PROPEL: PeRsOnalised PrEhabilitation in acute myeloid Leukaemia

PeRsOnalised PrEhabilitation in AML

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ABSTRACT

Introduction: Treatment for Acute Myeloid Leukaemia (AML) requires multiple courses of intense chemotherapy, often with stem cell transplant (SCT); resultant fatigue is debilitating. Prehabilitation (supportive care interventions such as exercise, nutrition, psychological wellbeing) may improve fatigue, easing treatment completion

Methods: To inform a trial of multiphasic, multimodal personalised prehabilitation (MMPP), a scoping review of supportive-care interventions delivered to adults with AML undergoing treatment (induction or consolidation chemotherapy, +/- SCT), was completed. Two surveys were conducted to capture, i) stakeholder perceptions on haematology centre capacity and deliverability of prehabilitation and ii) awareness and access to prehabilitation services for persons with AML.

Results: 36 trials addressing a range of interventions were identified, only one incorporated prehabilitation (exercise-only prior to SCT). Studies were small, testing one component of prehabilitation, with variability of outcomes and timing of interventions. Seventy healthcare professionals and 43 people with AML responded to the survey which confirmed the need for better support, with no UK hospitals having systematic access to MMPP in standard practice.

Conclusions: There is a lack of prehabiliation services in the UK and an urgent need to establish the benefit of MMPP, on fatigue, emotional wellbeing and quality of life, in people receiving remission consolidation treatment for AML

INTRODUCTION

Acute myeloid leukaemia (AML) is the most common acute leukaemia; 5-year survival in adults is around 20% (1).

Treatment aimed at cure requires multiple courses of intensive chemotherapy and may include haemopoietic stem cell transplant (HSCT). Cancer related fatigue is a universal feature and persistent symptomatic burden for people with AML (2); it may be associated with states of anorexia, cachexia and sarcopenia (3), impacting recovery and wellbeing and a prognostic marker for poorer outcomes and shorter survival (2).

Prehabilitation aims to enhance general health and wellbeing prior to major treatments to enable completion of treatments (4).

Prehabilitation may improve fatigue and result in physical and psychological resilience, enabling completion of treatment courses, yet is not formally offered in the NHS. Uncertainty remains on the impact of prehabilitation for people with AML.

METHODS AND MATERIALS

Due to the lack of prehabilitation services in the UK and in response to a UK government research call for prehabilitation studies in cancer, we designed a RCT to determine if prehabilitation can improve functional outcomes and maximise completion of all intensive consolidation courses for patients with AML, including planning for HSCT.

To inform the development of the multiphasic, multimodal personalised prehabilitation (MMPP) intervention, a scoping review of supportive-care interventions delivered to adults with AML undergoing treatment (induction or consolidation chemotherapy, +/- SCT), was completed.

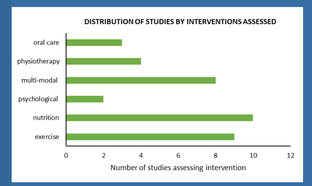
In addition, two surveys were conducted to capture, i) stakeholder perceptions on haematology centre capacity and deliverability of prehabilitation and ii) awareness and access to prehabilitation services for persons with AML.

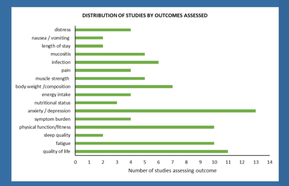
RESULTS

SCOPING REVIEW

Whilst identifying 36 RCTs addressing a range of supportive care interventions, only one trial incorporated prehabilitation as an exercise-only preparation phase and this was prior to HSCT (x). Most of the included trials tested an individual component, with nutrition being the most common intervention (10 trials), and not as an integrated prehabilitation package. All bar one of the included trials were small (≤100 patients); none were sufficiently powered to demonstrate (cost-) effectiveness.

There was variability in outcomes measured (16 outcomes reported in two or more studies) and considerable heterogeneity in the nature and timing of the interventions.





UK SURVEY

Seventy healthcare professionals and 43 people with AML responded to the survey which confirmed the need for better support, with no UK hospitals having systematic access to MMPP in standard practice and all willing to participate in PROPEL.

