

Dynamic prognostic evaluation of oral squamous cell carcinoma using net and conditional survival rates: A retrospective cohort study

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Abstract

Background

Cancer prognosis is conventionally evaluated using the overall survival rate (OSR); however, this metric may not adequately reflect cancer-specific outcomes, particularly in older patients. Net survival rate (NSR) and conditional survival rate (CSR) may provide complementary insights into long-term prognosis. This study investigated the prognostic evaluation of oral squamous cell carcinoma (OSCC) using the NSR and CSR.

Methods

A retrospective cohort of 783 patients with OSCC treated between 2000 and 2014 was analyzed. OSR and NSR were estimated using the Kaplan–Meier and Pohar–Perme methods, respectively. CSR was derived from survival estimates and compared across the clinicopathological factors. Prognostic determinants were assessed using the Cox proportional hazards model.

Results

NSR exceeded OSR, with the most discrepancy in patients aged ≥ 65 years, reflecting increased non-cancer-related mortality. CSR analysis demonstrated that the survival probability improved over time. Survival differences progressively decreased between early- and advanced-stage diseases. Site-specific differences persisted: tongue cancer showed favorable long-term outcomes, whereas buccal mucosa and floor of mouth cancers exhibited slower CSR improvement. Sex-related differences diminished after 3 years of follow-up.

Conclusion

NSR and CSR provide a dynamic and clinically meaningful evaluation of the prognosis of OSCC. Non-cancer mortality substantially influenced survival outcomes in older patients, whereas CSR revealed that the prognosis improved over time among long-term survivors, even in advanced-stage disease. These findings highlight the clinical utility of dynamic survival measures for individualized prognostic assessment and follow-up planning in patients with OSCC.

Introduction

The overall survival rate (OSR) has been widely used in clinical research and epidemiological surveys to evaluate cancer survival. The OSR indicates the proportion of patients who survive within a specified period, regardless of cause of death, and is often used for its calculation [1–4]. However, OSR does not

distinguish cancer-specific mortality from deaths due to other factors. In older patients, non-cancer-related deaths may underestimate OSR and obscure cancer-related prognosis [5].

To overcome the limitations of OSR, cancer-specific survival (CSS) is used; however, its utility is constrained by inaccuracies in cause-of-death classification and difficulty determining cancer-specific mortality [6]. In contrast, the net survival rate (NSR), introduced by Perme et al. in 2012, addresses these issues by estimating survival using life tables calibrated to background mortality [7]. This approach removes the influence of non-cancer deaths, enabling more accurate assessment of cancer-attributable mortality. Accordingly, NSR is used in international epidemiological research for comparisons across populations and time periods [8]. Although studies have demonstrated that the NSR more precisely reflects cancer-specific mortality [9, 10], few studies have applied it to patients with oral squamous cell carcinoma (OSCC) [11].

Another metric that is gaining attention is the conditional survival rate (CSR), which represents the probability of surviving an additional period given survival to a time point after diagnosis or treatment. CSR can be calculated using OSR, NSR, or CSS. By incorporating elapsed survival time into assessment, CSR provides time-dependent information, particularly for patients who have completed the initial cancer treatment [12]. Improvements in CSR have been reported in breast, colorectal [13, 14], and oral cancers [15]. However, the CSR of Japanese patients with OSCC remains unknown.

This study aimed to visualize the risk factors for OSCC and clarify prognostic changes over time by conducting a multifaceted survival analysis using OSR and NSR in Japanese patients with OSCC.

Patients and methods

Study population

This retrospective study examined patients with OSCC who presented to the Department of Oral and Maxillofacial Surgery at Kumamoto University Hospital between January 1, 2000, and December 31, 2014, and who underwent surgery as their initial treatment. Patients without a history of head and neck cancer (including oral cancer), prior radical resection, or pretreatment were included. The survival status was determined based on the medical records until March 31, 2025.

