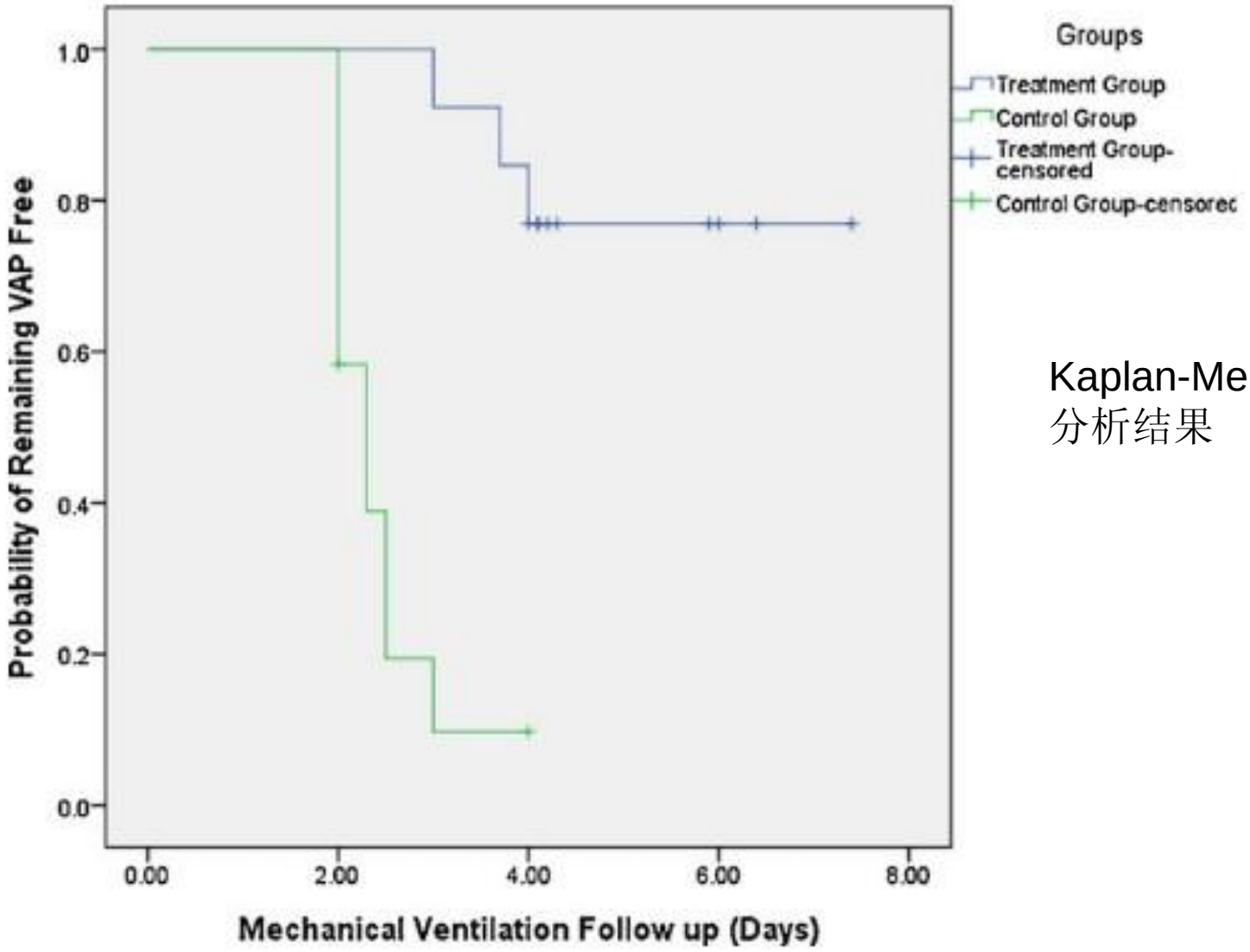
- A Kaplan–Meier analysis confirmed a significantly lower incidence of VAP in the experimental group than in the control group (p = 0.018) (Fig. 4).
- The duration of mechanical ventilation in the experimental group was 3.2 days (SD 1.3), while that in the control group was 5.9 days (SD 2.8)(p = 0.009);
- and the length of ICU stay was 4.8 days (SD 1.6) versus 9.8 days (SD 6.3) for the experimental and control groups, respectively (p = 0.019) (Table 2).
- No significant differences were identified between the two groups in terms of tracheostomy, length of hospital stay, or mortality.

