

for p53(-) vs 78.7% for p53(+); $P=0.002$, intermediate-risk group; 96.5% for p53(-) vs 90.7% for p53(+); $P=0.003$).

Conclusions: This study demonstrates that p53 accumulation based on IHC has prognostic impact in LNN-BC, and it gives the additional prognostic information for intrinsic phenotypes and the St Gallen consensus.

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Nuclear p53 protein and cell cytosol LDH expression as prognostic indicators to monitor FEC treatment in triple negative breast cancer

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Background: The p53 tumor suppressor is involved in the control of cell growth and programmed cell death. p53 mutations are most commonly seen in human cancer, with some estimate 25% of primary breast carcinomas. Approximately 10–17% of triple negative (lack of expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) invasive breast cancer is significantly associated with mutant p53 overexpression. This type of cancer displays more aggressive clinical behaviour, distinctive metastatic patterns and poorer prognosis when compared with other breast cancer subtypes. 5-Fluorouracil, Epirubicin and Cyclophosphamide (FEC) are usually combined to treat as the neo-adjuvant or adjuvant chemotherapy for breast cancer. Lactate dehydrogenase (LDH) is a stable cytoplasmic enzyme that is present in all cells. It is rapidly released into the cell-culture supernatant upon damage of the plasma membrane. In this study breast cancer cells were treated with single and combination use of FEC followed by the measurement of the level of nuclear p53 protein, cytosol LDH and DNA synthesis in 5-bromo-2'-deoxyuridine (BRDU).

Material and Methods: High levels of mutant p53 breast cancer cell line MDA-MB-231 was selected. The cells were cultured in flasks and 96 well plates with L-15 medium in assigned control, 0.6µg/mL 5-Fluorouracil, 0.5µg/mL Epirubicin, 0.6µg/mL Cyclophosphamide and FEC combination groups, respectively for 24 hours. At the harvest day, the cultured medium and cell homogenates of different groups were quantified by a photometric enzyme immunoassay, ELISA kit. The LDH released from damaged cells and DNA synthesis labelled with BRDU were measured by the nonradioactive colorimetric immunoassay.

Results: All four test groups demonstrated a statistically significant difference from control group and the most significant result was from the FEC group.

Group	p53 (pg/ml)	LDH (OD)	BRDU (OD)
Control	1.89±0.04	1.35±0.10	1.27±0.15
5-Fluorouracil	*0.71±0.001	*1.93±0.07	*0.94±0.03
Epirubicin	*0.65±0.006	*1.87±0.02	*0.86±0.02
Cyclophosphamide	*0.8±0.001	*2.12±0.02	*1.14±0.02
FEC	*0.32±0.001	*2.44±0.008	*0.57±0.03

Values are mean±SD (standard deviation); OD: Optical Density. * $p < 0.05$.

Conclusion: FEC regimen suppresses cell proliferation, nuclear p53 mutations and LDH. These three indicators may predict how triple-negative breast cancer patients would respond to various chemodrugs or regimens.

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New recurrence prediction model for breast cancer by data mining

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Background: Many studies were published to predict recurrence of breast cancer. The most frequently used methods to predict recurrence are the statistical technique of regression. However, Cox regression does not allow non-linear relations between the independent and dependent variables and low accuracy. A new technique based on machine learning has recently been proposed as a supplement or alternative to Cox regression. Our study aims to develop more accurate prediction model for recurrence of breast cancer.

Material and Methods: Data from 1480 patient with breast cancer from the department of surgery of Ajou university hospital were collected and recorded during the period 1994–2007 years. This study used 631 patients to be excluded in case of other cancer, man, and metastasis to other organ, stage IV, and follow up period under 5 years. Eight among 64 variables were selected with Pearson chi-square test. To obtain a reliable estimate

of model accuracy applied the holdout method that divided into 438 patients for training and 193 patients for testing. Since Cox regression is the most popular algorithm to build a predictive model for time-to-event data, this study compared accuracy of two algorithms; Cox regression and Support Vector Machine (SVM).

Results: The results of the univariate analysis used to determine the correlation between clinicopathologic variables and recurrence of breast cancer and showed a significant association between recurrence of breast cancer and variables such as histological grade ($p < 0.001$), local invasion of tumor ($p < 0.001$), HER2 ($p < 0.05$), number of tumor ($p < 0.001$), tumor size ($p < 0.001$), lymphovascular invasion ($p < 0.001$), estrogen receptor ($p < 0.05$) and number of metastatic lymph node ($p < 0.001$). For both model (Cox regression and SVM), a recurrence probability for each patient in the test set was calculated. The predictive accuracy of two models was computed using the area under Receiver Operation Curve (ROC) curve (AUC). SVM: AUC=0.842) was higher AUC than Cox regression (AUC=0.648). As compared by Adjuvant! Online software program, The AUC and accuracy of purposed model (0.842, 80.3%) was slightly higher than the adjuvant! online (0.7, 70.5%).

Conclusions: This study predicted recurrence of breast cancer which is as important as early detection of breast cancer. A parallelism of adequate treatment and follow-up by recurrence prediction prevent the recurrence of breast cancer. This study compared accuracy of models; Cox regression and SVM. SVM showed higher AUC than Cox regression. Our new model can predict more accurately recurrence of breast cancer than previous models.

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Ki-67 as a long-term prognostic factor in lobular breast cancer

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Background: Ki-67 has recently been introduced in the St Gallen consensus as an important prognostic factor in breast cancer. The aim of the present study was to specifically investigate the prognostic bearing of Ki-67 in a subgroup of lobular breast cancer.

Material and Methods: This population-based non-screening material consists of 212 patients (pts) with lobular breast cancer diagnosed between 1980 and 1991. The median follow-up time was 12 years and for those still living, 20 years (range 0.6–30 years). Clinical stage was recorded. The expression of Ki-67 in the tumour was assayed by immunohistochemistry (Mib-1 antibody).

Results: With this long follow-up time, 72 pts (34%) have died of breast cancer, 73 pts (34%) have died of other causes and 67 pts (32%) are alive. Among those alive there were five with local recurrences, one with regional recurrence and one with distant recurrence. At diagnosis the clinical stage was stage I in 90 pts (42%), stage II in 70 pts (33%), stage III in 41 pts (19%), stage IV in 7 pts (3.3%) and stage was undefined in 4 pts (1.9%). Ki-67 expression was categorized into four groups: 0 (0%), 1 (1–10%), 2 (11–30%) and 3 (>30%). A logrank test for trend shows that the null hypothesis of equal overall survival for these four groups could be rejected in favour of the trend alternative ($p=0.037$). High Ki-67 expression gives negative impact on survival.

Conclusions: Ki-67 expression seems to give long time prognostic information in lobular breast cancer and might thus be a useful tool in the adjuvant decision making.

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Body mass index is associated with breast cancer of large size and positive lymph nodes in pre-menopausal but not post-menopausal women

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Background: Obesity is known to be a risk factor for breast cancer. While many studies suggested that overweight would be associated with higher risk of breast cancer with higher grade tumours, greater tumour burdens and poorer prognosis, the association between body mass index (BMI) and breast cancer outcome is controversial. There is recent suggestion that the prognostic outlook of Chinese breast cancers might be somewhat different from those in the Western population. Western studies have shown that body mass index may affect important biological mechanisms related with breast cancer prognosis but there is limited data with regard to the impact of BMI upon breast cancer features in the Hong Kong Chinese population.

Methods: We conducted a preliminary retrospective study on 166 Hong Kong Chinese primary breast cancer patients seen as new cases during