DISCUSSION

The findings of the scoping review support the efficacy of our PPCP intervention components addressing fatigue and provides evidence that individual components of multimodal interventions can be successfully delivered in the AML population. Only one study included prehabilitation, yet data increasingly supports a role for prehabilitation in the cancer setting.

A multiphase prehabilitation approach may be needed by many individuals with cancer to prepare for subsequent treatments such as chemotherapy (5), and evidence in early-stage breast cancer suggests that higher baseline (pre-chemotherapy) cardiovascular fitness and muscular strength may be associated with higher rates of chemotherapy completion (6). This supports the potential utility of multiphase, multimodal prehabilitation in AML management.

THE PROPEL TRIAL

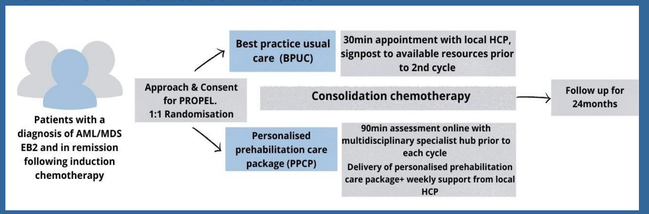
We have received NIHR funding to conduct a large pragmatic RCT to determine if prehabilitation interventions can improve functional outcomes and maximise completion of all intensive consolidation courses for patients, including planning for haemopoietic stem cell transplantation (HSCT), thereby potentially resulting in better treatment outcomes for people with AML and value for money for the NHS.

Aim: To establish the clinical impact and cost-effectiveness of best practice usual care (BPUC) compared to a multiphasic, multimodal personalised prehabilitation care package (PPCP) on fatigue, emotional wellbeing and quality of life (QoL) in patients receiving remission consolidation treatment for AML or high-risk myelodysplastic syndromes with excess blasts (MDS-EB2).

Design: Multicentre, open-label 1:1 randomised controlled trial comparing BPUC (best practice usual care) with PPCP (personalised prehabilitation care package) incorporating a 12-month internal pilot, parallel process evaluation and economic evaluation

Recruitment target: 600 patients over a period of 30months. First patient first visit (FPFV) expected early 2023.

Number of UK centres: 50 NHS sites



REFERENCES

1. *Burnett AK, Russell NH, Hills RK, Knapper S, Freeman S, Huntly B, et al. Defining the Optimal Total Number of Chemotherapy Courses in Younger Patients With Acute Myeloid Leukemia: A Comparison of Three Versus Four Courses. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2021;39(8):890-901.*
2. *Lacourt TE, Kavelaars A, Ohanian M, Shah ND, Shelburne SA, Futreal A, et al. Patient-reported fatigue prior to treatment is prognostic of survival in patients with acute myeloid leukemia. Oncotarget. 2018;9(58):31244-52.*
3. *Dunne RF, Loh KP, Williams GR, Jatoi A, Mustian KM, Mohile SG. Cachexia and Sarcopenia in Older Adults with Cancer: A Comprehensive Review. Cancers (Basel). 2019;11(12).*
4. *Macmillan Cancer Support. Prehabilitation for People with Cancer2020 10th March 2021. Available from: https://cdn.macmillan.org.uk/dfsmedia/1a6f23537f7f4519bb0cf14c45b2a629/1532-source/prehabilitation-for-peoplewith-cancer-tcm9-353994?_ga=2.117808841.1392116525.1614958821-1231098844.1592907207.*
5. *Santa Mina D, van Rooijen SJ, Minnella EM, Alibhai SMH, Brahmbhatt P, Dalton SO, et al. Multiphasic prehabilitation across the cancer continuum: a narrative review and conceptual framework. Front Oncol. 2021; 10: 598425.*
6. *An K-Y, Arthuso FZ, Kang D-W, Morielli AR, Ntoukas SM, Friedenreich CM, et al. Exercise and health-related fitness predictors of chemotherapy completion in breast cancer patients: pooled analysis of two multicenter trials. Breast Cancer Res Treat. 2021.*