

Background

Neuroendocrine (NE) carcinomas make up 5-10% of non-small cell lung cancers (NSCLC), but are reported to be aggressive and have a 5-year survival after surgery ranging from 13-90%.^{1,2} Assessment of Stage-1 NE tumor histologic grade of differentiation could clarify its effect on survival of NE NSCLC patients after surgical lobectomy.

Objective

To investigate the effects of histologic grade on survival of Stage-1 Neuroendocrine (T1N0 or T2N0) NSCLC patients after lobectomy using the SEER NIH cancer database.

Methods



Using the SEER NIH database, we identified patients who underwent lobectomy for primary Stage-1 Neuroendocrine NSCLC (T1N0M0 or T2N0M0) tumors from 1988-2013 and grouped by tumor histological grade:

Grade 1: Well Differentiated.

Grade 2: Moderately Differentiated.

Grade 3: Poorly Differentiated.

Kaplan-Meier survival analyses with log-rank test was performed between Grades within separate T1N0 and T2N0 populations.

We identified possible covariates from univariate analysis (Chi-squared χ^2 test, Fisher's exact test, ANOVA, and Student's t-test) and significant ($p \leq 0.05$) imbalances from univariate was used as a variable in the Cox regression model to investigate possible predictors of survival by tumor Grade.

Demographics	Grade I		Grade II		Grade III	
	T1N0	T2N0	T1N0	T2N0	T1N0	T2N0
(total n=515 pts)						
Age						
Mean Age (years)	71.4	72.1	72.4	72	72	72.9
SD	5.5	5.9	4.8	5.0	5.4	5.6
Gender*						
Male	51	19	11	10	44	52
Female	149	32	41	20	52	31
Race						
White	185	48	47	27	89	72
Black	8	3	2	2	5	8
Other	7	0	3	1	2	3
Era of Diagnosis						
1988-2003	14	11	12	9	23	13
2004-2013	186	42	40	22	73	70

Table 1: Univariate analyses of demographics of T1N0 and T2N0 patients with significance set at $p \leq 0.05$

Results

Histopathologic	Grade I		Grade II		Grade III	
	T1N0	T2N0	T1N0	T2N0	T1N0	T2N0
Tumor Size (mm)*						
Mean Tumor Size	17.6	33.2	19.1	33	20.3	41.4
SD	6.8	14.4	5.7	14.8	6.2	15.9
Tumor Location*						
Right Upper/Middle Lobe	80	12	19	14	45	34
Right Lower Lobe	38	15	10	8	14	16
Left Upper Lobe	32	11	11	3	27	22
Left Lower Lobe	45	9	12	6	10	9
Lymph Nodes Examined (LNE)						
0	8	3	3	1	3	2
1-5	74	20	20	16	38	30
6-10	48	15	15	5	24	22
11-20	34	7	8	5	15	17
>20	15	3	0	0	7	8

