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Identifying Premenopausal Patients with Early-Stage Hormone Receptor–Positive Node-Negative Breast Cancer at Minimal Risk of Distant Recurrence by Breast Cancer Index

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INTRODUCTION

- Adjuvant endocrine therapy for 5 years with ovarian function suppression (OFS) is recommended for premenopausal breast cancer patients with endocrine-sensitive tumors at high enough risk of recurrence, e.g. younger age, high grade tumor or nodal involvement.
- Genomic risk assessment may help to personalize OFS-based treatment selection. The Breast Cancer Index (BCI) test was previously confirmed as prognostic in premenopausal patients in the SOFT and TEXT trials [1].
- An adjusted Breast Cancer Index (BCI) model with an additional cutpoint was recently identified and validated to classify postmenopausal patients with HR+, N0 breast cancer with minimal (<5%) risk of distant recurrence within 10 years, even without receiving any adjuvant endocrine therapy [2].
- We evaluated the prognostic performance of the adjusted BCI model minimal-risk cutpoint in premenopausal patients with HR+ N0 breast cancer in SOFT and TEXT for supporting decision-making about OFS-containing adjuvant endocrine therapy.

METHODS

- The analysis included 1110 patients with N0 cancers from SOFT (randomly assigned to tamoxifen, exemestane+OFS or tamoxifen+OFS), and 915 patients from TEXT (assigned exemestane+OFS or tamoxifen+OFS) (**Table 1**).
- The new BCI cutpoint of 3.0, along with the current cutpoints (5.1 and 6.5), was used to re-classify the low-risk group as minimal risk or remaining as low risk; those in intermediate- or high-risk groups remained as previously classified.
- The primary endpoint was distant recurrence-free interval (DRFI). 10-year DR was reported as one minus Kaplan-Meier estimate of DRFI with pointwise 95% confidence intervals (CI). The median follow-up was 12 and 13 years for SOFT and TEXT trial, respectively

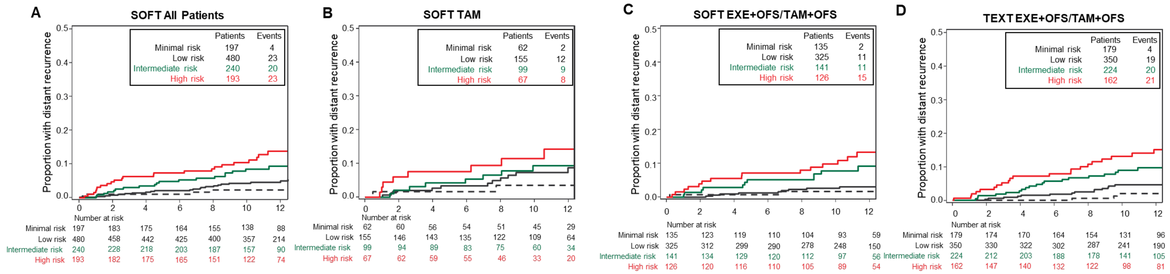
Table 1. Clinicopathologic characteristics of patients in HR+ N0 BCI cohorts of SOFT and TEXT, all patients and by treatment assignment in SOFT

	SOFT						TEXT	
	All N0		Tamoxifen		Exemestane+OFS or Tamoxifen+OFS		Exemestane+OFS or Tamoxifen+OFS	
	n	%	n	%	n	%	n	%
N in BCI analysis population	*1110*	*100.0*	*383*	*100.0*	*727*	*100.0*	*915*	*100.0*
Chemotherapy*								
No	715	64.4	240	62.7	475	65.3	545	59.6
Yes	395	35.6	143	37.3	252	34.7	370	40.4
Age at randomization								
<35	92	8.3	37	9.7	55	7.6	65	7.1
35-39	173	15.6	71	18.5	102	14.0	133	14.5
40-44	315	28.4	104	27.2	211	29.0	327	35.7
45-49	382	34.4	126	32.9	256	35.2	313	34.2
50+	148	13.3	45	11.7	103	14.2	77	8.4
Tumor size								
≤2 cm	824	74.2	284	74.2	540	74.3	646	70.6
>2 cm	278	25.0	94	24.5	184	25.3	265	29.0
Tumor grade*								
1	327	29.5	108	28.2	219	30.1	165	18.0
2	574	51.7	194	50.7	380	52.3	542	59.2
3	195	17.6	77	20.1	118	16.2	204	22.3
HER2 status+								
HER2–	984	88.6	337	88.0	647	89.0	795	86.9
HER2+	100	9.0	35	9.1	65	8.9	115	12.6

*Optional chemotherapy was prior to randomization in SOFT and after randomization in TEXT.
+Tumor grade and HER2 status were determined locally.
There were a few unknown tumor size, grade or HER2 status, not shown.

RESULTS

Figure 1. Kaplan-Meier estimates of DRFI in the SOFT and TEXT N0 cohorts according to the BCI risk groups of the adjusted BCI model. Minimal-risk group is indicated by a dashed black line.



