Survival Outcomes in Patients with Clinical Complete Response Following Neoadjuvant Chemotherapy: Is Omitting Surgery an Option?

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BACKGROUND

- Neoadjuvant chemotherapy (NCT) can reduce the extent of surgery both for the breast and for the axilla.
- In the last decade, it is widely used not only for locally advanced breast cancer, but also for some early-stage breast cancer patients with biologically aggressive subtypes, such as triple-negative and HER2+ disease, who would normally need adjuvant chemotherapy.
- Developments of new drugs and treatment combinations have increased the rates of response, and increased pathologic complete response (pCR) rates have led to the hypothesis that surgery to the primary site may not be necessary for a subset of patients.

OBJECTIVE

- As there are limited data on patients with clinical complete response (cCR) after NCT who did not undergo surgery, we sought to evaluate the survival outcomes of these patients using the National Cancer Data Base (NCDB).

METHODS

Patient Cohort

- Using the NCDB, we identified 93,417 women ≥18 years of age who were diagnosed with invasive breast cancer and received NCT between 2010 and 2015.
- In order to demonstrate the effect of NCT on survival, we extracted two different cohorts: a non-surgical and surgical cohort (**Figure 1**).

REFERENCE

Kuerer HM, Vrancken Peeters MTFD, Rea DW, Basik M, De Los Santos J, Heil J. Nonoperative Management for Invasive Breast Cancer After Neoadjuvant Systemic Therapy: Conceptual Basis and Fundamental International Feasibility Clinical Trials. Ann Surg Oncol. 2017 Oct;24(10):2855-2862.

METHODS

Statistical Analysis

- To assess differences in categorical and continuous variables, Pearson's Chi-squared, independent samples t-test and one-way ANOVA test were performed.
- Variables that are related with cCR with *p*-values <0.10 in the univariable analysis were entered into a multivariable binary logistic regression model.
- Kaplan-Meier survival curves were used to illustrate overall survival (OS) differences for the entire non-surgical cohort and subgroups.
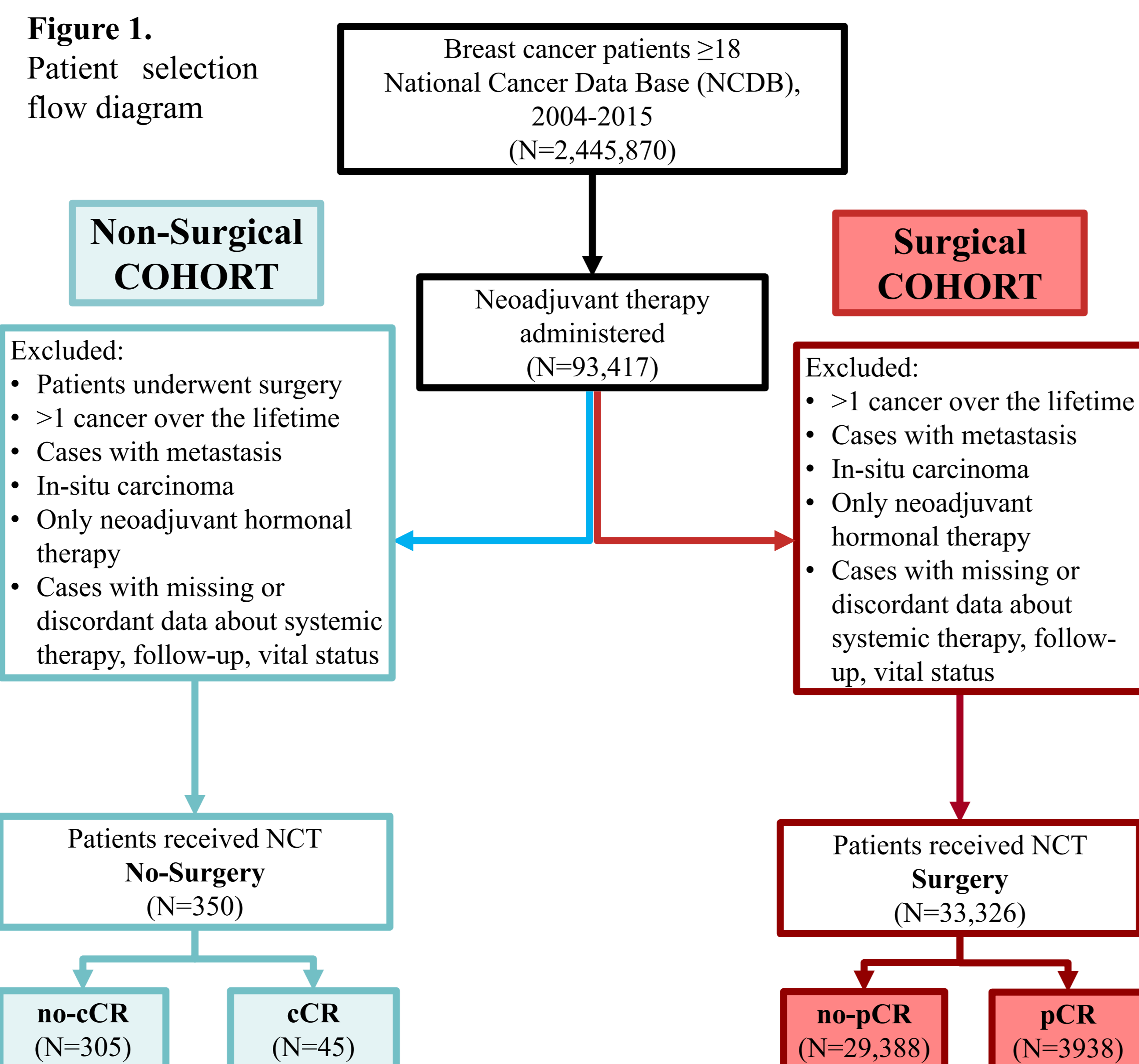- Log-rank tests with *p*-values <0.05 were considered statistically significant.

