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FATIGUE ASSESSMENT

P002

Clinical Correlates of Impaired Fatigue Scores in Quality-of-Life Evaluation for Long-Term Survivors of Breast Cancer

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Introduction: Quality of life (QOL) in survivors of premenopausal breast cancer (BC) is influenced by prolonged hormone therapy, secondary amenorrhea, and other factors. A proportion of premenopausal BC patients develop fatigue during follow-up. We aim to ascertain the clinical findings associated with severe fatigue in these patients.

Methods: Retrospective evaluation of patients with invasive BC diagnosed before menopause and with a disease-free status for 5–15 years after surgery. A subgroup of patients with fatigue scores > 50 (0–100 scale) on the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire were submitted to further in-depth analysis of clinical features. QOL testing was performed during routine follow-up visits at our center.

Results: Of 214 patients, 27 (12.6%) had fatigue scores > 50. Median age at diagnosis: 45.7 years (35–54 years). Median follow-up: 8.4 years (5.1–15 years). Previous postsurgical therapy: chemotherapy (21/27), hormone therapy (23/27), and radiotherapy (23/27). Of the 27, 9 had rheumatologic diseases (7 fibromyalgia, 1 psoriatic arthritis, 1 severe osteoarthritis); 8 had endocrine diseases (4 hypothyroidism, 2 overweight disorders, 1 parathyroid surgery, 1 diabetes mellitus); 8 were under psychiatric care (3 for alcohol and/or illicit substance abuse, 4 severe depression, 1 anxiety disorder); 4 had *Helicobacter*-associated chronic gastritis, 1 ulcerative colitis, and 1 chronic hepatitis. Blood testing disclosed mild hyperglycemia ($n = 5$), hypertransaminasemia ($n = 3$), and hypoferritinemia ($n = 3$). Low-grade thrombocytopenia ($n = 5$) was more common than anemia ($n = 1$). Common medications included benzodiazepines ($n = 16$), antidepressants ($n = 17$), nonsteroidal anti-inflammatories ($n = 12$), statins ($n = 4$), antihistamines ($n = 4$), and inhaled bronchodilators ($n = 4$). With a median follow-up of 8 months after QOL testing no BC relapse has been detected among the patients with severe fatigue.

Conclusions: More than 10% of long-term survivors of premenopausal BC reported severe fatigue in QOL testing. Concurrent rheumatic, endocrine, psychiatric, and hepatodigestive disorders were found in a proportion of these patients.

P003

Association of Fatigue with Other Tested Scales in EORTC Quality-of-Life Questionnaires for Breast Cancer Survivors

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Objectives: To correlate performance on the various scales of the European Organization for Research and Treatment of Cancer (EORTC) general (QLQ-C30) and breast-specific (BR23) quality-of-life (QOL) questionnaires according to the degree of fatigue for long-term disease-free premenopausal breast cancer patients.

Methodology: Two equally distributed groups of patients were defined according to a fatigue score of less than or more than 22.2 on the QLQ-C30. Performances on other QOL scales were compared between the groups using the Spearman rank correlation coefficient (ρ). Functional scores of 100 indicate best performance, and symptom scales of 100 indicate worst symptom burden.

Results: Among the 214 patients tested, mean fatigue scores were 3.4 and 42.6 in the low and high fatigue-score groups. The group with lower fatigue scores presented significantly better ($p = 0.0001$) mean scores on the following functioning scales of QLQ-C30: physical (95.4 vs. 79.1), role (96.5 vs. 73.9), emotional (87.6 vs. 62.3), cognitive (94.9 vs. 73.2), social (97.0 vs. 73.2), and overall (83.3 vs. 55.3). Mean scores of symptom burden were significantly better ($p = 0.0001$) for emesis (0 vs. 8.4), pain (5.6 vs. 37.9), dyspnea (0.8 vs. 11.7), insomnia (17.1 vs. 47.3), appetite loss (2.4 vs. 14.6), diarrhea (0.6 vs. 10.6), and financial problems (4.1 vs. 25.9). Scores were significantly better ($p = 0.001$) in QLQ-BR23 for body image (90.0 vs. 71.8), future perspective (76.8 vs. 50.0), and sexual functioning (31.2 vs. 22.3, $p = 0.006$). Also ($p = 0.0001$) for arm (10.2 vs. 29.3) and breast (8.6 vs. 23.6) symptoms, systemic therapy side effects (11.8 vs. 30.3), and upset by hair loss (8.6 vs. 26.9, $p = 0.003$).

Conclusions: Fatigue is correlated with worse functional and symptom scores on the EORTC general and breast QOL questionnaires for survivors of premenopausal breast cancer.