Table 2: Histopathologic traits of T1N0 & T2N0 NE patient. * $p < 0.05$

Overall Survival

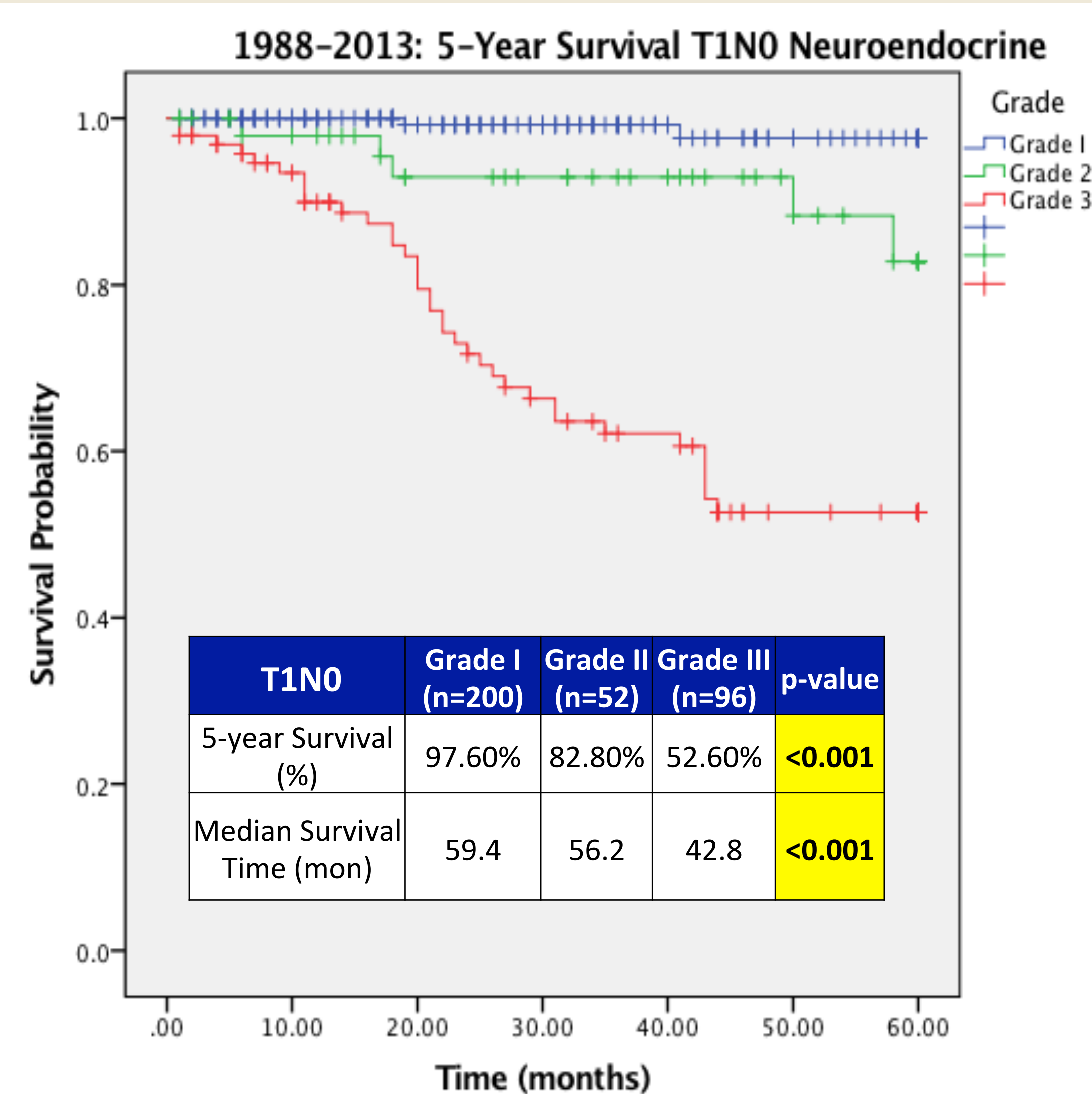


Figure 1: T1N0 Neuroendocrine patients Kaplan-Meier Survival by Grade of Differentiation; significance set at $p \leq 0.05$

