



postoperative fever. The study protocol was approved by the Research Ethics Committee of Shimane University (No.4041) and the Ethics Committee of Kagawa Prefectural Central Hospital (No.878). All patients received perioperative oral management (POM) by oral specialists between April 2012 and December 2018 at Kagawa Prefectural Central Hospital, Kagawa, Japan prior to lung cancer surgery. Bacteria counts from the dorsum of the tongue were measured on the day of pre-hospitalization, pre-operation, and post-operation, and background data was also collected retrospectively. In total, 441 consecutive patients were enrolled in the study.

All statistical analyses were performed using SPSS version 26.0 software (IBM Japan, Tokyo, Japan). The one-way analysis of variance (ANOVA) statistical test was used followed by the Bonferroni's multiple comparison test among each time point. Univariate and multivariate analyses of the risk factors for the duration of fever were conducted using logistic regression analysis (backward selection method) on each BMI group. A *p*-value less than 0.05 was considered statistically significant. Also, since a substantial number of patients had missing data, multiple imputation using an ordinal logistic imputation method was utilized, with the assumption that the missing data were missing at random.

## **RESULTS AND DISCUSSION**

In total, 441 consecutive patients (276 males and 165 females) were enrolled in the study. About their characteristics; the median age was 71.0 years, and the median BMI was 22.6 kg/m<sup>2</sup>. The performance status (PS) was 0 in 422 patients (95.7%), 1 in 11 patients (2.5%), 2 in 5 patients (1.1%), 3 in 2 patients (0.5%), and 4 in 1 patient (0.2%). The mean Brinkman index was 450.0. The median number of housemates was 1.0. The type of cancer was non-small cell carcinoma in 364 patients (82.5%), small cell carcinoma in 8 patients (1.8%), and other in 69 patients (15.6%). The cancer stage was 1 in 312 patients (70.7%), 2 in 68 patients (15.4%), 3 in 57 patients (12.9%), and 4 in 4 patients (0.9%). The median number of teeth was 22.0. The number of patients with dentures was 198 (44.9%) and 72 patients had a home dentist (16.3%). The median level of oral bacteria count at pre-hospitalization, pre-operation, and post-operation was 5.3, 4.6, and 4.5, respectively. Median white blood cell counts at pre-operation were 6.0 x 10<sup>3</sup>/μL and mean serum albumin values at pre-operation were 4.2 g/dL. The median estimated duration of hospitalization was 14.0 days. The median duration of hospitalization was 10.0 days. The median operation time was 223 minutes. There were 367 patients (83.2%) who experienced fever and the median duration of fever was 2.0 days.

Longitudinal data showed the results of the one-way ANOVA test, which manifested the significant differences in the oral bacteria count level between the time points (*p*<0.001). The median level of oral bacteria count at pre-hospitalization, pre-operation, and post-operation was 5.3, 4.6, and 4.5, respectively. The Bonferroni's multiple comparison test also showed significant

differences between pre-hospitalization and pre-operation ( $p < 0.001$ ) and between pre-hospitalization and post-operation ( $p < 0.001$ ). There was no significant difference between pre-operation and post-operation ( $p = 0.242$ ).

Logistic regression analysis manifested the potential risk factors of postoperative fever. In the total data, there were significant correlations between postoperative fever and BMI (OR: 0.92 [95% CI: 0.85-0.99],  $p = 0.03$ ), PS (OR: 0.38 [95% CI: 0.21-0.70],  $p < 0.01$ ), number of housemates (OR: 0.60 [95% CI: 0.42-0.86],  $p < 0.01$ ), and white blood cell count at pre-operation (OR: 0.86 [95% CI: 0.75-0.98],  $p = 0.02$ ) in multivariate analysis. In the underweight group, PS (OR: 0.04 [95% CI: 0.003-0.67,  $p = 0.02$ ]) and number of teeth remained (OR: 0.73 [95% CI: 0.53-0.99,  $p = 0.05$ ]) significantly associated with postoperative fever in multivariate analysis. In the normal weight group, only number of housemates (OR: 0.58 [95% CI: 0.37-0.92,  $p = 0.02$ ]) and white blood cell count at pre-operation (OR: 0.78 [95% CI: 0.67-0.91,  $p < 0.01$ ]) were significantly associated with postoperative fever in the multivariate analysis. In the overweight group, PS (OR: 0.05 [95% CI: 0.004-0.62,  $p = 0.02$ ]) and number of teeth (OR: 0.94 [95% CI: 0.89-0.99,  $p = 0.03$ ]) remained significant in the multivariate analysis.

This study was broadly divided into two main findings. First, the Bonferroni's multiple comparison test showed significantly higher oral bacteria counts at pre-hospitalization compared to pre- and post-operation ( $p < 0.001$ ). In other words, it has been shown that an initial pre-hospital POM intervention can reduce the level of oral bacterial counts, and that reduced bacterial counts can be maintained by pre-operative POM, and lower levels of oral bacterial counts can also be maintained postoperatively. Second, multivariate analysis showed that a lower number of teeth was significantly associated with postoperative fever in the underweight and overweight groups. In particular, BMI could be considered a risk factor for postoperative complications in various surgical sites as shown in the previous studies. For the interpretation of the relationship between oral health status (number of teeth) and postoperative fever could be designed to determine the risk factors associated with postoperative complications after surgery.

Therefore, we suggest that while a higher number of teeth and good occlusal function should be better for patients undergoing lung cancer surgery, it be important to reduce the oral plaque count through thorough POM. The greater the number of teeth of the lung cancer patients planning for surgical intervention, the more intense POM should be considered in perioperative management.

## **CONCLUSION**

The study showed that POM could reduce the level of oral bacterial counts, and that BMI could be one of the risk factors for postoperative fever after lung cancer surgery. The risk of postoperative complications could be lower with dentulous patients, and the appropriate POM would be essential for prevention of complication in lung cancer patients by dental specialists.