Oral Health Status and Development of Ventilator-Associated Pneumonia: A Descriptive Study
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Ventilator-associated pneumonia (VAP) is defined as pneumonia in a patient receiving mechanical ventilation that was neither present nor developing at the time of intubation. VAP increases mortality, length of stay, and cost. Oral health status can be compromised by critical illness and by mechanical ventilation and is influenced by nursing care. However, the extent of oral changes in critically ill patients and the relationship between oral health status and development of VAP have not been extensively studied.

A major risk factor for VAP is colonization of the oropharynx by potential pathogens such as *Staphylococcus aureus*, *Streptococcus pneumoniae*, and gram-negative rods. Several factors contribute to the importance of oral health status in the development of VAP.
Within 48 hours of admission to the intensive care unit (ICU), patients have changes in oral flora to predominantly gram-negative organisms, which include more virulent organisms. Dental plaque can provide an environment for microorganisms that cause VAP, and dental plaque of patients in the ICU can be colonized by potential respiratory pathogens such as methicillin-resistant Staphylococcus aureus and Pseudomonas aeruginosa. In addition, abnormalities in salivary flow may place patients at risk for overgrowth of organisms in the oropharynx. Circulation of saliva in the mouth provides mechanical removal of debris and plaque, and saliva contains both innate and specific immune components active in controlling oral microorganisms. Thus, salivary volume and amounts of salivary immune components such as lactoferrin and immunoglobulin A may influence oropharyngeal colonization and development of VAP. Tubes traversing the oral cavity that keep the mouth open may contribute to the accumulation of dental plaque by exacerbating xerostomia (dry mouth). Many medications also reduce salivary flow.

Oral health status in critically ill adults is an important issue, but it has not been well studied. The specific aim of this study was to describe the relationship between oral health status and the development of VAP. Specifically, we examined the relationship between oral health status, as indicated by assessment of the oral cavity, cultures of oral specimens, salivary volume, and salivary immune components, and development of VAP, as indicated by the Clinical Pulmonary Infection Score (CPIS). In addition, we determined changes in oral health status during the first 7 days of intubation and mechanical ventilation and the relationships between microbial colonization of the oropharynx and colonization of the trachea over time.

Methods
Design and Sample
A nonexperimental, longitudinal, descriptive design was used. The study was approved by the Virginia Commonwealth University Office of Research Subjects Protection and was carried out in accordance with the ethical standards set forth in the Helsinki Declaration of 1975. Subjects were recruited from the medical respiratory ICU at Virginia Commonwealth University Health Systems in Richmond, Va. This 12-bed unit has about 1000 admissions each year; approximately 50% of the patients admitted require mechanical ventilation.

All patients admitted to the unit were reviewed for potential enrollment in the study. Patients receiving mechanical ventilation were enrolled within 24 hours of intubation. Because reintubation increases the risk for VAP, patients who already had had endotracheal intubation during the current hospital admission were excluded. Data were obtained during a period of up to 7 days or until extubation. Because clinical evidence of VAP occurs after 48 hours of intubation, data on VAP and oral health were collected on days 1 (baseline), 4, and 7.

Measurement and Quantification of Key Variables
Oral Health Status. Evaluation of oral health status had 5 components:
1. a baseline count of decayed, missing, and filled teeth;
2. an assessment of the oral cavity;
3. a culture of an oral specimen;
4. measurement of salivary volume; and
5. analysis of 2 salivary immune components: immunoglobulin A and lactoferrin.

Assessment of the oral cavity consisted of visually scoring 9 components:
1. dental plaque,
2. inflammation,
3. bleeding,
4. purulence,
5. candidiasis,
6. calculus,
7. stain,
8. caries, and
9. salivary flow (observed salivary volume).

The assessments were documented by using a 100-mm visual analog scale (VAS) for each component. These components were chosen on the basis of previous work and were developed in conjunction with a dental hygiene faculty member and a biostatistician.

