

Adherence to the Mediterranean Diet and Healthy Aging: A Narrative Review over the Last Decade

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ABSTRACT

Objective: Even though modern medicine has significantly contributed to the extension of human lifespan, it has failed to delay the upsurge of chronic diseases. Health benefits of the Mediterranean diet are well established. Thus, adherence to this diet pattern may be the key to healthy aging. The aim of this review is to investigate the potential benefits of the Mediterranean diet on healthy aging.

Methods: A literature search of three databases (ScienceDirect, MEDLINE and The Cochrane Library) was conducted in order to trace all relevant studies published between January 1st 2010 and June 6th 2020 that focused on the impact of adherence to the Mediterranean diet on the physical and mental well-being of individuals aged 60 or older.

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Results: Twenty-two studies fulfilled the selection criteria and were classified into six groups, according to the main outcome of each study: mental health (eight studies), frailty (6), cardiovascular risk factors (3), plasma levels of uric acid (1), length of hospital stay (1), and aging mechanisms (3). Based on these studies, the protective role of Mediterranean diet on depression, cardiovascular and frailty risk was established. Moreover, adherence to the Mediterranean diet resulted in reduced plasma uric acid levels as well as decreased length of hospital stay and mortality risk among patients who were urgently admitted for any cause in a tertiary hospital. In contrast, results on the effect of Mediterranean diet on cognition were controversial, as studies presented positive or neutral correlations.

Conclusions: This review provides evidence on the association between adherence to the Mediterranean diet and healthy aging and highlights the importance of conducting more studies among seniors in order to provide further insight into this matter.

Keywords: Mediterranean diet, healthy aging, elderly, review.

INTRODUCTION

Aging is a natural and multifactorial process that is taking place at the genetic, molecular and cellular level of human organs and systems (1). The globe population is getting older. Although modern medicine managed to extend the human lifespan, it failed to delay the upsurge of chronic diseases (2). For example, approximately 30 million people suffer from Alzheimer's dementia worldwide, and by 2050 it is expected that this number will increase dramatically (3-5).

In the 1960s, Ancel Keys was the first to observe improvement in cardiometabolic risk factors, specific types of cancer and other nutrition related diseases by adhering to an eating pattern, present in Greece and Southern Italy, that was characterized by low intake of saturated fat and high consumption of vegetable oils and was defined as the "Mediterranean diet". Important conclusions of Keys' research include the positive correlation of premature death with the Western type diet that was characterized by high daily intake of saturated fats, the negative correlation of premature death with monounsaturated fatty acids' intake, and the neutral effect of polyunsaturated fatty acids, proteins, carbohydrates and alcohol in cardiovascular morbidity and mortality (6). Mediterranean diet not only contributes to an extended lifespan but also to a better quality of life in the elderly (7, 8). Research shows that 10 mg/day of extra virgin olive oil, the main oil used in Mediterranean diet, may lower plasma levels of glucose, LDL cholesterol and ox-LDL and reduce insulin resistance (9).

Several validated questionnaires are used in order to assess adherence to the Mediterranean diet (AdMedD) such as the MedDiet score (Mediterranean diet score), the t-MED (10), MAI (Mediterranean adequate index), DS (dietary score), PREDIMED score, MSDPS (Mediterranean-style dietary pattern score), mMDS (modified Mediterranean diet score) and others (11, 12).

The objective of our study was to review the available literature published within last decade regarding AdMedD and its impact on physical and mental health in individuals aged 60 or older.

MATERIALS AND METHODS

Search strategy

A literature search of three databases (ScienceDirect, MEDLINE and The Cochrane Library) was conducted in order to trace all relevant studies published between January 1st 2010 and June 6th 2020, using either "adherence to Mediterranean diet" as keyword or related term "Mediterranean diet score" as a search criterion. Also, "older adults" or "elderly" were used as a second search term.

