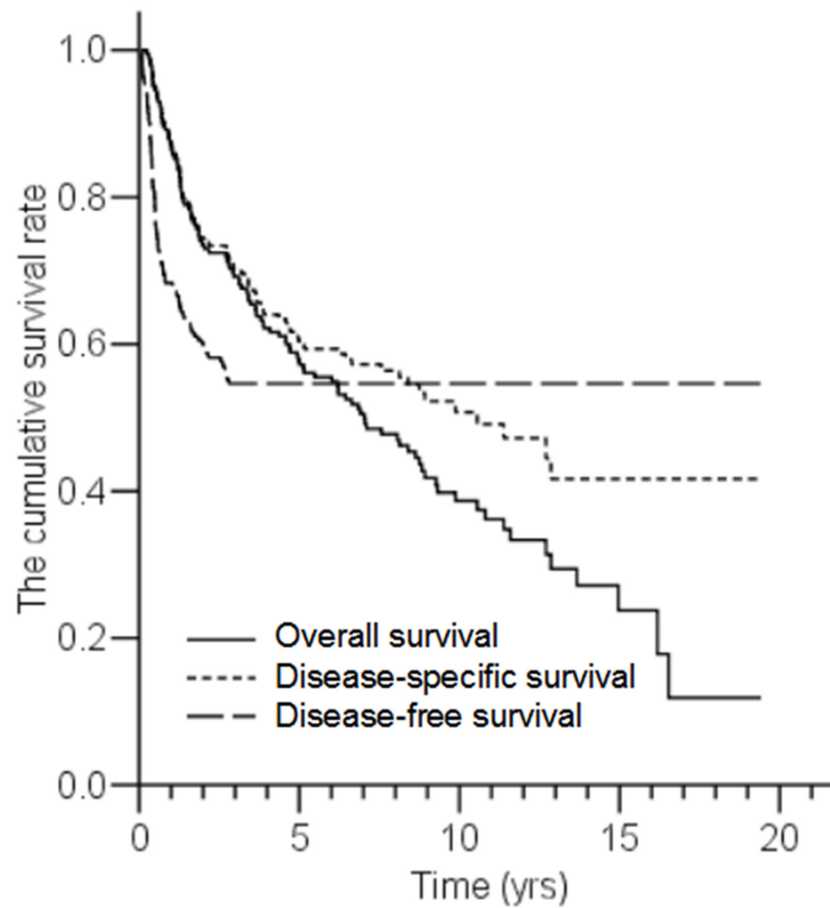
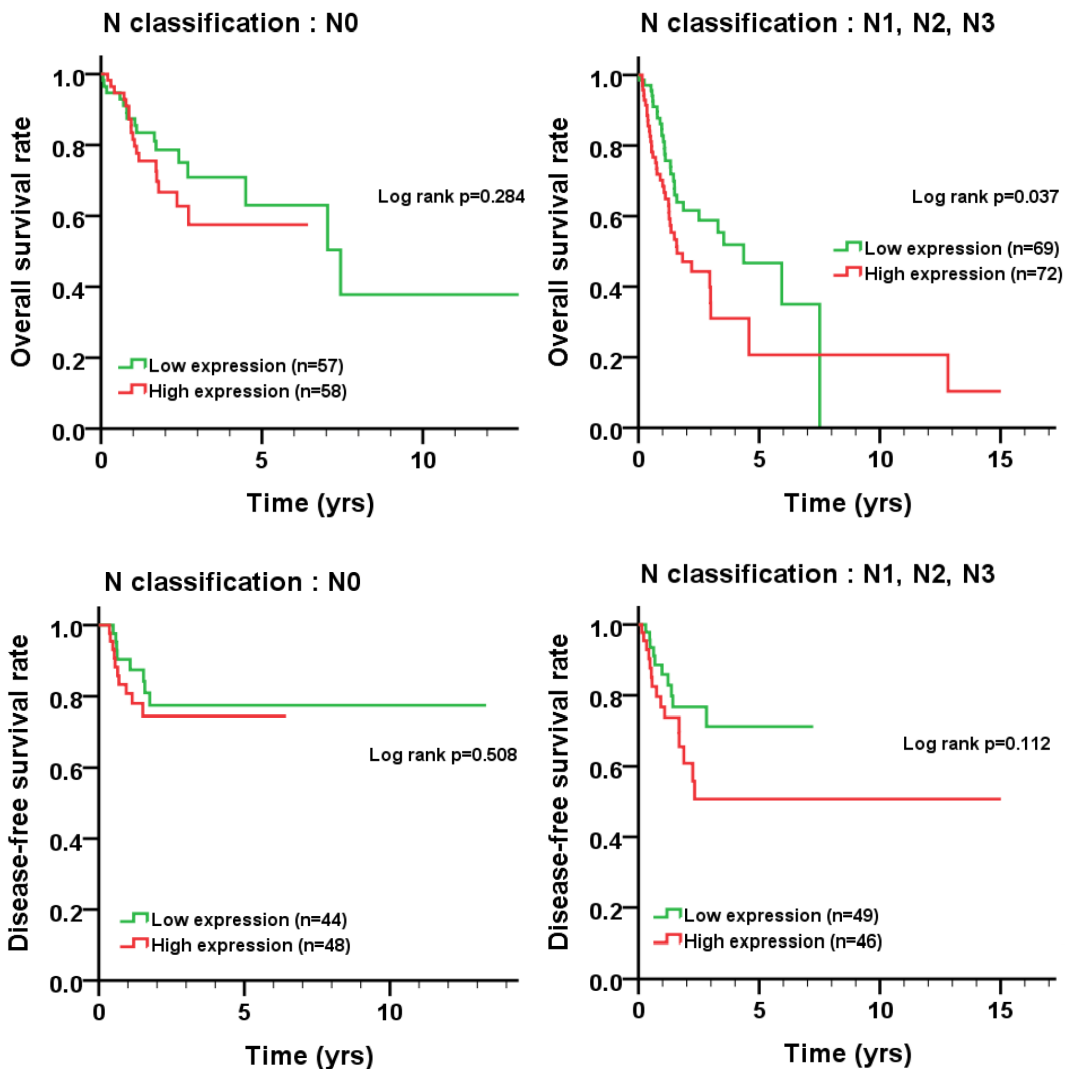


