5th EAPC Research Forum

A novel Cachexia Classification for Palliative Cancer Care: Synthesis of systematic literature review and nominal experts' focus group

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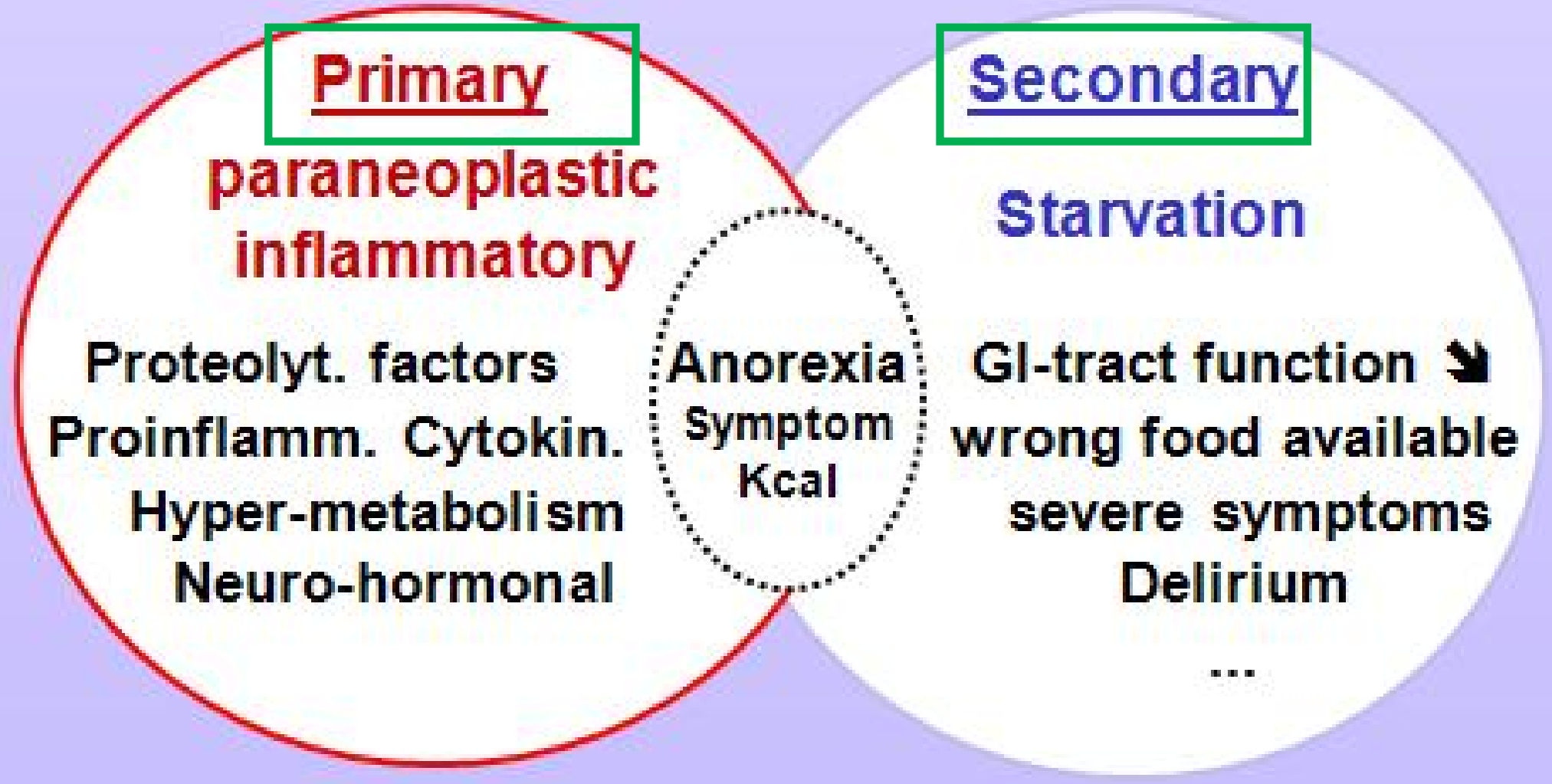
Background

The current definition of cancer cachexia (2 criteria: weight loss, anorexia) does poorly guide practice.

To monitor clinical decisions, alleviate suffering and develop tailored anti-cachexia interventions, a novel cachexia classification system, adjusted for palliative care, is required

Anorexia / cachexia syndromes



Impact: psychosocial and physical function

Systematic literature reviews

a) Factors to classify cachexia — EAPC-08 Abstract #35

b) Secondary causes for impaired oral intake — EAPC-08 Abstract #170

c) Psycho-social consequences of cachexia — MASCC-07 #107

Consensus process

- Clinical cancer cachexia academic experts
- Focus group round 1
- Focus group round 2
- Core experts → send out for Delphi

Factors to classify cachexia

Objectives

- To **identify any system** developed with the purpose to classify cancer cachexia or cancer patients with cachexia
- To **identify any factor/indicator/descriptor** (cachexia, patient-related, disease-related) that can be used to classify, categorize, or group cancer cachexia or cancer patients with cachexia, or to predict its clinical course (cachexia process);

