

CANCER-RELATED FATIGUE

CLINICAL CASE DISCUSSION

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DISCLOSURE

Personal financial interests: NO DISCLOSURES TO DECLARE

Institutional financial interests:

- TERNI Hospital: Novartis-GSK, Merck Sharp & Dohme, Roche, Bristol-Myers Squibb, Boehringer Ingelheim, Sanofi-Aventis, Pfizer, Astra Zeneca, Astellas, Eli Lilly, Helsinn
- PERUGIA Hospital: Novartis-GSK, Merck Sharp & Dohme, Roche, Bristol-Myers Squibb, Boehringer Ingelheim, IPSEN, Astra Zeneca

Non-financial interests: leadership role in any other medical society

President of the NCSO (Italian Network for Supportive Care in Oncology)
from June 2014 to June 2017; Vice-President from June 2017 to June 2020

CASE PRESENTATION

- Patient with non-small cell lung cancer (T3, N0, M0, stage IIB) submitted to 4 cycles of adjuvant chemotherapy with cisplatin/vinorelbine
- 3 months after the end of chemotherapy the patient presented fatigue which strongly ameliorate **with physical exercise, psychoeducation and psychooncological support**



FATIGUE: DEFINITION

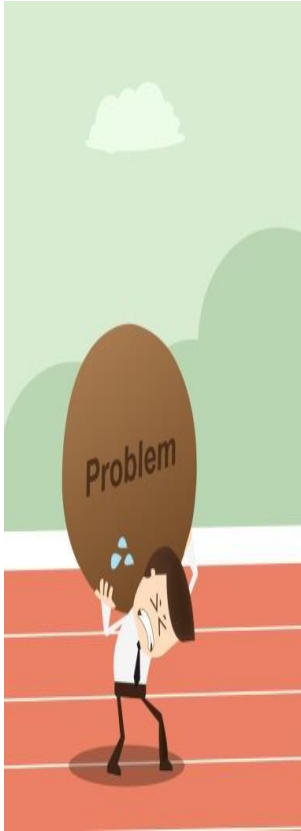
Cancer-related fatigue (CRF) is a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer and/or cancer treatment that is not proportional to recent activity and interferes with usual functioning

In comparison to the fatigue experienced by healthy individuals, CRF is often not alleviated by rest or sleep

CRF: INCIDENCE

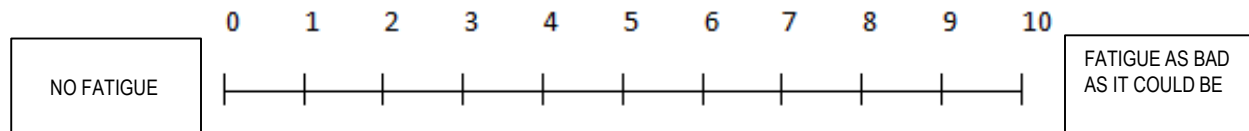
CRF can occur before, during and even long after anti-cancer treatment has been completed

- up to 40% of patients report CRF at diagnosis
- 80% and 90% of patients during chemotherapy and radiotherapy, respectively
- 17%-21% or 33%-53% of patients when strict criteria or other criteria are applied, respectively, in the post-treatment phase



CRF: SCREENING AND DIAGNOSIS

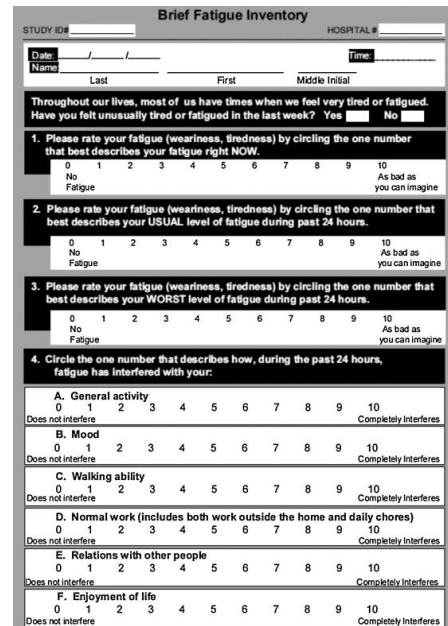
- All cancer patients should be routinely screened for the presence and severity of fatigue from the point of diagnosis onward, at regular intervals during therapy and aftercare and if clinically indicated **(level of evidence II, grade of recommendation B)**
- Screening should be done using brief and validated tools with established cut-off values for severity (e.g., Numerical Rating Scale) **(level of evidence II, grade of recommendation B)**



