Supplemental Tables for:
Modified ypTNM Staging Classification for Gastric Cancer after Neoadjuvant Therapy: A Multi-institutional Study
Chang-ming Huang et al.

Supplemental Table 1. Five-year Overall Survival Probabilities for Different ypTNM Subgroups in the Development Cohort and the Validation Cohort.

Development Cohort

5y-OS	N0	N1	N2	N3
T1	69.9% (n=93)	42.4% (n=42)	19.3% (n=13)	20.0% (n=5)
T2	54.9% (n=92)	32.0% (n=70)	29.7% (n=43)	26.1% (n=17)
T3	54.3% (n=173)	32.6% (n=189)	22.8% (n=209)	16.2% (n=156)
T4a	36.5% (n=105)	33.7% (n=149)	24.4% (n=146)	10.9% (n=160)
T4b	26.2% (n=23)	37.5% (n=24)	23.1% (n=35)	15.7% (n=47)

Validation cohort

5y-OS	N0	N1	N2	N3
T1	79.1% (n=17)	100.0% (n=3)	- (n=2)	100.0% (n=1)
T2	46.1% (n=19)	16.1% (n=12)	54.5% (n=11)	38.9% (n=10)
T3	78.3% (n=26)	65.7% (n=19)	25.0% (n=17)	25.3% (n=25)
T4a	41.3% (n=19)	58.5% (n=17)	36.4% (n=16)	13.6% (n=36)
T4b	33.3% (n=3)	- (n=2)	25.0% (n=4)	0.0% (n=7)

In the validation cohort, one of two patients with T1N2 disease and one of two patients with T4bN1 disease were censored. Therefore, overall survival was not calculated. OS, overall survival.

Supplemental Table 2. Univariate Analyses for Overall Survival in the Development and the Validation Cohort.

Variable	Development cohort (n=1791)			Validation cohort (n=266)		
	HR	95%CI	*p*	HR	95%CI	*p*
Region						
China	NA			REF		
Italy	NA			0.85	0.60-1.21	0.358
Year of operation						
2004-2009	REF			REF		
2010-2015	1.03	0.91-1.17		1.12	0.78-1.61	0.542
Center						
FMUUH	NA			REF		
IMIGASTRIC	NA			0.82	0.56-1.20	0.314
QUAH	NA			0.92	0.61-1.38	0.687
Age						
<45	REF			REF		
45-59	1.06	0.85-1.32	0.596	0.73	0.44-1.21	0.223
60-75	1.11	0.90-1.38	0.323	0.82	0.50-1.35	0.439
>75	1.5	1.15-1.95	0.003	0.68	0.30-1.55	0.359
Race						
White	REF					
Black	0.84	0.68-1.04	0.103			
Others*	0.83	0.69-0.99	0.04	REF		
Unknown	0.5	0.07-3.54	0.486	0.85	0.60-1.21	0.358
Sex						
Female	REF			REF		
Male	1.05	0.91-1.20	0.499	0.93	0.63-1.35	0.686
Site						
Upper	REF			REF		
Middle	0.77	0.65-0.91	0.003	0.66	0.45-0.96	0.029
Lower	0.88	0.72-1.06	0.175	0.63	0.38-1.05	0.077
Overlapping	1.06	0.85-1.33	0.602	1.19	0.59-2.38	0.627
NOS	1.28	0.98-1.67	0.068	1.19	0.29-4.86	0.808
Histological type						
General types	REF			REF		
Special types	1.31	1.15-1.50	<0.001	1.14	0.81-1.60	0.46
Size						
≤2cm	REF			REF		
>2cm, ≤5cm	1.35	1.10-1.64	0.003	1.6	0.73-3.50	0.244
>5cm	1.49	1.22-1.83	<0.001	2.05	0.94-4.47	0.07
Linitis plastica	1.75	1.16-2.65	0.008	4.37	1.38-13.81	0.012
Unknown	1.23	0.98-1.55	0.073	2.73	0.96-7.79	0.061
Surgical procedure						
Partial gastrectomy	REF			REF		
Total gastrectomy	1.28	1.12-1.46	<0.001	1.09	0.77-1.54	0.632
Gastrectomy, NOS	1.39	1.18-1.65	<0.001			
Grade						

