Identification of women at high risk of breast cancer and in need of supplemental screening - a cohort study

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ABSTRACT

Background. Mammography screening reduces breast cancer mortality, but a proportion of breast cancers are missed and are detected at later stages or develop in between screening intervals. We developed a risk model using negative mammograms that identifies women likely to be diagnosed with breast cancer before or at next screen.

Methods. A prediction model was developed using mammographic features (fibro-glandular density, microcalcifications and masses), age, a polygenic risk score, body mass index, use of hormone replacement therapy, family history of breast cancer, and menopausal status.

Results. The model predicted 2-year risks for use in bi-annual screening. The area under the receiver operating curve (AUC) reached 0.77.

Conclusions. This risk model could improve mammography screening by identifying women that are in need of additional examination procedures. There is also a substantial proportion of women with low breast cancer risk who will have little benefit from the screening.

OBJECTIVES

• Build and validate the KARMA risk model that predicts breast cancer risk and is adapted to the mammography screening setting.
• Construct the first risk model based on mammographic features, lifestyle factors, and a 313 SNP polygenic risk score.
• Identify women that have a negative screening mammogram but are at high risk of being diagnosed with breast cancer until the next mammography screen.
• Risk stratify women into groups who need additional examination procedures and groups that have little benefit from screening.

REFERENCES

3. ACR BI-RADS atlas. American College of Radiology
4. NICE guideline. National Collaborating Centre for Cancer (UK). A fourth low-risk category was added.

RESULTS

Womens’ 2-year risks were determined by mammographic density (OR 1.4 / SD), microcalcifications (OR 1.8 / SD), masses (OR 2.0 / SD), and PRS (OR 1.6 / SD). Postmenopausal women had slightly lower risk estimates. When adding bilateral breast asymmetries to the model, the full model reached a discrimination performance of AUC 0.77.

The model predicted 2-year risks for use in bi-annual screening and was expanded by including age, a polygenic risk score (PRS), body mass index, use of hormone replacement therapy, breast cancer onset in family, and menopausal status. Relative risks were calculated per standard deviation (SD) for each risk factor using conditional logistic regression. Two-year absolute risks were calculated based on the relative risks, national breast cancer incidence rates, and competing mortality from other death causes than breast cancer.

CONCLUSIONS

• After a negative mammogram at screening, 25% of the women have moderate or high 2-year breast cancer risk. 48% of the women have an average risk and 27% of the women have a low risk.
• The risk model has the potential to improve mammography screening by identifying women that are at high risk of an interval or advanced cancer. In addition, the risk model could identify those women that have little benefit from mammography screening.

Methods

OBJECTIVES

RESULTS

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CONCLUSIONS