



# The association of oral health with length of stay and mortality in the intensive care unit

Erika Caroline Steinle<sup>1</sup> · Jessica Antonia Montovani Pinesso<sup>1</sup> · Leonardo Bernardi Bellançon<sup>2</sup> · Solange de Paula Ramos<sup>1</sup> · Gabriela Fleury Seixas<sup>2</sup>

Received: 25 July 2022 / Accepted: 28 March 2023 / Published online: 5 April 2023  
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2023

## Abstract

**Objectives** To analyze the relationship between the oral and systemic health status of adult patients admitted to the intensive care unit (ICU) with the length of stay and mortality.

**Material and methods** A daily oral examination and oral hygiene were performed in patients admitted to an adult ICU. Dental and oral lesions, systemic health status, the need for mechanical ventilation, length of stay, and mortality were registered. Multivariate linear and logistic regression analyses were performed to identify associations between length of stay and death of patients, respectively, with oral and systemic health status.

**Results** In total, 207 patients were included, 107 (51.7%) male. Ventilated patients presented an increased length of stay ( $p < 0.001$ ), mortality ( $p < 0.0001$ ), number of medications ( $p < 0.0001$ ), edentulism ( $p = 0.001$ ), mucous lesions and bleeding ( $p < 0.0001$ ), oropharyngitis ( $p = 0.03$ ), and drooling ( $p < 0.001$ ) compared to non-ventilated patients. The number of days in the ICU was associated with mechanical ventilation ( $p = 0.04$ ), nosocomial pneumonia ( $p = 0.0001$ ), end-stage renal disease ( $p < 0.0007$ ), death ( $p < 0.0001$ ), mucous bleeding ( $p = 0.01$ ), tongue coating ( $p = 0.001$ ), and cheilitis ( $p = 0.01$ ). Mortality was associated with length of stay in the ICU ( $p < 0.0001$ ), number of medications ( $p < 0.0001$ ), and the need for mechanical ventilation ( $p = 0.006$ ).

**Conclusion** ICU patients present poor oral health. Soft tissue biofilm and mucous ulcerations were associated with the length of stay in the ICU, but not with the mortality rate.

**Clinical relevance** Mucous lesions are associated with an increased length of stay in the ICU, and critically ill patients should receive oral care to control oral foci of infection and mucous lesions.

**Keywords** Intensive care units · Oral health · Hospital infection

## Introduction

Oral care and hygiene have been recommended for patients admitted to intensive care units (ICUs) to prevent the colonization of oral surfaces with pathogenic biofilm and reduce the risk of development of ventilator-associated pneumonia, lower respiratory tract infections, and other

infectious foci [1–5]. However, the majority of hospitalized patients, including those admitted to the ICU, present oral lesions and infectious foci before hospitalization, including dental caries (29.9 to 40%), residual tooth roots (19.7%), periodontal disease (34 to 41.9%), gingivitis (58.7%), mucosal lesions (36%), and oral abscesses (1.6%) [5–8]. Considering that most ICU patients are critically ill, these oral lesions and foci of infection can increase the risk of complications from the primary diseases [7, 9], post-surgical complications [10, 11], or the development of novel active local or systemic infections [6, 11, 12]. In addition, ICU patients may develop new oral lesions such as mucositis and pressure oral ulcers [9, 13, 14], gingivitis [15], dry mouth [14], tongue coating, and oral candidosis [12] as a consequence of their critically ill health status, clinical procedures, the use of medications, and the need for mechanical ventilation [9, 13, 14].

✉ Gabriela Fleury Seixas  
fleuryseixas@gmail.com

<sup>1</sup> Research Group On Tissue Regeneration, Adaptation, and Repair, Center of Biological Sciences, State University of Londrina, Londrina, PR, Brazil

<sup>2</sup> Research Group On Tissue Regeneration, Adaptation, and Repair, North Parana University, Rua Marselha, Londrina 678, Brazil

Some studies employing oral hygiene associated with dental care have been shown to decrease the incidence of respiratory infections, especially ventilator-associated pneumonia in intubated patients [2, 4, 16]. However, there is poor evidence that a decreased incidence of ventilator-associated pneumonia in patients receiving oral hygiene could reduce their mortality rate and length of stay in the ICU [16]. In addition, poor oral hygiene and a poor oral health status are also a concern in critically ill patients admitted to the ICU, with or without intubation or mechanical ventilation. For example, poor oral health could increase the risk of infection at the site of spinal surgery [11] which could increase the hospital stay and mortality rate of patients. Other authors observed that deep odontogenic infections requiring ICU attendance increased the risk of nosocomial pneumonia, length of stay, and mortality rate of patients, especially patients who were smokers [17]. On the other hand, patients admitted to the ICU after surgical procedures to remove esophageal cancer and who received oral hygiene presented reduced bacteremia and days of fever, despite no differences in length of ICU stay [18]. These results suggest oral care and hygiene have the potential to prevent complications that increase morbidity and mortality in non-intubated ICU patients but may not reduce the time of ICU stay. However, there is still little evidence in the literature to establish a correlation between oral health status and length of stay of patients in the ICU. It has also not been established whether, despite oral hygiene and dental care, oral lesions and dental foci of infections could present a correlation with the mortality rate of patients in the ICU.

The objective of this research was to evaluate the oral health status of adult patients admitted to the ICU of a public hospital and identify associations with the general health status, length of stay in the ICU, and mortality rate. The study hypothesis was that poor oral health may be associated with longer ICU stays and increased frequency of ICU deaths, even for patients receiving adequate oral hygiene care.

## Material and methods

### Study design and study population

This is a longitudinal observational study of patients admitted to the ICU of Irmandade Santa Casa de Londrina (ISCAL), Londrina, Brazil, from July to August 2018. ISCAL is a philanthropic hospital that almost exclusively serves patients of the Brazilian public health system, the Unified Health System (SUS). There were 24 beds available in the adult ICU during the research period. Participants were included in the study by consecutive sampling, and all adult patients who remained hospitalized in the ICU for more than 24 h were eligible.

The following exclusion criteria were considered: patients under 18 years of age, the impossibility of handling the patient due to medical request, systemic instability, last-minute cardiorespiratory arrest, any other condition that made oral clinical examination impossible, and an absence of authorization by patients or their relatives.

The included patients were evaluated daily until the moment of ICU discharge or death. Two previously trained and calibrated dentists performed oral care and hygiene, as well as data sampling. A total of 207 patients admitted to the ICU were evaluated. The number of patients was determined considering a relative frequency of 36.6% of hospitalized patients presenting with oral lesions [7]. A minimum number of 151 patients was established to obtain a statistical power of 80% and an alpha error of 5%.