Caspase-3 expression in tumorigenesis and prognosis of buccal mucosa squamous cell carcinoma

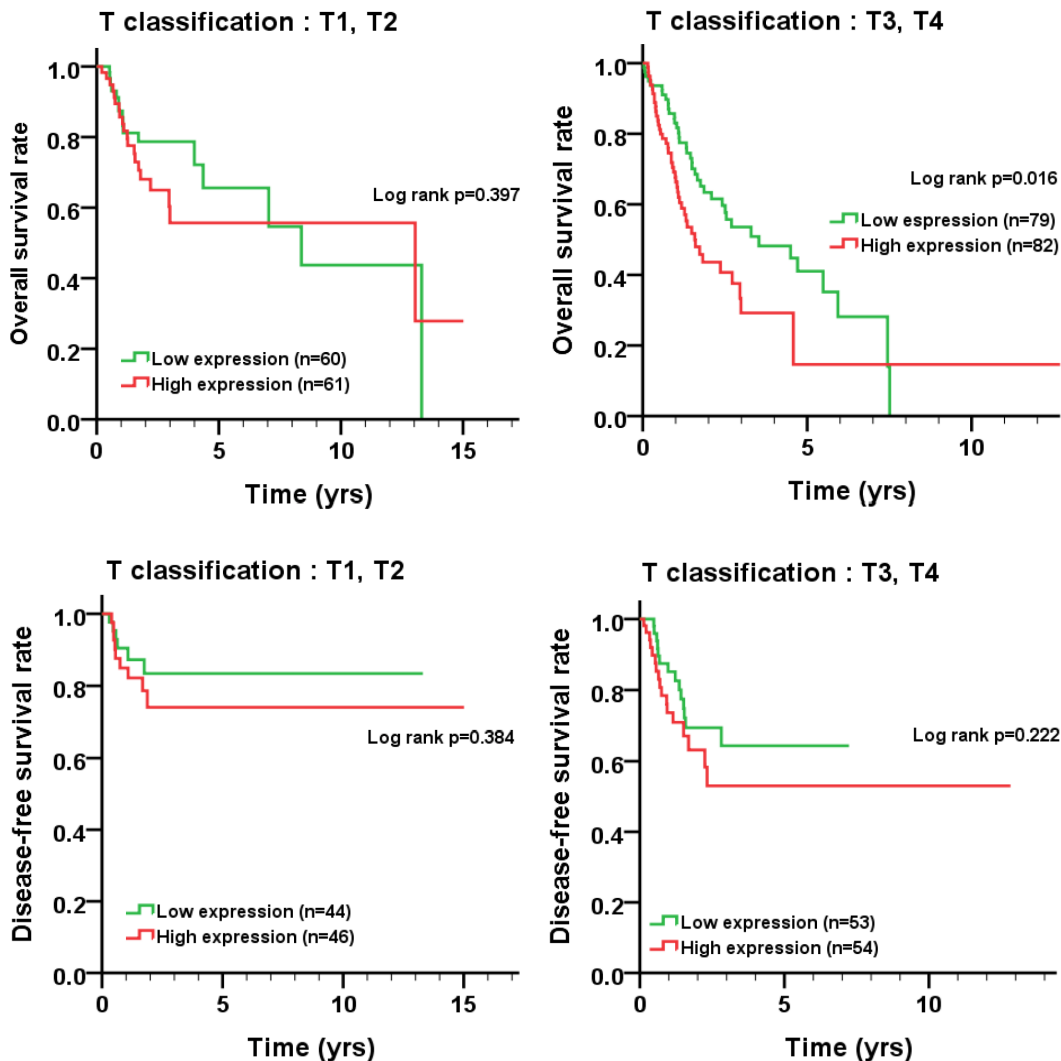
