

Oral care and bacteremia risk in mechanically ventilated adults

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OBJECTIVE: Transient bacteremia occurs in healthy populations from toothbrushing. With the high incidence of bacteremia in the intensive care unit and toothbrushing as an oral care method, this study examined the incidence and clinical significance of transient bacteremia from toothbrushing in mechanically ventilated adults.

METHODS: Prospective pre- and post-test with all subjects (N = 30) receiving a toothbrushing intervention twice per day (up to 48 hours). The planned microbial analysis used DNA typing to identify organisms from oral and blood cultures collected immediately before, 1 minute, and 30 minutes after the interventions.

RESULTS: Seventeen percent of subjects had oral cultures that were positive for selected pathogens before the first toothbrushing intervention. None of the subjects had evidence of transient bacteremia by positive quantitative blood cultures before or after the toothbrushing interventions. Patient characteristics were not statistically significant predictors for systemic inflammatory response syndrome, length of hospital stay, or length of intubation.

CONCLUSION: The toothbrushing intervention did not induce transient bacteremia in this patient population. (Heart Lung® 2010;39:S57–S65.)

Critically ill patients are a vulnerable population, susceptible to nosocomial infections that can increase their length of stay, hospital costs, and mortality rates. Clinically apparent bloodstream infection is one of the most common nosocomial infections and is a leading cause of mortality in hospitalized patients. Bloodstream infection accounts for 15% of all nosocomial infections.¹ Significant evidence exists that bacteremia (viable bacteria in the circulating

blood) occurs in healthy populations in association with procedures that involve the oral cavity, including toothbrushing.²⁻⁶ Bacteremia in healthy populations from toothbrushing is classified as transient bacteremia because the bacteria are rapidly (within minutes) eliminated by the reticuloendothelial system.⁷⁻⁹ Transient bacteremia does not usually cause disease in healthy people and is often undetected because it may not have clinical manifestations. However, mechanically ventilated critically ill patients may be at risk for transient bacteremia that leads to subsequent clinical bloodstream infections. Clinically apparent bloodstream infections are accompanied by detectable systemic signs and symptoms, such as systemic inflammatory response syndrome (SIRS). SIRS criteria describe the clinical response due to either noninfective or infective causes and serve as an alert to the inflammation process.¹⁰ The endotracheal tube of mechanically ventilated adults facilitates bacterial adherence to the mucosa, causes xerostomia, and alters the first lines of defense in these patients, increasing their risks of clinically significant bacteremia.¹¹ The oral cavity is bacterial laden with more than 700 species,^{12,13} and oral bacteria of the intubated patient has been shown to become more

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virulent during the first 48 hours of hospital admission.¹⁴ The proximity of bacteria in the oral cavity to the highly vascularized gingival lining and the mechanical action of toothbrushing increase the chance of translocation into the bloodstream.¹³ Therefore, it is important to explore the risks of toothbrushing in mechanically ventilated adults, including the relationship of toothbrushing to the incidence of transient bacteremia in mechanically ventilated critically ill adults.

There are many studies examining the link between oropharyngeal colonization and the development of ventilator-associated pneumonia (VAP),¹⁵⁻¹⁷ which has influenced the development of interventions to prevent VAP. These interventions often include toothbrushing, despite the lack of published reports regarding risks of toothbrushing in mechanically ventilated adults.⁴⁻⁶ Toothbrushing is a commonly reported method of oral care in mechanically ventilated adults in the United States and European countries.¹⁸⁻²⁰ Because of the high incidence and impact of bacteremia on health care resources, and the interest in toothbrushing as a potential intervention to prevent VAP, data regarding the risks of toothbrushing on transient bacteremia and clinical bloodstream infections in this population are important.

The goals of our study as prospectively designed were to determine (1) the incidence of transient bacteremia related to toothbrushing in mechanically ventilated critically ill adults; (2) the relationship of oral microbial cultures and dental plaque scores to the incidence of transient bacteremia, clinical outcomes, and indicators of infection; and (3) the relationships among patient characteristics and clinical outcomes.

MATERIALS AND METHODS

Study design

This study was a prospective pre- and post-test design in which all subjects received a toothbrushing intervention twice daily while enrolled in the study (for up to 48 hours). Transient bacteremia was assessed at each toothbrushing intervention. Subject participation ended at extubation.