### Ethics approval and consent to participate

The data collection procedures were performed after approval of the study from the Ethics Committee in Research Involving Human Beings of ISCAL—Irmandade Santa Casa de Londrina (protocol no. 3.202.350). Patients or their guardians (in cases of unconsciousness) were informed of the research objectives, and data collection was performed only after authorization and signing of the written free and informed consent form. All research procedures followed the ethical principles of the Declaration of Helsinki (2013) [19].

### Demographic data and systemic health

Demographic information and patient health conditions were collected from medical records. The data collected were as follows: age, sex, the medical specialty that referred the patient to the ICU, length of stay in the ICU, previous outpatient hospitalization, smoking, alcoholism, number of daily medications (analgesic, steroids, sedatives, non-steroidal anti-inflammatory drugs, antibiotics) during hospitalization in the ICU, chronic systemic diseases, neurological and cardiac alterations, infectious diseases present at the time of hospitalization, the presence of syndromes, intubation, and the need for mechanical ventilation.

The patients were examined every other day until they were discharged from the ICU or died. The ICU attends patients from hospital wards whose health status has worsened and who need intensive care, post-surgical patients, and patients from emergency care who need immediate life support in the ICU. The need for mechanical ventilation and the development of nosocomial pneumonia at any time during the stay in the ICU were recorded.

## Oral health status

The analysis of oral health status was performed as described by Carrilho Neto et al. [7], using a dental clinical mirror, a number 5 dental probe, and artificial illumination. An oral examination was performed to record the presence of dental caries, gingivitis, and periodontal disease; lesions in oral mucosa; the use of dental prosthesis; and the dental plaque index. The examination was performed by two dentists, previously trained and calibrated, with a kappa index of agreement  $> 0.98$  between interindividual and intraindividual performance.

Patients were examined and classified as edentulous or dentate (partial and total). Wearing of dental prosthesis, type of oral prosthesis, and the quality and hygiene of prosthesis were recorded. The use of orthodontic appliances was also recorded.

Active caries was recorded as dental cavities, detected by probing on the tooth surface or with the naked eye, with evidence of enamel or cementum breakdown and exposed dentine, or dentine and pulp. Residual dental roots and the presence of dental abscesses were also recorded.

The dental plaque index was registered on the first day of ICU admission, after which oral hygiene was performed daily to avoid the formation of large amounts of dental plaque during the ICU stay. Scores 2 and 3 of the dental plaque index of Loe and Silness [20] were used to record the presence of dental plaque visible by the naked eye (score 2) and the presence of abundant dental plaque inside periodontal pockets (or gingival margin) and on the tooth surface (score 3).

Periodontal disease was clinically evaluated by the presence of suppuration in the gingival margin, tooth mobility, and the presence of dental calculus or gingival recession. Gingivitis has been reported when the gingival margin and interdental papillae appear swollen and red. Periodontal probing was not performed in the periodontal disease evaluation, or for recording scores of 0 to 1 of the dental plaque index [20], due to the risk of evoking bleeding and bacteremia in critically ill patients. Spontaneous gingival bleeding was observed in some patients.

Drooling was recorded as the continuous overflowing of saliva from the mouth due to hypersalivation or the incapacity to swallow the entire volume of produced saliva. A dry mouth was characterized by the inability to secrete enough volume of saliva to moisten lips and oral mucosa.

Lips and oral mucosa were examined daily to detect ulcers (with or without spontaneous bleeding), nodules, blisters, white spots and plaques, candidiasis, abscess, fistula, erythematous areas, pseudomembranous deposits removable by scraping, or any other mucous alterations.

All ICU patients, whether included in the study or not, underwent the oral hygiene protocol recommended by the Brazilian Association of Intensive Medicine (AMIB), which

consists of performing oral hygiene with a small toothbrush, vacuum suction, use of chlorhexidine 0.12%, and hydration of the lips with essential fatty acid (EFA). This protocol was adopted by ISCAL as part of the ventilator-associated pneumonia prevention protocol.

## Statistical analysis

The normal distribution of the data was determined by the Shapiro–Wilk test. Parametric data are expressed as mean and standard deviation and non-parametric data as median and quartiles from 25 to 75%. The comparison between patients with and without mechanical ventilation was performed using the Student *t* test or Mann–Whitney *U* test. Categorical data are expressed as frequency and differences between groups, tested using the chi-square test with Yates' correction or Fisher's exact test. The odds ratio and 95% confidence interval of having oral lesions in ICU patients with health comorbidities and smoking are calculated and presented with the chi-square test with Yates' correction or Fisher's exact test. The association between the length of hospital stay and systemic and oral health conditions was determined using the multivariate linear regression analysis, with a stepwise backward adjustment. The presence of multicollinearity of the independent variables was detected through the variance inflation factor. The association of general and oral health conditions with mortality was determined using multivariate logistic regression analysis with stepwise backward adjustments. Differences between groups or associations between variables were considered significant if  $p < 0.05$ .

## Results

In total, 207 patients participated in the study, of whom 100 (48.3%) were female and 107 (51.7%) were male. No patients were hospitalized due to oral disease, deep dental infections, or oral disease complications. During the study period, all patients newly admitted to the ICU were eligible for inclusion in the study.

Since oral foci of infection have been suggested to increase the risk of pneumonia in mechanically ventilated patients, we also investigated the oral health status in ventilated and non-ventilated patients. Age, length of stay in the ICU, number of medications used daily, and frequency of pneumonia were higher in patients undergoing mechanical ventilation (Table 1). Most patients were referred to the ICU after general surgery (post-surgical recovery and care) and cardiology and had diabetes and hypertension but did not require mechanical ventilation (Table 1). The patients were considered as diabetic according to the medical evaluation, and they maintained controlled blood glucose during

