Rehabilitation of the Older Cancer Patient

Lodovico Balducci, M.D.
Moffitt Cancer Center
Tampa, Florida
Rehabilitation of the older cancer patient

• Is cancer treatment effective in older individuals?
• Chronologic age vs physiologic age: which patient should be treated?
• Short and long term complications of cancer and its treatment
Rehabilitation of the older cancer patient

• Is cancer treatment effective in older individuals? Yes, but…..
Lymphoma and Age: Same Treatment, Same Benefits

CGA and benefits of chemotherapy

Tucci et al, Cancer 2011
Cancer and aging: the growth of the population

Yancik et al, Semin Oncol, 2004
Rehabilitation of the older cancer patient

- Chronologic age vs physiologic age: which patient should be treated?
Indice di fragilità e eta' fisiologica

The trajectory of aging

Decreased functional reserve

Functional dependence
Polymorbidity

Death

STRESS

GENETICS
ENVIRONMENT
Assessment of aging

- Life expectancy
- Treatment tolerance
- Outcome

Cure
Prolongation of survival
Symptom Management
Prolongation of active life expectancy
Assessment of aging

Laboratory
• Circulating inflammatory markers
• Leukocyte telomeres length

Clinical
• Comprehensive Geriatric Assessment
• Functional assessment
Geriatric assessment and life-expectancy

<table>
<thead>
<tr>
<th>RISK FACTORS</th>
<th>Odd ratio</th>
<th>SCORE</th>
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<tbody>
<tr>
<td>AGE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-64</td>
<td>1.9</td>
<td>1</td>
</tr>
<tr>
<td>65-69</td>
<td>2.8</td>
<td>2</td>
</tr>
<tr>
<td>70-74</td>
<td>3.7</td>
<td>3</td>
</tr>
<tr>
<td>75-79</td>
<td>5.4</td>
<td>4</td>
</tr>
<tr>
<td>80-84</td>
<td>8.3</td>
<td>5</td>
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<tr>
<td>&gt;85</td>
<td>16.2</td>
<td>7</td>
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<tr>
<td>Male sex</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>comorbidity</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Cáncer</td>
<td>2.1</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>2.3</td>
<td>2</td>
</tr>
<tr>
<td>CHF</td>
<td>2.3</td>
<td>2</td>
</tr>
<tr>
<td>BMI &lt; 25</td>
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<td>1</td>
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<tr>
<td>Smoking</td>
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<td>2</td>
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<tr>
<td>Function</td>
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<td></td>
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<tr>
<td>grooming</td>
<td>2.0</td>
<td>2</td>
</tr>
<tr>
<td>Financial management</td>
<td>1.9</td>
<td>2</td>
</tr>
<tr>
<td>Walking one block</td>
<td>2.1</td>
<td>2</td>
</tr>
<tr>
<td>Push and pull weighty objects</td>
<td>1.5</td>
<td>1</td>
</tr>
</tbody>
</table>

Lee et al., JAMA, 2006
CGA AND FOUR YEARS MORTALITY RATE

![Bar chart showing CGA and four years mortality rate with different age groups and mortality rates. The chart includes categories for >80, 70-79, and 50-69 age groups, with varying bars representing the number of deaths.](chart.png)

LEE ET AL, JAMA, 2006
A new instrument
## Heme model

<table>
<thead>
<tr>
<th>Item</th>
<th>0 points</th>
<th>1 point</th>
<th>2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBP</td>
<td>( \leq 72 )</td>
<td>( &gt; 72 )</td>
<td></td>
</tr>
<tr>
<td>IADL</td>
<td>26–29</td>
<td>10–25</td>
<td></td>
</tr>
<tr>
<td>LDH*</td>
<td>0–459</td>
<td>0.45–0.57</td>
<td>( &gt; 459 )</td>
</tr>
<tr>
<td>Chemotox</td>
<td>0–0.44</td>
<td>0.45–0.57</td>
<td>( &gt; 0.57 )</td>
</tr>
</tbody>
</table>

*ULN = 618

DBP = diastolic blood pressure; LDH = lactate dehydrogenase; ULN = upper limit of normal.
Heme model

Trend $p < 0.001$
Cstat $0.65–0.77$

- Int. low
- Int. high
- High
## Non-heme model

<table>
<thead>
<tr>
<th>Item</th>
<th>0 points</th>
<th>1 point</th>
<th>2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECOG PS</td>
<td>0</td>
<td>1–2</td>
<td>3–4</td>
</tr>
<tr>
<td>MMS</td>
<td>30</td>
<td>&lt; 30</td>
<td>&lt; 30</td>
</tr>
<tr>
<td>MNA</td>
<td>&gt; 27.5</td>
<td>0–27.5</td>
<td>&gt; 0.57</td>
</tr>
<tr>
<td>Chemotox</td>
<td>0–0.44</td>
<td>0.45–0.57</td>
<td>&gt; 0.57</td>
</tr>
</tbody>
</table>

