Predictive value of geriatric oncology screening and geriatric assessment of older patients with cancer

A randomized clinical trial protocol (PROGNOSIS-RCT)

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ABSTRACT

Introduction: Comprehensive geriatric assessment (CGA) has been shown to reduce frailty in older patients in general. In older patients with cancer, frailty affects quality of life (QoL), physical function, and survival. However, few studies have examined the effect of CGA as an additional intervention to antineoplastic treatment. This protocol presents a randomized controlled trial, which aims to evaluate the effects of CGA-based interventions in older patients with cancer and Geriatric 8 (G8) identified frailty.

Materials and Methods: This randomized controlled trial will include patients, age 70+ years, with solid malignancies and G8 frailty (G8 ≤ 14). Patients will be separated into two groups, with different primary endpoints, depending on palliative or curative antineoplastic treatment initiation, and subsequently randomized 1:1 to either CGA with corresponding interventions or standard of care, along with standardized antineoplastic treatment.

A geriatrician led CGA with corresponding interventions and clinical follow-up will be conducted within one month of antineoplastic treatment initiation. The interdisciplinary CGA will cover multiple geriatric domains and employ a standard set of validated assessment tools.

Primary endpoints will be physical decline measured with the 30-s Chair-Stand-Test at three months (palliative setting) and unplanned hospital admissions at six months (curative setting). Additional outcomes include QoL, treatment toxicity and adherence, occurrence of polypharmacy, potential drug interactions, potential inappropriate medications, and survival. The primary outcomes will be analyzed using a mixed model regression analysis (30-s chair stand test) and linear regression models (unplanned hospitalizations), with an intention to treat approach. Power calculations reveal the need to enroll 134 (palliative) and 188 (curative) patients.

Discussion: The present study will examine whether CGA, as an additional intervention to antineoplastic treatment, can improve endpoints valued by older patients with cancer. Inclusion began November 2020 and is ongoing, with 37 and 29 patients recruited April 15th, 2021.

Registration: NCT04686851

Abbreviations: ADL, Activities of Daily Living.; CCI, Charlson's Comorbidity Index.; CGA, Comprehensive Geriatric Assessment.; CIRS-G, Cumulative Illness Rating Scale –Geriatric.; 30-s CST, 30 s Chair Stand Test.; DFS, Decease-free survival.; ELFI, Elderly Functional Index Score.; EORTC-QLQ-ELD14, European Organization for Research and Treatment of Cancer –Quality of Life Questionnaire-Elderly 14 item.; EORTC-QLQ-C30, European Organization for Research and Treatment of Cancer –Quality of Life Questionnaire – Core 30 item.; G8, geriatric eight screening tool.; GDS, Geriatric Depressions Scale.; HGST, Hand Grip Strength Test.; IADL, Instrumental Activities of Daily Living.; MNA, Mini Nutritional Assessment.; NCI-CTCAE, The National Cancer Institute's Common Terminology Criteria for Adverse Events.; OS, Overall survival.; PDI, Potential Drug Interactions.; PFS, Progression-free survival.; PIM, Potential Inappropriate Medications.; PP, polypharmacy.; QoL, Quality of Life.; RCT, Randomized controlled trial.; SD, Standard Deviations.; START/STOPP, Screening Tool to Alert doctors to Right Treatment/Screening Tool of Older People's Prescriptions..

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1. Introduction

Frailty in older patients with cancer is associated with an increased risk of loss of quality of life (QoL), decline in physical function, postoperative complications, reduced ability to tolerate chemotherapy, hospitalization, and decreased survival [1–5]. Frailty is the result of decreased physiological reserve of organ function, leading to increased vulnerability to stressors such as antineoplastic treatment [6]. Multiple factors, such as previous disease and genetics, influence this age-related loss of functional reserve and the development of comorbidity in older persons. This creates high diversification where patients range from fit to frail with varying comorbidity [6]. Vulnerable and frail patients constitute over half of all older patients with cancer [1]. Moreover, older patients with cancer receiving palliative antineoplastic treatment may prefer improved QoL and physical autonomy to prolonged survival [7–10]. Hence, the treatment goals for these patients may differ from that of a younger counterpart [11–14]. This heterogeneity in frailty, comorbidity, and treatment preference in older patients with cancer, necessitates a personalized and multifactorial evaluation [15].