Figure 1. Patient selection flow diagram

RESULTS

Variables	Non-Surgical Cohort				Surgical Cohort			
	All Patients	Response to NCT			All Patients	Response to NCT		
		cCR	No cCR	p-value		pCR	No pCR	p-value
	N=350 (100%)	N=45 (12.9%)	N=305 (87.1%)		N=33,326 (100%)	N=3938 (11.8%)	N=29,388 (88.2%)	
Age				0.9				<0.001
Median (23-90)	54 (23-88)	54 (33-79)	54 (23-88)		52 (18-90)	50 (20-90)	52 (18-90)	
Follow-up (months)				<0.001				<0.001
Median (3-156)	30 (1-80)	37 (15-80)	29 (1-75)		37 (1-86)	43 (3-85)	36 (1-86)	
Race				0.69				0.72
Non-Hispanic White	238 (68%)	33 (73.3%)	205 (67.2%)		25,448 (76.4%)	3022 (76.7%)	22,426 (76.3%)	
Non-Hispanic Black	90 (25.7%)	10 (22.2%)	80 (26.2%)		5711 (17.1%)	657 (16.7%)	5054 (17.2%)	
Other	22 (6.3%)	2 (4.4%)	20 (6.6%)		2167 (6.5%)	259 (6.6%)	1908 (6.5%)	
Charlson/Deyo Comorbidity				0.45				<0.001
Score	299 (85.4%)	41 (91.1%)	258 (84.6%)		29,072 (87.2%)	3540 (89.9%)	25,532 (86.9%)	
0	35 (10%)	4 (8.9%)	31 (10.2%)		3593 (10.8%)	348 (8.8%)	3245 (11%)	
1	12 (3.4%)	0	12 (3.9%)		537 (1.6%)	39 (1%)	498 (1.7%)	
2	4 (1.1%)	0	4 (1.3%)		124 (0.4%)	11 (0.3%)	113 (0.4%)	
3								
AJCC Clinical Stage*				0.32				<0.001
I	14 (4.2%)	0	14 (4.8%)		2256 (6.9%)	467 (12.1%)	1789 (6.2%)	
II	150 (45.3%)	18 (43.9%)	132 (45.5%)		18,056 (55.5%)	2191 (56.9%)	15,865 (55.3%)	
III	167 (50.5%)	23 (56.1%)	144 (49.7%)		12,238 (37.6%)	1196 (31%)	11,042 (38.5%)	
Histology				0.20				<0.001
IDC	315 (90%)	38 (84.4%)	277 (90.8%)		28,059 (84.2%)	3540 (89.9%)	24,519 (83.4%)	
ILC	13 (3.7%)	1 (2.2%)	12 (3.9%)		2101 (6.3%)	142 (3.6%)	11959 (6.7%)	
IDC + ILC	13 (3.7%)	4 (8.9%)	9 (3%)		1275 (3.8%)	93 (2.4%)	1182 (4%)	
Other	9 (2.6%)	2 (4.4%)	7 (2.3%)		1891 (5.7%)	163 (4.1%)	1728 (5.9%)	
MBR Grade*				0.50				<0.001
