Disease control using low-dose-rate brachytherapy is unaffected by comorbid severity in oral cancer patients

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Objective: The aim of this study was to evaluate the outcome and complications of low-dose-rate brachytherapy (LDR-BT) for oral cancer according to comorbidity.

Methods: The records of a total of 180 patients who received LDR-BT for T1-2N0M0 oral cancers between January 2005 and December 2007 were analysed. The comorbidities of the patients were retrospectively graded according to the Adult Comorbidity Evaluation-27, and the relationships between the comorbidity grades and survival, disease control and the incidence of complications were analysed.

Results: The 2 year overall survival rates of patients with no comorbidity, Grade 1, Grade 2 and Grade 3 comorbidity were 87%, 85%, 76% and 65%, respectively, and the reduction in the survival rate according to comorbid severity was significant in a univariate analysis ($p=0.032$) but not in a multivariate analysis including other clinical factors. Cause-specific survival, locoregional control and local control were not related to the comorbidity grade, or any other clinical factors. Grade 2 or 3 complications developed in 27% of the patients. The incidence of complications was unrelated to the comorbidity grade.

Conclusion: The disease control of oral cancer and the incidence of complications after LDR-BT were not related to comorbid severity. LDR-BT is a useful and safe treatment for patients regardless of the presence of severe comorbidity.

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Surgery is a major modality for the treatment of head and neck cancer. However, many head and neck cancer patients are older people and have significant medical comorbidities [1]. Pre-treatment comorbidities, such as cardiovascular and respiratory disease, sometimes impair patients' post-operative recovery, and patients with severe comorbidity have an increased risk of operative death or death from head and neck cancer [2].

Radiotherapy is another major modality for the treatment of head and neck cancer that enables the preservation of structure and function. Low-dose-rate brachytherapy (LDR-BT) has played a particularly important role in the treatment of early oral cancer because it delivers a high radiation dose to a limited volume while sparing the surrounding tissues and yields results similar to those of surgery. Moreover, the patients' physical and mental stress levels are considered to be lower than those for surgery or external-beam radiotherapy (EBRT) because the LDR-BT sources are implanted under local anaesthesia and LDR-BT has a low incidence of complications [3–12]. Therefore, LDR-BT is performed at our institution even for the treatment of patients judged to be inoperable by surgeons or anaesthetists because of advanced age, severe comorbidity or any other reason.

Although various studies have shown that the comorbidity grade is a strong predictor of survival and disease control in patients who have undergone surgery, EBRT or combined therapy for head and neck cancer [1, 13–15], the influence of comorbidity on the outcome of LDR-BT has not been reported. In this study we evaluated the relationship between comorbidity and the outcome and complications after LDR-BT for oral cancer.

Methods and materials

Patients

Between January 2005 and December 2007, 180 patients with untreated T1-2N0M0 squamous cell carcinoma in the oral cavity underwent LDR-BT in the Department of Diagnostic Radiology and Oncology at Tokyo Medical and Dental University Hospital. The patients comprised 58 females and 122 males, ranging in age from 24 to 90 years (median age 64 years). The numbers of smokers, ex-smokers and non-smokers at the time of diagnosis were 62, 34 and 70, respectively; the history of smoking was unknown in 14 patients. The numbers of drinkers and non-drinkers were 89 and 77, respectively; the history of drinking was unknown in 14 patients. The Eastern Cooperative Oncology Group (ECOG) performance status (PS) was 0 in 115 patients, 1 in 45 patients, 2 in 16 patients, and 3 in 4 patients. Of the 180 patients in total, 122 had

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tongue cancer, 25 had cancer of the floor of the mouth, 13 had cancer of the buccal membrane, 13 had cancer of the gum, 2 had cancer of the lip, and 5 had cancer of the hard palate. According to the Union of International Cancer Control classification, the T stage was T1 in 61 patients and T2 in 119 patients.

