Change of geriatric morbidity and muscle mass of elderly patients with malignant disease after treatment with palliative and adjuvant chemotherapy

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Observational non invasive

Summary

ID

NL-OMON41437

Source
ToetsingOnline

Brief title
CHARMING

Condition

- Muscle disorders
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
cancer-induced muscle loss, chemotherapeutic induced muscle wasting

Research involving
Human

Sponsors and support

Primary sponsor: Albert Schweitzer Ziekenhuis
Source(s) of monetary or material Support: Albert Schweitzerziekenhuis + stichting ORAS

Intervention

Keyword: Aged (MeSH term), Chemotherapy, Geriatric assessment, Sarcopenia (MeSH term)

Outcome measures

Primary outcome

Primary outcome:

- Correlation sarcopenia and overall survival

Primary study parameter:

- Sarcopenia (measured by slice-o-matic using CT-images)

Primaire uitkomstmaat:

Secondary outcome

Secondary study parameters

1. Geriatric assessment:

- Comorbidity and medical history (charlson comorbidity index)

- Polypharmacy (5 or more different medicines)

- Quality of life (by EORTC QLQ-C30 questionnaire)

- Nutritional status (minimal nutritional assessment)

- Cognitive disorders (minimal mental state evaluation and clock drawing test)

- Physical condition and muscle power (short physical performance battery,

steep ramp test, hand grip strength, gait speed)

- Mood (geriatric depression scale)

- (Instrumental) Activities of Daily life (Lawton and Brody index, Barthel

index)

2. Treatment success

Unsuccessful completion of chemotherapeutic treatment is concluded in the

presence of one of the following events:

1. Dose reduction

2. Delay of chemotherapeutic cycle

3. Cancellation of treatment because of any reason, except disease progression.

3. Biological markers:

1. Serum, inflammatory markers (CRP, interleukins)

2. Isolated DNA and single nucleotide polymorphisms in a biopsy of the skin.

Study description

Background summary

Ageing is an important phenomenon in the Dutch population. Cancer is the most common cause of death since 2008 and we assume that the incidence of cancer will increase because of this. More than half of the patients with oncologic disease is at an advanced age. This leads to a serious increase of the elderly population with oncologic disease in hospitals. In these vulnerable group of patients there are large differences in physiologic reverse capacity because of cognition, comorbidity, nutritional status and impaired mobility. Those differences are not always corresponding with age. Identifying the people, who will benefit from invasive oncologic treatment, is elusive. Geriatric assessment is considered as gold standard of evaluating patient vitality and physiological reserve and has shown to be an important diagnostic tool in the prediction of all cause mortality and chemotherapeutic toxicity in elderly patients undergoing oncologic treatment. Geriatric assessment prior to oncologic treatment, however, has limitations. It can be executed in all

elderly people to predict clinical outcome and treatment tolerability, but the assessment is time-consuming and the necessity of screening the entire elderly population undergoing chemotherapy remains unclear. It is desirable to determine a combination of markers that could be used during routine clinical practice to assess the risk of complicated oncologic treatment.

Secondly, sarcopenic obesity is associated with impaired daily functioning en the presence of sarcopenia could be a predictor of overall mortality. According to the European concensus sarcopenia is defined as a loss of muscle due to age in combination with impaired muscle power or function. In the literature several methods to measure body composition are reported. Determination of the lumbal skeletal index by slice o matic is internationally validated. There are also signs that endocrinologic factors influence the development of sarcopenia. Advanced age results in an increase of the amount of visceral adipose tissue. This causes more production of pro-inflammatory cytokins. These biomarkers are chronically elevated in elderly people and possibly cause the development of sarcopenia as well. It is possible to determine the prevalence of cellular senescence in skin biopsy. Senescence is defined as arrest during the cell cycle and plays a role in cellular pathways in the process of aging. Senescence will occur if DNA repair mechanisms are activitated. The cell looses the ability to proliferate. The question is if could be a predictor of overall surivival.

We hypothesize that geriatric markers, sarcopenia and biological markers predict progression free and overall survival and chemotherapeutic toxicity in elderly patients with cancer. This study is powered on the effect size of sarcopenia on the overall survival as this is our primary question.

Study objective

The aim of this study is to assess the prognostic value of sarcopenia and geriatric markers for survival and treatment tolerability and fluctuation of this value between several oncologic conditions. Secondly, we focus on the value of repeated CGA as this is important for effective geriatric interventions in routine geriatric care and the prognostic value of treatment adjustments based on CGA.

Primary objective:
1. Is sarcopenia (by CT imaging) prior to chemotherapeutic treatment correlated with overall survival?

Secundary objectives:
2. Is sarcopenia (by CT imaging) prior to chemotherapeutic treatment correlated with PFS and grade 3-4 chemotherapeutic toxicity?
3. Is dosage of chemotherapy per cm2 lean body mass related to PFS, OS, grade 3-4 chemotherapeutic toxicity and dose density of chemotherapy?
4. What is the value of geriatric markers in the prediction of PFS, OS and

chemotherapeutic toxicity in older patients with malignant disease?
5. Which combined geriatric markers provide the most accurate prediction of PFS, OS and chemotherapeutic toxicity in older patients with malignant disease?
6. Are biological markers (senescence in a skin biopt, single nucleotide polymorphisms, interleukins or other laboratory markers) related to PFS, OS and grade 3-4 chemotherapeutic toxicity?
7. Which definition of sarcopenia provides the best prediction of PFS, OS and chemotherapeutic toxicity?

Study design

Prospective multi centre cohort study

Study burden and risks

Number of research moments: 4 during 1 year. Duration: 60-75 min each
Number of laboratory research: 4 times
Number of skin biopsies: Once after inclusion

Research persons fill independently 2 questionnaires per research moment. Further questionnaires and examination take place together with the researcher during research moments. Physical examiniation contains low invasive tests such as gait speed, a short period of cycling and measuring muscle power. Disadvantages contain time investment of the research person and some questionnaires might be confronting. (for example: the geriatric depression scale) Participation in laboratory research and donating biopsy of the skin is voluntary. If the research person doesn't want to participatie it is still possible to join other aspects of the study.

Diagnostic imaging (CT) is performed during routine patient care. If that is not the case, measurement of muscle mass by slice-o-matic will be voided. Therefore, research persons are not exposed to extra radiation. The study has no influence on the regular oncologic treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patients with malignant disease
2. 65 years of age and older
3. Patients undergoing chemotherapeutic treatment.

Exclusion criteria

1. Previous systemic chemotherapeutic treatment during the last 3 months.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-05-2015
Enrollment:	450
Type:	Actual

Ethics review

Approved WMO

Date:	20-05-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL47633.101.15