

# 学位論文の要旨

氏名 古谷 龍人

学位論文名 Effects of Age on Postoperative Oral Function in Older Adults With Oral Squamous Cell Carcinoma and Its Cutoff Values: A Cross-Sectional Study

発表雑誌名 Scientific Reports  
(巻, 初頁~終頁, 年) (15(1), 9741, 2025)

著者名 Tatsuhito Kotani, Yuhei Matsuda, Mayu Takeda, Reon Morioka, Yukiho Shimamura, Rie Osako-Sonoyama, Hiroto Tatsumi, Masako Fujioka-Kobayashi, Takahiro Kanno

## 論文内容の要旨

### INTRODUCTION

According to the National Comprehensive Cancer Network (NCCN) guidelines, surgery is the first choice of treatment for oral squamous cell carcinoma (OSCC), and several modalities are added as adjuncts depending on the cancer stage. In recent years, the development of immune checkpoint inhibitors and photoimmunotherapy has increased treatment options for advanced OSCC. A phase 2 open-label, multicenter study of photoimmunotherapy in patients with locoregional, recurrent head and neck squamous cell carcinoma reported a median overall survival of 9.3 months. Novel therapies are expected to improve survival. The standard primary outcome for OSCC is the 3- or 5-year survival rate. There are variations among reports, but the 5-year survival rate is approximately 50%. While survival and disease-free survival rates are important, Japan's super-aged society requires a reconsideration of outcomes in older patients. Lohr reported that the 5Ds (death, disease, disability, dissatisfaction, and discomfort) are important for outcome measurements. However, disability, dissatisfaction, and discomfort are considered when selecting treatment. Therefore, soft outcome considerations and the definition of OSCC in older adults should be considered.

Japan has the world's oldest population, and Shimane Prefecture is a regional city with one of the largest aging populations. The number of treated older adults with OSCC has been increasing. Karino et al. reported the case of an 89-year-old patient with advanced tongue cancer who strongly desired treatment. The patient was selected for treatment with an emphasis on the recovery of oral function, as well as survival rate. A good outcome was achieved after treatment

maintaining oral intake. Consideration was given to soft outcomes after treatment. This case shows that survival rate is not always the primary outcome. Klingelhöffer et al. reported a hazard ratio of 2.26 for the effect of age on tumor-related survival, with a cutoff value of  $\geq 65$  years. There are no reports on the cutoff value of age related to oral function.

A common understanding of the definition of oral function has emerged. In Japan, oral hypofunction was registered as a disease by the National Health Insurance in 2018. In 2021, Matsuda et al. defined postoperative oral dysfunction in three categories. Postoperative oral dysfunction significantly reduces quality of life. OSCC patients have a higher rate of suicide. Local tumor control and maintenance of oral function should be considered. A cutoff value for the age at which oral function may be compromised should be considered. This study hypothesized that older age is associated with lower oral function after OSCC treatment.

### **MATERIALS AND METHODS**

This cross-sectional study collected background data and evaluated the oral function (microorganisms, oral dryness, occlusal force, tongue pressure, masticatory function and eating assessment tool [EAT-10]) of 102 patients from September 2019 to December 2023. The following patient background data were collected from electronic medical records: sex, age, primary tumor site, clinical cancer stage, treatment method, presence of neck dissection, presence of reconstructive surgery, and body mass index. Multiple linear regression analysis (forced entry method) was conducted, considering confounding factors. Analysis of the receiver operating characteristic (ROC) curves and the area under the curve (AUC) was used to examine the sensitivity and specificity of each oral function measurement to detect the high-risk age for postoperative oral dysfunction. Each patient was assigned an estimated propensity score, which was the predicted probability of postoperative oral dysfunction based on the cutoff score reported in a previous study. Finally, multivariable logistic regressions were also performed by applying propensity scores to adjust for group differences using the inverse probability of treatment weighting (IPTW). The study protocol was approved by the Research Ethics Committee of Shimane University (No. 4041).

### **RESULTS AND DISCUSSION**

In total, 102 patients with OSCC were enrolled: 74 (72.5%) males and 28 (27.5%) females with a mean age of 69.6 years. Microorganisms, masticatory function, and occlusal force were significantly correlated with age. For masticatory function, the cutoff age was 84 years when the point of the maximum AUC was 0.68, and the curve was used to determine the cutoff. For occlusal force, the cutoff age was 75 years when the point of maximum AUC was 0.70, and the curve was used to determine the cutoff. When the cutoff age was 75 years, the odds ratio for

association with masticatory function was 2.49 ( $P=0.08$ ). The odds ratio indicating an association with occlusal force was 4.32 ( $P=0.01$ ).

The age distribution of the enrolled patients with OSCC affected the quality of the study. The median age of this study was 69.6 years, and the oldest patient was 92 years.

This study has two major findings. First, age affects the occlusal force and masticatory function after treatment. The components of the occlusal force include the number of remaining teeth, masticatory muscle groups, and their dominant and trigeminal nerve. Muscle strength declines with aging in healthy older adults. In addition, the number of remaining teeth decreases in older adults. According to Eichner's classification, those in category C are particularly prone to a decline in occlusal strength. Another report stated that the occlusal force decreases when the number of remaining teeth is less than 19. The population in this study included 41 (40.2%) patients with gingival cancer. Therefore, it is reasonable that age- and treatment-related factors independently influenced the decline of postoperative oral function. The pathological decline in occlusal strength may lead to a decrease in food diversity and nutritional deficiencies. Decision-making should take into account the possibility that the occlusal strength of older patients with OSCC may decline more than expected and consider the planning of prosthetic treatment.

Masticatory function deteriorates over time. Mastication is related to occlusal function; however, the major difference is the contribution of oral motor skills. Mastication requires food to be repeatedly placed on the occlusal support zone by coordinated movements. Mastication involves brain activity. The sizes of the cerebellum and cortex decline with age. The decline in the physiological function and the organic changes caused by surgery are thought to enhance the decline in masticatory function.

The second major finding was that the cutoff value for age at risk of developing postoperative dysfunction in patients with OSCC was 75 years. A review of the cutoff values for various outcomes in patients with OSCC showed that the overall survival was 65 years. Therefore, the age of 75 years is the first in the world to define older patients with OSCC based on soft outcomes.

## **CONCLUSION**

Age at the time of OSCC treatment is an independent factor related to postoperative oral function (masticatory function and occlusal strength), and the incidence of oral dysfunction is approximately 2–4 times higher in patients aged > 75 years, suggesting the need for caution in selecting treatment methods and managing the postoperative course.