

# MRI-identified multidimensional nodal features predict survival and concurrent chemotherapy benefit for stage II nasopharyngeal carcinoma

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**SUPPLEMENTARY TABLE 1.** The pattern of failures and cause of deaths

Variables	Number (%)
<b>Pattern of failures</b>	
Total No. of patients	45
*Distant metastasis alone	18 (40.0)
Local failures alone	17 (37.8)
Regional failures alone	8 (17.8)
Local and regional failures	1 (2.2)
Local and/or regional failures	26 (57.8)
Distant + local + regional failures	1 (2.2)
<b>Cause of deaths</b>	
Total No. of patients	42
Distant metastasis	18 (42.9)
No cancer causes	12 (28.6)
Local or regional failure	7 (16.7)
Radiation-related complications	3 (7.1)
Unknown causes	1 (2.3)
Other malignant tumors	1 (2.3)

\*Distant metastatic sites: 14 bone metastasis, 10 liver metastasis, 12 lung metastasis and one retroperitoneal lymph node metastasis.

**SUPPLEMENTARY TABLE 2.** The incidences of acute and late toxicities between IMRT and CCRT groups

Acute toxicities	Grade1-4			Grade3-4		
	IMRT	CCRT	P	IMRT	CCRT	P
Number of patients	158	84	-	158	84	-
Mucositis	148 (93.7)	80 (95.2)	0.841	17 (10.8)	12 (14.3)	0.422
Leukopenia	57 (36.1)	59 (70.2)	< 0.001*	2 (1.3)	11 (13.1)	< 0.001*
Gastrointestinal reaction	46 (29.1)	48 (57.1)	< 0.001*	1 (1.3)	0 (0)	> 0.999
Ear toxicity	14 (8.9)	15 (17.9)	0.041*	0 (0)	1 (1.2)	0.350
Thrombocytopenia	8 (5.1)	12 (14.3)	0.011*	0 (0)	1 (1.2)	0.350
Anemia	3 (1.9)	7 (8.3)	0.041*	0 (0)	0 (0)	-
Late toxicities	Grade1-4			Grade3-4		
	IMRT	CCRT	P	IMRT	CCRT	P
No. of patients	140	78	-	140	78	-
Subcutaneous fibrosis	60 (38.0)	42 (53.8)	0.123	5 (3.6)	4 (5.1)	0.840
Hearing impairment	57 (40.7)	30 (38.5)	0.752	2 (1.4)	1 (1.3)	> 0.999
Hypoglossal nerve injuries	11 (7.9)	11 (14.1)	0.148	0 (0)	0 (0)	-
Temporal lobe necrosis	3 (2.1)	0 (0)	0.496	0 (0)	0 (0)	-

Data are numbers of patients, with percentages in parenthesis; \* = with significance; CCRT = concurrent chemoradiotherapy. IMRT = intensity-modulated radiotherapy

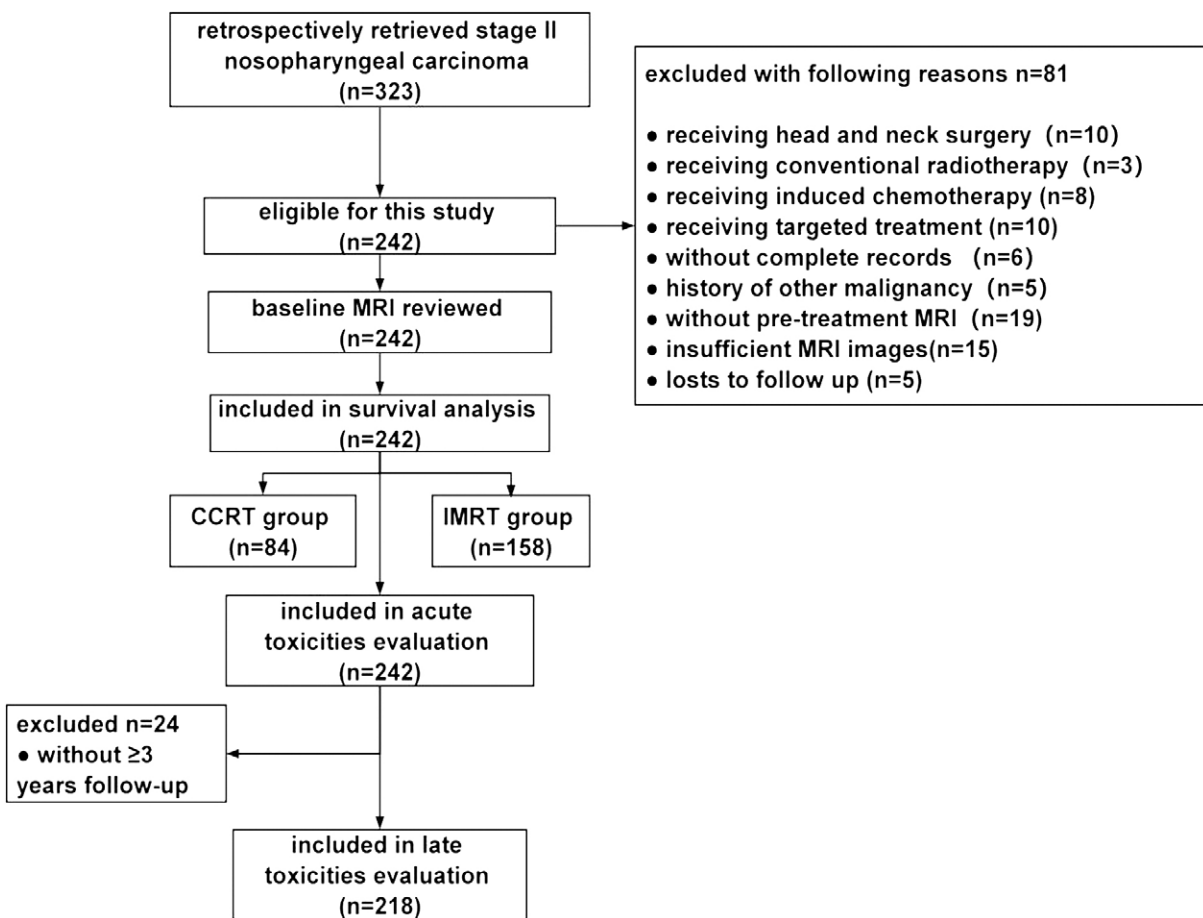
SUPPLEMENTARY TABLE 3. Univariate and multivariate analyses on OS

