Are there the specific prognostic factors for triple-negative subtype of early breast cancers (pT1-2N0M0)?

T1-2 위험 병종 삼중음성유방암의 예후인지

Reviews: 삼중음성유방암은 삼중음성유방암병에 비해 초기에 해
도 더 나중 예후 보다는 것이 알려져 있다고 하며, 특히 삼중음성
유방암의 초기 치료림에 정형적 예후인자들 적용이 중요하
다. 본 연구에서는, T1-2 위험 병종 삼중음성유방암의 나머
예후와 관련된 예후인자를 보고하고자 하였다.

방법: 1995년부터 2008년까지 고령학과의 원리과 암성성양에서
유방암으로 진단받고 사망한 환자 중 위험 병종 안으로 위험
군이 아닌 나머지 병원을 대상으로 하였다. 이 중에서 희소한 수용체
및 HER2 수용체 없이 외래 기기는 하면 등도 재긴 환자들을 포함시켰
다. 우기의 추적 분석을 통해 삼중음성유방암 및 비중음성
유방암 환자들의 산업적적 특징을 분석하였다.

결과: 179명 (22.9%)의 환자들 삼중음성유방암군으로 분류되
았고, 삼중음성유방암군에서 65% 해당 환자들에서 65% 나온 환
자군보다 더 낮은 무병수명을 보였다 (p=0.028). 대비 화학
요법에서 32% 이내의 낮은 반도가 삼중음성유방암과 관련된
독립적인 예후인자로 나타났으며, Ki-67가 낮은 화기 화학요법에
서 삼중음성유방암의 독립적으로 유의하게 관련성이 보였다.

결론: 본 연구에서, T1-2 위험 병종 삼중음성유방암에서
 연구와 전문적인 예후인자들을 이용해 나머지 나온 예후를 연구하였
았으며, Ki-67는 위험성 유방암 등에서 연구된 것과 달리, 삼중
음성유방암의 예후인자가 될 것으로 생각된다.

학력저자: 배재영
T1-2간, 성형외과 학자 51% 고령학과 병원장 현직으로

Are there the specific prognostic factors for triple-negative subtype of early breast cancers (pT1-2N0M0)?

Background

Breast cancer is a heterogeneous disease, encompassing a number of distinct biological entities that are associated with specific morphological and immunohistochemical features and clinical behavior. Triple-negative breast cancer (TNBC) accounts for 10–20% of all breast carcinomas. Patients with TNBC typically have inferior prognosis compared to patients with other subtypes of breast cancer. The poor prognosis of TNBC is associated with the aggressive course of the tumor, increased risk of distant metastasis, and the lack of specific treatment[1]. TNBC has a pattern of rapid recurrence following discontinuation of therapy, and the peak risk of recurrence is within three years[2]. However, the peak risk period, the risk of recurrence declines rapidly and recurrence becomes rare[3]. The initial management of TNBC patients is therefore very important, even in early stages of the disease. There was unmet clinical need for the development of biomarkers for TNBC in order to identify patients with poor prognosis, thus, more significant efforts have been made to improve clinical outcome of TNBC patients so far. As part of these efforts, various immunohistochemical molecules have been studied, and p53 and Ki-67 markers are being actively investigated. p53 functions in maintenance of genomic stability, cell cycle regulation, and the induction of apoptosis[4]. Duplication of these functions appears to play an important role in carcinogenesis. Since non-functional mutated p53 accumulates in the nuclei of tumor cells, immunohistochemical

1) Patients

Patients with available reports on hormone receptor and human epidermal growth factor receptor-2 (HER2) status were selected among 1200 breast cancer patients who were female and underwent surgical resection at the Korea University Anam Hospital Seoul, Korea between August 1995 and December 2006. Patients were excluded if they had lymph node metastasis, distant metastasis, or T3 (tumor > 5 cm) tumors. All of the subjects underwent surgical treatment and standard adjuvant chemotherapy and/or radiotherapy. All included patients were clinically followed up by the end of year 2010. The median follow-up period was 78.12 ± 38.45 months. Clinico-pathological data were collected from medical records and analyzed retrospectively. These data included age at surgery, tumor stage and histologic grade, surgical procedure, adjuvant therapy, receptor status and clinical follow-up data. Tumors were staged according to the 7th edition of the American Joint Committee on Cancer tumor–node–metastasis (AJCC 7th TNM)[5]. Grades were grouped from 1 to 3 by pathologic reports of our hospital.

