

# Young Age is Associated with Increased Locoregional Recurrence in Node-Positive Breast Cancer with Luminal Subtypes

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## INTRODUCTION

The effect of biological subtypes within breast cancer on prognosis is influenced by age at diagnosis. We investigated the association of young age with locoregional recurrence (LRR) according to hormone receptor status

## METHODS

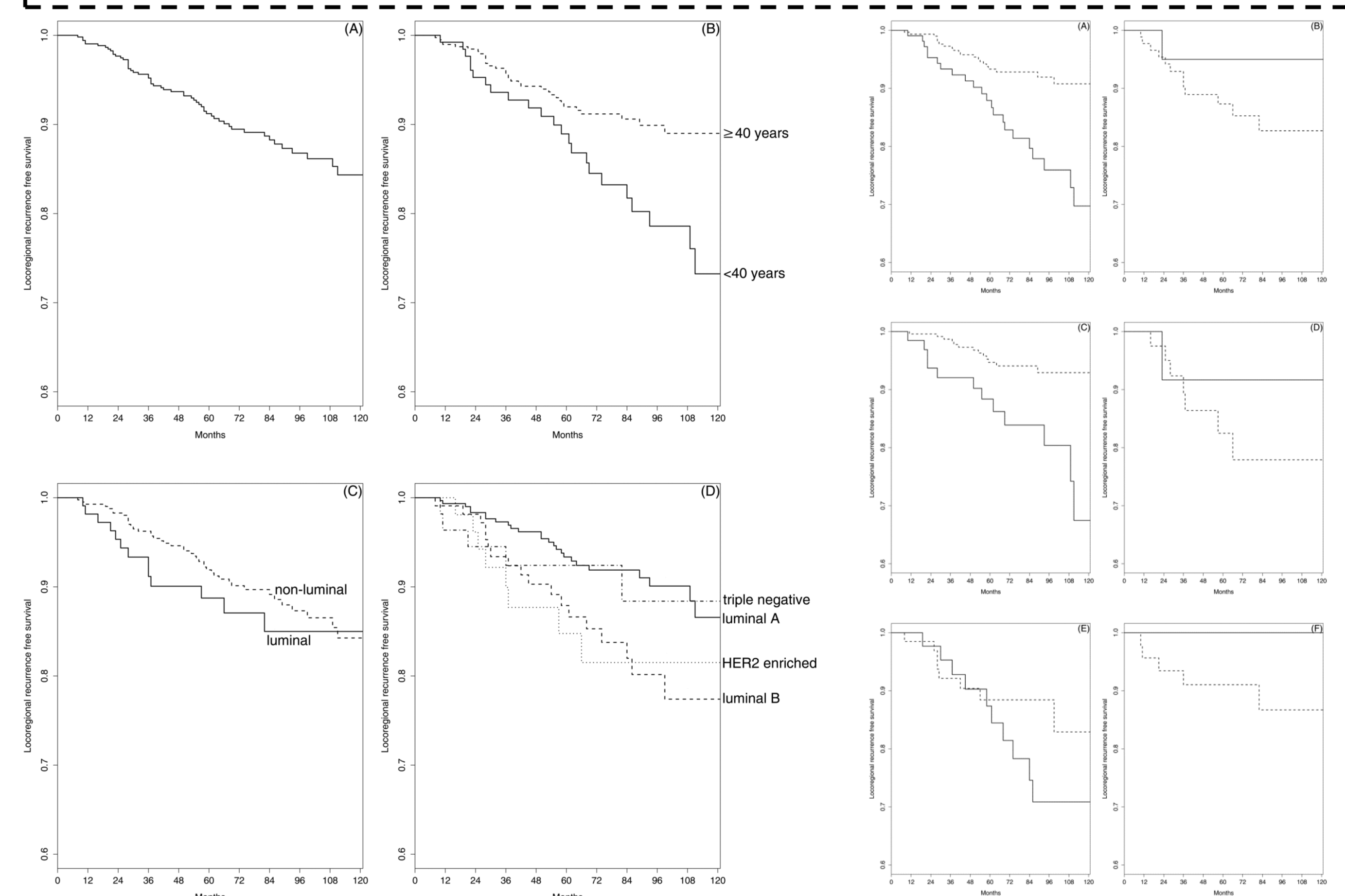
Medical records of 524 Korean breast cancer patients with positive lymph nodes between 1999 and 2010 who received curative surgery and adjuvant chemotherapy were reviewed retrospectively. Biological subtype was determined by immunohistochemical markers including estrogen receptor (ER), progesteron receptor (PR) and human epidermal growth factor receptor type 2 (HER2); luminal A (ER or PR+, HER2-,  $n = 304$ ), luminal B (ER or PR+, HER2+,  $n = 109$ ), HER2-enriched (ER-, PR-, HER2+,  $n = 55$ ) and triple negative (ER-, PR-, HER2-,  $n = 56$ ).