This study analyzed the following variables: age (< 65 vs. ≥65 years), sex, primary tumor site, clinical stage (cStage), and clinical macroscopic tumor type. Demographic and clinical data, including age, sex, and the primary tumor site, were collected from medical records and diagnostic imaging at the time of diagnosis. Cancer stages were classified according to the 7th edition of the Union for International Cancer Control (UICC) TNM classification [16], and clinical growth patterns. Local invasion and cervical lymph node metastasis were preoperatively evaluated using a combination of computed tomography (CT), magnetic resonance imaging, positron emission tomography–CT, and ultrasonography.

This study was approved by the Ethics Committee of Kumamoto University (RINRI 1928). The study was conducted in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments. Owing to the retrospective nature of this study, the requirement for informed consent was waived. However, patients were allowed to refuse participation on an opt-out basis (RINRI1427).

Statistical analysis

Overall survival was defined as the time from initial diagnosis to death from any cause. Surviving patients at the end of the follow-up period were censored on the date of the last confirmed survival. Kaplan–Meier curves were constructed, and the log-rank test was used to compare survival differences between groups based on each variable. Subsequently, the 5-year CSR was calculated for patients who survived for a defined period after diagnosis. Net survival was estimated using the Pohar–Perme estimator within a relative survival framework. Expected population mortality was obtained from the Japanese cohort life tables provided by the National Cancer Center Japan and matched according to age, sex, and calendar year. CSR was defined as the probability of surviving an additional y years, given that a patient had already survived x years after diagnosis. In this context, x represents the number of years a patient has survived and y represents the number of additional years the patient is expected to survive. Therefore, CSR is calculated as follows:

$$CSR(y|x) = \frac{S(x+y)}{S(x)}$$

where $S(x)$ is the relative survival at time x .

The 5-year CSR was estimated at 1, 2, 3, 4, and 5 years after the initial diagnosis. Cox proportional hazards models were used to identify factors influencing 5-year CSR.

All statistical analyses were performed using R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria) and EZR version 1.68 (Saitama Medical Center, Jichi Medical University, Saitama, Japan). EZR is a modified version of R Commander designed to add statistical functions frequently used in biostatistics [17]. The relsurv package was used to estimate the Pohar-Perme estimator [18]. All p -values were two-sided, and statistical significance was set at $p < 0.05$.

Results

Patient selection and baseline characteristics

The patient selection flowchart is shown in Fig. 1. Of the initial 828 cases, patients who discontinued follow-up within 1 month after surgery were excluded. Patients with carcinoma in situ were excluded

because of their favorable prognosis. Patients with jaw-central type and unclassifiable growth patterns were excluded. Finally, 783 patients were included.

Table 1 presents the baseline characteristics of the study population. Patients aged ≥ 65 years accounted for 59.8% of the cohort. The tongue was the most common primary tumor site. Although the number of stage III cases was relatively small, the distribution of the other clinical stages and growth patterns was well balanced.

Comparison of 5-year and 10-year OSR and NSR

Table 2 presents the 5- and 10-year OSR and NSR stratified by various factors. The p-values shown in Table 2 were derived from log-rank tests comparing 10-year OSR among the categories of each factor. In nearly all subgroups, the NSR exceeded the OSR, with the difference being pronounced among patients aged ≥ 65 years (5-year OSR vs. NSR: 76.8% vs. 83.8%; 10-year OSR vs. NSR: 62.8% vs. 69.4%). Based on the 5-year and 10-year OSR and NSR, women exhibited higher survival rates than men. Among the primary tumor sites, tongue cancer had the most favorable prognosis. For maxillary gingival cancer, no difference was observed in the 10-year survival rate between the OSR and NSR (10-years OSR: 64.5%, 10-years NSR: 63.6%). As the clinical stage progressed, the difference between OSR and NSR increased, particularly in stage IV (5-year OSR/NSR; 66.3%/69.5%; 10-year OSR/NSR; 59.5%/62.6%). Among the clinical growth patterns, the superficial type had the best prognosis, whereas the endophytic type had the poorest using the 5-year and 10-year OSR and NSR.

