

**PSYCHO-EDUCATIONAL AND REHABILITATIVE INTERVENTION FOR THE
ONCOLOGICAL PATIENT WITH CACHEXIA AND HIS CAREGIVER: A FEASIBILITY
STUDY**

Number of the study: 73/2019/SPER/IRCCSRE

Official date: 18th March 2019

Background

Today, cachexia still remains a largely underestimated and undertreated condition. Approximately half of all patients with advanced cancer experience cachexia, with the prevalence rising above 80% in the last weeks of life¹⁻³. According to the recent definition of the European Society for Clinical Nutrition and Metabolism, cachexia also known as ‘Cancer-related malnutrition’⁴, is a syndrome which includes an ‘objective’ component (e.g. inadequate food intake, weight loss, inadequate physical activity, muscle mass loss, metabolic derangements and catabolism) and a ‘subjective’ component (e.g. anorexia, fatigue, early satiety, taste alterations, distress, loss of concentration and interest in daily activities) that due to their complex interdependence, require a multi-professional approach²⁻⁵.

Cancer cachexia is a continuum with three stages of clinical relevance: pre cachexia, cachexia, and refractory cachexia³⁻⁵. Given the multifaceted pathophysiology and heterogeneous presentation of cancer cachexia, a personalized approach to the patient is necessary to ensure the best possible adherence to the therapeutic proposal⁶, with particular attention to patients in palliative care, where a 20% dropout index is detected⁷. According to recent literature, a multimodal approach should ensure sufficient energy and protein intake, maintaining physical activity and muscle mass, and reducing systemic inflammation where present^{3,4}. Core component interventions would therefore include nutritional support, physical activity, and exercise. The physical activity seems to be a very important anabolic stimulus especially for patients on chemotherapy. Little is known about its efficacy in the advanced stages of disease³⁻⁵.

The evidence based practice show the difficulty of compliance to the all components, in a study it is reported that the intake of supplements and NSAIDs are the most abandoned components^{8,9}. Exercise can attenuate the effects of cancer cachexia by modulating muscle metabolism, reducing insulin resistance and decreasing the inflammatory cascade^{10,11}. The most recent review in collaboration with Cochrane on this subject examined the safety, acceptability and efficacy of exercise in adult patients with cachexia, but no RCTs studied physical activity programs in the advanced disease¹². Despite this, the review highlighted two studies^{13,14} that could have enrolled cachectic patients, but did not clearly report them in the inclusion criteria. Both studies reported no adverse effects.

Cheville¹³ in an RCT investigated the feasibility and the impact on physical well-being of a program of physical activity in oncological patients, with a life expectancy of greater than six months undergoing radiotherapy. He found subjective improvement in physical performance in the group of intervention that participated in a program of physical exercise, in the absence of improvements measured with objective scales.

Oldervoll conducted a RCT¹⁴ to investigate the improvement of fatigue and physical performance after eight weeks of physical exercise in cancer patients with prognosis less than two years. He did not report any differences with respect to the main outcome, but he recorded an statistically significant improvement in the intervention group in muscle strength measured with Grip strength test and in resistance to walking, measured with the Shuttle Walk Test.

Considering the characteristics of the patient with cachexia-anorexia, it is important that the exercise program is tailored, feasible even at home, and it has ‘key-component’ resistance exercises, which stimulate the building of muscle mass, increase of strength, and reduce the inflammatory response⁶⁻¹⁰. The authors who have studied this topic propose an intervention variable between 5 and 8 weeks^{13,14} and a moderate exercise intensity. Other important components of the physical activity program aimed at motivating the patient and supporting compliance are goal-setting^{13,14} and stretching and relaxation exercises¹⁵.

Many qualitative studies have shown that the cancer cachexia is associated with psychosocial distress both for patients and their families, with severe consequences on the quality of life and also on the bereavement depression¹⁶⁻²¹. The psychosocial effects of cancer cachexia are

defined as negative emotions associated with a reduced dietary intake, an involuntary weight loss and the social consequences of these symptoms^{16,17}.

The weight loss generates a visible physical changes, creating emotional distress^{16,17}. The self image is an important dimension of the personal identity and the negative changes, like protruding bones or the impossibility of wearing clothes, may lead to an altered self-perception. The patients often don't feel comfortable meeting people because their body image is unfamiliar to them, resulting an alienation from one's self^{16,17}.