Setting and sample

The study was conducted in an 820-bed tertiary care, university teaching hospital in the Southeast. Subjects were recruited from the surgical trauma, medical respiratory, and neuroscience intensive

care units (ICUs). All patients admitted to 1 of the 3 ICUs were reviewed for potential enrollment. Inclusion criteria included mechanical ventilation, age greater than 18 years, intubated less than 24 hours, invasive catheter in place less than 24 hours to decrease the likelihood of organisms already present in the line, no documented evidence of clinical bloodstream infection before enrollment, having at least 1 tooth, and hemoglobin greater than 7 g/dL. Edentulous patients were excluded because dental plaque assessments were a critical variable for this study and could not be assessed in patients with no teeth. Persons with a hemoglobin level of less than 7 g/dL were excluded from the study to reduce risks of repeated blood sample collection.

The study was reviewed and approved by the university's institutional review board. All subjects who met inclusion criteria were assessed for the ability to provide informed consent through gesturing or writing. If subjects had medications that impaired cognition or were unable to provide informed consent due to their illness, the legally authorized representative provided informed consent.

Because studies of transient bacteremia related to toothbrushing in the critically ill have not been reported in the literature, the sample size was based on estimations from other related studies. Several studies examining the development of bacteremia after toothbrushing in healthy populations^{3,5,6,21,22} demonstrated the development of transient bacteremia in sample sizes of 11 to 40 subjects per group. In the study performed by Lucas et al,³ subjects were randomly allocated into 4 groups, including a manual toothbrushing group with a sample size of 32 and 2 electric toothbrushing groups with sample sizes of 35 and 33. The investigators reported a greater intensity of bacteremia at 30 seconds after both the electric toothbrushing interventions. In another study,²¹ the investigators examined the incidence of bacteremia at 30 seconds and 2 minutes after toothbrushing in 11 healthy subjects. The investigators reported an increase in the incidence of bacteremia after toothbrushing. Therefore, a sample of 30 subjects was enrolled.

Procedures

Before the first toothbrushing intervention, demographic data were collected and each subject received an oral health assessment, which included an oral microbial culture. Three blood samples for quantitative culture (lysis filtration) were collected

at the first toothbrushing (before toothbrushing, 1 minute after the toothbrushing intervention, and 30 minutes after the intervention) to examine the incidence of transient bacteremia that occurs within seconds and is eliminated within minutes. A second set of blood samples was obtained during the last scheduled toothbrushing intervention 48 hours later (Fig 1) as repeated data. Subjects with 1 postintervention blood culture were sufficient to examine the incidence of transient bacteremia. Operational definitions of key study variables are listed in Table I.

Toothbrushing intervention. The toothbrushing intervention was performed on all enrolled subjects using a standardized protocol guided by the recommendations of the American Dental Association for healthy adults.²³ The mouth was divided into 4 dental quadrants (right upper, right lower, left upper, left lower). Proceeding in a defined pattern, every tooth in each quadrant was brushed for 5 strokes (forward to backward) on lingual (tongue side), buccal (cheek side), and biting surfaces, using a soft pediatric toothbrush and toothpaste (Biotene toothpaste, Laclede, Inc, Rancho Dominguez, CA). The palate and tongue were also brushed. Each quadrant, the palate, and the tongue were rinsed with a total of 15 mL of mouthwash (Biotene, Laclede, Inc) using a transfer pipette. A Yankauer suction catheter was used as needed to suction excess saliva and mouthwash from the subject's mouth as the intervention was performed. Finally, a measured amount of moisturizing gel (OralBalance, Laclede, Inc) was applied to all soft surfaces of the oral cavity and lips using a green Toothette swab (Sage Products, Inc, Cary, IL). The 2-minute toothbrushing intervention was repeated twice per day over the study period (48 hours or until extubation if extubated before 48 hours). Subjects were withdrawn from the study after endotracheal tube extubation; data to that point were used in the analysis. All of the subjects' toothbrushing was provided by the principal investigator during the 48-hour period, and any comfort oral care (including swabbing the mouth with mouthwash) provided by the hospital staff was documented. Hospital staff was instructed not to provide toothbrushing to subjects enrolled in the study during the study period.