Analysis of 5-Year CSR

Figure 2 presents the 5-year CSR calculated from CSR. In all patients, the CSR improved with each passing year from the time of diagnosis, although changes beyond the third year were modest (Fig. 2a). CSR steadily increased from 84.7% to 97.1% in patients aged < 65 years, whereas patients aged ≥ 65 years showed limited improvement (from 76.8% to 81.7%) (Fig. 2b). Initial differences in CSR between men and women were observed; however, these differences gradually diminished over time (Fig. 2c). Tongue cancer had the most favorable outcomes among primary tumor sites. Lesions in the buccal mucosa and oral floor initially showed gradual improvement in CSR but demonstrated marked improvement in CSR from the second or third year of treatment. Conversely, the maxillary gingiva and palate exhibited a reduction in CSR starting in the third year (Fig. 2d). Patients with stage IV disease showed the most significant early improvement (from 66.3% to 90.0%), with the most pronounced gains occurring within the first two years (Fig. 2e). Patients with endophytic growth showed the most markedly improvement (from 71.6% to 87.1%) (Fig. 2f). Similar trends were observed for the CSR calculated from the NSR (**Supplementary Fig. 1**).

Multivariable analysis of factors affecting CSR

Table 3 shows the results of the multivariate Cox proportional hazards analyses using the OSR to identify prognostic factors for subsequent survival at baseline, 3 years, and 5 years. Landmark analyses were performed at 3 and 5 years to evaluate the prognostic factors for subsequent survival among patients who survived at each respective time point. At 0 years, age (≥ 65 years), sex (female), and clinical stage (stages II–IV) were identified as prognostic factors. At the 3-year mark, age (≥ 65 years), anatomical site (buccal and oral floor), and clinical stage (stages II–IV) were identified as prognostic factors. At 5 years, only age (≥ 65 years) was a prognostic factor. At the baseline landmark, age ≥ 65 years was associated with poorer survival. A significant association was observed at the 3- and 5-year time points. Regarding sex differences, women had a significantly lower hazard of death at baseline than men (adjusted hazard ratio [aHR], 0.66; 95% confidence interval [CI], 0.46–0.94; $p = 0.023$). However, no significant association was observed at the 3-year or 5-year landmarks. Among the primary tumor sites, tongue cancer showed a favorable prognosis. At the 3-year landmark, buccal and oral floor tumor sites were significantly associated with a higher hazard ratio (aHR, 2.97, $p = 0.004$ and aHR, 2.79, $p = 0.030$). At the 5-year landmark, neither the buccal nor oral floor tumor sites were significantly associated with subsequent survival (aHR, 1.24, $p = 0.681$ and aHR, 2.11, $p = 0.206$). Stages II–IV were significantly associated with poorer subsequent survival at the 3-year landmark. However, no significant association between clinical stage and subsequent survival was observed at the 5-year follow-up. No clinical proliferation pattern was identified as a prognostic factor.

Discussion

We attempted to clarify prognostic dynamics that cannot be captured by conventional evaluations by examining 5-year CSR. Few studies have used NSR [15, 19] or CSR in head and neck cancers [15, 20–23]. This study is the first to report the NSR and CSR of head and neck cancers in a Japanese population. To our knowledge, no study has conducted subgroup analyses based on sex, primary tumor sites, or growth patterns in Japanese population with head and neck cancer, underscoring our findings.

When comparing OSR and NSR, the impact of non-cancer deaths was pronounced in patients aged ≥ 65 years, with the difference in survival narrowing by approximately 7%. NSR reflects only cancer-specific deaths, whereas OSR includes all types of deaths. In older patients, cardiovascular diseases and age-related conditions increasingly contribute to non-cancer death, lowering OSR [5]. These findings align with the geriatric perspective that prognosis is influenced more by age-related conditions than by cancer itself [24]. Although NSR is expected to be higher than OSR, OSR occasionally exceeded NSR at some time points in the present study. This reversal may reflect differences in background mortality between the study and general populations used to estimate expected survival and statistical variability during long-term follow-up, particularly when the number of patients at risk becomes small. Therefore, the differences between OSR and NSR should be interpreted cautiously during later follow-ups. Previous studies of head and neck cancer have also demonstrated the utility of NSR for evaluating long-term outcomes [25]. Taken together, these findings suggest that NSR should be considered as a complementary measure to OSR, particularly when evaluating long-term survival in older patients with OSCC.