The involuntary and rapidity loss of weight is the cause of concern because it is associated with the fear of the imminent death^{20,21}. Consequently, some patients strive to eat more, despite the sense of satiety, expressing unrealistic demands of meals to families. More often, the patients have insight into their clinical condition and they are more aware of short-term prognosis than their families^{20,21}. The family caregivers undertake a series of practices dedicated to satisfy the nutritional needs of patients, such as cooking different foods and spending a lot of time to buy new foods that can stimulate the appetite of their loved ones¹⁹. The food represent in all cultures a symbolic meaning of care and love because it has value of nourishment of life. Therefore, the families increase the activities on behalf of food with the aim to offer a good care to the patients^{16,17}. Many patients have difficulties to refuse food prepared with great care by family members, consequently they eat more and more and lastly they choose to close themselves in a social retreat in order to not create further discussion²⁰.

Changes in eating habits disrupt the relational balances, also associated with previous roles¹⁹. Wives of men having cancer reported suffering for the lack of appreciation in their cooking, while female patients can feel a sense to burden to husbands for shopping and cooking. The patients who live with their partners report more eating related distress than the patients who live alone²².

All this data confirms that the cancer cachexia is a complex relational experience which involves the patient-family diad. The health care professionals should therefore move beyond the simple physical assessment and explore the illness experience from a socio-psychologic perspective, thus responding also to emotional needs of the patients and their families.

Studies on psycho-educational approaches to support patients and their families are increasing²³⁻²⁵.

Currently, there are three known studies that provide evidence about the important role of psychosocial interventions in the management of cancer cachexia²³⁻²⁵.

A phase II cluster-randomized exploratory trial²³, carried out in 50 advanced cancer patients, explored the deliverability, acceptability and patient-perceived effects of a psychosocial intervention on weight-related distress (WRD) and eating related distress (ERD). The trial found that patients supported by the intervention reported lower levels of WRD and ERD, compared with the group that received usual supportive care. The validity of these findings were limited by a flaw of the study design in which the experimental group received the intervention prior to baseline data collection, in addition to fewer recruited patients than estimated.

A nested study of this explanatory trial²⁴ investigated the WRD and the ERD in 26 carers of advanced cancer patients, by adopting a controlled before-and-after design. Data was gathered from 12 non-randomised carers before and after the intervention and 14 control group carers. The median of ERD decreased only in the exposed carers, while the median of WRD decreased in both group but to a greater and more significant extent in the exposed group ($p=0.02$). Qualitative analysis suggested psychosocial intervention to be helpful for carers of advanced cancer patients by providing information, reassurance, and support for self-management. However, these findings should be considered with caution for the weak quasi-experimental design, the small sample size, and the baseline difference between the groups.

A mixed-methods qualitative research study²⁵ developed a complex family-centered psychosocial intervention to help patients with incurable cancer and their family caregivers cope with involuntary weight loss and worsening appetite. This intervention was delivered during face-to-face consultation between 16 patient-family caregiver dyads and a trained clinician. Although 15

dyads reported benefits, the finding should be read considering a number of shortcomings such as the small sample, the intervention development at a single center and its delivery by a single nurse researcher.

It is therefore useful to contribute to the debate on the cachexia, so that we can develop reproducible and effective psycho-educational interventions.

Objectives of the Study

Primary objective: to evaluate the feasibility of a psycho-educational intervention on cachexia combined with a physiotherapy intervention on the cancer patient and his caregiver.

Secondary objective: improve the quality of life of patient and caregiver, acceptability of the intervention, adherence to each of the two psycho-educational and rehabilitative components.

What does this study contribute?

There are no studies on psycho-social interventions on dyads associated with rehabilitative interventions to support more functional relationships to the management of cachexia. The two psycho-educational and rehabilitative components have a strong rationale, common objectives and modalities with respect to the care of the patient and the family, compared with the multimodal approaches explored in the literature. We will evaluate the feasibility of the intervention in the population and context studied, estimating the effect of the intervention for a future multicenter efficacy study.

Methodology

Study design

Mixed methods study, non-pharmacological interventional perspective.

Sample and setting

Population of cancer patients with irreversible cachexia and their caregivers assisted by Palliative Care Unit, Azienda Usl - IRCSS of Reggio Emilia. The number of consecutive patients identified is 30.