- Kaplan-Meier分析证实了VAP的发生率实验组显著低于对照组（p=0.018）（图4）。
- 机械通气的持续时间实验组为3.2天（SD1.3），而对照组为5.9天（SD2.8）(p=0.009)；
- 住ICU的时间实验组是4.8天(SD 1.6)和对照组是9.8天(SD 6.3),(p=0.019)(表2)。
- 两组在气管造口术、住院时间或死亡率之间没有显著差异。

3. Results

- The microorganisms that caused VAP in this study are shown in Table 2. In this trial, 13 patients acquired VAP.
- From the microbiological analysis, it was evident that 8 of these episodes were monomicrobial, whereas the others were polymicrobial episodes.
- The 5 polymicrobial VAP cases occurred exclusively in the control group.

- 本研究中引起VAP的微生物如表2所示。在这项试验中，13例获得VAP。
- 从微生物学分析，很明显，8例是单一菌血症，而其他是多种微生物引起的。
- 5例多种微生物VAP仅发生在对照组。



Kaplan-Meier
分析结果

Fig. 4. Probability of remaining ventilator-associated pneumonia (VAP) free.

Table 2
Clinical outcome and microorganisms causing ventilator-associated pneumonia (VAP).

Clinical outcome	Experimental group (N = 13) N (%) or mean (SD)	Control group (N = 12) N (%) or mean (SD)	p value
Acquired VAP	3 (23.1%)	10 (83.3%)	0.003
Duration of mechanical ventilation (day)	3.2 (SD 1.3)	5.9 (SD 2.8)	0.009
Length of ICU stay (day)	4.8 (SD 1.6)	9.8 (SD 6.3)	0.019
Length of hospital stay (day)	9.8 (SD 3.7)	21.8 (SD 25.0)	0.126
Tracheostomy	0 (0%)	2 (16.7%)	0.125
Mortality	1 (7.7%)	4 (33.3%)	0.109
Microorganisms causing VAP	**Experimental group (N = 13) N (%)**	**Control group (N = 12) N (%)**	**p value**
VAP			
Monomicrobial VAP	3 (100%)	5 (50%)	0.118
Polymicrobial VAP	0 (0%)	5 (50%)	
Gram positive bacilli			
S. aures	1 (33.3%)	5 (50%)	0.612
S. pneumonia	1 (33.3%)	1 (10%)	0.326
Gram negative bacilli			
Pseudomonas aeruginosa	0 (0%)	2 (20%)	0.400
Stenotrophomonas maltophilia	0 (0%)	1 (10%)	0.569
Escherichia coli	0 (0%)	2 (20%)	0.400
Klebsilella supp.	1 (33.3%)	2 (20%)	0.631
Candida albicans	0 (0%)	2 (20%)	0.400

4. Discussion

- In the ICU, nosocomial pneumonia is the most common infection, and there is a 6–20-fold increase in the rate of nosocomial pneumonia for patients who are mechanically ventilated (Celis et al., 1988; Chastre and Fagon, 2002; Torres et al., 1990).
- The incidence of VAP varies from 7% to 70% in different studies (Alp and Voss, 2006; Safdar et al., 2005).
- In this pilot study, although the nurses adhered to the measures for preventing VAP, such as hand hygiene, avoiding routine changes of ventilator circuits, and maintaining the patients' semi-recumbent position, VAP still occurred in 13 out of 25 (52%) patients.

- 在ICU，医院获得性肺炎是最常见的感染，并机械通气的病人比不带机的病人患肺炎高6~20倍。
- VAP的发生率在不同的研究中从7％到70％。
- 在这个试验性研究，虽然护士坚持预防VAP的措施，如手卫生，避免改变常规的呼吸机回路，维持患者的半卧位，但该研究的25例患者中还是有13例（52％）发生VAP。

4. Discussion

- The relatively high incidence of VAP in our pilot study might have been due to an overall increase in the need to make multiple attempts at intubation in the experimental and control groups. It has not been possible to determine if this was a significant risk factor in this pilot study.
- A larger sample and a thorough statistical analysis are needed for us to fully understand the independent effect that each of the risk factors has on the development of VAP.