SUPPLEMENTARY MATERIALS



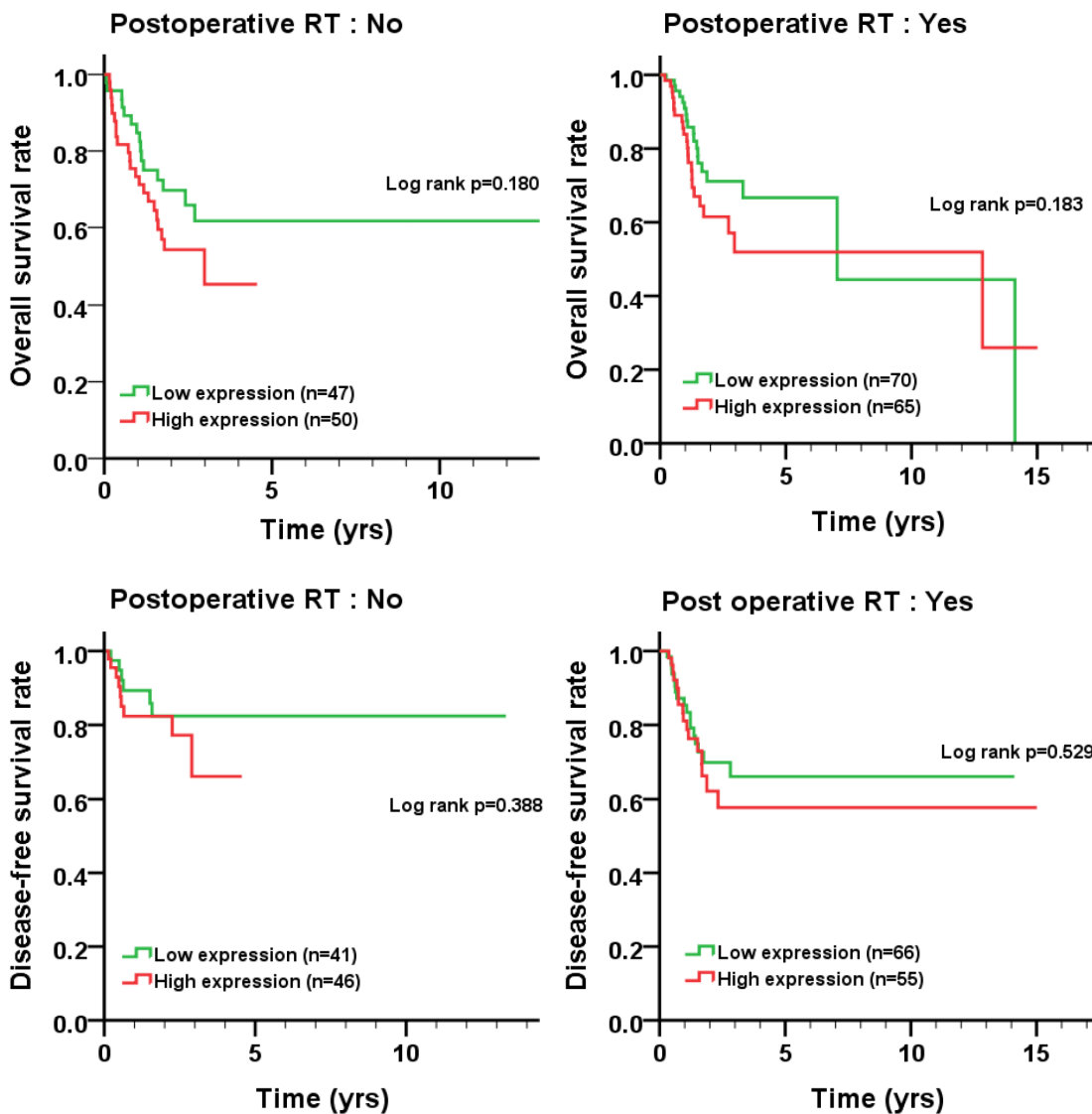
Supplementary Figure 1: Cumulative survival rate for patients with BMSCC.



