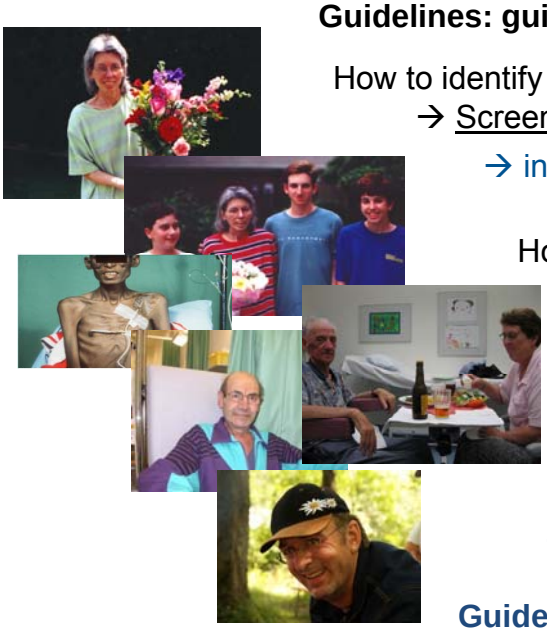
Pre-congress seminar PRC / EAPC-RN

Guidelines and treatment – the next steps

Cancer Cachexia

Florian Strasser

Guidelines: guide which questions?



How to identify patients having cachexia?
→ Screening or „name the *obvious*“

→ in routine HCP lines of care

How to assess patients with cachexia to treat *right*?

→ Who coordinates cachexia care?

How to *design* clinical cachexia trials?

→ will change practice (?)

Guidelines for routine care?

Chronos and Chairos

Where are we with cancer cachexia to produce „meaningful“ guidelines?

Is it the „*right*“ time?

The Cancer Cachexia Framework is „out“ for 16 months:

- Experiences from data collections, education, clinical trials
- Common Assessments for *updated* Framework are needed
- Agreed-on standard management requires validation

Fearon K & Strasser F, et al. Lancet Oncology 2011; 5th february

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Cancer Cachexia Framework: key features

From „anorexia/cachexia syndrome“ to cancer cachexia

„Muscle loss relevant for physical function, not reversible by nutrition, caused by decreased intake and alt. metabolism“

Diagnostic criteria: based on weight loss and BMI

Domains: Muscle/(Fat)
Nutritional Intake & „Appetite“-Symptoms
Catabolic tumor, inflammation, and hormones
Neuro-muscular and emotional function

Phases: from early to cachexia to refractory cachexia

Severity described by weight loss and BMI

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Cancer Cachexia Framework: 16 Months later
Experiences from **clinical patient data collections**

. Few longitudinal, full domains, standard clinical mgmt[1]
. Few cachexia clinics, full domains, standard clinical mgmt[2]
. Specialized clinical labs[3]
. Longitudinal, full domains, mgmt usual care[4]
. Longitudinal, some domains, mgmt usual care[5]
. Cross-sectional, some domains, mgmt usual care[6]

Support from experiences
→ Muscle loss matters: it correlates with survival[4]
→ Cachexia ≠ starvation / malnutrition, age-sarcopenia
→ Phases make sense

1: Edinburgh-group , Montreal-group, (both completed, not fully analysed)
2: MDACC (Del Fabbro E et al. J Palliat Med 2011 Jul 27); St.Gallen (not fully analysed)
3: Toronto-group (various publications)
4: Alberta-group (many publications)
5: Barbera, OLH
6: EPCRC-CSA-Data; other by several groups (Oslo, Rotterdam, ...)

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Cancer Cachexia Framework: 16 Months later
Experiences from **clinical patient data collections, education** and **clinial trials**

Unclear issues
→ Diagnostic criteria: sufficient WL & BMI, or Nintake too?
→ Appetite may re-considered in domains ≠ Nintake[1]
→ Tumorbiology (dynamics, responsiveness) is important, but how measure?
→ Physical and psychological function: are they domains of cancer cachexia or conceptualized as impact ?
→ Can severity (WL, BMI) interpreted without standard managment information (e.g., upper GI-tumor, H&N)

1: EPCRC-CSA-Data (Solheim T et al, manuscript in preparation)

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Challenge #1 to move towards consensual assessment
Phases: Biology of cachexia versus Severity

Biological driven Tumor not responsive and/or catabolic active	„late“ cachexia Prognosis < 3 mts „severe“ cachexia

Pat. 43j, Pancreas-ca, Adeno, liver mets,
Bili 36; 4 mts 8% WL, BMI 22; CRP 82

Pat. 53, SCC-HN, refuses chemoth, last tx >2j, WL 18%, 6 mts,
BMI 19, incident pain, PS 3, CRP 2, god waits, family ready

→ Which variables drive clinical judgment?

