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Assessment of Preference for Hormonal Treatment-Related Health States among Patients with Breast Cancer

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ABSTRACT

Objectives: 1) To obtain preference scores from patients with breast cancer in Singapore for different stages of breast cancer and hormonal therapy-related adverse effects, and 2) to determine the association of patients' demographic and clinical characteristics with those preference scores. **Methods:** A total of 22 health states were used to elicit preference values from 64 patients with breast cancer. At each interview, 14 health states were randomly selected and rated by the patient using the visual analogue scale and standard gamble methods to derive health state preference scores, which were recalibrated to the scale of 0 (death) and 1 (perfect health). **Results:** Mean adjusted visual analogue scale scores ranged from 0.25 (no recurrence with ischemic cerebrovascular events) to 0.82 (no recurrence with no adverse effects). Mean adjusted standard gamble scores ranged from 0.31 (distant recurrence with chemotherapy-related adverse effects) to 0.80 (no recurrence with no

adverse effects). Adverse effects ischemic cerebrovascular events and spine fracture resulted in the greatest decline in health state preference scores. Age, ethnicity, education level, and prior chemotherapy were associated with preference scores. Having children was not found to be associated with the preference scores. **Conclusions:** Taking into account disease progression and hormonal therapy-related adverse effects as well as their impact on health-related quality of life, this study quantifies patients' preference for various breast cancer-related health states. The findings offer valuable information for future cost-utility analysis of breast cancer treatments.

Keywords: breast cancer, preference, standard gamble, VAS.

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Introduction

Breast cancer is one of the leading causes of morbidity and mortality among women in the world. Its substantial lifetime treatment expenditure ranges from US \$20,000 to US \$100,000 per patient, with hospitalization and outpatient therapies largely contributing to the magnitude of those expenditures [1–4]. In Singapore, breast cancer is the most common cancer with the highest mortality rate in the female population [5]. Moreover, it is estimated that there are 1430 new breast cancer cases every year, and this number increases at 3% annually [6,7]. Each woman in Singapore has approximately a 6.1% chance of developing breast cancer in her lifetime, and the age-adjusted incidence among Singaporean women is one of the highest in Asia [6,7].

In addition to local treatments such as surgery and radiotherapy, systemic treatments for breast cancer such as hormonal, chemo-targeted, and molecular-targeted drug regimens are significant in their roles as standard treatment [8]. Over the years, the effectiveness of hormonal therapies such as tamoxifen and aromatase inhibitors has been well established for the

management of estrogen-receptor-positive breast cancer [9–12]. Furthermore, adjuvant hormonal therapy has been progressively essential in breast cancer treatment because of the increasing incidence of early stage breast malignancy and the rising number of breast cancer survivors. In addition to providing a significant reduction in disease recurrence and death, however, various hormonal therapies are associated with adverse effects on patients' quality of life [13,14]. The presence of adverse effects can lead to discontinuation of therapy and it may be more important to patients than clinicians have yet understood [15]. Indeed, successful treatment is greatly affected by patients' management and tolerance of adverse effects. Although the impact of cancer therapies on survival may be indistinct, their effect on patients' quality of life is expected to be decidedly negative. To understand patients' preference for different treatment outcomes, utility values can be used to quantify the impact on patients' health-related quality of life (HRQOL).

In previous utility assessment studies, the number of breast cancer-related health states and treatment adverse effects evaluated has been limited [16–19], and no study has been conducted in an

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Asian population. This study aimed to elicit preferences for different stages of breast cancer and adverse effects related to hormonal therapies in patients in Singapore, and also aimed to identify associations of patients' demographic and clinical characteristics with those preference scores. Such preference data will be useful for future cost-utility analyses and could improve clinical decisions regarding breast cancer therapies.

Methods

Health States

A total of 22 health states (death, perfect health, worst health, and current health, along with 18 hypothetical health states relating to different stages of breast cancer and adverse effects of hormonal therapies) were developed in a previous study through literature review and validation by an oncology expert panel [20]. The health state descriptions illustrated common hormonal treatment-associated adverse effects (cataract, hip fracture, wrist fracture, spine fracture, vaginal bleeding, hot flushes, musculoskeletal disorder, pulmonary embolism, endometrial cancer, deep vein thrombosis, and ischemic cardiovascular events) and breast cancer-related disease stages (no recurrence, locoregional recurrence, distant recurrence, and new contralateral breast cancer). These health states were used in the present study.

