

	Positive	20(4.0)	4(20.0)	3(0.9)	1(33.3)	13(13.1)	2(15.4)	4(5.3)	1(25.0)
	Negative	481(96.0)	286(59.5)	323(99.1)	220(68.1)	86(86.9)	34(39.5)	72(94.7)	32(44.4)
Size of flap (Length of skin island)									
	No	105(21.0)	64(61.0)	67(20.6)	50(74.6)	11(11.1)	2(18.2)	27(35.5)	12(44.4)
	0-10cm	159(31.7)	97(61.0)	101(31.0)	72(71.3)	32(32.3)	12(37.5)	26(34.2)	13(50.0)
	10-15cm	131(26.2)	69(52.7)	86(26.4)	53(61.6)	29(29.3)	9(31.0)	16(21.1)	7(43.8)
	15-20cm	72(14.4)	37(51.4)	47(14.4)	26(55.3)	22(22.2)	11(50.0)	3(3.9)	0.0000
	≥20cm	34(6.8)	23(67.7)	25(7.7)	20(80.0)	5(5.1)	2(40.0)	4(5.3)	1(25.0)
Flap type									
	Anterolateral thigh flap	270(53.9)	148(54.8)	191(58.6)	119(62.3)	46(46.5)	14(30.4)	33(43.4)	15.0000
	Fibular flap	10(2.0)	8(80.0)	10(3.1)	8(80.0)	0	NA	0.0000	NA
	Radial forearm flap	75(15.0)	51(68.0)	53(16.3)	41(77.4)	10(10.1)	4(40.0)	12(15.8)	6(50.0)
	Latissimus dorsi flap	7(1.4)	2(28.6)	1(0.3)	0.0000	5(5.1)	2(40.0)	1(1.3)	0.0000
	Pectoralis myocutaneous flap	34(6.8)	17(50.0)	4(1.2)	3(75.0)	27(27.3)	14(51.9)	3(3.9)	0.0000
	Direct close or regional flap	105(21.0)	64(61.0)	67(20.6)	50(74.6)	11(11.1)	2(18.2)	27(35.5)	12.0000
Perioperative complications^{&}									
	Surgical site infection	59(11.8)	24(40.7)	37(11.4)	16(43.2)	12(12.1)	5(41.7)	10(13.2)	3(30.0)
	Pulmonary infection	80(16.0)	46(57.5)	58(17.8)	38(65.5)	9(9.1)	3(33.3)	13(17.1)	5(38.5)
	Chyle leakage	19(3.8)	9(47.4)	13(4.0)	6(46.2)	4(4.0)	3(75.0)	2(2.6)	0.0000
	Orocutaneous fistula	38(7.6)	14(36.8)	17(5.2)	9(52.9)	11(11.1)	2(18.2)	10(13.2)	3(30.0)
	Flap necrosis	17(3.4)	4(23.5)	12(3.7)	4(33.3)	3(3.0)	1(33.3)	2(2.6)	0.0000
	Hematoma	15(3.0)	10(66.7)	11(3.4)	9(81.8)	0	NA	4(5.3)	1(25.0)
	Delirium	21(4.2)	10(47.6)	12(3.7)	7(58.3)	7(7.1)	3(42.9)	2(2.6)	0.0000
	Wound dehiscence	44(8.8)	19(43.2)	31(9.5)	14(45.2)	1(1.0)	1(100.0)	12(15.8)	4(33.3)
	DVT	8(1.6)	6(75.0)	7(2.1)	6(85.7)	0	NA	1(1.4)	0.0000
Postoperative adjuvant therapy									
	Radiotherapy	310(61.9)	177(57.1)	202(62.0)	136(67.3)	53(53.5)	16(30.2)	55(72.4)	25(45.5)
	Chemotherapy	9(1.8)	4(44.4)	6(1.8)	3(50.0)	3(3.0)	1(33.3)	0.0000	NA
	Radio-chemotherapy	100(20.0)	63(63.0)	75(23.0)	54(72.0)	15(15.2)	4(26.7)	10(13.2)	5(50.0)
	Radiotherapy and anti-EGFR therapy	22(4.4)	13(59.1)	9(2.8)	5(55.6)	9(9.1)	6(66.7)	4(5.3)	2(50.0)
	Chemotherapy and anti-EGFR therapy	12(2.4)	9(75.0)	10(3.1)	7(70.0)	2(2.0)	2(100.0)	0.0000	NA
	Radio-chemotherapy and anti-EGFR therapy	24(4.8)	16(66.7)	24(7.4)	16(66.7)	0	NA	0.0000	NA
	None	24(4.8)	8(33.3)	0	NA	17(17.2)	7(41.2)	7(9.2)	1(14.3)