Salivary flow determined by using the VAS was significantly correlated with the objective measurement of salivary volume ($r = 0.70; P = .006$). Number of teeth decayed was significantly correlated with VAS caries ($r = 0.83; P < .001$). In addition, VAS items not expected to change over time were highly correlated on different days (caries, $r = 0.90, P < .001$; stain, $r = 0.94, P < .001$). This assessment tool provided greater discrimination than categorical scoring systems do; data collectors were extensively trained and
were periodically retested to maintain interrater reliabilities greater than 0.90.

Cultures of oral specimens were evaluated microscopically (Gram stain) and semiquantitatively. Each culture was scored on a 3-point scale identical to the CPIS scale used to describe cultures of tracheal aspirates:

1 = no growth or few bacteria,
2 = moderate or large number of bacteria, and
3 = large number of bacteria and same bacteria seen on Gram stain.

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Oral comfort care did not affect pneumonia risk.

After the oral assessment, a sample of saliva was collected from the sublingual pocket on the dependent side of the mouth by means of a salivette (Sarstedt Inc, Newton, NC). The salivette was centrifuged to recover the saliva, and the volume of the recovered saliva was measured. Levels of salivary immunoglobulin A and lactoferrin were determined by using an enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, Minn). Aliquots of saliva samples were stored at -70°C until assay. All assays were performed in triplicate.

Ventilator-Associated Pneumonia. Development of VAP was determined by using the CPIS.23-25 With the CPIS, points are assigned to 6 easily obtained variables:

1. body temperature,
2. white blood cell count,
3. tracheal secretions,
4. oxygenation (ratio of PaO₂ to fraction of inspired oxygen),
5. findings on chest radiograph (radiologist’s report), and
6. cultures of tracheal aspirates (microscopic examination and semiquantitative culture of tracheal secretions, scored by using the same scale as for the oral cultures).

Points for each variable of the CPIS are summed, yielding a total CPIS (range 0-12), which provides a range of scores for data analysis. Although some investigators26,27 have used the CPIS as a dichotomous measure of VAP (CPIS = 6 indicates pneumonia, and CPIS <6 indicates no pneumonia), other investigators12,23,28 have used the entire range of scores to describe the clinical development and progression of pulmonary infection over time. We used the full range of scores to describe the risk of VAP.

Several other risk factors may contribute to the development of VAP. Descriptive data related to these risk factors also were collected, including demographics and severity of illness as determined by scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II. Demographic data included sex, race, age, previous use of antibiotics, reason for intubation, type of intubation, intubation process, and reason for admission to the ICU.

Procedure

For each patient, if inclusion criteria were met, the study was explained to the patient’s legally authorized representative and consent was obtained. Data were collected from time of enrollment in the study through day 7 of intubation or until extubation. Oral health status and CPIS were determined 3 times during the study: within 24 hours of intubation (baseline, at time of enrollment), at 72 to 96 hours after intubation (during day 4 of intubation, corresponding to the definition of early-onset VAP29), and at 144 to 168 hours after intubation (during day 7 of intubation, corresponding to late-onset VAP29). Data related to other risk factors for VAP were collected daily and included information on ventilator support, enteral nutrition, and selected medications.

As salivary volume decreased, risk of pneumonia increased.

Data Analysis

Descriptive statistics were used to summarize the characteristics of the study population; percentages were calculated for discrete variables and means and SDs for continuous variables. A general forward selection multiple regression analysis was used to model the relationship between oral health status and CPIS at day 4. Day 4 was chosen because the sample size at day 7 was small because of loss of patients (extubation or death). Variables examined included baseline CPIS, oral assessment scores, salivary volume, salivary immunoglobulin A, salivary lactoferrin, and demographic variables. The final model had the highest overall analysis of variance F ratio (F_6,21 = 4.86, P = .006) and adjusted $R^2$ ($R^2_{adj} = 0.52$). Model parameters are presented in Table 1. Finally, model assumptions were checked by examining the residual by predicted plot, the normal quantile plot of the residuals, and regression diagnostics.
Results

Characteristics of the Sample

The characteristics of the sample are summarized in Table 2. The 66 patients (mean age 55 years, 58% men) were ethnically diverse: 59% black, 35% white, 3% Asian, and 1.5% Hispanic. Patients remained in the study for a mean of 4.2 days. A total of 37 patients (56%) remained in the study through day 4; 21 (32%), through day 7. Because patients remained in the study only while intubated and receiving mechanical ventilation, an important reason for attrition was extubation; death related to critical illness was another source of attrition. Most of the patients (65%) were intubated because of respiratory failure; the remainder were intubated to provide airway control.