Preference Assessment

Study design and subjects

This cross-sectional study was approved by the National Health Group Domain Specific Review Boards and was conducted in the Cancer Centre of National University Cancer Institute, Singapore, from November 2011 to January 2012.

Patients could be recruited for this study if they were female, diagnosed with breast cancer, able to communicate in English or Mandarin, at least 21 years old, and able to function without apparent cognitive impairment. Patients with breast cancer were identified by the hospital pharmacy system on the basis of hormonal and chemotherapy agents prescribed specifically for breast cancer treatment. Potential respondents were invited to participate in the study during their consultation or chemotherapy appointments. All respondents who completed the interview were reimbursed with Singapore \$30 for their participation.

Study interviews

The face-to-face study interviews were conducted by two trained interviewers in either Mandarin or English, depending on patient preference. An interview script was preplanned and carefully followed to reduce interviewer bias or inconsistency. The respondents were asked to provide sociodemographic information as well as their breast cancer treatment history, including their experiences with symptoms or diseases after breast cancer diagnosis. Patients also rated their current health status on a five-point poor-to-excellent scale.

Each health state description was displayed on a laminated card. The descriptions for different health domains of the health states were presented in different colored text to help patients understand and contrast the various health states. Because 22 health states were considered to be too many for accurate evaluation as well as too much of a burden for respondents, a core random sample approach was applied to select 14 health states for each interviewee [21]. Each patient assessed the same core set of 4 health states (death, perfect health, worst health, and current health) and an additional set of 10 other health states that were selected by a random number generator. All health

states were presented in a random sequence to reduce potential biases due to presentation order or respondent fatigue.

Preferences can be measured by both direct and indirect methods. The indirect method, or the use of generic HRQOL instruments, was not selected because Singapore-specific population-based values for generic HRQOL instruments, such as the EuroQol five-dimension (EQ-5D) questionnaire, are not available. Instead, two direct valuation methods, the visual analogue scale (VAS) and standard gamble (SG) methods, were used in this study. For elicitation of health state preferences using VAS, a rating scale was displayed as a line with distinct intervals from 0 to 100. Respondents were asked to read and understand all 14 cards with health state descriptions and then rank the various health states on the scale in descending order according to their preference. The most preferred state and the least preferred state, which might or might not be death, were anchored at the 100 and 0 marks, respectively. Respondents were then asked to give each of the remaining health states a value between 0 and 100, with the intervals between adjacent health states reflecting the differences in preference as deemed by the patients [22–25].

In the SG assessment, a color schematic diagram illustrating a probability wheel on a computer screen was used as a visual support to facilitate comprehension of the process. Respondents were offered three options: 1) to live in a particular health state under evaluation with certainty for the rest of her life; 2) to have p probability of living in perfect health for the rest of her life with a $(1 - p)$ probability of immediate death; and 3) to indicate that the previous two options were equal. The probability p was varied at an increment of 5% until the respondent switched to a different option or chose the third option. If any health state was rated to be worse than death in the VAS assessment, the respondents were also asked to choose between immediate death and a gamble of perfect health and that particular health state [22–25].

Statistical Analysis

Preference scores obtained for each health state were presented by means, medians, and SDs. Raw preference scores obtained from both VAS and SG techniques were calibrated to the scale of 0 (death) and 1 (perfect health) [22]. For VAS assessment, if death was indicated as the least preferred health state, the preference score for the other health states would take the scale value of its placement. In cases in which death was not indicated as the least preferred health state, the formula $(x - d)/(100 - d)$, where d and x denote the scale value of death and the particular health state, respectively, was used for the calculation of the adjusted preference score. In the SG method, if a health state was perceived to be worse than death, the formula for calibration was as follows: adjusted preference score = $-p/(1 - p)$, where p is the probability, or raw preference score, of that particular health state. If the health state was perceived to be more desirable than death, the preference score for the health state was equal to the probability p [22].

Because of the small sample size, nonparametric tests were used in the data analysis. The Wilcoxon signed rank test was used to examine the difference in preferences among the health states and the difference between VAS- and SG-derived preference scores. Spearman's correlation coefficient, the Mann-Whitney U test, and the Kruskal-Wallis test were performed where appropriate to determine the association between patient characteristics (i.e., age, ethnicity, language version, education level, having children, experience with chemotherapy, and experience with hormonal therapy) and preference scores. In addition, the Mann-Whitney U test was used to examine the association between experience of the common adverse effects of hormonal therapy (i.e., hot flushes and musculoskeletal disorder) and the preference scores of the corresponding health states. All

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