Assessment of sarcopenia and frailty in TCT selection

Professor Nicole Kiss
Deakin Institute for Physical Activity and Nutrition

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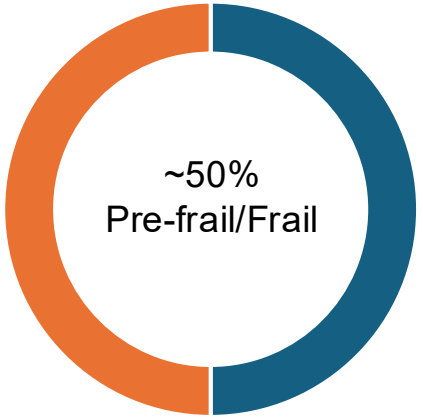
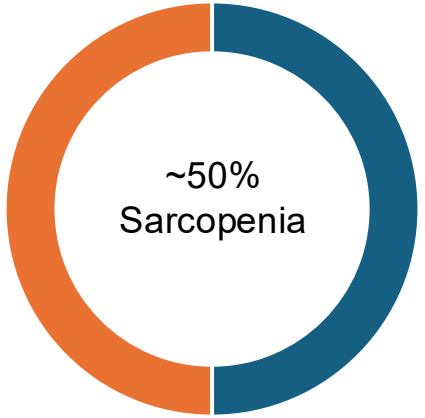
Frailty and Sarcopenia

- Increasingly recognised as important considerations in treatment planning for people with cancer
- Cancer therapies are significant stressors
  - Challenge physiologic reserves
- Affect people of all ages, but higher prevalence in older adults
- Increase risk of adverse outcomes





Ethun 2017, Sia 2025, Williams 2020

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Sarcopenia and adverse outcomes

859 patients with Acute Leukaemia or Myelodysplastic Syndrome treated with Allo-HCT:

- Independent predictor of non-relapse mortality (HR 1.58)
- Longer LOS (37.2 vs. 31.5 days, p<0.001)
- Lower overall survival at 2-years (65.2% vs. 66.9%, p<0.001)

Armenian et al., 2019

320 patients with Hodkin's Lymphoma or NHL treated with Auto-HCT:

- 2.0 higher odds longer LOS
- 3.7 higher odds ICU admission
- 6.4 higher odds unplanned readmission
- 2.5 higher odds all-cause mortality
- Odds even higher if sarcopenic obesity
  (adjusted for well established confounders)

Armenian et al., 2020

Frailty and adverse outcomes

136 patients receiving CAR-T for relapsed or refractory Multiple Myeloma:

- No difference in high grade toxicities
- Inferior efficacy outcomes (median survival 14 months in frail patients and not reached in non frail patients, p=0.028)

Davis et al., 2024

Systematic review of 16 studies in patients with AML treated with intensive systemic therapies:

- Worse overall survival (6 of 7 studies)
- Higher grade toxicity (1 study)
- Delayed neutrophil recovery (1 study)

Sia et al., 2025

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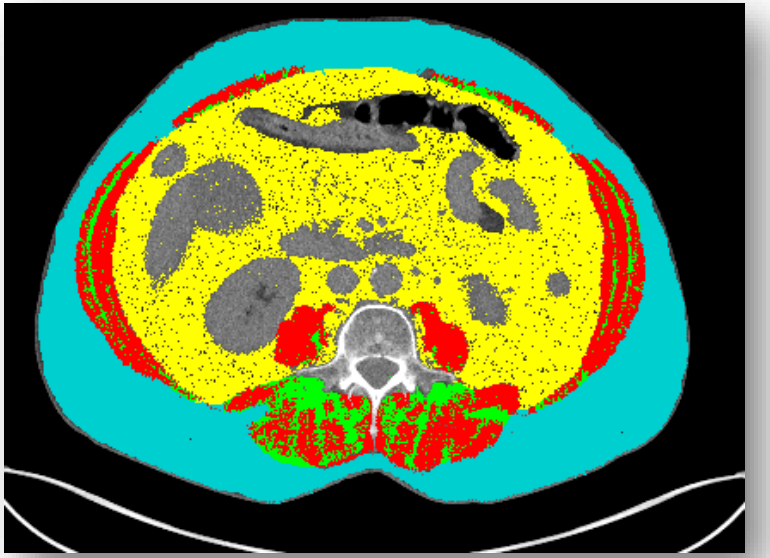
Table 1. 2018 operational definition of sarcopenia

Probable sarcopenia is identified by Criterion 1.
Diagnosis is confirmed by additional documentation of Criterion 2.
If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe.

