

Supplementary Information for

Establishment and validation of a prognostic nomogram for patients with locoregionally advanced nasopharyngeal carcinoma incorporating clinical characteristics and dynamic changes in hematological and inflammatory markers during concurrent chemo-radiation

Qin Liu^{1,2†}, Lingyu Ma^{1,2†}, Huangrong Ma¹, Li Yang^{1,2*} and Zhiyuan Xu^{1,2*}

¹Clinical Oncology Center, The University of Hong Kong-Shenzhen Hospital, Shenzhen, Guangdong Province, 518053, P.R.China.

²Shenzhen Key Laboratory of Translational Research on Recurrent/Metastatic Cancer, The University of Hong Kong - Shenzhen Hospital. Shenzhen, Guangdong Province, 518053, P.R.China.

*Correspondence:

Yang Li, PhD

yangl1@hku-szh.org

Zhiyuan Xu, MD

xuzy@hku-szh.org

†These authors contributed equally to this work

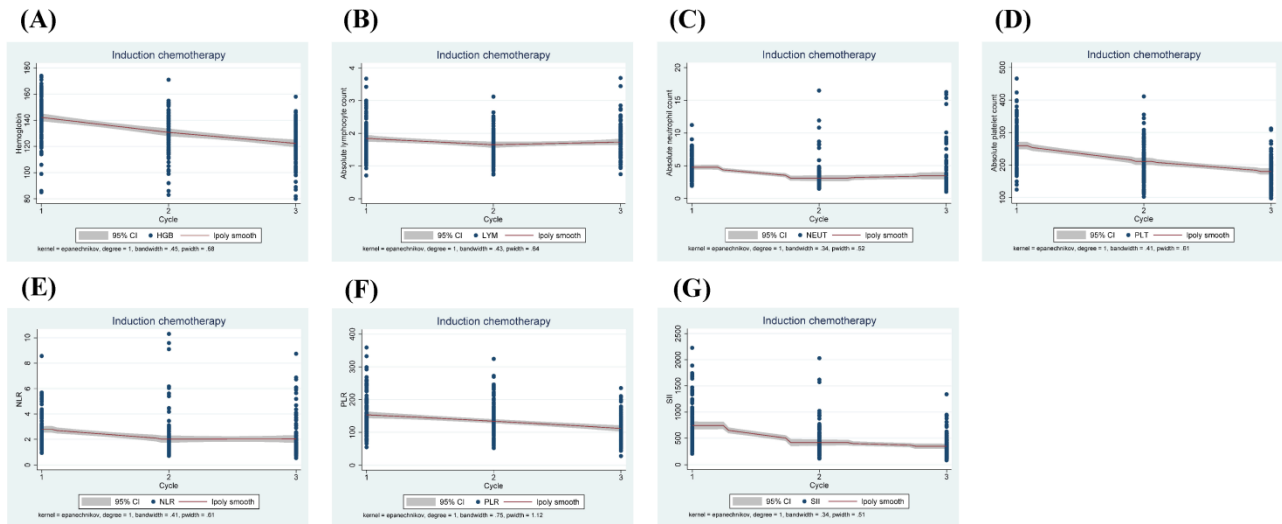
Table of Contents

Supplementary Tables 1-8

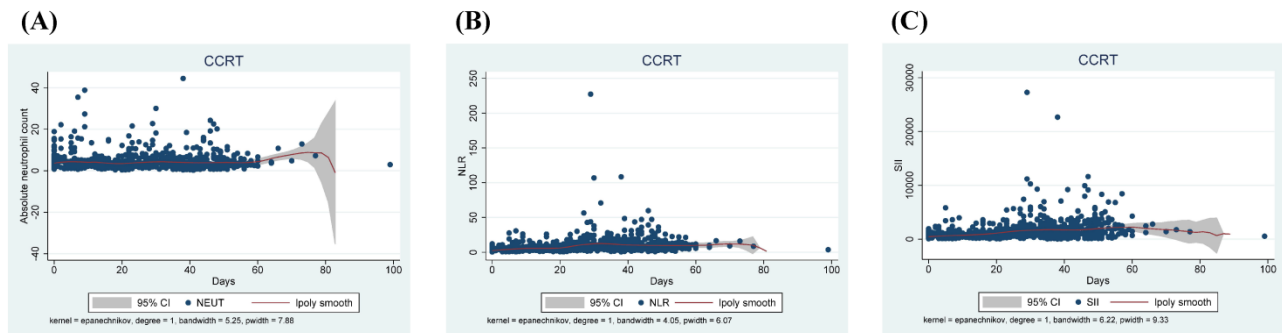
Supplementary Figures 1-5

$\Delta p/bLYM$	Lymphocyte count post-IC/baseline lymphocyte count
$\Delta e/bLYM$	Lymphocyte count at end of treatment/baseline lymphocyte count
$\Delta e/pLYM$	Lymphocyte count at end of treatment/lymphocyte post-IC
$\Delta minLYM$	Minimum lymphocyte count during CCRT/lymphocyte count post-IC
$\Delta p/bPLT$	Platelet count post-IC/baseline platelet count
$\Delta e/bPLT$	Platelet count at end of treatment/baseline platelet count
$\Delta e/pPLT$	Platelet count at end of treatment/platelet post-IC
$\Delta minPLT$	Minimum platelet count during CCRT/ platelet count post-IC