CRF, cancer-related fatigue

CRF: SCREENING AND DIAGNOSIS

- Patients who screen positive for CRF (values of 4 out 10 or higher indicating moderate to severe fatigue) should undergo a comprehensive and focused assessment with the aim to identify treatable contributing issues and comorbid conditions **(level of evidence II, grade of recommendation B)**
- The Brief Fatigue Inventory (BFI, a reliable and easily understood questionnaire, validated in many languages, in clinical screening and research) integrates the assessment of fatigue severity and its impact on important functional domains



The image shows a sample of the Brief Fatigue Inventory (BFI) questionnaire. It includes fields for STUDY ID, HOSPITAL #, Date, Name (Last, First, Middle Initial), and Time. The questionnaire consists of several sections with rating scales from 0 to 10, where 0 is 'No Fatigue' and 10 is 'As bad as you can imagine'. The sections are:

- 1. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your fatigue right NOW.
- 2. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your USUAL level of fatigue during past 24 hours.
- 3. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during past 24 hours.
- 4. Circle the one number that describes how, during the past 24 hours, fatigue has interfered with your:
 - A. General activity
 - B. Mood
 - C. Walking ability
 - D. Normal work (includes both work outside the home and daily chores)
 - E. Relations with other people
 - F. Enjoyment of life

CRF: SCREENING AND DIAGNOSIS

- the comprehensive and focused assessment should involve:
 - ✓ a focused fatigue history
 - ✓ a thorough physical examination
 - ✓ a status of the underlying malignant disease
 - ✓ a review of body systems
 - ✓ a mental status examination
 - ✓ a minimum battery of laboratory tests

(level of evidence II, grade of recommendation B)



CRF: CONTRIBUTING ISSUES



- ANAEMIA
- SYMPTOM BURDEN
 - Pain, anxiety, depression, dyspnoea, sleep dysfunction
- MEDICAL COMORBIDITIES
 - Endocrinopathies (hypothyroidism, hypogonadism, diabetes mellitus), cardiopulmonary disorders, hepatic, renal and neurological dysfunctions, adrenal insufficiency, infections

CRF: CONTRIBUTING ISSUES



- NUTRITIONAL AND FLUID IMBALANCES
 - Weight loss, changes in caloric intake, fluid and electrolyte imbalances, gastrointestinal tract motility disorders
- MEDICATIONS
 - Opioids, sedating agents (hypnotics, neuropathic agents, antihistamines), beta blockers
- CANCER THERAPY
 - Chemotherapy, radiotherapy, surgery, immunotherapy, hormone therapy, molecularly targeted agents

CRF: TREATMENT

- PHARMACOLOGICAL TREATMENT
- NON-PHARMACOLOGICAL INTERVENTIONS
 - PHYSICAL EXERCISE
 - PSYCHOSOCIAL TREATMENT
 - MIND-BODY INTERVENTIONS





PHARMACOLOGICAL TREATMENTS



Not recommended

- **PSYCHOSTIMULANTS**

- Methylphenidate, modafinil
- Dexmethylphenidate, dexamphetamine, long-acting methylphenidate, armodafinil

[II, D]

[II, D]

- **ANTIDEPRESSANTS**

- Paroxetine

[II, D]

- **ACETHYLCHOLINE INHIBITORS**

- Donepezil

[II, D]

- **OTHER DRUGS**

- Eszopiclone, TRH, megestrol, ATP, melatonin

[II, D]