Oral microbial culture. A swab of the oral cavity for microbial culture was performed immediately preceding the first toothbrushing intervention. The oral cavity was swabbed in the following order using a single swab: upper and lower buccal and lingual gingival margin (obtaining organisms from gum line and tooth

surface), and palate. The oral microbial cultures were performed using BBL Culture Swab Plus collection and transport media (Becton, Dickinson and Co, Sparks, MD) and were analyzed using standard operations for the clinical microbiology laboratory. Cultures were analyzed and quantified for the following potentially pathogenic organisms: viridans group Streptococci, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus spp.*, *Klebsiella pneumoniae*, and *Candida spp.* These organisms are most commonly cited as causes of bloodstream infections in mechanically ventilated patients.²⁴ Positive cultures were frozen and stored for comparison with blood culture organisms by DNA typing. We prospectively planned the microbial analysis using multi-locus sequence typing to identify species at the strain level. Multi-locus sequence typing is a relatively new and powerful technique that involves molecular comparison of collections of essential genes also referred to as the "housekeeping" genes.²⁵ There is considerable polymorphism (variability) in housekeeping genes between species and even between strains of the same species, making these housekeeping genes attractive targets for DNA typing. Comparison of DNA sequences from isolates found in blood cultures and oral cultures would enhance the determination of whether the isolates were identical or different, and differentiate transient bacteremia from the intravenous line or sample contamination from bacteremia of oral origin. DNA typing would reduce the likelihood that confounding variables in the ICU (eg, the presence of invasive lines, frequent and invasive procedures, intubation, comorbidities, and immunosuppression) would adversely affect the analysis.

Dental plaque. Dental plaque was assessed using the University of Mississippi Oral Hygiene Index²⁶ with observations augmented by use of a plaque disclosing agent visible only in ultraviolet light (fluorescein). The University of Mississippi Oral Hygiene Index assesses every tooth, dividing each tooth into 10 sections (5 sections for the buccal surface and 5 sections for the lingual surface). Each section of every tooth is scored for the presence or absence of plaque, yielding a score for each tooth from 0 (no plaque) to 10 (plaque in every section). The mean plaque score for the subject was then calculated by dividing the total score by the number of teeth.

Decayed, missing, and filled (DMF) teeth inventory. Each subject was also assessed for the total number of DMF teeth (a numeric assessment) as a measure of preexisting oral health on initial study enrollment.