Grade 1	9 (4.5%)	0	9 (4.9%)		2831 (9.7%)	239 (7.5%)	2592 (10%)	
Grade 2	63 (31.3%)	5 (26.3%)	58 (31.9%)		11,653 (40.2%)	1033 (32.4%)	10,620 (41.1%)	
Grade 3	129 (64.2%)	14 (73.7%)	115 (63.2%)		14,556 (50.1%)	1915 (60.1%)	12,641 (48.9%)	
ER Status*				0.10				<0.001
Positive	168 (48.8%)	15 (36.6%)	153 (50.5%)		21,527 (64.9%)	2005 (51.3%)	19,522 (66.7%)	
Negative	176 (51.2%)	26 (63.4%)	150 (49.5%)		11,628 (35.1%)	1900 (48.7%)	9728 (33.3%)	
PR Status*				0.23				<0.001
Positive	129 (32.5%)	12 (29.3%)	117 (38.6%)		18,004 (55.4%)	1603 (41.2%)	16,401 (56.2%)	
Negative	215 (62.5%)	29 (70.7%)	186 (61.4%)		15,095 (45.6%)	2289 (58.8%)	12,806 (43.8%)	
HER2 Status*				0.46				<0.001
Positive	96 (29.3%)	14 (35%)	82 (28.5%)		8327 (26.1%)	1369 (36.8%)	6958 (24.7%)	
Negative	232 (70.7%)	26 (65%)	206 (71.5%)		23,622 (73.9%)	2355 (63.2%)	21,267 (75.3%)	
Receptor Status*				0.53				<0.001
HR+/HER2-	123 (37.5%)	12 (30%)	111 (38.5%)		15,450 (48.4%)	1156 (31.1%)	14,294 (50.7%)	
HR+/HER2+	45 (13.7%)	5 (12.5%)	40 (13.9%)		5796 (18.2%)	819 (22%)	4977 (17.6%)	
HR-/HER2+	51 (15.5%)	9 (22.5%)	42 (14.6%)		2520 (7.9%)	547 (14.7%)	1973 (7%)	
HR-/HER2-	109 (33.2%)	14 (35%)	95 (33%)		8164 (25.6%)	1199 (32.2%)	6965 (24.7%)	
Radiation Therapy*				<0.001				<0.001
Yes	106 (30.8%)	33 (73.3%)	73 (24.4%)		26,019 (78.3%)	2914 (74.1%)	23,105 (78.9%)	
No	238 (69.2%)	12 (26.7%)	227 (75.6%)		7211 (21.7%)	1016 (25.9%)	6195 (21.1%)	
Adjuvant Endocrine Therapy*				0.07				<0.001
Yes	62 (19.5%)	12 (29.3%)	50 (18.1%)		22,126 (67.7%)	2165 (56.1%)	19,961 (69.3%)	
No	256 (80.5%)	29 (70.7%)	227 (81.9%)		10,548 (32.3%)	1695 (43.9%)	8853 (30.7%)	

Table 1. Clinico-pathologic features of non-surgical and surgical cohorts; NCDB, 2010-2015.
* Missing data not included and percentages calculated for available data.

