Risk factors and clinical characteristics of loco-regional relapse in local advanced breast cancer treated with neoadjuvant chemotherapy following mastectomy and radiotherapy: a single-center experience for non-pathological complete responders

Liang Huang (Department of Breast Surgery, Fudan University Shanghai Cancer Center/Cancer Institute, Shanghai, China)

BACKGROUND: To investigate the prognostic factors that could possibly affect the local-regional recurrence (LRR) of breast cancer patients without achieving pathological complete response (pCR) after neoadjuvant chemotherapy, and built a prognostic nomogram to predict patients' outcome.

METHODS: The retrospective analysis included consecutively 510 patients who had locally advanced breast cancer received NCT followed by surgery and radiotherapy at Shanghai Cancer Center from 1999 to 2011. Multivariate analyses were used to identify independent predictors of LRR. The primary end point was time to LRR as first event.

RESULTS: Median follow-up for the entire study population was 61 months (rang 5 to 128 months). 62 LRR events had occurred after median 61 months of follow-up. The five-year cumulative incidence of local recurrence and regional recurrence was 8.63% and 4.31% separately. Luminal A had lowest local-region recurrence rate (6.44%), luminal B subtype have highest LRR rate (22.86%). Hormone receptor positive and HER2 negative subgroup have similar locally and regional recurrences rate, while HER2 positive and triple negative subgroups have higher locally failure (p=0.012). A multivariate analysis was performed that positivity for ≥4 lymph nodes and Ki-67 index ≥14% were independent factors for LRR-free recurrence. According to our prognostic model, the 5-year LRR free survival rates in low, median and high-risk groups were 95.5%, 89.1%, 67.1%, respectively (log-rank test $p < 0.001$). In relevant literature, the annual risk of local-regional recurrence peaked between two or three years after the initial diagnosis. In contrast, the annual recurrence rate curve of high risk subgroup for neoadjuvant patients exhibited one peak near 1 year (17% per annum). Median and low-risk subgroup had not obvious recurrence peak.

CONCLUSION: Positivity for ≥4 lymph nodes and Ki-67 index ≥14% were independent factors for LRR-free recurrence. This prognostic model has a considerable clinical value in predicting local-regional recurrence, which could help clinicians to design an appropriate local-regional treatment specifically and surveillance individually. Potential is also highlighted for the design of post-neoadjuvant adjuvant studies in these high-risk populations.

TABLE. Univariate and multivariate analysis of time to locoregional recurrence

	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
Age (≥50y vs. < 50y)	1.387	0.841-2.288	0.200		-	
Menopause status (pre vs. post)	1.493	0.907-2.459	0.115		-	
pT (T1 vs. T2/3)	2.158	1.207-3.860	0.010	1.625	0.902-2.926	0.106
pN (N0/1 vs. N2/3)	3.489	1.950-6.242	<0.001	3.295	1.828-5.939	<0.001
MP (3/4 vs. 2-0)	1.594	0.968-2.623	0.067		-	
ER (positive vs. negative)	0.724	0.440-1.193	0.205		-	
PR (positive vs. negative)	0.806	0.488-1.333	0.401		-	
HER2 (positive vs. negative)	1.61	0.942-2.776	0.081		-	

	7					
Ki67 (≥14% vs. < 14%)	3.105	1.884-5.119	<0.001	2.897	1.701-4.937	<0.001
nuclear grade (1/2 vs. 3)	2.205	1.310-3.710	0.003	1.371	0.787-2.390	0.266
LVI (positive vs. negative)	0.936	0.545-1.606	0.809		-	
clinical response (CR/PR vs. SD/PD)	1.506	0.915-2.479	0.107		-	
Chemo regimen (non-Taxel vs Taxel)	0.961	0.560-1.650	0.886		-	

FIGURE. Kaplan-Meier curves for LRFS (A) and OS (B) according to the prognostic model. Annual local regional recurrence hazard rate (C) according to the prognostic model.