CAUSATIVE MECHANISMS—CENTRAL OR PERIPHERAL

P004

**Persistent Fatigue in Post-Treatment Survivors:
Are Fatigue Perceptions an Important Central Etiology**
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Cancer-related fatigue (CRF) is a highly prevalent and distressing side effect of treatment that can affect all aspects of quality of life. CRF persists in the post-treatment survivorship period for some cancer patients, but this persistence is not fully explained by diagnosis or treatment variables. Qualitative data show that patients hold specific beliefs or attributions about fatigue that may influence central interpretation of this symptom and severity outcomes. Attributions or specific beliefs, thoughts, and emotions that patients hold about CRF may play an important role in the etiology and persistence of fatigue, but that role has not been previously examined.

Objectives: The specific research questions addressed were: What beliefs do cancer patients hold about CRF? What is the independent contribution of beliefs/attribution on intensity of fatigue when other covariates are controlled?

Methods: Population cohorts of nonmetastatic breast, prostate, and colorectal cancer survivors (6–18 months; 2–3 years; and 5–6 years) post-treatment were identified through the Princess Margaret Hospital cancer registry and sent a questionnaire package that included the Fatigue Symptom Perception Questionnaire (FSPQ), CES-D short form, STAI-S, MSAS-SF, Charlson comorbidity index, and WHO Disability Assessment Schedule. Demographic and clinical variables were abstracted from charts. We conducted a hierarchical regression multivariate analysis to examine the additional variance explained in fatigue severity when disease, treatment, and other symptom covariates are controlled.

Results: Overall, patients reported fatigue as cyclical, and they had low perceived consequences of fatigue and treatment control. Compared with prostate cancer survivors, breast cancer and colorectal patients reported higher emotional responses to fatigue. Fatigue attributions explained additional variance in fatigue severity when other variables were controlled in the analysis.

Conclusions: The study results suggest that fatigue attributions like other symptoms that are interpreted as part of a central psychological-information processing system may play an important role in the central etiology of fatigue. This role should be examined in future research. Understanding patient perceptions of CRF and the role of those perceptions in predicting intensity of CRF in cancer survivors is critical to the design of clinical interventions.

**Levels of Peripheral Blood Cells During External-Beam Radiation
Therapy: Relationship with Fatigue**

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Objectives: To determine association between levels of peripheral blood cells and fatigue symptoms of men with nonmetastatic prostate cancer receiving external-beam radiation therapy (EBRT). EBRT is the second most common treatment modality used for treatment of nonmetastatic prostate cancer. Up to 71% of prostate cancer patients complain of fatigue during EBRT, which decreases their quality of life.

Methods: An exploratory and longitudinal study design. Men with prostate cancer who schedule to receive EBRT were enrolled under active protocol (NCT00852111). All study participants completed the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) and had peripheral blood drawn at 3 time points: baseline (D0), midpoint (D21), and EBRT completion (D42). One-way repeated-measures analysis of variance (ANOVA) and multivariate linear regression were used for data analysis.

Results: The preliminary analysis included 34 prostate cancer patients. Results showed significant changes of fatigue scores, red blood cells (RBCs), hematocrit, hemoglobin, absolute basophil count, absolute lymphocyte count, and absolute reticulocyte count over time in patients during EBRT compared with baseline ($p \leq 0.05$). At all 3 time points, decreasing hemoglobin ($\beta = -2.5$, $p < 0.01$) and increasing absolute reticulocyte count ($\beta = 0.26$, $p < 0.01$) and absolute basophil count ($\beta = 233.0$, $p < 0.01$) predict worsening fatigue.

Conclusions: The study findings provide empirical evidence of the significant association in this population between worsening fatigue and changes in blood counts levels associated with anemia and inflammation. Interventions that address anemia and inflammation related to EBRT may reduce the fatigue symptoms experienced by these subjects.

P005

**Peripheral and Central Markers of Fatigue in Men
Receiving Localized Radiation Therapy**

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Objective: To explore potential markers of peripheral and central fatigue in men with localized prostate cancer receiving external-beam radiation therapy (EBRT).

Method: Questionnaires and peripheral blood were collected at baseline (D0), midpoint (D21), and endpoint (D42) of EBRT. Fatigue was measured by the revised Piper Fatigue Scale. Aldolase and MCP-1 levels were explored as markers of peripheral and central fatigue, respectively; both were measured using ELISA from serum samples. Muscle strength and cognitive function were measured by hand-grip dynamometer and STROOP test, respectively. Descriptive statistics and *t*-tests were used to analyze the changes and differences of means between groups.