**Table 1** Age, sex, and systemic health of patients admitted to the ICU, submitted or not to mechanical ventilation during the observation period

|                          | Total (n=207) | Mechanical ventilation |                   | p value |
|--------------------------|---------------|------------------------|-------------------|---------|
|                          |               | Yes (n=35, 21.2%)      | No (n=172, 78.2%) |         |
| Days in the ICU (median) | 2 [1-4]       | 5 [3-11]               | 1 [1-3]           | <0.0001 |
| Mortality rate           | 43 (20.7%)    | 25 (71.4%)             | 18 (10.4%)        | <0.0001 |
| Age (mean ±SD)           | 61.6 ± 18.0   | 60.2 ± 18.3            | 68.4 ± 4.5        | 0.01    |
| Sex                      |               |                        |                   |         |
| Male                     | 107 (51.7%)   | 21 (60%)               | 86 (50%)          |         |
| Female                   | 100 (48.3%)   | 14 (40%)               | 86 (50%)          | 0.13    |
| Number of medications    | 14 [10-21]    | 13 [9-17]              | 22 [17-26]        | <0.0001 |
| Nosocomial pneumonia     | 17 (8.2%)     | 6 (17.1%)              | 11 (6.4%)         | 0.04    |
| Smoker                   | 38 (18.4%)    | 7 (20%)                | 31(18%)           | 0.66    |
| Alcoholic                | 10 (4.8%)     | 3 (8.5%)               | 7 (4%)            | 0.45    |
| Diabetes                 | 51 (%)        | 11 (31.4%)             | 40 (23.5%)        | 0.99    |
| Hypertension             | 135 (65.2%)   | 24 (68.5%)             | 111(64.3%)        | 0.07    |
| End-stage renal disease  | 7 (3.4%)      | 2 (5.7%)               | 5 (2.9%)          | 0.63    |
| Medical specialty        |               |                        |                   |         |
| General surgery          | 58 (28%)      | 13 (37.1%)             | 45 (26.1%)        |         |
| Cardiology               | 53 (25.6%)    | 14 (40%)               | 39 (22.6%)        |         |
| Orthopedics              | 28 (13.5%)    | 1 (2.8%)               | 27 (15.7%)        |         |
| Neurosurgery             | 28 (13.5%)    | 7 (20%)                | 21 (12.2%)        |         |
| Angiology                | 23 (11.1%)    | 3 (8.5%)               | 20 (11.6%)        |         |
| Nephrology               | 8 (3.8%)      | 3 (8.5%)               | 5 (2.9%)          |         |
| Pneumology               | 7 (3.4%)      | 4 (11.4%)              | 3 (1.7%)          |         |
| Gastroenterology         | 1 (0.48%)     | -                      | 1 (0.5%)          |         |
| Urology                  | 1 (0.48%)     | -                      | 1 (0.5%)          | 0.04    |
| Previous hospitalization | 119 (57.5%)   | 24 (68.5%)             | 95 (55.2%)        | 0.64    |

the entire period of hospitalization. Approximately 57% of patients had been hospitalized in other sectors and were admitted to the ICU due to a worsening clinical condition or the need for surgery (Table 1).

The median days of ICU stay were higher in patients who developed pneumonia [5 (3 to 12) days;  $p < 0.0001$ ] than those who did not [2 (1 to 3) days]. The frequency of deaths (relative risk (RR): 1.53; 95%CI: 4.1 to 52.9;  $p = 0.01$ ) in patients with pneumonia was higher ( $n = 9$ ; 47%) than in those who did not develop pneumonia ( $n = 35$ ; 18.5%).

Regarding oral health status, 144 (69.6%) patients were totally or partially dentate and 63 (30.4%) were completely edentulous. Regarding the use of dental prostheses, 23 (54.8%) patients were wearing complete dentures, 13 (31%) had removable partial dentures, and 6 (14.2%) had protocol-type prostheses on implants. The hygiene of the dentures was considered poor in all patients, with food residues, microorganism colonies, calcified deposits, and pigmentations. No patients undergoing mechanical ventilation wore prostheses during the intubation period. The main oral findings observed in the patients are described in Table 2. The presence of large amounts of dental plaque and calculus at first examination was more frequent in dentate patients who did not require mechanical

ventilation (Table 2). Edentulism, mucous lesions and bleeding, oropharyngitis, and drooling were more frequent in mechanically ventilated patients. Two patients (9.6%) were using fixed orthodontic appliances.

Patients who developed nosocomial pneumonia presented a higher frequency of caries and oral bleeding (Table 2).

Regarding mucosal lesions, the ulcer was the most frequent oral lesion ( $n = 32$ ; 65.3%), followed by blisters ( $n = 6$ ; 12.3%), white lesions ( $n = 5$ ; 10.2%), macules ( $n = 4$ ; 8.2%), nodule ( $n = 1$ ; 2%), and hematoma ( $n = 1$ ; 2%).

Considering a possible association between general health status and oral health status, it was calculated the odds ratio (OR, 95% confidence interval) of having oral lesions in ICU patients with the most frequent health comorbidities (diabetes and hypertension) and smoking. Diabetic patients had an increased frequency of dental calculus (OR: undefined,  $p = 0.01$ ) and mucous lesions (OR: 2.33, 95%CI: 1.14–4.77,  $p = 0.02$ ). However, diabetes did not increase the odds ratio for presenting edentulism (OR: 0.62, 95%CI: 0.29–1.33,  $p = 0.28$ ), dental plaque (OR: 4.42, 95%CI: 0.55–35.2,  $p = 0.18$ ), dental caries (OR: 0.48, 95%CI: 0.45–2.13,  $p = 1.00$ ), tongue coating (OR: 1.67, 95%CI: 0.69–4.05,  $p = 0.30$ ), dry lips (OR: 1.63, 95%CI: 0.53–5.02,  $p = 0.45$ ), and angular cheilitis