2) Immunohistochemical Staining

Tumor tissues from surgical specimen were immunohistochemically stained using monoclonal antibodies (mouse anti-human estrogen receptor (ER) or progesterone receptor (PR) monoclonal antibody, DAKO Inc. Seoul, Korea after slicing and embedding in paraffin. The sliced, paraffin-embedded tissues were deparaffinized with xylene and sequentially hydrated with 100%, 90%, 80% and 70% ethanol solutions. The samples were incubated with an ethanol and H2O2 solution, cleared with phosphate buffered saline (PBS), left at room temperature for 20 minutes and mixed with normal serum to block nonspecific intrinsic reactions. Tissues were then incubated with biotinylated secondary anti-rat antibody, cleansed three times with PBS for 20 minutes, reacted with a streptavidin biotinylated peroxidase complex and dyed with a diaminobenzidine solution and hematoxylin for contrast. HER2 positivity was defined as an intensity of 3+ by IHC or as gene amplification ratio of ≥2.2 by fluorescence in situ hybridization (FISH) in the case of an intensity of 1+ or 2+ by IHC. The Ki-67 expression status (percentage) was considered positive when at least 10% of cells showed moderate to strong staining and a negative (<10%) group. The p53 expression status was interpreted as positive when at least 10% of the tumors showed moderate to strong nuclear staining and a negative (<10%) group. ER and PR data were acquired from the pathologic report. TNBC was defined all negative to ER, PR & HER2 and the others were grouped to non-TNBC.

3) Fluorescence in situ Hybridization (FISH)

FISH was performed using 4 um-thick serial sections according to the guidelines of the HER2 FISH kit.
초 록

대상: 삼중유성암은 삼중유성암에 비해 초기에 해적
도가 나가 예후를 보지 않는 경우가 많으며, 따라서 삼중유성
암의 초기 치료를 위해서 정확한 예후판정을 하는 것이 중요하
다. 본 연구에서는, T1-2 질병 적정한 삼중유성암의 나이, 
예후와 관련된 예후인자를 찾아보기 위하여, 1998년
부터 2008년까지의 10년간 삼중유성암 암자 중, 
T1-2 질병 질병
적정한 삼중유성암 126예를 대상으로 하였다.

Background

Breast cancer is a heterogeneous disease, encompassing a number of distinct biological entities that are associated with specific morphological and immunohistochemical features and clinical behavior.

Triple-negative breast cancer (TNBC) accounts for 10–20% of all breast carcinomas. Patients with TNBC typically have inferior prognoses compared to patients with other subtypes of breast cancer. The poor prognosis of TNBC is associated with the aggressive course of the tumor, increased risk of distant metastasis, and the lack of specific treatment.

TNBC has a pattern of rapid recurrence following diagnosis, and the peak risk of recurrence is within three years. However, after the peak risk period, the risk of recurrence declines rapidly and recurrence becomes rare.

The initial management of TNBC patients is therefore very important, even in early stages of the disease. There was unmet clinical need for the development of biologic markers for TNBC in order to identify patients with poor prognoses, thus, more significant efforts have been made to improve clinical outcomes of TNBC patients so far. As part of these efforts, various immunohistochemical molecules have been studied, and p53 and Ki-67 markers are being actively investigated.

p53 functions in maintenance of genomic stability, cell cycle regulation, and the induction of apoptosis. Disruption of these functions appears to play an important role in carcinogenesis. Since non-functional mutated p53 accumulates in the nuclei of tumor cells, immunohistochemical

H&E staining for p53 has been used as a popular surrogate marker for its mutational status. p53 mutations are present in 18–25% of primary breast cancers and are well known to reduce patients' survival, although the exact mechanism has not been determined. Because mutated p53 helps to predict good response to anthracycline based chemotherapy, it is expected as promising prognostic factor.

The proliferation marker Ki-67 has repeatedly been confirmed as an independent predictive and prognostic factor for early breast cancer. Breast cancer with high Ki-67 expression responds better to chemotherapy, but is associated with poor prognosis. This phenomenon is similar to the triple-negative paradox, in which TNBC shows poorer survival, despite a higher response rate to neoadjuvant chemotherapy. TNBC is associated with higher expression of Ki-67 than non-TNBC.

Our aim was to study the relationships between early TNBC prognoses and markers p53 and Ki-67, in order to identify the predictive or prognostic value of p53 and Ki-67 among patients with early TNBC, and therefore enable better assessment of the need for close follow-up.

Patients and Methods

1) Patients

Patients with available reports on hormone receptor and human epidermal growth factor receptor-2 (HER2) status were selected among 1,200 breast cancer patients who were female and underwent surgical resection at the Korea University Anam Hospital (Seoul, Korea) between August 1998 and December 2006.

Patients were excluded if they had lymph node metastasis, distant metastasis, or T3 (tumor > 5 cm) tumors. All of the subjects underwent surgical treatment and standard adjuvant chemotherapy and/or radiotherapy. All included patients were clinically followed up by the end of year 2010. The median follow-up period was 78.12 ± 38.43 months. Clinico-pathological data were collected from medical records and analyzed retrospectively.

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3) Fluorescence in situ Hybridization (FISH)

FISH was performed using 4 µm-thick serial sections according to the guidelines of the HER2 FISH kit.