$\Delta p/bNEUT$	Neutrophil count post-IC/baseline neutrophil count
$\Delta e/bNEUT$	Neutrophil count at end of treatment/baseline neutrophil count
$\Delta e/pNEUT$	Neutrophil count at end of treatment/neutrophil post-IC
$\Delta minNEUT$	Minimum neutrophil count during CCRT/neutrophil count post-IC
$\Delta p/bHGB$	Hemoglobin count post-IC/baseline hemoglobin count
$\Delta e/bHGB$	Hemoglobin count at end of treatment/baseline hemoglobin count
$\Delta e/pHGB$	Hemoglobin count at end of treatment/hemoglobin post-IC
$\Delta minHGB$	Minimum hemoglobin count during CCRT/hemoglobin count post-IC
$\Delta p/bNLR$	NLR post-IC/baseline NLR NLR (neutrophil-to-lymphocyte ratio) = neutrophil count ($10^9/L$)/lymphocyte count ($10^9/L$)
$\Delta e/bNLR$	NLR at end of treatment/baseline NLR
$\Delta e/pNLR$	NLR at end of treatment/NLR post-IC
$\Delta maxNLR$	Maximum NLR during CCRT/NLR post-IC
$\Delta p/bSII$	SII post-IC/baseline SII SII (systemic inflammatory index) = platelet count ($10^9/L$) x neutrophil count ($10^9/L$) / lymphocyte count ($10^9/L$)
$\Delta e/bSII$	SII at end of treatment/baseline SII
$\Delta e/pSII$	SII at end of treatment/SII post-IC
$\Delta maxSII$	Maximum SII during CCRT/SII post-IC
$\Delta p/bPLR$	PLR post-IC/baseline PLR PLR (platelet-to-lymphocyte ratio) = platelet count ($10^9/L$)/lymphocyte count ($10^9/L$)
$\Delta e/bPLR$	PLR at end of treatment/baseline PLR
$\Delta e/pPLR$	PLR at end of treatment/PLR post-IC
$\Delta maxPLR$	Maximum PLR during CCRT/PLR post-IC
$\Delta p/bCA$	Calcium level post-IC/baseline calcium level