- 5-year OS for the cCR and no-cCR groups (non-surgical cohort) was 96.8% and 69.8% (*p*=0.004), respectively (Figure 2a).
- 5-year OS for the pCR and no-pCR groups (surgical cohort) was 87.3% and 77.8% (*p*<0.001), respectively (Figure 2b).
- 5-year OS was 79% for the surgical cohort and 74.8% for the non-surgical cohort (*p*=0.003) (Figure 3a).
- **5-year OS was 92.5% for the surgical cohort patients with pCR and 96.8% for the non-surgical cohort patients with cCR (*p*=0.15) (Figure 3b).**
- In multivariable analysis, clinical stage ≤T2 (OR:6.56; 95% CI 2.48-17.32; *p*<0.001) and nodal positivity (OR:5.02; 95% CI 1.71-14.69; *p*=0.003) were significant predictors for cCR following NCT for non-surgical cohort.
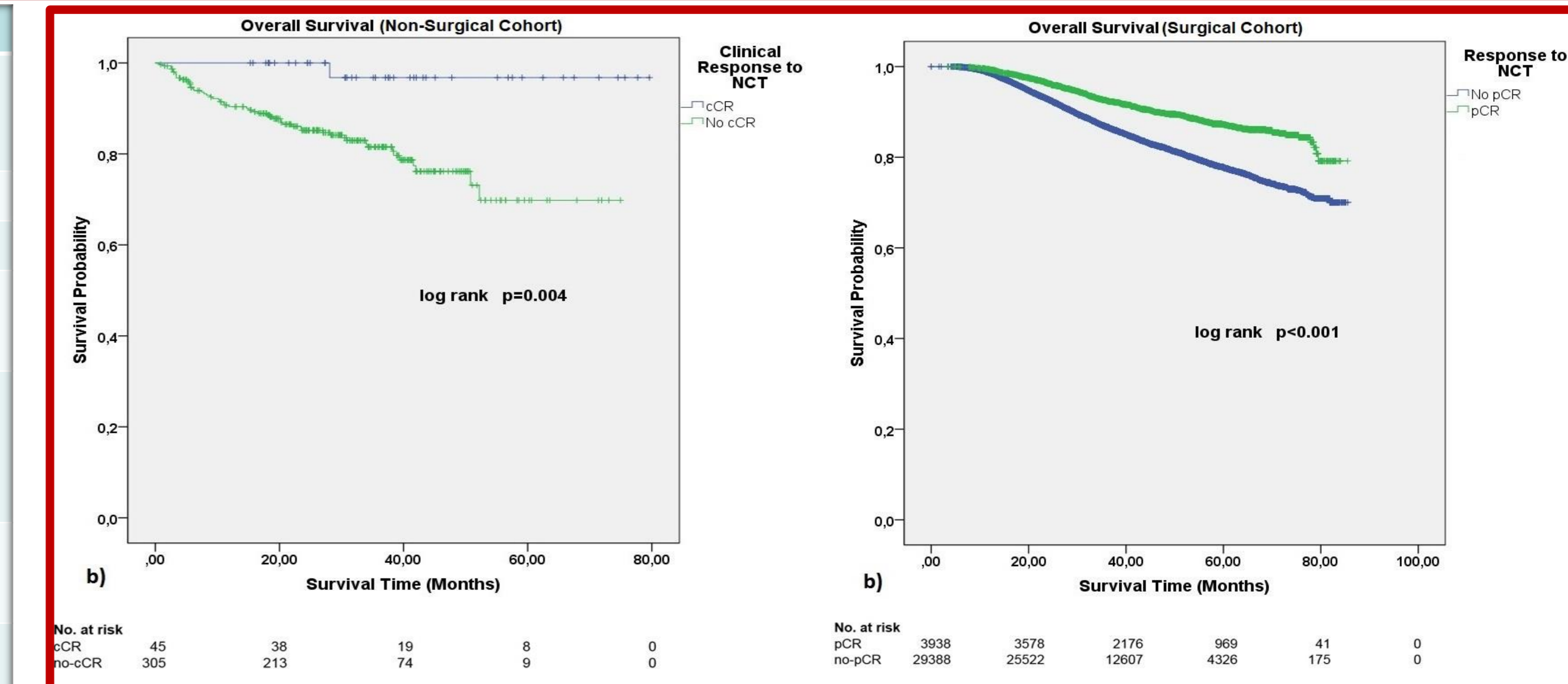

Figure 2a. Kaplan-Meier survival plots for non-surgical cohort grouped as cCR vs. no cCR