Selection criteria

Only full-text original articles published in English language and evaluating individuals aged 60 or over at baseline were included. Secondary analyses, reviews, guidelines, meeting summaries, comments, unpublished abstracts or studies conducted in animals were excluded. There was no restriction on study design or sample characteristics apart from age. □

RESULTS

Twenty-two publications fulfilled our inclusion criteria, as shown in Table 1. They were classified into six groups, according to the main outcome of each study. The first group comprised eight studies focusing on the effect of AdMedD on mental health disorders, including organic brain disorders such as cognitive impairment and Alzheimer's dementia, and psychiatric disorders, mainly depression (23-29). The second group consisted of six studies that reported outcomes related to frailty (17, 30-34). The third group included three studies on AdMedD cardiovascular related outcomes (35-37). The fourth and fifth groups each included one study on the effect of AdMedD on plasma levels of uric acid (38) and hospital length of stay (LOS) (39), respectively. Finally, the sixth group consisted of three studies dealing with the effect of AdMedD on aging mechanisms (1, 40, 41).

Of all included studies, 13 presented results exclusively from Mediterranean countries, including Italy (1, 29, 30, 40), Spain (17, 36, 37), Greece (34, 38, 39), France (33), Israel (32) and a compilation of Mediterranean islands (Cyprus, Malta, Sardinia, Sicily, Mallorca, Menorca, Lesbos, Samothrace, Cephalonia, Crete, Corfu, Limnos, Ikaria, Syros, Naxos, Zakynthos, Salamina, Kassos, Rhodes, Karpathos, Tinos, Imbros and the rural region of Mani) (27). Seven studies sampled non-Mediterranean populations from the USA (22, 31), Australia (23, 24, 26), Sweden (25) and Brazil (28), and two mixed Mediterranean and non-Mediterranean populations from multicenter studies in five European countries: Italy, France, UK, The Netherlands and Poland (35, 41).

All studies used a variety of Mediterranean diet scores, including the Mediterranean diet (MedDiet) score (0-9 items) (8, 10) that was used in six studies (22, 23, 25, 28, 31, 32), the Mediterranean diet score (0-55 items) (13), which was utilized in six studies (1, 27, 34, 38, 39, 40), the PREDIMED 14-item score (14) that was used in four studies (29, 30, 36, 37), the MEDI score (15) which was utilized in two studies (24, 33), the NU-AGE index (16) that was used in one study (35), the MEDAS score (0-14 items) that was developed according to the PREDIMED study (17, 18) and was used in one study (17), and the Mediterranean diet score (0-18) (19) that was utilized in one study (41). Finally, in one study, both

Mediterranean diet scores (0-9 items and 0-55 items) were used (26). □

DISCUSSION

The term "Mediterranean diet" was initially used by Ancel Keys in the 60's in order to describe the eating pattern observed in Greece and Southern Italy, that was characterized by high consumption of vegetables, legumes, fruits, nuts, cereals, olive oil and fish, moderate intake of cheese and yoghurt, low intake of meat and poultry and regular small quantities of wine with meals (20). It is an established healthy-eating diet pattern that has consistently demonstrated beneficial effects on cognitive, musculoskeletal, cardiovascular and metabolic diseases (21).

A literature review of the last decade was conducted in order to elucidate the effect of AdMedD on healthy aging. Twenty-two full-text original articles dealing with individuals aged 60 or over were identified and classified into six groups based on the assessed parameters, including mental health disorders, frailty, cardiovascular risk factors, levels of serum uric acid, length of hospital stay and aging mechanisms (Table 1).

Concerning mental health disorders, Roberts *et al.* studied 5 233 residents aged 70-89 from Olmsted County, Minn., USA, and found that AdMedD was associated with a reduced risk of mild cognitive impairment and Alzheimer's disease (22). Similarly, Hardman *et al.* concluded that AdMedD was significantly correlated with better cognition, alongside with antidementia medications, in 93 individuals aged 60-90 from 15 independent living aged care villages around Melbourne, Australia (23). In contrast, Cherbuin and Anstey assessed 1 528 Australians aged 60-64 and concluded that AdMedD was not protective against cognitive decline, but excessive caloric intake and high intake of monounsaturated fats was predictive of mild cognitive impairment (24). Titova *et al.* could also not elicit a link between AdMedD and cognitive impairment among 1 016 individuals aged 70 living in the community of Uppsala, Sweden (25). Moreover, Hosking *et al.* showed that the Mediterranean-Dash intervention for neurological delay (MIND) diet, but not also the Mediterranean diet, was associated with reduced odds of 12-year cognitive impairment in 1 220 elderly individuals aged 60-64 from Canberra, Australia (26).

