

1 Original research

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3 Correlation between degree of bone invasion and prognosis in carcinoma of the mandibular
4 gingiva: soft tissue classification based on UICC classification

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18 Footnote:

19 Authors declare no conflict of interest.

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1 **Abstract**

2 Objective: The criteria for T4 staging of carcinoma of the mandibular gingiva are
3 controversial. Oral cancer staged as T4 implies “invasion to an adjacent organ,” such as the
4 skin, extrinsic muscles of the tongue, masticator space, or mandibular bone. In this study, we
5 compared different T classifications and retrospectively investigated the correlation between
6 each classification and the prognosis of patients with carcinoma of the mandibular gingiva.

7 Methods: We investigated 81 patients with squamous cell carcinoma of the mandibular
8 gingiva treated at two institutions.

9 Results: There was a significant correlation between soft tissue classification and local
10 recurrence ($P < 0.05$) and that the correlation with prognosis is borderline significant ($P =$
11 0.05).

12 Conclusions: Soft tissue classification, which does not consider bone invasion, was the most
13 useful for diagnosis, selecting the appropriate surgical procedure, and assessing the
14 correlation to prognosis. We recommended using this classification to define T4. Because this
15 classification is not new but is based on International Union Against Cancer classification, it
16 could be easily adopted. However, the current study is a retrospective analysis of a small
17 number of patients. A multi-institutional, prospective study is necessary to determine the
18 appropriate criteria for the TNM staging of carcinoma of the mandibular gingiva.

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20 Key words: Carcinoma of mandibular gingiva; Oral cancer; UICC classification; T
21 classification; Bone invasion

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1 **1. Introduction**

2 The T4 criteria for carcinoma of the mandibular gingiva are challenging and
3 controversial. Oral cancer staged as T4 implies “invasion to an adjacent organ” such as the
4 skin, extrinsic muscles of the tongue, masticator space, or mandibular bone [1]. Carcinoma of
5 the mandibular gingiva originates from the gingiva, which is located just above the
6 mandibular bone. Unlike other oral cancers, carcinoma of the mandibular gingiva can easily
7 invade to the mandibular bone. Because the mandibular bone is adjacent to the mandibular
8 gingiva, a small carcinoma of the mandibular gingiva (such as T1 or T2) could unexpectedly
9 be potentially classified as T4. This phenomenon is inadequate for the concept of T
10 classification because such tumors are not suitable for the classical T classification system.
11 Consequently, various T4 criteria and T classifications have been reported for bone invasion
12 in carcinoma of the mandibular gingiva. The International Union Against Cancer (UICC) has
13 defined T4 cancer with bone invasion as invasion to the cortical bone [1]. The Japan Society
14 for Oral Tumors (JSOT) has defined T4 cancer with bone invasion as invasion to the
15 mandibular canal [2-6]. This T4 criterion is based on a multicenter retrospective study of 1187
16 cases from 24 institutions of the Department of Oral Surgery. In Japan, many oral surgeons
17 have applied this T4 criterion [5,6]. In recent years, Ebrahimi et al. [7] recommended revising
18 the T staging system such that tumors are classified as T1–T3 based on size and are then
19 upgraded by one T stage in the presence of medullary bone invasion. In addition, some
20 reports have suggested that tumor size is well correlated with adverse prognosis, and that
21 bone invasion is not an independent predictor of survival [8-10]. As seen above, there are still
22 no universally accepted criteria to define T4 for cancer of the mandibular gingiva.

23 In this study, we reconsidered the T4 criteria for carcinoma of the mandibular gingiva.
24 Therefore, we investigated the correlation between each T4 criterion and the prognosis of
25 patients with carcinoma of the mandibular gingiva.

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2. Patients and Methods

1 *2-1. Patients*

2 A total of 81 patients with carcinoma of the mandibular gingiva who had undergone
3 primary surgical excision with curative intent were retrospectively assessed. Of these, 53
4 patients visited the Department of Oral and Maxillofacial Surgery, Nagasaki University
5 Hospital (Nagasaki, Japan), between 2001 and 2013, and 28 patients attended the Department
6 of Oral and Maxillofacial Surgery, Kobe University Hospital (Kobe, Japan), between 2007
7 and 2012. The study cohort included patients with histologically confirmed diagnoses of
8 squamous cell carcinoma and a minimum follow-up of 12 months. Inoperable cases which
9 patients have distant metastasis and hesitated to consent to surgical intervention were
10 excluded.

11 Overall survival (OS) and disease-specific survival (DSS) were calculated from the
12 time of initial examination to the time of death or the time of last follow-up. Local control
13 (LC) was calculated from the time of initial examination to the time of local disease
14 recurrence or the last follow-up.