Factors to classify cachexia

Search strings & databases

2 search strings:

A) cachexia OR anorexia OR weight loss OR loss of appetite OR loss of weight OR wasting syndrome OR eating problem OR protein malnutrition OR energy malnutrition

B) Neoplasm* OR cancer*

Databases:

MedLine, Cochrance, Embase, PsycINFO, CinAhl

Factors to classify cachexia

Inclusion criteria

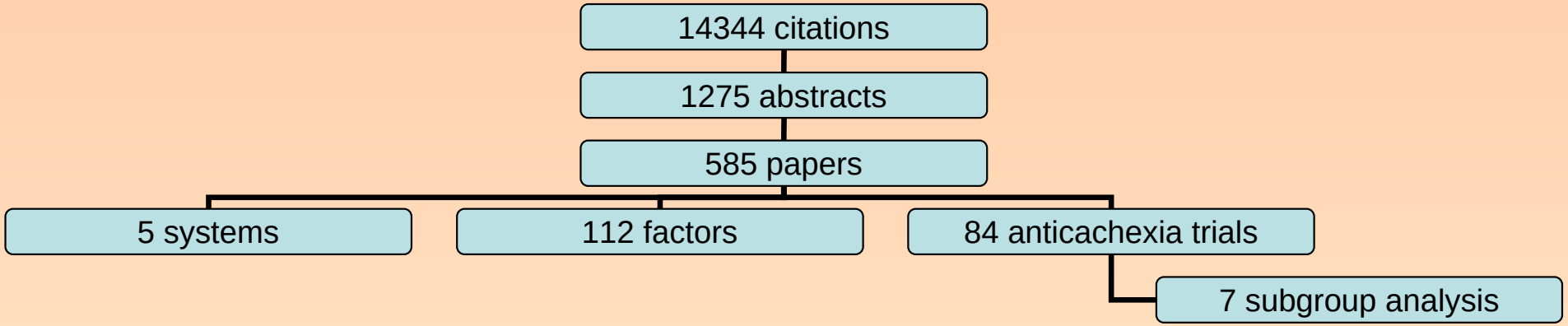
The paper addresses anything like cachexia, anorexia, loss of appetite, malnutrition in the widest range including clinical features of tumor.

It is about cancer. (Exclusion of Survivors, AIDS, COPD etc)

A classification-(system) or an undefined factor/indicator/descriptor to classify, categorize or group cachexia, patients with cachexia or clinical progress of cachexia or to predict response to an type of anticachectic treatment.

Factors to classify cachexia

Retrieved papers



Interrater-reliability

Citation level: random selection of 10% screened blinded, Agreement >95% required on exclusion.

Abstract level: random selection of 10% screened blinded, Agreement >95% required on inclusion.

Factors to classify cachexia

Outcomes

- Studies had to use weight loss as outcome. Various definitions of WL were applied. Some studies distinguished just weight losing and weight stable Subjects. Most of the studies used 5% or 10% of preillness weight as cut-off. A part from them requiered WL of 5% or 10 % over 6 Months for the definition of cachexia.

Challenge: another systematic review on weight loss thresholds?

Factors to classify cachexia

Single Factors

1) Body composition
2) Nutritional intake
3) Symptoms
4) Inflammation
5) Metabolism
6) Eating regulating hormones
7) Resting energy expenditure
8) Catabolic/anabolic factors
9) Muscle strenght

Challenge: how do value these factors, how define a classification system?

Challenge:

Symptoms in cachexia assessment: „A family of distinct characters“

A Symptoms mirroring the pathogenesis of cachexia

Early satiety, appetite loss, no desire to eat, weakness

B Symptoms and syndromes causing starvation

Pain, vomiting, dyspnea,

C Symptoms reflecting the impact of cachexia

Fatigue, eating-related distress

Cachexia definition and characteristics:
Consensus processes

Is a systematic literature review the sufficient base for a (novel) classification?

→ **Consensus process of academic clinical cancer cachexia experts needed**

Can a systematic literature review be made before a consensus process is underway?

→ **Experts‘ brainstorming and narrowing down supported the design of the SLR**

Cachexia definition and characteristics: Consensus processes

Three phases of a consensual Delphi-type process: brainstorming, narrowing down, and quantification.

The application of the Delphi-technique in palliative cancer care for the development of assessment instruments and decisions on drugs was reported.

Biondo PD, Nekolaichuk CL, Stiles C, Fainsinger R, Hagen NA. Applying the Delphi process to palliative care tool development: lessons learned. Support Care Cancer. 2007 Oct 30

De Lima L, Krakauer EL, Lorenz K, Praill D, Macdonald N, Doyle D. Ensuring palliative medicine availability: the development of the IAHPC list of essential medicines for palliative care. JPSM 2007;33(5):521-6

Cachexia definition and characteristics: Consensus processes – Brainstorming

First round of focus groups: decision-guiding factors for cancer cachexia

“What are the key factors which guide your clinical decision making as clinical cachexia experts to manage cachexia in your daily practice?"

