The Evolving Role of the 21 Gene Recurrence Score in the Neoadjuvant Setting

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ABSTRACT

Background: Oncotype DX 21 gene recurrence score (21-GRS) has been extensively validated for use in the adjuvant setting, and studies demonstrate that it may help to select which patients benefit from neoadjuvant chemotherapy (NACT) and neoadjuvant hormonal therapy (NAHT). Despite this, there is little data regarding how frequently it is used in the neoadjuvant setting. We assessed the use of the 21-GRS in the neoadjuvant setting and the relationship between recurrence scores and response to neoadjuvant therapy.

Methods: The National Cancer Database (NCDB) was queried from 2010 – 2016 to identify patients who received NACT or NAHT prior to definitive surgical management, and those having a 21-GRS. We compared pretreatment clinical T and N to final pathologic T and N to assess response to treatment. Multivariable analysis was then used to determine predictors for the use of the 21-GRS in the NACT and NAHT setting and its association with neoadjuvant treatment response.

Results: A total of 25,372 patients were identified who received either NACT or NAHT; 17,588 (69.3%) received NACT and 7,884 (30.7%) received NAHT. A 21-GRS was utilized in 2710 (10.7%), among whom, 335 (12.4%) received NACT and 2375 (87.6%) received NAHT. There was a significant uptrend in the overall use of the 21-GRS in any neoadjuvant setting from 185 (7.3%) in 2010 to 662 (12.8%) in 2016 (p<0.0001). While the rate of use in all patients receiving NACT remained stable at ~2% (31 to 70) there was a significantly increased use of the 21-GRS in all patients receiving NAHT from 22.6 to 35.0% (154 to 592) (p<0.0001). In patients with an available 21-GRS, the NACT patients were younger at 54.2 years than NAHT patients at 67.3 years (p<0.0001). Significant factors associated with use of a 21-GRS in the NACT cohort were lower grade and lobular histology. Significant factors associated with use in the NAHT cohort were younger age, lower Charleson/Deyo score, lobular histology, lower grade and the presence of LVI. The mean 21-GRS scores were significantly different between those having NACT 30.0 versus NAHT 16.3 (p<0.0001). The T and N response rates to NACT with a 21-GRS were 46.5% and 14.1% respectively. The T and N response rates to NAHT with an available 21-GRS were 23.6% and 1.9% respectively. The T and N complete response rates to NACT with an available 21-GRS were 2.4% and 9.8% respectively while the T and N compete response to NAHT with an available 21-GRS was 0.3% and 1.7% respectively.

Conclusions: Despite more limited data, oncologists are increasingly incorporating the use of the 21-GRS in the neoadjuvant setting. Lower 21-GRS scores predict the selection of NAHT while higher score predict the selection of NACT, suggesting its proper use. Although its use is increasing, it remains limited in this national dataset. Further validation and efforts to define specific indications for its use preoperatively may increase adoption of the 21-GRS in the neoadjuvant setting.

PURPOSE

- Evaluate trends in use of the 21-GRS use in neoadjuvant setting
- Evaluate whether the 21-GRS is predictive of selection of NACT and NAHT
- Evaluate whether the 21-GRS score correlated with down staging based on treatment modality

METHODS

- The National Cancer Database was queried between 2010-2016 for patients who received either NACT or NAHT and had an available 21-GRS and definitive surgical treatment
- Multivariable analysis was performed
- Comparison of pre-treatment clinical stage to post-treatment pathologic stage individualized for T and N, characterized a response as any decrease in T stage or any N stage