**Table 2** Oral health status of patients admitted to the ICU

|                                      | Total ( <i>n</i> = 207) | Mechanical ventilation |                      | <i>p</i> value    | Pneumonia            |                      | <i>p</i> value    |
|--------------------------------------|-------------------------|------------------------|----------------------|-------------------|----------------------|----------------------|-------------------|
|                                      |                         | Yes ( <i>n</i> = 35)   | No ( <i>n</i> = 172) |                   | Yes ( <i>n</i> = 17) | No ( <i>n</i> = 190) |                   |
| Edentulous                           | 63 (30.4%)              | 19 (54.2%)             | 44 (25.6%)           | <b>0.006</b>      | 4 (23%)              | 59 (31%)             | 0.59              |
| Dental plaque <sup>1</sup>           | 130 (62.8%)             | 16 (45.7%)             | 114 (66.2%)          | <b>0.03</b>       | 13 (76.4%)           | 117 (61.5%)          | 0.29              |
| Caries                               | 56 (6.2%)               | 6 (17.1%)              | 50 (29%)             | 0.20              | <b>10 (58.8%)</b>    | <b>46 (24.2%)</b>    | <b>0.004</b>      |
| Residual root                        | 13 (21.7%)              | 2 (5.7%)               | 11 (6.4%)            | 0.87              | 3 (17.6%)            | 10 (5.2%)            | 0.07              |
| Tooth mobility                       | 29 (14%)                | 2 (5.7%)               | 27 (15.7%)           | 0.17              | 2 (11.7%)            | 26 (13.6%)           | 1.00              |
| Dental calculus                      | 128 (61.8%)             | 15 (42.8%)             | 113 (65.7%)          | <b>0.02</b>       | 12 (70.8%)           | 116 (61%)            | 0.59              |
| Gingival bleeding                    | 10 (4.8%)               | 2 (5.7%)               | 8 (4.6%)             | 0.68              | 2 (11.7%)            | 8 (4.2%)             |                   |
| Periodontal suppuration <sup>2</sup> | 2 (0.9%)                | 2 (5.7%)               | -                    | 0.17              | -                    | 2 (1%)               | -                 |
| Mucous bleeding <sup>3</sup>         | 12 (5.8%)               | 11 (31.4%)             | 1 (0.6%)             | <b>0.01</b>       | <b>11 (64.7%)</b>    | <b>1 (0.5%)</b>      | <b>&lt;0.0001</b> |
| Oral candidiasis                     | 3 (1.4%)                | 1 (2.8%)               | 2 (1.2%)             | 1.00              | -                    | 3 (1.5%)             | -                 |
| Tongue coating                       | 164 (79.2%)             | 26 (74.3%)             | 138 (80.2%)          | 0.49              | 16 (94.1%)           | 148 (77.9%)          | 0.20              |
| Mucous lesions                       | 49 (22.7%)              | 15 (42.8%)             | 34 (19.7%)           | <b>0.007</b>      | 3 (17.6%)            | 46 (24.2%)           | 0.57              |
| Hairy tongue                         | 1 (0.5%)                | 1 (5.7%)               | -                    | 0.17              | -                    | 1 (0.5%)             | -                 |
| Dry lips                             | 182 (87.9%)             | 31 (88.5%)             | 151 (87.8%)          | 0.79              | 16 (94.1%)           | 166 (87.3%)          | 0.81              |
| Angular cheilitis                    | 181 (87.8%)             | 31 (68.8%)             | 150 (87.2%)          | 0.88              | 17 (100%)            | 164 (86.3%)          | 0.82              |
| Oropharyngitis                       | 32 (15.4%)              | 12 (34.3%)             | 20 (11.6%)           | <b>0.03</b>       | 3 (17.6%)            | 29 (15.2%)           | 0.72              |
| Drizzling                            | 20 (9.6%)               | 17 (48.5%)             | 3 (1.7%)             | <b>&lt;0.0001</b> | 4 (23%)              | 16 (8.4%)            | 0.06              |

<sup>1</sup>Presence of visible dental plaque in the first evaluation

<sup>2</sup>Visible suppuration of gingival sulcus

<sup>3</sup>Ulceration of mucous membranes with spontaneous bleeding

(OR: 0.82, 95%CI: 0.37–1.79,  $p = 0.77$ ). Hypertension was the more frequent comorbidity among ICU patients, but presented no increased frequency associated with edentulism (OR: 0.72, 95%CI: 0.40–1.32,  $p = 0.29$ ), dental plaque (OR: 1.32, 95%CI: 0.42–4.17,  $p = 0.85$ ), dental caries (OR: 0.92, 95%CI: 0.46–1.82,  $p = 0.95$ ), dental calculus (OR: 2.25, 95%CI: 0.83–7.45,  $p = 0.10$ ), tongue coating (OR: 1.57, 95%CI: 0.80–3.10,  $p = 0.24$ ), mucous lesions (OR: 1.45, 95%CI: 0.74–2.87,  $p = 0.31$ ), dry lips (OR: 1.56, 95%CI: 0.67–3.62,  $p = 0.40$ ), and angular cheilitis (OR: 0.86, 95%CI: 0.43–1.72,  $p = 0.81$ ). Smokers had no increased odds ratio (95%CI) than dentate patients presenting edentulism (OR: 1.38, 95%CI: 0.57–3.22,  $p = 0.34$ ), dental plaque (OR: undefined;  $p = 0.50$ ), dental caries (OR: 1.86, 95%CI: 0.67–5.17,  $p = 0.34$ ), dental calculus (OR: undefined;  $p = 0.21$ ), tongue coating (OR: 0.91, 95%CI: 0.34–2.43,  $p = 1.00$ ), mucous lesions (OR: 2.24, 95%CI: 0.32–22.38,  $p = 0.43$ ), dry lips (OR: 0.55, 95%CI: 0.18–1.63,  $p = 0.44$ ), angular cheilitis (OR: 0.47, 95%CI: 0.19–1.14,  $p = 0.15$ ), and oropharyngitis (OR: 0.30, 95%CI: 0.03–2.36,  $p = 0.32$ ).

The length of stay in the ICU was associated with the need for mechanical ventilation, the development of pneumonia, end-stage renal disease, and death. In addition, there was an association between the length of stay in the ICU with oral alterations, including the presence of mucous bleeding, tongue coating, and cheilitis (Table 3).

Oral bleeding was considered to be any source of bleeding that was not of gingival/periodontal origin, which could be a mucous lesion of traumatic origin, caused by dryness or other complications. Patients with oral bleeding stayed a longer median time [9 (3 to 19) days,  $p = 0.02$ ] in the ICU than patients without oral bleeding [2 (1 to 4) days]. Patients with tongue coating stayed more days in the ICU ( $5.4 \pm 5.3$  days,  $p = 0.008$ ) than those without tongue coating ( $3.4 \pm 3.0$  days). Median days in the ICU were not different [2 (1 to 4) days,  $p = 0.68$ ] between patients with and without cheilitis.

Edentulism was not included in the multivariate linear regression due to collinearity with dental plaque and dental caries variables. Median days of ICU stay were increased in edentulous patients [ $p = 0.02$ ; 3 (1 to 5) days] compared to dentate and partially dentate patients [2 (1 to 3) days].

During the observation period, 43 (20.77%) patients died. Only the length of hospital stay, the use of multiple drugs, and the need for mechanical ventilation were associated with patient death (Table 4). Among the oral alterations, only oropharyngitis was associated with patients' death during the study period (Table 4). However, the presence of oropharyngitis did not significantly increase the relative risk (RR: 1.04; 95% confidence interval: 0.81 to 1.33;  $p = 0.77$ ) of death in relation to patients without oropharyngeal secretion.