NA: Not Applicable

^{a:} Neck dissection for the ENE side was counted: **SOND:** Supra-omohyoid neck dissection (Level I-III); **extended SOND:** extended supra-omohyoid neck dissection (Level I-IV); **RND:** Radical neck dissection (Level I-V)

&: Some cases had multiple complications.

HPV: Human papillomavirus; **DVT:** Deep venous thrombosis.

Supplementary Table 2. The characteristics of primary or recurrent oral lesions in patients with unilateral ENE nodes

Variables	The whole groups		The PL group		The RL group		The INM group	
	N(%)	The DFS rate	N(%)	The DFS rate	N(%)	The DFS rate	N(%)	The DFS rate
Primary or recurrent subsite								
Buccal mucosa	73(14.6)	38(52.1)	41(12.6)	25(12.6)	11(11.1)	7(63.6)	21(27.6)	6(28.6)
Floor of mouth	137(27.3)	79(57.7)	84(25.8)	61(25.8)	48(48.5)	15(31.3)	5(6.6)	3(60.0)
Retromolar trigone	20(4.0)	10(50.0)	19(5.8)	10(52.6)	1(1.0)	0.0000	0.0000	NA
Upper Gingiva	22(4.4)	19(86.4)	16(4.9)	15(93.8)	2(2.0)	1(50.0)	4(5.3)	3(75.0)
Tongue	201(40.1)	113(56.2)	132(40.5)	88(66.7)	31(31.3)	9(29.0)	38(50.0)	16(42.1)
Hard palate	28(65.6)	18(64.3)	18(5.5)	11(61.1)	3(3.0)	2(66.7)	7(9.2)	5(71.4)
Lower Gingiva	20(4.0)	13(65.0)	16(4.9)	11(68.8)	3(3.0)	2(66.7)	1(1.3)	0.0000
Pathologic grade								
I	69(13.8)	35(50.7)	30(9.2)	23(76.7)	20(20.2)	5.0000	19(25.0)	7(36.8)
II	356(71.1)	208(58.4)	245(75.2)	159(64.9)	62(62.6)	25(25.0)	49(64.5)	24(49.0)
III	76(15.2)	47(61.8)	51(15.6)	39(76.5)	17(17.2)	6(35.3)	8(10.5)	2(25.0)
T classification*								
T1	10(2.0)	7(70.0)	2(0.6)	2(100.0)	4(4.0)	1(25.0)	4(5.3)	4(100.0)
T2	105(21.0)	62(59.0)	67(20.6)	47(70.2)	21(21.2)	7(33.3)	17(22.4)	8(47.1)
T3	284(56.7)	166(58.5)	182(55.8)	127(70.0)	57(57.6)	20(35.1)	45(59.2)	19(42.2)
T4	102(20.4)	55(53.9)	75(23.0)	45(60.0)	17(17.2)	8(47.1)	10(13.2)	2(20.0)
Size of oral lesion								
0-2cm	13(2.6)	8(61.5)	5(1.5)	4(80.0)	4(4.0)	1(25.0)	4(5.3)	3(75.0)
2-4cm	165(32.9)	99(60.0)	104(31.9)	74(71.2)	34(34.3)	11(32.4)	27(35.5)	14(51.9)
4-6cm	248(49.5)	145(58.5)	157(48.2)	108(68.8)	53(53.5)	22(41.5)	38(50.0)	15(39.5)
>6cm	75(15.0)	38(50.7)	60(18.4)	35(58.3)	8(8.1)	2(25.0)	7(9.2)	1(14.3)
DOI>10mm								
Yes	239(47.7)	133(55.6)	153(46.9)	100(65.4)	59(59.6)	23(39.0)	27(35.5)	10(37.0)
No	262(52.3)	157(60.0)	173(53.1)	121(70.0)	40(40.4)	13(32.5)	49(64.5)	23(46.9)
Midline involvement								
Yes	100(20.0)	53(53.0)	64(19.6)	40(62.5)	20(20.2)	8(40.0)	16(21.1)	5(31.3)
No	401(80.0)	237(59.1)	262(80.4)	181(69.1)	79(79.8)	28(35.4)	60(78.9)	28(46.7)
PNI								
Yes	122(24.4)	67(54.9)	82(25.2)	55(67.1)	26(26.3)	9(34.6)	14(18.4)	3(21.4)
No	379(75.6)	223(58.8)	244(74.9)	166(68.0)	73(73.7)	27(37.0)	62(81.6)	30(48.4)
Bone destruction (oral lesion)								
Yes	93(18.6)	43(46.2)	60(18.4)	32(53.3)	23(23.2)	7(30.4)	10(13.2)	4(40.0)
No	408(81.4)	247(60.5)	266(81.6)	189(71.1)	76(76.8)	29(38.2)	66(86.8)	29(43.9)

