

Number of positive nodes did not affect management decision. Regional radiotherapy was given to the axilla from an anterior field, 50 Gy D_{max} in 25 daily fractions. Outcomes of recurrence and 'breast cancer specific survival' (BCSS) were assessed.

Results: 387 patients with 1–3 positive nodes who received ART were identified. The number with 1, 2 or 3 nodes involved was 222, 106 and 59 respectively. Median follow up was 129 months (5–247). There were 28 (7%) RR, with median time to recurrence of 50 months (12–175). Estimated RR free survival (SE) was 95.3% (0.011) at 5 years, 93.1% (0.014) at 10 years.

Univariate survival analysis demonstrated that 1 node positive status predicted a lower risk of RR compared to those with 2/3 nodes positive (HR 0.376, 95% CI 0.173–0.815, $p = 0.013$.) This remained significant on multivariate analysis, adjusting for tumour grade and tumour size ($p = 0.02$).

Estimated BCSS (SE) was 85.8% (0.018) at 5 years, 72.4% (0.024) at 10 years, with appearances of improved survival in the 1 node positive group; however, this was of borderline significance, $p = 0.086$.

Conclusion: RR is uncommon in 1–3 node positive patients treated with ART, but the risk is significantly lower in the 1 node positive sub-group. Less aggressive strategies of regional management should be considered and investigated for these patients.

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Clinical Significance of Stem Cell Phenotype (CD44⁺/CD24⁻) Relating to Molecular Subtype of Breast Cancer – a Multi-institutional Retrospective Study

J. Kang¹, G. Gong¹, H.J. Lee¹, Y.K. Bae², A. Lee³, E.Y. Cho⁴, J.S. Lee⁵, K.S. Suh⁶, D.W. Lee⁷, W.H. Jung⁸. ¹Asan Medical Center, Pathology, Seoul, Korea; ²Yeungnam University College of Medicine, Pathology, Daegu, Korea; ³Catholic University of Korea College of Medicine, Pathology, Seoul, Korea; ⁴Samsung Medical Center, Pathology, Seoul, Korea; ⁵Chonnam National University Medical School, Pathology, Gwangju, Korea; ⁶Chungnam National University College of Medicine, Pathology, Daejeon, Korea; ⁷Soonchunhyang University Hospital, Pathology, Seoul, Korea; ⁸Yonsei University Gangnam Severance Hospital, Pathology, Seoul, Korea

Background: The breast is the first solid organ that has been discovered its cancer stem cells. CD44⁺CD24⁻ Lineage⁻ tumorigenic cells showed stem cell properties. However, the clinicopathologic significance of stem cell phenotype has not been clarified yet. To investigate the prognostic significance of stem cell phenotype (CD44⁺/CD24⁻) in breast cancer cells and its relation to molecular subtype, we performed a multi-institutional retrospective study.

Materials and Methods: From 8 institutions of South Korea, 1401 consecutive breast cancer cases were collected which were resected from 1997 to 2003. Median follow-up period is 73.1 month. Immunohistochemical (IHC) stainings of ER, PR, EGFR, CK5/6, CK14, c-kit, CD44 and CD24 were done on slides of 64 tissue microarray blocks. To identify the stem cell phenotype (CD44⁺/CD24⁻), double IHC staining for CD44 and CD24 was done. The status of HER2/neu amplification was investigated by dual-color silver-enhanced *in situ* hybridization (SISH). Clustering of CD44/CD24 expression pattern was done using k-means clustering (stem cell phenotype). In addition, clustering of stem cell phenotype and molecular subtype markers was done using k-modes clustering. Univariate and multivariate survival analyses were done using Kaplan-Meier method and cox regression test.

Results: Seven hundred forty five cases were analyzed which had all available IHC stain, SISH results and follow up data. CD44/CD24 expression pattern was classified into stem cell rich/poor phenotype using k-means clustering. The pattern of stem cell phenotype and molecular subtype markers was classified into five subtypes using k-modes clustering. Those were hormone receptor positive and stem cell rich subtype (19.5%), hormone receptor positive and stem cell poor subtype (41.3%), basal-like subtype (4.7%), null subtype (23.2%) and HER2 positive subtype (11.3%). The hormone receptor positive and stem cell rich subtype shows best prognosis, followed by basal-like, hormone receptor positive and stem cell poor, null, and HER2 positive subtypes ($p < 0.001$, log-rank test) and the significance remained after adjustment with TNM stage.

Conclusions: By clustering analysis, hormone receptor positive breast cancer is divided stem cell rich/poor phenotypes. The stem cell rich phenotype shows better prognosis than stem cell poor phenotype. The stem cell phenotype could be a prognostic marker in hormone receptor positive type. In addition, the stem cell rich phenotype is associated with basal-like and null subtypes and stem cell poor phenotype is associated with HER2 positive subtype.