- 该研究的VAP发病率相对较高的可能是由于在实验组和对照组需要多次插管。但在这项试验研究，一直未能确定这是否是一个显著风险因素。

- 这需要一个更大的样本和一个全面的统计分析，我们才能充分了解每一个风险因素对VAP的发展的独立效果。

4. Discussion

- Oropharyngeal colonization plays an important role in the pathogenesis of VAP. Johanson et al. (1969) reported an association between oropharyngeal colonization and the risk of developing VAP. A subsequent study confirmed that oropharyngeal colonization is a risk factor for VAP (Bonten et al., 2001).
- In intubated patients, bacteria-laden nasal and oral secretions were collected above the endotracheal tube cuff and below the glottis. VAP developed when this subglottic secretion traveled down to the lower respiratory tract if leakage occurred around the cuff.

- 口咽部定植菌在VAP的发病机制中起着重要的作用。Johanson等人1969年报告了一个口咽部定植是VAP发生的相关危险因素。随后的研究证实，口咽部定植是VAP的危险因素。
- 气管插管的病人，鼻腔和口腔分泌物内的细菌聚集在气管导管cuff上面和声门下面。如果cuff发生漏气，声门下分泌物将向下到达下呼吸道时将引起VAP的发生。

4. Discussion

- Studies on the use of an endotracheal tube with a dorsal lumen above the cuff for removing subglottic secretions found that the incidence of VAP could be decreased by 50% (Kollef et al., 1999; Mahul et al., 1992; Valles et al., 1995).
- Similarly, in this study the incidence of VAP in the experimental group (23.3%) was 60% less than the control group (83.3%).

- 研究发现，使用cuff上面有一个背腔的气管导管清除声门下分泌物，VAP的发病率可以减少50％。

- 类似地，在此研究VAP的实验组的发病率（23.3％）较对照组（83.3％）低60％。

4. Discussion

- This preliminary result supports further research on the continuous clearance of oral secretions by the saliva ejector, which was designed with five holes for effective suctioning.This might have contributed to a substantial decrease in the collection of subglottic secretions and, hence, in a reduction in the rate of VAP.

- 初步结果支持深入研究在使用带有5个孔的唾液排出器持续清除口腔分泌物。这可能是一个重大贡献，在减少声门下分泌物，降低VAP的发生率方面。

4. Discussion

- A saliva ejector costs US$0.06. In terms of resource impact, the proposed intervention in this study might be a good alternative to continuous subglottic suction in preventing VAP in the ICU. A formal costing study is warranted to explore the question of whether improvements in cost might be realized if patient outcomes are improved and the length of stay is reduced. The findings could be particularly useful in developing countries with limited resources, where the prevalence of nosocomial infections is generally higher (Alp et al., 2011).

- 一个唾液排出器的成本约为0.06美元。在资源方面，本研究中所提出的干预措施可能是一个很好的替代持续声门下吸引预防VAP。正式的成本的核算，需要探索的问题是病人预期是否改善和住院日是否减少。调查结果显示，可能是在发展中国家资源有限，院内感染的患病率通常更高。

4. Discussion

- Mechanical ventilation and additional days in the ICU require more resources and cause an increase in healthcare expenses. A longer duration of mechanical ventilation also exposes patients to a greater risk of morbidity and mortality (Jimenez et al., 1998; Cook et al., 1998). For instance, Ely et al. (1999) found a relationship between ventilation duration and mortality. They noted that patients who were ventilated for 1–7 days had a mortality rate of 33%, and that a subsequent increase in ventilator days increased the mortality rate.