Low	REF			REF		
High	1.38	1.20-1.59	<0.001	1.6	1.12-2.27	0.009
Gx	1.04	0.79-1.38	0.758	1.63	0.80-3.32	0.183
ypT category						
T1	REF			REF		
T2	1.57	1.15-2.13	0.004	2.72	1.13-6.51	0.025
T3	1.96	1.51-2.56	<0.001	2.2	0.93-5.21	0.073
T4a	2.5	1.92-3.27	<0.001	3.74	1.61-8.67	0.002
T4b	2.92	2.13-4.02	<0.001	6.36	2.41-16.82	<0.001
ypN category						
N0	REF			REF		
N1	1.67	1.40-1.99	<0.001	1.32	0.77-2.25	0.315
N2	2.09	1.75-2.49	<0.001	1.95	1.18-3.22	0.009
N3	3.3	2.77-3.94	<0.001	3.48	2.26-5.35	<0.001
LNs examined						
<15	REF			REF		
≥15	0.83	0.74-0.94	0.002	1.07	0.58-1.97	0.84
ypTNM staging (AJCC 8th)						
I	REF			REF		
II	1.68	1.33-2.13	<0.001	1.26	0.69-2.31	0.443
III	2.87	2.30-3.59	<0.001	2.86	1.66-4.95	<0.001
Modified ypTNM staging						
IA	REF			REF		
IB	1.74	1.15-2.66	0.009	1.4	0.51-3.84	0.511
II	2.98	2.01-4.42	<0.001	2.11	0.82-5.43	0.119
IIIA	3.83	2.58-5.67	<0.001	3.17	1.25-8.05	0.015
IIIB	6.2	4.17-9.22	<0.001	5.96	2.38-14.94	<0.001
Adjuvant radiotherapy						
None	REF			NA		
Yes	1.12	0.96-1.32	0.159	NA		
Adjuvant chemotherapy†						
None	NA					
Yes	NA			0.94	0.67-1.31	0.719

Abbreviations: NOS, not otherwise specified; LNs, Lymph nodes; Gx, Grade can't evaluate; NA, Not applicable.

Others*, American Indian/AK Native, Asian/Pacific Islander.

†In the SEER database, category record" Chemotherapy recode (yes, no/unk)" does not distinguish between preoperative and postoperative chemotherapy in detail.

Supplemental Table 3. Time-Dependent Univariate Cox Analysis of the Staging System for Patients with Gastric Cancer after Neoadjuvant Therapy.

Variable	Development cohort			Validation cohort		
	HR	95%CI	p	HR	95%CI	p
	Baseline (N=1791)			**Baseline (N=266)**		
ypTNM staging (AJCC 8th)						
I	REF		<0.001	REF		<0.001
II	1.68	1.33-2.13	<0.001	1.26	0.69-2.31	0.443
III	2.87	2.30-3.59	<0.001	2.86	1.66-4.95	<0.001
Modified ypTNM staging						
IA	REF		<0.001	REF		<0.001
IB	1.74	1.15-2.66	0.009	1.40	0.51-3.84	0.511
II	2.98	2.01-4.42	<0.001	2.11	0.82-5.43	0.119
IIIA	3.83	2.58-5.67	<0.001	3.17	1.25-8.05	0.015
IIIB	6.20	4.17-9.22	<0.001	5.96	2.38-14.94	<0.001
	1 Year (N=1440)			**1 Year (N=215)**		
ypTNM staging (AJCC 8th)						
I	REF		<0.001	REF		0.001
II	2.26	1.69-3.02	<0.001	1.25	0.65-2.39	0.507
III	3.69	2.78-4.88	<0.001	2.50	1.37-4.55	0.003
Modified ypTNM staging						
IA	REF		<0.001	REF		<0.001
IB	1.70	1.04-2.77	0.035	1.36	0.44-4.24	0.592
II	3.49	2.21-5.51	<0.001	2.39	0.84-6.83	0.104
IIIA	4.38	2.77-6.91	<0.001	3.44	1.21-9.78	0.020
IIIB	6.71	4.22-10.67	<0.001	5.47	1.93-15.5	0.001
	2 Year (N=856)			**2 Year (N=154)**		
ypTNM staging (AJCC 8th)						
I	REF		<0.001	REF		0.090
II	2.29	1.57-3.36	<0.001	0.93	0.42-2.06	0.866
III	3.44	2.38-4.99	<0.001	1.75	0.85-3.63	0.130
Modified ypTNM staging						
IA	REF		<0.001	REF		0.017
IB	1.59	0.88-2.88	0.125	0.94	0.28-3.16	0.925
II	3.05	1.75-5.30	<0.001	1.39	0.46-4.22	0.559
IIIA	3.89	2.23-6.78	<0.001	1.81	0.59-5.57	0.299
IIIB	5.08	2.83-9.11	<0.001	3.52	1.17-10.61	0.026
	3 Year (N=542)			**3 Year (N=120)**		
ypTNM staging (AJCC 8th)						
I	REF		<0.001	REF		0.978
II	1.59	1.00-2.52	0.050	0.99	0.38-2.56	0.986
III	2.80	1.80-4.36	<0.001	1.08	0.41-2.85	0.874
Modified ypTNM staging						
IA	REF		<0.001	REF		0.262
IB	1.43	0.70-2.93	0.324	0.45	0.11-1.82	0.261
II	2.28	1.17-4.48	0.016	1.16	0.37-3.63	0.805
IIIA	3.50	1.79-6.86	<0.001	0.63	0.16-2.52	0.512
IIIB	4.54	2.20-9.37	<0.001	1.67	0.47-5.93	0.425
	4 Year (N=376)			**4 Year (N=86)**		