ECOG PS = Eastern Cooperative Oncology Group performance status; MMS = mini-mental status; MNA = mini-nutritional assessment.
Non-heme model

Trend p < 0.001
Cstat 0.62–0.66
Aging and complications of cancer treatment

- **Surgery**
  Increased mortality (emergency surger)
  Increased length of stay and deconditioning

- **Radiation Therapy**
  Mucositis
  Damage of surrounding organs
Aging and complications of cancer treatment

- Hormonal therapy
  Deep vein thrombosis
  CHF

- Cytotoxic chemotherapy
  Myelosuppression
  Mucositis
  Fatigue
  Cardiotoxicity
  Neurotoxicity
Aging and long term complications of systemic cancer treatment

- AML/MDS
- Cardiac dysfunction
- Cognitive Decline
- Fatigue
- Peripheral neuropathy
- Ostoporosis
Rehabilitation of the older cancer patient

• Short and long term complications of cancer and its treatment

Where rehabilitation is needed
Rehabilitation issues

• Fatigue

• Cognition

• Peripheral neuropathy
Most Common Symptoms of Cancer Survivors

- Fatigue
- Abdominal pain
- Sleep disturbances
- Depression
- Hypertension
- COPD
- Fear of cancer recurrence
# Prevalence of Fatigue European Population

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>51%</td>
<td>55%</td>
<td>0.406</td>
</tr>
<tr>
<td>75</td>
<td>59%</td>
<td>68%</td>
<td>0.005</td>
</tr>
<tr>
<td>80</td>
<td>58%</td>
<td>68%</td>
<td>0.045</td>
</tr>
<tr>
<td>85</td>
<td>79%</td>
<td>87%</td>
<td>0.126</td>
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</table>
Fatigue as a predictor of

- Mortality
- Decreased Mobility
- Disability and functional dependence
- Cognitive Decline
- Decreased Social Interactions
Causes and mechanisms of fatigue

- Comorbidity
- Physiology
  Muscle mass
  Hypoxia and hypoxemia
  Sarcopenia
- Cognitive decline
- Biology
  Mitochondria
  Inflammation
  Telomeres
- Isolation
- Depression
- Lifestyle

Avlund Aging Clin Exper Res, 2010, 100-115
Management of fatigue

- Patient choice
- Exercise
- Nutrition
- Treatment of anemia
- Psychostimulants
- Antidepressants
- Alternative medicine
Exercise

• 70 RCS
• 4881 patients
• Exercise reduced fatigue significantly during and following cancer treatment
• People who benefited most from exercise were those with the lowest baseline degree of fatigue

Fong et al, BMJ 2012, 344. e70

<table>
<thead>
<tr>
<th>Study</th>
<th>% with breast cancer</th>
<th>No</th>
<th>Mean (SD)</th>
<th>No</th>
<th>Mean (SD)</th>
<th>Difference (95% CI)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Piper fatigue scale</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yuan 2007</td>
<td>100</td>
<td>8</td>
<td>3.9 (1.7)</td>
<td>7</td>
<td>4.2 (1.7)</td>
<td>-0.3 (-2.0 to 1.5)</td>
<td>-1.4 (-3.2 to 0.5)</td>
</tr>
<tr>
<td>Yuan 2007</td>
<td>100</td>
<td>7</td>
<td>2.8 (1.9)</td>
<td>7</td>
<td>4.2 (1.7)</td>
<td>-1.4 (-3.2 to 0.5)</td>
<td>-1.4 (-3.2 to 0.5)</td>
</tr>
<tr>
<td>Daley 2007</td>
<td>100</td>
<td>34</td>
<td>--</td>
<td>38</td>
<td>--</td>
<td>-1.0 (-1.8 to -0.1)</td>
<td>-1.0 (-1.8 to -0.1)</td>
</tr>
<tr>
<td>Pooled estimate (random effect)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: P=0.636, I²=0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Beck depression inventory** |                      |    |           |    |           |                     |                     |
| Segar 1998                   | 100                  | 16 | 5.5 (2.1) | 8  | 10.0 (2.0)| -4.5 (-6.2 to -2.8) | -6.0 (-10.2 to -1.8) |
| Daley 2007                   | 100                  | 34 | --        | 38 | --        | 0.3 (-4.0 to 4.6)  | 0.3 (-4.0 to 4.6)  |
| Von Gruenigen 2009           | 0                    | 23 | 8.6 (7.2) | 22 | 8.3 (7.4) | -5.8 (-10.1 to -1.5)| -5.8 (-10.1 to -1.5) |
| Kaltsasou 2011              | 100                  | 14 | 16.5 (1.7)| 13 | 22.3 (7.7)| -4.1 (-6.5 to -1.8) | -4.1 (-6.5 to -1.8) |
| Pooled estimate (random effect) |                    |    |           |    |           |                     |                     |
| Test for heterogeneity: P=0.132, I²=47% |                      |    |           |    |           |                     |                     |
# Causes of Anemia