The comorbidities of all the patients were retrospectively graded using the Adult Comorbidity Evaluation-27 (ACE-27), which included 27 different cogent comorbid ailments composed of various organ system disorders (such as cardiovascular, respiratory, gastrointestinal, renal, endocrine, neurological and immunological systems), psychiatric and rheumatological disorders, previous or coexistent malignancy, alcohol abuse and body weight. According to the degree of organ decompensation and the prognostic impact, comorbidity was divided into a three-category severity system defined as mild (Grade 1), moderate (Grade 2) or severe (Grade 3). The overall comorbidity grade was defined according to the highest ranked single comorbidity. In cases where two or more Grade 2 comorbidities occurred in different organ systems, the overall comorbidity score was designated as Grade 3 [1].

Treatment

The treatment policy and method of performing LDR-BT for oral cancer used at our institution have been described previously [3–9]. The usual dose prescribed for the treatment of tongue cancer with linear sources of caesium-137 or iridium-192 was 70 Gy over a period of 5–7 days, and the dose distribution was always calculated using computer dosimetry after implantation. The dose usually prescribed for other areas of the oral cavity was 80–90 Gy, achieved with the permanent implantation of gold-198, or 70 Gy over a period of about 7 days using mould therapy with gold-198. However, because the implantation of linear sources was more invasive than the implantation of grain sources, when patients with tongue cancer were clinically judged as being unable to withstand treatment with linear sources because of a poor activities of daily living score, they were treated with grain sources of gold-198. Patients with thick tumours were treated with EBRT at a dose of 30–40 Gy prior to LDR-BT, and the LDR-BT dose prescribed was about 90% of the dose prescribed in patients treated with LDR-BT alone. Chemotherapy was not combined with LDR-BT simultaneously.

Analysis

The median follow-up period for all patients after the start of LDR-BT was 26 months, and the range was from 2.2 to 54 months. The median follow-up period for the surviving patients without locoregional recurrence ($n=94$) was 27 months, and the range was 12–54 months.

The relations between comorbidity and clinical or treatment factors were analysed using a χ^2 test. The overall survival, cause-specific survival, locoregional control and local control were calculated using the Kaplan–Meier method, and the log-rank test was used for a univariate analysis of the relation between the survivals or disease controls and the comorbidity grade. These survivals or

disease controls and eight clinical factors (age, sex, smoking, alcohol, primary site, T stage, PS and comorbidity) were compared using the Cox proportional hazards test, and a p -value of <0.0064 was considered statistically significant in the multivariate analysis to obtain an overall significance level of 5% [16]. Complications were graded according to the Common Terminology Criteria for Adverse Events v4.0, and the relations between the rates of occurrence and clinical factors (age, sex, smoking, alcohol, primary site, T stage, PS and comorbidity) were analysed using logistic regression; a p -value of <0.0064 was considered to indicate a statistically significant difference in a multivariate analysis to obtain an overall significance level of 5% [16].

Results

Correlation between comorbidity grade and clinical factors

According to the ACE-27 grading, 52 patients (29%) were Grade 1, 34 patients (19%) were Grade 2, 8 patients (4%) were Grade 3, and 86 patients (48%) had no comorbidity. The relations between the comorbidity grade and the clinical factors are shown in Table 1. The comorbidity grade was significantly related to age, PS, primary site and LDR-BT source, respectively. The percentage of patients who were more than 65 years old among the patients with no comorbidity, Grade 1 comorbidity, Grade 2 comorbidity and Grade 3 comorbidity was 28%, 62%, 68% and 75%, respectively ($p<0.001$). The percentage of patients with a PS of 2 or 3 among the patients with no comorbidity, Grade 1 comorbidity, Grade 2 comorbidity and Grade 3 comorbidity was 0%, 10%, 29% and 63%, respectively ($p<0.001$). The difference in primary site according to comorbidity grade was significant ($p=0.015$), and the percentage of patients with tongue cancer among the patients with no comorbidity, Grade 1 comorbidity, Grade 2 comorbidity and Grade 3 comorbidity was 78%, 63%, 47% and 75%, respectively. The LDR-BT source was dependent upon the primary site, but the percentage of patients who were treated with gold-198 grains for tongue cancer among the patients with no comorbidity, Grade 1 comorbidity, Grade 2 comorbidity and Grade 3 comorbidity was 12%, 24%, 69% and 67%, respectively ($p<0.001$). The relationship between comorbidity grade and sex, smoking, alcohol, T stage or EBRT was not significant.