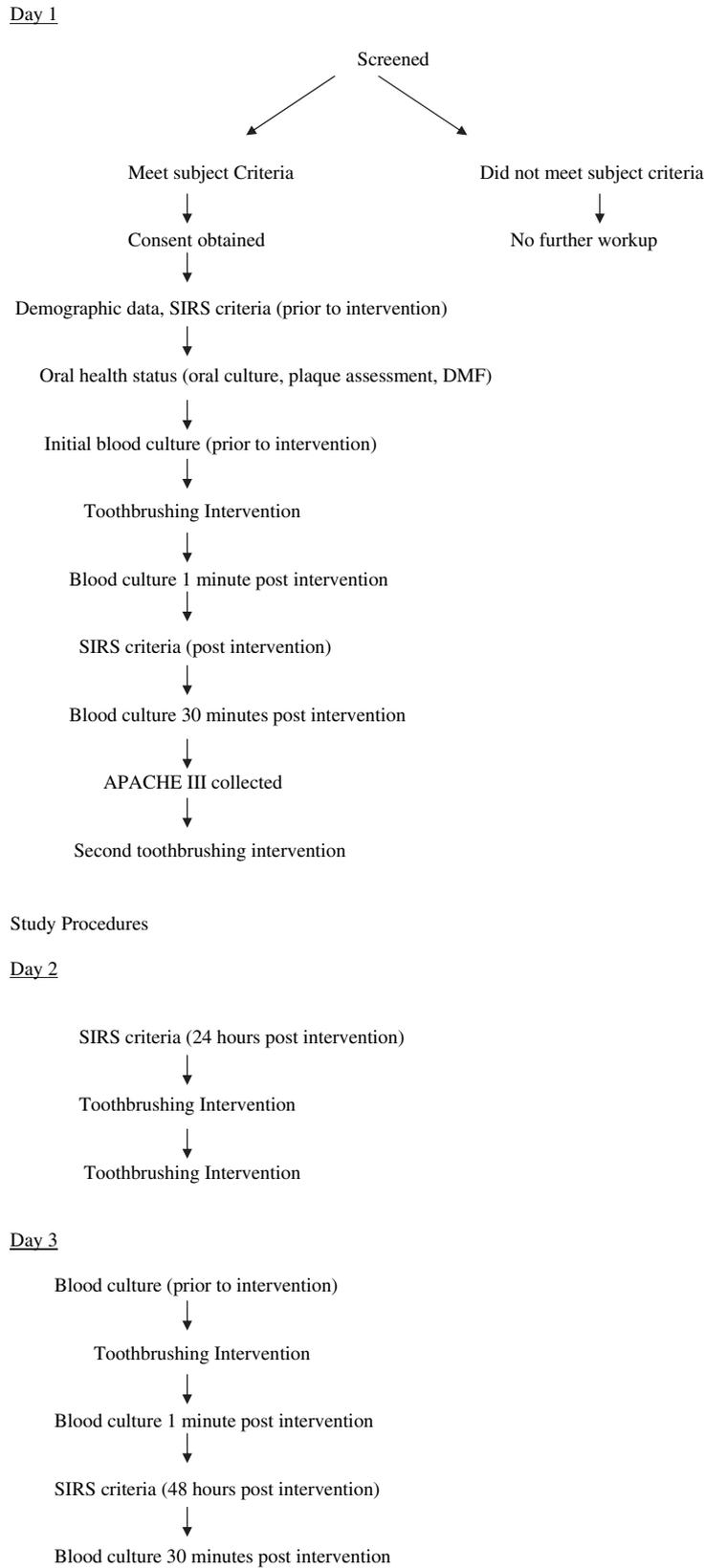


Fig 1 Study procedures. SIRS, systemic inflammatory response syndrome; DMF, decayed, missing, and filled; APACHE III, Acute Physiology and Chronic Health Evaluation III.

Table I
Key study variables

Dependent variables	Operational definition
1. Incidence of transient bacteremia	1. Positive postintervention blood culture (1 or 30 min)
2. Clinical outcomes	2. a. SIRS criteria (heart rate > 90, respiratory rate > 20 or P _a CO ₂ < 32 mm Hg, WBC > 12,000 mm ³ or < 4000 mm ³ or > 10% bands, temperature > 38 °C or < 36 °C) b. Days of hospital stay and length of intubation
3. Clinical indicators of infection	3. WBC > 12,000, body temperature > 38 °C, results of blood cultures drawn for clinical indications or clinical diagnosis
Independent variables	Operational definition
1. Toothbrushing intervention	1. Twice per day (separated by at least 8 h), defined protocol based on American Dental Association guidelines
2. Oral health status	2. Dental plaque score, DMF assessment, oral microbial culture
3. Patient characteristics	3. Severity of illness score, empiric antibiotics, age, gender, ethnicity, race

SIRS, systemic inflammatory response syndrome; WBC, white blood cell; DMF, decayed, missing, and filled.

Measurement of key variables

Incidence of bacteremia. The incidence of transient bacteremia was defined by the presence and quantity of bacteria or microbes in the bloodstream after the toothbrushing intervention (1 or 30 minutes postintervention). Bacteremia was measured by quantitative blood cultures with specific surveillance for the following bacteria: viridans group Streptococci, *S. aureus*, *P. aeruginosa*, *Enterococcus spp.*, and *K. pneumoniae*. In addition, we conducted surveillance for *Candida spp.* Blood cultures were obtained for all subjects immediately preceding the first intervention. Blood for quantitative culture was obtained from an intravenous catheter (in place for < 24 hours at study enrollment) following hospital policy using aseptic technique. Blood samples were obtained at 3 time points (before intervention, 1 minute postintervention, and 30 minutes postintervention) at both the first intervention and at the last scheduled toothbrushing intervention (48 hours after first intervention). Each blood sample consisted of a minimum of 1.5 ml of blood collected in pediatric isolator laboratory tubes (Wampole Laboratories, Division Carter Wallace, Cranbury, NJ). Blood samples were plated on 3 plates (2 blood agar plates and 1 chocolate agar) and incubated for 7 days.