	HR	95% CI	p	HR	95% CI	p
ypTNM staging (AJCC 8th)						
I	REF		<0.001	REF		0.748
II	1.49	0.81-2.74	0.196	0.66	0.19-2.27	0.504
III	3.00	1.69-5.34	<0.001	0.65	0.17-2.44	0.523
Modified ypTNM staging						
IA	REF		<0.001	REF		0.246
IB	2.46	0.84-7.19	0.101	0.36	0.07-1.87	0.223
II	3.28	1.16-9.33	0.026	0.56	0.13-2.47	0.444
IIIA	5.84	2.06-16.55	0.001	0.20	0.02-1.96	0.168
IIIB	8.08	2.7-24.21	<0.001	1.48	0.33-6.64	0.605
	5 Year (N=275)			**5 Year (N=70)**		
ypTNM staging (AJCC 8th)						
I	REF		0.003	REF		0.809
II	1.81	0.81-4.08	0.151	0.97	0.16-5.82	0.973
III	3.47	1.58-7.63	0.002	0.48	0.04-5.37	0.551
Modified ypTNM staging						
IA	REF		0.009	REF		0.552
IB	1.87	0.52-6.71	0.338	0.11	0.01-1.45	0.093
II	3.19	0.95-10.77	0.061	0.32	0.04-2.45	0.271
IIIA	4.67	1.36-16.04	0.014	0.33	0.03-3.73	0.374
IIIB	6.57	1.74-24.83	0.005	0.57	0.05-6.36	0.652

Supplemental Table 4. Comparison of the Prognostic Performances of the AJCC 8th ypTNM Staging System and the Modified ypTNM Staging System for Patients with Inadequate Lymph Nodes (<15) Retrieved and Adequate Lymph Nodes (≥15) Retrieved in the Development Cohort.

Variable	ypTNM staging (AJCC 8th)	Modified ypTNM staging	*p* value*
Inadequate Lymph Nodes (<15) Retrieved			
Harrell's C index*	0.588 (0.561-0.615)	0.611 (0.583-0.639)	0.006
AIC†	5371.33	5345.04	<0.001
Likelihood ratio chi-square‡	51.05	103.69	<0.001
Mean difference in BIC with 95%CI limits♯	17.82 (-6.64, 39.86)		
NRI with 95%CI limits	14.84% (-1.95%, 32.43%)		0.082
IDI with 95%CI limits	0.028 (-0.002, 0.053)		0.070
Adequate Lymph Nodes (≥15) Retrieved			
Harrell's C index*	0.596 (0.575-0.618)	0.641 (0.618-0.665)	<0.001
AIC†	7984.25	7917.07	<0.001
Likelihood ratio chi-square‡	81.34	174.86	<0.001
Mean difference in BIC with 95%CI limits♯	59.50 (25.27, 84.42)		
NRI with 95%CI limits	37.35% (21.12%, 56.60%)		<0.001
IDI with 95%CI limits	0.050 (0.022, 0.078)		<0.001