Survival

The 2 year overall survival rate and the cause-specific survival rate of all 180 patients were 83% and 87%, respectively. Between 2.2 and 41 months (median 17 months) after the start of LDR-BT, 36 patients died from oral cancer ($n=28$), other malignancies ($n=5$), benign disease ($n=2$) or an unknown cause ($n=1$).

According to the comorbidity grade, the 2 year overall survival rate and cause-specific survival rate were 87% and 88%, respectively, in patients with no comorbidity;

Table 1. Correlation between comorbidity group and clinical factors

	Grade of comorbidity according to ACE-27 (n)				p-value
	No	Grade 1	Grade 2	Grade 3	
Total	86	52	34	8	
Sex					
Female	31	18	6	3	0.249
Male	55	34	28	5	
Age (years)					
Range (median)	24–90 (57)	33–88 (71)	31–85 (72)	58–82 (69)	
≤65	62	20	11	2	<0.001
>65	24	32	23	6	
Smoking					
Smoker	33	15	10	4	0.849
Ex-smoker	14	11	7	2	
Non-smoker	34	20	14	2	
Unknown	5	6	3	0	
Alcohol					
Drinker	43	25	18	3	0.759
Non-drinker	38	21	13	5	
Unknown	5	6	3	0	
PS					
0	72	31	12	0	<0.001
1	14	16	12	3	
2	0	4	8	4	
3	0	1	2	1	
Primary site					
Tongue	67	33	16	6	0.018
Floor of the mouth	12	6	6	1	
Buccal membrane	2	7	4	0	
Gum	2	4	6	1	
Hard palate	2	1	2	0	
Lip	1	1	0	0	
T stage					
1	31	17	11	2	0.912
2	55	35	23	6	
LDR-BT source					
Au	27	27	29	6	<0.001
Cs	21	7	3	0	
Ir	38	18	2	2	
EBRT					
Yes	9	2	6	0	0.137
No	77	50	28	8	

ACE-27, Adult Comorbidity Evaluation-27; LDR-BT, low-dose-rate brachytherapy; PS, ECOG performance status; EBRT, external-beam radiotherapy.

85% and 86%, respectively, in patients with Grade 1 comorbidity; 76% and 85%, respectively, in patients with Grade 2 comorbidity; and 65% and 88%, respectively, in patients with Grade 3 comorbidity (Figure 1a,b). The overall survival rate decreased according to the severity of the comorbidities, and this tendency was significant in the univariate analysis ($p=0.032$) but not in a multivariate analysis including clinical factors ($p=0.914$). The cause-specific survival rate did not differ significantly according to the comorbidity grade in the univariate ($p=0.358$) or multivariate ($p=0.931$) analysis.

Although the overall survival rates or the cause-specific survival rates of younger patients, women, patients with T1 oral cancer, or patients with PS 0 were higher than those of elderly patients, men, patients with T2 oral cancer or patients with PS 1–3, respectively, the Cox proportional hazard test revealed that the overall survival and the cause-specific survival after LDR-BT were unaffected by any clinical factors (Table 2).

Disease control

The 2 year locoregional control rate and the local control rate of all 180 patients were 56% and 79%, respectively.

According to the comorbidity grade, the 2 year locoregional control rate and the local control rate were 58% and 77%, respectively, in patients with no comorbidity; 56% and 82%, respectively, in patients with Grade 1 comorbidity; 51% and 77%, respectively, in patients with Grade 2 comorbidity; and 75% and 100%, respectively, in patients with Grade 3 comorbidity (Figure 1c,d). A correlation between the locoregional control or the local control and the severity of the comorbidities was not found.