Clinical outcomes. Clinical outcomes measured were SIRS, hospital length of stay, and length of

intubation. Transient bacteremia in healthy individuals leads to no more than a slight increase in temperature;⁸ however, the relationship of transient bacteremia to clinical outcomes in mechanically ventilated adults is unclear. Bloodstream infections can lead to sepsis, increased ICU and hospital stay, and increased use of resources.^{27,28} The criteria for diagnosing SIRS were collected on each subject at enrollment, 24 hours, and 48 hours postintervention. A diagnosis of SIRS was determined using the American College of Chest Physicians/Society of Critical Care Medicine definition (Table I).¹⁰ The criteria for SIRS determination were collected and entered into the study database for each participant. The determination was made using the calculation functions of the database. Length of hospital stay and length of intubation were calculated for each subject and served as outcome data in the final analysis.

Clinical indicators of infection. White blood cell count and body temperature were collected on study admission (before the first intervention), at 24 hours, and at 48 hours after the first intervention. We were interested in signs of clinical infection from bacteria in the bloodstream that could lead to poor clinical outcomes. Therefore, white blood cell count and body temperature were collected from the medical record. Results of blood cultures drawn for clinical

indications or clinical diagnosis were also collected during the study period and for 1 week after the last study intervention. In the event clinical blood cultures were positive after the toothbrushing intervention, these organisms would be compared with organisms found in the mouth by DNA typing.

Oral health status. Oral health status was measured by the collection of an oral microbial culture, dental plaque assessment, and DMF inventory. The oral microbial culture provided the species present and quantitative count of the species in the mouth. The dental plaque assessment provided information regarding the amount of dental plaque present in the mouth before the toothbrushing intervention. The DMF inventory provided information regarding the subject's preexisting oral hygiene condition. Although we did not measure pocket depth or specifically assess for periodontitis or gingivitis, we did visually inspect the oral cavity for sores, bleeding, and general appearance.

Patient characteristics. Demographic data and severity of illness determined by the Acute Physiology and Chronic Health Evaluation (APACHE) III score were also collected on each patient. These data were analyzed as predictors of clinical outcomes (SIRS, length of intubation and hospital stay).

Data analysis

JMP 11.0 statistical analysis software (SAS Institute Inc, Cary, NC) was used to analyze data. Characteristics of the sample were summarized with descriptive statistics. Nominal logistic regression was used to determine whether the APACHE III score, dental plaque assessment, and DMF score were predictors of the presence of SIRS. Linear regression was used to determine whether the APACHE III score, dental plaque assessment, and DMF score were predictors of the clinical outcomes (length of intubation and hospital stay).

RESULTS

Sample characteristics

Thirty subjects were enrolled from the surgical trauma, medical respiratory, and neuroscience ICUs (Table II). The subjects were representative in terms of ethnicity, race, and gender of the population at the university medical center where the study was conducted.

Transient bacteremia

The primary goal of the study was to determine the incidence of transient bacteremia related to

Table II
Sample characteristics

Ethnicity	
Hispanic	3%
Non-Hispanic	97%
Race	
Black/African American	52%
White	48%
Gender	
Female	37%
Male	63%
Age	46 y (SD 17)
Length of intubation	2.7 d (SD 2.8)
Length of hospital stay	20 d (SD 20)
Empiric antibiotic	87%
ICU	
MRICU	33%
STICU	37%
NSICU	30%

SD, standard deviation; ICU, intensive care unit; MRICU, medical respiratory intensive care unit; STICU, surgical trauma intensive care unit; NSICU, neuroscience intensive care unit.

toothbrushing in mechanically ventilated critically ill adults. All subjects received a postintervention blood culture needed to define transient bacteremia and complete the first arm of the study. Transient bacteremia was examined at each toothbrushing intervention as a unit of analysis for the primary aim; all 30 subjects had 1 set of useable blood culture data. Eighty percent of subjects were extubated before day 3; therefore, a second set of blood culture data was not obtained. Six subjects (20%) remained intubated for greater than 48 hours, and a second set of blood culture data was obtained from them at the last intervention (48 hours after the first intervention). This data served as an extra set of blood cultures and was also analyzed for transient bacteremia. None of the subjects had evidence of transient bacteremia by positive quantitative blood cultures before or after the toothbrushing interventions.

