Prediction of health-related quality of life from longitudinal self-reported symptom patterns in adult survivors of childhood cancer

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Survivors of childhood cancer are at risk for developing various late effects in their adult life. Predicting health-related quality of life (HRQoL) from longitudinal patterns of patient-reported symptoms allows early detection of high-risk subgroups and offers opportunities for interventions tailored to specific patterns of symptoms.

A total of 721 adult survivors of childhood cancer, enrolled in both the Childhood Cancer Survivor Study and St. Jude Lifetime Cohort Study, were analyzed. Outcomes included two HRQoL measures, physical and mental component summary scores (PCS and MCS) collected through the 36-Item Short Form Survey (SF-36) questionnaire. Potential predictors were demographic, clinical and longitudinal symptom-pattern variables. Demographic predictors included sex, age at first survey, age at diagnosis of cancer, race, and educational attainment at the first survey. Clinical predictors included cancer type and treatment exposures including sites of radiotherapy and use of specific chemotherapy drugs within the first five years of cancer treatment. A total of 37 symptoms, categorized into 10 domains, were collected across three time points 2000, 2009 and 2013 as part of the comprehensive questionnaires of the two cohort studies. HRQOL was collected through the most recent CCSS or SJLIFE surveys, whichever occurred later. For each individual symptom item or domain of symptoms, we extracted various longitudinal symptom-patterns (features) hypothesized to affect HRQoL. These patterns include development/disappearance and count increase/decrease between two consecutive assessment points, and chronic presence/absence over the three time-points.

For prediction modeling, we used Elastic Net variable selection, first using only demographic and clinical predictors, followed by adding the 283 symptom-pattern as potential predictors. We used Bayesian Information Criterion (BIC) to select the best Elastic Net tuning parameters, and employed Intra-class correlation (ICC) and Area Under the Curve (AUC) for dichotomous HRQoL status (impaired vs. not impaired) as measures of prediction performance, estimated by a 10-fold cross-validation.

For MCS, selected predictors in the final model included 10 symptom-pattern variables involving anxiety and depression domains, but not demographic or clinical variables. By including symptom-pattern predictors, ICC (cross-validated version in parenthesis) improved from 0.06 (0.04) to 0.63 (0.59) and AUC improved from 0.60 (0.55) to 0.91 (0.89). For PCS, 18 selected variables included age, educational attainment, and symptom-based variables involving movement problems, pain, fatigue, sensation abnormality, and cardiac symptom domains. ICC and AUC improved from 0.22 (0.21) to 0.59 (0.52) and from 0.77 (0.75) to 0.92 (0.88) with and without the inclusion of symptoms.

In conclusion, our analysis revealed that longitudinal symptom patterns could successfully predict mental and physical HRQOL in childhood cancer survivors. In particular, self-reported symptoms have stronger predictive power for MCS, which outweighs the influence of cancer/treatment type. In addition, chronic suffering of a symptom/domain appears highly predictive of HRQoL as hypothesized. Furthermore, in the absence of symptom data, baseline demographic and clinical variables are better predictors of PCS compared with MCS.