RESPONSE TO LETTER Factors Predicting Positive Sentinel Lymph Node **Biopsy in Clinically Node-Negative Breast Cancer** [Response to Letter]

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Dear editor

We thank Dr. Bao-Hua et al for their insightful comments on our paper, and we appreciate the continued opportunity to discuss our manuscript titled "Factors Predicting Positive Sentinel Lymph Node Biopsy in Clinically Node-Negative Breast Cancer".

Dr. Bao-Hua et al believe that the characteristics included in this study such as tumor focality in final pathology and locoregional recurrence contribute little to surgical decision-making, as they cannot be identified before surgery. Another concern of Dr. Bao-Hua was that since the discussion part mentioned that the purpose of the study was identifying noninvasive predictors, postoperative features such as tumor size in final pathology should not be included in the analysis. The reason we chose to include post-operative variables was chiefly to compare and confirm the accuracy of pre-operative variable values. In fact, pre-operative and post-operative variables such as surgical pathology, tumor size, and focality were concordant. In the case that there was discordance among these variables, we would have had to investigate the reasons and exclude them from the study. One of the clinical variables that turned out to have a significant impact on the prediction of sentinel lymph node biopsy (SLNB) positivity was tumor size in final pathology, this variable has been identified in several previous publications as the strongest predictive factor of the risk of sentinel lymph node (SLN) positivity.^{1–3}

Regarding Dr. Bao-Hua's questions about the statistical analysis, we would like to clarify that the analysis was conducted by two independent biostatisticians. Both analyses' conclusions were similar. All variables that were analyzed in the simple logistic regression were subsequently analyzed in the multiple regression analysis.

Dr. Bao-Hua also stated that common potential predictors such as menstrual status, body mass index (BMI), comorbidity, and surgical history were not described, which may lead to information bias. We have looked at those factors in the literature and found no convincing argument that they will correlate to predicting SLNB positivity. These variables may play a role if the aim of this study was to look at the risk factors for cancer development. For BMI specifically, the concern of information bias would be reasonable if the method used to detect the SLN in our patient population was methylene blue only, as it affects the identification rate of SLNB. However, in our institution, we used radioactive isotope injection with a gamma detection probe on all patients included in this study.

For patients with SLN micrometastasis. According to the landmark IBCSG 23-01 study that followed breast cancer patients with axillary micrometastasis for almost a 10-year period, there is no difference in prognosis if ALND was performed or omitted.⁴ Therefore, we do not perform ALND on patients with axillary micrometastasis in our practice, as recommended by international guidelines.^{5,6} In turn, we considered this group of patients as having negative SLN. No prognosis analysis on patients with micrometastasis was conducted in this present study since it was not within the study scope; however, this area may be explored further in future studies.

133

Dr. Bao-Hua asks a very important question about what changes we have implemented in our breast cancer management multidisciplinary team. Notably, we have implemented the rule that all patients identified to have prominent axillary lymph nodes (ALN) by our breast radiologist would undergo an ultrasound (US) guided ALN biopsy as it appeared to be a strong predictor of SLN positivity. Also, we are in the process of conducting a prospective multicentric study to further predict the factors resulting in SLNB positivity. The results of this future study will hopefully be more representative of the population of breast cancer patients in Saudi Arabia, and the setting will be more controlled.

Finally, we understand Dr. Bao-Hua's observation on the setting of the study; however, our institution has the largest tertiary breast cancer care center in our country and is the chief referral center in the Kingdom of Saudi Arabia. Also, our center has been implementing the use of SLNB for a longer period than other centers in the country. In the future prospective study that we are leading, we have invited the involvement of multiple breast cancer care centers in Saudi Arabia due to the current widespread use of SLNB.

In summary, we want to thank Dr. Bao-Hua et al for their invaluable comments and continued interest in our research.

Disclosure

The authors report no conflicts of interest in this communication.

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