ESMO PRECEPTORSHIP
SUPPORTIVE & PALLIATIVE CARE
SESSION 1

“REHABILITATION AN EMERGING INTEGRAL PART OF SUPPORTIVE AND PALLIATIVE CARE”

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What is rehabilitation?
Function/Disability approach not diagnosis driven
ICF-Model: Body-Activity-Participation
Rehab-Interventions: Exercise-Food-Mind-Soul-Spirit

Cancer Rehabilitation
Both tumor and anticancer treatment impact function
Sarcopenia, cachexia and cancer outcomes
Muscle, nerve and brain toxicity of anticancer treatments
Cancer-specific patients’ needs

Rehabilitation in supportive care
Fatigue, CINP, Body Image, Sexuality, Mucositis, …

Rehabilitation in palliative care
Value- and goal directed interventions close to EOL
DISCLOSURE information Florian Strasser

Institutional financial interests (KSSG): Unrestricted industry grants for clinical research: Helsinn, Celgene, Fresenius  Participation in company-lead clinical trial: Novartis

Leadership roles: Society on Sarcopenia, Cachexia and Wasting Disorders (SCWD): Board member – Swiss Society Medical Oncology: National representative oncological rehabilitation - European Society for Medical Oncology, Palliative and Supportive Care / Designated Centers Working Group: past Chair (2014-2017) - Swiss Group Clinical Cancer Research (SAKK), Working Group Supportive and Palliative Cancer Care: past Chair (2002-2016) - Multinational Association of Supportive Care in Cancer (MASCC),  Working Group Nutrition and Cachexia: past Co-Chair (until 2016)

Punctual advisorship (advisory boards, expert meetings) that have been paid to my institution - not to me directly: Danone, Grünenthal, Helsinn, ISIS Global, Mundipharma, Novartis, Novelpharm, Obexia, Ono Pharmaceutical, Psioxus Therapeutics, PrIME Oncology, Sunstone Captial, Vifor
Rehabilitation, is defined as "a set of measures that assist individuals, who experience or are likely to experience disability, to achieve and maintain optimum functioning in interaction with their environments" (WHO, 2011)

Typically delivered by multiprofessional and extended teams: physio-, sport-, ergo-, logotherapy, nutritionists, psychooncology, art-, music-, integrative therapies, social support, and of course APNs, doctors (oncology-rehabilitative-supportive-palliative)

(http://www.who.int/topics/rehabilitation/en)
International Classification of Functioning, Disability and Health: ICF

Description of patients’ condition not only diagnosis-based (ICD-10), but from a holistic functional perspective integrating personal situation in everyday life, work place and leisure.

Health condition

- Body Functions & Structure
- Activity
- Participation

(disorder or disease)

Environmental:
- familiar, relationship, residential- and work situation, transportation, ...
- Issues influencing function

Personal:
- Special background of life and life style, demography: Age, gender, psychosocial experiences, environment

Self-efficacy, -management
Independence
Meaning of life

Muscle, Skin, Gut, ...
CINeuroP, CRFatigue, ...
Metabolism, Immune, ..

walk, eat, think, do
Daily life, work, leisure
Sexuality, shower, ..

Contextual factors

Environmental Factors

Personal Factors
Rehabilitation-relevant Diagnose

Impaired physical function due to malnutrition because of secondary causes, cancer cachexia due to active tumor and emotional distress associated with existential threat and depressive reaction.

Mesothelioma epitheloid

Cisplatin/Pemetrexed --Pembrolizumab

Opioid-toxicity, neuropathic pain syndrome

Pain syndrome

Malnutrition, cachexia
Rehabilitation interventions to achieve goals

Cooperation («coordinated delivery»)

Individual planing of modules as individual therapy and/or Group therapies also presentations and **education** programs

Physio- and/or ergotherapy are **mandatory**, also included is nutrition, sporttherapy, psycho-oncology, social support, mind-bodytherapies (Yoga, MBSR), art-, musictherapy, often integrative medicine

Quelle: In Anlehnung an Zerriebel (2013)
Rehabilitation interventions

Herr X nahm an einer kontrollierten Bewegungstherapie teil. Er beteiligte sich:

- an der Gymnastik
- am muskulären Aufbautraining
- an physiotherapeutischen Einzelmassnahmen
- an psychologischen Gesprächen
- an der progressiven Muskelrelaxation
- an Atemübungen
- an Spaziergängen
- an der Klangmeditation
- an der Ernährungsberatung
- an der Wassergymnastik