**Table 3** Multivariate linear regression between the length of stay of the patients in the ICU, medical procedures, and systemic and oral health

|                          | Multivariate linear regression |      |          |                                | Adjusted multivariate linear regression |      |          |                                |
|--------------------------|--------------------------------|------|----------|--------------------------------|---|------|----------|--------------------------------|
|                          | Coef                           | SE   | <i>F</i> | <i>p</i>                       | Coef                                    | SE   | <i>F</i> | <i>p</i>                       |
| Age                      | 0.03                           | 0.02 | 1.03     | 0.30                           |   |      |          |                                |
| Sex                      | −0.61                          | 0.66 | 0.85     | 0.35                           |   |      |          |                                |
| Alcoholic                | −2.93                          | 1.75 | 2.80     | 0.09                           |   |      |          |                                |
| Smoking                  | 1.42                           | 2.16 | 1.49     | 0.22                           |   |      |          |                                |
| Mechanical ventilation   | 2.02                           | 1.10 | 3.37     | <b>0.05</b>                    | 2.00                                    | 0.97 | 4.25     | 0.04                           |
| Nosocomial pneumonia     | 3.08                           | 1.24 | 6.13     | <b>0.01</b>                    | 3.69                                    | 1.00 | 13.55    | 0.001                          |
| Previous hospitalization | −1.21                          | 0.69 | 3.09     | 0.08                           |   |      |          |                                |
| Antibiotics              | 1.19                           | 0.73 | 2.61     | 0.10                           |   |      |          |                                |
| Number of medications    | −0.09                          | 0.05 | 2.62     | 0.10                           |   |      |          |                                |
| Hypertension             | 0.20                           | 0.68 | 0.08     | 0.76                           |   |      |          |                                |
| Diabetes                 | −1.15                          | 0.85 | 1.81     | 0.17                           |   |      |          |                                |
| End-stage renal disease  | 5.49                           | 1.81 | 9.18     | <b>0.002</b>                   | 5.66                                    | 1.64 | 11.82    | 0.0007                         |
| Death                    | 4.69                           | 1.00 | 21.72    | <b>0.0006</b>                  | 4.55                                    | 0.88 | 26.33    | <0.0001                        |
| Dental plaque            | 0.76                           | 1.38 | 0.31     | 0.57                           |   |      |          |                                |
| Caries                   | 0.88                           | 0.93 | 0.90     | 0.34                           |   |      |          |                                |
| Residual root            | 0.71                           | 1.38 | 0.26     | 0.60                           |   |      |          |                                |
| Tooth motility           | −0.02                          | 1.07 | 0.002    | 0.98                           |   |      |          |                                |
| Dental calculus          | −0.83                          | 1.33 | 1.38     | 0.53                           |   |      |          |                                |
| Gingival bleeding        | −0.83                          | 1.54 | 0.29     | 0.58                           |   |      |          |                                |
| Oral bleeding            | 4.47                           | 2.37 | 3.53     | <b>0.06</b>                    | 5.71                                    | 2.20 | 6.74     | 0.01                           |
| Candidosis               | −0.69                          | 2.02 | 0.11     | 0.73                           |   |      |          |                                |
| Tongue coating           | −2.44                          | 0.79 | 9.44     | <b>0.002</b>                   | −2.30                                   | 0.73 | 9.83     | 0.001                          |
| Mucous lesions           | 0.47                           | 0.80 | 0.34     | 0.56                           |   |      |          |                                |
| Drooling                 | 1.32                           | 1.95 | 0.46     | 0.49                           |   |      |          |                                |
| Dry lips                 | −0.97                          | 1.49 | 0.42     | 0.51                           |   |      |          |                                |
| Cheilitis                | −1.50                          | 1.48 | 1.01     | 0.31                           | −2.16                                   | 0.91 | 5.58     | 0.01                           |
| Oropharyngitis           | 0.62                           | 1.06 | 0.34     | 0.55                           |   |      |          |                                |
| Constant                 | −5.53                          | 4.61 | 1.26     | 0.26                           | −7.23                                   | 3.52 | 4.20     | 0.04                           |
|                          |                                |      |          | <b><math>r^2 = 0.45</math></b> |   |      |          | <b><math>r^2 = 0.40</math></b> |

## Discussion

The results of the study demonstrate that patients admitted to the ICU had poor oral health status, with a high frequency of dental plaque, calculus, dry lips, cheilitis, and tongue coating. This highlights the importance of the adopted hygiene protocol to control microorganism colonization of dental and mucous surfaces during ICU hospitalization. However, oral lesions such as periodontitis, residual roots, and dental caries are chronic foci of oral infections that could not be adequately treated during the ICU stay and may lead to complications of health status, especially when microorganisms were aspirated by mechanically ventilated patients. These oral foci of infections were not significantly more frequent in patients submitted to mechanical ventilation. However, active caries were significantly more

frequent in patients who developed nosocomial pneumonia. These dental and periodontal foci of infections were also not associated with length of stay and mortality rate in ICU patients. However, the diagnosis of periodontal disease may be underestimated due to the lack of periodontal probing and radiographic examination. This is an unavoidable limitation of oral health screening in ICU patients.

On the other hand, mucous lesions with and without spontaneous bleeding, oropharyngitis (presence of pus or pseudomembranous secretion in oropharynges), and drooling were frequent problems found in mechanically ventilated patients. The majority of mucous lesions seemed to be pressure ulcers caused by traumatic procedures of intubation and maintenance of the ventilation apparatus. Although the mortality rate is higher in mechanically ventilated patients, these mucous lesions were not associated with the overall mortality rate in the ICU.