- 机械通气和额外的住ICU天数需要更多的资源，导致医疗费用的增加。长时间机械通气还会使患者发病率和死亡率的风险更大。例如，Ely等1999年发现通气时间和死亡率之间的关系。他们指出，机械通气1-7天患者死亡率为33%，而随后增加机械通气天数，则死亡率就增加了。

4. Discussion

- In this pilot study, significant decreases in the duration of mechanical ventilation and length of ICU stay were found in the experimental group. The duration of the patients' mechanical ventilation and the length of their ICU stay decreased from 5.9 (SD 2.8) to 3.2 (SD 1.3) days, and from 9.8 (SD 6.3) to 4.8 (SD 1.6) days, respectively. COS appears to have been effective in preventing VAP, hence resulting in a significant reduction in the duration of mechanical ventilation and length of ICU stay.

- 在本研究中发现，实验组在机械通气的持续时间和ICU住院时间显著下降。病人机械通气的持续时间和住ICU时间下降的长度分别从5.9天（SD 2.8）到3.2天（SD 1.3），9.8天到（SD 6.3）4.8天（SD 1.6）。COS似乎已有效地防止VAP，因此，显著减少机械通气时间和住ICU时间。

4. Discussion

- Although only those participants who had received mechanical ventilation for more than 48 h were included in the analysis, and the groups did not differ in demographics, reasons for intubation, co-morbidity, and risk factors for VAP (Table 1), we could not exclude the possibility that VAP was reduced because of earlier extubation in the experimental group. In addition, before being discharged from the ICU, the patients were extubated and all of them were followed up for the occurrence of pneumonia after 48 h.

- 但只分析了接受机械通气时间超过48小时的病人，并且在人口统计，插管原因，基础疾病和VAP的危险因素没有显着差异的组（表1），我们不能排除因实验组尽早拔管造成VAP降低的可能性。此外，在转出ICU之前，病人拔管48小时后，全部随访肺炎的发生。

4. Discussion

- Therefore, it was likely that the reduction in the length of the ICU stay was attributable to COS. The differences in the length of the hospital stay, tracheostomy, and mortality between the experimental and control groups do not appear to be statistically significant. Taking into consideration the small sample size in this pilot study, these results should be interpreted with caution.

- 因此，它是可能由于COS缩短住ICU时间。住院时间、气管切开以及死亡率之间的差异，实验组和对照组没有统计学意义。考虑到本研究的样本量，这些结果应该是谨慎解读。

4. Discussion

- Hoem (2008) contended that indicators of statistical signicance should be used flexibly rather than mechanically.For example, much higher p-values may be expected to indicate statistical significance in very small data sets, while for large studies p-values much smaller than 0.05 may be needed to indicate important features in the data.

- Hoem（2008）认为，统计学指标的意义应该灵活,而不是机械地使用。例如，在非常小的数据集，更大的P值有统计学意义，而对于大型研究的p值比0.05更小，可能更有统计学意义。

4.1. Limitations

- The findings of this research should be considered in light of its limitations.
- First, recruiting participants who are receiving mechanical ventilatory support for clinical study poses particular challenges (Chlan et al., 2009). Our results are limited by the small size of our sample. Further studies with larger samples are warranted to evaluate whether COS can decrease the incidence of VAP.
- Second, our findings represent the practices of only one hospital. We do not know if these practices are followed at other sites. A multisite study would be necessary to determine whether these findings also occur at other sites.

- 该研究的结果有其局限性。
- 首先，招募接受机械通气支持的临床研究的参加者是个特殊的挑战（Chlan等，2009）。我们的研究结果被我们的样本较小限制了。较大样本的进一步的研究是必要的，以评估是否COS可减少VAP的发生率。
- 第二，我们的结果只有代表该医院的做法。我们这样做不知道是否与其他医院的结果一致。多点研究将是必要的，以确定这些结果也出现在其他医院。

4.2. Implications for future research

- Although there was a positive trend toward the use of the intervention, it would be unwise to advocate the use of COS in practice.
- Instead, the results of this pilot study can be used as a guide in the design and implementation of a full-scale, definitive randomized controlled clinical trial (RCT).

- 虽然干预是有效的，但在实践中提倡使用COS，这将是轻率的。
- 相反，这项试验研究结果可以作为一个全面的、明确的随机对照临床试验（RCT）的设计和实施的指南。

4.2.1. Sample size calculation

- One reason to conduct a pilot study is to provide information for use in calculating the sample size of a subsequent main study (Arain et al., 2010). This seems especially sensible in situations where no data are available from previous studies to inform this process. Preliminary data collected from the current study were used to estimate the sample size requirements for the definitive RCT on COS. The expected event rates in the control group and treatment group were 83.3% and 23.1%, respectively.

