correspondence

Risk Assessment in Population-Based Breast Cancer Screening

TO THE EDITOR:

Yala et al[1] reported on the multinational validation of the Mirai artificial intelligence–based mammography-based breast cancer risk model. The study included 62,185 screening mammograms and 3,815 incident cancers diagnosed within 5 years of study entry. Concordance indices ranged from 0.75-0.84 for the 5-year risk model across seven screening sites. It was concluded that the risk tool could offer broad and equitable improvements in breast care.

The authors advance the important inclusion of image-based data to further refine existing models for the assessment of breast cancer risk. The identification of women who, after a negative screen, may benefit from supplemental screening could lead to earlier detection of breast cancers and potentially improved prognoses as previously described.[2] The goal of equitable improvements in care is also essential for broad implementation. We, therefore, read this study with great interest and applaud the authors for their undertaking. However, there are several aspects of this study that require clarification.

First, in regard to the study design, typically in a population-based screening program, there are similar proportions of women attending screening and developing breast cancer each year over the 5-year period. However, Table A4 shows that 42%-82% of the cancers were diagnosed in the first year of the 5-year study. Therefore, the distribution of cases over time suggests that the study sample might not have represented a population-based screening setting. In addition, the estimation of the area under the curve (AUC) for the 5-year period included all women with follow-up from 0 to 5 years. In combination with the distribution of the cancers over time, the average risk projection time was weighted closer to 1 year rather than 5 years. This study design may, therefore, limit the generalizability of the results in assessing risk in a population-based screening program.

Second, we have questions regarding the cancers diagnosed within six months of the initial screen. As is well stated in the article, accurate risk assessment is essential for the success of risk-based breast cancer screening. Table 2 shows high 1-year AUCs ranging from 0.78 (95% CI, 0.73 to 0.84) to 0.90 (95% CI, 0.89 to 0.92) across the different sites. After removal of cancers diagnosed within 6 months of screening, Supplemental Table A5 reports a drop in the 1-year AUC of approximately six points. It is unclear if mammograms at the time of diagnosis were included in the main table or why there is such a difference in the results shown in the supplemental table and which AUCs should be considered more clinically relevant for risk assessment in population-based screening.

Third, in regard to the comparison of the author's Mirai risk model with the Tyrer-Cuzick model, clinical guidelines were used to define the sensitivity and specificity of the Tyrer-Cuzick model for women at $\geq$ 20% lifetime risk.[3-5] Furthermore, the specificity of the Tyrer-Cuzick model was used to find an operating point of the Mirai model at the same specificity and then, this specificity was used to determine the cost of mammography screening. The method assumes that the two models are well calibrated, ie, show good correlation between the predicted probabilities for breast cancer and the actual proportions of breast cancers in the population.[6] However, if the model is not well calibrated, an operating point may need to be established for each imaging site in a postanalysis, on the basis of retrospective data, to define a target specificity and/or sensitivity. It would be helpful for the authors to further clarify the method of calibration of the Mirai model.

Fourth, the authors discuss using 5-year risk assessment to enable more effective screening and prevention efforts of high-risk populations. Our view is that a risk model for effective screening should be designed to assess the risk of breast cancer in the interval between the just-performed screen and the next scheduled screen to identify women who need supplemental screening. This could result in fewer false-positive high-risk women sent for supplemental screening compared with using 5-year risk assessment. By contrast, a 5-year risk assessment could be too short a time for use in primary prevention considering that the development of a breast cancer takes more than five years. Treating a developing cancer could not be considered primary prevention.

In summary, we support the aim of Yala et al[1] to leverage both the mammography screening infrastructure and image-based data to further refine breast cancer risk assessment. However, study design, analysis procedure, and model calibration require clarification so that the generalizability of the reported results and the methodology potentially adopted in other breast cancer screening settings may be determined.

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