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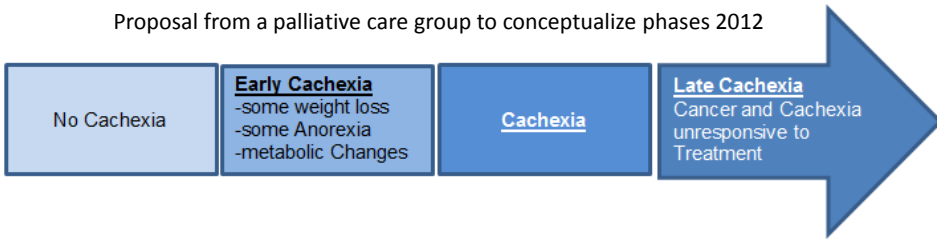
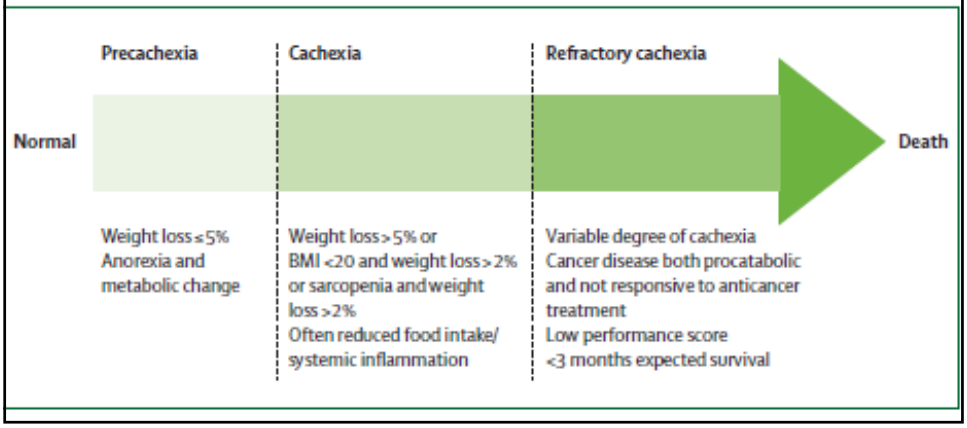
Proposal from a palliative care group to conceptualize phases 2012



The original publication



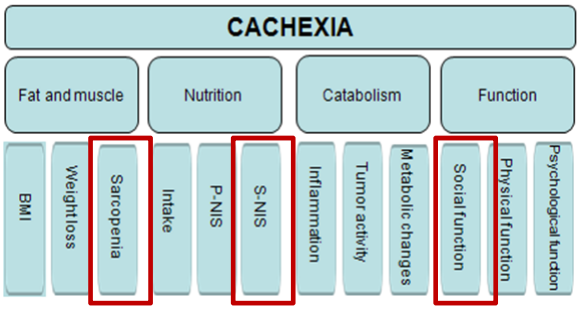
Challenge #2 to move towards consensual assessment
Domains: Clinical Mgmt Standards vs Domains

Clinical Mgmt standards Settings of care S-NIS / Co-morbidities	Various domains „found“ in same patient, incuding different biologies

Pat. 53, SCC-HN, refuses chemoth, last tx >2j, WL 18%, 6 mts, BMI 19, incident pain, PS 3, CRP 2, god waits, family ready

→ Is a domain – description approach helpful to guide mgmt?
→ Can symptom clusters and collections of variables guide?

Vrgl. Pat. bone met lumbal, plexus infiltration left leg, drug addict, existential suffering, anxiety, infection-delir, venous puncture hurts



Cachexia

Storage	**Weight loss (%, vs usual), BMI** **fluid retention/obesity**
Intake	**Intake kcal/Protein** **Anorexia, satiety,** chemosensory
Potential	**Tumor [catabolic] activity** **C-reactive protein**
Performance	**Physical functioning** **Psychological motivation**

Age-related **Sarcopenia:** Co-“morbidity“

S-NIS: **SECONDARY** nutrition impact symptoms: Complications of cancer / treatment ≠ cachexia

Function: Phenomenology of the biology **NOT impact**

Challenge #3 to move towards consensual assessment
Domains: Riskfactors for difficult mgmt versus impact

Physical and/or emotional function decreased Co-morbidities (wheelchair)	Impact of cachexia on physical functioning, on emotions, social role

Pat. 72, RCC, mediastinal, kidney, CRP 210, WL 14.5% / 4 mts, refractory to chemo (3 lines), PS 2, active physical, motivated

→ Is the domain „Potential“ an indicator of (un-) responsiveness of cachexia to multimodal treatment?
→ Impact of the syndrome on role function etc. ≠ same!