### Patient characteristics

	Age < 40 ( $n = 129$ )	Age $\geq 40$ ( $n = 395$ )	$p$
Type of operation			.31
breast conserving	53 (41.1)	184 (46.6)	
mastectomy	76 (58.9)	211 (53.4)	
Pathologic T stage			.30
1-2	113 (87.6)	360 (91.1)	
3-4	16 (12.4)	35 (8.9)	
N stage			.17
1	75 (58.1)	241 (61.0)	
2	23 (17.8)	87 (22.0)	
3	31 (24.0)	67 (17.0)	
AJCC stage			.61
II	75 (58.1)	241 (61.0)	
III	54 (41.9)	154 (39.0)	
no. of dissected LN	mean, 20.8	mean, 20.1	.36
Lymph node ratio			.47
$\leq 0.2$	72 (55.8)	236 (59.7)	
$> 0.2$	57 (44.2)	159 (40.3)	
resection margin			.77
$\geq 2$ mm	105 (81.4)	326 (82.5)	
$< 2$ mm	24 (18.6)	69 (17.5)	
Histologic grade			.62
low	9 (7.0)	34 (8.6)	
intermediate	44 (34.1)	155 (39.2)	
high	70 (54.3)	189 (47.8)	
unknown	6 (4.7)	17 (4.3)	
Hormone receptor			.14
negative	21 (16.3)	90 (22.8)	
positive	108 (83.7)	305 (77.2)	
Estrogen receptor			.18
negative	31 (24.0)	121 (30.6)	
positive	98 (76.0)	274 (69.4)	
Progesterone receptor			.10
negative	30 (23.3)	124 (31.4)	
positive	99 (76.7)	271 (68.6)	
HER2 overexpression			$< .01$
negative	74 (57.4)	286 (72.4)	
positive	55 (42.6)	109 (27.6)	

## RESULTS

During median follow up of 84 months, the 10-year locoregional recurrence free survival rate (LRRFS) was 84.3% for all patients. Patients  $< 40$  years showed significantly worse 10-year LRRFS than  $\geq 40$  years (73.2% vs. 89.0%, respectively,  $p = .01$ ). The difference of the 10-year LRRFS between two age groups was particularly remarkable in luminal subtypes (69.7% for  $< 40$  years vs. 90.8% for  $\geq 40$  years,  $p < .01$ ). After multivariate analysis, which used luminal subtypes in  $\geq 40$  years as reference, luminal subtypes in  $< 40$  years were significantly associated with increased risk of LRR (Hazard ratio, 2.33; 95% CI, 1.28 - 4.22;  $p < .01$ )



The 10-year LRRFS by age and subtypes

	All (%)	LA (%)	LB (%)	HER2 (%)	TN (%)	$p$ value
All	84.3	86.6	77.4	81.5	88.4	<b>.05</b>
$< 40$ years	73.2	67.5	70.8	91.7	100.0	.49
$\geq 40$ years	89.0	92.9	82.9	77.9	86.7	<b>.01</b>
$p$ value	<b>.01</b>	<b><math>&lt; .01</math></b>	.55	.42	.36	

### Multivariate analysis for LRRFS

	HR	95% CI	$p$ value
Luminal vs. non-luminal			
Age $\geq 40$			
luminal	1.00		
non-luminal	1.40	0.65 - 3.01	.39
Age $< 40$			
luminal	2.33	1.28 - 4.22	$< .01$
non-luminal	0.66	0.09 - 4.95	.68
four biological subtypes			
Age $\geq 40$			
luminal A	1.00		
luminal B	2.33	1.00 - 5.42	.05
HER2-enriched	2.46	0.91 - 6.66	.08
triple negative	1.37	0.44 - 4.29	.59
Age $< 40$			
luminal A	2.87	1.29 - 6.37	.01
luminal B	3.58	1.50 - 8.54	$< .01$
HER2-enriched	1.57	0.20 - 12.27	.67
triple negative	0	0	.96

## CONCLUSION

Young age breast cancer patients with positive lymph nodes had a higher risk of LRR than more older patients. This detrimental effect of young age on LRR was confined in luminal subtypes