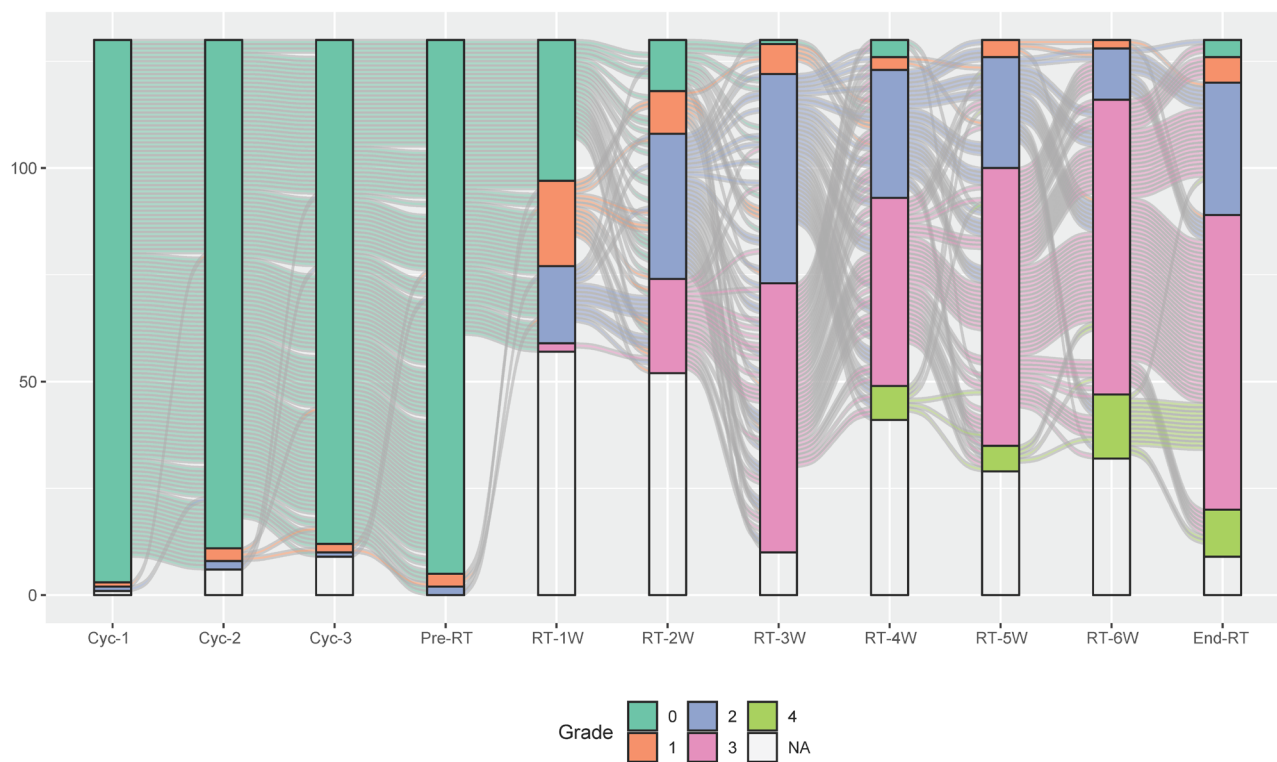
Supplementary Table 1. Calculations of dynamic changes in hematological and inflammatory markers



Supplementary Figure 1. Changes in hematological and inflammatory markers during induction chemotherapy, including hemoglobin(A), lymphocyte(B), neutrophil(C), platelet(D), NLR(E), PLR(F) and SII(G).



Supplementary Figure 2. Changes in neutrophils(A), NLR(B), SII(C) during concurrent chemoradiation.



Supplementary Figure 3. Changes in degree of lymphopenia during treatment. Lymphopenia was graded according to the CTCAE v4.0.

Induction chemotherapy	Coefficient (95%CI)	P-value
Continue	-0.054 (-0.097, -0.012)	0.012
Baseline	Reference	
Cycle 2	-0.178 (-0.255, -0.102)	<0.001
Cycle 3	-0.106 (-0.191, -0.021)	0.015
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	-0.163 (-0.175, -0.152)	<0.001
Pre-RT	Reference	
Week 1	-0.623 (-0.731, -0.515)	<0.001
Week 2	-0.997 (-1.091, -0.903)	<0.001
Week 3	-1.169 (-1.262, -1.076)	<0.001
Week 4	-1.208 (-1.308, -1.074)	<0.001
Week 5	-1.259 (-1.352, -1.167)	<0.001
Week 6	-1.347 (-1.442, -1.252)	<0.001
End-RT	-1.226 (-1.327, -1.126)	<0.001

Supplementary Table 2. Kinetics of absolute lymphocyte counts during induction chemotherapy and concurrent chemo-radiation

