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Prediction of Breast Cancer Risk and Tumor Aggressiveness in the Athena Breast Health Network

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BACKGROUND

Introduction:

- Breast cancer (BC) risk models are important tools to estimate a woman's risk for developing invasive BC.
- Risk models are used to guide screening, risk reducing medication & supplemental imaging guidance. [1,2]
- Most models currently predict the risk to develop BC versus no cancer, rather than the subtype of BC.
- This poses limitations as BC varies widely in its aggressiveness and biology.
- Evaluating models for their ability to predict different subtypes of BC is important for personalized recommendations about screening and prevention.

Athena Cohort:

- The Athena Breast Health Network (Athena) is a University of California (UC) and Sanford Health initiative integrating clinical care and research to drive improvements in breast screening.



Figure 1: Athena Workflow

RESEARCH QUESTION & AIMS

1. Assess the association of 5-year invasive cancer risk level by the Breast Cancer Surveillance Consortium version 3 (BCSCv3) model and the development of aggressive or non-aggressive cancer in the Athena UCSF Cohort

2. We aim to better understand whether a risk model predicts specific BC types to better inform its use in risk assessment and prevention strategies

METHODS

Risk Assessment:

- BC risk was assessed by the BCSCv3 risk model. High risk was defined as ≥1.67% 5-year BCSCv3 risk.

Cancer Data & Classification of Aggressiveness:

- Incident BC were identified by cancer linkage with the San Francisco Mammography Registry and the UCSF cancer registry (complete through Dec. 2018 and Jan. 2022 respectively).
- Tumor aggressiveness was defined in two ways.
  - Advanced or non-advanced cancer was classified by the AJCC prognostic pathologic stage (≥2 stage is advanced, < stage 2 is non-advanced).
  - Faster and slower growing cancer considered tumor biology only, where one or more of the following criteria defined faster: HR-negative, HER2-positive, and/or grade 3, all other were slower growing cancers.

Statistical Approach:

- We used logistic regressions to examine associations between BCSCv3 5-year risk score and BC incidence and tumor aggressiveness.

RESULTS – BCSCv3 RISK ASSESSMENT

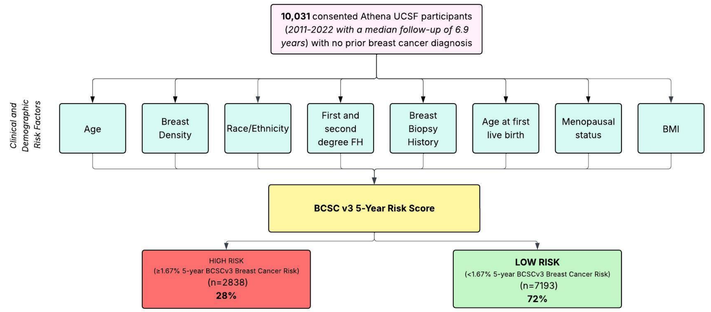


Figure 2: Athena BCSC v3 Risk Model Input and Risk Classification

RESULTS - CANCER REGISTRY LINKAGE

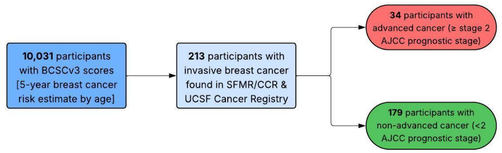


Figure 3: Cancer Registry Linkage Results - AJCC Prognostic Stage

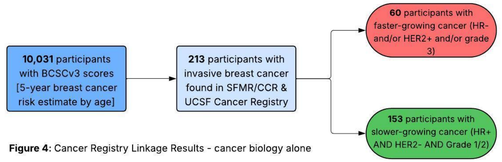


Figure 4: Cancer Registry Linkage Results - cancer biology alone

RESULTS – BCSCv3 RISK & CANCER OUTCOMES

BCSC Risk and Cancer Stage

- The median 5-year BCSCv3 risk score for women with and without breast cancer was **1.73%** and **1.38%** respectively (p<0.001).
- The average 5-year BCSCv3 risk score for women with advanced and non-advanced cancers was **1.67%** and **1.74%,** respectively.
- The average 5-year BCSCv3 risk score for women with faster and slower growing cancers was **1.65%** and **1.76%**, respectively.

RESULTS – BCSCv3 & CANCER OUTCOMES

Table 1: The likelihood of developing breast cancer in the Athena cohort by BCSC risk stratum

	ODDS RATIO	95% CI	P VALUE
Invasive Breast Cancer vs. no cancer	1.89	1.38 - 2.61	P<0.0001
Non-advanced cancer vs. no cancer (< AJCC prognostic stage 2)	3.08	1.87-5.08	P<0.0001
Advanced cancer vs. no cancer (≥ AJCC prognostic stage 2)	1.24	0.56-2.77	P=0.59
Slower-growing cancer vs. no cancer (HR+ and HER2- and grade 1-2)	2.02	1.39-2.92	P<0.0001
Faster-growing cancer vs. no cancer (HR- and/or HER2+ and/or grade 3)	1.62	0.87-2.98	P=0.123

DISCUSSION

Impact on Clinical Practice:

- The BCSCv3 model predicts non-advanced, less-aggressive cancers, but not advanced cancers. We see similar findings in the BCSC version 2 model.[4]
- Women with high 5-year BCSCv3 risk might be more likely to benefit from endocrine risk-reducing medications as non-advanced and slower-growing cancers are primarily hormone-receptor positive.[5]
- Prophylactic use is shown to reduce the incidence of estrogen receptor (ER) positive cancers (sometimes by over 50%). They have been shown to have little effect on reducing the incidence of ER-negative cancers.[6]

Subtype-Specific Risk:

- The BCSC consortium recently developed a 6-year advanced breast cancer risk model that specifically identifies individuals who are at risk for AJCC pathologic prognostic stage II or higher cancers.[6]

The WISDOM Study:

- The second iteration of WISDOM Study (WISDOM 2.0) specifically aims to understand who is at risk for developing aggressive breast cancer (www.thewisdomstudy.org).

Future Work:

- The analysis using the recently developed BCSC advanced cancer model is ongoing.

CONCLUSION

- The BCSCv3 model strongly predicts for less aggressive breast cancers, suggesting it could be used to optimally guide the use of prophylactic selective estrogen receptor modulator (SERM) medications .
- Reliable models to predict aggressive cancers are needed to guide recommendations about screening frequency and supplemental imaging. The recently developed BCSC advanced cancer model may provide better discrimination for those at risk for advanced cancers.

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