	Authors, country, year of publication	Number of participants	Age of participants (years)	Follow-up	Results	Mediterranean diet score used
First group: mental health disorders						
1	Roberts <i>et al.</i> , USA, 2010 (22)	5233	70 - 89	7.2 years	AdMedD (adherence to Mediterranean diet) was associated with a reduced risk of mild cognitive impairment and Alzheimer's disease.	MedDiet score (0-9 items) (8)
2	Hardman <i>et al.</i> , Australia, 2017 (23)	93	60 - 90	-	AdMedD was significantly correlated with better cognition alongside with antimentia medications	MedDiet score (0-9 items) (8)
3	Cherbuin and Anstey, Australia, 2012 (24)	1528	60 - 64	Four years	AdMedD was not found to be protective against cognitive decline.	MEDI Score (0-9 items) (15)
4	Titova <i>et al.</i> , Sweden, 2013 (25)	1016	70	Five years	No significant association between AdMedD and cognitive decline	MedDiet score (0-9 items) (8)
5	Hosking <i>et al.</i> , Australia, 2019 (26)	1220	60 - 64	12 years	The Mediterranean-Dash intervention for neurological delay (MIND) diet, but not the Mediterranean diet, showed an association with reduced odds of cognitive impairment.	MedDiet score (0-9 items) (8) AND MedDiet score (0-55 Items) (13)
6	Masana <i>et al.</i> , Mediterranean islands, 2018 (27)	2687	≥65	Six years	AdMedD was associated with absence of depression.	MedDiet score (0-55 Items) (13)
7	Bastos <i>et al.</i> , Brazil, 2020 (28)	545	≥60	-	Moderate and high adherence to Mediterranean diet were associated with a lower prevalence of common mental health diseases, such as depression	MedDiet score (0-9 items) (8)
8	Vicinanza <i>et al.</i> , Italy, 2020 (29)	143	73.1 ± 8.35	-	AdMedD may protect geriatric patients with multimorbidity from development of depressive symptoms.	14-item PREDIMED score (18)
Second group: frailty						
1	Barrea <i>et al.</i> , Italy, 2019 (30)	84	60 - 85	-	Positive association of the Mediterranean diet with the hand grip strength in active elderly women	14-item PREDIMED score (18)
2	Shahar <i>et al.</i> , USA, 2012 (31)	2220	70 - 79	Eight years	AdMedD was positively associated with faster walking speed.	MedDiet score (0-9 items) (8)
3	Tepper <i>et al.</i> , Israel, 2018 (32)	117	>60	-	AdMedD was associated with lower risk of falls and greater muscle strength. AdMedD was associated with a better six-min walk test and 10-min walk test in participants aged >75	MedDiet score (0-9 items) (8)
4	Rahi <i>et al.</i> , France, 2018 (33)	560	≥75	Two years	AdMedD was associated with significantly reduced frailty risk, incident slowness, poor muscle strength and low physical activity.	MEDI score (0-9 items) (15)
5	M.León-Muñoz <i>et al.</i> , Spain, 2014 (17)	1815	≥60	3.5 years	AdMedD was associated with a reduced risk of frailty and slow walking.	MEDAS score (17)

