

# Adherence to Mediterranean Diet and Nutritional Status: Impact on Clinical Outcomes in Hospitalized Elderly Patients

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## Article Info

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## Abstract

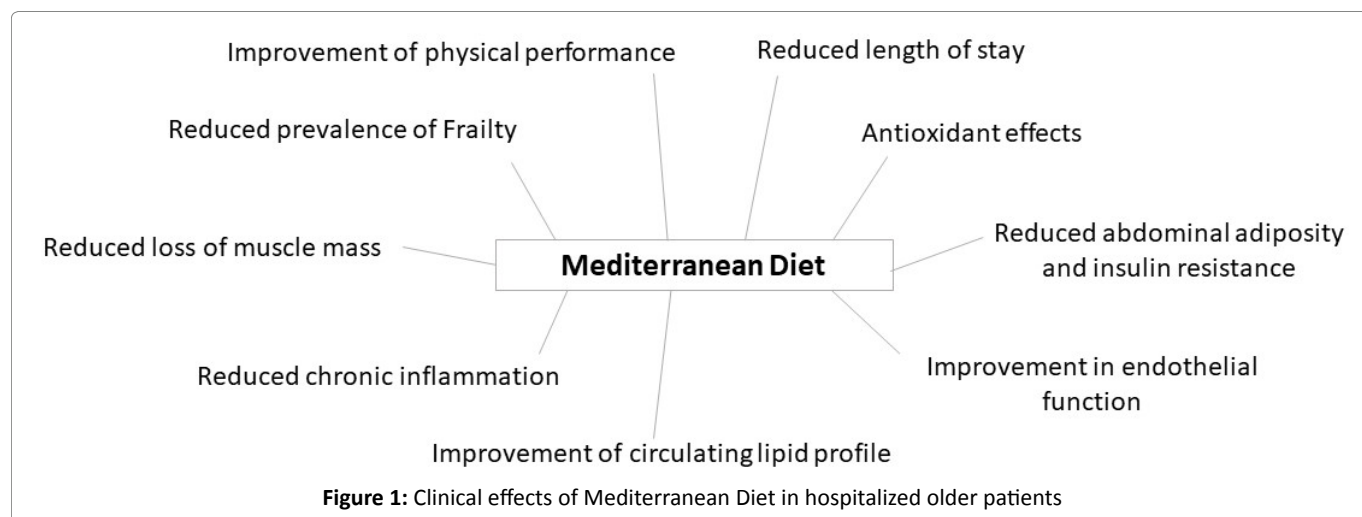
Malnutrition is associated to poor clinical outcomes, especially in hospitalized patients. High prevalence of low-grade chronic inflammation, low skeletal muscle mass, and insulin resistance are often found in malnourished patients. Increasing evidence shows how these effects can be partially reverted through an adequate intake of food or using specific dietary supplementation. In this scenario, Mediterranean Diet (MD) demonstrated positive effects on the nutritional status, with important clinical finding in hospitalized patients such as low rate of length of stay and in-hospital mortality.

The aim of this review is the summary of the main evidence about the role of Mediterranean diet on health and clinical outcomes in hospitalized elderly patients.

## Introduction

Aging is characterized by higher prevalence of several condition such as malnutrition, comorbidities, changes in body composition and chronic low grade inflammation<sup>1-4</sup>. A strong association exists between malnutrition and systemic inflammation. Most conditions that require hospitalization in acute wards are associated with a pro-inflammatory state. This can promote a reduction in both appetite and calorie intake, with an increased risk of malnutrition. On the other hand, malnourished patients are characterized by chronic inflammation<sup>5,6</sup>. Important changes are observed in body composition during aging and malnutrition. Indeed, aging is characterized by progressive loss of muscle mass associated to increase in fat mass<sup>7</sup>. Adipose tissue tends to accumulate at the visceral level, promoting insulin resistance and high levels of circulating pro-inflammatory cytokines<sup>5,8</sup>. Malnutrition induces loss of skeletal muscle mass, with similar effects to those of aging on both the metabolic and the inflammatory status<sup>9-12</sup>. Lifestyle exerts an important effect on quality of aging<sup>13,14</sup>.

