Utility of the CPS+EG scoring system in triple-negative breast cancer treated with neoadjuvant chemotherapy

#4042

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Background

- Pathologic complete response (pCR) after neoadjuvant chemotherapy (NACT) is associated with superior disease free (DFS) and overall survival (OS).[1]
- This association is strongest in triple-negative breast cancer (TNBC).[1]
- Post-neoadjuvant therapy has become a standard option for patients not achieving a pCR after NACT, especially in HER2+ disease and TNBC.[2,3]
- The CPS+EG system, based on pre-treatment clinical (CS) and post-treatment pathologic stage (PS), grade and estrogen receptor status, leads to a refined estimate of prognosis after NACT in all comers and HR+/HER2-.[4,5,6]

Here, we investigate if CPS+EG scoring provides a superior estimate of prognosis in TNBC after NACT to select patients for post-neoadjuvant therapy.

Patients and Methods

Trial design

10526 patients have been treated within 9 prospective randomized neoadjuvant trials conducted by the German Breast Group (GBG) and the Arbeitsgemeinschaft Gynäkologische Onkologie-Breast (AGO-B) study group until 2013. All trials investigated anthracycline and taxane-based chemotherapy regimens. The CPS+EG score was calculated as depicted in **Figure 1**. ER, PgR, HER2 and grade were assessed on pretreatment core biopsies. For this analysis we only included patients with HER2-negative disease. Excluded patients and reasons are summarized **Figure 2**. The primary goal was to investigate if CPS+EG scoring provides a superior estimate of prognosis in TNBC after NACT to select patients for post-neoadjuvant therapy.

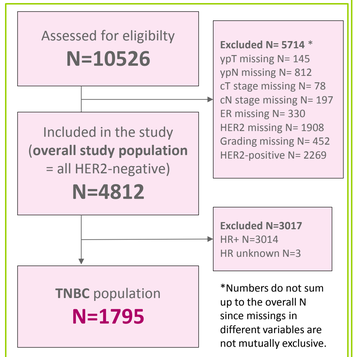
Statistical consideration

Disease-free survival (DFS) was plotted as Kaplan Meier curves. Local progression during NACT was not counted as an event. Log-rank p-values were calculated to compare different stages or risk scores. Five-year survival analysis (DFS), including percentage of survival and associated 95% confidence intervals, was conducted using IBM SPSS Statistics 25.

Figure 1: CPS+EG score point assignment

Clinical Stage		
I	0	T1N0; T0N1mi, T1N1mi
IIA	0	T0N1; T1N1; T2N0
IIB	1	T2N1; T3N0
IIIA	1	T0-2N2
IIIB	2	T4N0-2
IIIC	2	Any T N3
Pathologic Stage		
0	0	T0/isN0
I	0	T1N0; T0N1mi, T1N1mi
IIA	1	T0N1; T1N1; T2N0
IIB	1	T2N1; T3N0
IIIA	1	T0-2 N2
IIIB	1	T4 N0-N2
IIIC	2	Any T N3
Tumor Biologic Factors		
ER negative	1	
Nuclear grade 3	1	