Induction chemotherapy	Coefficient (95%CI)	P-value
Continue	-40.212 (-44.993, -35.430)	<0.001
Pre-Chemo	Reference	
Cycle 2	-49.467 (-57.259, -41.675)	<0.001
Cycle 3	-80.199 (-89.791, -70.608)	<0.001
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	1.296 (1.100, 1.493)	<0.001
Pre-RT		
Week 1	1.917 (0.921, 2.914)	<0.001
Week 2	3.771 (3.028, 4.514)	<0.001
Week 3	2.633 (2.097, 3.169)	<0.001
Week 4	9.976 (4.973, 14.979)	<0.001
Week 5	10.559 (8.243, 12.875)	<0.001
Week 6	7.696 (6.179, 9.213)	<0.001
End-RT	7.556 (6.320, 8.792)	<0.001

Supplementary Table 3. Kinetics of absolute platelet counts during induction chemotherapy and concurrent chemo-radiation

Induction chemotherapy	Coefficient (95%CI)	<i>P</i> -value
Continue	-0.661 (-0.971, -0.352)	<0.001
Pre-Chemo	Reference	
Cycle 2	-1.667 (-2.133, -1.202)	<0.001
Cycle 3	-1.303 (-1.924, -0.682)	<0.001
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	0.035 (-0.038, 0.108)	0.348
Pre-RT	Reference	
Week 1	0.287 (-0.673, 1.246)	0.558
Week 2	0.149 (-0.542, 0.839)	0.673
Week 3	-1.116 (-1.716, -0.516)	<0.001
Week 4	0.450 (-0.194, 1.094)	0.171
Week 5	1.085 (0.450, 1.721)	0.001
Week 6	-0.563 (-1.234, 0.108)	0.100
End-RT	0.273 (-0.410, 0.957)	0.433

Supplementary Table 4. Kinetics of absolute neutrophil counts during induction chemotherapy and concurrent chemo-radiation

Induction chemotherapy	Coefficient (95%CI)	<i>P</i> -value
Continue	-9.875 (-10.994, -8.757)	<0.001
Pre-Chemo	Reference	
Cycle 2	-11.161 (-12.761, -9.562)	<0.001
Cycle 3	-19.718 (-21.955, -17.481)	<0.001
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	-2.509 (-2.901, -2.116)	<0.001
Pre-RT	Reference	
Week 1	1.102 (-0.940, 3.145)	0.290
Week 2	-9.643 (-11.484, -7.803)	<0.001
Week 3	-11.342 (-13.015, -9.669)	<0.001
Week 4	-8.369 (-10.408, -6.329)	<0.001
Week 5	-12.814 (-15.315, -10.312)	<0.001
Week 6	-20.383 (-23.106, -17.660)	<0.001
End-RT	-14.866 (-17.580, -12.151)	<0.001

Supplementary Table 5. Kinetics of hemoglobin during induction chemotherapy and concurrent chemo-radiation

Induction chemotherapy	Coefficient (95%CI)	<i>P</i> -value
Continue	-0.383 (-0.549, -0.217)	<0.001
Pre-Chemo	Reference	
Cycle 2	-0.770 (-1.090, -0.451)	<0.001
Cycle 3	-0.758 (-1.090, -0.426)	<0.001
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	2.481 (0.730, 4.233)	0.005
Pre-RT	Reference	
Week 1	-11.094 (-20.869, -1.319)	0.026
Week 2	-44.208 (-55.406, -33.011)	<0.001
Week 3	-19.728 (-28.546, -10.909)	<0.001
Week 4	10.690 (-3.776, 25.156)	0.148
Week 5	-12.381 (-27.062, 2.300)	0.098
Week 6	-38.967 (-52.324, -25.610)	<0.001
End-RT	33.048 (18.524, 47.573)	<0.001

