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**METABOLOMIC PROFILE OF HEALTHY DIETARY PATTERNS
ASSOCIATED WITH FRAILITY IN ADULT HUMANS**

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ABSTRACT

INTRODUCTION

Frailty, as defined by the WHO, is a condition characterized by diminished physical and physiological reserves, increasing vulnerability to adverse health outcomes. As global life expectancy rises, frailty becomes a critical public health concern. Recent research indicates that healthy dietary patterns, such as the Mediterranean Diet (MD), rich in polyphenols with antioxidative and anti-inflammatory properties, are associated with a reduced risk of frailty. Metabolomics, through metabotyping, can identify metabolic profiles or signatures related to specific diseases or complex conditions like frailty. Establishing these metabolic profiles can help detect individuals at higher risk of developing frailty, and it is a step towards personalized nutrition at the group level by classifying individuals with similar metabotypes.

HYPOTHESIS AND OBJECTIVES

The hypothesis is that specific metabolic signatures associated with healthy dietary patterns mediate the relationship between dietary patterns and frailty. Consequently, these metabolic signatures may aid in identifying individuals at higher risk of developing pre-frailty and progressing to frailty.

This study has two primary objectives: The first is to conduct a systematic review of existing data on the mediating role of metabolites in the relationship between healthy dietary patterns and frailty. This review serves as a preparatory phase for the NUTRIFRAIL study.

The second objective is to summarize and describe the baseline characteristics of the NUTRIFRAIL cohort study population after the first year, comparing the robust and pre-frail groups to identify preliminary findings or emerging trends.

MATERIALS AND METHODS

This study consists of two separate but interconnected parts. The first part is a systematic review that serves as a preparatory stage for the NutriFrail cohort study. The second part is a descriptive study of the baseline characteristics of the NutriFrail cohort after the first year.

The systematic review of the literature was performed by searching MEDLINE (PubMed) and Google Scholar (the first 20 pages – 200 relevant articles) from May 2024 to June 2024. Studies with observational and randomized controlled designs were included. Studies had to involve human participants, both males and females, and focus on elderly individuals with an average age of 60 years or older. The studies had to evaluate the consumption of, or adherence to, clearly defined dietary patterns, including information on the frequency of consumption, involve the detection of metabolomic biomarkers associated with these dietary patterns, and consider frailty or pre-frailty as the primary outcome, with a clear definition of frailty and description of the assessment methods used.

Additionally, studies had to investigate the correlation between biomarkers or metabolic profiles (signatures), dietary patterns, and frailty status.

A portion of this section has been concealed due to the confidential character of this work.

RESULTS

The findings indicate that adherence to healthy dietary patterns, such as the Mediterranean Diet Score (MDS), Alternative Healthy Eating Index (AHEI), and Mediterranean-DASH Diet Intervention for Neurodegenerative Delay (MIND), is negatively associated with frailty. High-quality diets, indicated by higher levels of scores like the Revised Food Score (RFS), and specific dietary components, including high intake of plant protein, fruits, and vegetables, are also linked to a reduced risk of frailty. Conversely, a high Dietary Inflammatory Index (DII) score is associated with an increased risk of frailty. Moreover, the review found that several metabolites are positively correlated with healthy dietary patterns, such as docosahexaenoic acid (DHA) with RFS, aMED, MIND, and DASH, and various triglycerides and phosphatidylcholine metabolites with MDS, AHEI, and MIND. Higher consumption of plant protein is associated with elevated levels of tryptophan betaine and indole-3-propionic acid. Additionally, higher consumption of fruits and vegetables is associated with increased levels of hippuric acid. Conversely, other metabolites, including glycoprotein acetyls, monounsaturated fatty acids (MUFA), and saturated fatty acids (SFA), show negative associations with these dietary patterns. Finally, the review concludes that metabolic signatures significantly mediate the relationship between diet and frailty.

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CONCLUSIONS

Certain dietary patterns have an inverse association with frailty. Metabolomics allows for the creation of metabolomic signatures of these dietary patterns. These MSs may mediate the relationship between dietary patterns and frailty, suggesting that it might be possible to use metabolomic signatures for metabotyping and identifying certain metabotypes more prone to frailty. This represents a step towards both personalized and group-based nutrition and management of frailty.

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