

of less than <0.05 was considered as indicative of statistically significant difference.

**Results:** Pretreatment CA15.3 levels ranged from 3.3 to 237.6 U/ml. Elevated CA15.3 levels (>28 U/ml) were found in 21 (8.5%) patients. Statistical analysis revealed that preoperative serum CA15.3 levels were directly related to tumor size ( $p=0.015$ ) and lymph node involvement ( $p=0.009$ ), while no significant relationship between CA15.3 measurements and age, histological type, grade, HER2/neu positivity, ER and PR status was observed. In the univariate analysis, high CA15.3 levels were significantly associated with a lower probability of disease free survival (DFS) in the overall group of patients ( $p=0.0001$ ). On the contrary, multivariate regression method showed that CA15.3 was not an independent risk factor for a shorter DFS, with a hazard ratio of 0.177 (95% CI 0.074–0.422;  $p=0.001$ ).

**Conclusions:** In this study of 247 cases of pT1–2 infiltrating breast carcinomas, high preoperative CA15.3 levels correlate with large size tumors and the presence of lymph node metastases and suggest that this antigen could be possibly used as a complementary prognostic marker.

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### TNBC Has Disproportionately Poor Prognosis Among AJCC Stages

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**Background:** Subtypes defined by clinicopathological criteria are similar to but not identical to intrinsic subtypes and represent a convenient approximation. Not only previous known prognostic factors, such as lymph node status, tumor size, and patient's age but also molecular subtypes might be some correlations with breast cancer's prognosis, especially similar stages.

**Methods:** 1305 women diagnosed and/or treated with invasive breast cancer during 1989–2004 at Asan Medical Center were studied. Primary endpoint (locoregional, and distant metastasis) and secondary endpoint (OS) were evaluated using chi-square tests and Cox proportional hazards models. Breast cancer samples were categorized into molecular subtypes based on immunohistochemical profiles. Samples that were ER- or PR-positive and Her-2/neu-negative were classified as luminal A, samples that were ER- or PR-positive and Her-2/neu-positive were classified as luminal B, samples that were ER- and PR-negative and Her-2/neu positive were classified as Her-2/neu-enriched, and samples that were ER-, PR- and Her-2/neu-negative were classified as triple-negative.

Parameter	TNBC	Her-2/neu	Luminal A	Luminal B	p-value
Number	256(19.6)	220(16.9)	564 (43.2)	265 (20.3)	
Tumor size (mm)	27.0 (±19.7)	32.6 (±23.4)	27.2 (±17.2)	24.9 (±12.4)	<0.001
Age(years)					<0.001
<35	40(15.6)	19(8.6)	36(6.4)	26(9.8)	
35–49	143(55.9)	110(50.0)	361(64.0)	151(57.0)	
>50	73(28.5)	91(41.4)	167(29.6)	88(33.2)	
Stage					<0.002
I	84(32.8)	72(32.7)	178(31.6)	83(31.3)	
II	155 (60.5)	111 (50.5)	343 (60.8)	148 (55.8)	
III	13 (5.1)	32 (14.5)	40 (7.1)	32 (12.1)	
IV	4 (1.6)	5 (2.3)	3 (0.5)	2 (0.8)	
p53					<0.006
-	135 (52.9)	90 (40.9)	492 (87.4)	199 (76.0)	
+	120 (47.1)	130 (59.1)	71(12.6)	63(24.0)	
Type					0.01
IDC	254 (99.2)	219 (99.5)	545 (96.6)	260 (98.1)	
ILC	2 (0.8)	0	19 (3.4)	5 (1.9)	
Others	0	1 (0.5)	0	0	
Chemotherapy					<0.001
no	25 (9.8)	31 (14.1)	203 (36.4)	93 (35.4)	
yes	229 (90.2)	189 (85.9)	354 (63.4)	170 (64.6)	
unknown					
OP					<0.001
BCO	79 (30.9)	31 (14.1)	148 (26.2)	45 (17.0)	
MRM	177 (69.1)	189 (85.9)	416 (73.8)	220 (83.0)	
LN					<0.021
(-)	158 (62.5)	120 (55.6)	286 (51.7)	131 (50.8)	
(+)	95 (37.5)	96 (44.4)	267 (48.3)	127 (49.2)	