(1) Low muscle strength
(2) Low muscle quantity or quality
(3) Low physical performance



Cruz Jentof et al., 2018

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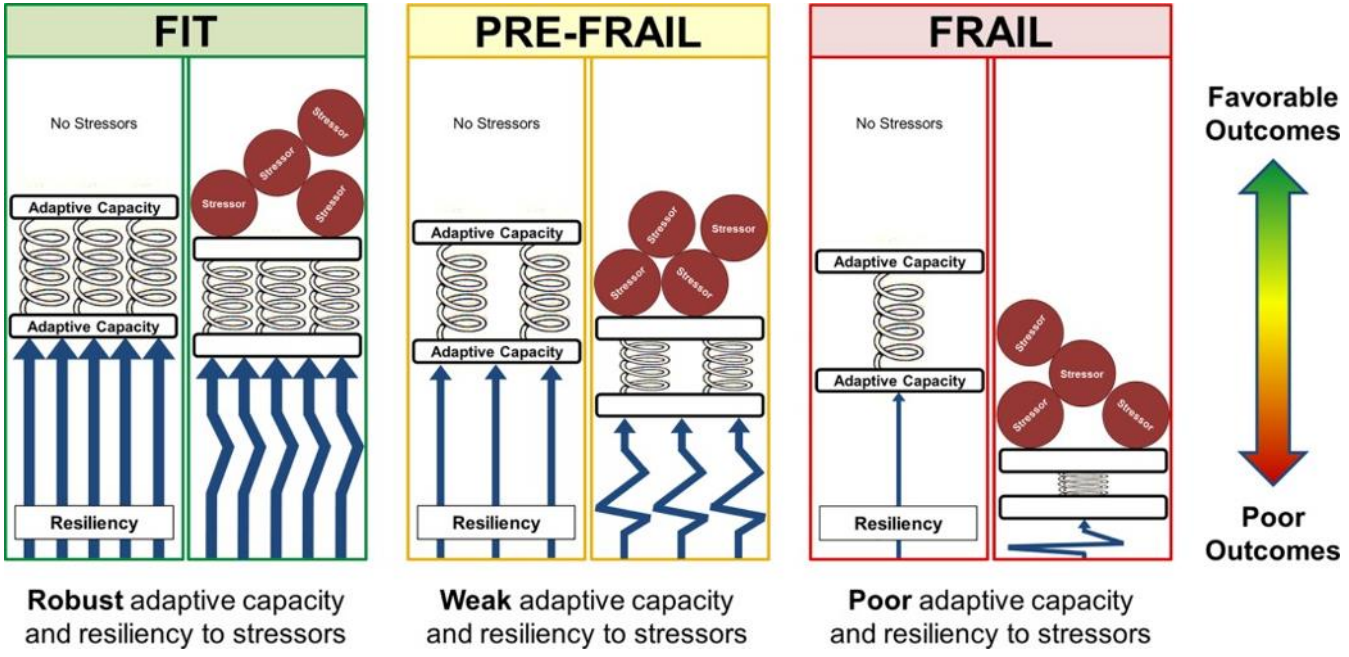

CA A Cancer J Clinicians, Volume: 67, Issue: 5, Pages: 362-377, First published: 21 July 2017, DOI: (10.3322/caac.21406)

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What are the opportunities to:

1. Better define risk
2. Support equitable access to TCT
3. Enable safer, individualized treatment decisions for older adults

Screening and Assessment

- Screening for sarcopenia and frailty may complement conventional methods for predicting patients at risk of adverse outcomes
  - Karnofsky Performance Score or ECOG
  - HCT comorbidity index
- Screening as a tool for risk stratification to:
  - Support clinicians to offer optimal and appropriate treatment intensity for an individual
  - Identify patients who require further assessment and potential intervention
  - Enable pathways to prehabilitation