Supplementary Figure 2: Survival curves depicting overall survival and disease-free survival according to caspase-3 expression pattern in oral cancer patients without (N0) and with (N+N2+N3) lymph node metastasis from TCGA database.



Supplementary Figure 3: Survival curves depicting overall survival and disease-free survival according to caspase-3 expression pattern in oral cancer patients with small (T1+T2) and larger (T3+T4) tumor size from TCGA database.



Supplementary Figure 4: Survival curves depicting overall survival and disease-free survival according to caspase-3 expression pattern in oral cancer patients without (No) and with (Yes) postoperative RT from TCGA database.

Supplementary Table 1: Demographical characteristics and pathological outcomes and disease-specific survival of BMSCC patients

Variable	No.	CHR	<i>p</i> -Value*
Sex			
Female	4	1.00	
Male	181	0.49	0.227
Age, y			
≤ 40	25	1.00	
41-50	58	1.49	0.301
51-60	56	1.53	0.272
>60	46	1.47	0.327
Cell differentiation			
Well	51	1.00	
Moderate	125	1.70	0.045
Poor	9	5.32	<0.001
AJCC pathological stage			
I	65	1.00	
II	47	1.30	0.428
III	19	2.81	0.006
IV	54	4.48	<0.001
T classification			
T1	70	1.00	
T2	70	2.14	0.005
T3	12	4.58	<0.001
T4	33	3.20	<0.001
N classification			
N0	141	1.00	
N1	19	2.90	<0.001
N2	25	5.69	<0.001
Postoperative RT			
No	134	1.00	
Yes	51	2.31	<0.001
Postoperative CT			
No	181	1.00	
Yes	4	0.57	0.573

AJCC, American Joint Committee on Cancer; CHR, crude hazard ratio; RT, radiotherapy; CT, chemotherapy.

**p* values were estimated by Cox's regression.

Supplementary Table 2: The score ratios of caspase-3 in CTAN/tumor tissues of BMSCC patients

Cleaved caspase-3 (CC-3)			
CTAN/tumor ratio	Patient numbers	Percentage	Cumulative percentage
0.00	62	39.1	98.1
2.00	1	0.8	
Total	53	39.8	
Missing value	80	60.2	
Total	133	100.0	
Caspase-3 (C-3)			
CTAN/tumor ratio	Patient numbers	Percentage	Cumulative percentage
0.00	36	24.0	24.8
0.29	1	0.7	25.5
0.33	5	3.3	29.0
0.40	7	4.7	33.8
0.50	9	6.0	40.0
0.57	2	1.3	41.4
0.60	4	2.7	44.1
0.67	6	4.0	48.3
0.75	7	4.7	53.1
0.80	8	5.3	58.6
0.83	14	9.3	68.3
0.86	2	1.3	69.7
1.00	26	17.3	
1.20	5	3.3	
1.25	4	2.7	
1.33	1	0.7	
1.50	2	1.3	
1.67	2	1.36	
2.00	4	2.7	
Total	145	96.7	
Missing value	5	3.3	
Total	150	100.0	

Supplementary Table 3: The comparison of caspase-3 expression between tumor adjacent normal and tumor tissues in oral cancer patients from TCGA database

Variables	Tumor adjacent normal		Tumor		Z	p-Value*
	Mean±SD	Median	Mean±SD	Median		
	(n=29)		(n=303)			
Caspase-3	66.44±8.65 ^d	67.36	71.19±6.87 ^{cd}	71.38	-2.908	0.004

SD, standard deviation.