15 This study is approved by the ethics committees of the Nagasaki University Hospital.

16 *2-2. Surgical procedure*

17 TNM classification was defined using inspection, palpation, and some imaging findings
18 like Panorama X-ray, computed tomography (CT), magnetic resonance imaging (MRI), and
19 ultrasonic echo. The oral surgeons made a final clinical TNM diagnosis by reference to
20 radiologist's findings. Surgical procedure was depends on TNM classification. The extent of
21 resection was decided considering from above the clinical elements. In all cases, ≥ 15 mm
22 safety margin far from tumor was fundamentally set both the bone and soft tissue. Thereby,
23 marginal or segmental resections were consequently chose. All patients underwent surgery
24 with curative intent. Elective neck dissection was not performed routinely in our institutions.

25 *2-3. T4 criteria*

1 UICC defines that T4a is moderately advanced local disease prescribed as tumor
2 invades adjacent structures (e.g., through cortical bone, into extrinsic muscle of tongue like
3 genioglossus, hyoglossus, palatoglossus, and styloglossus, and skin of face). And T4b is very
4 advanced local disease prescribed as tumor invades masticator space, pterygoid plates, or
5 skull base, and/or encases internal carotid artery.

6 The T4 criteria described by UICC, JSOT, Ebrahimi et al., and soft tissue classification were
7 evaluated [1-7]. The T4 criteria required by each classification system are listed in Table 1.
8 Each classification system is fundamentally based on the UICC TNM classification [1], with
9 differences mainly regarding the degree of bone invasion. JSOT defined T4 as invasion to the
10 mandibular canal [2-6]; Ebrahimi et al. [7] classified it as T1–T3 according to UICC
11 classification, followed by an upgrade of one T stage in the presence of medullary bone
12 invasion. The soft tissue T4 criteria do not consider the contribution of bone invasion. These
13 T4 criteria were re-classified from the aspect of bone invasion. Two oral surgeons and a
14 radiologist decided the grade of bone invasion using panoramic X-ray pictures and CT
15 images.

16 *2-4. Statistical analysis*

17 Statistical analyses were performed using StatMate IV (ATMS Co., Tokyo, Japan). The
18 significance of categorical data was assessed using χ^2 tests or Fisher's exact tests, as
19 appropriate. DSS and LC were calculated using the Kaplan–Meier method, and significance
20 was evaluated using the log-rank test. $P < 0.05$ was considered significant.

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1 **3. Results**

2 *3-1. Patient characteristics*

3 Demographics of the patient cohort are summarized in Table 2. The male-to-female
4 ratio was 0.88, with 38 male subjects. The mean age at diagnosis was 69.4 years (range, 36–
5 92 years). Marginal resection was performed in 40 (49.4%) cases and segmental resection in
6 41 (50.6%). Local recurrence occurred in 18 (22.2%) patients during the follow-up period.
7 Five-year OS was 74.2%, and 5-year DSS was 83.1%. The mean follow-up period was 40.8
8 months for the entire patient series (range, 1–119 months).

9 Sixty-five patients were classified as UICC T4 (80.2%), whereas 29 (35.8%) patients
10 were classified as JSOT T4. According to the criteria described by Ebrahimi et al., 29 (35.8%)
11 patients had T4 cancer, while according to soft tissue classification, 17 (21.0%) had T4 cancer.

12 *3-2. Correlation between T4 criteria and type of surgical resection*

13 When T4 cases were compared with T1–T3 cases, segmental resection was
14 significantly more common in T4 cases (regardless of classification). However, segmental
15 resection was performed in only 60.0% of UICC T4 cases compared with >85% of T4 cases
16 according to the other three classifications (Table 3).

17 *3-3. Correlation between T4 criteria and pathological nodal status*

18 In our cases, total 31 patients had pathological nodal metastasis. Lymph node
19 metastasis cases had a significant relationship with OS and DSS ($P < 0.05$). Considering the
20 relationship between each T classification and lymph node metastasis, the rates of lymph node
21 metastasis of each T4 were from 35.3% to 44.8% (Table 4). There were no significant
22 relations each T4 criteria and lymph node metastasis. These results indicated that it was able
23 to compare the relationship between each T4 criteria and prognosis.

24 *3-4. Correlation between T4 criteria and prognosis*

25 We next evaluated OS, DSS, and LC among the different T4 classifications. In patients

1 with T4 cancer according to UICC classification, OS was 73.9% compared with 78.8% in
2 patients with T1–T3 cancer. According to JSOT classification, OS was 70.3% in patients with
3 T4 cancer compared with 75.4% in patients with T1–T3 cancer. Using classification described
4 by Ebrahimi et al., OS was 77.4% in patients with T4 cancer compared with 73.1% in patients
5 with T1–T3 cancer. Finally, OS was 67.6% in T4 cases and 76.7% in T1–T3 cases according
6 to soft tissue classification (Figure 1).