OXFORD

JNCI: Journal of the National Cancer Institute, 2025, **117(7)**, 1316–1339
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Review

Frailty and outcomes in adults undergoing systemic anticancer treatment: a systematic review and meta-analysis

Jessica Pearce, MBBS[1,2,*], Sally Martin, MBChB, MSc[2], Sophie Heritage, MBBChir, MA[3], Emma G. Khoury, MRes, MBChB[4], Joanna Kucharczak, MBBChir, MA[5], Thitikorn Nuamek, MD[6], David A. Cairns, PhD[7], Galina Velikova, MD, PhD[1,2], Suzanne H. Richards, PhD[8], Andrew Clegg, MBBS, MD[9], Alexandra Gilbert, MBBS, PhD[1,2]

[1]Leeds Institute of Medical Research at St James's, University of Leeds, Leeds LS2 9JT, United Kingdom
[2]Leeds Institute of Oncology, Leeds Teaching Hospitals National Health Service Trust, Leeds LS9 7TF, United Kingdom
[3]Royal Papworth Hospital National Health Service Foundation Trust, Cambridge CB2 0AY, United Kingdom
[4]Academic Cancer Sciences Unit, University of Southampton, Southampton SO16 6YD, United Kingdom
[5]Department of Oncology, Cambridge University Hospitals, University of Cambridge, Cambridge CB2 0SP, United Kingdom
[6]Clinical Oncology, The Christie National Health Service Foundation Trust, Manchester M20 4BX, United Kingdom
[7]Leeds Cancer Research UK Clinical Trials Unit, University of Leeds, Leeds LS2 9JT, United Kingdom
[8]Leeds Institute of Health Sciences, University of Leeds, Leeds LS2 9NL, United Kingdom
[9]Academic Unit for Ageing and Stroke Research, Bradford Institute for Health Research, Bradford BD9 6RJ, United Kingdom

*Corresponding author: Jessica Pearce, MBBS, Patient Centred Outcomes Research Group (PCOR), Level 5, Clinical Sciences Building, St James' University Hospital, Beckett Street, Leeds LS9 7TF, United Kingdom (j.pearce@leeds.ac.uk).

- 58 studies, 9 frailty assessment tools evaluated
- 2 tools demonstrated prognostic value for survival, toxicity, treatment tolerance:
- Geriatic-8
- Vulnerable elders survey-13

Questions and possible answers (score)

Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
☐ 0: severe decrease in food intake ☐ 1: moderate decrease in food intake ☐ 2: no decrease in food intake

Weight loss during the last 3 months
☐ 0: weight loss > 3 kg ☐ 1: does not know ☐ 2: weight loss between 1 and 3 kgs ☐ 3: no weight loss

Mobility
☐ 0: bed or chair bound ☐ 1: able to get out of bed/chair but does not go out ☐ 2: goes out

Neuropsycholgical problems
☐ 0: severe dementia or depression ☐ 1: mild dementia or depression ☐ 2: no psychological problems

Body mass Index (BMI: weight in kg/height in m²)
☐ 0: BMI < 19 ☐ 1: BMI = 19 to BMI < 21 ☐ 2: BMI = 21 to BMI < 23 ☐ 3: BMI = 23 and > 23

Takes more than three medications per day
☐ 0: yes ☐ 1: no

In comparison with other people of the same age, how does the patient consider his/her health status?
☐ 0: not as good ☐ 0.5: does not know ☐ 1: as good ☐ 2: better

Age
☐ 0: > 85 ☐ 1: 80-85 ☐ 2: < 80

Total score (0-17)

Age

Score = 1 point for age 73-84, 3 points for age ≥ 85

In general compared to other people your age, would you say your health is:

☐ Poor ☐ Fair ☐ Good ☐ Very good ☐ Excellent

Score = 1 point for fair or poor

How much difficulty on, *average*, do you have with the following activities:	No difficulty	A little difficulty	Some difficulty	A lot of difficulty	Unable to do
a. Stooping, crouching or kneeling?	☐	☐	☐	☐	☐
b. Lifting or carrying objects as heavy as 4.5 kg?	☐	☐	☐	☐	☐