Skull base involvement

Yes	20(4.0)	8(40.0)	14(4.3)	6(42.9)	5(5.0)	1(20.0)	1(1.3)	1(100.0)
No	481(96.0)	282(58.6)	312(95.7)	215(68.9)	94(95.0)	35(37.2)	75(98.7)	32(42.7)

NA: Not Applicable.

*: T classification of the RL or INM group was based on the pathological characteristics of their prior primary lesions according to AJCC system.

Supplementary Table 3. The characteristics of metastatic lymph nodes and ENE features in patients with unilateral ENE nodes

Variables	The whole groups		The PL group		The RL group		The INM group		
	N(%)	The DFS rate	N(%)	The DFS rate	N(%)	The DFS rate	N(%)	The DFS rate	
ENE found via preoperative imaging									
	Yes	216(43.1)	98(45.4)	137(42.0)	72(52.6)	44(44.4)	13(29.5)	35(46.1)	13(37.1)
	No	285(56.9)	192(67.4)	189(58.0)	149(78.8)	55(55.6)	23(41.8)	41(53.9)	20(48.8)
ICCR-subclassification									
	ENEMA	108(21.6)	65(60.2)	68(20.9)	49(72.1)	24(24.2)	8(33.3)	16(21.1)	8(50.0)
	ENEMI	393(78.4)	225(57.3)	258(79.1)	172(66.7)	75(75.8)	28(37.3)	60(78.9)	25(41.7)
Fusion of oral lesion and metastatic lymph node									
	Yes	2(0.4)	0.0	2(0.6)	0.0	0.0	NA	0.0	NA
	No	499(99.6)	290(58.1)	324(99.4)	221(68.2)	99(100.0)	36(36.4)	76(100.0)	33(43.4)
Maximum size of ENE nodes									
	Mean ± standard deviation	3.6±1.2		3.6±1.2		3.6±1.3		3.7±1.3	
Number of lymph nodes									
	Mean ± standard deviation	21±12.7		21±12.6		21.9±11.8		21.6±14.0	
Number of metastatic lymph nodes									
	Mean ± standard deviation	4±4.1		3±4.1		4.9±4.5		3.8±3.3	
Number of ENE nodes									
	Mean ± standard deviation	2±2.2		2±2.4		1.9±1.7		2.0±1.8	
Sides of ENE lymph nodes									
	Ipsilateral	416(83.0)	246(59.1)	279(85.6)	192(85.6)	74(74.7)	27(36.5)	63(82.9)	27(42.9)
	Contralateral	85(17.0)	44(51.8)	47(14.4)	29(61.7)	25(25.3)	9(36.0)	13(17.1)	6(46.2)
Level of ENE nodes									
	I-III	422(84.2)	244(57.8)	278(85.3)	190(68.3)	82(82.8)	32(39.0)	62(81.6)	22(35.5)
	IV-V	48(9.6)	28(58.3)	32(9.8)	20(62.5)	8(8.1)	1(12.5)	8(10.5)	7(87.5)
	Both	31(6.2)	18(58.1)	16(5.0)	11(68.8)	9(9.1)	3(33.3)	6(7.9)	4(66.7)
Soft tissue involvement									