Therefore, the International Society of Geriatric Oncology recommends that all patients with frailty and cancer, age 70 years or more, are offered a comprehensive geriatric assessment (CGA) [16,17]. CGA is a multidimensional, interdisciplinary diagnostic process with corresponding interventions focused on improving the overall health in older patients with frailty. It addresses core domains related to frailty, including functional status, comorbidity, cognition, mental health, social status and support, nutrition, and polypharmacy [18,19]. CGA is considered the cornerstone of geriatric care and the gold standard for health assessment in older adults. CGA with corresponding interventions has been demonstrated to reduce frailty in older patients [20]. Furthermore, in an in-hospital (non-oncologic) setting, early CGA with corresponding interventions decreases mortality and the risk of institutionalization [21]. Identifying and treating factors leading to frailty may therefore, counteract frailty and improve outcomes for older patients with cancer.

CGA with corresponding interventions is time and resource consuming and may not be needed in all patients. The International Society of Geriatric Oncology recommends a two-step approach, starting with a geriatric oncology screening to identify individuals with frailty who would benefit from a CGA [16]. Several screening tools for identifying frailty in older patients with cancer have been developed. The Geriatric 8 (G8) is among the most investigated tools, with high sensitivity and fair specificity in predicting CGA-frailty [22,23]. The G8 is based on the Mini Nutritional Assessment, with scores ranging from 0 to 17 and a cut-off for frailty at G8 ≤ 14 [24]. The G8 has previously been applied in several Danish studies, with percentages of G8 frailty in older patients with cancer ranging from 50 to 72% [25–29].

Frailty identified through CGA is strongly associated with increased risk of chemotherapy toxicity, functional decline, and mortality in older patients with cancer [30]. Until recently, research has primarily examined CGA as a means to guide oncologic treatment, as opposed to viewing CGA as an additional intervention, thus evidence is sparse [31]. The GERICO study, a randomized control trial (RCT) examining older patients with colorectal cancer receiving either adjuvant or first line palliative chemotherapy, and screened as frail with the G8, recently found that CGA with corresponding interventions reduced chemotherapy toxicity, increased chemotherapy treatment completion and increased physical functioning [27]. Preliminary results from two ongoing RCTs with mixed cancer populations support the chemotherapy toxicity findings [32,33]. Furthermore, preliminary results from an additional ongoing RCT study suggest that CGA has a positive effect on the QoL Elderly Functional Index Score (score related to physical functioning), treatment continuation, and unplanned hospital admissions [34]. Also, an interventional study of 407 Danish older patients with cancer found a potential improvement in 90-day mortality [35]. However, only the GERICO-study screened for frailty before offering CGA as an intervention. Thus, the effects of CGA as an additional intervention to oncological treatment in older patients with different cancers, who are identified as frail with the G8, remains to be confirmed in an RCT.

2. Study Objectives

2.1. Primary Objectives

To investigate whether CGA based interventions as an additional intervention to oncologic treatment vs. oncologic treatment alone can

i. prevent physical decline at 3 months follow-up in G8-frail older patients initiating palliative oncologic treatment
ii. decrease unplanned hospital admission at 6 months follow-up in G8-frail older patients initiating curative oncologic treatment

2.2. Secondary Objectives

To establish whether CGA and clinical follow-up as an additional intervention to oncologic treatment vs. oncologic treatment alone in patients initiating either palliative or curative oncologic treatment can

i. decrease treatment-related toxicity (grade 3+) measured at 6 months
ii. increase the proportion of patients completing planned first line palliative or curative intended oncologic treatment
iii. enhance quality of life within 6 months
iv. decrease polypharmacy (PP), potential drug interactions (PDI), and potentially inappropriate medications (PIM) at 3 months
v. enhance cancer-specific and overall survival at 6 months

3. Methods

3.1. Study Setting and Design

This is a single center study consisting of two RCTs with parallel groups (i.e., subjects who are enrolled to receive oncologic treatment with palliative vs curative intent) conducted in collaboration between the Department of Oncology and the Department of Geriatric Medicine at the University Hospital of Odense.