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TABLE. The Simple "SARC-F" Sarcopenia Questionnaire (0-10 points)[3]

Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the last year?	None = 0 1-3 falls = 1 4 or more falls = 2

SARC-F with calf circumference independent prognostic ability in haematology (HR 2.37)
However, low sensitivity for detecting low muscle mass in people with cancer

da Anunciacao et al., 2025

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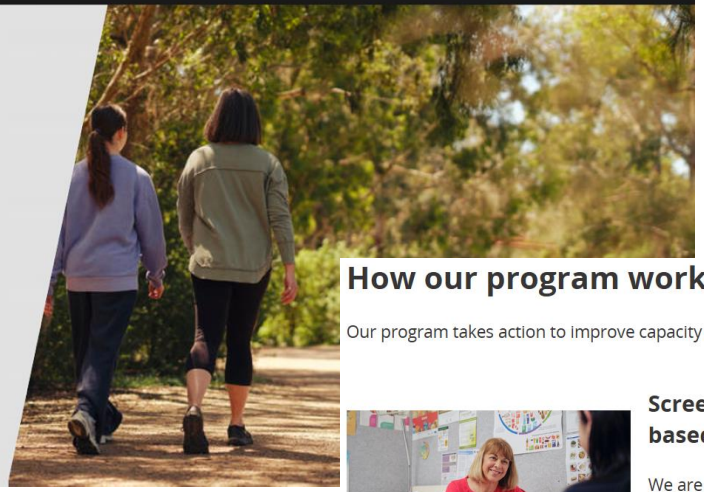
Establishing Pathways to Improved Care for Cancer-related Sarcopenia



Improving access to the right care at the right time

We aim to improve access to quality care for cancer-related low muscle mass (sometimes referred to as sarcopenia) and enhance treatment outcomes for individuals with low muscle mass across Australia.

How our program works

Our program takes action to improve capacity for cancer treatment, leading to better cancer outcomes.

Screening tool and referral pathway to evidence-based care

We are developing and validating a short and simple screening tool to identify people with cancer at risk of low muscle mass and referral pathways to overcome barriers to accessing timely nutrition and exercise care.

URL: deakin.edu.au/epiccs

Transforming care within cancer services

In a stepped wedge trial at 4 rural and specialist cancer centres across Australia, the screening tool and referral pathway will be embedded in clinical practice to assess the impact on access to care, the workforce, clinical outcomes and health care costs.