Baseline counts of decayed, missing, and filled teeth (Table 2) indicated that many patients had oral health problems before admission. Interestingly, the number of times per day that oral comfort care was given did not affect day 4 CPIS ($P = .81$) and did not differ significantly between patients in whom VAP developed and those in whom it did not.

The risk of VAP as evidenced by mean CPIS consistently increased over time (Table 3). Of the 31 patients with complete data through day 4, a total of 8 (26%) had a score of 6 or higher on the CPIS.

Relationship Between Oral Health Status and VAP

Factors significantly related to day 4 CPIS were APACHE II scores ($P = .007$), day 4 salivary volume ($P = .02$), interaction between baseline CPIS and APACHE II ($P < .001$), and interaction between baseline CPIS and plaque ($P = .01$). An inverse relationship was observed between salivary volume and day 4 CPIS; as salivary volume decreased, CPIS increased. Because our model has 2 interaction terms (baseline CPIS × APACHE II and baseline CPIS × plaque), the effect of plaque on day 4 CPIS could not be directly interpreted.

Table 1 Model parameter estimates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate (SE)</th>
<th>t ratio</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>APACHE</td>
<td>0.172 (0.055)</td>
<td>3.14</td>
<td>.007*</td>
</tr>
<tr>
<td>Salivary volume</td>
<td>-0.002 (0.001)</td>
<td>-2.61</td>
<td>.02†</td>
</tr>
<tr>
<td>CPIS1</td>
<td>-0.098 (0.202)</td>
<td>-0.49</td>
<td>.63</td>
</tr>
<tr>
<td>Plaque</td>
<td>0.005 (0.017)</td>
<td>0.28</td>
<td>.79</td>
</tr>
<tr>
<td>CPIS1 × APACHE</td>
<td>-0.165 (0.0325)</td>
<td>-5.06</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>CPIS1 × Plaque</td>
<td>-0.034 (0.012)</td>
<td>-2.76</td>
<td>.01†</td>
</tr>
</tbody>
</table>

* Significant at $P < .01$.
† Significant at $P < .05$.
Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; CPIS, Clinical Pulmonary Infection Score.

Table 2 Characteristics of the sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55</td>
<td>25-93</td>
</tr>
<tr>
<td>Score on Acute Physiology and Chronic Health Evaluation II</td>
<td>20.35</td>
<td>4-41</td>
</tr>
<tr>
<td>No. of decayed teeth</td>
<td>1.08</td>
<td>0-7</td>
</tr>
<tr>
<td>No. of missing teeth</td>
<td>13.85</td>
<td>0-36</td>
</tr>
<tr>
<td>No. of filled teeth</td>
<td>0.82</td>
<td>0-9</td>
</tr>
<tr>
<td>Total No. of decayed, missing, and filled teeth</td>
<td>15.75</td>
<td>0-36</td>
</tr>
<tr>
<td>Oral care, No. of times per day</td>
<td>2.58</td>
<td>0-7</td>
</tr>
</tbody>
</table>

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Table 3 Clinical Pulmonary Infection Score (CPIS) and oral health status variables by study day