**Table 4** Multivariate logistic regression between death and systemic and oral health status of ICU patients

| Variables                | Multivariate logistic regression |              |               | Adjusted regression |            |          |
|--------------------------|----------------------------------|--------------|---------------|---------------------|------------|----------|
|                          | Odds ratio                       | 95%CI        | <i>p</i>      | Odds ratio          | 95%CI      | <i>p</i> |
| Age                      | 1.03                             | 0.98–1.08    | 0.20          |                     |            |          |
| Sex                      | 1.04                             | 0.25–4.37    | 0.94          |                     |            |          |
| Alcoholism               | 4.66                             | 0.14–146.19  | 0.38          |                     |            |          |
| Smoking                  | 1.68                             | 0.19–14.55   | 0.63          |                     |            |          |
| Mechanical ventilation   | 11.69                            | 2.31–58.99   | <b>0.002</b>  | 5.89                | 1.19–17.44 | 0.001    |
| Nosocomial pneumonia     | 1.70                             | 0.21–13.66   | 0.61          |                     |            |          |
| Previous hospitalization | 0.73                             | 0.18–2.87    | 0.65          |                     |            |          |
| Antibiotics              | 0.40                             | 0.06–2.39    | 0.32          |                     |            |          |
| Number of medications    | 1.27                             | 1.13–1.43    | <b>0.0001</b> | 1.20                | 1.11–1.31  | <0.0001  |
| Hypertension             | 0.64                             | 0.15–2.73    | 0.55          |                     |            |          |
| Diabetes                 | 2.94                             | 0.61–14.14   | 0.17          |                     |            |          |
| End-stage renal disease  | 0.30                             | 0.01–7.75    | 0.47          |                     |            |          |
| Days in ICU              | 1.58                             | 1.21–2.01    | <b>0.0001</b> | 1.40                | 1.17–1.67  | 0.0002   |
| Edentulism               | 0.32                             | 0.01–7.01    | 0.47          |                     |            |          |
| Dental plaque            | 0.07                             | 0.005–11.80  | 0.31          |                     |            |          |
| Dental caries            | 2.72                             | 0.30–24.56   | 0.36          |                     |            |          |
| Residual root            | 1.51                             | 0.12–18.49   | 0.74          |                     |            |          |
| Tooth motility           | 2.36                             | 0.38–22.22   | 0.29          |                     |            |          |
| Dental calculus          | 0.92                             | 0.006–138.13 | 0.97          |                     |            |          |
| Gingival bleeding        | 0.29                             | 0.01–5.18    | 0.40          |                     |            |          |
| Oral bleeding            | 0.06                             | 0.009–4.98   | 0.21          |                     |            |          |
| Tongue coating           | 0.98                             | 0.15–6.12    | 0.98          |                     |            |          |
| Mucous lesions           | 0.42                             | 0.09–1.90    | 0.26          |                     |            |          |
| Drooling                 | 0.17                             | 0.007–4.16   | 0.27          |                     |            |          |
| Dry lips                 | 1.03                             | 0.04–21.67   | 0.98          |                     |            |          |
| Cheilitis                | 13.21                            | 0.36–484.59  | 0.16          |                     |            |          |
| Oropharyngitis           | 0.11                             | 0.01–0.88    | <b>0.03</b>   | 0.16                | 0.02–0.89  | 0.03     |

Smoking had been investigated as a predictor of increased length of stay of patients in ICU [17, 21–23]. Although smoking had been associated with increased incidence of early pneumonia in trauma patients in ICU, no association with length of stay and mortality was identified [21]. Others also did not find an association between smoking with the length of stay in the ICU for patients who suffered hemorrhagic aneurysms [23]. On the other hand, smoking was associated with increased length of stay in cardiac surgery patients [22] and incidence of pneumonia in patients admitted to ICU due to deep odontogenic infections [17]. These results suggest that smoking could increase the risk of staying in the ICU depending on patients' diseases. Of note, a limitation of our study was there was no medical record of the number of cigarettes per day and previous history of smoking. Time and amount of exposure to tobacco may increase the prevalence and severity of periodontal disease and caries [24–26], as well as comorbidities and mortality in ICU patients. Alcohol dependence was also associated with increased prevalence of complications and mortality in ICU patients [27], as well as

increased prevalence of oral lesions [28]. However, medical records also did not detail the amount and frequency of alcohol consumption by ICU patients. Nevertheless, caution should be taken in interpreting the absence of an association between the length of stay and mortality in the present study with alcoholism, since a low number of patients were considered alcohol addicted. The addition of information on glomerular filtration rate and biochemical glycemic control is suggested for future studies as a way to make its assessment more detailed.

Although oral foci of infections were not significantly different in mechanically ventilated patients (and these patients stayed longer in the ICU), oral bleeding and tongue coating were associated with an increased length of ICU stay. This suggests that despite oral hygiene care, the presence of microorganism colonies on mucous membranes or the bleeding of mucous membranes was associated with the worsening of the patient's health status and complications. This could be a result of a poor health condition, including oral health, a complication in the primary disease, or adverse effects of medications. Nevertheless, mortality in the ICU was

associated with the main factors associated with a longer ICU stay (mechanical ventilation, number of medications) but not with oral health status, except for oropharyngitis.

Oral hygiene and dental care in ICU patients have been claimed to decrease the incidence of nosocomial pneumonia and other complications, especially in patients with mechanical ventilation [2, 6, 16, 29]. Some studies reported a reduced incidence of nosocomial ventilator-associated pneumonia in patients submitted to oral hygiene [29], while other studies did not find significant differences [3]. In the present study, pneumonia was still more frequent in mechanically ventilated patients than in non-ventilated ones, despite daily hygiene care. Previous studies demonstrated that oral hygiene could reduce ventilator-associated pneumonia to a prevalence range of 10% [30], 11.2% [29], and 37.8% [3] on the fifth day. A similar frequency of ventilator-associated pneumonia (17.8%) has been reported by other authors in intubated patients submitted to oral hygiene care [5]. This suggests that in our study, oral hygiene care was in agreement with the expected prevalence and incidence of pneumonia in mechanically ventilated and non-ventilated patients. Nevertheless, oral foci of infection may harm or be associated with other health problems leading to an increased length of stay in the ICU but not mortality rate. Thus, the presence of a qualified dentist within the ICUs, as a member of the health team, is of fundamental importance for the early diagnosis of injuries and treatment when necessary, in addition to training the nursing team regarding oral care and assistance in the implementation of bundles for the control of infections and improvement in the prognosis and quality of life of patients.

Previous studies have demonstrated that oral hygiene per se did not decrease stay time in the ICU or mortality rates [3, 16, 29]. Thus, do other oral health problems contribute to the worsening of health status and increasing length of stay in the ICU? Our results suggest that there is no significant association between chronic foci of oral infections, such as dental caries and periodontal disease, with stay time and mortality in the ICU. However, the development of mucous lesions (oral bleeding and tongue coating) was present in patients that had a long ICU stay. Some of these lesions could be preventable and treated by ICU staff and dental surgeons through oral hygiene, mucous hydration, and care to avoid the formation of oral pressure and traumatic ulcers. A previous study estimated that approximately 45.4% of intubated patients develop pressure ulcers in the oral mucosa [13], while our study presented mucous lesions in approximately 42% of ventilated patients. Of concern, the development of pressure ulcers in intubated patients has been associated with microbial colonization of oral mucosa [13]. This highlights the importance of maintaining oral hygiene in mechanically ventilated patients and monitoring the development of pressure ulcers.