In this study, we dynamically captured temporal changes in prognosis by analyzing the 5-year CSR, which is useful for predicting the prognosis among long-term survivors. The clinical relevance of CSR in head and neck cancer has been increasingly recognized in recent years [15, 22, 26]. As CSR is heavily influenced by mortality during the initial period after diagnosis, early outcomes are strongly affected by factors such as tumor stage and comorbidities [27]. Our finding of a marked improvement in CSR during the early follow-up period supports this concept. Merrill et al. previously reported that the estimated 5-year CSR increased over time and eventually plateaued after approximately 5–10 years [28]. Other studies have similarly shown that mortality rates tend to stabilize after 3–4 years [20, 22]. Our findings were consistent with these previous observations, suggesting that the risk of cancer-related mortality decreases substantially among patients who survive the initial post-diagnosis period.

The CSR analysis yielded two important results. First, regardless of clinical stage, patients who survived the initial period after diagnosis demonstrated progressively improved prognosis over time. Moreover, the survival gap between advanced-stage (cStage III/IV) and early-stage (cStage I/II) disease narrowed from a difference of 26.0% at baseline to 2.7% at follow-up, consistent with those of previous reports [22]. This suggests that even patients with advanced-stage disease who survive the early post-treatment period may achieve favorable long-term outcomes. Therefore, these results highlight the importance of management during initial treatment [29] and support CSR in providing realistic prognostic information for long-term survivors.

Second, long-term prognosis varied according to the primary tumor site. Tongue cancer showed favorable outcomes, whereas maxillary gingival and palate cancers demonstrated variable survival outcomes, likely reflecting anatomical constraints and treatment complexity [30]. Because a limited number of patients with palate cancer were included, these findings should be interpreted cautiously, owing to limited statistical power. Buccal mucosa and floor of mouth cancers exhibited a more moderate improvement in prognosis over time than those of other oral cancer sites. Previous studies have reported relatively high recurrence rates for buccal mucosa cancer [31–33]. This may be explained by the anatomical characteristics of the buccinator muscle, which serves as the primary barrier to tumor extension. Once the tumor invades beyond the buccinator muscle into the buccal fat space, local spread and peripheral infiltration may occur more readily [32, 34]. Furthermore, preserving oral function is often challenging, and the complexity of the reconstructive surgery may negatively influence the treatment outcomes. Similarly, floor of mouth cancer is associated with a high risk of local recurrence, mandibular invasion, and cervical lymph node metastasis, necessitating prolonged surveillance [35]. The persistent risk of recurrence and treatment-related complications may contribute to the slower improvement in CSR observed at these sites. These findings reaffirm that the long-term prognosis of oral cancer differs substantially according to the primary tumor site and suggest the need for site-specific and individualized treatment strategies, particularly for buccal mucosa and floor of mouth cancers.

Sex-based analyses showed slightly poorer survival outcomes in men, consistent with previous studies [15, 36]. This difference may be associated with the higher prevalence of smoking and alcohol consumption in men. National surveys in Japan have reported substantially higher rates of alcohol

consumption and smoking among men than among women [37, 38]. In addition, men have been reported to exhibit a higher incidence of second primary tumors than women (5.5% vs. 3.4%) [39]. The sex-related difference in prognosis became less pronounced after approximately 3 years of follow-up, suggesting that the impact of sex on long-term survival may be limited. Similar trends have been reported in other head and neck cancers, where prognostic differences between sexes are thought to be primarily associated with early treatment response and treatment-related complications rather than with long-term disease control [2].