According to the primary site, the 2 year local control rate of patients with tongue cancer was 79% (74% in patients with no comorbidity, 87% in patients with Grade 1 comorbidity, 75% in patients with Grade 2 comorbidity and 100% in patients with Grade 3 comorbidity, $p=0.464$), that of patients with cancer of the floor of the mouth was 84% (92% in patients with no comorbidity,

Figure 1. (a) Overall survival, (b) cause-specific survival, (c) locoregional control and (d) local control according to absence and grade of comorbidity.

83% in patients with Grade 1 comorbidity, 67% in patients with Grade 2 comorbidity and 100% in patients with Grade 3 comorbidity, $p=0.609$), that of patients with cancer of the buccal membrane was 62% (100% in patients with no comorbidity, 57% in patients with Grade 1 comorbidity and 50% in patients with Grade 2 comorbidity, $p=0.566$), that of patients with cancer of the gum was 92%, that of patients with hard palate was 60% and that of patients with cancer of the lip was 100%.

No clinical factors were significantly related with the locoregional control or the local control (Table 3).

Survival after locoregional failure

Local recurrence was observed in 41 patients (20 (23%) with no comorbidity, 11 (21%) with Grade 1 comorbidity, 10 (29%) with Grade 2 comorbidity and 0 with Grade 3 comorbidity) during the follow-up period. The kind of salvage therapy used for local recurrence is shown according to the comorbidity grade in Figure 2a.

Although the overall survival after the diagnosis of local recurrence among patients with Grade 1 comorbidity, of whom 90% underwent salvage surgery or repeat LDR-BT, was much higher than that of patients with Grade 2 comorbidity, of whom 70% underwent salvage surgery or repeat LDR-BT, the difference in the overall survival after the diagnosis of local recurrence according to the comorbidity grade was not statistically significant (Figure 2b, $p=0.103$).

Cervical lymph node metastasis was observed in 63 patients (29 (34%) with no comorbidity, 19 (37%) with Grade 1 comorbidity, 13 (38%) with Grade 2 comorbidity and 2 (25%) with Grade 3 comorbidity). Neck dissection was performed in 25 (86%) patients with no comorbidity, 14 (74%) patients with Grade 1 comorbidity, 8 (62%) patients with Grade 2 comorbidity and 1 (50%) patient with Grade 3 comorbidity (Figure 2c). The reduction in the overall survival rate according to the severity of the comorbidities at 2 years was significant (Figure 2d, $p=0.012$).

A synchronous diagnosis of both local recurrences and cervical lymph node metastasis was made in 4 patients,

Table 2. Relation between overall and cause-specific survival and clinical factors

	Overall survival			Cause-specific survival		
	HR	95% CI	Multi- <i>p</i>	HR	95% CI	Multi- <i>p</i>
Age (years)						
≤65	1			1		
>65	1.605	0.697–3.694	0.266	1.665	0.624–4.437	0.308
Sex						
Female	1			1		
Male	1.771	0.781–4.017	0.171	1.045	0.341–3.199	0.939
Smoking						
Smoker	1			1		
Non-smoker	0.779	0.316–1.924		1.236	0.446–3.424	
Ex-smoker	0.509	0.175–1.478		0.482	0.131–1.775	
Unknown	0.502	0.101–2.480	0.595	0.285	0.031–2.589	0.342
Alcohol						
Drinker	1			1		
Non-drinker	0.669	0.271–1.655		0.369	0.125–1.091	
Unknown	–	–	0.385	–	–	0.072
Primary site						
Tongue	1			1		
Other oral cavity	1.012	0.479–2.139	0.975	0.994	0.421–2.348	0.988
TNM stage						
1	1			1		
2	1.511	0.674–3.385	0.316	1.664	0.645–4.295	0.292
PS						
0	1			1		
1	2.732	1.061–7.037		3.876	1.311–11.459	
2	2.582	0.780–8.545		2.327	0.534–10.146	
3	6.497	1.025–41.192	0.108	6.953	0.602–80.325	0.090
ACE-27						
No	1			1		
Grade 1	0.794	0.312–2.020		0.723	0.258–2.028	
Grade 2	1.121	0.403–3.121		0.951	0.299–3.024	
Grade 3	1.191	0.214–6.621	0.914	0.718	0.072–7.199	0.931

ACE-27, Adult Comorbidity Evaluation-27; CI, confidence interval; HR, hazard ratio; PS, ECOG performance status; multi-*p*, multi-variate *p*-value.

and a metachronous diagnosis was made in 14 patients. Distant metastases were found in 11 patients during the follow-up period, but none of these metastases were observed prior to the locoregional failure.