Participants, enrolled in a larger departmental prospective cohort study (PROGNOSIS-G8), who are identified as frail according to the G8 screening, and who are eligible for antineoplastic treatment, will be offered randomization to CGA with corresponding interventions or standard of care as a supplement to standard oncologic treatment. Patients will be separated into two groups, with different endpoints, depending on palliative or curative antineoplastic treatment initiation. Thereafter, patients will be randomized 1:1 to either intervention or control group. Apart from this, the two RCT studies will be identical in regards to the study setup, randomization, stratification, intervention, and follow-up. Patient enrollment began November 2020 and is expected to end in 2022. (Fig. 1).

3.2. Geriatric assessment

3.2.1. Participants

3.2.1.1. Eligibility Criteria. Inclusion Criteria

i. Patients age 70 years or more with solid malignancies who speak Danish and are able to give informed consent
ii. Patients identified as frail according to the G8 (G8 ≤ 14)
iii. Patients initiating any oncologic (medical or radiation) first line treatment in palliative or curative setting, including chemotherapy as monotherapy, adjuvant or neoadjuvant chemotherapy, immunotherapy, targeted therapy, radiotherapy as monotherapy, radiotherapy in combination with surgery or medical antineoplastic treatment (chemotherapy, targeted therapy, immunotherapy).

Exclusion Criteria

i. Patients who have been treated with antineoplastic treatment for another cancer diagnosis within the past twelve months
ii. Patients who have had a consultation in the geriatric outpatient clinic within the past twelve months

3.3. Recruitment Procedure and Randomization

Older patients presenting at the Department of Oncology outpatient clinic will be screened with the G8 before oncologic treatment initiation as part of standard departmental procedure.

Eligible patients will be invited to consider participation and will be provided with oral and written information about the study by the principal investigator or medical staff associated to the study. All participants will be asked to give written consent before study inclusion.

Participants will be randomized 1:1 to either intervention or control group through a REDCap randomization module. Randomization will be conducted using blocks of 8 and will be stratified for dichotomized G8 score (G8 > 11 or G8 ≤ 11) and sex. A cut-off value of 11 was chosen to ensure even distribution of participants with moderate or severe G8 frailty between the control and the intervention groups.

3.4. Blinding

The CGA with corresponding interventions and follow-up will be documented in the patient's electronic medical record, which can be accessed by both patient and medical staff the Department of Oncology and Geriatric Medicine. Therefore, it is not possible to blind participants, oncologic, and geriatric staff to allocation. However, the biostatistician performing the analyses will be blinded to patient allocation.

3.5. The Control Group

Patients allocated to the control group will receive standard oncologic care following national guidelines for the respective cancer