Oral health status

The second study goal was to examine the relationship of oral microbial cultures and dental plaque scores to the incidence of transient bacteremia and clinical outcomes. Oral microbial cultures: Five subjects (17%) had positive oral cultures for organisms other than normal oral flora before the first

toothbrushing intervention. Organisms other than the normal flora identified in positive oral cultures were *S. pneumoniae*, *coagulase-negative Staphylococcus*, *Escherichia coli*, *S. aureus*, and *P. aeruginosa*.

Dental plaque score and decayed, missing, and filled assessment

The mean dental plaque score on admission to the study was 58% (Table III). The range of dental plaque was 18% to 100%. The DMF assessment had a mean score of 11.3 with a range from 3 to 27. Results from this oral health assessment are similar to those found in previous studies by our research team.²⁹ None of the subjects had open mouth sores or gum bleeding during the intervention.

Relationships among oral health measures, patient characteristics, clinical outcomes, and indicators of infection

The third study goal was to examine the relationships among patient characteristics and clinical outcomes. The mean APACHE III score was 60.8 with a range from 24 to 121 (Table III). Analysis of SIRS revealed 23% of subjects had positive SIRS criteria on study admission. SIRS criteria were identified by the presence of 2 or more of the indicators (Table I). Subjects who were positive for SIRS with 2 or more criteria present remained positive during the study period. No subjects negative for SIRS criteria became positive during the study period. Logistic regression was used to predict SIRS on the basis of the APACHE score, DMF assessment, and

plaque score. Plaque, DMF and APACHE score were not found to be independent predictors of SIRS (likelihood ratio chi-square = .79, $P = .85$). Linear regression was also used to explore the relationship of plaque, DMF, and APACHE score to hospital length of stay and length of intubation. The relationship among the variables was not statistically significant. Blood cultures collected for clinical purposes during the study period and within 1 week after the last intervention were also analyzed. All blood cultures obtained for clinical suspicion of infection were negative for microbial growth.

DISCUSSION

The primary goal of this study was to explore the effects of toothbrushing on the incidence of transient bacteremia in mechanically ventilated adults. Secondary aims were to examine the relationship of oral microbial cultures and dental plaque score on the incidence of transient bacteremia, clinical outcomes, and indicators of infection, and the relationship of patient characteristics to clinical outcomes such as SIRS, length of intubation, and length of hospital stay. There have been no published reports examining the relationship of oral care to bacteremia in mechanically ventilated adults. This study did not support an increased risk of transient bacteremia from toothbrushing in critically ill mechanically ventilated adults. Although 17% of subjects had positive oral cultures for potential pathogens before initiation of the toothbrushing intervention, none of the subjects had positive study blood cultures, and all blood cultures drawn for clinical purposes were negative. Positive oral microbial cultures and increased dental plaque score were

Table III
Oral health and clinical outcomes

Oral health assessment	Mean (range or standard deviation SD)
Dental plaque score	58% (range 18%-100%)
DMF	11.3 (range 3-27)
APACHE III	60.8 (range 24-121)
SIRS (positive for at least 2 criteria)	23%
Length of intubation	2.7 d (SD 2.8)
Length of hospital stay	20 d (SD 18.9)

SD, standard deviation; DMF, decayed, missing, and filled; APACHE III, Acute Physiology and Chronic Health Evaluation III; SIRS, systemic inflammatory response syndrome.

not correlated with SIRS, length of intubation, or length of hospital stay.

Blood cultures are the standard for clinical diagnosis of bacteremic episodes in the critically ill.³⁰ Quantitative culture of organisms using lysis filtration, which provides direct information regarding species and bacterial load (number of colony forming units) in small volumes of blood, is not commonly used clinically, because the added expense³¹ and time³² required for analysis are generally not clinically justified. However, quantitative culture techniques, used in this study, permit sensitive detection of low colony forming units even with small volume samples.