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Age				
< 50	Ref	-	Ref	-
≥ 50	3.461 (1.732, 6.916)	< 0.001*	3.995 (1.931, 8.266)	< 0.001*
Sex			/	/
Male	Ref	-		
Female	0.905 (0.455, 1.802)	0.776		
AJCC 8th T stage			/	/
T1	Ref	-		
T2	1.419 (0.746, 2.698)	0.286		
AJCC 8th N stage			/	/
N0	Ref	-		
N1	0.588 (0.272, 1.271)	0.177		
AJCC 8th subgroup			/	/
T1N1M0	Ref	-		
T2N0M0	1.858 (0.779, 4.430)	0.162		
T2N1M0	1.295 (0.653, 2.569)	0.459		
GTVnx volume (cm <sup>3</sup> ),			/	/
< 13.7	Ref	-		
≥ 13.7	1.233 (0.629, 2.416)	0.542		
GTVnd volume (cm <sup>3</sup> )				
< 29.1	Ref	-	/	/
≥ 29.1	2.629 (1.256, 5.504)	0.010*		
Lateral of RPLNs				
None	Ref	-		/
Unilateral	1.111 (0.564, 2.188)	0.760		
Bilateral	1.338 (0.566, 3.161)	0.507		
LN located in level III				
Yes	Ref	-	Ref	-
No	3.449 (1.846, 6.441)	<0.001*	2.349 (1.087, 5.074)	0.030*
LN size (cm)				
MAD < 2.2	Ref	-	Ref	-
MAD ≥ 2.2	2.138 (1.165, 3.923)	0.014*	1.696 (0.776, 3.706)	0.185
Number of positive LN				
0	Ref	-	Ref	-
1	0.141 (0.037, 0.531)	0.004*	1.120 (1.032, 1.456)	0.002*
2	0.700 (0.286, 1.714)	0.435	0.605 (0.236, 1.555)	0.297
3	0.499 (0.181, 1.377)	0.180	0.461 (0.160, 1.331)	0.152
4	2.051 (0.740, 5.678)	0.167	1.455 (0.476, 4.449)	0.510
≥ 5	2.251 (0.732, 6.924)	0.157	0.754 (0.197, 2.885)	0.680
† ENE grade				
Grade 0	Ref	-	/	

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Grade 1, 2	0.870 (0.395, 1.919)	0.731		
Grade 3	1.162 (0.505, 2.674)	0.724		
CNN				
No	Ref	-	Ref	-
Yes	2.110 (1.122, 3.967)	<b>0.020*</b>	1.411 (0.678, 2.933)	0.357