- 进行试点研究的其中一个原因是提供在随后的主研究中计算样本量（Arain等，2010）。这似乎可在没有数据的情况下，从前面的研究了解这个过程。对于COS初步数据的收集可从目前明确的RCT的研究来估计样本量需求。在预期VAP发生率在对照组和实验组分别为83.3%和23.1%。

4.2.1. Sample size calculation

- In a power analysis, the sample size for each group was estimated at 10 to reach a power of 0.8 with a 0.05 significance level, using G-power. Based on this calculation, the pilot study has already met sample size requirements for hypothesis testing. However, variance estimates obtained from pilot studies can be subject to substantial sampling errors. Treatment effects may be under- or overestimated because of the imprecision inherent in data from small samples (Sim and Lewis, 2012; Leon et al., 2011).

- 在动力分析中，对每组的样本量估计为10，达到0.8的power与0.05的显着性水平，采用G-power。在此基础上计算，该试验研究对假设检验已经达到样本量要求。然而，方差从试点研究获得的估计值可能会受到实质性的抽样误差。因为数据不精确的小样本，治疗效果可能会被低估或高估了（Sim and Lewis，2012 ;Leon等，2011）。

4.2.1. Sample size calculation

- Therefore if not used cautiously, the results of pilot studies can potentially mislead sample size or power calculations (Kraemer et al., 2006). Alternatively, it is common in practice to determine a required sample size by an estimate based on data from previous similar trials. In determining sample size requirements for the definitive RCT, VAP data from a previous study on the continuous aspiration of subglottic secretions conducted by Valles et al. (1995) were used for the estimation. The sample and data collection methodology were nearly identical to those in this study.

- 因此，如果不慎重使用，试点研究的结果有可能误导样本大小或功率的计算（Kraemer等，2006）。或者，常见的做法是通过以前类似试验的数据以确定所需的样本大小。Valles等（1995）关于持续声门下吸引的研究的VAP数据被用于估计明确的RCT需要的样本量。在本研究中，样本和数据收集方法几乎相同的。

4.2.1. Sample size calculation

- Previous data showed that the VAP rates in the control group and treatment group were 32.5% and 18.4%, respectively. Based on the conditional assumption of a type 1 error of 0.05 and a power of 80%, the sample size required would be 149 per group. We anticipate recruiting a total sample size of approximately 331 to accommodate a potential attrition rate of 10% among the participants.

- 以前的数据显示，VAP的发生率在对照组和实验组分别为32.5%和18.4%。基于一类错误的条件0.05和80%的假设，每组所需样本量将是149例，我们预计参与者中10%的潜在损耗率，总样本量约331例。

4.2.2. Adjudication of VAP

- Careful adjudication of VAP can reduce random errors, and consistent decision-making requires strict criteria. In this open-label pilot study, the diagnostic criteria of VAP were standardized and agreed upon by all of the ICU physicians, who were not members of the research team.After training, they screened all of the participants in both the experimental and control groups daily for the occurrence of VAP. Disagreement between adjudicators would be resolved through discussion and consensus decision-making. Because these adjudications were made by physicians who were aware of the patients' treatment assignments, they were reviewed by the research team to ensure consistency and completeness.

- 谨慎诊断VAP可以减少随机误差，而一致的决策需要严格的标准。在这个开放的试验研究中，由非研究小组的成员的所有的ICU医生统一意见并对VAP的诊断标准进行了标准化。培训结束后，他们每天筛选所有参与者包括实验组和对照组里发生VAP的。评判员之间有分歧的将通过讨论和协商来决策。由于这些判决来自进行了病人治疗任务的医生，他们需要研究小组修订，以确保一致性和完整性。

4.2.2. Adjudication of VAP

- To further enhance the diagnostic accuracy of VAP, endotracheal aspirate was collected for culture not only at the time of intubation, but also repeated for any participant with a clinical suspicion of VAP.
- The diagnostic value of endotracheal aspirate was confirmed in a recent randomized trial conducted by the Canadian Critical Care Trials Group (2006) that involved 740 patients in 28 ICUs in Canada and the United States. They compared a diagnosis of VAP based on endotracheal aspirate culture with a diagnosis based on bronchoalveolar lavage culture and found no difference in clinical outcomes.