Results: The 38 subjects enrolled were grouped into high fatigue (HF) and low fatigue (LF) based on changes in fatigue scores during EBRT, using baseline as control. Fatigue scores increased significantly from baseline to midpoint in the HF ($p < 0.01$) and the LF ($p = 0.03$) groups and remained elevated at completion of EBRT in both groups ($p = 0.01$). Aldolase levels significantly increased from baseline to midpoint ($p = 0.05$) in the LF group, but not in the HF group ($p = 0.31$). There were no significant changes in MCP-1 levels over time during EBRT for both groups ($p = 0.27$ – 0.98); however, MCP-1 concentrations trended towards significance different at midpoint between the groups ($p = 0.09$). No significant changes in maximum voluntary contraction (MVC) and static fatigue were noted over time during EBRT compared with baseline in both groups ($p = 0.30$ – 0.82), and the number of wrong answers and reaction time from STROOP test in both groups were nonsignificant ($p = 0.07$ – 0.87).

Conclusions: Fatigue is associated with increased aldolase concentration in prostate cancer patients during EBRT. Aldolase may serve as a physical and a central marker of fatigue in this population. Further studies exploring and validating biomarkers of physical and central fatigue will be necessary to identify novel interventional targets.

P006

FATIGUE INTERVENTIONS

P008

Exploring Attention-Restorative Theory and Its Use in Fatigue Management

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Fatigue is a common and distressing symptom of long-term illness, palliative care conditions, and cancer, and a concern for families, carers, and health care practitioners. Attention Restorative Theory (ART) was developed by Kaplan (1995) following his interest in restoring mental attention within the "person-environment interaction." Within this framework, restorative events have 4 core components: "being away" (that is, distinct from routine), "fascination," "extent" (that is, scope), and "compatibility."

Objectives: To explore enjoyable routines and activities of people experiencing fatigue related to long-term illnesses. To analyze identified activities within an ART framework by mapping emergent themes with the core components of mental restoration. To determine if a novel intervention based on restoring mental attention should be considered for people with long-term illnesses.

Methods: A qualitative approach was used to obtain knowledge about a discrete population of people who experience fatigue as a result of a long-term illness or palliative care condition. Participants ($n = 25$) were approached to participate from a local hospice, a podiatry clinic, and service user representative groups. Semi-structured interviews lasting no more than 45 minutes were conducted using an interview guide in which the emphasis was on describing activities that were enjoyed, rather than dwelling on the limitations of fatigue.

Results: Participants reported enjoying creative arts, baking, reading (all types), watching motor bike racing, singing, word games, or having a facial, as would be expected based on individual personalities and characteristics. Emergent themes were social coherence, nurturing, purposeful, fascinating, and expansive. Safety and contributing to the community were noteworthy attributes that did not easily integrate into the ART framework.

Conclusions: The ART approach has interesting prospects and scope within fatigue management. Further research is required to explore potential interventions that in time may prove to be beneficial in addressing the mental and possibly emotional dimensions of fatigue.

P009

Fighting Fatigue: Designing a Multidisciplinary Intervention for Cancer-Related Fatigue

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Objectives: This program was developed in response to the pervasiveness of fatigue reported by cancer patients. Patients of the Northeast Cancer Centre (NECC), including those receiving care at one of 14 Community Oncology Clinic Network (COCN) sites, are routinely screened for distress using the Edmonton Symptom Assessment System (ESAS). Patients reporting cancer-related fatigue (CRF) were referred to the Supportive Care Program (SCP) for individual interventions, including psychosocial, nutrition, and physiotherapy services. To ensure access for patients to receive guidance encompassing a variety of strategies for CRF, a psychoeducational class was developed by an inter-professional team within the SCP at NECC.

Methods: The SCP created an inter-professional committee to develop an interactive, psychoeducational class for cancer patients. The focus was multidimensional, supported with current evidence-based guidelines on fatigue, and developed with expertise from the fields of social work, neuropsychology, nutrition, and physiotherapy. Additional input was received from a group of cancer survivors. A electronic slide presentation and patient workbook highlight objectives, including understanding CRF, learning management strategies, and building a personalized plan. The class is professionally facilitated by members of the SCP and offered monthly at the NECC. Patients are welcome to bring caregivers. Several strategies to promote the intervention included centre-wide distribution of posters and information sessions for oncology health care providers.

Results: An integrated psychoeducational intervention targeting CRF was created and offered to patients of the NECC beginning in spring 2012. Initial feedback via formal evaluation was overwhelmingly positive as it related to patients receiving evidence-based guidelines to self-manage CRF.

Conclusions: To improve accessibility for patients throughout Northeastern Ontario, this intervention will be offered by telemedicine in fall 2012. In future research, patient-reported outcomes for the management of CRF will be tracked.