Figure 2: Consort statement

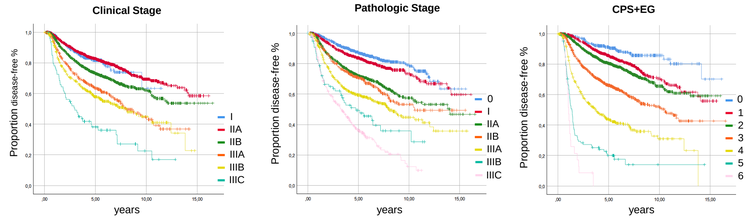


Results

In HER2- patients, CPS+EG leads to a refined estimate of prognosis (**Figure 3a**). TNBC patients who achieved a pCR had a 5-year DFS of 86% (n=822, 45.8%), whereas patients with residual stage I had a 5-year DFS of 77.5% (n=383; 21.3%). CPS+EG score was unable to identify non-pCR patients with a sufficiently good prognosis, to avoid post-neoadjuvant therapy (**Figure 3b**). The best prognostic TNBC CPS+EG groups (score 1/2) in non-pCR patients had a 5-year DFS of 77.5% and 74.4%, respectively (n=362; 37.2%) (**Figure 3b**). CPS+EG identified a small group of patients (n=26; 3.2%) at high risk of recurrence despite pCR, mainly based on initial stage (CS+EG score > 3; 5-year DFS 61.4%) that might benefit from additional treatment (**Figure 3b**). However, prognosis of patients with a CPS+EG score of 3 (5-year DFS: 64%), could be further discriminated by pCR (5-year DFS: 83.9% vs 49.7%) (**Figure 4**).

Figure. 3a: HER2-

DFS stratified according to clinical stage, pathologic stage and CPS+EG



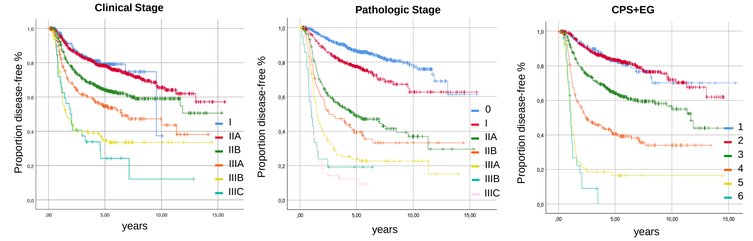
CS (N=4812)	5-year DFS rate	95% CI		N	%
0	0	0	0	0	0
I	0.817	0.778	0.856	442	9.2
IIA	0.829	0.811	0.847	1917	39.8
IIB	0.732	0.707	0.757	1418	29.5
IIIA	0.635	0.588	0.682	479	10.0
IIIB	0.579	0.532	0.626	482	10.0
IIIC	0.382	0.266	0.498	74	1.5

PS (N=4812)	5-year DFS rate	95% CI		N	%
0	0.872	0.852	0.892	1256	26.1
I	0.838	0.814	0.862	1116	23.2
IIA	0.721	0.692	0.750	1090	22.7
IIB	0.708	0.663	0.753	448	9.3
IIIA	0.593	0.550	0.636	549	11.4
IIIB	0.494	0.376	0.612	78	1.6
IIIC	0.364	0.303	0.425	275	5.7

CPS-EG (N=4812)	5-year DFS rate	95% CI		N	%
0	0.913	0.884	0.942	420	8.7
1	0.856	0.834	0.878	1136	23.6
2	0.805	0.785	0.825	1715	35.6
3	0.660	0.629	0.691	992	20.6
4	0.439	0.388	0.490	417	8.7
5	0.200	0.120	0.280	106	2.2
6	0.000	0.000	0.000	26	0.5

Figure 3b: TNBC

DFS stratified according to clinical stage, pathologic stage and CPS+EG



CS (N=1795)	5-year DFS rate*	95% CI		N	%
0	0	0	0	0	0
I	0.791	0.734	0.848	234	13.0
IIA	0.783	0.752	0.814	751	41.8
IIB	0.639	0.594	0.684	479	26.7
IIIA	0.546	0.466	0.626	170	9.5
IIIB	0.347	0.261	0.433	129	7.2
IIIC	0.242	0.077	0.407	32	1.8

PS (N=1795)	5-year DFS rate*	95% CI		N	%
0	0.864	0.839	0.889	822	45.8
I	0.775	0.730	0.820	383	21.3
IIA	0.489	0.428	0.550	292	16.3
IIB	0.394	0.290	0.498	89	5.0
IIIA	0.239	0.153	0.325	109	6.1
IIIB	0.190	0.021	0.359	21	1.2
IIIC	0.122	0.044	0.200	79	4.4