*p values were estimated by Wilcoxon signed-rank test.

^ap<0.001; ^bp<0.001; ^cp<0.001; ^dp<0.001; ^ep=0.011; ^fp=0.001.

Supplementary Table 4: Association of caspase-3 expression with pathological outcomes in oral cancer patients from TCGA database

Variable	No. (%)	Caspase-3		
		Mean±SD	Median	<i>p</i> -Value
Sex				
Female	100 (33.0)	70.21±6.83	70.08	0.080*
Male	203 (67.0)	71.68±6.85	71.56	
Age, y				
≤ 40	13 (4.3)	66.70±6.13 ^{abc}	67.01	0.006[‡]
41-50	37 (12.2)	71.76±5.96 ^a	71.21	
51-60	81 (26.7)	71.58±6.58 ^b	71.65	
61-70	92 (30.4)	69.85±7.25 ^d	70.14	
>70	80 (26.4)	72.82±6.76 ^{cd}	72.92	
Cell differentiation				
Well	48 (16.0)	69.59±6.65	69.60	0.173 [‡]
Moderate	191 (63.7)	71.36±6.56	71.49	
Poor	61 (20.3)	71.95±7.65	72.65	
AJCC pathological stage				
I, II	76 (27.1)	71.41±6.33	71.21	0.772*
III, IV	204 (72.9)	71.15±6.73	71.41	
T classification				
T1, T2	123 (43.2)	71.44±6.53	71.39	0.629*
T3, T4	162 (56.8)	71.06±6.75	71.43	
N classification				
N0	117 (45.7)	71.00±6.11	71.43	0.733*
N1, N2	139 (54.3)	71.29±7.00	71.39	

AJCC, American Joint Committee on Cancer.

**p* values were estimated by student's T test.

[†]*p* values were estimated by Kruskal-Wallis 1-way ANOVA test.

[‡]*p* values were estimated by 1-way ANOVA test.

[§]*p* values were estimated by Mann-Whitney U test.

^a*p*=0.022; ^b*p*=0.017; ^c*p*=0.003; ^d*p*=0.002.

Supplementary Table 5: The expression levels of caspase-3 for overall survival and disease-free survival in oral cancer patients from TCGA database

Variable	No. (%)	Overall survival				Disease-free survival				
		CHR (95% CI)	<i>p</i> -Value	AHR (95% CI)	<i>p</i> -Value [*]	CHR (95% CI)	<i>p</i> -Value	AHR (95% CI)	<i>p</i> -Value [†]	
Caspase-3 expression	Low	150 (50.0)	1.00		1.00		1.00		1.00	
	High	150 (50.0)	1.52 (1.07–2.16)	0.020	1.45 (0.92–2.78)	0.107	1.39 (0.80–2.43)	0.246	1.25 (0.71–2.19)	0.446

AJCC, American Joint Committee on Cancer; CHR, crude hazard ratio; CI, confidence interval; AHR, adjusted hazard ratio.
^{*}*p*-value were adjusted for cell differentiation (moderate, poor vs. well), AJCC pathological stage (stage II, III, IV vs stage I), postoperative RT by multiple Cox's regression.
[†]*p*-value were adjusted for cell differentiation (moderate, poor vs. well), AJCC pathological stage (stage II, III, IV vs stage I) by multiple Cox's regression.

Supplementary Table 6: Distribution of scores for cleaved caspase-3 and caspase-3 expression in BMSCC patients

Cleaved caspase-3 (CC-3)			
Score	Number	Percentage	Cumulative percentage
0.00	114	61.6	61.6
1.00	13	7.0	68.6
2.00	36	19.5	88.1
3.00	16	8.6	96.8
4.00	6	3.2	100.0
Total	185	100.0	
Caspse-3 (C-3)			
Score	Number	Percentage	Cumulative percentage
0.00	5	2.7	2.7
2.00	13	7.0	9.7
3.00	19	10.3	20.0
4.00	37	20.0	40.0
5.00	60	32.4	72.4
6.00	46	24.9	97.3
7.00	5	2.7	100.0
Total	185	100.0	