PHARMACOLOGICAL TREATMENTS

Not recommended

- **NUTRICEUTICAL INTERVENTIONS**



- Wisconsin ginseng [II, D]
- L-carnitine [II, D]
- Coenzyme Q10 [II, D]
- Astagalus, guarana, mistletoe [II, D]



PHARMACOLOGICAL TREATMENTS

Recommended



- **CORTICOSTEROIDS**

- Dexamethasone, methylprednisolone [II, B]
(for short-term use in the advanced cancer patients)

NON-PHARMACOLOGICAL INTERVENTIONS

- **PHYSICAL EXERCISE**
- **PSYCHOSOCIAL TREATMENT**
- **MIND-BODY INTERVENTIONS**
 - Mindfulness-based stress reduction
 - Yoga
 - Acupuncture

PHYSICAL EXERCISE

- The role of physical exercise in patients with CRF during both active treatment and for those who have completed treatment has been documented by multiple systematic reviews and meta-analyses.
- Despite much evidence for exercise an exact exercise prescription in patients with CRF does not exist.
- Some guidelines encourage 150 minutes of moderate aerobic exercise, such as fast walking, cycling, or swimming, per week with an additional 2 to 3 days per week of strength training such as weight lifting unless contraindicated (e.g., extensive lytic bone metastases, fever or infection).

NON-PHARMACOLOGICAL INTERVENTIONS

Recommended



PHYSICAL EXERCISE

Moderate intensity, aerobic and functional resistance exercise is recommended in patients with CRF [I, B]

Aerobic, resistance and moderate physical exercise in patients with CRF provides symptomatic relief in depression, anxiety, pain, and muscle strength [II,B]



PSYCHOSOCIAL TREATMENT

- Information on the multi-factorial nature of CRF and its potential causes and influencing factors should be given
- Counseling should include recommendations for energy preservation, task prioritisation, activity pacing and advice on how to delegate less important activities (may be supported by brochures or interactive media)



PSYCHOSOCIAL TREATMENT

- Psychoeducation may be helpful for patients to identify sources of psychosocial distress and to eliminate stress-producing activities when possible and to find a balance between rest and activity during the day (using diary techniques, including subjective rating of each activity in terms of the perceived level of fatigue).
- Cognitive behavioral therapy is generally used to address the following factors: coping with the experience of cancer; fear of disease recurrence; dysfunctional thoughts and beliefs regarding fatigue, sleep dysregulation, etc.

NON-PHARMACOLOGICAL INTERVENTIONS

Recommended



- **PSYCHOSOCIAL TREATMENT**

- ✓ information and counseling to educate cancer patients about ways to prevent fatigue are recommended [II,B]
- ✓ psychoeducation is recommended to help patients to identify source of psychosocial distress and to eliminate stress producing activities [II,B]
- ✓ cognitive-behavioral therapy is recommended to improve CRF [II,B]

NON-PHARMACOLOGICAL INTERVENTIONS

not recommended

- **MIND-BODY INTERVENTION**

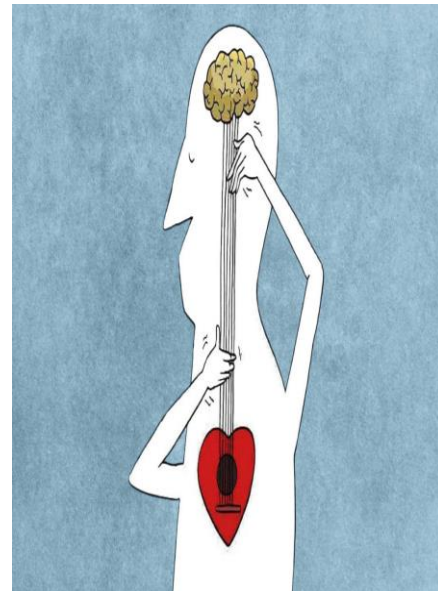
- ✓ Mindfulness-based stress reduction
- ✓ Yoga
- ✓ Acupuncture



[II, D]

[II, C]

[II, D]



Cancer-related fatigue: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up †

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Thank you