7 Using UICC classification, DSS was 82.8% in patients with T4 cancer compared with
8 84.0% in patients with T1–T3 cancer. According to JSOT classification, DSS was 82.1% in
9 T4 cases and 83.3% in T1–T3 cases. According the classification system described by
10 Ebrahimi et al., DSS was 80.4% and 84.6% in T4 and T1–T3 cases, respectively. Finally,
11 according to the soft tissue classification system, DSS was 67.6% in patients with T4 cancer
12 compared with 87.2% in those with T1–T3 cancer (Figure 2). There was no significant
13 difference between OS and DSS in patients with T4 cancer compared with those with T1–T3
14 cancer using any classification system. However, DSS in soft tissue T4 cases, which did not
15 consider bone invasion, had a trend toward unfavorable prognosis ($P = 0.05$).

16 LC in UICC cases T4 was 75.8% compared with 72.2% in T1–T3 cases. LC in JSOT
17 T4 cases was 68.7% compared with 78.3% in T1–T3 cases. Using classification described by
18 Ebrahimi et al., LC was 62.8% in T4 cases and 78.3% in T1–T3 cases. Soft tissue T4 cases
19 exhibited a LC of 57.9% compared with that of 79.8% in T1–T3 cases (Figure 3). There was
20 no significant difference in LC between T4 and T1–T3 using the UICC and JSOT
21 classifications. In contrast, tumors classified as T4 by classification described by Ebrahimi et
22 al. and soft tissue classification recurred significantly more frequently. Moreover, considering
23 the detail of the soft tissue classification, invasion to the skin of face was not associated with
24 bad prognosis. In fact, when cases in which invasion to the exterior skin was observed were
25 excluded from the soft tissue classification, 5-year DSS of the soft tissue classification was

1 significantly worse in T4 (62.6%) cases than in T1–T3 (77.2%) cases ($P = 0.02$). Therefore,
2 soft tissue T4 tumors that invade to the interior or posterior organs had worse prognosis.

3 *3-5. Recurrence and prognosis*

4 We compared OS and DSS between cases with and without local recurrence. Data
5 revealed that prognosis was significantly worse in patients who experienced recurrence ($P =$
6 0.05).

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1 **4. Discussion**

2 Several institutions of the Department of Oral Surgery in Japan adopt the JSOT T4
3 criteria [3,6] because the UICC T4 criteria seem inadequate. Carcinoma of the mandibular
4 gingiva originates from the gingiva, which is located just above the mandibular bone.
5 Therefore, it can more easily invade to the bone marrow compared with other head and neck
6 cancers. In our patient cohort, >80% of cases were classified as T4 when the UICC criteria
7 were applied. Hence, the UICC classification system is inadequate because of an imbalance in
8 the T distribution.

9 Muvke et al. [11] identified bone invasion by postoperative histopathological analysis
10 in 15.5% of patients in whom bone invasion could not be diagnosed preoperatively.
11 Furthermore, Mohammad et al. [12] compared the diagnostic accuracy of cone-beam
12 computed tomography (CT) and panoramic radiography for assessing mandibular invasion by
13 lower gingival carcinoma using postoperative histopathological findings. The mean
14 sensitivity for cone-beam CT was 89% compared with that of 73% for panoramic radiography.
15 Taken together, these studies suggest that carcinoma of the mandibular gingiva with bone
16 invasion is more common than expected; therefore, the preoperative diagnosis of bone
17 invasion using UICC classification is difficult.

18 Some studies reported that cancer cells extended along the inferior alveolar nerve when
19 carcinoma infiltrated the mandibular canal [13]. Therefore, segmental mandibulectomy or
20 hemimandibulectomy was performed such patients [14]. However, many other reports
21 suggested that oral squamous cell carcinoma rarely extended along the nerve [15-20].
22 Histopathologically, carcinoma of the mandibular gingiva is divided into the following two
23 types: expansive and infiltrative [20-22]. The mechanism underlying this carcinoma has not
24 been well elucidated. Nevertheless, it is possible that a specific cell-adhesion factor exists that
25 adheres to nerves more readily. Although further studies are needed to analyze this, there is

1 little current evidence to support the implementation of the JSOT T4 criteria for bone
2 invasion.

3 To further explore local recurrence, we evaluated the specific regions of recurrence.
4 The rate of local recurrence was higher in tumors that invaded adjacent soft tissues compared
5 with those without local invasion. Most instances of recurrence were from the soft tissues of
6 organs adjacent to the mandible, particularly interior and posterior organs such as the
7 masticator space. Nomura et al. [16] reported that tumors recurred from the mucosa around
8 the resection margin after both marginal and segmental resection, and they suggested that
9 sufficient resection of soft tissue is important for preventing recurrence. Many other studies
10 reported that invasion of the mandibular bone was not related to outcomes among patients
11 with carcinoma of the mandibular gingiva [11, 23-26]. In general, superficial extent of
12 carcinoma in soft tissue is broader than that in bone from CT or MRI images. Then, when the
13 surgical margin was decided considering soft tissue, it is more likely to be able to remove the
14 tumor in mandibular bone consequently. Moreover, it is easy to decide surgical margin in
15 bone because of form of mandible. Mucke et al. [11] reported that cancer recurrence was
16 associated with OS, which is consistent with the current study. It is important to control local
17 recurrence from the adjacent soft tissue rather than the bone.