Complications

Grade 2 or 3 complications occurred in 49 patients between 3 and 43 months after the start of LDR-BT (median 10 months). The rate of occurrence of Grade 2 or 3 complications was 33% in patients with no comorbidity, 23% in patients with Grade 1 comorbidity, 19% in patients with Grade 2 comorbidity and 25% in patients with Grade 3 comorbidity. 51 Grade 2 complications developed in 44 patients (24%), and 4 Grade 3 complications developed in 4 patients (3%, Table 4). Three patients who had Grade 3 osteonecrosis of the jaw had received LDR-BT for tongue cancer; one of these patients who had no comorbidity developed this complication after salvage surgery for a local recurrence in the tongue, another patient who had no comorbidity developed this complication after gold-198 grains were implanted for the treatment of a second primary cancer in the lower gum, and one patient who had a Grade 1 comorbidity developed this complication after undergoing a neck dissection. One patient developed a Grade 3 fistula between the floor of the mouth and the skin after intra-arterial chemotherapy for cervical lymph

node metastasis was repeatedly performed. None of the differences according to comorbidity grade were significant, and none of the clinical factors influenced the incidence of complications (Table 5).

Discussion

The 5 year overall survival rate, cause-specific survival rate, locoregional control rate and local control rate of the patients who received LDR-BT for early oral cancer have been reported to be 46–95%, 76–95%, 67–70% and 70–93%, respectively, and the incidence of severe soft-tissue and bone complications after LDR-BT has been found to be 2.9–5% of patients with oral tongue cancer and 24% of patients with cancer of the floor of the mouth [3–5, 8–11, 17–19]. Prognostic factors for survival and tumour control reportedly include age, T stage and macroscopic appearance, while no clinical factors related to complications have been identified.

Although the correlation between comorbidity and survival or disease control has not yet been analysed among oral cancer patients treated with LDR-BT, comorbidity is known to be a strong predictor of survival among patients treated with surgery, EBRT or combined therapy. Patients with head and neck cancer often have accompanying medical problems, most notably in the cardiovascular and respiratory systems, and these problems are

Table 3. Relation between locoregional and local control and clinical factors

	Locoregional control			Local control		
	HR	95% CI	Multi- <i>p</i>	HR	95% CI	Multi- <i>p</i>
Age (years)						
≤65	1			1		
>65	1.410	0.823–2.416	0.211	2.106	0.940–4.720	0.070
Sex						
Female	1			1		
Male	1.381	0.788–2.419	0.260	1.004	0.444–2.271	0.992
Smoking						
Smoker	1			1		
Non-smoker	1.138	0.632–2.048		1.366	0.562–3.320	
Ex-smoker	0.699	0.358–1.366		0.755	0.268–2.128	
Unknown	0.636	0.236–1.716	0.490	1.313	0.402–4.285	0.711
Alcohol						
Drinker	1			1		
Non-drinker	0.774	0.433–1.384		0.490	0.199–1.209	
Unknown	–		0.387	–	–	0.122
Primary site						
Tongue	1			1		
Other oral cavity	0.888	0.537–1.470	0.645	1.004	0.482–2.092	0.991
TNM stage						
1	1			1		
2	1.194	0.734–1.943	0.474	1.377	0.663–2.858	0.391
PS						
0	1			1		
1	1.014	0.542–1.895		1.363	0.552–3.365	
2	1.547	0.650–3.682		4.480	1.450–13.844	
3	1.740	0.368–8.225	0.701	3.572	0.394–32.407	0.061
ACE-27						
No	1			1		
Grade 1	0.971	0.568–1.658		0.499	0.215–1.160	
Grade 2	0.987	0.492–1.978		0.460	0.163–1.298	
Grade 3	0.351	0.074–1.661	0.591	0.000	0	0.353