Inclusion criteria

- Age of 18 years or older
- Good command of the Italian language
- Written informed consent
- Histologically confirmed tumor diagnosis
- Presence of irreversible cachexia and cachexia (ESPEN3-5 guidelines, MUST calculation)
- Patients who have identified a caregiver
- Patients and family members are informed of the diagnosis and the objectives of the therapies and who have reported awareness of the disease phase (evaluated by the palliative doctor).

Exclusion criteria

- Patients with prognosis less than three months to enable the rehabilitative intervention
- Presence of important mental disorder or dementia
- Severe sensory deficit
- Presence of diffuse bone metastases that put the patient at risk of fracture during rehabilitation exercise.

Intervention

The intervention involves two activities, psycho-educational and rehabilitation. The operators involved in the intervention will receive pre-intervention training and supervision.

Training for operators

The training includes two afternoons of 4 hours each, over a three-week period, during which the main theories on family types will be traced with particular focus on the context of palliative care and the management of the patient / caregiver dyad. The contents will focus on the characteristics and methods of conducting a psycho-educational intervention, specifically related to the cancer cachexia. The theoretical part will be integrated into the practical part through the analysis of clinical cases proposed by nurses and physiotherapists, in particular, with the request to analyze the functioning of the dyads related to food management. This part will be conducted by the PI of the study, Unit of Psycho-Oncology, Scientific Direction, Ausl - IRCSS of Reggio Emilia.

Psycho-educational intervention

The intervention is structured during a face-to-face consultation between a patient–family caregiver dyad and a trained nurses. It is designed to help patient and family caregivers cope with involuntary weight loss and declining appetite by seeking to strengthen individual and dyadic coping resources. The intervention includes 3 weekly meetings for outpatients (Palliative Care Unit, Azienda Usl - IRCSS of Reggio Emilia) which address the following topics consecutively to help patients and their family members talk about weight and eating-related problems and solutions:

- ‘Mapping to change eating habits tool’ to aid the patient and the family caregiver in talking about their own experience of the patient’s change in weight and eating habits (for example, role of the family caregiver during the preparation of meals, modalities, meanings associated with food, reactions of the patient). The nurse should empower patients and their family carers to understand the nature, course, and biological mechanisms of cachexia and acknowledge its negative effects (e.g., patients’ weight loss, reduced appetite, early satiety). At the end of the meeting, the nurse will collect the main needs reported by the patient and caregiver with respect to both the management of mealtimes and the experiences associated with them and will ask the dyad to observe their own relational dynamics with respect to the role that food takes during the day. To conduct this meeting and collect the data, the nurse uses the tool for evaluating family functioning to construct a first map of the interaction of the dyad.

- Sharing of data collected during the first meeting both by the nurse and the dyad. The nurse will propose practical examples of different ways of managing food in the care of the cancer patient and proposing other ways to support the patient. In particular, the nurse will facilitate talking about each perspective, feelings and food, and how the patient and family carer help each other manage weight and eating related problems. These reflections are embedded in a naturalistic conversation.

- Final reevaluation meeting based on the needs that emerged.

- Proposal of a follow-up meeting to be agreed upon, based on the needs emerged and the clinical condition of the patient.

For the first month, at the end of each meeting and thereafter, as requested by the team, there is a supervision with the PI and Psycho-Oncology Unit, to which the nurses will report what emerged from the interview with the dyad, to set the next meeting based on the shared analysis of the needs that emerged and the interaction methods detected.

The intervention of psycho-education is in continuity with the other figures of the care team, which can be activated according to the needs that emerged (doctor, psychologist, nutritionist). The palliativist doctors will be informed of any information needs on the prognosis or on the clinical condition that may emerge during the psycho-educational intervention. If during the monitoring and supervision phase the need for a specialized psychotherapeutic course emerges, the psychologist of

the Psycho-Oncology Unit with skills in palliative care will be activated, particular attention will be given to patients with irreversible cachexia. Team meetings, which take place twice a week may be an additional space for sharing and discussion on the global management of the patients.

Rehabilitative intervention

The intervention is conducted by two trained physiotherapists and includes:

- 3 individual outpatient sessions (times T0, T1 and T2; see table), in which the physiotherapist, after evaluating the patient, sets up with him a program of personalized reinforcement exercises, which can be performed at home, even with the use of weights and / or elastic bands with different strength, if indicated.
- 3 home sessions of exercises per week; self-managed by the patient, or carried out with the help of the caregiver, for a total of at least 18 sessions in 6 weeks (24 in 8 weeks).