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Mean (SD)</th>
<th>Day 4 Mean (SD)</th>
<th>Day 7 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPIS</td>
<td>3.66 (1.74)</td>
<td>4.26 (2.02)</td>
<td>4.50 (1.79)</td>
</tr>
<tr>
<td>Score on visual analog scale for oral assessment (millimeters from zero anchor)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plaque</td>
<td>21.27 (23.66)</td>
<td>22.72 (20.47)</td>
<td>24.32 (29.01)</td>
</tr>
<tr>
<td>Salivary flow</td>
<td>31.86 (28.12)</td>
<td>31.53 (30.95)</td>
<td>26.79 (24.10)</td>
</tr>
<tr>
<td>Measured salivary volume, µL</td>
<td>357.2 (483.4)</td>
<td>305.9 (448.4)</td>
<td>133.5 (286.9)*</td>
</tr>
<tr>
<td>Immunoglobulin A, g/L</td>
<td>3.5 (4.9)</td>
<td>2.6 (5.8)</td>
<td>3.0 (7.3)</td>
</tr>
<tr>
<td>Lactoferrin, µg/mL</td>
<td>398.5 (155.2)</td>
<td>992.5 (181.4)</td>
<td>535.2 (111.0)</td>
</tr>
</tbody>
</table>

* Significant at $P < .01$. 

Table 1

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Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; CPIS, Clinical Pulmonary Infection Score.
The complex relationship between day 4 CPIS and plaque, APACHE II scores, and baseline CPIS was evaluated by using contour plots. In order to generate the plots, plaque scores were collapsed into 3 categories: low (cleanest teeth), moderate, and high (most plaque). Figure 1 shows the relationship of these categories to day 4 CPIS across a range of APACHE II scores for patients who did not have pneumonia at baseline (CPIS <5). The contour plots are color keyed such that color wavelength is associated with day 4 CPIS (larger wavelength indicates higher CPIS); yellow, orange, and red areas correspond to day CPIS scores ≥6 (indicating pneumonia).

In the most critically ill, increases in dental plaque increased the risk of pneumonia.

In patients with the cleanest teeth (Figure 1, left panel), higher baseline CPIS was predictive of a slight decrease in day 4 CPIS for patients whose APACHE II scores were greater than 26. However, for patients whose APACHE II scores were less than 26, increases in baseline CPIS were predictive of increased day 4 CPIS. Similar patterns held for patients with moderate plaque (Figure 1, middle panel) and the most plaque (Figure 1, right panel), although the breakpoint for APACHE II score was 23 in the patients with moderate plaque and 21 in the patients with the most plaque.

In all categories, when APACHE II and baseline CPIS were held constant, plaque increases were associated with increased day 4 CPIS. The model indicates that increased plaque was most predictive of pneumonia in patients with high APACHE scores and lower baseline CPIS.

Changes in Oral Health Status During the First 7 Days of Intubation

Data related to oral health status on study days 1 (baseline), 4, and 7 are presented in Tables 3 and 4. Salivary volume decreased over time, with significant differences between day 1 and day 7 (t test, P = .003). Dental plaque consistently increased over time, although the differences were not significant. Baseline plaque score was highly correlated with day 4 plaque score (r = 0.65, P < .001). Baseline salivary lactoferrin was positively correlated with day 4 plaque score (P = .01). Other correlations were not significant.

Temporal Relationships in Microbial Colonization

We examined both the concordance between and timing of oral and tracheal colonization. The number
of organisms present in cultures of oral specimens increased from day 1 to day 4 and remained high on day 7 (Figure 2). Potential pathogens were detected in the cultures: *S. aureus* in 4 patients, *P. aeruginosa* in 1 patient, and *Acinetobacter baumanii* in 1 patient. Importantly, in each instance, the organism was present in oral cultures on the same sampling day or before the appearance of the organism in cultures of tracheal aspirates.

We tested the agreement between oral culture scores and tracheal aspirate scores by using a weighted $\kappa$ statistic. The analysis revealed significant agreement on all 3 study days between oral swab score and tracheal aspirate score (day 1, $P = .02$; day 4, $P < .001$; day 7, $P = .008$).

**Discussion**

VAP is associated with increased healthcare costs, morbidity, and mortality. Several factors increase the risk for VAP. Although strong data link certain risk factors to VAP, the influence of oral health status has not been examined extensively. We found that the oral health of critically ill patients is often compromised at the time of admission and deteriorates over time, and that a relationship exists between oral health status and VAP.