18 Summarizing the four different classifications, the UICC and JSOT T4 criteria are
19 strongly related to bone invasion because tumors are classified as T4 when they invade to the
20 bone marrow or the mandibular canal. Ebrahimi et al.'s classification is moderately related to
21 bone invasion because the tumor upgrade of one T stage in the presence of medullary bone
22 invasion. In contrast, soft tissue T4 classification is unrelated to bone invasion. In the present
23 study, UICC- and JSOT T4-related bone invasion had no effect on OS, DSS, and LC. In
24 contrast, the Ebrahimi et al. T4, which diminished the influence of bone invasion, had no
25 effect on OS or DSS but lead to significant decreases in LC. Soft tissue T4, which does not

1 consider bone invasion, had an almost significant relationship with DSS and lead to
2 significant decreases in LC. Therefore, it is more important to consider the surgical margin in
3 soft tissue than in bone though we must not ignore the factor of bone invasion.

4 The UICC defines T4 as invasion to an adjacent organ. It is possible to adopt the bone
5 invasion criterion to the T4 criteria for other oral cancers such as cancers of the tongue, oral
6 floor, and buccal mucosa. However, carcinoma of the mandibular gingiva differs from other
7 oral cancers because it can easily invade to the bone marrow because of the thin gingiva.
8 Specifically, it is inadequate to regard the mandibular gingiva and the mandibular bone as
9 different organs; although they are histologically different tissues, they are anatomically the
10 same organ. As such, soft tissue classification evaluated in the present study is not a new
11 classification but is based on the UICC classification. Various reports including the current
12 study have demonstrated the importance of considering controlling recurrence in soft tissue. It
13 is unnecessary to develop a new classification; instead, the current, well-defined UICC
14 classification should be expanded; it has distinct advantages and disadvantages.

15 TNM staging directly affects treatment strategy and the prediction of prognosis. T4 is
16 strongly correlated with segmental resection compared with T1–T3. However, when only
17 UICC T4 cases were evaluated in the current study, segmental resection was performed in
18 only 60.0%. UICC T classification is inadequate when deciding treatment strategy. For
19 predicting prognosis, each classification was unrelated to OS and DSS. However, soft tissue
20 classification was almost significantly related to DSS and significantly related to local
21 recurrence. The soft tissue T4 criterion, which is UICC T4 without bone invasion, was the
22 most effective for defining T4.

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1 **5. Conclusions**

2 The present study suggests that there is no relationship between bone invasion and
3 prognosis, and that T classification should be reconsidered. Because of long-term use of
4 UICC classification, we recommend modifying UICC classification to the soft tissue
5 classification for carcinoma of the mandibular gingiva. However, the current study is a
6 retrospective analysis of a small number of patients. As such, a multi-institutional, prospective
7 study is necessary to determine the appropriate criteria for the TNM staging of carcinoma of
8 the mandibular gingiva.

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1 **References**

- 2 [1] Sobin LH, Gospodarowicz MK, Wittekind C, eds. TNM classification of malignant
3 tumors, 7th edition. New York: Wiley-Blackwell; 2009.
- 4 [2] Fujibayashi T, Kanda S, Ohashi Y, Sasaki T, Imai Y, Gotoh S. The controversial point in
5 T classification of gingival carcinomas. *Head and Neck Cancer* 1999; 25: 453-460.
- 6 [3] Sasaki T, Imai Y, Fujibayashi T. Nes proposal for T classification of gingival carcinomas
7 arising in the maxilla. *Int J Oral Maxillofac Surg* 2004; 33: 349-352.
- 8 [4] Tei K, Totsuka Y, Iizuka T, Ohmori K. Marginal resection for carcinoma of the
9 mandibular alveolus and gingiva where radiologically detected bone defects do not extend
10 beyond the mandibular canal. *J Oral Maxillofac Surg* 2004; 62: 834-839.
- 11 [5] Omura K. Current status of oral cancer treatment strategied: surgical treatments for oral
12 squamous cell carcinoma. *Int J Clin Oncol* 2014; 19: 423-430.
- 13 [6] Izumo T, Kirita T, Ariji E, Ozeki S, Okada N, Okabe S, et al. General Rules for Clinical
14 and Pathological Studies on Oral Cancer: A Synopsis. *Jpn. J. Clin. Oncol* 2012; 42:
15 1099-1109.
- 16 [7] Ebrahimi A, Murali R, Gao K, Elliott MS, Clark JR. The Prognostic and Staging
17 Implications of Bone Invasion in Oral Squamous Cell Carcinoma. *Cancer* 2011; 117:
18 4460–4467.
- 19 [8] Platz H, Fries R, Hudec M, Tjoa AM, Wagner RR. The prognostic relevance of various
20 factors at the time of the first admission of the patient: retrospective DOSAK study on
21 carcinoma of the oral cavity. *J Maxillofac Surg* 1983; 11: 3-12.
- 22 [9] Overholt SM, Eicher SA, Wolf P, Weber RS. Prognostic factors affecting outcome in
23 lower gingival carcinoma. *Laryngoscope* 1996; 106: 1335-1339.
- 24 [10] Soo KC, Spiro RH, King W, Harvey W, Strong EW. Squamous carcinoma of the
25 gums. *Am J Surg* 1988; 156: 281-285.