The contents of the intervention focus on:

- an educational component that stimulates patient self-management regarding physical activity, fatigue management, and goal-setting.
- The drafting of the personalized program of reinforcement exercises and the delivery of a booklet to help the patient perform the exercises at home, keeping a diary on the number of exercises, the duration, the number of repetitions and any critical issues that prevent completion of the defined program.
- Training for stretching and relaxation exercises, to be carried out at the end of each session.

Data collection strategies

Recruitment will last one year and all patients assisted by Palliative Care Unit will be evaluated during this period. Each patient will be offered both interventions (psycho-educational and rehabilitative) and will not be given the possibility to choose just one. All replies and reasons for any refusal to participate will therefore be kept.

For each participant, basic information will be collected regarding: age, sex, marital status, family unit, education, profession, religious practice, location of the primary tumor, date of diagnosis, KPS, immediately after giving informed consent through these sources:

- direct request to the patient and / or caregiver
- UCP folder
- Matilde computerized file system.

Analysis

The evaluation will be carried out by trained operators who carry out their work outside the clinical area of the study and who will not have contact with the patients and families involved in the study in order to protect the data collection.

Primary objective: for the feasibility, the proportion of number of dyads who completed the intervention / involved dyads will be evaluated. Compliance will be assessed for each individual component (psycho-social and rehabilitative intervention). The overall intervention will be evaluated feasible if there is compliance greater than or equal to 50 percent to both interventions.

Secondary objectives:

The effects of the intervention will be evaluated on:

- quality of life and anorexia-cachexia syndrome related distress: Functional Assessment of Anorexia-Cachexia Therapy (FAACT)
- caregiver burden: Zarit Burden Scale

- family functioning in the palliative care setting: Family Functioning index
- physical performance Superior Arts: Hand-Grip strength test
- physical performance Lower Arts: 30 seconds sit-to stand test
- adherence to each of the two components (psycho-educational and rehabilitative) through participation in meetings and clinical diaries
- acceptability of the intervention through ad-hoc semi-structured interviews.

Measurement Scale

- Functional Assessment of Anorexia-Cachexia Therapy (FAACT)^{26,27}

Evaluation scale for anorexia-cachexia related distress. It is a tool that derives from the Functional Assessment of Cancer Therapy-General (FACT-G), includes several sub-scales, developed and validated to measure the quality of life related to health status, in particular in cancer patients undergoing therapy: wellness physical, social / family well-being, emotional well-being and functional well-being. To these 4 sub-scales, which contain a total of 28 items, 12 specific items were added on problems related to the presence of anorexia-cachexia. Each item can be assigned a score ranging from 0 'Not at all' to 4 'Very much'; higher scores indicating greater quality of life. The questionnaire can be self-completed or administered by a trained person.

In our study we will use only the sub-scale related to anorexia-cachexia self-compiled by the patient²⁷.

- Zarit burden scale²⁸⁻³⁰

The Zarit Burden Interview (ZBI) is a 22-item instrument for measuring the caregiver's perceived burden of providing family care. The 22 items are assessed on a 5-point Likert scale, ranging from 0 = 'never' to 4 = 'nearly always'. Item scores are added up to give a total score ranging from 0 to 88, with higher scores indicating greater burden. The questions focus on major areas such as caregiver's health, psychological well-being, finances, social life and the relationship between the caregiver and the patient.

This scale has been widely used for many years, has been translated into 18 languages²⁹, Italian validation is available³⁰.

In our study it will be self-compiled by the caregiver.

- Family Relationship Index³¹

Evaluation scale composed by 12 items with a true / false answer, self-compiled, specifically used to evaluate family functioning in the palliative care setting. It is used as a screening tool to preventively assess families at risk of developing psychological distress associated with a disease with poor prognosis. It is based on the perception of family members and their level of cohesion, expression, and resolution of conflicts. The scale identifies five family types that are distributed along a continuum by families with good adaptation to the disease (supportive and able to face and resolve conflicts) to dysfunctional families with poor adaptation (hostile and silent, where a high index of anger is detected or latent). There is a defined intermediate family type that is placed between these types of family functioning (with good adaptation and poor adaptation).