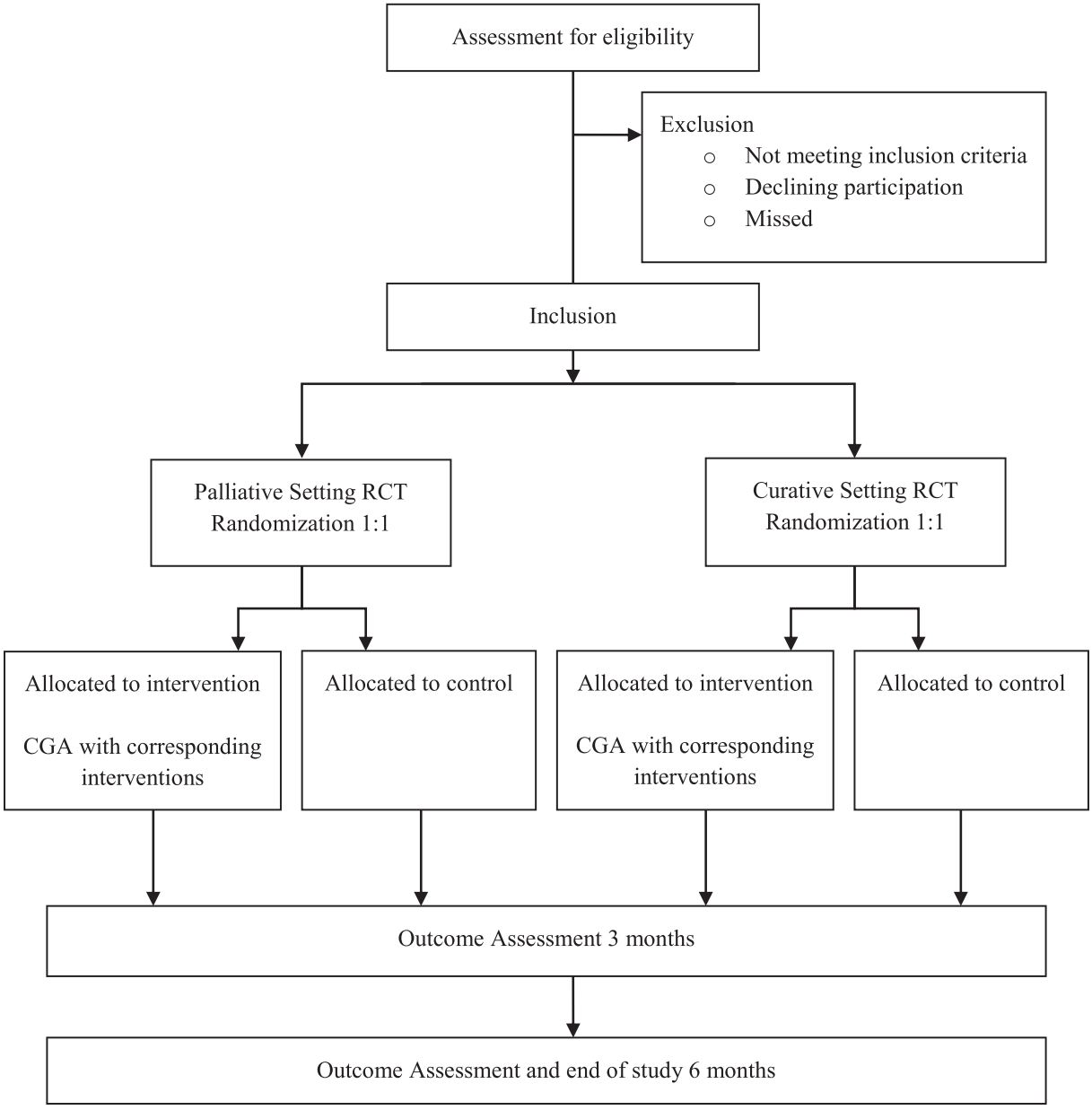

Fig. 1. Title: PROGNOSIS-RCT Trial Design. Footnotes: Abbreviations: RCT Randomized Controlled Trial, CGA Comprehensive.

diseases at the discretion of the treating oncologist. All health issues will be assessed by either the oncologist or the general practitioner, as is common practice.

3.6. The Intervention

Patients allocated to the interventional group will receive a CGA with corresponding interventions in addition to standard oncologic care.

The CGA will be a physician-led, multidimensional, interdisciplinary assessment including major geriatric syndromes and will take approximately 60–120 min to perform. A geriatric resident or specialized geriatrician and a geriatric nurse will perform the CGA within the first month of oncologic treatment initiation. The CGA will be performed in conjunction with other appointments at the hospital, if possible. For participants with a long hospital commute, an at-home CGA consultation may be conducted to reduce patient transportation. The domains in the CGA include cognition, emotional status, comorbidity, functional status, physical function, polypharmacy, weight-loss and nutritional status, fall risk, and social support. The domains will be assessed using validated tests within a fixed setup based on the Geriatric Core Dataset (Table 1) [36]. A tailored intervention will be formed based on individually identified health issues. If indicated, physical performance and the need for rehabilitation will be evaluated by an authorized physical therapist, while the nutritional status and the need for dietary interventions will be evaluated by a dietician. A follow-up session will be scheduled approximately one month after the initial CGA. If indicated, additional follow-up sessions may follow (Table 1).

3.7. Primary Outcomes

3.7.1. Functional Decline (palliative treatment RCT)

Functional decline will be assessed using the 30 s chairs stand test (30-s CST) and will be measured at baseline and at 3 months, in accordance with standard practice [47]. An available chair with a seat height of 42–44 cm will be used to ensure comparability between measurements performed in-hospital and at-home [48].