<table>
<thead>
<tr>
<th>Cause</th>
<th>NHANES III</th>
<th>Olmstead county</th>
<th>Biella</th>
<th>Chicago</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe def</td>
<td>16%</td>
<td>15%</td>
<td>16%</td>
<td>25%</td>
</tr>
<tr>
<td>Anemia of inflammation</td>
<td>34%</td>
<td>36%</td>
<td>17%</td>
<td>10%</td>
</tr>
<tr>
<td>B12 and folate deficiency</td>
<td>14%</td>
<td></td>
<td>6%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>12%</td>
<td>8%</td>
<td>15%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Hematological malignancies</td>
<td></td>
<td></td>
<td>7.4%</td>
<td></td>
</tr>
<tr>
<td>Thalassemia</td>
<td></td>
<td></td>
<td>4.5%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Unknown</td>
<td>24%</td>
<td>33%</td>
<td>26%</td>
<td>44%</td>
</tr>
</tbody>
</table>
Pharmacologic treatment of fatigue

- Methyphenidate
- Modafinil
- Guarana
- Antidepressants
Other interventions

- Psychotherapy
- Sleep hygiene
Figure 1 – Algorithm for diagnosis and treatment of cancer-related fatigue.

Cancer diagnosis is attained

Multidisciplinary assessment

Anamnesis and physical examination
- Nutritional, metabolic and hormonal status: anemia, hypothyroidism, menopause, water-electrolyte imbalance, dehydration, malnutrition.
- Comorbidities: cardiological assessment, pulmonary diseases
- Pain assessment and adequate therapy implementation

YES

Treat diagnosed pathologies

NO

Screen for cancer-related fatigue before starting any therapy

Apply questionnaire: Visual Analog Scale

Mild (1 to 3)

Non-pharmacological treatment
- Cognitive-behavioral therapy
- Individual counseling for stress and anxiety management
- Sleep therapy
- Physical exercises: avoid in patients with associated diseases and contraindications, such as: metastases with osteolytic lesions and imminent fracture risk, for instance
- Acupuncture

Moderate to severe (4 or higher)

Pharmacological treatment
- Methylphena
date: 5 mg 2x day (up to 20 mg/day)
- Guarana (dry extract): 50 mg 2x day
- Antidepressants if fatigue is accompanied by depression
- Modafinil: 100 to 200 mg in the morning
- Corticoids: for patients with terminal or advanced cancer due to side effects

Cognitive complications: Does chemotherapy cause dementia?

• Yes: Heck et al, J Am Ger Soc, 2008, SEER data, 18,000.00 patients. Diagnosis of dementia more common at three years in chemotherapy patients

• No. Baxter et al, J Am Ger Soc, 2009: SEER data. 21, 362.00 women. No dementia. Aging was not a risk factor for dementia
Ahles et al, JCO, 2010
Difference between standardized (Z) scores of the chemotherapy-exposed survivors of breast cancer and reference subjects. 15-WLT, 15-Word Learning Test; DOT, Design Organization Test; LDST, Letter Digit Substitution Test; MMSE, Mini-Mental State Examination.

Koppelmans V et al. JCO 2012;30:1080-1086
Blood–brain barrier integrity

Changes in cognition, and brain structure and function

Genetic susceptibility

DNA damage and telomere length

Oestrogen or testosterone reduction

Cytokine deregulation

Problems that breast cancer survivors reported more often

• More frequent forgetting
• More difficulty finding words
• Problem worsening over time
The syndrome of Aeneas
Conclusion

• Cancer and cancer treatment are a cause of disability and functional dependence
• Appropriate choice of patient and of cancer treatment is the first step toward preventing disability
• The mechanism of disability and functional dependence are multiple and interactive
Conclusions

• Exercise, nutrition, management of anemia, lifestyle may ameliorate fatigue and functional dependence

• Cognitive complications are real and are a cause of disability. The management at present is unknown
Conclusions

A research agenda should include:
• Better understanding of fatigue and aging
• Prevention of cognitive and neurologic complications
• Management of emotional disorders
• Management of social complications and assistance of the caregiver
Comment on peut se tromper en faisant la guerre au vieillissement et au cancer