- 1 [11] Mücke T, Hölzle F, Wagenpfeil S, Wolff KD, Kesting M. The role of tumor
2 invasion into the mandible of oral squamous cell carcinoma. *J Cancer Res Clin Oncol*
3 2011; 137: 165–171.
- 4 [12] Momin MA, Okochi K, Watanabe H, Imaizumi A, Omura K, Amagasa T, et al.
5 Diagnostic accuracy of cone-beam CT in the assessment of mandibular invasion of lower
6 gingival carcinoma: Comparison with conventional panoramic radiography. *Eur J Radiol*
7 2009; 72: 75–81.
- 8 [13] Zupi A, Mangone GM, Piombino P, Califano L. Perineural invasion of the lower
9 alveolar nerve by oral cancer: A follow-up study of 12 cases. *J Craniomaxillofac Surg*
10 1998; 26: 318-321.
- 11 [14] Totsuka Y, Usui Y, Tei K, Kida M, Mizukoshi T, Notani K, et al. Results of
12 surgical treatment for squamous carcinoma of the lower alveolus: Segmental vs. marginal
13 resection. *Head Neck* 1991; 13: 114-120.
- 14 [15] Marchetta FC, Sako K, Murphy JB. The periosteum of the mandible and intraoral
15 carcinoma. *Am J Surg* 1971; 122: 711-713.
- 16 [16] Nomura T, Shibahara T, Cui NH, Noma H. Patterns of mandibular invasion by
17 gingival squamous cell carcinoma. *J Oral Maxillofac Surg* 2005; 63: 1489-1493.
- 18 [17] O'Brien CJ, Adams JR, McNeil EB, Taylor P, Laniewski P, Clifford A, et al.
19 Influence of bone invasion and extent of mandibular resection on local control of cancers
20 of the oral cavity and oropharynx. *Int J Oral Maxillofac Surg* 2003; 32: 492-497.
- 21 [18] Pandey M, Rao LP, Das SR, Mathews A, Chacko EM, Naik BR. Patterns of
22 mandibular invasion in oral squamous cell carcinoma of the mandibular region. *World J*
23 *Surg Oncol* 2007; 5: 12-17.

- 1 [19] Rao LP, Das SR, Mathews A, Naik BR, Chacko E, Pandey M. Mandibular invasion
2 in oral squamous cell carcinoma: investigation by clinical examination and
3 orthopantomogram. *Int J Oral Maxillofac Surg* 2004; 33: 454-457.
- 4 [20] Shaw RJ, Brown JS, Woolgar JA, Lowe D, Rogers SN, Vaughan ED. The influence
5 of the pattern of mandibular invasion on recurrence and survival in oral squamous cell
6 carcinoma. *Head Neck* 2004; 26: 861-869.
- 7 [21] Wong RJ, Keel SB, Glynn RJ, Varvares MA. Histological pattern of mandibular
8 invasion by oral squamous cell carcinoma. *Laryngoscope* 2000; 110: 65-72.
- 9 [22] Brown JS, Lowe D, Kalavrezos N, D'Souza J, Magennis P, Woolgar J. Patterns of
10 invasion and routes of tumor entry into the mandible by oral squamous cell carcinoma.
11 *Head Neck* 2002; 24: 370-383.
- 12 [23] Ash CS, Nason RW, Abdoh AA, Cohen MA. Prognostic implications of mandibular
13 invasion in oral cancer. *Head Neck* 2000; 22: 794-798.
- 14 [24] Dubner S, Heller KS. Local control of squamous cell carcinoma following marginal
15 and segmental mandibulectomy. *Head Neck* 1993; 15: 29-32.
- 16 [25] Pandey M, Rao LP, Das SR, Shukla M. Tumor stage and resection margins not the
17 mandibular invasion determines the survival in patients with cancers of oro-mandibular
18 region. *Eur J Surg Oncol* 2009; 35: 1337-1342.
- 19 [26] Patel RS, Dirven R, Clark JR, Swinson BD, Gao K, O'Brien CJ. The prognostic
20 impact of extent of bone invasion and extent of bone resection in oral carcinoma.
21 *Laryngoscope* 2008; 118: 780-785.