Various rehabilitative interventions delivered by a team working
- Goal-steered
- Transprofessional
- Humanistic

So arbeiten wir: zielgesteuert, transprofessionell, menschennahe
The goal of **Rehabilitation** is the maintenance or the recovery of the best possible autonomy (societal participation)

1. **Reverse** impairments of body functions and structures as good as possible through **mechanism based** approaches
2. **Normalize** activity-disorders through **training** as good as possible or to develop and exploit **functional compensation opportunities** for relevant disorders
3. **Facilitate** best possible participation, also through **adaption of environmental factors** (Family, Living place, Work place, ..)
4. Inclusion of **personal factors** (Age, Experiences, …)
5. Conveyance of **preventive strategies** (Noxes, Habits, …)

**Rehabilitation is indicated also in chronic diseases and non-curative («palliative») situations**

Silver J et al. Support Care Cancer 2015;23:3633–43
DefReha 2.0
Rehabilitationsziele:

Dem Patienten ist es richtig wichtig ("what matters most") mit der Familie zu sein, der Natur nahe zu sein und sich bewegen zu können und kreative Arbeit.

Als spezifische Rehabilitationsziele beschreibt der Patient:

Ziel 1: Zu Kräften zu kommen, Zusammensitzen zum Essen, ohne Schmerzen in die Natur/in den Wald gehen, Tango tanzen und nicht mehr limitiert zu sein in der Kreativität durch Kraftprobleme und Schmerzen.

Ziel 2: Verbesserung der Ernährung, ein Zielgewicht ist 61 kg, ein Halbjahresziel 64 kg. Lernen den Einfluss von Gesellschaft und Stimmung auf die Ernährung besser zu verstehen, Schlucken zu regulieren, kein saures Aufstossen mehr zu haben.


Ziel 5: Vertrauen wieder bekommen in die Kreativität, Bilder machen für die Familie oder für sich selber oder andere Wege zu bekommen um die Kreativität wieder zu verbessern.


Rehabilitation goals

What matters most to you?
Family, nature, move, creativity

Goal 1: strength, sitting on the eating table, be in nature without pain, dance tango

Goal 2: improved nutrition, weight 64 kg, understand eating

Goal 3: improve self responsability and illness understanding, self efficacy through medication management

Goal 4: Deal with scoliosis

Goal 5: Confidence in own creativity, reblossom it

Goal 6: pain control, learn to do self

Goals are SMART

S  Specific
M  Measurable
A  Attainable
R  Realistic
T  Timed
Goals-setting is important in rehabilitation

Goal setting and strategies to enhance goal pursuit for adults with acquired disability participating in rehabilitation

Figure 2. Forest plot of comparison: 1 Goal setting (with or without strategies to enhance goal pursuit) versus no goal setting, outcome: 1.1 Health related quality of life or self-reported emotional status.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Std. Mean Difference IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blair 1991</td>
<td>-1.377</td>
<td>0.924</td>
<td>53</td>
<td>-1.855</td>
<td>0.766</td>
<td>26</td>
<td>14.7%</td>
<td>0.54 [0.06, 1.02]</td>
</tr>
<tr>
<td>Coole 2012</td>
<td>-26.2</td>
<td>13.3</td>
<td>26</td>
<td>-32.5</td>
<td>11.9</td>
<td>29</td>
<td>13.7%</td>
<td>0.49 [-0.04, 1.03]</td>
</tr>
<tr>
<td>Duncan 2003</td>
<td>-25.4</td>
<td>21.6</td>
<td>7</td>
<td>-33.5</td>
<td>22.6</td>
<td>7</td>
<td>7.2%</td>
<td>0.34 [-0.72, 1.40]</td>
</tr>
<tr>
<td>Evans 2002</td>
<td>14.46</td>
<td>2.73</td>
<td>13</td>
<td>11.7</td>
<td>2.29</td>
<td>26</td>
<td>11.0%</td>
<td>1.11 [0.39, 1.82]</td>
</tr>
<tr>
<td>Fredenburgh 1993</td>
<td>12.08</td>
<td>26.1</td>
<td>15</td>
<td>4.79</td>
<td>20.63</td>
<td>15</td>
<td>10.9%</td>
<td>0.30 [-0.42, 1.02]</td>
</tr>
<tr>
<td>Hanwood 2012</td>
<td>44.8</td>
<td>10.4</td>
<td>38</td>
<td>35.9</td>
<td>10.1</td>
<td>31</td>
<td>14.4%</td>
<td>0.86 [0.36, 1.35]</td>
</tr>
<tr>
<td>Scott 2004</td>
<td>25.02</td>
<td>3.63</td>
<td>15</td>
<td>20.79</td>
<td>4.78</td>
<td>24</td>
<td>11.5%</td>
<td>0.95 [0.26, 1.63]</td>
</tr>
<tr>
<td>Sewell 2005</td>
<td>0.62</td>
<td>1.41</td>
<td>63</td>
<td>0.89</td>
<td>1.29</td>
<td>58</td>
<td>16.6%</td>
<td>-0.20 [-0.56, 0.16]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>230</td>
<td>216</td>
<td>100.0%</td>
<td>216</td>
<td>0.53 [0.17, 0.88]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.16; Chi² = 20.74, df = 7 (P = 0.004); I² = 66%
Test for overall effect: Z = 2.91 (P = 0.004)