How to deal with co-morbidities in daily practice?
Adapt a Risk-Factor Concept like the ECS-CP?

Muscle & Fat	Nutritional intake	Catabolic drive	Muscle Fct & Psycholog.
. Weight loss . BMI	. >20kcal BW . >0.6 g Prot/BW	. Tumor responsive . CRP	. 15 min resist. Training/d . Willing to move
(edema)	(catabolism)	(Co-morbid.)	(Co-morbidities)

Framework is taken up well, some issues to clarify, now time to move for consensus on assessment, and then guidelines

→How good are current guidelines?
→ Do they cover the main aspects required?

Dieticians Association of Australia:
Evidence based practice guidelines for the nutritional management of cancer cachexia
Nutrition & Dietetics 63 (2006) S3-32

European Society of Clinical Nutrition and Metabolism:
ESPEN guidelines on enteral nutrition: non-surgical oncology
Clinical Nutrition 25 (2006) 245-59

Australia & New Zealand Society of Palliative Medicine
Guide to Ethical Principles of Hydration and Nutrition
http://www.anzspm.org.au/guidelines/hydration.html (1999)

European Association for Palliative Care
Guidelines on artificial nutrition versus hydration in terminal cancer patients
Nutrition 12 (1996) 163-7

Clinical practice guidelines on cancer cachexia in advanced cancer patients
with a focus on refractory cachexia

Current status of cancer cachexia guidelines

Assessment:
. Not sufficiently defined step-wise approach from
Screening → Clinical Assessment → Phase definition → ...

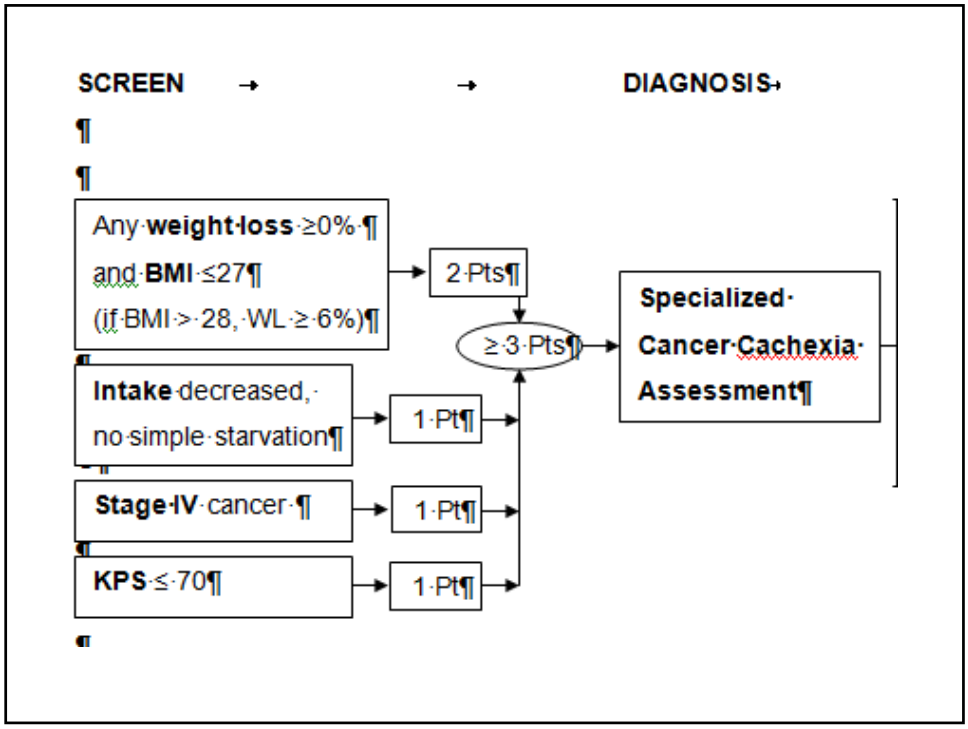
Subjective symptoms: Appetite, early satiety, nausea, vomiting, disturbances of taste or smelling, other gastrointestinal symptoms, weakness, disease-related burden, well-being
History Weight change, speed of weight loss, percentage of normal intake
Clinical examination Inspection of mouth, abdomen, hydration status, oedema, body weight, perceived physical strength
Laboratory examination CRP, blood sugar profile, testosterone
Activity monitoring Performance status (ECOG or Karnofsky), upper limb hand-grip dynamometry, body-worn activity meters
Body Composition Cross-sectional imaging (CT or MRI), dual energy x-ray imaging (DEXA), anthropometry (mid-arm muscle area), bioelectrical impedance analysis (BIA)