- 为进一步提高VAP诊断的准确率，不仅在插管时收集气管吸引物去培养，而且临床上有任何VAP怀疑的参与者还需重复。
- 气管内吸引物的诊断价值由加拿大重症监护实验小组最近（2006）在加拿大和美国进行的一项随机试验涉及740例中28例住ICU患者证实。他们比较了VAP的诊断基于气管吸引物培养与支气管灌洗培养，没有发现不同的临床结果。

4.2.2. Adjudication of VAP

- Owing to budgetary constraints, we were unable to use adjudication committees to conduct a blinded assessment of outcomes in this pilot study.
- The time-consuming nature of adjudication and the associated manpower costs in using this more stringent adjudication process would have diverted research funds from study infrastructure, data acquisition, or analysis.
- However, for a definitive RCT, a blinded assessment to ensure the rigorous adjudication of clinical outcomes is definitely an important issue to consider.

- 由于预算限制，我们无法使用审判委员会对该研究成果进行盲法评估。
- 然而，对于一个确定的随机对照试验，进行盲法评估以确保严格的临床结果评审是需要考虑的重要的问题。

4.2.3. Training, safety, and regulatory issues

- Before commencing the study, the research team gave all nursing staff in the ICU training on how to apply the saliva ejector and provide continuous oral suctioning.
- Return demonstrations by nurses were assessed to ensure proper application and use of the device. Given the novelty of the intervention, the training provided an opportunity to develop consistent practices to confirm the competencies and skills required for the investigation to be conducted with accuracy and precision. This is critical, especially if multiple sites and investigators are engaged in the study.

- 在研究开始之前，研究小组对所有护理人员在如何应用唾液排出器，提供持续的口腔吸痰做了培训。
- 由示范反馈对护士进行评估，以确保设备的合理应用。鉴于新的干预，培训为调查进行的准确性和精确度，提供了一个机会来确认能力和技能的需求。这是至关重要的，特别是如果多个医院和调查人员正在从事该项研究。

4.2.3. Training, safety, and regulatory issues

- The intervention itself was well received by nurses and patients, and the pilot study evolved quite well. All of the patients completed the intervention, and no adverse event was associated with COS.
- The saliva ejector was tolerated well, and no safety concerns were identified. Although the saliva ejector has been approved for use in dental surgery for suctioning, its application for the prevention of VAP is considered off-label. Currently, COS is an investigational intervention.

- 干预本身是护士和患者的一致好评,与试点研究进程很好。所有的患者完成了COS干预，且无不良事件。
- 唾液排出器的接受性很好，未发现安全隐患。虽然唾液排出器已被批准用于牙科手术吸痰，其用于预防VAP的应用还未被批准。目前，持续口腔吸引是一种临床试验干预措施。

5. Conclusion

- The incidence of VAP is high in mechanically ventilated patients. VAP brings an increase in morbidity and mortality, lengthens hospital stays, and raises healthcare costs. Preventing VAP is always preferable to treating it.
- COS may have an important role to play in reducing the rate of VAP, decreasing the duration of mechanical ventilation, and shortening the length of stay of patients in the ICU. The results of this pilot study warrant a full-scale RCT to ensure that the effects are real and that the intervention will have long-term benefits.
- Much work is needed to establish its efficacy as a non-invasive intervention in the prevention of VAP.

- VAP的发病率在机械通气患者中是很高的。VAP带来的的发病率和死亡率增加，延长住院时间，并提高医疗成本。预防VAP总比治疗VAP更可取。
- COS可能在降低VAP的发生率，减少机械通气时间，缩短病人住院时间和住ICU时间上有重要作用。这项研究的结果保证一个完整的随机对照试验，以确保干预的效果是真实的和它带来的长远利益。
- 确立它是一种作为预防VAP的非侵入性干预的有效性，还需要更多的工作。

- Conflict of interest

  None declared.
- Funding

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- Ethical approval

  Ethical approval was given by the Ethics Committee of the St. Paul's Hospital and the Human Subjects Ethics Sub-committee of The Hong Kong Polytechnic University (reference number: HSEARS20081021004-01).