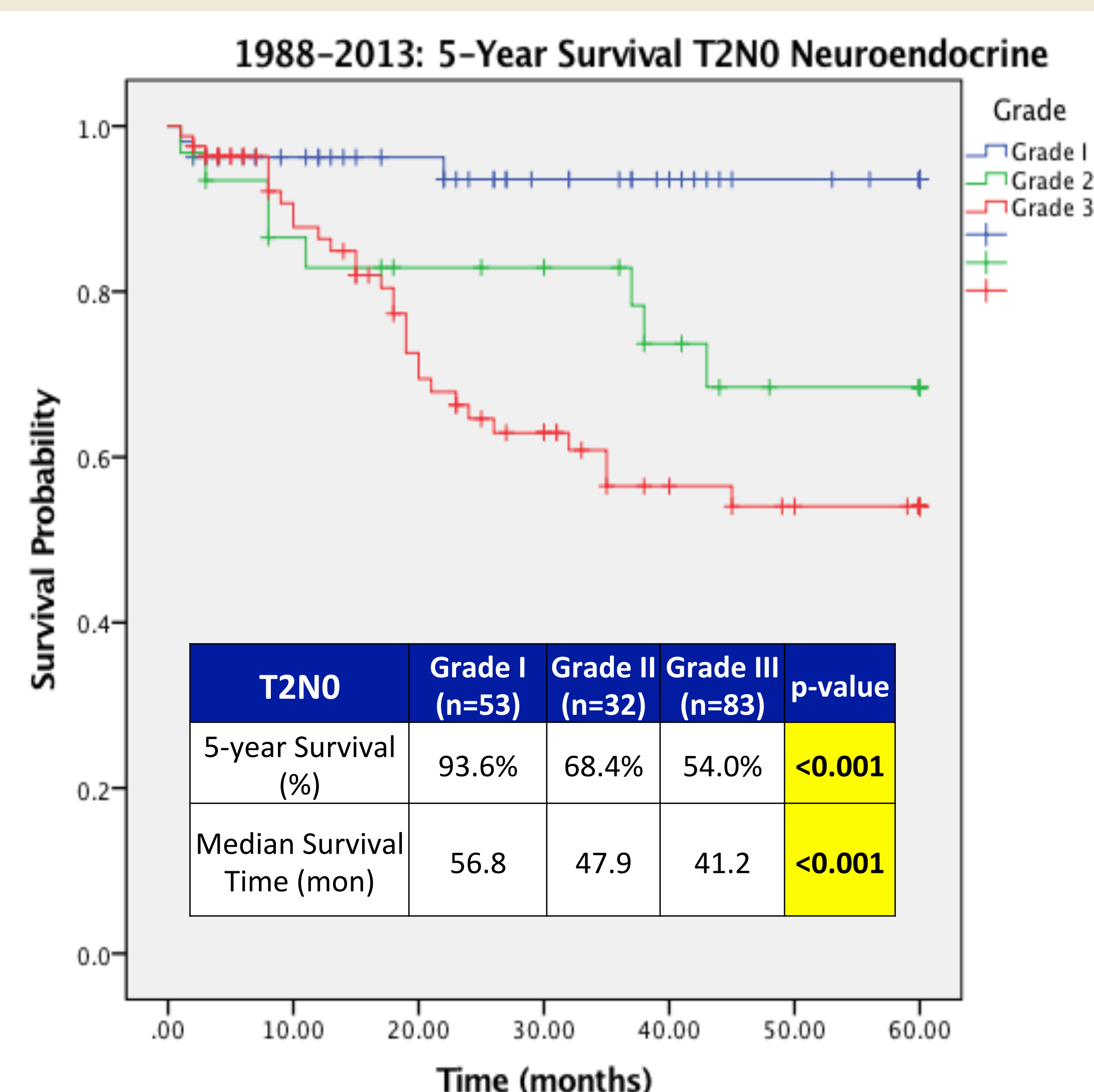


Figure 2: T2N0 Neuroendocrine patients Kaplan-Meier Survival by Grade of Differentiation; significance set at $p \leq 0.05$

T1N0 Cox Regression Analysis

Covariate	HR (95% CI)	p-value
Grade		<0.001
Grade 1	0.029 (0.007-0.125)	<0.001
Grade 2	0.229 (0.086-0.608)	0.003
Grade 3	1	-
Tumor Location		0.604
RUL or RML	1	-
RLL	1.668 (0.744-3.739)	0.214
LUL	1.072 (0.477-2.407)	0.867
LLL	1.456 (0.569-3.726)	0.433
Gender		
	1.002 (0.533-1.883)	0.994
Tumor Size		
	1.031 (0.981-1.083)	0.23

Table 3: T1N0 Cox proportional hazards analysis of cancer-specific survival. HR = Hazards Ratio; CI = Confidence Interval

T2N0 Cox Regression Analysis

Covariate	HR (95% CI)	p-value
Grade		0.018
Grade 1	0.172 (0.050-0.591)	0.005
Grade 2	0.611 (0.233-1.601)	0.316
Grade 3	1	-
Tumor Location		0.014
RUL or RML	1	-
RLL	3.603 (1.560-8.317)	0.003
LUL	1.560 (0.604-4.029)	0.358
LLL	1.012 (0.273-3.754)	0.986
Gender		
	1.122 (0.537-2.343)	0.76
Tumor Size		
	1.009 (0.987-1.031)	0.428

Table 4: T2N0 Cox proportional hazards analysis of cancer-specific survival. HR = Hazards Ratio; CI = Confidence Interval

Conclusions

Grade 3 NE patients had significantly worst survival than Grade 1 & 2 in both T1N0 & T2N0 patient populations. In T1N0 patients, the death rate for Grade 1 and Grade 2 patients was only 2.9% and 22.9% of the death rate for Grade 3, respectively. In T2N0 patients, the death rate for Grade 1 was only 17.2% of the death rate for Grade 3. In the T2N0 group, tumor location was found to be an independent risk factor affecting survival by Grade, a new finding past studies did not find. However, female gender, lymph node dissection, African-American ethnicity, and tumor size were not found to significantly impact survival, unlike past studies.^{3,4} These results suggest that histologic grade should be considered when determining adjuvant therapy and prognosis for surgically resected Stage-1 neuroendocrine carcinoma patients

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References

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