Mediterranean Diet (MD) is characterized by a high intake of vegetables, fruits, cereals, legumes and nuts, with extra-virgin olive oil as the main source of fat. MD also includes moderate consumption of fish, white meats, and eggs. Conversely, foods such as red meat and processed meat, and foods high in sugar and fat contents are consumed less frequently<sup>5,15,16</sup>. MD exerts several positive effects on serum lipoprotein levels, endothelium vasodilatation, insulin resistance, metabolic syndrome, antioxidant capacity, inflammation, and coagulation markers (Figure 1)<sup>17,18</sup>. Such evidence could justify how MD associates with a lower mortality from all causes, and a lower incidence of several chronic diseases such as obesity, type



2 diabetes, neurodegenerative disease and certain type of cancer<sup>5,16</sup>. However, the exact mechanisms through which MD exerts its beneficial effects is not known<sup>19</sup>. The increased consumption with MD of dried fruit rich in omega-6 and omega-3 fatty acid and plant sterols could play an important role in reducing LDL-cholesterol levels and coronary heart disease risk<sup>19</sup>. The high vegetable fiber content also appears to contribute to lowering of circulating LDL cholesterol levels through a reduction in intestinal reabsorption of cholesterol and bile acids<sup>20</sup>. Several nutrients from a range of diverse foods appear to have synergistic and interactive role on inflammatory state, as shown by several studies<sup>19,21,22</sup>. This evidence has been confirmed in the NU-AGE (European Project on Nutrition in Elderly People) study, where lower plasma level of inflammatory markers was associated with high adherence to comprehensive Mediterranean diet strategy<sup>23</sup>. The low energy intake consequent to satiety induced by inhibiting gastric emptying by intestinal hormones may contribute to reduce the incidence of obesity, insulin resistance, and cancer rate<sup>19</sup>. In this scenario, MD plays a central role in the healthy aging process. In fact, increasing evidence shows correlation between MD and higher longevity, with a delayed onset of health problems<sup>24,25</sup>. Several studies showed the role of nutritional supplements in malnourished patients on different clinical outcomes. Some studies also investigated nutritional intervention strategies in hospitalized patients. In the NOURISH (Nutrition effect On Unplanned Readmissions and Survival in Hospitalized patients) study, a multicentre and randomized trial, oral implementation with beta-hydroxy-beta-methylbutyrate was associated with a lower rate of 90-day mortality compared to placebo group. In the EFFORT (The Effect of Higher Protein Dosing in Critically Ill Patients) trial, an individualized nutritional support led to significantly lower incidence of severe complications and mortality compared to standard hospital food<sup>26-28</sup>. Among individuals aged 70-90 years, adherence to a MD and healthful lifestyle led to

more than 50% lower rate of all-causes and cause-specific mortality<sup>29</sup>. Furthermore, in the PREDIMED (in Spanish: PREvención con DIeta MEDiterránea) trial, Mediterranean diet supplemented with extra-virgin olive oil or with mixed nuts was associated with a reduced risk of cardiovascular and metabolic diseases by about 30% over five years<sup>28,30</sup>. The aim of this review is the summary of the main evidence about the role of Mediterranean diet on health and clinical outcomes in hospitalized elderly patients.

### Mediterranean diet and inflammation

In our recent work, we found significant differences on clinical and biochemical parameters as well as clinical outcomes between hospitalized older patients who are adherent to MD and those who are not<sup>5</sup>. Adherence to MD was assessed by the Italian Mediterranean Index, and patients were classified into tertiles, the lowest indicating the worst adherence to MD. The mean age was higher in Tertile II and III compared to Tertile I, whereas haemoglobin, lymphocytes, serum albumin and total cholesterol levels were lower in Tertile I and II with respect to Tertile III<sup>5</sup>. Bach-Faig A. et al. showed how high adherence to MD is associated with high plasma concentrations of  $\beta$ -carotene, folates, vitamin C,  $\alpha$ -tocopherol and HDL cholesterol<sup>31</sup>. Data about serum total cholesterol are different among studies<sup>5,32-34</sup>. High adherence to MD showed association with reduction in serum markers of inflammation such as C-reactive protein (CRP), as well as circulating cytokines, increased serum adiponectin levels<sup>6</sup>. However, other studies did not show any significant effect of MD on circulating cytokine levels<sup>35-37</sup>. With respect to patients with low MD adherence, we found lower serum levels of Neutrophil Lymphocyte Ratio (NLR), erythrocyte sedimentation rate (ESR), CRP and ferritin, as well as Interleukin 6 (IL-6) and Tumor Necrosis Factor (TNF) in patients with high adherence to MD<sup>5</sup>. The association between insulin resistance and poor adherence to MD was also demonstrated. Evidence suggests a link between high adherence to the Mediterranean diet

and reduction of abdominal obesity, insulin resistance, and systemic inflammation<sup>38,39</sup>.

