**Systematic Monitoring and Treatment of Physical Symptoms to Alleviate Fatigue in Patients With Advanced Cancer: A Randomized Controlled Trial.**

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**Summary Handout by Anjana Ranganathan, MD**

**Background:** Cancer-related fatigue is common (prevalence 74%) and multi-dimensional with physical, emotional and cognitive components. Treatment options in cancer pts are scare and some guidelines advise optimizing management of other physical symptoms.

**Hypothesis:** Monitoring and protocolized treatment of physical symptoms will have a more favorable effect on the severity of fatigue than standard symptom management. This will also be more effective than standard care in decreasing symptom burden, interference of fatigue with daily life, anxiety and depressed mood, and in improving quality of life.

**Methods Review:**
- **Population:** Ambulatory pts with an advanced, solid malignancy, receiving palliative treatment with a fatigue score \( \geq 4 \), ECOG PS \( \leq 2 \) and life expectancy \( \geq 4 \) months. Pts were excluded for recent involvement in experimental treatments, anxiety/ depression requiring psychiatric care, severe co-morbidity causing fatigue, NH residence, or severe cognitive impairment. (Netherlands)
- **Intervention:** Pts were assigned (1:1; computer generated randomization) to protocolized pt-tailored treatment (PPT) of symptoms or standard care (CAU). PPT entailed four appointments (1 wk, 2-4 wks, 5-6 wks and 8-10 wks) with a nurse who assessed nine symptoms on a 0 – 10 numeric rating scale (NRS). Pts received a non-pharmacologic education for symptom scores \( \geq 1 \) and a medical intervention for scores \( \geq 4 \) (pts specifically not educated about fatigue).
- **Outcome Studied:** Primary - Fatigue dimensions (Multidimensional Fatigue Inventory – MFI). Secondary - fatigue NRS score, interference of fatigue with daily life (BFI-I), symptom burden (EORTC QLQ-C30), quality of life (EORTC QLQ-C30), anxiety and depression (HADS) were measured at baseline and after 1, 2 and 3 months.
- **Statistics:** Differences between the groups over time were assessed by using linear mixed modeling.

**Results:**
- (Primary Outcome) Decrease in MFI-General Fatigue in the PPT group compared to CAU (effect size/ p-value: T1 0.27/ 0.007; T2 0.35/ 0.005; T3 0.27/ 0.07). Scores on MFI-Reduced Activity and Reduced Motivation improved significantly; however, scores on MFI-Physical Fatigue and Mental Fatigue were not significantly different.
- (Secondary Outcomes) Significant decrease over time in: intensity of fatigue, symptom burden, interference of fatigue with daily life and in anxiety in PPT group compared to CAU group. No significant difference in course of depression or quality of life in the two groups.

**Authors Conclusions:** In fatigued pts with advanced cancer, nurse-led monitoring and protocolized treatment of physical symptoms is more effective than standard of care in improving physical symptoms, reducing fatigue intensity, improving interference of fatigue with daily life and reducing anxiety.

**Reviewers Critique:**
- Maximum effect size on primary outcome was small (0.35; goal 0.5); however, this is comparable to exercise and pharmacologic interventions (0.23 and 0.28).
- Challenging to show fatigue and symptom improvement in patients with advanced cancer over time. Despite improvements, as the disease progresses, fatigue and symptoms burden may increase rapidly.
- Enrollment on the study was based on providers offering participation; there was no systematic screening of all patients (selection bias).
- Small, single center study limited to only Caucasian patients; lacks generalizability.
- Outcome was measured based on patient questionnaire (reporting bias).
- Component of the intervention that was responsible for the beneficial effect is unclear (care vs extra attention).
**Summary For Practice Implications:** Providers should consider adopting a systematic method for protocolized monitoring and treatment of physical symptoms as part of the routine care of patients with advanced cancer.