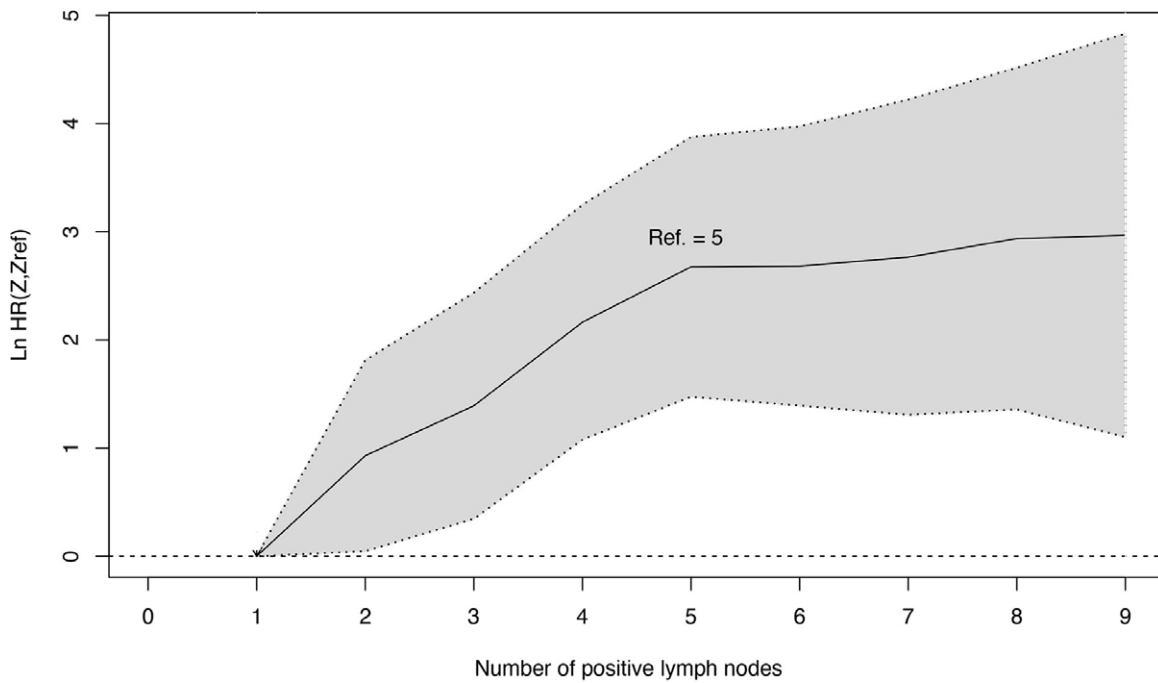
\* with significance; † ENE Grade 0, none; Grade 1, LN infiltrating surrounding fat; Grade 2, matted nodes; and Grade 3, LN infiltrating adjacent muscle and (or) vessels and/or skin.

CCRT = concurrent chemoradiotherapy; CI = confidence interval; CNN = central nodal necrosis; ENE = extranodal extension; GTVnx/GTVnd = gross target volume of nasopharyngeal tumor/lymph nodes; IMRT = intensity-modulated radiotherapy; LN = lymph node; MAD = maximum diameter; OS = overall survival; RPLN = retropharyngeal lymph node



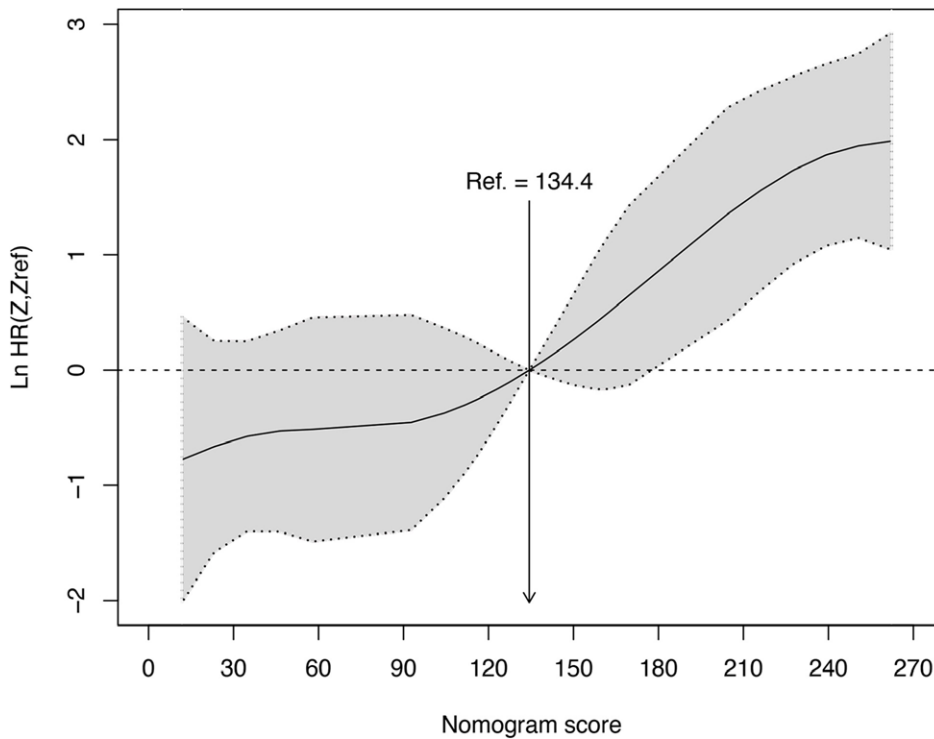
SUPPLEMENTARY FIGURE 1. Flow chart for patient inclusion.

CCRT = concurrent chemoradiotherapy; IMRT = intensity-modulated radiotherapy



**SUPPLEMENTARY FIGURE 2.** Linear correlation between the nomogram-derived prognostic score and hazard of death. The gray bands indicate the 95% confidence interval.

HR = hazard ratio; Ref = reference



**SUPPLEMENTARY FIGURE 3.** P-splines based smooth hazard ratio (HR) between number of positive nodes and hazard of overall death.

Ref = reference