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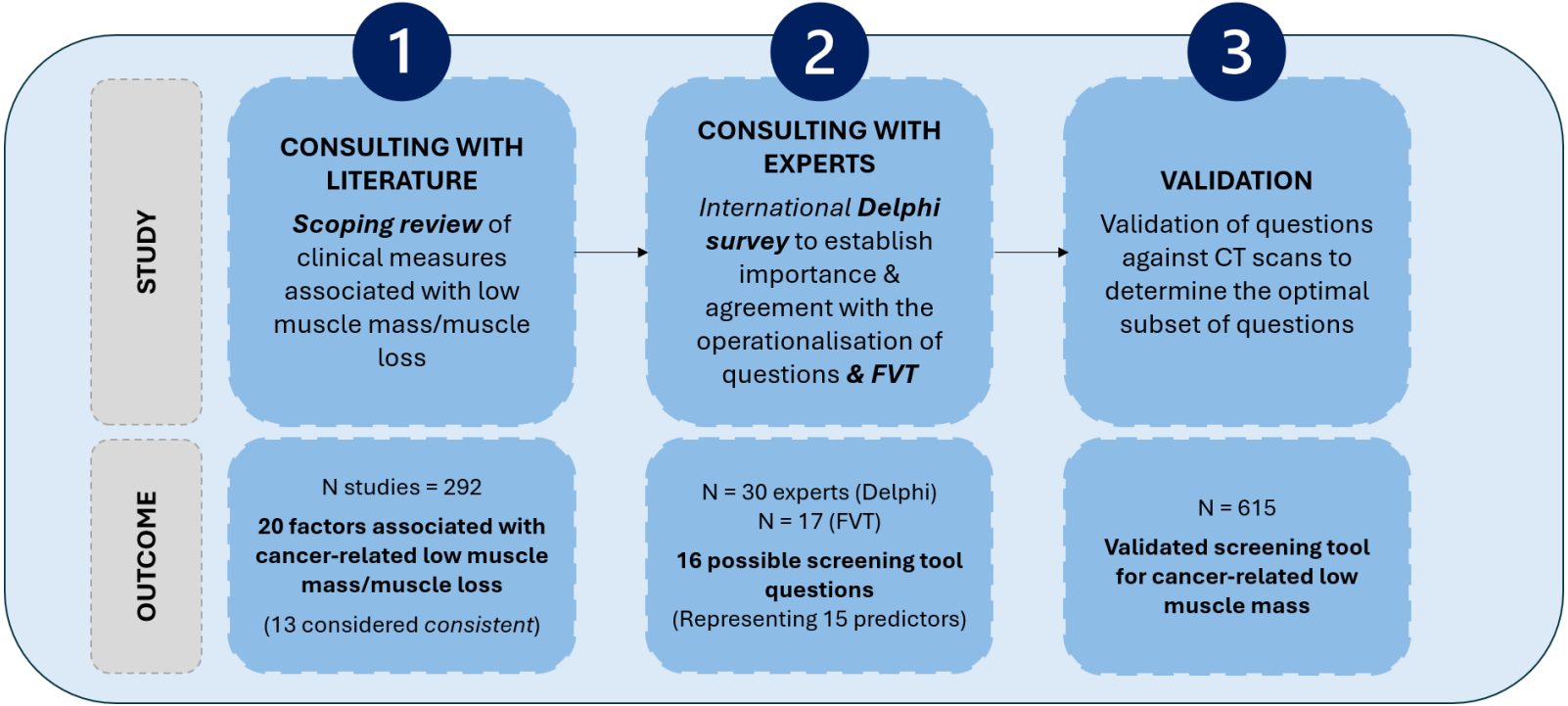
Developing the screening tool (M-Screen)



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Assessment

- Evidence from systematic review of 61 studies that frailty assessment reduces toxicity, improves treatment completion and QoL
- Well established that low muscle mass is associated with dose limiting treatment toxicities and earlier termination of treatment.
- COSA position statement and toolkit https://cancermalnutritionandsarcopenia.org.au/

Hamaker et al 2022, Surov et al., 2021, Palmela et al., 2017

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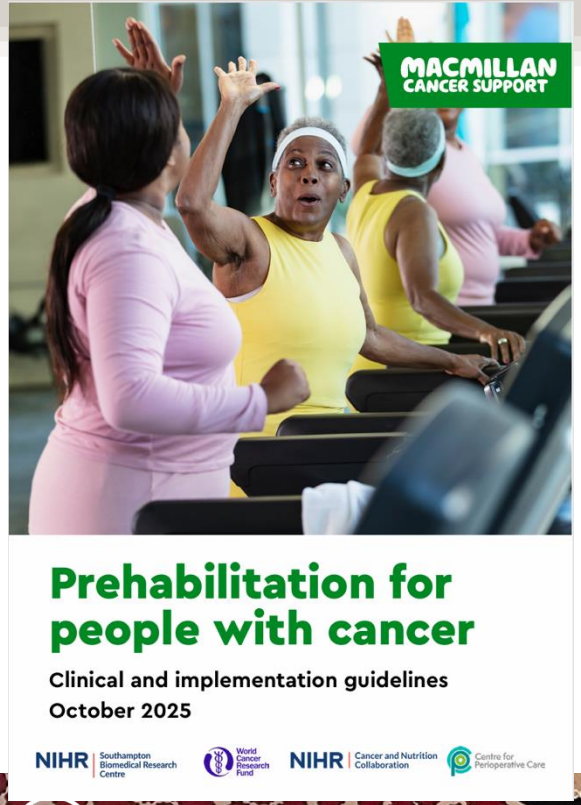
Considering prehabiliation and rehabilitation