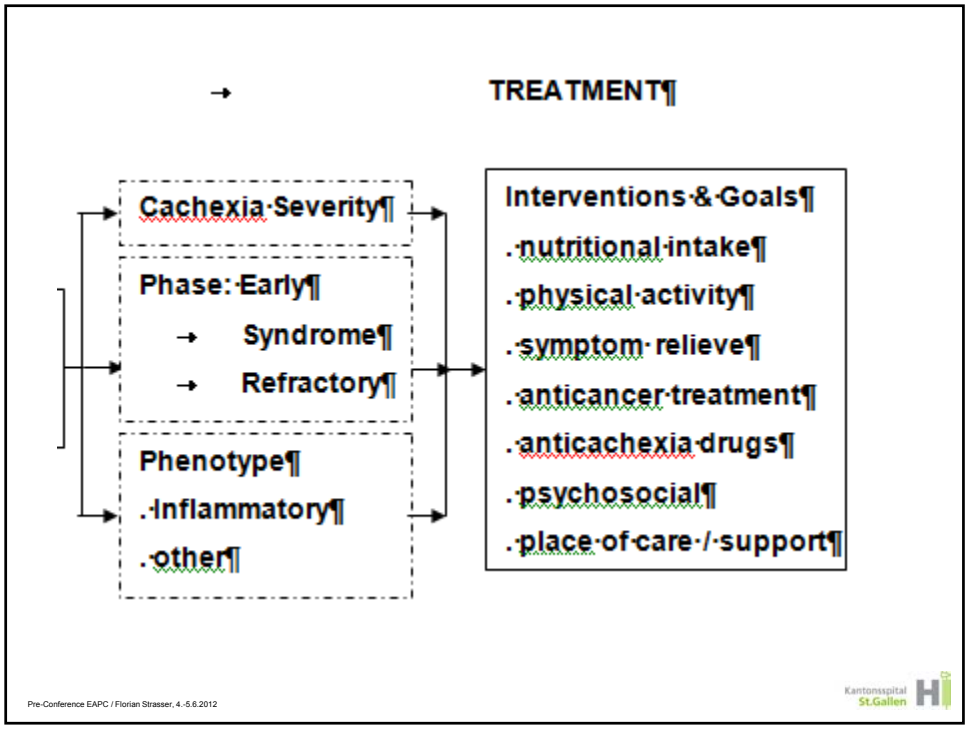
EPCRC-GL: do not guide
- Levels of assessment
- Phase definition

Treatment
. Nutrition –focused (ESPEN, Australia)
. EPCRC: developped mainly for patients close to end-of-life

Cancer Cachexia: Guidelines next steps
Content

Assessment:
- Build into routine care lines
- Tackles coordinators of cachexia care
- Content based on Framework:
  "Diagnosis – Domains – Phases – Severity"
- Screen → Assess → Priorize → Phase → tx


SCREEN → → DIAGNOSIS
Any weight loss ≥0%
and BMI ≤27
(if BMI > 28, WL ≥ 6%)
2 Pts
≥ 3 Pts
Specialized Cancer Cachexia Assessment
Intake decreased, no simple starvation
1 Pt
Stage IV cancer
1 Pt
KPS ≤ 70
1 Pt


→ TREATMENT
Cachexia Severity
Phase: Early
→ Syndrome
→ Refractory
Phenotype
. Inflammatory
. other
Interventions & Goals
. nutritional intake
. physical activity
. symptom relieve
. anticancer treatment
. anticachexia drugs
. psychosocial
. place of care / support
Pre-Conference EAPC / Florian Strasser, 4.-5.6.2012
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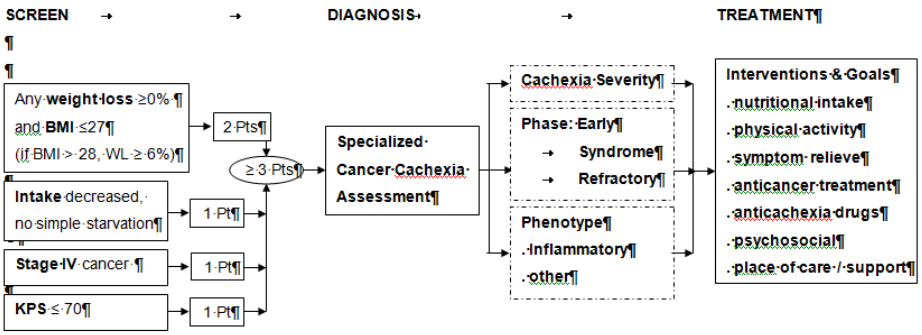
How could an Assessment – Approach look like