**Results:** Triple negative breast cancer was 256 patients (19.6%), luminal A; 564 (43.2%), Her-2/neu positive breast cancer 220 (16.9%), and luminal B 265 (20.3%) (Table 1). Median follow up was 60months, triple negative breast cancer carried worse prognosis than other typed breast cancer before 3 years but it was so disproportionately represented among each stages after 3 years, and luminal A breast cancers were better survival

than other typed breast cancer every stages Triple negative breast cancer carries a poor prognosis so is disproportionately represented among all stages. On multivariate survival analyses, AJCC stage, lymph node status, and breast cancer subtypes were independent prognostic factors.

**Conclusion:** Breast cancer subtypes have heterogeneous effects on disease free survival in a silimar stage, but disproportionately among all stages. Her-2/neu positive and triple negative breast cancer are seem to be independent prognostic factors in a limited sized analysis.

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### Immunohistochemical P53 Over-expression and Hormonal Therapy Benefit in Invasive Breast Cancer

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**Purpose:** To confirm prognostic and predictive values of immunohistochemical p53 accumulation, we analyzed the prognostic role of p53, particularly in invasive breast cancer patients according to the intrinsic subtypes by hormone receptor and HER2 status.

**Materials and Methods:** Data about p53 immunohistochemistry results along with estrogen receptor (ER), progesterone receptor (PgR), and HER2 of 60 hospitals' own patients were retrospectively retrieved from web-based database of Korean Breast Cancer Society (KBCS). A total of 15,598 patients diagnosed between 1997 and 2004 were enrolled in this analysis. The chi square test was used to determine the differences in variables between pairs of groups. Overall survival (OS) and breast cancer specific survival (BCSS) were estimated by the Kaplan-Meier method. Log-rank tests were used for the comparison of survival curves. Multivariate analyses were performed using stratified Cox's proportional hazard regression model. A model with interaction terms of p53 by both hormonal therapy and chemotherapy was evaluated to determine the treatment benefit from both modalities.

**Results:** Immunohistochemical p53 over-expression was statistically associated with advanced pathological stage; higher tumor grade; hormone receptor (HR) negativity; and HER2 positivity. The median follow-up for this cohort of patients was 53 months. The 5-year OS was 88.0% for positive p53 patients, and 91.3% for negative p53 patients ( $P<0.0001$ ). The 5-year BCSS was 88.5% for positive p53 patients, and 91.8% for negative p53 patients ( $P<0.0001$ ). In a multivariate analysis, p53 over-expression was a weak but independent prognostic factor (Hazard ratio (HR)=1.17; 95% CI, 1.01–1.34 for OS and HR=1.39; 95% CI, 1.12–1.73 for BCSS). Its poor prognostic value was prominently valid in the luminal A (HR+ and HER2-) subtype for OS and BCSS with a hazard ratio of 1.44 (95% CI, 1.08–1.93) and of 1.47 (95% CI, 1.09–1.99) respectively, compared to those in the other subtypes. The hazard ratios of p53 over-expression for OS/BCSS were 1.27 (95% CI, 0.98–1.66)/1.26 (95% CI, 0.96–1.65), 1.25 (95% CI, 0.96–1.60)/1.21 (95% CI, 0.94–1.57), and 0.94 (95% CI, 0.73–1.20)/0.92 (95% CI, 0.71–1.18) in luminal B (HR+ and HER2-), HER2 over-expressing, and basal-like subtype, respectively. The model with interaction terms revealed that hormonal therapy has a significant interaction with p53 status ( $p=0.002$  and  $0.007$  for OS and BCSS, respectively), resulting in insignificant prognostic value of p53 status ( $p=0.268$  and  $0.296$  for OS and BCSS, respectively). The interaction between chemotherapy and p53 status was not found in this model.

**Conclusions:** Immunohistochemical p53 over-expression has an independent prognostic value, especially in luminal A invasive breast cancer, most likely caused by differential treatment benefits from hormonal therapy according to the immunohistochemical p53 status.

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### Clinical Dilemmas in Bilateral Breast Cancer

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**Background:** Women with breast cancer are at an increased risk of bilateral breast cancer(BBC), a disease with a relatively poor prognosis. This review aims to highlight clinical difficulties in treating women with