ACE-27, Adult Comorbidity Evaluation-27; CI, confidence interval; HR, hazard ratio; PS, ECOG performance status; multi-*p*, multi-variate *p*-value.

often related to smoking and alcohol consumption. Thus, such patients often have a high risk of adverse outcomes because cancer treatment can involve both complex operations and prolonged radiotherapy. The survival rate has been shown to exhibit a consistent downward trend from patients with no comorbidity to patients with severe comorbidity, and an increase in the number of comorbidities has also been associated with a high incidence of post-operative complications [1, 13, 14].

In this study, we used ACE-27 to grade the comorbidities. ACE-27 is a modification of the Kaplan–Feinstein index [20]. Recently, ACE-27 has become a common method for scoring comorbidity [21]. Moderate (Grade 2) or severe (Grade 3) comorbidities according to the ACE-27 criteria have been reported in 17–47% of all head and neck cancer patients [1, 13–15]. Borggreven et al [15] performed surgery in 100 patients (17%, grade 0; 36%, Grade 1; 34%, Grade 2; 13%, Grade 3) with Stage II–IV oral cavity or oropharyngeal cancer and reported that the 5 year overall survival rate of patients with grade 0–2 comorbidity was 64% and that of patients with Grade 3 comorbidity was 29% ($p=0.039$). Terhaard et al [21] also analysed 666 patients (64%, Grade 0; 19%, Grade 1; 12%, Grade 2; 5%, Grade 3) with cancer of the parotid gland, oral cavity, submandibular gland, pharynx or larynx treated with surgery, EBRT, combined therapy, chemotherapy or no therapy, and reported that not only overall survival but

also the disease-free survival period was significantly affected by the ACE-27 comorbidity grade. In our study, overall survival was significantly correlated with the comorbidity grade in a univariate analysis, but cause-specific survival, locoregional control and local control were not related to the comorbidity grade. Some patients with high comorbidity grades died from the comorbidity or associated disease. Moreover, while disease control from the start of LDR-BT until locoregional or local failure did not differ according to the comorbidity grade, after the occurrence of disease failure, a difference in survival according to the comorbidity grade (which was correlated with salvage therapy) was noted. The comorbidity grade was strongly correlated with age and PS, but none of the clinical factors affected survival or disease control in the multivariate analysis. This result may indicate that, because comorbidity is associated with several clinical factors including age and PS, the relation between overall survival and clinical factors including comorbidity was not significant in the multivariate analysis. However, because the locoregional control and local control after LDR-BT for oral cancer were unaffected by the severity of the comorbidities, LDR-BT appears to be a safe and useful treatment for patients with early tongue cancer regardless of the comorbidity grade.

Only a few reports have analysed the correlation between comorbidity and complications in head and neck

Figure 2. Salvage therapies for local recurrence (a) and overall survival after diagnosis of local recurrence according to absence and grade of comorbidity (b). Salvage therapies for lymph node metastasis (c), and overall survival after diagnosis of lymph node metastasis according to absence and grade of comorbidity (d). Ch, chemotherapy; EBRT, external-beam radiotherapy.

cancer treatment. Borggreven et al [15] reported that the comorbidity grade was a predictor of post-operative complications in head and neck cancer patients who had been treated surgically. Moreover, McGurk et al [2] reported that patients with pre-existing cardiovascular

disease had a 1.5-fold greater risk of developing major (life-threatening) and intermediate (hospital-stay-prolonging) post-operative complications, while patients with respiratory disease had a 1.8-fold greater risk of developing major and intermediate post-operative complications.