	Yes	232(46.3)	121(52.2)	152(46.6)	91(59.9)	42(42.4)	13(31.0)	38(50.0)	17(44.7)
	No	269(53.7)	169(62.8)	174(53.4)	130(74.7)	57(57.6)	23(40.4)	38(50.0)	16(42.1)
Muscular invasion									
	Yes	246(49.1)	122(49.6)	157(48.2)	91(58.0)	51(51.5)	16(31.4)	38(50.0)	15(39.5)
	No	255(50.9)	168(65.9)	169(51.8)	130(76.9)	48(48.5)	20(41.7)	38(50.0)	18(47.4)
Arterial encasement									
	Yes	15(3.0)	2(13.3)	10(3.1)	2(20.0)	3(3.0)	0.0	2(26.3)	0.0
	No	486(97.0)	288(59.3)	316(96.9)	219(69.3)	96(97.0)	36(37.5)	74(97.4)	33(44.6)
Internal jugular cancer embolism									
	Yes	48(9.6)	16(33.3)	29(8.9)	12(41.4)	13(13.1)	2(15.4)	6(7.9)	2(33.3)
	No	453(90.4)	274(60.5)	297(91.1)	209(70.4)	86(86.9)	34(39.5)	70(92.1)	31(44.3)
Lymph node necrosis									
	Yes	132(26.3)	56(42.4)	88(27.0)	44(50.0)	25(25.3)	6(24.0)	19(25.0)	6(31.6)
	No	369(73.7)	234(63.4)	238(73.0)	177(74.4)	74(74.7)	30(40.5)	57(75.0)	27(47.4)
Bone involvement									
	Yes	50(10.0)	25(50.0)	35(10.7)	19(54.3)	9(9.1)	2(22.2)	6(7.9)	4(66.7)
	No	451(90.0)	265(58.8)	291(89.3)	202(69.4)	90(90.9)	34(37.8)	70(92.1)	29(41.4)
Lymph node ratio (LNR)*									
	Mean ± standard deviation	0.26±0.29		0.26±0.28		0.24±0.24		0.28±0.28	
Number ratio between ENE and excised nodes&									
	Mean ± standard deviation	0.19±0.27		0.18±0.25		0.14±0.17		0.19±0.25	

NA: Not Applicable

*: The number of metastatic nodes divided by the total number of excised nodes.

&: The number of ENE nodes divided by the total number of excised nodes.

Supplementary Table 4. Summary of death causes of patients with unilateral ENE nodes

Variables	N(%)			
	The whole groups	The PL group	The RL group	The INM group
Death causes (Overall)				
locoregional recurrence	94(44.6)	53(50.5)	25(39.7)	16(27.2)
Distant metastasis	54(25.6)	29(27.6)	12(19.0)	13(30.2)
Distant metastasis and locoregional recurrence	55(26.1)	20(19.0)	22(34.9)	13(30.2)
Non-oncologic cause	8(3.8)	3(2.9)	4(6.3)	1(2.3)

Supplementary Table 5. The Cox regression DFS survival analysis of the characteristics of patients with unilateral ENE nodes