It is important to point out that patients undergoing hospitalization, including ICU attendance, had a poor oral health status [5, 7], which could worsen if they do not receive oral care [6]. Although we did not identify an association between the oral foci of infections with the length of stay and mortality rate in the ICU, it should be pointed out that the accumulation of dental plaque on hard and soft tissues could be a potential risk for developing complications, such as nosocomial pneumonia, post-surgical infection, or bacteremia.

Death was associated only with systemic factors. Although we did not identify any association between the foci of oral infections and mortality, it is important to point out that an increased mortality rate in the ICU had been described in ventilated patients due to septic shock or multiple organ failure secondary to abdominal and pulmonary infections [31]. Other factors that could contribute to the increased rate of mortality were age, stay time in hospital, and severity of illness scores [32].

We concluded that the majority of the patients admitted to the ICU presented poor oral hygiene and a poor oral health status and require dental care during their stay in the ICU. However, the presence of oral foci of infection, in patients under oral hygiene care, did not increase the time in the ICU and mortality rate. The presence of ulcerations and bleeding from oral mucosa is a concern in both ventilated and non-ventilated patients.

**Acknowledgements** The authors thank the Coordination for the Improvement of Higher Education Personnel (CAPES-Brasil), Irmandade Santa Casa de Londrina (Londrina-Brasil), and the company Dental Clean (Londrina, Brazil).

**Author contribution** E.C.S: patient care, data collection, data analysis, and paper writing.

J.A.M.P: patient care, data collection, data analysis, and paper writing.

L.B.: patient care, data collection, and paper writing.

S.P.R: study design, data analysis, and paper writing.

G.F.S: project supervisor, study design, patient care, data collection, data analysis, and paper writing.

**Data Availability** Patient data are confidential, but the authors make themselves available to share the data from the spreadsheets obtained with those responsible for the journal, if necessary.

## Declarations

**Ethical approval** The data collection procedures were approved by the Ethics Committee in Research Involving Human Beings of ISCAL-Irmandade Santa Casa de Londrina (protocol no. 3.202.350).

**Informed consent** Patients or their guardians (in cases of unconsciousness) were informed of the research objectives, and data collection was performed only after authorization and signing of a written free and informed consent.