RESULTS

Table 1. Patient Characteristics

	NACT (N=17588)					NAHT (N=7784)				
	Not Performed		Performed		p-value	Not Performed		Performed		p-value
	n	%	*n*	%		*n*	%	*n*	%	
# of patients	17253	98.10	335	1.90		5409	69.49	2375	30.51	
21-GRS, mean ± SD (range)			29.99 ± 17.97 (0-95)	-				16.25 ± 8.12 (0-90)	-	
Age (years), mean ± SD (range)	54.25 ± 12.31 (18-90)		53.39 ± 12.21 (24-87)		0.2082	69.76 ± 12.53 (21-90)		61.45 ± 10.35 (24-90)		**<.0001**
≤50	6673	38.68	135	40.30		400	7.40	384	16.17	
51-70	8940	51.82	169	50.45	0.8336	2232	41.26	1543	64.97	**<.0001**
>70	1640	9.51	31	9.25		2777	51.34	448	18.86	
Race/Ethnicity										
White	11382	65.97	235	70.15		4333	80.11	1945	81.89	
Black	3732	21.63	59	17.61	0.2805	539	9.96	199	8.38	0.0686
Hispanic	1239	7.18	26	7.76		295	5.45	114	4.80	
Asian/Other/Unknown	900	5.22	15	4.48		242	4.47	117	4.93	
Charlson/Deyo Comorbidity Index										
0	14681	85.09	289	86.27		4079	75.41	1991	83.83	
1	2041	11.83	35	10.45	0.7296	952	17.60	282	11.87	**<.0001**
≥2	531	3.08	11	3.28		378	6.99	102	4.29	
Histology										
Ductal	16689	96.73	297	88.66	**<.0001**	4495	83.10	1899	79.96	**0.0009**
Lobular	564	3.27	38	11.34		914	16.90	476	20.04	
Grade										
1	525	3.04	25	7.46		1526	28.21	748	31.49	
2	3968	23.00	126	37.61	**<.0001**	2733	50.53	1329	55.96	**<.0001**
3	11793	68.35	160	47.76		847	15.66	194	8.17	
Other/Unknown	967	5.60	24	7.16		303	5.60	104	4.38	
LVI										
Yes	9800	56.80	200	59.70		3714	68.66	1776	74.78	
No	4116	23.86	73	21.79	0.5507	883	16.32	274	11.54	**<.0001**
Unknown	3337	19.34	62	18.51		812	15.01	325	13.68	
Days from dx to definitive surgery, mean ± SD	187.80 ± 60.65		193.60 ± 80.45		0.1899	161.51 ± 116.46		138.51 ± 104.85		**<.0001**
Days from dx to treatment, mean ± SD	35.69 ± 27.66		43.84 ± 30.69		**<.0001**	30.85 ± 31.10		29.88 ± 26.49		0.1581
Clinical T Stage										
0 & 1	3070	17.79	81	24.18		2248	41.56	1039	43.75	
2	8556	49.59	167	49.85	**<.0001**	2038	37.68	1045	44.00	**<.0001**
3	3370	19.53	70	20.90		607	11.22	225	9.47	
4	2257	13.08	17	5.07		516	9.54	66	2.78	
Clinial N Stage										
0	8463	49.05	193	57.61		4271	78.96	2147	90.40	
1	6520	37.79	108	32.24	**0.0073**	912	16.86	216	9.09	**<.0001**
2 & 3	2270	13.16	34	10.15		226	4.18	12	0.51	
Clinial Stage Group										
I	2055	11.91	54	16.12		2109	38.99	996	41.94	
II	9743	56.47	202	60.30	**0.0020**	2451	45.31	1261	53.09	**<.0001**
III	5455	31.62	79	23.58		849	15.70	118	4.97	

Figure 1. Trends in 21-GRS Use

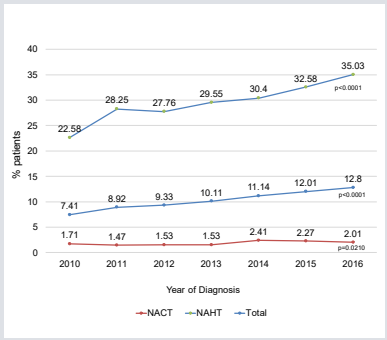
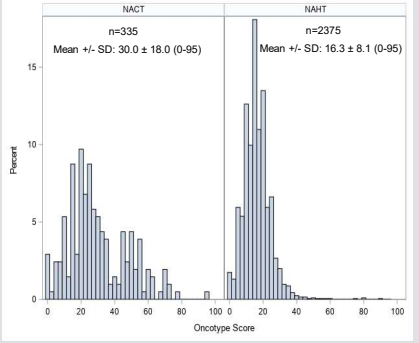


Figure 2. Distribution of 21-GRS Scores



There was a significant uptrend in the use of 21-GRS in both any neoadjuvant setting from 185 (7.4%) to 662 (12.8%) patients from 2010 to 2016 (p<0.0001) as well as in the NAHT setting from 154 (22.6%) to 592 (35.0%) (p<0.0001)

There was a significant difference in the mean 21-GRS score in patients selected for NACT (N=337) 30.0 ± 18.0 (range 0-95) while the NAHT (N=2384) mean 21-GRS score was 16.3 ± 8.1 (range 0-90) (p <0.0001)

FINDINGS

- There was a significant uptrend in the use of the 21-GRS in any neoadjuvant setting from 185 in 2010 to 662 in 2016 (p<0.001)
- The use of the 21-GRS score to select patients for NAHT significantly increased from 154 in 2010 to 591 in 2016 (21.9 to 35%) (p<0.001)
- The mean 21-GRS scores were significantly different in patients selected for NACT (N=335) 30.0 ± 18.0 (0-95) versus NAHT (N=2384) 16.3 ± 8.1 (0-90) (p <0.0001)

CONCLUSIONS

- The 21-GRS score is being increasingly used by oncologists to help select neoadjuvant treatment modality despite limited prospective data and small retrospective studies supporting its use in this setting
- Lower 21-GRS scores are associated with selection of NAHT suggesting its proper use and the inverse, high Oncotype scores predict neoadjuvant chemotherapy choice
- Further validation of the use of the 21-GRS in the neoadjuvant setting is needed

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