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- 伦理批准

  获得圣保罗医院的伦理委员会和香港理工大学人体试验伦理委员会的伦理批准（参考号：HSEARS20081021004-01）。

References

- Alp, E., Voss, A., 2006. Ventilator associated pneumonia and infection control. Annals of Clinical Microbiology and Antimicrobials 5, 7.
- Alp, E., Leblebicioglu, H., Doganay, M., Voss, A., 2011. Infection control practice in countries with limited resources. Annals of Clinical Micro- biology and Antimicrobials 10, 36.
- American Association of Critical-Care Nurses, 2008. Ventilator Associated Pneumonia. Retrieved from http://classic.aacn.org/AACN/practiceA-lert.nsf/Files/VAP/$file/Ventilator%20Associated%20 Pneumonia%2011-2007.pdf (accessed 30.12.11).
- American Thoracic Society, 2005. Guidelines for the management of adults with hospital-acquired, ventilator-associated pneumonia,and healthcare-associated pneumonia. American Journal of Respira tory and Critical Care Medicine 171, 388–416.
- Arain, M.R., Campbell, M.J., Cooper, C.L., Lancaster, G.A., 2010. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Medical Research Methodology 10, 67.
- Bonten, M., Bergmans, D., Gaillard, C., 2001. Prevention of ventilator-associated pneumonia by oral decontamination: a prospective, randomised, double-blind, placebo-controlled study.
- American Journal of Respiratory and Critical Care Medicine 164, 382–388.
- CanadianCriticalCareTrialsGroup,2006.Arandomized trialofdiagnostic techniques for ventilator-associated pneumonia. New England Journal of Medicine 355, 2619–2630.
- Celis, R., Torres, A., Gatell, J.M., Almela, M., Rodriguez-Roisin, R., AgustiVidal,A.,1988.Nosocomialpneumonia:amultivariateanalysisofrisk and prognosis. Chest 93, 318–324.
- Chastre, J., Fagon, J.Y., 2002. Ventilator-associated pneumonia. American Journal of Respiratory and Critical Care Medicine 165, 867–903.
- Chawla, R., 2008. Epidemiology, etiology, and diagnosis of hospital-acquired pneumonia and ventilator-associated pneumonia in Asian countries. American Journal of Infection Control 36 (4 Suppl.), S93–S100.

References

- Johanson, W.G., Pierce, A.K., Stanford, J.P., 1969. Changing pharyngeal bacterial flora of hospitalized patients: emergence of gram-negative bacilli. New England Journal of Medicine 154, 1137–1140.
- Joshi, N., Russell, L., Bruce, H.H., 1992. A predictive risk index for noso- comial pneumonia in the intensive care unit. American Journal ofMedicine 93, 135–142.
- Julious, S.A., 2005. Sample size of 12 per group rule of thumb for a pilot study. Pharmaceutical Statistics 4, 287–291.
- Koenig, S.M., Truwit, J.D., 2006. Ventilator-associated pneumonia: diag- nosis, treatment, and prevention. Clinical Microbiology Reviews 19 (4), 637–657.
- Kollef,M.,1999.Thepreventionofventilator-associatedpneumonia.New England Journal of Medicine 340, 627–634.
- Kollef, M.H., Skubas, N.J., Sundt, T.M., 1999. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. Chest 116, 1339–1346.
- Kraemer, H.C., Mintz, J., Noda, A., Tinklenberg, J., Yesavage, J.A., 2006.Caution regarding the use of pilot studies to guide power calculations for study proposal. Archives of General Psychiatry 63, 484–489.
- Leon, A.C., Davis, L.L., Kraemer, H.C., 2011. The role and interpretation of pilot studies in clinical research. Journal of Psychiatric Research 45, 626–629.
- Mahul, P., Auboyer, C., Jospe, R., Ros, A.,Guerin, C., Khouri, Z.E., Galliez, M.,Dumont,A.,Gaudin,O.,1992.Preventionofnosocomialpneumoniain intubated patients: respective role of mechanical subglottic secretion drainage and stress ulcer prophylaxis. Intensive Care Medicine 18, 20–25.
- Oikkonen, M., Aromaa, U., 1997. Leakage of fluid around low-pressure tracheal tube cuffs. Anaesthesia 52, 567–569.
- Powers, J., Brower, A., Tolliver, S., 2007. Impact of oral hygiene on pre- ventionof ventilator-associated pneumonia in neuroscience patients.Journal of Nursing Care Quality 22, 316–321.