22 **Figure legends**

23 Figure 1.

1 Comparison of Kaplan–Meier curves for 5-year overall survival of T4 and T1–T3 tumors. A,
2 UICC classification; B, JSOT classification; C, Ebrahimi’s classification; D, soft tissue
3 classification.

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5 Figure 2.

6 Comparison of Kaplan–Meier curves for 5-year disease-free survival of T4 and T1–T3 tumors.
7 A, UICC classification; B, JSOT classification; C, Ebrahimi’s classification; D, soft tissue
8 classification.

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10 Figure 3.

11 Comparison of Kaplan–Meier curves for 5-year local control of T4 and T1–T3 tumors. A,
12 UICC classification; B, JSOT classification; C, Ebrahimi’s classification; D, soft tissue
13 classification.

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Fig. 1

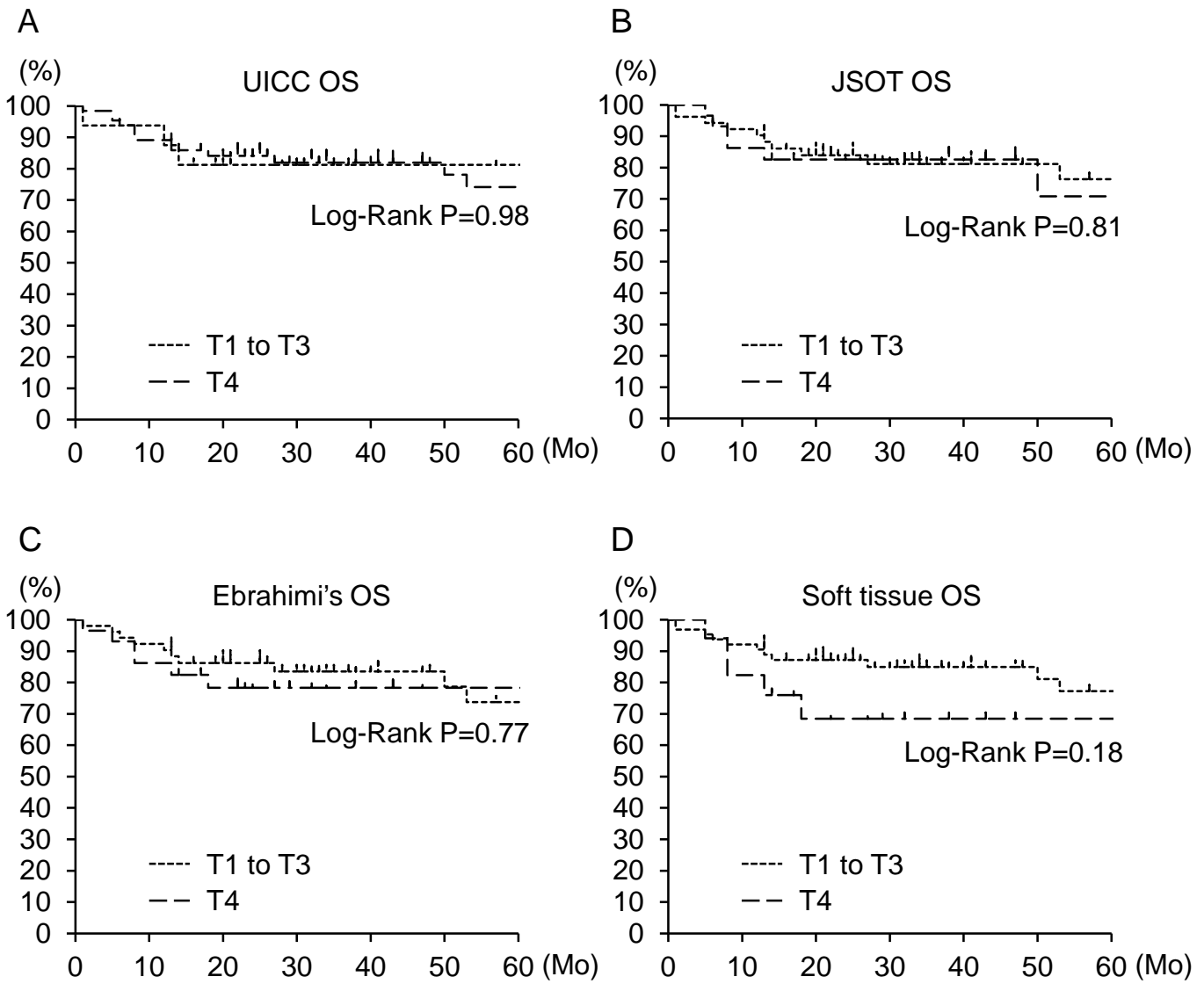


