

Fatigue during radiotherapy for early-stage breast cancer and its relationship to irradiated volumes, IL-6sR and anxiety and depression: towards a prognostic model

Dr Nick Courtier

ABSTRACT

Introduction

Fatigue is the most troublesome untreated symptom during radical breast radiotherapy. This situation persists due to an uncertain aetiology and an inability to identify patients at high risk of experiencing significant fatigue during subsequent radiotherapy. Aetiological investigations of the current study concentrated on discriminating the radiotherapy-specific effects on fatigue, in a context encompassing multiple psychological and physiological covariates. Prognostic aspects sought to characterise a 'high-risk' patient.

Methods

The study cohort comprised 100 women, diagnosed with Stage 0 to IIA breast cancer, and prescribed standard whole breast irradiation to 40Gy in 15 fractions over three weeks. The use of systemic therapies was an exclusion criterion. A cytokine-induced sickness behaviour model framed the study investigations, and provided a theoretical link between localised radiotherapy and systemic fatigue. The outcome fatigue was assessed before, during and four weeks after radiotherapy, using the Functional Assessment of Chronic Illness Therapy Fatigue Subscale. Volumes of tissue irradiated were derived from dose-volume histogram analysis; concentrations of the cytokine interleukin-6 soluble receptor were established via enzyme-linked immunosorbent assay. Multivariable analysis determined the factors that contributed to fatigue and generated a prognostic model that classified participants to fatigued or non-fatigued groups.

Results

38% of participants experienced significant fatigue during radiotherapy, with the remainder little affected. The fatigued group recorded relatively elevated pre-radiotherapy levels of depression, and particularly anxiety, as measured by the Hospital Anxiety and Depression Scale. Depression uniquely accounted for 34% of the variance in pre-treatment fatigue. During radiotherapy, depression level and interleukin-6 soluble receptor concentration were significantly elevated in the fatigued group compared to the non-fatigued group ($p < 0.0001$, $p = 0.01$, respectively). The volume of tissue irradiated significantly affected peripheral interleukin-6 soluble receptor concentration ($p = 0.003$), but was not significantly associated with fatigue. A model comprising pre-treatment fatigue, anxiety and activity level (as measured by the International Physical Activity Questionnaire) reliably classified 82% of the study participants to the correct fatigue outcome (sensitivity 71.1%; specificity 88.7%).

Conclusion

Psychological mood is the strongest predictor of fatigue before and during radiotherapy. Inter-related data is consistent with the concept that a lower psychological mood prior to radiotherapy relates to a distinct immunological and behavioural response during radiotherapy. These aetiological insights may inform fatigue treatment pathways, and ensure the targeting of future interventions at early breast cancer patients at a high risk of experiencing fatigue.