39 studies (27 RCTs, 6 cluster-RCTs, 6 quasi-RCTs), 2846 participants; Disorders: musculoskeletal, brain injury, chronic pain, mental health conditions, and cardiovascular disease; 2 Studies few cancer pts

Körperliche Funktion

6-Min-Gehtest bei Eintritt am 12.12.2018:
Start: Puls: 108/min  O2: 95%  Blutdruck: 97/67 mmHg
Ende: Puls: 117/min  O2: 93%  Blutdruck: 106/72 mmHg

6-Min-Gehtest bei Austritt am 09.01.2019:
Start: Puls: 104/min  O2: 95%  Blutdruck: 115/73 mmHg
Ende: Puls: 108/min  O2: 93%  Blutdruck: 131/70 mmHg

Gehstrecke: Eintritt: 420 m  Austritt: 518 m  Soll: 435 m
Prozentuale Veränderung: 23 %  Absolute Veränderung: 98 m

Five-times-sit-to-stand: Eintritt 13,7 sec; 17.12. 9 sec; 7.1. 8.4 sec; Austritt 9.1. 8.1 sec (41% besser)

Handkraft rechts / links kg: Eintritt 34/27; 7.1. 37/32; Austritt 43/40

Ernährungsstatus
Gewicht Eintritt 56kg, Austritt 63 kg (ohne Oedeme)
Mittelarm re Umfang Austritt 22 cm; Unterschenkel re Umfang Austritt 33.5 cm

Somatische und psychische Symptomerfassung:
Eintritt:
Schmerz 5/10  Fatigue 6/10 (kognitiv 4/10, körperlich 5/10, 4/10 emotional),
Angst 3/10  Depression 3/10
Nausea 0/10  Appetit 0/10  Dyspnoe 0/10

Austritt 09.01.2019
Schmerzen 1/10  Fatigue 2/10
Angst 0/10  Depression 0/10
Nausea 0/10  Anorexie 0/10  Atemnot 0/10

Quality of life 0/10 «perfekt»

Outcomes physical and symptomatic
Also HADS
Patient danced Tango!
Cancer Rehabilitation: evidence & referrals

- In many patients it seems to work: evidence?
  - The intervention is not well defined for components of rehab-interventions spectrum of cancer patients including curative and non-curative pts
  - For single interventions, mainly physical activity good data
  - For standardized Rehab Clinics some data

- In many patients it seems to work: why so poor referral?
  - Lack of knowledge of services, how to refer, who will profit
  - Lack of recognition / documentation functional deficits
  - Inadequate awareness to screen for rehabilitation needs

Callistus Nwosu A et al. Support Care Cancer 2012;20:3247–54
Cheville AL et al. Supp Care Cancer 2009;17:61-7
Cancer Rehabilitation: which patients do I see in my practice who I should refer?