Variables	The whole groups		The PL group		The RL group		The INM group	
	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)
Treatment group	<0.001	<0.001(1.295~1.785)	NA		NA		NA	
ENE found via preoperative imaging	<0.001	<0.001(1.365~2.969)	<0.001	<0.001(1.917~5.430)	0.078		0.375	
ICCR-subclassification	0.437		0.418	0.030(0.261~0.935)	0.612		0.399	
Fusion of oral lesion and metastatic lymph nodes	0.012		0.003	0.018(1.422~40.671)	NA		NA	
Maximum size of ENE nodes	<0.001	0.036(0.696~0.988)	<0.001		0.066		0.775	
Number of lymph nodes	0.255		0.005		0.026	0.017(1.004~1.046)	0.830	0.082(0.936~1.004)
Number of metastatic lymph nodes	0.539		0.570		0.301		0.085	
Number of ENE nodes	0.206		0.037		0.602		0.346	
Level of ENE nodes	0.974		0.812		0.238		0.040	
The side of the ENE nodes	0.167		0.343		0.856		0.933	
Soft tissue involvement	0.012		0.004		0.210		0.634	
Muscular invasion	<0.001		<0.001		0.088		0.466	
Arterial encasement	<0.001	0.035(1.047~3.584)	<0.001	0.010(1.917~5.430)	0.013		0.475	
Internal jugular cancer embolism	<0.001	0.016(1.103~2.616)	0.001		0.012		0.571	
metastatic node necrosis	<0.001	0.010(1.125~2.350)	<0.001		0.017	0.011(1.175~3.487)	0.458	0.079(0.893~7.647)
Bone involvement	0.205		0.071		0.142		0.251	
HPV status	0.066		0.856		0.707		0.920	
LNR	0.024	0.031(0.095~0.891)	<0.001		0.734		0.152	0.021(<0.001~0.367)
Number ratio between ENE and excised nodes	0.002	0.008(1.486~14.602)	<0.001	0.001(1.532~4.820)	0.844		0.809	0.048(1.057~47134.133)

DFS: Disease-free survival.

NA: Not Applicable

HPV: Human papillomavirus; LNR: Lymph node ratio.

Supplementary Table 6. The Cox regression TTR analysis of the characteristics of patients with unilateral ENE nodes.

Variables	The whole groups		The PL group		The RL group		The INM group	
	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)
Treatment Group	<0.001	<0.001(1.292~1.796)	NA		NA		NA	
ENE found via preoperative imaging	<0.001	<0.001(1.397~3.070)	<0.001	<0.001(1.709~4.667)	0.049		0.294	0.085(0.883~6.846)
ICCR-subclassification	0.303		0.395	0.076(0.300~1.062)	0.448		0.374	

Fusion of oral lesion and metastatic lymph nodes	0.047		0.016		NA		NA
Maximum size of ENE nodes	<0.001	0.031(0.691~0.982)	<0.001		0.031		0.916 0.090(0.408~1.067)
Number of lymph nodes	0.087		0.002		0.163		0.805 0.024(0.919~0.994)
Number of metastatic lymph nodes	0.647		0.726		0.320	0.056(0.993~1.708)	0.111
Number of ENE nodes	0.210		0.059		0.654	0.013(0.366~0.888)	0.362
Level of ENE nodes	0.776		0.757		0.182	0.021(1.137~4.760)	0.061
Side of ENE nodes	0.252		0.459		0.943		0.978
Soft tissue involvement	0.021		0.005		0.331		0.709
Muscular invasion	<0.001		0.001		0.077		0.533
Arterial encasement	<0.001		<0.001	<0.001(2.002~8.561)	0.023		0.827 0.094(0.014~1.397)
Internal jugular cancer embolism	<0.001	0.001(1.332~3.056)	<0.001		0.004	0.008(1.307~6.200)	0.447
metastatic node necrosis	<0.001		<0.001		0.010		0.545 0.027(1.154~11.080)
Bone involvement	0.223		0.092		0.176		0.296
HPV status	0.697		0.732		0.535		0.920
LNR	0.018	0.005(0.092~0.872)	<0.001		0.911	0.047(<0.001~0.912)	0.168 0.025(<0.001~0.397)
Number ratio between ENE and excised nodes	0.002	0.007(1.530~15.379)	<0.001	0.001(1.560~4.944)	0.953		0.715

TTR: Time-to-relapse.

NA: Not Applicable.

HPV: Human papillomavirus; LNR: Lymph node ratio.