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6	Ntanasi <i>et al.</i> , Greece, 2018 (34)	1740	≥65	-	Adherence to the Mediterranean diet was associated with lower odds of frailty.	MedDiet score (0-55 Items) (13)
Third group: cardiovascular diseases						
1	Jennings <i>et al.</i> , five European centres, 2019 (35)	1294	65 - 79	One year	One-year AdMedD reduced cardiovascular risk, as showed by the significant reduction in robust measures of vascular health, including systolic blood pressure in males and augmentation index, that evaluates systemic arterial stiffness, in females	NU-AGE index (16)
2	Dominguez-Rodriguez <i>et al.</i> , Spain, 2020 (36)	284	≥70	One year	AdMedD was associated with a lower risk of cardiovascular death, cardiac transplantation or decompensated heart failure at one year follow up after cardiac resynchronization therapy.	14-item PREDIMED score (14)
3	Miró <i>et al.</i> , Spain, 2018 (37)	991	>70	2.1 ± 1.3 years	There was no link between AdMedD and reduced mortality after an episode of acute heart failure. However, AdMedD was associated with a reduced prevalence of re-admission to hospital after an episode of acute heart failure.	14-item PREDIMED score (14)
Fourth group: blood levels of uric acid						
1	Chrysochoou <i>et al.</i> , Greece, 2011 (38)	538	75 ± 6	Four months	MedDiet score was inversely associated with uric acid levels in males but not in females	MedDiet score (0-55 items) (13)
Fifth group: hospital length of stay (LOS)						
1	Lampropoulos <i>et al.</i> , Greece, 2020 (39)	183	>65	Two years	Each extra unit of the Mediterranean diet score decreased LOS by 0.3 days. Mortality risk decreased 13% per each unit increase of MedDiet score	MedDiet score (0-55 items) (13)
Sixth group: aging process						
1	Bonaccorsi <i>et al.</i> , Italy, 2018 (40)	475	92.6 ± 2.6	One year	AdMedD contributes to longevity by improving various anthropometric and bioelectrical parameters, including calf circumferences, specific resistance and specific impedance	MedDiet score (0-55 Items) (13)
2	Cesari <i>et al.</i> , Italy, 2018 (1)	421	93.1 ± 3.2	-	AdMedD contributes to longevity by protecting against the development of endothelial dysfunction, as evidenced by higher levels of circulating progenitor CD34 ⁺ and endothelial progenitor CD34 ⁺ /KDR ⁺ cells	MedDiet score (0-55 Items) (13)
3	Clements <i>et al.</i> , five European countries, 2017 (41)	120	65 - 79	One year	Mediterranean diet can reduce the elevated secretion of adipokine, resistin after <i>ex vivo</i> stimulation of peripheral blood mononuclear cells.	Mediterranean diet score (0-18 items) (19)

TABLE 1. Characteristics of the 22 included studies

With respect to psychiatric disorders, in a sample of 2 687 older people aged >65 living in the

Mediterranean basin, Masana *et al.* concluded that AdMedD was associated with absence of de-

pression (27). Similarly, Bastos *et al.* explored a population of 545 elders from São Paulo City, Brazil, and found that a moderate or high MedDiet score that was related to lower prevalence of common mental health diseases such as depression (28). Apart from that, Vicinanza *et al.* observe that, among 143 Italian geriatric patients, AdMedD may provide protection from the development of depressive symptoms, ultimately promoting healthy aging (29).

Regarding frailty, a major geriatric syndrome characterized by low muscle strength, Barrea *et al.* studied 84 Italian females aged 60-85 and reported that PREDIMED score was positively correlated with hand grip strength (HGS), which is the most frequently used indicator of muscle functional capacity for clinical purposes (30). Furthermore, in a population of 2 225 Americans aged 70-79, Shahar *et al.* observed that walking speed over eight years was faster among those with higher MedDiet score at baseline and that these differences remained significant over a period of eight years, thus suggesting a long-term effect of diet on mobility performance with aging (31). Similarly, Tepper *et al.* observed that, among 117 Israelis with type-2 diabetes and age over 60, AdMedD was associated with a lower risk for falls and an increased muscle strength, as measured by the Berg balance test and grip strength using a Jamar dynamometer, respectively. Interestingly, among participants aged over 75, after adjustment for gender, BMI, and physical activity, AdMedD was associated with a longer distance achieved in the six-min walk test and a higher walking speed in the 10-min walk test (32). Apart from that, in the French 'Three-City-Bordeaux study', which included 560 initially non-frail participants aged >75, Rahi *et al.* observed that older adults with the highest MedDiet score (6-9 items) had a significantly 68% frailty risk reduction compared to those in the lowest MedDiet score category (0-3 items). More specifically, high MedDiet scores were related to a significantly reduced risk of incident slowness, poor muscle strength and low physical activity (33). Furthermore, in a prospective cohort study that included 1 815 Spanish community-dwelling individuals aged ≥ 60 , León-Muñoz *et al.* noticed that AdMedD was associated with a decreasing risk of frailty and especially a reduced risk of slow walking and weight loss (17). Finally, Ntanasi *et al.* observed that, among 1 740 Greeks aged >65, each additional

unit in the MedDietScore was associated with a 5%, 4% and 7% decrease in the odds for frailty according to the Fried definition, Frailty index, and Tilburg frailty indicator, respectively (34).