Although blood cultures are the most common clinical method for diagnosing bacteremia, this method alone would not provide a definitive link between bacteremia and bacteria of oral origin due to toothbrushing. We planned to further strengthen the understanding of the relationship between oral and blood isolates by comparing organisms obtained from oral and blood cultures by DNA typing, but we were unable to do so because none of the blood cultures yielded the organisms of interest. Given the literature reporting transient bacteremia in healthy populations with oral manipulations in studies with similar sample sizes,^{4-6,33} we were surprised that there were no blood isolates obtained for comparison. Because transient bacteremia from toothbrushing has historically been demonstrated in healthy individuals and individuals with periodontitis or gingivitis,^{34,35} we anticipated that transient bacteremia related to toothbrushing would be evident in critically ill mechanically ventilated adults. Notably, 2 recent studies using sensitive methodology similar to this study^{35,36} also failed to demonstrate any bacteremia after toothbrushing in healthy individuals without gum disease. For example, Hartzell et al³⁶ examined the incidence of bacteremia in 30 healthy subjects using two 20-mL aerobic and anaerobic culture bottles collected before and after a toothbrushing intervention. The study found 0% bacteremia after toothbrushing in this population. Another study by Forner et al³⁵ examined the incidence of bacteremia after toothbrushing, chewing, and scaling in 60 systemically healthy individuals. Quantitative blood cultures similar to cultures used in this study were obtained before and after the toothbrushing intervention. Subjects with healthy periodontium did not develop transient bacteremia from toothbrushing or chewing. A limitation of our study may be the use of empiric antibiotics in 87% of subjects, which may have increased the result of negative blood cultures. The subjects were receiving the following antibiotics

before and during the study period: piperacillin/tazobactam, cefoxitin, levofloxacin, cefazolin, gentamicin, vancomycin, ceftriaxone, erythromycin, azithromycin, metronidazole, and cefepime.

Neither oral health nor severity of illness influenced the incidence of SIRS, length of stay, clinical infection, or length of intubation. Although subjects exhibited poor oral hygiene with greater than 50% of tooth surfaces covered with dental plaque, this was not associated with clinical outcomes. Poor oral health has been linked to other systemic and nosocomial infections, including VAP.¹⁵⁻¹⁷ This study focused on the first 72 hours after intubation; all subjects were enrolled within the first 24 hours of intubation, and the mean length of intubation was 2.7 days. Results may have differed if subjects had been intubated longer or enrolled later in their ICU stay. Because oral flora changes to more virulent pathogens in mechanically ventilated patients after 48 hours of intubation, the risk of developing transient bacteremia from those pathogens may have been increased. Therefore, further research is needed to fully understand potential risks and benefits related to toothbrushing. The sample size was estimated on the basis of studies in healthy populations; interpretation of results is limited by the small sample size.

Although we obtained measures of oral health (including oral microbial cultures, dental plaque scores, DMF, presence of bleeding and mouth sores), we did not specifically assess for gingivitis or periodontitis. Gingivitis or periodontal disease provides opportunities for bacterial overgrowth, and richly vascularized and often ulcerated tissues associated with these diseases are susceptible to bacterial invasion.⁹ Thus, gingivitis and periodontitis do increase the risk of bacteremia related to invasive dental procedures in healthy populations.^{34,35} Further research is needed in mechanically ventilated populations to assess gum disease and the relationship to bacteremia and other systemic infections.

CONCLUSIONS

Toothbrushing is a common oral care strategy and an effective method of removing dental plaque and preventing gum disease.³⁷ The role of toothbrushing in reducing the risk of VAP and promoting patient comfort is a continuing area of nursing research. However, potential benefits of the procedure must be balanced against potential risks; definitive study of the risk/benefit ratio is an opportunity for further investigation. Understanding the incidence and clinical relevance of transient bacteremia of oral

origin in the ICU is important to assist in standardizing safe and effective oral care for the critically ill. Our toothbrushing intervention did not induce transient bacteremia in critically ill mechanically ventilated patients. This study contributes to knowledge related to the risks of bacteremia from toothbrushing in mechanically ventilated adults and assists in guiding future research focused on standardizing safe and effective oral care in this population.

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