Supplementary Table 7. The Cox regression TTR analysis of demographics and treatment in patients with bilateral ENE nodes

Variables	The whole groups		The PL group		The RL group		The INM group	
	Univariate Analysis	Multivariate analysis(OR,95%CI)	Univariate Analysis	Multivariate analysis(OR,95%CI)	Univariate Analysis	Multivariate analysis(OR,95%CI)	Univariate Analysis	Multivariate analysis(OR,95%CI)
Treatment group	0.038							
Age	0.301		0.746		0.364		0.572	
Sex	0.622		0.843		0.640		0.716	
Histories of smoking and alcohol	0.297		0.631		0.658		0.445	
Comorbidities	0.310		0.252		0.026		0.418	
History of prior treatment	0.079		0.150		NA		0.723	
Ipsilateral neck dissection	0.702		0.379		0.861		0.882	
Contralateral neck dissection	0.509		0.459		0.586		0.592	
En-bloc resection	0.067		0.097	0.032(0.287~0.946)	0.428		NA	

Surgical margin	0.008	0.006(1.322~5.114)	0.258	0.019	0.019(1.270~13.884)	0.390
Flap size	0.150		0.373	0.932		0.077
Flap type	0.892		0.625	0.507		0.087
Postoperative adjuvant therapy	0.018	0.020(0.727~0.974)	0.880	0.450		0.338
HPV status	0.725		0.719	0.549		0.713
Perioperative complications	0.018	0.047(1.006~2.485)	0.007	0.003(1.375~4.666)	0.542	0.172

TTR: Time-to-relapse.

NA: Not applicable.

*: Including a case whose primary lesions were found both in the tongue and thyroid, but mostly the tongue.

HPV: Human papillomavirus.

Supplementary Table 8. The Cox regression TTR analysis of metastatic lymph nodes in patients with bilateral ENE nodes.

Variables	The whole groups		The PL group		The RL group		The INM group	
	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)	Univariate analysis	Multivariate analysis(OR,95%CI)
ENE found via preoperative imaging	0.079		0.698		0.261		0.210	
ICCR-subclassification	0.005	0.060(0.966~5.585)	0.017		0.351		0.308	
Fusion of oral lesion and metastatic lymph nodes	0.194		0.108		0.282		0.159	
Maximum size of ENE nodes	<0.001	0.039(1.013~1.661)	0.003		0.540		0.009	0.004(1.243~3.058)
Number of ipsilateral lymph nodes	0.621		0.604	0.072(0.996~1.101)	0.515		0.110	
Number of contralateral lymph nodes	0.397		0.819		0.257		0.690	
Number of ipsilateral metastatic lymph nodes	0.774		0.794		0.233	0.013(0.666~0.952)	0.281	
Number of contralateral metastatic lymph nodes	0.849		0.578		0.069		0.099	0.099(0.975~1.334)
Number of ipsilateral ENE nodes	0.631		0.358		0.685		0.885	
Number of contralateral ENE nodes	0.500		0.262		0.556		0.091	
Level of ipsilateral ENE nodes	0.956		0.498		0.046		0.432	
Level of contralateral ENE nodes	0.866		0.294		0.812		0.562	
Bilateral ENE nodes in I-III level	0.947		0.725		0.009	0.001(2.228~20.259)	0.432	
Fusion of ipsilateral metastatic lymph nodes	0.329		0.195		0.697		0.797	
Fusion of contralateral metastatic lymph nodes	0.261		0.693		0.887		0.317	
Soft tissue involvement	0.007		0.020	0.055(0.006~0.060)	0.092		0.201	
Muscular invasion	0.004		0.004	0.016(0.336~17.346)	0.115		0.185	
Arterial encasement	0.001	0.092(0.957~1.806)	0.044	0.010(1.258~5.344)	0.223		0.042	
Internal jugular cancer embolism	0.045		0.718	0.054(0.013~1.037)	0.002	<0.001(8.582~1305.690)	0.050	
metastatic node necrosis	0.630		0.845		0.007		0.977	
Bone involvement	0.056		0.084		0.668		0.494	
HPV status	0.725		0.719		0.549		0.713	
LNR	0.53		0.955		0.085		0.02	

Number ratio between ENE and excised nodes

0.114

0.834

0.837

0.118

NA: Not Applicable.