The study sample was a diverse group, with African Americans and women well represented. Severity of illness was appropriate for a large urban medical center, and the VAP rate was similar to the rate reported in the literature. Interestingly, the number of decayed, missing, and filled teeth in our sample is similar to that reported by Fourrier et al (mean 6, SD 8) in a sample of patients in Europe.

Others have examined dental plaque in ICU patients, but we focused exclusively on patients receiving mechanical ventilation, restricted the study to the first 7 days of intubation, and included oral health status...
parameters other than plaque. In a study by Scannapieco et al., a total of 34 patients in a medical respiratory ICU had mean plaque scores significantly greater than those of outpatients in a preventive dentistry clinic. Fourrier et al. found an increase over time in dental plaque on premolar teeth in 15 ICU patients examined on study days 0 and 5. El-Solh et al. examined dental plaque in 49 elderly long-term care residents at the time of admission to the ICU and found that dental plaque was worse in those who were subsequently colonized with respiratory pathogens than in those who were not colonized. Scannapieco et al. did not examine the relationships between VAP and dental plaque and oral colonization. Fourrier et al. found that colonization of dental plaque with potential pathogens was significantly associated with subsequent nosocomial infections (not limited to VAP).

Our data support a link between increases in dental plaque and the development of VAP. The relationship was not straightforward but was influenced by interactions among dental plaque, baseline severity of illness, and baseline pulmonary infection status. The effect of increased plaque was most predictive of pneumonia in patients with high APACHE scores and lower baseline CPIS. The effect of oral care interventions on VAP has not been shown, but as plaque-reduction interventions are tested, patients who have the highest severity of illness but do not yet have signs of pulmonary infection might derive the most benefit. The differential benefits of plaque reduction in particular subgroups of patients require additional investigation.

Association of plaque scores and risk for VAP may be due to the potential for dental plaque to harbor pathogens responsible for VAP in the microbially rich biofilm. Scannapieco et al., Fourrier et al., and El-Solh et al. all found potential VAP pathogens, including S. aureus and P. aeruginosa, in the oral cavities of ICU patients. We also cultured these organisms from oral and tracheal secretions. Potential pathogens were present in oral specimens at the same time as or before the appearance of the pathogens in tracheal secretions, similar to the findings in elderly subjects reported by El-Solh et al.

We observed that lower baseline salivary volumes were associated with increased day 4 CPIS (and risk of VAP). Because of the importance of salivary flow in mechanical removal of oral organisms and in distribution of salivary immune components throughout the oral cavity, this finding was not surprising. Although our examination was restricted to the first 7 days of ventilation, the reduction in salivary volume over time might contribute to increases in risk for VAP beyond the period we studied. Many of the medications given to critically ill patients (including benzodiazepines, haloperidol, and meperidine) can affect salivary volume. Methods of increasing oral mucosal hydration merit investigation.

Our data further indicate that levels of innate and specific immune components in the mouth, particularly salivary lactoferrin and immunoglobulin A, do change during critical illness. The role of salivary immune factors has not been thoroughly investigated and might provide additional insights into risk factors for VAP.

We developed an oral VAS to address difficulties with previous bedside oral evaluation tools. Our assessment tool has tested reliability and validity, includes multiple parameters of oral health status, and is designed to evaluate those parameters as continuous measures. Some of the individual items on the VAS (eg, caries) are not expected to change during hospitalization; these items provide a mechanism for ongoing evaluation of interrater reliability in individual patients or groups of patients. Of note, we were able to maintain a greater than 0.90 interrater reliability throughout the study with minimal training.

Dental plaque and salivary volume can be determined by bedside clinicians and are associated with risk for VAP. These factors are theoretically amenable to alteration by nursing interventions, although oral care interventions in adults receiving mechanical ventilation have not been tested extensively. However, current oral care is focused on comfort rather than plaque removal or stimulation of salivary flow. We are testing the effect of specific oral care interventions on removal of plaque and reduction of the incidence of VAP in patients in a surgical, medical, and neuroscience ICU.

Good salivary flow enhances the removal of oral organisms, reducing pneumonia.

Optimal oral care should focus on plaque removal and stimulation of salivary flow.
REFERENCES

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