Figure 2b. Kaplan-Meier survival plots for surgical cohort grouped as pCR vs. no pCR
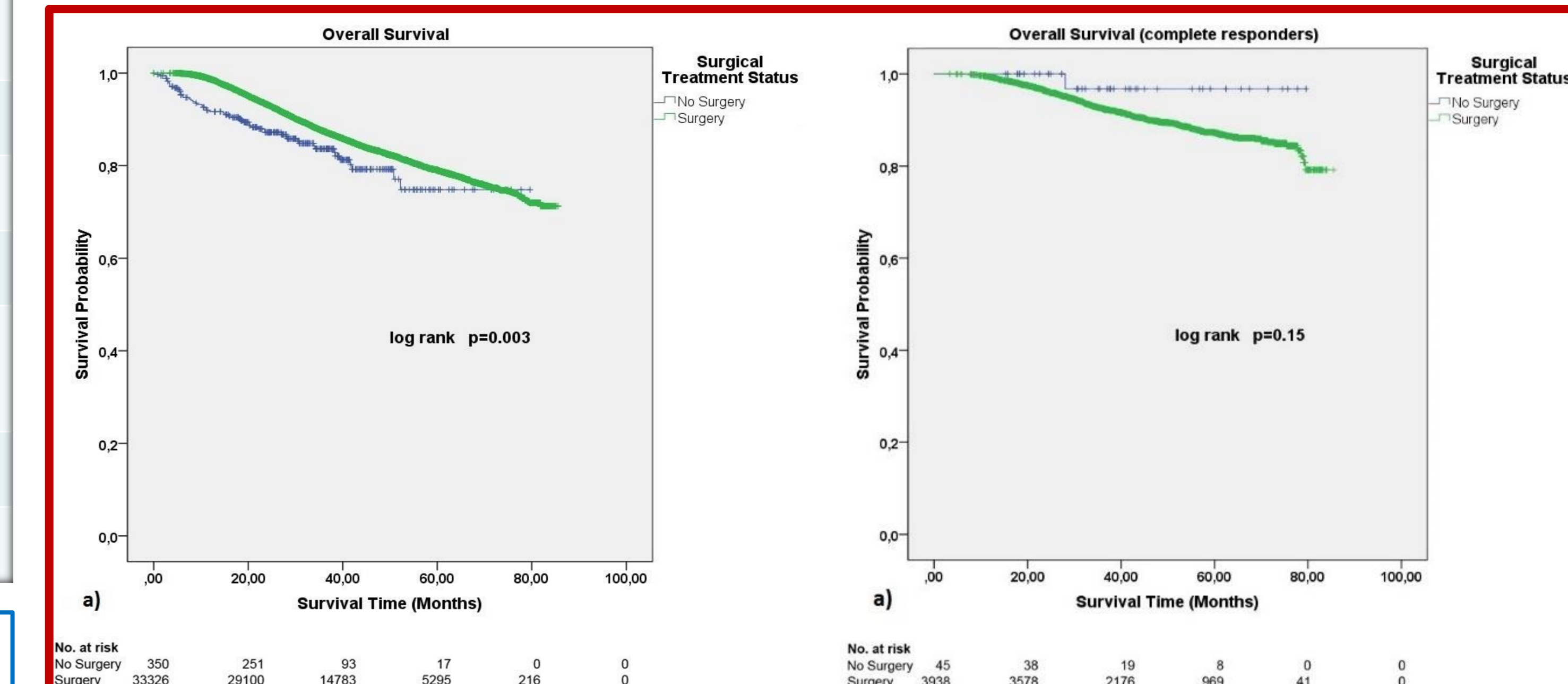

Figure 3a. Kaplan-Meier survival plots for NCT patients who received surgery vs. those who did not.

Figure 3b. Kaplan-Meier survival plots for NCT patients with cCR without surgery vs. cCR with surgery.

CONCLUSIONS

- Omission of surgery for selected group of patients with cCR after NCT may be the next step in advancement in breast cancer care.
- This retrospective cohort study demonstrated that active surveillance or de-escalating therapy to the primary tumor site and administering radiotherapy instead could be a possible option to consider in patients who achieved cCR after NCT as part of a clinic trial.
- The results from ongoing trials along with new drug combination therapies and improved imaging and biopsy techniques may help physicians identify patients who may not need surgery to the breast following NCT.