### **Effect of Mediterranean diet on body composition, sarcopenia, frailty, and functional autonomy**

MD also impacts on body composition. In fact, adherence to MD was associated with reduced weight gain and reduced increase in waist circumference in young people, as well as with lower total and regional adiposity in aged women<sup>40-42</sup>. In the elderly, physical function and muscle strength are also improved by physical activity (i.e. resistance training). Moreover, growing evidence suggests that physical activity improves serum inflammatory markers<sup>43-45</sup>. Body composition may also change with exercise, showing an increase in fat free mass and a reduction in adipose depots<sup>46</sup>. However, some studies report conflicting results showing no effects of physical activity on body composition in elderly patients<sup>47,48</sup>

In elderly population, we found higher percentage of fat free mass (FFM) and muscle mass (MM) and lower percentage of fat mass (FM) in Tertile III (high MD adherence) as compared to Tertiles II and I<sup>5</sup>. No differences were found among Tertile groups in total body water (TBW), intracellular water (ICW), and extracellular water (ECW). Furthermore, arm, thigh and waist circumference were found higher in patients with greater adherence to MD<sup>5</sup>. High adherence to the MD is associated with better muscle health and function, with higher performance in Short Physical Performance Battery (SPPB), grip strength, walking speed, and lower risk of sarcopenia<sup>49</sup>. However, studies are not conclusive in demonstrating a reduction in the risk of sarcopenia, but evidence a protective role on frailty and functional disability<sup>50</sup>. Indeed, Hashemi et al. found a lower prevalence of sarcopenia among individuals in third Tertile (12%) compared to first Tertile (21%)<sup>51</sup>. According to the InCHIANTI (Aging in Chianti) study, subjects with greater adherence to MD showed lower risk of developing frailty after a 6-year period follow-up<sup>52</sup>. Moreover, the highest quartile of MD adherence was associated with higher performance on 30-s chair stands in men and 6-min walking speed in women<sup>53</sup>. In our study, patients in Tertile III showed greater preservation of the activity daily and instrumental activity daily living, with lower overall prevalence of Fried criteria for Frailty (weight loss, exhaustion, low physical activity, low walking speed and low grip strength), with respect to Tertiles II and I<sup>5</sup>. In a 8-year period follow up, the walking speed was faster in the group with higher MD adherence at baseline, with respect to lower MD adherence<sup>54</sup>.

### **Mediterranean Diet, Length of stay and in-hospital mortality**

Malnutrition is associated with higher costs of hospitalization, rate of length of stay and mortality<sup>55</sup>. Deutz

et al. highlighted how an oral nutritional supplement with high-protein plus beta-hydroxy-beta-methylbutyrate was associated with decreased post-discharge mortality and improved nutritional status<sup>26</sup>. We showed a benefit of high adherence to MD on clinical outcomes in hospitalized elderly patient<sup>5</sup>. We found that length of stay was shorter in Tertile III compared to Tertile II and Tertile I, while no differences were found on in-hospital mortality. However, malnutrition (evaluated with the Mini Nutritional Assessment) showed a significant association with in-hospital mortality.

### **Conclusion**

Nutritional status in hospitalized older patient plays an important role on several clinical outcomes. Adherence to MD is associated to better lipid profile and lower chronic systemic inflammation, as well as a reduction in abdominal obesity and insulin resistance. Furthermore, adherence to MD shows lower overall prevalence of frailty and higher physical performance. Lastly, MD regimen significantly reduces length of stay with lower hospitalization costs and better well-being of the patients.

### **Author Contributions**

A.L.B, F.B., G.V. equally contributed to the manuscript. All authors have read and agreed to the published version of the manuscript.

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### **Conflicts of Interest**

The authors declare no conflict of interest.

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