Clinical growth patterns showed differences in the survival outcomes. Although the endophytic type tended to exhibit a poorer prognosis, it did not reach statistical significance in the Cox proportional hazards model and was not identified as an independent prognostic factor. Previous studies have demonstrated a propensity for poor prognosis in the endophytic type [40], which is consistent with the results of the current study. This finding may have been influenced by potential confounding factors, such as differences in the primary tumor site, stage distribution, and treatment modalities. Therefore, the observed association should be interpreted with caution, and further investigation with a larger cohort and adjustment for confounding factors is required.

The incorporation of NSR and CSR into clinical practice may contribute to more individualized treatment strategies for oral cancer management. The NSR provides an estimate of cancer-related survival that accounts for expected mortality from causes other than cancer and may provide complementary information to the OSR, particularly in older patients and those with significant comorbidities. In addition, CSR provides dynamic prognostic information by demonstrating that survival probability may improve once the initial high-risk period has passed. This may support more realistic prognostic counseling and help guide patient expectations regarding the long-term survival. Furthermore, CSR-based risk trajectories may contribute to optimizing follow-up strategies by reducing unnecessary surveillance in patients whose risk declines over time while supporting prolonged monitoring in groups with persistently elevated risk or slower CSR recovery. Thus, the integration of the NSR and CSR may facilitate more personalized treatment planning, improve patient communication, and enhance shared decision-making.

This study has some limitations. First, patient comorbidities and systemic conditions before treatment were not evaluated adequately. Second, because this was a retrospective single-center study, institution-specific biases in patient characteristics and treatment strategies may have influenced our results. Third, the number of patients with certain primary tumor sites was limited, which may have reduced the statistical power of the site-specific analyses. In addition, recurrence and secondary primary tumors were not systematically assessed. Therefore, tumor-specific outcomes, such as disease-free survival, could not be sufficiently evaluated. Finally, the possibility of overfitting should be considered, particularly in later landmark analyses, where the number of patients and events was limited. Although multivariable Cox models were used to adjust for potential confounding factors, the limited number of events may have resulted in unstable estimates. In light of these limitations, further validation through multicenter collaborative studies and prospective investigations is required.

In conclusion, the integration of OSR, NSR, and CSR provides a more comprehensive and dynamic assessment of OSCC prognosis. NSR demonstrated that non-cancer-related mortality substantially influenced survival outcomes in older patients, whereas CSR revealed that prognosis improved over time among patients who survived the initial post-treatment period, even in advanced-stage disease. Furthermore, long-term prognostic patterns differed according to the primary tumor site, with buccal mucosa and floor of mouth cancers showing persistently slower recovery based on CSR. These findings suggest that dynamic survival measures, such as the NSR and CSR, may complement OSR analysis by providing more realistic prognostic information and supporting individualized follow-up and treatment strategies in patients with OSCC.

Declarations

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Competing interests

The authors declare that they have no competing interests.

Data availability statement

The datasets generated and/or analyzed in this study are not publicly available, but they are available from the corresponding author on reasonable request.

Ethics approval

The study was conducted in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki and its later amendments. Owing to the retrospective nature of this study, the requirement for informed consent was waived by the Ethics Committee of Kumamoto University. However, patients were allowed to refuse participation on an opt-out basis (RINRI1427).

Author contribution statement

KS and MH conceived this study. KS and KH performed the statistical analyses. KS and MH interpreted the results. KK, TY, HN, KY, SG, and YN acquired the clinical data. AH, RY, and HN supervised this study. All authors reviewed the manuscript draft and revised it critically to enhance the intellectual content. All authors have approved the final version of the manuscript to be published.

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Tables

Tables are available in the Supplementary Files section.