3.7.2. Unplanned Hospital Admissions (curative treatment RCT)

The number of unplanned hospital admissions within the first 6 months of antineoplastic treatment initiation will be assessed. All hospitalizations that were not planned or foreseen, including both non-emergency and emergency admissions with durations longer than 24 h, or if hospital admission included an overnight stay, will be registered. Date of unplanned hospitalizations, department in which the participant is hospitalized, duration of stay, and diagnosis at discharge, will be obtained from medical records.

3.8. Secondary Outcomes

3.8.1. Quality of Life

Participants will be asked to complete the European Organization for Research and Treatment of Cancer (EORTC)-QLQ-C30 and QLQ–ELD14 at baseline and at 3- and 6-months follow-up. The EORTC-QLQ-C30 includes 30 questions involving a global health scale, five functional scales, three symptom scales, and six single items; similarly, the QLQ-ELD14 questionnaire includes two physical scales and five symptom scales [49,50].

QoL will be reported using the summary score and the Elderly functional index score (ELFI Score) derived from the two validated QoL questionnaires [51,52]. The summary score is a higher order factor model based on the QLQ-C30, excluding overall quality of life and the single item scale financial impact. The score is calculated as a mean of all summed items, giving all scales equal weight. Scores range from 0 to 100, and a clinically significant change is defined as 0.5 (moderate change) or more [52]. The ELFI-score represents the physical role and social functioning scales from the QLQ-C30 and the mobility scale from the QLQ-ELD14. The ELFI-score ranges from 0 to 100, with higher scores indicating higher physical functioning QoL. No minimal clinically important difference has been established for the ELFI score [51].

Table 1
CGA assessment tools with corresponding interventions.

CGA Domains	Assessment Tool*	Cut-off values*	Possible Interventions
Comorbidity	CIRS-G CCI Medical review and physical examination**		Referral for further evaluation, initiation or optimizing of (non-oncologic) treatments
Functional Status	Katz ADL Lawton IADL		Initiation community-based health care services or referral to occupational therapist
Polypharmacy	START/STOPP criteria adapted to Danish conditions Review of prescription medications		Medication changes if indicated
Cognition	Mini-Cog cut-off Interview of relative/caregiver	<3/5	Assessment of cognition and referral for further investigation, Initiation community-based health care services
Mood	GDS Interview of relative/caregiver	>5/15	Initiation of medical therapy, non-medical therapy advice, notifying caregivers
Nutrition and Weight loss	MNA Weight loss	≤11/15 >5% of total body weight	Assessment and treatment of potential underlying causes (non-oncologic), nutritional advice, prescription of nutritional supplements and/or referral to dietician.
Physical Function	HGST*** 30-s CST*** Patient-reported loss of strength within last 3 months	sex and age adjusted	Referral to physical therapist/ community-based exercise programs guided by physical therapist
Fall risk	Self-reported falls within 12 months	>1	Fall risk assessment and intervention on identified risk factors
Social Support	Social network and home care?		Initiation or adjustment of community-based health care services if indicated. Involvement of relatives/caregivers.

* Cut-off values indicated if applicable.
** Including blood samples, ECG, and further imaging if needed.
*** Cut-off sex- and age-adjusted Abbreviations: CIRS-G Cumulative Illness Rating Scale –Geriatric [37], CCI Charlson's Comorbidity Index [38], ADL Activities of Daily Living [39], IADL Instrumental Activities of Daily Living [40], START/STOPP Screening Tool to Alert doctors to Right Treatment/Screening Tool of Older People's Prescriptions [41,42], GDS Geriatric Depressions Scale [43], MNA Mini Nutritional Assessment [44], HGST Handgrip strength test [45], 30-s CST 30 s Chair Stand Test [46].

3.8.2. Treatment Toxicity

Treatment toxicity grade 3+ (Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0) occurring within the first 6 months of antineoplastic treatment initiation will be registered. This is carried out by staff, mainly nurses, in the oncologic department on specific pre-printed templates. Grade 3 + treatment toxicities resulting in hospitalisations, changes in antineoplastic treatment, or initiation of additional supportive care will be abstracted from the electronic patients records. The relationship between toxicity, treatment and other causes for hospitalization will be reviewed by one of the oncology specialists on the study team.