In our study, the scale will be used to collect data useful for the evaluation of family functioning specifically associated with cachexia and the role of food in assistance (Do we talk about it in the family? Do we tend to avoid the subject? Is it possible to talk about the emotional problems related to cachexia? Is the problem faced or avoided). The scale will be self-completed separately by the patient, the caregiver (pre-intervention) and the nurse involved in the study during the psycho-educational intervention as support in the evaluation of the dyad interaction modalities.

There is a validated version in Italian³¹.

- Hand-Grip strength test³²

Test administered using a dynamometer, to quantitatively and objectively measure the isometric muscle strength of the patient's upper limbs. The best out of three attempts is accounted for. This test has been validated for patients with stroke outcomes, elderly and healthy adults. It has been used as a measure of physical performance in some studies with patients with oncological pathology, even at an advanced stage.

- 30 seconds sit-to stand test³³

It evaluates functionally the strength of the lower limbs. The test counts the number of times the patient can get up from a chair without arms within a period of 30 seconds. This test has been validated for patients with osteoarthritic and elderly problems. It has been used as a measure of physical performance in some studies with patients with oncological pathology, even at an advanced stage.

- Ad-hoc semi-structured interviews aimed at the dyad one month after the intervention. The interviews will be conducted by a research nurse (G.A.) trained in qualitative research and focus groups and by the PI of the study for a total of 7 interviews. The dyads will be chosen on the basis of pre and post intervention results, with particular attention to identifying the participants who have reported good adherence to the intervention and participants who have reported difficulties.

- Ad hoc semi-structured interviews with nurses and physiotherapists who participated in the study. The interviews will be conducted by the research nurse (G.A.) and by the PI of the study for a total of 4 interviews corresponding to the operators involved (2 nurses and 2 physiotherapists).

Data analysis

The data analysis will be conducted by the Clinical and Statistical Studies Unit - IRCCS Reggio Emilia.

Sample size: since it is a pilot study to collect data on the feasibility of the intervention, the formal calculation is not carried out but is identified in 30 patients, according to criteria of opportunity and feasibility, the sample for the main objective. The statistical analysis will be descriptive: the primary endpoint will be represented with descriptive statistics tools (average, median, minimum, maximum, remarkable percentiles, central tendency index (with 95% CI), standard deviation, shape indexes.

secondary endpoints: descriptive representation (for T0, T1, T2 and T3) of the endpoints and of the variations detected between T0 and T3.

Ethical considerations

Access to clinical documentation

The researchers responsible for completing the Basic Information Sheet (Annex 11 Evaluation Scales) will collect only the data contained in the form (personal data and clinical data), by consulting the clinical documentation held by the Palliative Care Unit (Azienda USL - IRCCS of Reggio Emilia). The information collected will be limited to those contained in the form and aimed at carrying out psycho-educational and rehabilitative interventions. Please note that, to protect the privacy of all those involved:

- it is expected that the names of the dyad (patient / caregiver) will appear only in the aforementioned form, combined with a code
- in all the remaining forms, the patient will be identified exclusively with a code
- the data will be presented and published in aggregate form, without reporting information that can be traced back to the individual patient, the family caregiver, or the individual professional.

The study documentation will be collected and managed at one of the centers involved in the study (Palliative Care Unit, Azienda USL - IRCCS of Reggio Emilia). It will be kept and made available for any required inspections by regulatory authorities.

Consent to participation in the study

All study participants will be informed in detail by the investigator of the aims and objectives of the study, and must sign specific informed consent for the study and processing of personal data which will be filed together with the study documentation. The consent to participate in the study is requested and collected by the proposing doctor or by the researcher in charge of the T0 assessment. Each participant has the right to withdraw their membership in the study at any time.

The study will be conducted in accordance with this protocol, any amendments will be introduced and authorized and follow the ethical principles of the Helsinki Declaration.

Table time for the evaluation secondary outcomes.

Assessment	T0 (before intervention)	T1 (2 weeks after T0)	T2 (4 weeks after T0)	T3 (8 weeks after T0)
Functional Assessment of Anorexia-Cachexia Therapy (FAACT; patient)	x			x
Zarit Burden Interview (ZBI; caregiver)	x			x
Family Function Index (FFI; patient and caregiver)	x			
Hand-Grip (patient)	x	x	x	x
Sit-to-Stand (30CST; patient)	x	x	x	x
N sessions for rehabilitative intervention		x	x	x
N sessions for psycho-educational intervention			x	
Hoc semi-structured interviews (dyads)				x
Hoc semi-structured interviews (operators)				x

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