Denehy et al. BMC Cancer (2025) 25:532
https://doi.org/10.1186/s12885-025-13898-3

BMC Cancer

STUDY PROTOCOL Open Access

Rehabilitation after bone marrow transplant compared with usual care to improve patient outcomes (REBOOT): protocol for a randomised controlled trial

Linda Denehy[1,2,3*], Shaza Abo[1,4], Christopher Swain[1], Camille E. Short[1,5], Nicole Kiss[6], Amit Khot[3,7], Eric Wong[8], Duncan Purtill[9,10], Clare O'Donnell[11], Marlena Klaic[12], Catherine L. Granger[1], Michelle Tew[13], Tim Spelman[2], Vinicius Cavalheri[14,15†], Lara Edbrooke[1,2,3†] and on behalf on the REBOOT research team

Abstract

Background Haematological cancer affects more than 1.3 million people around the world annually and accounted for almost 800,000 deaths globally in 2020. The number of patients with these cancers undergoing bone marrow transplant is increasing. Of note, this intensive treatment is associated with complex and multifactorial side effects, often impacting nutritional status, physical functioning and overall health-related quality of life. The primary aim of this study is to investigate the effectiveness of an eight-week multidisciplinary rehabilitation intervention compared with usual care on the physical function domain of the European Organisation for the Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30 version 3) in patients with haematological cancer following bone marrow transplant.

Methods This is a multisite, pragmatic two-arm parallel-group, randomised controlled trial (RCT) with stratified randomisation, powered for superiority, recruiting 170 participants at 30 days following either allogeneic or autologous bone marrow transplant (ACTRN12622001071718). Recruitment sites include three Australian university affiliated teaching hospitals. Participants are eligible if aged ≥ 18 years, treated for haematological cancer with allogeneic or autologous bone marrow transplant and can walk independently. The intervention group will receive eight weeks of twice weekly telehealth-based exercise classes, an initial and follow up dietetics consult, post exercise protein supplements, and a home-based physical activity program, all with embedded behaviour change strategies. The primary outcome is patient reported physical function measured using the EORTC QLQ-C30 version 3. Secondary outcomes include other domains of the EORTC QLQ-C30, fatigue, physical function, physical activity levels, frailty, body composition, sarcopenia and nutrition assessment. We will also undertake a health economic analysis alongside the trial and a process evaluation exploring intervention fidelity, causal mechanisms as well as contextual influences through qualitative enquiry.

†Vinicius Cavalheri and Lara Edbrooke are joint senior authors and contributed equally to this work.
*Correspondence:
Linda Denehy
ldenehy@unimelb.edu.au
Full list of author information is available at the end of the article

nutrients MDPI

Systematic Review

Nutritional Prehabilitation Intervention in Hematological Patients Undergoing Bone Marrow Transplant: A Systematic Review of the Literature

Luca Falcone [1], Stefano Mancin [1,2], Elena Azzolini [1,2], Francesco Colotta [1], Sergio Ferrante [2], Manuela Pastore [2], Sara Morales Palomares [3], Diego Lopane [1,2], Marco Sguanci [4], Simone Cosmai [1], Daniela Cattani [1,2], Emanuele Cereda [5,*], Riccardo Caccialanza [5] and Beatrice Mazzoleni [1]

[1] Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, Pieve Emanuele, 20090 Milan, Italy; luca.falcone@st.hunimed.eu (L.F.); stefano.mancin@humanitas.it (S.M.); elena.azzolini@humanitas.it (E.A.); francesco.colotta@humanitasresearch.it (F.C.); diego.lopane@hunimed.eu (D.L.); simone.cosmai@hunimed.eu (S.C.); daniela.cattani@humanitas.it (D.C.); beatrice.mazzoleni@hunimed.eu (B.M.)
[2] IRCCS Humanitas Research Hospital, Via Manzoni 56, Rozzano, 20089 Milan, Italy; sergio.ferrante@grupposandonato.it (S.F.); manuela.pastore@humanitas.it (M.P.)
[3] Department of Pharmacy, Health and Nutritional Sciences (DFSSN), University of Calabria, 87036 Rende, Italy; sara.morales@unical.it
[4] A.O. Polyclinic San Martino Hospital, Largo R. Benzi 10, 16132 Genova, Italy; marco.sguanci@unicampus.it
[5] Clinical Nutrition and Dietetics Unit, Fondazione IRCCS Policlinico San Matteo, 27100 Pavia, Italy; r.caccialanza@smatteo.pv.it
* Correspondence: e.cereda@smatteo.pv.it