Fig. 2

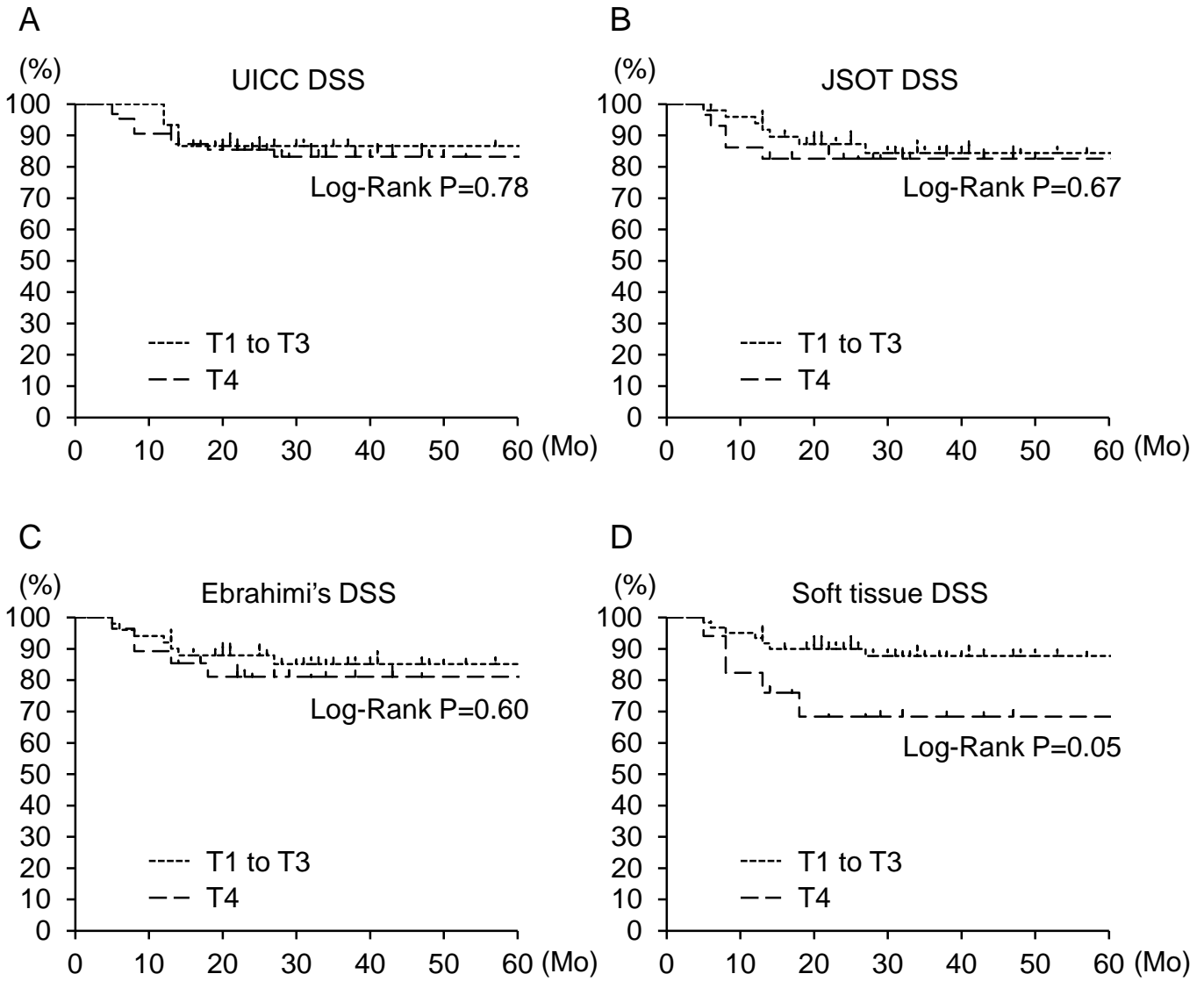


Fig. 3

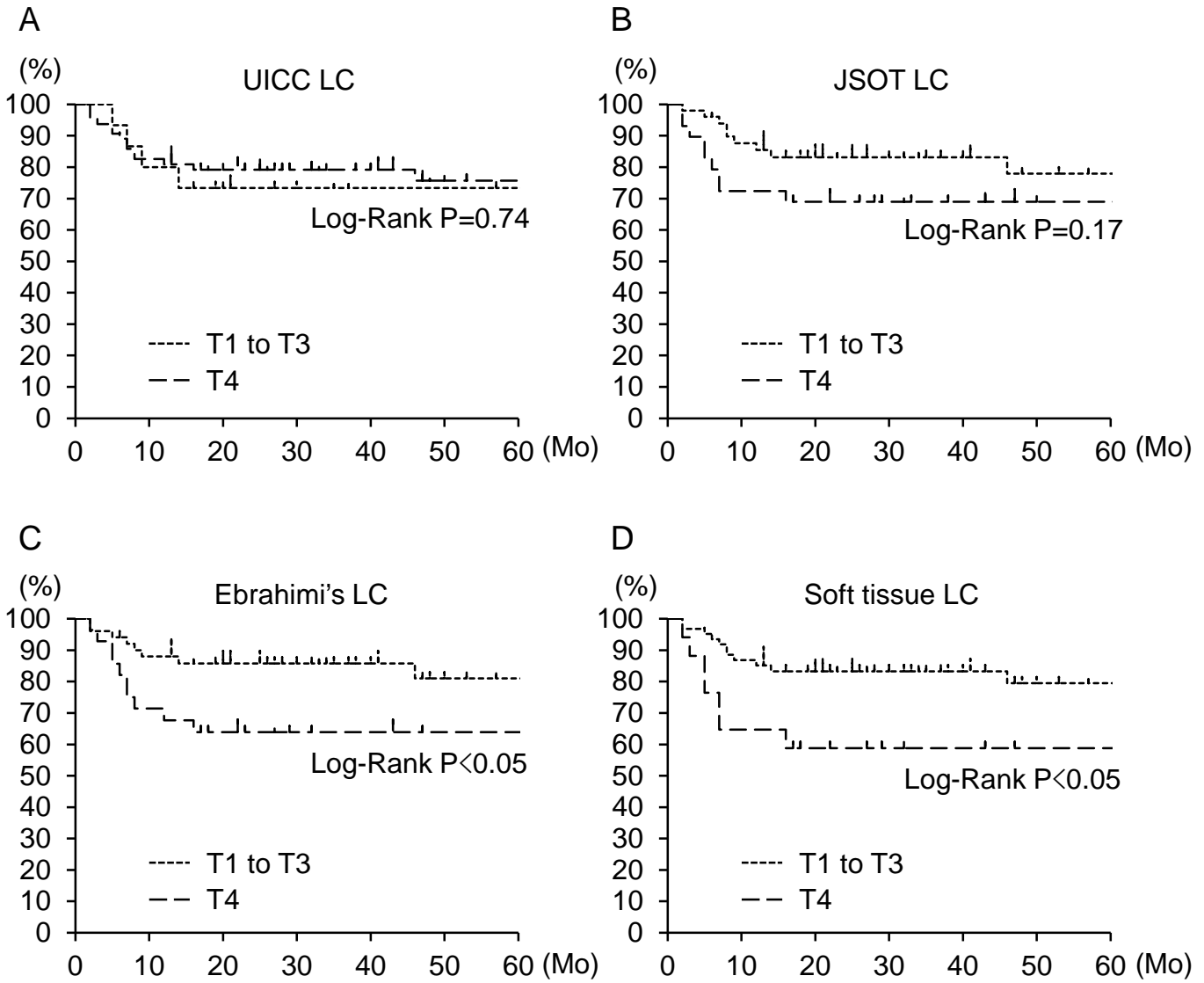


Table 1. Classification of each classifications

Classification	Feature
UICC	T4 of oral cancer means 'invasion to the adjacent organ', such as the skin, extrinsic muscles of the tongue, masticator space, or mandibular bone.
JSOT	Modified UICC classification: T4 about mandibular bone invasion means invasion to the mandibular canal
Ebrahimi et al.'s	Modified UICC classification: 1 T stage upstaged in the presence of medullary bone invasion.
Soft tissue	Another aspect of UICC classification: T4 means invasion to the adjacent organ except bone invasion

Table 2. Demographic characteristics of patients.

Characteristics	No. of cases(%)
Gender	
Male	38 (46.9)
Female	43 (53.1)
Age	
≥71	41 (50.6)
≤70	40 (49.4)
T4 criteria	
UICC	
T4	65 (80.2)
T1 to T3	16 (19.8)
