Acute Ovarian Failure Abstract for the North American Symposium on Late Complications after Childhood Cancer

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Title
Predicting Acute Ovarian Failure in Female Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study (CCSS)

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Abstract

Background
Acute ovarian failure (AOF), which is the permanent loss of menstruation within 5 years of cancer diagnosis or failure to achieve menarche before age 18, is an established late effect of cancer treatment. Precise individual risk prediction of AOF may direct appropriate counseling and fertility preservation. We sought to develop and validate a risk prediction model as the initial step to creating an AOF risk scoring system for clinical use.

Methods
Treatment exposure and self-reported menstrual history information were obtained from 5,886 female participants in the CCSS (median age at evaluation = 13 years (range: 5-26 years)). Alkylating agent exposure was quantified using the cyclophosphamide equivalent dose (CED). Three classes of candidate risk prediction models, i.e. logistic regression models, random forests, and support vector machines, were developed and evaluated using 100 random training-test data splits. Model performance including discrimination, predictive power, and calibration were assessed with the AUC, the average positive predictive value (AP), and calibration plots respectively. The final model was externally validated using the St. Jude Lifetime Cohort Study (SJLIFE).

Results
AOF occurred in 354 survivors (6.0%) following cancer treatment. Final models from each class performed very well, with internally validated AUCs above 0.80 and APs above 0.50. Calibration plots indicated good calibration, with the observed and predicted number of cases aligning well for low and high risk patients. Since the prediction performance of the three models was similar, the logistic regression model was selected as the final model for external validation due to its simple interpretation compared to the random forest and support vector machine. Predictors in the final model included ovarian radiation dose, exposure to preparatory regimens for a bone marrow transplant, age at cancer diagnosis, and CED. When externally validated, the model was calibrated, with an AUC of 0.96 and an AP of 0.91.

Conclusions
The logistic regression model performed very well during both internal and external validation, indicating the excellent ability of the model to predict the risk of AOF. A risk scoring system will be developed using the final logistic regression model to provide individual risk prediction for AOF to childhood cancer patients.