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Original article

Evaluation of the prognostic stage in the 8th edition of the American Joint Committee on Cancer in locally advanced breast cancer: An analysis based on SEER 18 database



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ABSTRACT

Background: The new "prognostic stage" in the 8th edition of the American Joint Committee on Cancer (AJCC) incorporated important biologic factors such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2), histologic grade and TNM stage into one system. The objective of this study was to evaluate the "prognostic stage" in locally advanced breast cancer (LABC) based on the Surveillance, Epidemiology, and End Results (SEER) 18 database.

Methods: 10053 LABCs diagnosed between 2010 and 2013 were enrolled. TNM stage was based on AJCC 7th edition. Comparisons of biologic factor proportions among stage changes were performed using Pearson's chi-square test. Breast cancer-specific survival (BCSS) and overall survival (OS) were estimated using the Kaplan-Meier method and log rank testing with pairwise comparisons between different stages was conducted. Cox models were fitted to assess the independent prognostic factors.

Results: The prognostic stage grouped LABC into six stages: IB-IIIC among which IB-IIIA had a relatively better survival. It reassigned 74% LABCs to a different tumor stage. 60.4% cases in grade III and 68.3% cases with triple negative breast cancer were upstaged while 57.1% cases with ER/PR dual positivity were down staged. It was an independent prognostic factor of LABC. There were statistically significant survival differences among stage IB-IIIA, IIIB and IIIC. Among each TNM stage, there were statistically significant survival differences among stage changes.

Conclusions: The prognostic stage provided accurate prognostic information for LABC compared with anatomic TNM stage. It will lead to accuracy in prognosis prediction and optimal treatment selection, and therefore, better outcomes.

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1. Introduction

Breast cancer treatment should take into account both anatomic factors and biology characteristics [1]. The classic TNM staging system is based strictly on anatomic factors; it does not consider the prognostic impact of tumor biology. However, the advances in understanding breast cancer biology have resulted in the identification and validation of biologic markers of prognosis and treatment benefit [2].

Accordingly, the integration of both anatomic and biologic classification into one staging system was an unmet need. It helps to understand why patients who are staged similarly have

* Corresponding author. E-mail address: 13671852284@163.com (H. Chen). significantly different outcomes based on tumor biology. Numerous studies proposed incorporating biologic factors into TNM stage. But most of them evaluated smaller groups of patients [3–7].

A new "prognostic stage" in the recently published eighth edition of the American Joint Committee on Cancer (AJCC) system included estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2), histologic grade and conventional TNM variables into one staging system. Although it is only based on unpublished data from the National Cancer Data Base (NCDB), expert panel believes that additional data from other large populations of patients with full prognostic factor information and increasing longer follow-up will become available in the coming years [8].

Locally advanced breast cancer (LABC) is a great challenge in the treatment of breast cancer because a great proportion of patients will eventually relapse. Standard factors that traditionally defined an advanced stage are potentially overruled by other biologic factors. Patients with advanced stage disease but favorable tumor biology had better clinical outcomes than those with stage I disease and unfavorable tumor biology [9]. LABC is commonly treated as a whole cohort. Anatomic TNM stage does not predict the clinical outcome precisely while incorporating biologic characteristics may refine the prognostic information and have as or more importance on selecting locoregional or systemic treatments, and as a result, lead to a better outcome.

The Surveillance, Epidemiology, and End Results (SEER) database is characterized with high quality and broad coverage, so we conducted a validation study based on SEER database to evaluate the new "prognostic stage" in LABC.

2. Materials and methods

2.1. Patient population

This retrospective study employed data derived from the National Cancer Institute's limited use SEER 18 registry databases that were released in November 2016. We identified female invasive ductal carcinoma (IDC) cases (with International Classification of Disease for Oncology, third edition (ICD-0-3) code of 8500) with AICC IIIA-C stage (T3N1M0 excluded) diagnosed between 2010 and 2013. Patients with more than one primary cancer, having metastatic disease at diagnosis, diagnosed at death or autopsy only, age >80 years old, AJCC stage III NOS, unknown HER2 status or unknown histologic grade were excluded. TNM stage was based on a derived AJCC 7th edition. Prognostic stage for these cases was based on the prognostic stage system in the 8th edition of AICC [8]. Poorly differentiated and anaplastic histological grades were considered grade III disease. Borderline ER or PR status was considered positive as ER/PR positivity was defined as >1% positive now.

We obtained permission to access the files of SEER program custom data with additional treatment fields such as radiation therapy and chemotherapy. The informed consent was not required because personal identifying information was not involved. This study was reviewed and approved by the Institutional Review Board of Obstetrics and Gynecology Hospital of Fudan University.

2.2. Statistical analysis

Comparisons of the proportions of biologic factors among the upstage or downstage classifications were performed using Pearson's chi-square test with Fisher's exact test. Follow-up cut-off was 31 December 2013. Overall survival (OS) was computed from the time of diagnosis of breast cancer to the time of death from any cause or last follow-up with patients still alive at last follow-up censored. Breast cancer-specific survival (BCSS) was computed from the time of diagnosis of breast cancer to the time of death from breast cancer with patients who died of other causes or still alive at last follow-up censored. Survival outcomes were estimated using the Kaplan-Meier product limit method and log rank testing with pairwise comparisons between different stages was conducted. Adjusted hazard ratios (HRs) with 95% confidence intervals were calculated using Cox proportional hazards model to assess the factors independently associated with survival. Two-sided P < 0.05 was considered statistically significant. All the statistical analysis was performed using SPSS 19.0 software package (SPSS, Chicago, IL, USA).

Table 1Patient and tumor characteristics of LABC.

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