Predicting fatigue severity in oncology patients one week following chemotherapy

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Background and Purpose

Effective symptom management is a critical component of cancer treatment. Computational tools that predict the course and severity of these symptoms have the potential to assist oncology clinicians to personalize the patient's treatment regimen more efficiently and provide more aggressive and timely interventions. Cancer-related fatigue (CRF) is the most common symptom associated with cancer and its treatments. CRF has a negative impact on patients' ability to tolerate treatments and on their quality of life. One of the limitations to effective treatment of CRF is the availability of a valid and reliable model to predict the severity of CRF.

The objective of this pilot study was to generate a predictive model for fatigue severity at one week after chemotherapy (CTX) administration (T2) using 28 demographic and clinical characteristics that were collected just prior to CTX administration (T1) in a sample of 1042 cancer patients undergoing CTX.

Methods

Oncology outpatients (n=1042) who were receiving CTX for breast, lung, gynecological, or gastrointestinal cancers were recruited as part of the parent grant (CA134900). Patients beginning their 2nd or 3rd cycle of CTX were assessed over two complete CTX treatment cycles (i.e., 6 assessments).

In this pilot study, we used support vector regression (SVR) with a polynomial kernel to predict the severity of the evening fatigue between two different time points during a cycle of CTX using demographic and clinical data.

Demographic and Clinical Designs

- The primary dataset contained a total of 1042 patients with 28 predictors. Patients with missing data were removed. No imputation was performed. The resulting dataset (n=689) was split into training and testing datasets, containing 75%/25% (n=518, n=171) of patients, respectively. The mean evening fatigue score observed at T1 was 5.39 (range 0.0-10.0) and at T2 was 5.66 (range 0.15-10.0).
- Training data were pre-processed for center and scale and were used to train the model. 10-times 10-fold cross-validation root-mean-square error (RMSE) was used to select the optimal model using the smallest value. Only training data were used.
- Model performance was evaluated with a Bland-Altman plot and correlation between predicted and observed Evening Fatigue scores at T2. Observed scores were provided by the testing set.

Predictors in the Final Model

Demographic: Age (years), Gender, Highest level of education, Body mass index, Ethnicity, Married/partnered, Lives alone, Currently employed, Annual household income, Child care responsibilities, Adult care responsibilities

Clinical: Karnofsky Performance Status, Comorbidity profile, Number of metastatic sites, Cancer diagnosis, Years from diagnosis to start of CTX, Number of prior cancer treatments, Hemoglobin level, Exercise on a regular basis, CTX cycle length, Morning fatigue (LFS) at T1, Evening fatigue (LFS) at T1, Morning energy at T1, Evening energy at T1, Attentional fatigue at T1, CES Depression Scale, State Anxiety Scale, General Sleep Disturbance Scale

Results

The Prediction Model

The final values used for the model were degree = 1, scale = 0.01 and Cost C = 1. The final model RSME was 1.514816. The performance score (RSME/mean) was 0.269.

The mean evening fatigue score predicted by the model at T2 was 5.57. The range of evening fatigue scores predicted by the model at T2 was 2.515 - 8.83.

Results (Continued)

Figure 1. Scatter plot of observed and predicted Evening Fatigue scores at time 2 in the test dataset (n=171). Predicted values were produced by the model developed using the training data, and observed values are provided by the testing dataset. Pearson's correlation = 0.62 (p-value < 2.2e-16).

Figure 2. Bland-Altman plot showing the level of agreement between predicted and observed values of Evening Fatigue at T2 (n=171). Predicted values were produced by the model developed using the training data, and observed values are provided by the testing dataset.

Figure 3. Histogram of observed and predicted Evening Fatigue scores at time 2 in the test dataset (n=171). Predicted values were produced by the model developed using the training data, and observed values are provided by the testing dataset.

Discussion

Relative Contributions of the Demographic and Clinical Variables

- The five predictors with the highest importance were: evening fatigue at T1, morning fatigue at T1, attentional function at T1, sleep disturbance at T1, and performance status at T1.
- The five predictors with the lowest importance were: living alone, caregiver to adult, level of education, cycle length, and number of metastatic sites.
- Hemoglobin values had a low importance as a predictor, suggesting anemia is not a major contributor to the level of evening fatigue following chemotherapy.
- Overall, clinical characteristics associated with cancer and its treatment, including cancer diagnosis, had low importance in the model.
- These findings suggest that the experience and mechanisms of CRF may be general and not cancer specific.

Conclusions

This type of predictive model can be used to identify high risk patients, educate patients about their symptom experience, and improve the timing of pre-emptive and personalized symptom management interventions. These results suggest that the integration of demographic and clinical data can enhance clinical prognostic prediction, which will contribute to the development of precision cancer medicine. Our methods may be generalizable to other symptoms associated with cancer and its treatment (e.g., sleep disturbance, depression, anxiety).

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