Detailed protocol based on the verbal statements of the experts and a summary of key findings

Cachexia Expert Focus Groups (n=11)

"What are the key factors which guide your clinical decision making as clinical cachexia experts to manage cachexia in your daily practice?"

- **Absolute degree of weight loss reflecting body storage *(past)***
- **Weight loss dynamics or speed of weight loss *(past or present)***
- **Inflammation, a key factor of hypermetabolism *(present)***
- **Hypermetabolism *(present)***
- **Upper GI tract: early satiety, chronic nausea, gut works *(present)***
- **Central drive to eat (motivation), hunger, central food reward *(present)***
- **Secondary impairment of ability for oral nutritional intake *(future)***
- **Loss of muscle mass and muscle strength *(present)***
- **Body composition patterns: loss of fat, presence of edema *(present)***
- **Likelihood of improvement of muscle function *(future)***
- **Likelihood to influence cancer disease *(future)***
- **Co-morbidities (ability to eat, catabolic, physical function) *(future)***

Cachexia definition and characteristics: Consensus processes – Narrowing down [1]

<u>Second round of focus groups: factors to classify cancer cachexia, considering literature</u>

Copy of the amalgamated key findings from the first rounds

"What are the key factors which guide your clinical decision making as clinical cachexia experts to manage cachexia in your daily practice?"

Preliminary evidence from systematic reviews of literature was provided

Detailed protocol based on the verbal statements of the experts and a summary of key findings

Systematic literature reviews

a) Factors to classify cachexia EAPC-08 Abstract #35

14’344 citations → **127 papers**

Nine groups of factors: Body compartments (fat mass, muscle mass), decreased nutritional intake, decreased muscle strength, eating-related hormones, metabolism (fat, protein, carbohydrates), symptoms, energy expenditure, inflammation, anabolic/catabolic fct.

5 papers used >2 factors, 1 multivariate analysis: **NO systems**

Variety of definitions of weight loss

b) Secondary causes for impaired oral intake EAPC-08 Abstract #170

14’344 citations → 43 papers (18 original)

c) Psycho-social consequences of cachexia MASCC-07 #107

5000 citations → 12 papers: no consensus

Factors to classify cachexia
Papers using >1 factor

Autors	Title	Factors used in multivariate analysis
Fearon	**Definition of cancer cachexia**	CRP>10, Kcal <1500/d WL 10%
Fouladiun	Body composition incancer patients on palliative care	Caloric Intake Whole Body fat in DEXA Serumaalbumin
Ravasco	Nutritional deterioration in cancer: the role of disease and diet	Cancer stage and location Duration of disease Energy and Protein intake Surgery and chemotherapy
Scott	The systemic inflfammatory response	Age, Tumor type weight loss CRP KPS fatigue
Bosaeus	Dietary intake and resting energy expenditure in relation to weight loss	Food record+interwiev+1/3 U-nitro(for validation) REE, Basal metabolic rate(BMR)

BUT: only 1 multivariate analyis (for Survival)

Cachexia definition and characteristics: Consensus processes – Narrowing down[2]

Experts core group (VB, KF, FS): definition, diagnosis, key characteristics, considering literature

Based on amalgamated key findings from the first two rounds, results of the systematic literature reviews, and own expert opinions:

Preparation of a Delphi document to quantify experts opinion on definition, diagnosis, and key characteristics.

Cancer Cachexia definition

Statement 1a: Cancer cachexia associated with a negative energy and protein balance. Over its course it is associated with functional impairment. A key definition feature is ongoing loss of skeletal muscle mass.

Statement 1b: A fundamental characteristic of cachexia is muscle wasting which is not fully reversed or responsive to conventional nutritional support.

Statement 1c: Cachexia in cancer is different from transient starvation

EPCRC Consensus reached after SLRs, focus groups, narrowing down, core experts, Lofoten May 2008

Cancer Cachexia diagnosis

Key components (domains) of cancer cachexia

- **Loss of weight loss >5% last 6 months, ongoing last 1-2 months**
  - **In most patients loss of BMI reflects loss of muscle mass**
  - **In patients with fluid retention, large tumor mass, or obesity (>30kg/m2), muscularity needs to be measured directly or weight loss is >15%/6**

Three main domains:

- **Anorexia** (central, taste, satiety, bowel) **/ reduced food intake**
- **Catabolic drive** (inflammation and/or tumor)
- **Decreased muscle mass, strenght, and physical function**

Impact:
Psychosocial consequences
Physical function

EPCRC Consensus reached after SLRs, focus groups, narrowing down, core experts, Lofoten May 2008

Conclusion:

A long journey towards a new Cancer Cachexia Assessment & Classification Tool

→ Combination of experts consensus und systematic literature review is (was for us) interactive NOT sequential

Tool to manage patients with cancer cachexia

- **Key components simple: screen**
- **Advanced instrument**

→ Use for management in clinical practice

→ Define distinct cachexia phenotypes

THANK YOU!

David Blum
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Julie Hess
Kim Baumann
Tora Skeidsvoll
Ben Tan
Vickie Baracos
Ken Fearon
Jochen Walker
Daniel Kaufmann
EPCRC!