**Conflict of interest** The authors declare no competing interests.



## References

- Ory J, Mourgues C, Raybaud E, Chabanne R, Jourdy JC, Belard F, Guerin R, Cosserant B, Faure JS, Calvet L, Pereira B, Guelon D, Traore O, Gerbaud L (2018) Cost assessment of a new oral care program in the intensive care unit to prevent ventilator-associated pneumonia. *Clin Oral Investig* 22:1945–1951. <https://doi.org/10.1007/s00784-017-2289-6>
- Bellissimo-Rodrigues WT, Meneguetti MG, Gaspar GG, Nicolini EA, Auxiliadora-Martins M, Basile-Filho A, Martinez R, Bellissimo-Rodrigues F (2014) Effectiveness of a dental care intervention in the prevention of lower respiratory tract nosocomial infections among intensive care patients: a randomized clinical trial. *Infect Control Hosp Epidemiol* 35:1342–1348. <https://doi.org/10.1086/678427>
- de Lacerda Vidal CF, Vidal AK, Monteiro JG Jr, Cavalcanti A, Henriques APC, Oliveira M, Godoy M, Coutinho M, Sobral PD, Vilela CA, Gomes B, Leandro MA, Montarroyos U, Ximenes RA, Lacerda HR (2017) Impact of oral hygiene involving toothbrushing versus chlorhexidine in the prevention of ventilator-associated pneumonia: a randomized study. *BMC Infect Dis* 17:112. <https://doi.org/10.1186/s12879-017-2188-0>
- Choi MI, Han SY, Jeon HS, Choi ES, Won SE, Lee YJ, Yang JH, Baek CY, Shim H, Mun SJ (2022) The influence of professional oral hygiene care on reducing ventilator-associated pneumonia in trauma intensive care unit patients. *Br Dent J* 232:253–259. <https://doi.org/10.1038/s41415-022-3986-3>
- Takahama A Jr, de Sousa VI, Tanaka EE, Ono E, Ito FAN, Costa PP, Pedriali M, de Lima HG, Fornazieri MA, Correia LS, Cardoso LTQ, de Maio Carrilho CMD (2021) Analysis of oral risk factors for ventilator-associated pneumonia in critically ill patients. *Clin Oral Investig* 25:1217–1222. <https://doi.org/10.1007/s00784-020-03426-x>
- Bellissimo-Rodrigues WT, Meneguetti MG, Gaspar GG, de Souza HCC, Auxiliadora-Martins M, Basile-Filho A, Martinez R, Bellissimo-Rodrigues F (2018) Is it necessary to have a dentist within an intensive care unit team? Report of a randomised clinical trial. *Int Dent J* 68:420–427. <https://doi.org/10.1111/idj.12397>
- Carrilho Neto A, De Paula RS, Sant'ana AC, Passanezi E (2011) Oral health status among hospitalized patients. *Int J Dent Hyg* 9:21–29. <https://doi.org/10.1111/j.1601-5037.2009.00423.x>
- Silva AP, Caruso P, Jaguar GC, Carvalho PA, Alves FA (2014) Oral evaluation and procedures performed by dentists in patients admitted to the intensive care unit of a cancer center. *Support Care Cancer* 22:2645–2650. <https://doi.org/10.1007/s00520-014-2233-0>
- Choi BK, Kim MS, Kim SH (2020) Risk prediction models for the development of oral-mucosal pressure injuries in intubated patients in intensive care units: a prospective observational study. *J Tissue Viability* 29:252–257. <https://doi.org/10.1016/j.jtv.2020.06.002>
- Ishikawa S, Yamamori I, Takamori S, Kitabatake K, Edamatsu K, Sugano A, Oizumi H, Kato H, Suzuki J, Sato K, Yusa K, Sadahiro M, Iino M (2021) Evaluation of effects of perioperative oral care intervention on hospitalization stay and postoperative infection in patients undergoing lung cancer intervention. *Support Care Cancer* 29:135–143. <https://doi.org/10.1007/s00520-020-05450-9>
- Mirzashahi B, Tonkaboni A, Chehrassan M, Doosti R, Kharazifard MJ (2019) The role of poor oral health in surgical site infection following elective spinal surgery. *Musculoskelet Surg* 103:167–171. <https://doi.org/10.1007/s12306-018-0568-2>
- Abe T, Futamura K, Goto N, Ohara K, Ogasa T, Tomosugi T, Okada M, Hiramitsu T, Narumi S, Watarai Y (2022) Oral/oesophageal candidiasis is a risk factor for severe infection after kidney transplantation. *Nephrology (Carlton)* 27:97–103. <https://doi.org/10.1111/nep.13959>
- Kim SH, Nah HS, Kim JB, Kim CH, Kim MS (2021) Relationships between oral-mucosal pressure ulcers, mechanical conditions, and individual susceptibility in intubated patients under intensive care: a PCR-based observational study. *Biol Res Nurs* 23:557–567. <https://doi.org/10.1177/1099800421998071>
- Eduardo FP, Bezinelli LM, Gobbi MF, Bergamin LG, de Carvalho DLC, Correa L (2022) Oral lesions and saliva alterations of COVID-19 patients in an intensive care unit: a retrospective study. *Spec Care Dentist*. <https://doi.org/10.1111/scd.12705>
- Rezaei S, Rezaei K, Mahboubi M, Jarahzadeh MH, Momeni E, Bagherinasab M, Targhi MG, Memarzadeh MR (2016) Comparison the efficacy of herbal mouthwash with chlorhexidine on gingival index of intubated patients in intensive care unit. *J Indian Soc Periodontol* 20:404–408. <https://doi.org/10.4103/0972-124X.194269>
- Zhao T, Wu X, Zhang Q, Li C, Worthington HV, Hua F (2020) Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev* 12:CD008367. <https://doi.org/10.1002/14651858.CD008367.pub4>
- Rautaportas N, Furuholm J, Uittamo J, Saloniemi M, Puolukka T, Snall J (2021) Deep odontogenic infections-identifying risk factors for nosocomial pneumonia. *Clin Oral Investig* 25:1925–1932. <https://doi.org/10.1007/s00784-020-03500-4>
- Mizuno H, Mizutani S, Ekuni D, Tabata-Taniguchi A, Maruyama T, Yokoi A, Omori C, Shimizu K, Morimatsu H, Shirakawa Y, Morita M (2018) New oral hygiene care regimen reduces postoperative oral bacteria count and number of days with elevated fever in ICU patients with esophageal cancer. *J Oral Sci* 60:536–543. <https://doi.org/10.2334/josnusd.17-0381>
- World Medical A (2013) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 310:2191–2194. <https://doi.org/10.1001/jama.2013.281053>
- Loe H, Silness J (1963) Periodontal disease in pregnancy. I. Prevalence and severity *Acta Odontol Scand* 21:533–551. <https://doi.org/10.3109/00016356309011240>
- Harrell KN, Lee WB, Rooks HJ, Briscoe WE, Capote W, Dart BWT, Hunt DJ, Maxwell RA (2023) Early pneumonia diagnosis decreases ventilator-associated pneumonia rates in trauma population. *J Trauma Acute Care Surg* 94:30–35. <https://doi.org/10.1097/TA.0000000000003808>
- Kao KD, Lee SKC, Liu CY, Chou NK (2022) Risk factors associated with longer stays in cardiovascular surgical intensive care unit after CABG. *J Formos Med Assoc* 121:304–313. <https://doi.org/10.1016/j.jfma.2021.04.020>
- Hammer A, Ranaie G, Erbguth F, Hohenhaus M, Wenzl M, Killer-Oberpfalzer M, Steiner HH, Janssen H (2020) Impact of complications and comorbidities on the intensive care length of stay after aneurysmal subarachnoid haemorrhage. *Sci Rep* 10:6228. <https://doi.org/10.1038/s41598-020-63298-9>
- Robbins J, Ali K (2022) How do periodontal indices compare among non-smokers, tobacco and e-cigarette smokers? *Evid Based Dent* 23:116–117. <https://doi.org/10.1038/s41432-022-0809-y>
- Beklen A, Sali N, Yavuz MB (2022) The impact of smoking on periodontal status and dental caries. *Tob Induc Dis* 20:72. <https://doi.org/10.18332/tid/152112>
- Salhi L, Seidel L, Lambert F, Albert A (2022) Predicting probing depth reduction after periodontal non-surgical treatment in smokers according to the nicotine dependence and the number of cigarette consumed. *Heliyon* 8:e10143. <https://doi.org/10.1016/j.heliyon.2022.e10143>
- Lowicka-Smolarek M, Kokoszka-Bargiel I, Knapik M, Smietanka K, Dyrda P, Mozdzen M, Kurczab M, Borkowski J and Knapik P (2022) Analysis of patients with alcohol dependence treated in silesian intensive care units. *Int J Environ Res Public Health* 19. <https://doi.org/10.3390/ijerph19105914>

28. Zupo R, Castellana F, De Nucci S, Dibello V, Lozupone M, Giannelli G, De Pergola G, Panza F, Sardone R, Boeing H (2021) Beverages consumption and oral health in the aging population: a systematic review. *Front Nutr* 8:762383. <https://doi.org/10.3389/fnut.2021.762383>
29. Galhardo LF, Ruivo GF, Santos FO, Ferreira TT, Santos J, Le MV, Pallos D (2020) Impact of oral care and antisepsis on the prevalence of ventilator-associated pneumonia. *Oral Health Prev Dent* 18:331–336. <https://doi.org/10.3290/j.ohpd.a44443>
30. Haghighi A, Shafipour V, Bagheri-Nesami M, GholipourBaradari A, YazdaniCharati J (2017) The impact of oral care on oral health status and prevention of ventilator-associated pneumonia in critically ill patients. *Aust Crit Care* 30:69–73. <https://doi.org/10.1016/j.aucc.2016.07.002>
31. van Wagenberg L, Witteveen E, Wieske L, Horn J (2020) Causes of mortality in ICU-acquired weakness. *J Intensive Care Med* 35:293–296. <https://doi.org/10.1177/0885066617745818>
32. Martin-Loeches I, Wunderink RG, Nanchal R, Lefrant JY, Kapadia F, Sakr Y, Vincent JL, Investigators I (2016) Determinants of time to death in hospital in critically ill patients around the world. *Intensive Care Med* 42:1454–1460. <https://doi.org/10.1007/s00134-016-4479-0>

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.