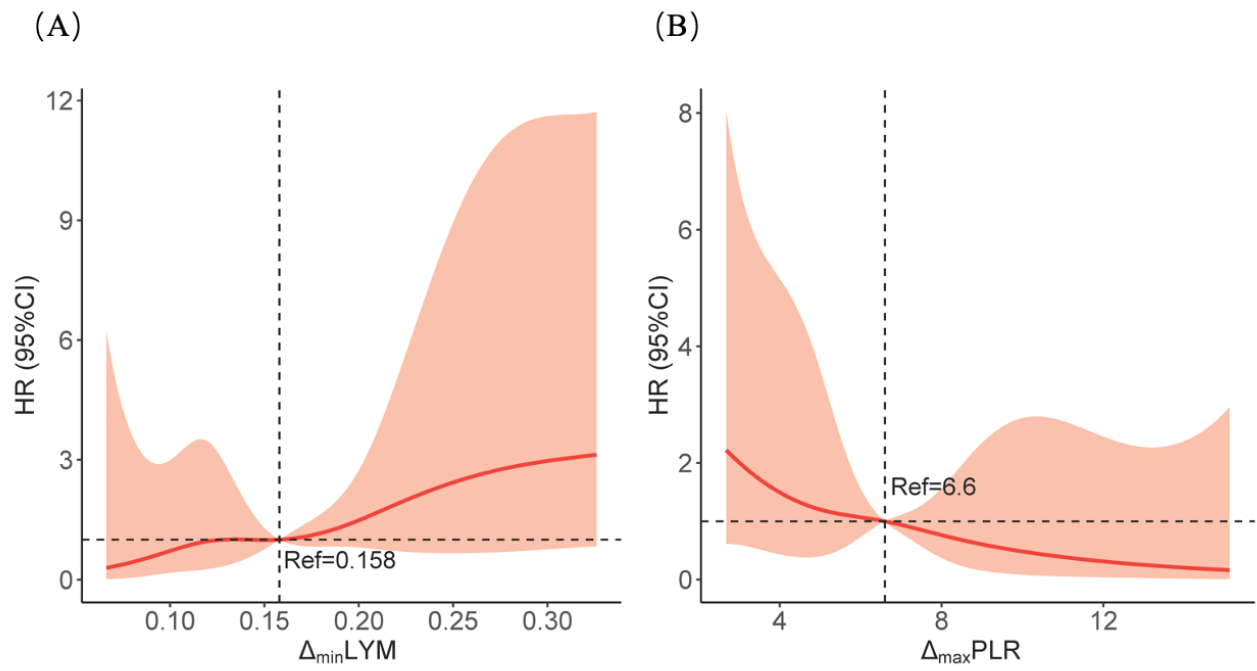
Supplementary Table 6. Kinetics of NLR during induction chemotherapy and concurrent chemo-radiation

Induction chemotherapy	Coefficient (95%CI)	<i>P</i> -value
Continue	-200.594 (-239.420, -161.768)	<0.001
Pre-Chemo	Reference	
Cycle 2	-329.570 (-405.963, -253.176)	<0.001
Cycle 3	-398.507 (-475.864, -321.150)	<0.001
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	246.008 (210.125, 281.890)	<0.001
Pre-RT	Reference	
Week 1	309.829 (164.839, 454.819)	<0.001
Week 2	430.763 (313.576, 547.951)	<0.001
Week 3	402.904 (307.987, 497.822)	<0.001
Week 4	1693.160 (1059.006, 2327.315)	<0.001
Week 5	1691.175 (1367.258, 2015.092)	<0.001
Week 6	1026.197 (753.922, 1298.473)	<0.001
End-RT	1701.652 (1398.537, 2004.766)	<0.001

Supplementary Table 7. Kinetics of SII during induction chemotherapy and concurrent chemo-radiation

Induction chemotherapy	Coefficient (95%CI)	<i>P</i> -value
Continue	-21.023 (-25.554, -16.493)	<0.001
Pre-Chemo	Reference	
Cycle 2	-19.036 (-27.597, -10.474)	<0.001
Cycle 3	-42.095 (-51.167, -33.024)	<0.001
Concurrent chemo-RT	Coefficient (95%CI)	
Continue	67.296 (60.697, 73.894)	<0.001
Pre-RT	Reference	
Week 1	56.599 (39.309, 73.890)	<0.001
Week 2	106.015 (83.153, 128.877)	<0.001
Week 3	230.986 (204.159, 257.813)	<0.001
Week 4	373.914 (312.909, 434.919)	<0.001
Week 5	342.554 (291.138, 393.970)	<0.001
Week 6	385.379 (330.940, 439.818)	<0.001
End-RT	460.227 (399.086, 521.367)	<0.001

Supplementary Table 8. Kinetics of PLR during induction chemotherapy and concurrent chemo-radiation



Supplementary Figure 4. Non-linear relationships between $\Delta_{\min}\text{LYM}$ and PFS (A) and between $\Delta_{\max}\text{PLR}$ and PFS (B) were modelled using RCS.