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Assessment: next steps

Consensus of clinical & academic experts needed

- Agreements — Principles of framework (Performance?)
  Basic/Screening – Clinical Priority - Research
  Secondary-NIS: are NOT cachexia
- Domains — are from the framework (no new domains)
- Assessments — those used in data collections / trials
  no new SLR‘s of all possible domains
- Consensus — formal Delphi, Levels A/B/C
  Experts: defined (clinical >30%, published)
  . as 2009-2011; new persons
- Results — Clinical flow recommendation
  Management of S-NIS, before diagnosis
  Tool: setting, limits, time frames; validate

7.2012 – 12.2012

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Cancer Cachexia: Guidelines next steps
Content

Assessment:
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Treatment:
- rule out Secondary- Nutrition Impact Symptoms
- basic multidimensional approach on all domains
- re-define interventions based on framework:
  . Phases: pre-cachexia – cachexia – refractory
  . Domains: phenotypes?
  . Riskfactors of patients' co-morbidities

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Cancer Cachexia: Guidelines next steps
Process

. Based on best available evidence (Lit), but still recommendation based on formal consensus when not (yet) evidence

. Modular: conceptualize „easy bits"
more comprehensive for specialized care
HCP-comptencies based: structure „independent"
Phase-specfic (new stage IV versus EOL)

. Endorsement by „all" societies in Europe (and beyond)
- Palliative: EAPC (AAHPM, JSPC,..)
- Nutrition: ESPEN (ASPEN, ...)
- Oncology: MASCC, ESMO (ASCO, JSCO, ...)

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The ESPEN –EPAAC – EAPC Guidelines

Representation of EAPC and „cachexia community“

Methodology high standard (content questions, AGREE, GRADE)

Endorsement seeked by many societies

Harmonized with Framework of Cancer Cachexia

- Domains
- Phases
- Multidimensional Interventions

Process started 4.12
Finish 2.13

Cancer Cachexia Guidelines for Clinical Trials

Working Group SCWD Society Sarcopenia, Cachexia ,Wasting Dieseases
. Patient Population
. Basic Management
. Outcomes

The evolution of clinical trial design in cancer cachexia: a systematic review based on the novel classification and definition criteria

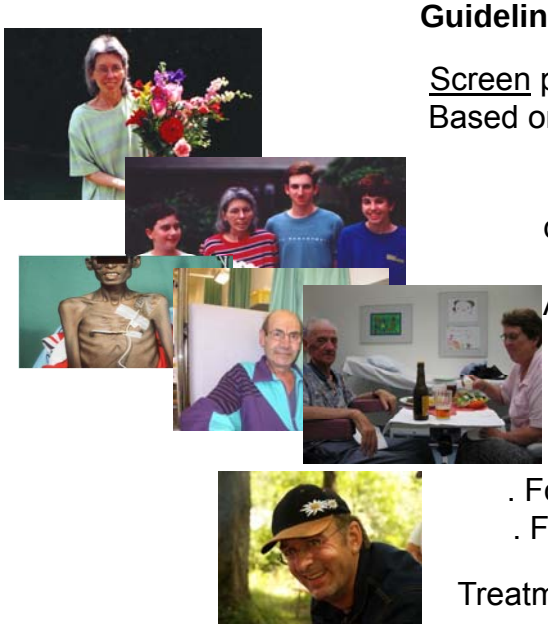
Lisa Martin [1,2], Aurelius Omlin[1], Vickie Baracos[2], Kenneth C. H. Fearon[3], Florian Strasser[1]

SLR: 64 articles, 38 ongoing trials

Heterogenity of patient population definitions

Many different outcome, if measured

Guidelines Conclusion



Screen patients in routine settings:
Based on the four domains, simple

Assess patients with four domains: phases, severity
Make care priority
Assess to guide treatment
by coordinantors of cachexia care

Guideline process:
. For assessment: EAPC-RN
. For treatment: with ESPEN

Treatment: let‘s do MENAC trial