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criteria; CI, Confidence interval; NRI, Net reclassification Index; IDI, Integrated discrimination improvement index.
* A higher Harrell's C index indicates higher discriminative ability
† Smaller AIC values indicate better optimistic prognostic stratification.
‡ A higher likelihood ratio chi-square score indicates better homogeneity.
♯ The BIC was used to assess the overall prognostic performance of different prognostic systems via bootstrap-resampling analysis
ψ NRI and IDI quantify the improvement by the new staging system in predicting the patient's 5-year survival.

Supplemental Table 5. Comparison of the Prognostic Performance of the AJCC 8th ypTNM Staging System and the Modified ypTNM Staging System for Patients with Low-Grade and High-Grade Tumors.

Variable	ypTNM staging (AJCC 8th)	Modified ypTNM staging	*p* value*
Development cohort			
Low grade			
Harrell's C index*	0.567 (0.530-0.604)	0.590 (0.551-0.629)	0.051
AIC†	2765.73	2748.39	<0.001
Likelihood ratio chi-square‡	20.79	42.13	<0.001
Mean difference in BIC with 95%CI limits♯	10.85 (-10.21, 24.78)		
NRI with 95%CI limits	14.84% (-2.00%, 42.93%)		0.096
IDI with 95%CI limits	0.034 (0.006, 0.054)		<0.001
High grade			
Harrell's C index*	0.590 (0.571-0.610)	0.622 (0.601-0.643)	<0.001
AIC†	9998.34	9953.35	<0.001
Likelihood ratio chi-square‡	107.10	156.10	<0.001
Mean difference in BIC with 95%CI limits♯	36.77 (0.90, 64.73)		
NRI with 95%CI limits	28.93% (9.35%, 46.75%)		<0.001
IDI with 95%CI limits	0.026 (0.002, 0.045)		0.019
Validation cohort			
Low grade			
Harrell's C index*	0.671 (0.600-0.742)	0.707 (0.627-0.788)	0.041
AIC†	379.78	377.67	0.348
Likelihood ratio chi-square‡	15.69	21.80	<0.001
Mean difference in BIC with 95%CI limits♯	-1.10 (-19.78, 9.03)		
NRI with 95%CI limits	35.55% (-32.14%, 75.73%)		0.548
IDI with 95%CI limits	0.041 (-0.067, 0.115)		0.436
High grade			
Harrell's C index*	0.626 (0.575-0.677)	0.658 (0.604-0.712)	0.044
AIC†	789.85	786.15	0.157
Likelihood ratio chi-square‡	16.17	23.88	<0.001
Mean difference in BIC with 95%CI limits♯	-6.19 (-16.69, 9.05)		
NRI with 95%CI limits	47.34% (-19.19%, 78.57%)		0.441
IDI with 95%CI limits	0.042 (-0.036, 0.104)		0.317

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criteria; CI, Confidence interval; NRI, Net reclassification Index; IDI, Integrated discrimination improvement index.

Supplemental Table 6. Comparison of the Prognostic Performance of the AJCC 8th ypTNM Staging System and the Modified ypTNM Staging System for Patients with Different Histological Types.