Table 4. Numbers of patients with complications according to comorbidity grade

CTCAE v4.0		Grade of comorbidity according to ACE-27 (n)			
Term	Grade	No	Grade 1	Grade 2	Grade 3
Mucositis oral	3	0	0	0	0
	2	24 (28%)	10 (24%)	5 (14%)	2 (25%)
	1	13 (15%)	13 (31%)	5 (14%)	0 (%)
Osteonecrosis of the jaw	3	2 (2%)	1 (2%)	0	0
	2	6 (7%)	1 (2%)	2 (6%)	1 (13%)
	1	0	0	0	0
Others	3	1 (fistula)	0	0	0
	2	0	0	0	0
	1	0	0	0	0

ACE-27, Adult Comorbidity Evaluation-27; CTCAE, Common Terminology Criteria for Adverse Events.

Table 5. Relation between incidence of Grade 2 or 3 complications and clinical factors

	OR	95% CI	Multi-p
Age (years)			
≤65	1		
>65	2.026	0.808–5.083	0.132
Sex			
Female	1		
Male	0.359	0.142–0.906	0.030
Smoking			
Smoker	1		
Non-smoker	1.160	0.429–3.138	
Ex-smoker	2.444	0.890–6.717	
Unknown	0.436	0.081–2.340	0.139
Alcohol			
Drinker	1		
Non-drinker	0.555	0.207–1.489	
Unknown	–	–	0.243
Primary site			
Tongue	1		
Other oral cavity	1.088	0.485–2.443	0.838
TNM stage			
1	1		
2	0.809	0.375–1.743	0.588
PS			
0	1		
1	1.755	0.653–4.718	
2	1.678	0.349–8.073	
3	0	0	0.735
ACE-27			
No	1		
Grade 1	0.405	0.165–0.995	
Grade 2	0.268	0.078–0.918	
Grade 3	0.360	0.046–2.803	0.113

CI, confidence interval; OR, odds ratio.

Ferrier et al [22] operated on 117 head and neck cancer patients whose comorbidities were graded according to ACE-27 (41%, Grade 0; 29.9%, Grade 1; 29.1%, Grade 2 or 3), and 21.4% of the patients in their series had major complications. Furthermore, the duration of anaesthesia and the comorbidity grade were significantly correlated with the incidence of complications according to a multivariate analysis. In patients treated with LDR-BT, the use of a spacer and computer dosimetry in patients with tongue cancer has been found to decrease the incidence of osteoradionecrosis of the mandible and soft-tissue complications. The use of a spacer and computer dosimetry is now performed routinely, and no clinical factors related to complications have been identified [3–11, 23, 24]. In our study, the incidence of complications was not correlated with the comorbidity grade.

The limitations of this study included the short follow-up period and the lack of an analysis of quality of life (QOL). Although cancer statistics generally cite 3 or 5 year survival rates, our outcome measures were the 2 year survival and disease control rates. Therefore, the disease control in patients with high comorbidity grades might be overvalued. However, because important post-treatment events, such as recurrence and cancer-related death, occur within the first 18 months after treatment in most cancer patients [1] and in view of our co-author's finding that most locoregional recurrences after LDR-BT for early tongue cancer occur within 2 years [25], a 2 year follow-up period was considered to be sufficient for

the analyses performed in this report. QOL has been increasingly used as an outcome parameter and must be given serious consideration when selecting a treatment [12]. The QOL of oral cancer patients treated with LDR-BT is relatively high whereas the QOL after surgery or EBRT is immediately reduced, and changes in only a few functions and symptoms after LDR-BT have been discovered to be affected by T stage, tumour site and complications. In this study, because comorbidity was not strongly correlated with the T stage or incidence of complications, we suspect that the change in QOL after LDR-BT for oral cancer was unaffected by the severity of the comorbidities.

Conclusion

The comorbidity grade of early oral cancer patients was strongly correlated with age and PS, and the severity of the comorbidities was related to overall survival but was not related to cause-specific survival, locoregional control, local control or the incidence of complications. LDR-BT is a safe and useful treatment for patients with early oral cancer regardless of the presence of severe comorbidity.

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