- Prolonged bed rest
One Week of Bed Rest: Muscle Atrophy and Whole-Body Insulin Resistance

Figure 1—One week of bed rest leads to a substantial decline in muscle mass. A: Whole-body lean mass declined by \(1.4 \pm 0.2 \text{ kg}\) following bed rest. B: CSA of m. quadriceps femoris declined by \(3.2 \pm 0.9\%\). Data represent mean ± SEM. *Significantly different from pre-bed rest value \((P < 0.05)\).

\[29 \pm 5\% \text{ decrease in whole-body insulin sensitivity}\]

During hospitalization 4.2%

Kouwd et al. JAMDA
2018, in press

**Fractional Muscle Protein Synthesis Rate**
1-2% per day

Dirks ML et al. Diabetes 2016;65:2862-75
Cancer Rehabilitation: which patients do I see in my practice who I should refer?

- Prolonged bed rest
- Patients with declining function and weight during anticancer treatments
  patients have also poorer survival and more toxicity if sarcopenic
- Decreasing function \(\Rightarrow\) if you ask!
Muscle wasting associated with the long-term use of mTOR inhibitors

<table>
<thead>
<tr>
<th>Drug use</th>
<th>Disease</th>
<th>Gender</th>
<th>Parameter</th>
<th>Prior to the start of the treatment</th>
<th>Following at least 6 months of treatment</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everolimus alone</td>
<td>Renal cell carcinoma</td>
<td>Male</td>
<td>Body weight (kg)</td>
<td>55.5</td>
<td>54.4</td>
<td>-2.9 to 0.8</td>
<td>0.262</td>
</tr>
<tr>
<td>Temsirolimus alone</td>
<td>Pancreatic neuroendocrine tumor</td>
<td>Female</td>
<td>SAT index (cm²/m²)</td>
<td>35.1</td>
<td>36.4</td>
<td>-6.3 to 8.8</td>
<td>0.722</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>VAT index (cm²/m²)</td>
<td>31.5</td>
<td>43.8</td>
<td>-0.2 to 24.7</td>
<td>0.053</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TAT index (cm²/m²)</td>
<td>66.6</td>
<td>80.2</td>
<td>-6.0 to 33.1</td>
<td>0.163</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SMT area at (cm²)</td>
<td>137.3</td>
<td>124.6</td>
<td>-22.0 to -3.3</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SMI (cm²/m²)</td>
<td>50.2</td>
<td>43.8</td>
<td>-11.7 to -1.0</td>
<td>0.022</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lean body mass (kg)</td>
<td>47.2</td>
<td>43.1</td>
<td>-6.9 to -1.3</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Serum albumin (g/dl)</td>
<td>3.7</td>
<td>3.5</td>
<td>-0.6 to 0.0</td>
<td>0.091</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CRP (mg/dl)</td>
<td>2.8</td>
<td>5.3</td>
<td>-0.6 to 5.5</td>
<td>0.105</td>
</tr>
</tbody>
</table>

SMT: skeletal muscle tissue; SMI: SM index (corrected for height)

Also data for sorafenib: promote muscle wasting (8% in 12 mts) by proteolytic systems

Toledo M J Cach Sarcop Musc 2016;7:48-59

→ Indication for monitoring protein intake, physical activity

Gywali B Molec Clin Oncol 2016;5:641-6
Loss of Muscle Mass During Chemotherapy Is Predictive for Poor Survival of 67 Patients With Metastatic Colorectal Cancer

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight change in 6 months before baseline</td>
<td></td>
</tr>
<tr>
<td>Gain &gt; 5%</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Stable</td>
<td>39 (58)</td>
</tr>
<tr>
<td>Loss 5% to 10%</td>
<td>15 (22)</td>
</tr>
<tr>
<td>Loss &gt; 10%</td>
<td>7 (10)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td></td>
</tr>
<tr>
<td>&lt; 20</td>
<td>4 (6)</td>
</tr>
<tr>
<td>20-24.9</td>
<td>21 (31)</td>
</tr>
<tr>
<td>25-29.9</td>
<td>37 (55)</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>5 (8)</td>
</tr>
<tr>
<td>SMI &lt; reference value*</td>
<td>38 (57)</td>
</tr>
<tr>
<td>MD &lt; reference value* muscle density</td>
<td>43 (64)</td>
</tr>
<tr>
<td>Sarcopenic obesity†</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

* Sex (63% male), age (66y, SD 11y), LDH, Comorbidity (CCI 1-2 28%, ≥3 5%), metastases (liver 18%, multiorgan 82%), chemo-tx line (2nd 23%), tumor progression