Prognosis of the adjusted BCI model in the SOFT & TEXT N0 cohorts:

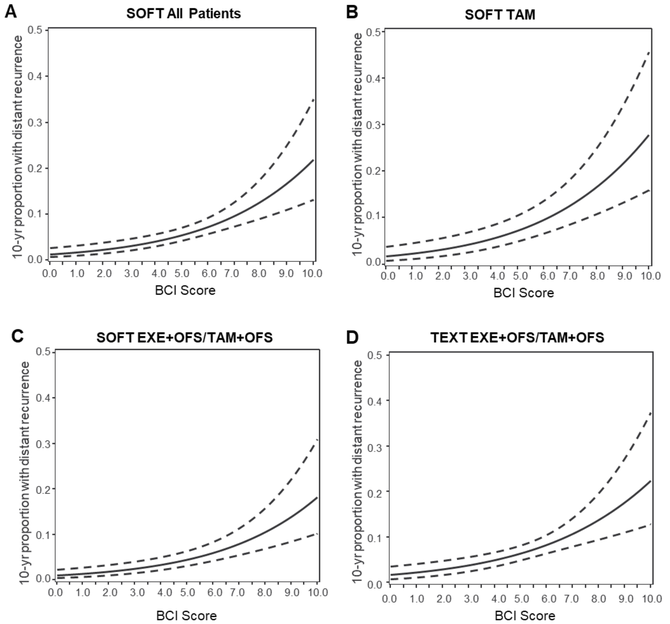
- In the SOFT cohort, the adjusted BCI model re-categorized 17.8% of patients as minimal risk and 43.2% as low risk; there were 21.6% and 17.4% as intermediate and high-risk based upon the current BCI model.
- In SOFT, the estimated 10-year risk of distant recurrence was 2.3% (95% CI, 0.9–6.0) among those patients re-classified as minimal risk, and for the revised low-risk group was 4.1% (95% CI, 2.6–6.5; HR low vs minimal risk, 1.93 [95% CI, 0.66-5.61]) (**Figure 1A, Table 2**).
- In the SOFT tamoxifen-assigned group, the estimated 10-year distant recurrence of 3.5% (95% CI, 0.9–13.3) and 7.2% (95% CI, 2.0–5.2) in the reclassified minimal- and low-risk groups (**Figure 1B, Table 2**). In the SOFT exemestane+OFS or tamoxifen+OFS treatment groups, the estimated 10-year of distant recurrence was 1.7% (95% CI, 0.4–6.6) and 2.7% (4.0–13.1) respectively (**Figure 1C; Table 2**).
- In the TEXT cohort (exemestane+OFS or tamoxifen+OFS), 19.6% and 38.3% of patients were re-categorized as minimal and low risk; estimated 10-year distant recurrence was 2.0% (95% CI, 0.7–6.2) and 4.6%, respectively (95% CI, 2.8–7.7; HR low vs minimal risk, 2.50 [95% CI, 0.85–7.36]). (**Figure 1D, Table 2**).

Table 2. Estimated distant recurrence probabilities at 10 years from randomization of the four risk groups of the adjusted BCI model in SOFT and TEXT N0 cohorts.

N0 Cohort	Patients, no. (%)	10-year Distant Recurrence, % (95% CI)
SOFT All	*n = 1110*	
BCI minimal risk	197 (17.8)	2.3 (0.9–6.0)
BCI low risk	480 (43.2)	4.1 (2.6–6.5)
BCI intermediate risk	240 (21.6)	8.4 (5.4–13.0)
BCI high risk	193 (17.4)	10.4 (6.8–15.9)
SOFT tamoxifen	*n = 383*	
BCI minimal risk	62 (16.2)	3.5 (0.9–13.3)
BCI low risk	155 (40.5)	7.2 (4.0–13.1)
BCI intermediate risk	99 (25.8)	9.3 (4.7–17.8)
BCI high risk	67 (17.5)	11.4 (5.6–22.6)
SOFT exemestane+OFS or tamoxifen+OFS	*n = 727*	
BCI minimal risk	135 (18.6)	1.7 (0.4–6.6)
BCI low risk	325 (44.7)	2.7 (1.4–5.3)
BCI intermediate risk	141 (19.4)	7.9 (4.3–14.2)
BCI high risk	126 (17.3)	9.9 (5.7–16.8)
TEXT All (exemestane+OFS or tamoxifen+OFS)	*n = 915*	
BCI minimal risk	179 (19.6)	2.0 (0.7–6.2)
BCI low risk	350 (38.3)	4.6 (2.8–7.7)
BCI intermediate risk	224 (24.5)	9.0 (5.7–13.9)
BCI high risk	162 (17.7)	13.1 (8.5–19.7)

SOFT minimal risk, 14.7% (29/197) had prior chemotherapy; TEXT minimal risk, 27.4% (49/179) had chemotherapy

Figure 2. Relation of the continuous BCI score with estimated probability of distant recurrence within 10 years of randomization in the SOFT and TEXT N0 cohorts.



- The estimated increasing function of 10-year distant recurrence in relation to the continuous BCI score is presented for all patients (**Figure 2A**) & patient subsets according to assigned treatment regimen (**Figure 2B and 2C**) in the SOFT N0 cohort; and for patients in the TEXT N0 cohort (**Figure 2D**).

CONCLUSIONS

- This study confirmed the prognostic ability of the adjusted BCI model minimal-risk cutpoint to re-classify a subset of premenopausal patients with HR+ N0 breast cancer estimated to have minimal risk of distant recurrence within 10 years.
- These findings suggest that patients categorized as minimal risk may derive only a small benefit from OFS-containing endocrine therapy regimens and may represent a subgroup for whom adjuvant tamoxifen alone would be adequate endocrine therapy.

ACKNOWLEDGEMENTS & REFERENCES

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1. O'Regan et al; PMID 39145953. 2. Jilderda et al; PMID 40145943.

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