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A Validated Web-based Nomogram for Predicting Positive Surgical Margins in Breast-conserving Therapy

R.G. Pleijhuis¹, A.B.G. Kwast², L. Jansen¹, J. de Vries¹, R. Lanting¹, J. Bart³, T. Wiggers¹, S. Siesling⁴, G.M. van Dam¹. ¹University Medical Center Groningen, Department of Surgery, Groningen, The Netherlands; ²Comprehensive Cancer Centre the Netherlands, Department of Epidemiology, Enschede, The Netherlands; ³University Medical Center Groningen, Department of Pathology and Laboratory Medicine, Groningen, The Netherlands; ⁴Twente University, Department of Health Technology and Services Research, Enschede, The Netherlands

Background: Breast-conserving therapy (BCT) is considered standard treatment for early-stage breast cancer. One of the most important risk factors for local recurrence following BCT is the presence of positive surgical margins. We aimed to develop and validate a user-friendly prediction model (nomogram) based on preoperatively obtainable variables to predict for positive surgical margins in BCT.

Patients and Methods: Breast cancer patients who underwent BCT throughout the North-East region of the Netherlands between June 2008 and July 2009 were selected from the Netherlands Cancer Registry ($n = 1185$). Results from multivariate logistic regression analyses served as the basis for development of the nomogram. Nomogram calibration and discrimination were assessed graphically and by calculation of a concordance index, respectively. Performance of the nomogram was validated on an external independent dataset ($n = 331$) from the University Medical Center Groningen.

Results: The following clinicopathological variables were associated with positive surgical margin status in BCT and were included in the final model: microcalcifications on mammogram (OR: 1.37), absence of preoperative MRI (OR: 1.80), suspicion of multifocality (OR: 2.81), non-palpable tumor (OR: 1.51), positive preoperative N-stage (OR: 1.73), large tumor size (OR: 1.33), high density of the breast (OR: 1.22), lobular histological type (OR: 2.90), high histological grade (OR: 1.44), positive ER status (OR: 1.80), and presence of DCIS (OR: 3.11). Concordance indices were calculated of 0.70 (95% CI: 0.66–0.74) and 0.69 (95% CI: 0.63–0.76) for the modeling and the validation group, respectively. Calibration of the model was considered good in both groups. A nomogram was developed as a graphical representation of the model.

Conclusions: We developed and validated a nomogram to predict the probability of positive surgical margins in BCT using preoperatively obtainable clinicopathological variables. Moreover, a web-based version (*Breast Conservation!*) of the nomogram is accessible at <http://www.breastconservation.com> (login name: review; password: ArrBaw5X). Our nomogram could support clinicians in counseling patients regarding the likelihood of requiring further surgery, identify high risk patients who could benefit from more extensive surgery, and allow for the stratification of patients in clinical trials.

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The Influence of Education Level On the Survival of Breast Cancer

K.T. Hwang¹, W. Han², H.C. Shin³, H.S. Kang⁴, Y.T. Bae⁵, Y.S. Jung⁶, S.H. Koh⁷, D.Y. Noh². ¹Seoul National University Boramae Hospital, Surgery, Seoul, Korea; ²Seoul National University College of Medicine, Surgery, Seoul, Korea; ³Seoul National University Hospital, Surgery, Seoul, Korea; ⁴National Cancer Center, Center for Breast Cancer, Goyang, Korea; ⁵Pusan National University Hospital, Surgery, Pusan, Korea; ⁶Ajou University School of Medicine, Surgery, Suwon, Korea; ⁷Kyung Hee University College of Medicine, Surgery, Seoul, Korea

Background: The prognostic role of education level (EL) in breast cancer has been not consistent but still controversial. We tried to investigate the role of EL as a prognostic factor of breast cancer.

Materials and Methods: Data of 36,299 primary breast cancer patients diagnosed between 1987 and 2008 from the Korean Breast Cancer Registry was analyzed. EL was classified into the low EL group (<12 years; $n = 13,178$) and the high EL group (≥ 12 years; $n = 23,121$) according to time spent in education.

Results: The high EL group had younger age, earlier tumor stage, more estrogen receptor positivity, less HER2 positivity, lower histologic grade, less lymphovascular invasion, and less body mass index compared to the low EL group. The high EL group received more lumpectomy and/or more adjuvant therapy than the low EL group regardless of tumor size, node positivity, tumor stage, and operation methods. Both overall survival rate and breast cancer specific survival rate of the high EL group were higher than those of the low EL group (log-rank test, both $P < 0.001$). The differences in survival rates between the high and low EL groups were more evident under clinicopathologically more favorable conditions.