3.8.3. Treatment Adherence

The number of participants completing scheduled antineoplastic treatment will assessed.

The initial treatment plan, including dosage reductions, dosage delays, treatment discontinuations, reasons for discontinuation/ delay/ reduction, date of first line treatment completion will be registered from medical records. Adherence will be registered from initiation of antineoplastic treatment until completion of treatment or until 6 months after treatment initiation.

Dosage reductions will be measured as a percentage of the planned dose. Dose delays will be measured in days, and discontinuations will be measured as the fraction of number of the given cycles per number of planned cycles, excluding discontinuations due to cancer progression.

3.8.4. Polypharmacy (PP), Potential Drug Interactions (PDI), and Potentially Inappropriate Medications (PIM)

PP, PDI, and PIM will be measured at baseline and 3 months follow-up. Participant medication prescriptions will be reviewed using electronic medical records and will be updated to reflect actual medication intake. The update will be based on patient history and registry of medication purchases within the past 4 months. Polypharmacy will be defined as 5 or more daily medications. Potential drug interactions will be evaluated using Stockleys' drug interaction database and potential inappropriate medications using the START/STOPP criteria adapted to Danish conditions [41,42,53].

3.8.5. Survival

Survival will be described as overall survival (OS), progression-free survival (PFS) (palliative setting RCT), and disease-free survival (DFS) (curative setting RCT) at 6 months follow-up. Time of death will be obtained from participants medical records. PFS and DFS will be measured from time of randomization until death of any cause or time to progression of cancer or time to relapse of cancer, respectively. OS will be measured from time of randomization to time of death from any cause.

3.8.6. Baseline Data

The following baseline data will be collected before randomization: age, sex, G8 score, type and stage of cancer, performance status (ECOG), initiation of curative or palliative oncologic treatment, civil status, Body Mass Index, Charlson's Comorbidity Index, Cumulative Illness Rating Scale-Geriatric, daily prescription medications, falls within the last 12 months, weight loss, intake of prescription nutritional supplements, exercise habits, and whether the participants are receiving home care or physical rehabilitation. (Table 2).

3.9. Data Management

All data will be stored in accordance with the Danish Data Protection Agency's laws. Baseline and outcome data retrieved from participant medical records, clinical measurements, and questionnaire responses will be stored in a REDCap Database designated for this study. Data regarding patient inclusion will be stored in a restricted Sharepoint data-managing platform.

Table 2
SPIRIT flow diagram.

Participant Timeline					
	Enrolment	Allocation	CGA and follow-up	Follow-up	
TIMEPOINT	-0-2 days	0	0-1 month	3 months	6 months
ENROLMENT					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS					
CGA with follow-up on interventions			←		
Standard oncologic care	←				→
Controls					
Standard oncologic care	←				→
ASSESSMENTS					
Baseline Data collection	X				
30-sec CST	X			X	
Unplanned hospitalizations					X
Quality of Life				X	X
Treatment toxicity					X
Treatment Adherence					X
PP,PDI,PIM				X	
Survival					X

Abbreviations: CGA Comprehensive Geriatric Assessment, 30-Sec CST 30 s Chair Stand Test, PP Polypharmacy, PDI Potential Drug Interactions, PIM Potential Inappropriate Medications.

3.10. Sample Size and Power

3.10.1. Physical Decline (Palliative Setting RCT)

A minimal clinically important difference for the 30-s CST has previously been established as 2.6 repetitions [54]. A recent cohort study published normative data for the 30-s CST in an adult Danish population. For persons aged 70 years or more a standard deviation (SD) between 3.04 and 5.00 was established [55]. With a significance level of 5%, 80% power, SD of 5, and allowing for a loss to follow-up of 20%, 134 participants (67 in each group) are needed to detect a minimal clinically important difference of 2.6 between the randomized groups.

3.10.2. Unplanned Hospital Admissions (Curative Setting RCT)

The NORDIC9-study showed admission rates of 56% for Scandinavian older patients with colon cancer [56]. In the INTEGRATE-study, an add-on CGA to oncologic treatment reduced 41% of unplanned hospital admissions in an Australian population of unscreened older patients with cancer of different origins [34].