Figures

Figure 1

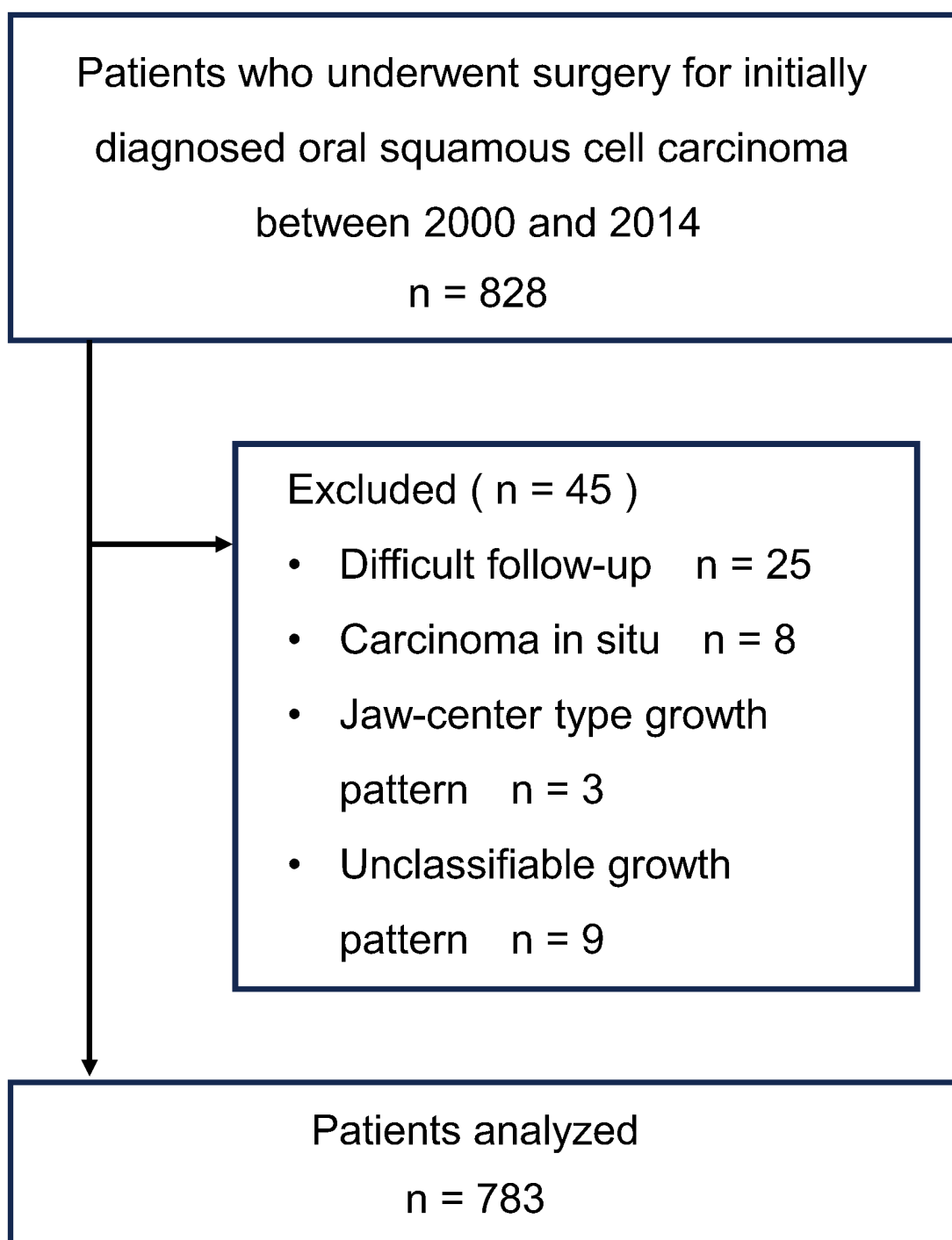
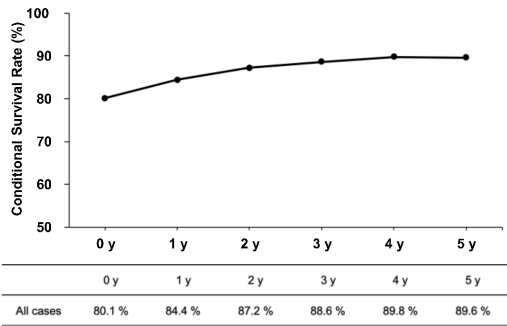