References

- Rello, J., Ollendorf, D.A., Oster, G., Vera-Llonch, M., Bellm, L., Redman,
- R., Kollef, M.H., 2002. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. Chest 122, 2115–2121.
- Chlan, L., Guttormson, J., Tracy, M.F., Bremer, K.L., 2009. Strategies for overcomingsiteandrecruitmentchallengesinresearch studiesbased in intensive care units. American Journal of Critical-Care Nurses 18 (5), 410–417.
- Cook, D., Walter, S., Cook, R., 1998. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Annals of Internal Medicine 129, 433–440.
- Craven, D.E., Steger, K.A., 1995. Epidemiology of nosocomial pneumo- nia: new perspective on an old disease. Chest 108 (Suppl.), 1S–16S.
- Ely, E.W., Baker, A.M., Evans, G.W., Haponik, E.F., 1999. The prognostic significance of passing a daily screen of weaning parameters. Inten- sive Care Medicine 25 (6), 581–587.
- Greene, R., Thompson, S., Jantsch, H., Teplick, R., Cullen, D.J., Greene, E.M., Whitman, G.J., Hulka, C.A., Llewellyn, H.J., 1994. Detection of pooled secretions above endotracheal-tube cuffs: value of plain radiographs in sheep cadavers and patients. American Journal of Roentgenology 163, 1333–1337.
- Hoem, J.M., 2008. The reporting of statistical significance in scientific journals. Demographic Research 18, 437–442.
- Horan, T.C., Andrus, M., Dudeck, M.A., 2008. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. American Journal of Infection Control 36, 309–336.
- Jimenez, P., Torres, A., Rodriguez-Roisin, R., de la Bellacasa, J., Aznar, R., Gatell, J., Agusti-Vidal, A., 1998. Incidence and etiology of pneumonia acquired during mechanical ventilation. Critical Care Medicine 17, 882–885.

References

- Safdar, N., Dezuflian, C., Collard, H.R., Saint, S., 2005. Clinical economic consequences of ventilator associated pneumonia: a systematic review. Critical Care Medicine 33, 2184–2193.
- Sim,J.,Lewis,M.,2012.Thesizeofapilotstudyforaclinicaltrialshouldbe calculated in relation to considerations of precision and efficiency. Journal of Clinical Epidemiology 65, 301–308.
- Smulders,K.,vanderHoeven,H.,Weers-Pothoff,I.,Vandenbroucke-Grauls,C.,2002. A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation.Chest121,858–862.
- Tablan, O.C., Anderson, L.J., Besser, R., Bridges, C., Hajjeh, R., 2004. Guide- lines for preventing health-care associated pneumonia, 2003: recom mendations of CDC and the Healthcare Infection Control Practices
- Advisory Committee. MMWR Recommendations and Reports 53 (RR03), 1–36 Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5303a1.htm (accessed 30.12.20).
- Torres,A.,Aznar,R.,Gatell,J.M.,Jimenez,P.,Gonzalez,J.,Ferrer,A.,Celis,R.,
- Rodriguez-Roisin, R., 1990. Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. American Review of Respiratory Disease 142, 523–528.
- Treece, E.W., Treece, J.W., 1982. Elements of Research in Nursing. Mosby, St.
- Louis.Valles, J., Artigas, A., Rello, J., Bonsoms, N., Fontanals, D., Blanch, L., Fernandez, R., Baigorri, F., Mestre, J., 1995. Continuous aspiration of subglottic secretions in preventing ventilator associated pneumonia. Annals of Internal Medicine 122, 179–186.
- van Belle, G., 2002. Statistical Rules of Thumb. John Wiley, New York.


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