Variable	ypTNM staging (AJCC 8th)	Modified ypTNM staging	*p* value*
Development cohort			
General types			
Harrell's C index*	0.585 (0.565-0.605)	0.614 (0.593-0.635)	<0.001
AIC†	10465.85	10417.61	<0.001
Likelihood ratio chi-square‡	87.84	140.10	<0.001
Mean difference in BIC with 95%CI limits♯	39.54 (4.27, 67.87)		
NRI with 95%CI limits	31.59% (9.90%, 39.47%)		<0.001
IDI with 95%CI limits	0.029 (0.009, 0.050)		<0.001
Special types			
Harrell's C index*	0.588 (0.588-0.621)	0.621 (0.586-0.657)	0.004
AIC†	3123.63	3102.59	<0.001
Likelihood ratio chi-square‡	51.44	76.48	<0.001
Mean difference in BIC with 95%CI limits♯	15.09 (-11.04, 32.57)		
NRI with 95%CI limits	19.14% (-6.77%, 71.88%)		<0.001
IDI with 95%CI limits	0.030 (-0.012, 0.080)		0.119
Validation cohort			
General types			
Harrell's C index*	0.656 (0.604-0.712)	0.692 (0.604-0.712)	0.040
AIC†	884.09	874.85	0.010
Likelihood ratio chi-square‡	27.29	40.53	<0.001
Mean difference in BIC with 95%CI limits♯	5.45 (-17.54, 17.95)		
NRI with 95%CI limits	48.47% (-10.35%, 76.88%)		0.138
IDI with 95%CI limits	0.036(-0.040, 0.092)		0.475
Special types			
Harrell's C index*	0.583 (0.508-0.658)	0.622 (0.546-0.699)	0.046
AIC†	389.19	384.42	0.092
Likelihood ratio chi-square‡	4.13	12.91	<0.001
Mean difference in BIC with 95%CI limits♯	2.51 (-16.60, 11.32)		
NRI with 95%CI limits	57.81% (-21.11%, 116.49%%)		0.201
IDI with 95%CI limits	0.064(-0.019, 0.133)		0.198

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criteria; CI, Confidence interval; NRI, Net reclassification Index; IDI, Integrated discrimination improvement index.

Supplemental Table 7. Multivariate Analyses for Overall Survival in the Development and the Validation Cohort (Including ypT and ypN category).

Variable	Development cohort (n=1791) Multivariate Model			Validation cohort (n=266) Multivariate Model		
	HR	95%CI	*p*	HR	95%CI	*p*
Age						
<45	REF		<0.001			
45-59	1.14	0.91-1.42	0.262			
60-75	1.27	1.02-1.58	0.032			
>75	1.72	1.32-2.26	0.000			
Race						
White						
Black						
Others*						
Unknown						
Site						
Upper	REF		0.004			
Middle	0.72	0.60-0.87	<0.001			
Lower	0.81	0.66-0.99	0.038			
Overlapping	0.80	0.63-1.03	0.080			
NOS	0.95	0.72-1.25	0.692			
Histological type						
General types	REF					
Special types	1.23	1.07-1.42	0.005			
Size						
≤2cm						
>2cm, ≤5cm						
>5cm						
Linitis plastica						
Unknown						
Surgical procedure						
Partial gastrectomy	REF		0.011			
Total gastrectomy	1.18	1.03-1.36	0.020			
Gastrectomy, NOS	1.25	1.05-1.49	0.012			
Grade						
Low	REF		0.042			
High	1.16	1.00-1.35	0.056			
Gx	0.90	0.68-1.19	0.457			
ypT category						
T1	REF		<0.001	REF		0.011
T2	1.35	0.99-1.84	0.058	2.20	0.90-5.36	0.084
T3	1.41	1.08-1.86	0.013	1.58	0.65-3.83	0.312
T4a	1.64	1.24-2.16	0.001	2.59	1.08-6.18	0.032
T4b	1.95	1.40-2.71	<0.001	3.93	1.44-10.71	0.008
ypN category						
N0	REF		<0.001	REF		<0.001
N1	1.55	1.29-1.85	<0.001	1.15	0.67-1.99	0.607
N2	1.99	1.66-2.39	<0.001	1.61	0.97-2.69	0.068
N3	3.32	2.73-4.04	<0.001	2.95	1.88-4.61	<0.001
LN examined						
<15	REF					
≥15	0.67	0.59-0.77	<0.001			

All significantly important prognostic factors in univariate analysis were considered in multivariate analyses, except for AJCC 8th ypTNM staging and the modified ypTNM staging.

Abbreviations: NOS, not otherwise specified; LNs, Lymph nodes; Gx, Grade can't evaluate; NA, Not applicable.

Others*, American Indian/AK Native, Asian/Pacific Islander.