Regarding the cardiovascular risk factors, the NU-AGE (New Dietary Strategies Addressing the Specific Needs of Elderly Population for Healthy Aging in Europe) study, conducted on 1 294 healthy participants aged 65 to 79 from five European centers (Bologna, Italy; Norwich, UK; Wageningen, the Netherlands; Warsaw, Poland; and Clermont-Ferrand, France) indicated that one-year AdMedD had the potential to reduce cardiovascular risk, as showed by the significant reduction in robust measures of vascular health, including systolic blood pressure in males and augmentation index, that evaluates systemic arterial stiffness, in females (35). Furthermore, Domínguez-Rodríguez *et al.* showed that, in 284 Spanish people aged >70, the risk of cardiovascular death, cardiac transplantation or decompensated heart failure at one year follow up after cardiac resynchronization therapy was significantly lower in those with Mediterranean diet compared to those with other food regimens (36). In contrast, the MEDIT-AHF study, that included 991 patients from seven Emergency Departments in Spain, did not find any link between high PREDIMED score and reduced mortality after an episode of acute heart failure. However, a high PREDIMED score was associated with low rates of rehospitalization during the next year, suggesting lesser severity of acute heart failure in these participants compared to those with low PREDIMED score (37).

In the fourth group, Chrysohoou *et al.* dealt with the impact of AdMedD on serum uric acid (UA) levels among 281 female (75 ± 6 years old) and 257 male (75 ± 7 years old) inhabitants of Ikaria, Greece, without known cardiovascular disease, and found that MedDiet score was inversely associated with UA levels in males but not in females (38).

In our fifth group, Lampropoulos *et al.* observed that, among 183 Greeks aged >65 who were urgently admitted for any cause to the Internal Medicine Department of Argolidos General Hospital, hospital LOS decreased by 0.3 days for each unit increase of MedDiet score. Moreover, they found that the mortality risk decreased 13% per each unit increase of MedDiet score (39).

Finally, concerning the aging process, the Mugello Working Study Group measured various anthropometric and bioelectrical parameters, including weight, ulnar length to estimate the height, body mass index (BMI), mid-upper arm circumference (MUAC), calf circumference (CC), waist circumference (WC), hip circumference (HC) and specific bioelectrical impedance vector analysis (BIVAsp), and concluded that AdMedD could partially explain the longevity of 298 nonagenarian residents of Mugello, Italy, as the MedDiet score was significantly correlated with CC, specific resistance and specific impedance in the whole sample, as well as with height in males (40). The same group has also reported that AdMedD contributed to the longevity of Mugello inhabitants by protecting against the development of endothelial dysfunction, as shown by the higher levels of circulating progenitor CD34+ and endothelial progenitor CD34+/KDR+ cells (1). Apart from that, the NU-AGE study revealed that AdMedD could decelerate many age-associated diseases that are accompanied by dysregulated immune function and excessive inflammation,

termed inflammaging, such as cardiovascular disease, rheumatoid arthritis, type 2 diabetes and cancer, by improving immune responses and, in particular, dendritic cell function (41). □

CONCLUSIONS

Our findings indicate that the Mediterranean diet has a protective role on depression, cardiovascular and frailty risk was revealed. Moreover, AdMedD resulted in reduced plasma uric acid levels and a decreased length of hospital stay and mortality risk among patients who were urgently admitted for any cause in a tertiary hospital. In contrast, results on the effect of AdMedD on cognition were not as clear, as studies presented positive or neutral correlations. Thus, additional studies among seniors on the association between AdMedD and healthy aging are recommended in order to provide further insight on this clinically important relationship. □

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