Abstract: Background: Nutritional interventions play a critical role in bone marrow transplant (BMT) patients. This review evaluates the effectiveness of nutritional strategies in mitigating post-transplant malnutrition and improving clinical outcomes. Methods: A systematic review was conducted using PubMed, CINAHL, Cochrane Library, and Embase. The search terms included "bone marrow transplant", "malnutrition", and "preoperative nutritional interventions". The quality of studies and risk of bias were assessed using the JBI framework, while evidence certainty was evaluated with the Oxford OCEBM. Results: Six studies were included (n = 3545 screened). The studies demonstrated predominantly high methodological quality and a low risk of bias, although heterogeneity in the treatments investigated and small sample sizes limited the evidence. Nutritional interventions significantly increased energy intake (26 vs. 24 kcal/kg/day, $p = 0.038$) and improved body weight (25% vs. 9%) with protein supplementation. Clinical complications decreased, including severe acute graft-versus-host disease (17.1% vs. 43.4%, $p = 0.001$) and pneumonia (27.6% vs. 52.7%, $p = 0.002$). The length of hospital stay (27 vs. 32 days, $p = 0.006$) and the need for parenteral nutrition (53% vs. 62%, $p = 0.03$) were also reduced. Overall survival improved with ≥50% adherence to prescribed TGF-beta2 intake (33 vs. 25.1 months, $p = 0.03$). Conclusions: Nutritional prehabilitation shows promise in improving BMT outcomes. Standardized nutritional programs could optimize care, although limitations in current evidence are clearly present. Larger randomized studies are needed to confirm findings and refine pre-transplant protocols.

check for updates

Citation: Falcone, L.; Mancin, S.; Azzolini, E.; Colotta, F.; Ferrante, S.; Pastore, M.; Morales Palomares, S.; Lopane, D.; Sguanci, M.; Cosmai, S.; et al. Nutritional Prehabilitation Intervention in Hematological Patients Undergoing Bone Marrow Transplant: A Systematic Review of the Literature. *Nutrients* **2024**, *16*, 4387. https://doi.org/10.3390/nu16244387

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Keywords: bone marrow transplantation; nutrition; prehabilitation; systematic review

1. Introduction

Cancer is one of the leading causes of mortality worldwide and remains a significant challenge in both the medical and healthcare fields. Hematological cancers account for approximately 6.5% of all cancer cases [1].

When conventional treatments prove ineffective or unsuitable, hematopoietic stem cell transplantation (HSCT) emerges as an advanced and complex therapeutic option for

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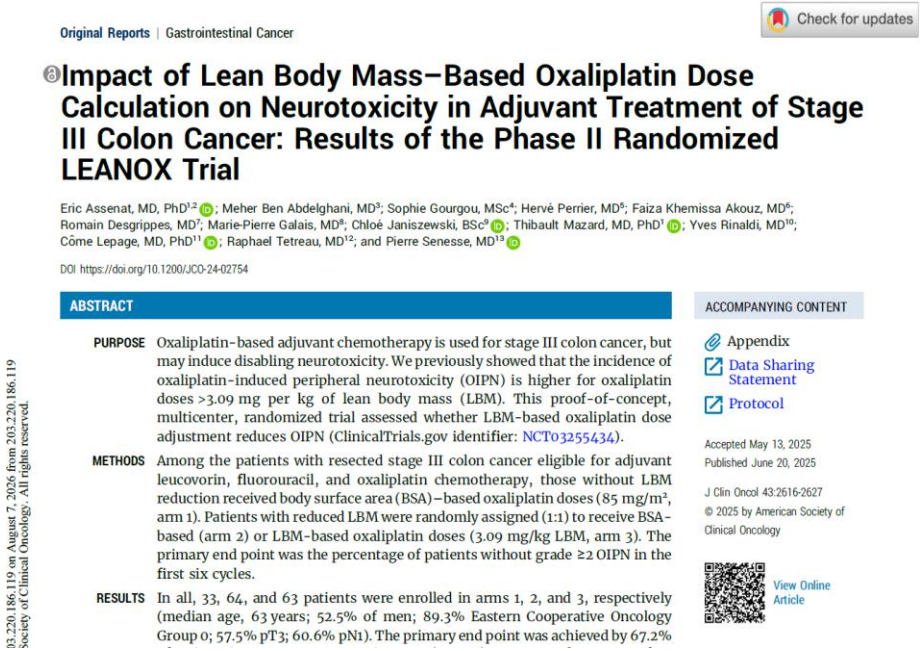
Future opportunities