With a significance level of 5%, 80% power, and allowing for a loss to follow-up of 20%, 188 participants (94 in each group) are needed to detect a mean difference between groups of 41%.

Hence, a total of 322 participants (those receiving treatment with both palliative and curative intent) will be included.

3.11. Data Analysis

Data analyses will be conducted using the intention to treat approach, followed by secondary per-protocol subgroup analyses. All outcome measures will be analyzed separately within each RCT group. Baseline characteristics will be described as means ± SD or medians (25th–75th percentiles) according to their distribution for quantitative variables, and numbers and percentages for categorical variables. Data on physical tests, QoL scores, PP, PDI, PIM, treatment toxicity and adherence, and unplanned hospital admissions will be described as means ± SD or medians (25th–75th percentiles) according to their distribution. Between-group differences in treatment adherence, treatment toxicity, and hospitalizations will be analyzed using linear regression models. In-group and between-group (intervention vs. control) differences in outcomes measured over time will be assessed using mixed model regression analysis taking the individual trajectories into account. OS, PFS and DFS will be assessed on hazards scale using survival regression models with time-varying covariates to account for immortal-time bias. PFS and DFS risk will be assessed taking the competing risk of death from other causes into account. Potentially confounding variables will be included in multivariable analyses (e.g., treatment modality, comorbidity). Results will be presented with 95% confidence intervals. Statistical analyses will be performed in collaboration with a biostatistician. STATA will be used for statistical analyses.

3.12. Ethics and Dissemination

The study was approved by the Regional Committees on Health Research Ethics for Southern Denmark (494998–20), and the Danish Data Protection Agency (20/17768). Participation is voluntary and declined participation or withdrawal will have no consequences on oncologic treatment decisions. Participants have the right to withdraw from the study at any time. The participants will be covered by the Danish "Complaint and compensation law in health care." To ensure participant safety, ongoing trials audits will be conducted yearly. Should a serious adverse event occur, the Regional Scientific Ethical Committee of Southern Denmark will audit the event within 2 weeks, independent of trial investigators. The RCT studies have been reported to clinicaltrials.gov (NCT04686851). The trial protocol complies with the SPIRIT guidelines [57]. Study results will be reported in compliance with CONSORT guidelines [58], published in international peer-reviewed journals, and presented at national and international conferences, irrespective of study findings.

3.13. Patient Public Involvement

Geriatric and cancer patient panels affiliated with Odense University Hospital were consulted before planning this study. Members of both committees responded positively towards the incorporation of a CGA in cancer treatment and expressed that maintenance of functional ability and quality of life were valuable effect measures.

4. Discussion

The present RCT study will evaluate the effect of CGA based interventions on physical decline, unplanned hospitalizations, QoL, treatment toxicity, and adherence, prescription medications, and survival in older patients initiating either palliative or curative oncologic treatment. The study is part of a larger departmental project comprised of a prospective cohort study in which all older patients, regardless of cancer site, will be screened for frailty with the G8 before inclusion. Simultaneously, participants will be enrolled in two RCT studies. Inclusion began November 1th, 2020 and is ongoing.

In this study, the effects of CGA, as a supplement to oncologic treatment, in preventing loss of physical function and QoL will be examined. Therefore, the CGA will be performed as early in the course of oncologic treatment as possible. Patients receive an extensive amount of information at the first oncologist appointment. Cohort pilot study participants reported that the addition of trial information and inclusion after the first appointment was burdensome. Therefore, to enhance recruitment, inclusion and intervention take place after the initiation of antineoplastic treatment.