Figure 1

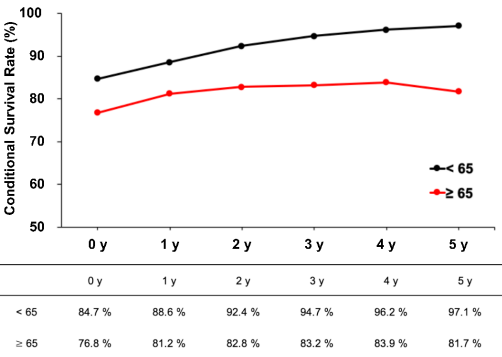
Study flowchart

Figure 2

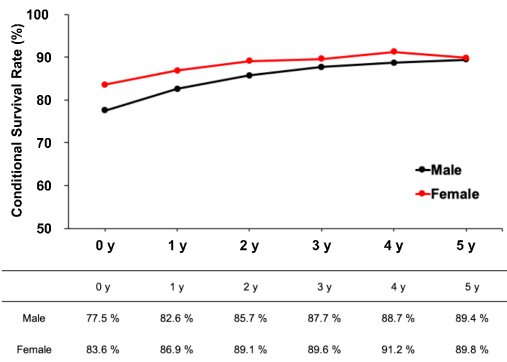
A All cases



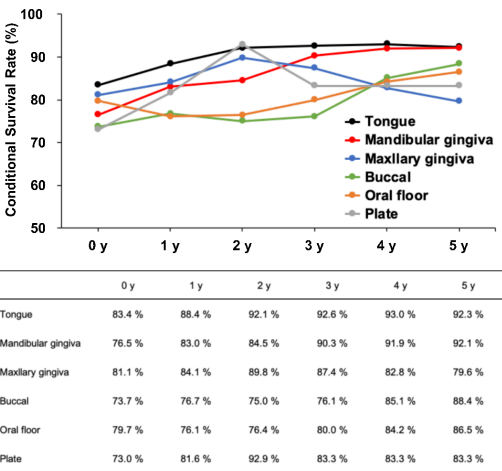
B Age



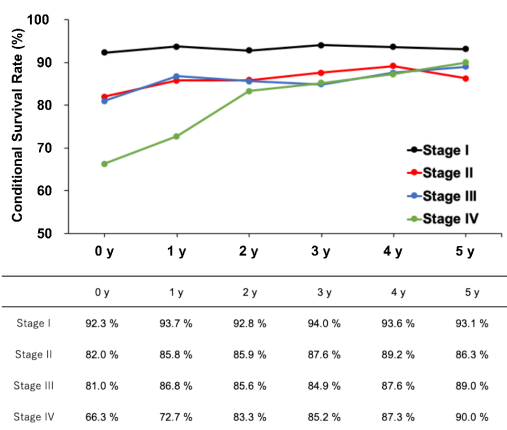
C Sex



D Primary tumor sites



E cStage



F Clinical growth pattern

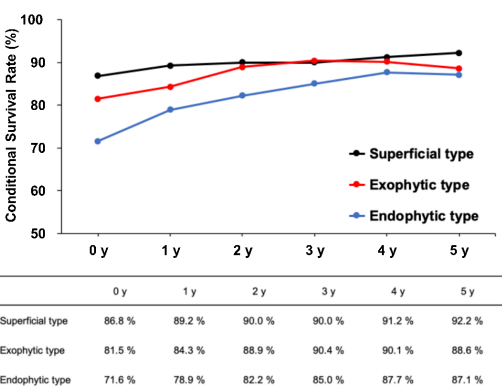


Figure 2

Conditional 5-year relative survival after diagnosis, based on the overall survival rate

Supplementary Files

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