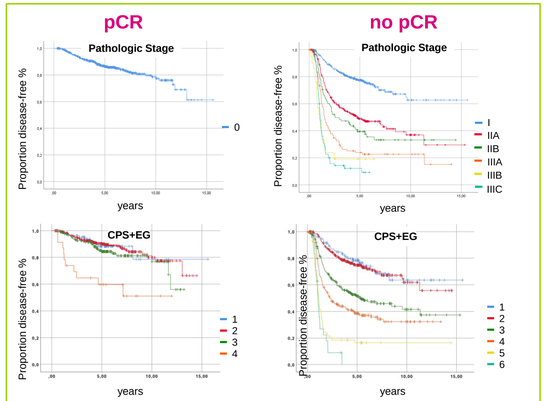
CPS-EG (N=1795)	5-year DFS rate*	95% CI		N	%
0	0	0	00	0	0
1	0.831	0.772	0.890	189	10.5
2	0.835	0.808	0.862	761	42.4
3	0.640	0.595	0.685	497	27.7
4	0.406	0.341	0.471	252	14.0
5	0.164	0.074	0.254	71	4.0
6	0.000	0.000	0.000	25	1.4

Table 1: Baseline characteristics

		complete database		HER2 negative CPS+EG cohort		TNBC CPS+EG cohort	
		N	valid %	N	valid %	N	valid %
All patients		10526		4812		1795	
pre-treatment clinical tumour stage	cT1	1184	11.3	666	13.8	322	17.9
	cT2	6481	62.0	2994	62.2	1120	62.4
	cT3	1585	15.2	645	13.4	215	12.0
	cT4a-c	586	5.6	263	5.5	45	2.5
	cT4d	612	5.9	243	5.1	92	5.1
pre-treatment clinical nodal status	cN0	5314	51.4	2550	53.1	1016	56.6
	cN1	4460	42.4	2001	41.6	678	37.8
	cN2	422	4.0	181	3.8	68	3.8
	cN3	133	1.3	74	1.5	32	1.8
Tumor grade	1	352	3.5	185	3.8	24	1.3
	2	5275	52.4	2437	50.6	491	27.4
	3	4447	44.1	2190	45.5	1280	71.3
ER status	Negative	4030	39.5	1982	41.2	1795	100.0
	Positive	6166	60.5	2830	58.8	NA	
HER-2 status	Negative	6349	73.7	4812	100.0	1795	100.0
	Positive	2269	26.3	NA		NA	
pCR (ypT0/Tis ypN0)		**2572**	**24.4**	**1256**	**26.1**	**822**	**45.8**

Figure 4: TNBC split by pCR status

DFS stratified according to pathologic stage and CPS+EG



CPS-EG (N=822)	5-year DFS rate	95% CI		N	%
0	-	-	-	-	-
1	0.880	0.809	0.951	101	12.3
2	0.887	0.858	0.916	487	59.2
3	0.839	0.784	0.894	208	25.3
4	0.614	0.416	0.812	26	3.2
5	-	-	-	-	-
6	-	-	-	-	-

CPS+EG: TNBC, pCR patients

CPS-EG (N=973)	5-year DFS rate	95% CI		N	%
0	-	-	-	-	-
1	0.775	0.679	0.871	88	9.0
2	0.744	0.689	0.799	274	28.2
3	0.497	0.436	0.558	289	29.7
4	0.382	0.315	0.449	226	23.2
5	0.164	0.074	0.254	71	7.3
6	0.000	0.000	0.000	25	2.6

CPS+EG: TNBC, non-pCR patients

* see Figure 3b for 5-yr DFS according to pathologic stage

Conclusions

- In TNBC the CPS+EG score does not lead to a clinically useful better categorization of patients into distinct prognostic groups beyond pCR and pathologic stage
- CPS+EG fails to identify a prognostic favourable subgroup not achieving a pCR, which might not be considered candidates for post-neoadjuvant stragies
- However, CPS+EG identifies a small subgroup of patients with TNBC and HER2- BC at high risk of recurrence despite a pCR. These are defined by G3 and clinical stage IIIB/C tumours.

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