JOST	
T4	29 (35.8)
T1 to T3	52 (64.2)
Ebrahimi et al's	
T4	29 (35.8)
T1 to T3	52 (64.2)
Soft tissue	
T4	17 (21.0)
T1 to T3	64 (79.0)
Resection type	
Marginal	40 (49.4)
Segmental	41 (50.6)
Local recurrence	
No	63 (77.8)
Yes	18 (22.2)
Overall survival	
Alive	66 (81.5)
Dead	15 (18.5)
Disease specific survival	
Alive	70 (86.4)
Dead	11 (13.6)

Table 3. Correlation between T4 criteria and surgical resection types.

		Marginal resection	Segmental resection	P value
UICC classification	T4	26	39	0.002
	T1-T3	14	2	
JSOT classification	T4	2	27	<0.001
	T1-T3	38	14	
Ebrahimi et al.'s classification	T4	4	25	<0.001
	T1-T3	36	16	
Soft tissue classification	T4	2	15	0.001
	T1-T3	38	26	

Table 4.

Rate of pathological nodal status among each T4.

	pN+	pN-	Total	Rate of pN+ (%)
UICC T4	25	40	65	38.5
JSOT T4	13	16	29	44.8
Ebrahimi T4	13	16	29	44.8
Soft tissue T4	6	11	17	35.3