Offering CGA to all referred older patients with cancer before oncologic consultation may be feasible [25,35]; however, a CGA is both time and resource consuming, and may be unnecessary for the fittest of older patients with cancer. Examining a select group of patients with frailty may strengthen the evidence of potential findings, as the CGA is conducted in patients, who we anticipate will benefit from the intervention. Therefore, a screening tool is needed to optimize frailty assessment and geriatric referrals. Currently, few RCT studies have examined the effects of CGA in older patients with various cancer sites receiving antineoplastic treatment. Only one of these studies specifically screened for frailty using the G8, though exclusively included patients with colorectal cancer stage II-IV [27]. This study showed a positive effect of receiving CGA on chemotherapy treatment completion. Likewise, a previous cohort study demonstrated an improvement in treatment adherence in older patients with cancer who were screened for frailty using the CGA-GOLD prior to CGA [59]. The screening tool used was a comprehensive patient administered assessment, including the entire EORTC-QLQ-C30, and was considerably more time-consuming than the G8, making it less feasible in a Danish clinical setting [59]. To ensure that the patients allocated to intervention are likely to benefit from a CGA, the current study has chosen to initially screen for frailty with the G8 at the first oncologic consultation.

Maintaining physical independence is considered of great importance regardless of the oncologic treatment intend [60]. Therefore, maintaining physical function in older patients with cancer should be a goal of both palliative antineoplastic treatment and supportive interventions.

Studies suggest that reduced instrumental activities of daily living (IADL) and nutritional status predict decline in activities of daily living (ADL) function in older patients initiating chemotherapy at 2–3 months follow-up [61]. However, the majority of older patients initiating antineoplastic treatment are not in need of assistance in IADL or ADL functions and due to a ceiling effect, changes in physical function over time might not be detected. Physical function measured by the 30-s CST at 3-month follow-up is highly feasible in a clinical setting due to its quick and simple execution [47]. The 30-s CST is a validated test, with low test-retest variability at measuring lower limb muscle strength and function [47]. The 30-s CST has previously been associated with physical independence and survival [62,63]. Its usefulness has been demonstrated in the olde cancer population, and normative data for the Danish older population has recently been published [55,64]. Hence, for this study a performance-based measurement, the 30-s CST, was selected.

Hospitalization of older patients has previously been shown to increase the risk of developing delirium, functional decline, and mortality for up to two years after discharge [65,66]. G8 frailty has been established as a risk factor for hospitalization in older patients with cancer [67]. Reducing unplanned hospital admission in patients with frailty receiving curative cancer treatment might therefore, benefits both patient health, as well as reduces healthcare costs.

With several ongoing clinical trials at the Department of Oncology, the fittest of the frail older patients may be less frequently included. Similarly, the frailest older patients might decline participation due to a lack of physical and psychological reserve. Thus, selection bias may occur.

To limit the risk of bias due to either underrepresentation of the fittest or the frailest of the frail older patients with cancer, several steps have been taken to ensure participation: Participant inclusion takes place after initial oncologic consultation, including patients with a broad representation of cancer sites, and the CGA may be performed at-home.

Previously, van Walree et al. has argued that the inhomogeneous methodological execution of CGA and follow-up has made it difficult to draw clear conclusions regarding the role of CGA in the treatment of older patients with cancer [23]. To increase comparability, the CGA performed in this study is based on a fixed setup of standard screening tools and predefined possible interventions. The fixed setup ensures uniform implementation of the CGA, independent of the setting in which it is performed. Furthermore, if a significant effect of an add-on CGA is shown, implementation in clinical practice is highly feasible, as the CGA interventions utilize the current healthcare framework. All offered interventions are standard treatments offered to frail older persons in Danish municipalities and geriatric outpatient clinics.

5. Conclusion

While recommendations for geriatric oncology screening, and offering CGA to older patients with cancer exist, the evidence for implementing CGA as a supplement to antineoplastic treatment is still sparse. We hope that this study will generate new knowledge on the effects of adding CGA, in the care of older patients with cancer and frailty receiving oncologic treatment.

Ethical Approval and Consent

This study, including the consent forms and written participant study information, has been granted ethical approval by the Regional Committees on Health Research Ethics for Southern Denmark (494998–20).

Patient Consent for Publication

Not applicable.

Availability of Data and Materials

Not applicable.

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Authors' contribution

Authorship follows the Vancouver guidelines.
AKWG, HMD, JR, ME, CML, PP, TLJ, and HJD were involved in the conception and design of the study. JR, ME, HJD and AKWG wrote the grant applications with input from PP, and TLJ. AKWG wrote the manuscript draft with input from JR. JR, ME, CML, PP, TLJ, HJD, AM and HMD reviewed and critiqued the manuscript and all authors approved the final published version.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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