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Impact of Lean Body Mass–Based Oxaliplatin Dose Calculation on Neurotoxicity in Adjuvant Treatment of Stage III Colon Cancer: Results of the Phase II Randomized LEANOX Trial

Eric Assenat, MD, PhD[1,2]; Meher Ben Abdelghani, MD[3]; Sophie Gourgou, MSc[4]; Hervé Perrier, MD[5]; Faiza Khemissa Akouz, MD[6]; Romain Desgrippes, MD[7]; Marie-Pierre Galais, MD[8]; Chloé Janiszewski, BSc[9]; Thibault Mazard, MD, PhD[1]; Yves Rinaldi, MD[10]; Côme Lepage, MD, PhD[11]; Raphael Tetreau, MD[12]; and Pierre Senesse, MD[13]

DOI https://doi.org/10.1200/JCO-24-02754

ABSTRACT

PURPOSE Oxaliplatin-based adjuvant chemotherapy is used for stage III colon cancer, but may induce disabling neurotoxicity. We previously showed that the incidence of oxaliplatin-induced peripheral neurotoxicity (OIPN) is higher for oxaliplatin doses >3.09 mg per kg of lean body mass (LBM). This proof-of-concept, multicenter, randomized trial assessed whether LBM-based oxaliplatin dose adjustment reduces OIPN (ClinicalTrials.gov identifier: NCT03255434).

METHODS Among the patients with resected stage III colon cancer eligible for adjuvant leucovorin, fluorouracil, and oxaliplatin chemotherapy, those without LBM reduction received body surface area (BSA)–based oxaliplatin doses (85 mg/m², arm 1). Patients with reduced LBM were randomly assigned (1:1) to receive BSA-based (arm 2) or LBM-based oxaliplatin doses (3.09 mg/kg LBM, arm 3). The primary end point was the percentage of patients without grade ≥2 OIPN in the first six cycles.

RESULTS In all, 33, 64, and 63 patients were enrolled in arms 1, 2, and 3, respectively (median age, 63 years; 52.5% of men; 89.3% Eastern Cooperative Oncology Group 0; 57.5% pT3; 60.6% pN1). The primary end point was achieved by 67.2%

ACCOMPANYING CONTENT

Appendix

Data Sharing Statement

Protocol

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J Clin Oncol 43:2616-2627

View Online Article

- Sarcopenia (low muscle mass) well known to lead to dose limiting treatment toxicities
- First study to compare dosing using BSA to LBM
- Using LBM-based oxaliplatin dose significantly reduced peripheral neurotoxicity and improved quality of life without affecting relapse-free survival and OS.

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Equitable access and informed treatment decisions

- Screen and assess for frailty and sarcopenia to support risk stratification beyond current conventional considerations
- Refer patients to prehabilitation who could benefit prior to treatment
- Rescreen and assess after treatment to determine who could benefit from rehabilitation
- Further opportunities for research:
  - Evaluation and implementation of risk stratification pathways informed by frailty and sarcopenia screening in TCT
  - Building on current prehabilitation and rehabilitation studies
    - How best to implement and deliver for people treated with TCT
  - Individualised dosing based on body composition

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