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low SMI at baseline (N = 67)</td>
<td>1.65 (0.85 to 3.18)*</td>
<td>.138</td>
</tr>
<tr>
<td>Low MD at baseline (N = 67)</td>
<td>2.38 (1.16 to 4.87)*</td>
<td>.018</td>
</tr>
<tr>
<td>≥ 9% muscle loss (n = 63)</td>
<td>4.47 (2.21 to 9.05)†</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

* not adjusted for WHO PS [1 52%, ≥2 8%], chemo [66% Capox±B, 15% Iri], 1° dose reduction [22%]

Severe sarcopenia (SP) might be associated with a decline of physical independence in older patients undergoing chemotherapeutic treatment (ChTh)

131 pts (age med 72 y), pre-SP 48%, SP 19%, severe SP 8% (n=10)*

(SP definition: LMM and walking speed ≤ 0.80 m/s or low handgrip strength (<26 kg male, <16 kg female)


IADL decline after ChTh: only severe SP associated (OR 6, CI 1–47) [per definition*] (uni- & multivariate) refractory/progressive disease despite ChTh (OR 7.5, 2-29)

CT-scan based Muscle mass (continuous scale)

<table>
<thead>
<tr>
<th>Functional Test</th>
<th>Coefficient</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking speed</td>
<td>-0.001</td>
<td>-0.01–0.01</td>
<td>0.74</td>
</tr>
<tr>
<td>FTSTS</td>
<td>-0.31</td>
<td>-0.51–0.11</td>
<td>0.002</td>
</tr>
<tr>
<td>Hand grip strength</td>
<td>0.04</td>
<td>-0.10–0.19</td>
<td>0.56</td>
</tr>
<tr>
<td>Steep ramp test</td>
<td>0.02</td>
<td>0.002–0.04</td>
<td>0.03</td>
</tr>
<tr>
<td>Timed up and go</td>
<td>0.002</td>
<td>-0.17–0.18</td>
<td>0.98</td>
</tr>
</tbody>
</table>

And: Non-linear associations of LMM (pre-sarcopenia) and decreased physical reserve → different entities

Monitor both muscle function and mass

functional tests measuring muscle strength and physical function

Rier HN et al. Supp Care Cancer 2018;26:1781–9
Oncologists underestimate (also) patient functional problems

Expectations of patients (n=202)

![Graph showing expectations of patients for different functional problems.

Documentation of oncologists

![Graph showing documentation of oncologists for different functional problems.

Patient-reported symptoms: collected from 467 persons (breast, lung, GU, GYN) at 4034 clinic visits. Clinician-reported symptoms: standard recorded by physicians & nurses at same visits.

Clinicians underestimate severity of patient-perceived symptom experiences including toxicities.

Atkinson TM et al. Support Care Cancer 2016;24(8):3669-76

Relative Strengths of Concordance of PRO vs ClinRO with Overall Health Status.

Cancer Rehabilitation: which patients do I see in my practice who I should refer?

- Prolonged bed rest
- Patients with declining function and weight during anticancer treatments. Patients have also poorer survival and more toxicity if sarcopenic.
- Decreasing function → if you ask!
- Increasing Fatigue
- CINP (chemo induced neuropathy)
- Multiple other impairments and information needs - even in far advanced pts

Rule of thumb: if several dimensions impaired and poor support consider inpatient rehab
Rehabilitative Palliative Care

Enabling people to live fully until they die

A challenge for the 21st century

Rebecca Tiberini, Specialist Palliative Care Physiotherapist, Hospice UK in July 2015

- Aim to maximise quality of life for patients and families
- Multidisciplinary approach
- Involve patient and family in care planning
- Optimise physical function and emotional wellbeing to highest extent possible
- Consistent with patient goals, priorities, and limitations
- Holistic
Rehabilitation in Palliative Care

- Died on the ward
- Discharged to home
- Transferred to hospices or nursing homes

528 Pts, Germany, Pall Care Unit
9.9 day length of stay
41% deceased
Karnofsky med 40

Loft of «good» is possible even if life is short

Conclusion

Cancer rehabilitation does focus on functional impairments of patients, works steered by goals and what matters most by teams applying a transprofessional collaborative approach.

Many patients under active anticancer treatment may profit from cancer rehabilitation, typical patients are those with lots of muscle mass, specific toxicities such as CINP, CRF, lymphedema, dysphagia and also emotional burden.

Screening patients for rehabilitation needs may encompass symptoms, FTSTS, and patients perception of specific impairments.