

Risk Factors and Diet Components Determining Adherence to the Mediterranean Diet in Acute Ischemic Stroke Patients: A Cross-Sectional Analysis of a Prospective Hospital Register Study

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Objectives: Low adherence to a Mediterranean diet (MeDi) is associated with increased incidence, mortality, and severity of acute ischemic strokes (AIS). Nevertheless, the explanatory factors associated with such results are unclear. Our aim was to investigate stroke risk factors associated with adherence to a MeDi in a prospective cohort of AIS patients. *Materials and Methods:* Patients admitted from February 2017 to February 2020 were included in this study. Adherence was measured using the 14-point Mediterranean Diet Adherence Screener (MEDAS). Demographic and clinical characteristics were compared with adherence with a univariate analysis. A binomial regression was used to investigate the independent association of premorbid factors and MeDi components with adherence. *Results:* There were 413 patients. Mean age was 68.6 (17.4), 176 (42.6%) women. Median MEDAS score was 6 (IQR 4–7) points. 253 patients (61.2%) had a low adherence (MEDAS \leq 6). In the univariate analysis, a low MEDAS was associated with lower education, diabetes, sedentary lifestyle, greater body mass index (BMI), lower alcohol consumption, and higher LDLc. In the regression analysis, younger age, lower education, functional disability, hypertension, sedentary lifestyle, and higher BMI were associated with lower MEDAS scores. Six MeDi components had particularly low patient adherence: seafood, legumes, olive oil, nuts, wine, and fruit. *Discussion:* These data indicate low adherence to MeDi in younger patients who are less educated and have existing cardiovascular risk factors, in particular hypertension, sedentary lifestyle, and higher BMI. Some components of the diet had a particularly low adherence. *Conclusions:* Tailoring diet prevention interventions to these specific populations, focusing on components with known less adherence, could improve adherence to a MeDi and the opportunity for secondary stroke prevention.

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Received March 17, 2021; revision received September 26, 2021; accepted September 30, 2021.

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1052-3057/\$ - see front matter

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<https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.106154>

Key Words: Mediterranean diet—Adherence—Ischemic stroke—Acute stroke—Risk factors
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Introduction

Ischemic stroke is a leading cause of disability and mortality worldwide.¹ The INTERSTROKE study reported a population attributable risk of 19% (95% CI 11–30%) due to an unhealthy diet, and the Global Burden of Disease Study demonstrated that 63.4% (56.5–67.8%) of disability-adjusted life years due to stroke could be attributed to dietary risks.^{2,3} Dietary patterns have been associated with decreased stroke incidence and mortality⁴). In particular, low adherence to a Mediterranean diet (MeDi) is associated with increased incidence and mortality of acute ischemic stroke (AIS), both in observation as well as in a large primary prevention clinical trial.^{5,6} Recently, a low pre-stroke adherence to a MeDi was associated with a higher severity at onset.⁷ The variables associated with low adherence to the MeDi in patients with AIS are unclear. Previous stroke comorbidities and sociodemographic factors may be associated with the specific components of the MeDi.^{8,9} Our aim was to investigate the risk factors and the MeDi components associated with adherence to the MeDi in a prospective cohort of AIS patients.

Patients and methods

Our institution is a teaching, non-profit, tertiary private hospital located in Santiago, Chile. From 1997, we have included all consecutive patients, 18 years or older, admitted to Clínica Alemana de Santiago with an acute stroke in our prospective stroke registry (Registro de Enfermedades Cerebrovasculares Clínica Alemana, RECCA).

In this cross-sectional analysis of our prospective hospital registry, we selected consenting patients with AIS and a complete 14-point Mediterranean Diet Adherence Screener (MEDAS) score who were admitted from February 2017 to February 2020. We excluded patients with transient ischemic attacks.

All variables were prospectively collected during patient hospitalization. Ischemic stroke was defined, according to current standard definitions, as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.¹⁰ The risk factors included any sociodemographic, cardiovascular, and comorbidities present before the incident event. Low education was defined as twelve or less years of formal education. Prior dependency was defined according to the modified Rankin Scale (mRS), a global seven-level measure of disability, where scores 0 to 2 indicate independence (minimal or no symptoms or some disability); scores 3 to 5 indicate, an increasing dependence from disability; and 6 is, death.¹¹ Hypertension, diabetes mellitus, hyperlipidemia, and mood disorders were considered present if patients had a prior clinical diagnosis or were under particular treatment. A

sedentary lifestyle was defined as less than 3 h of exercise per week and alcohol consumption as intake of more than 30 g per a week. All patients with suspected stroke were immediately assessed by the on-call neurologist, severity of the neurological impairment was measured using the National Institutes of Health Stroke Scale (NIHSS) and diagnosis confirmed with a neuroimaging stroke protocol consisting of non-contrast computed tomography scan, diffusion-weighted magnetic resonance imaging (DWI-MRI), either CT angiography (CTA) of the head and neck or magnetic resonance angiography, and computed tomography perfusion according to indication.¹²

Adherence to a MeDi was measured using the Spanish version of the MEDAS score, which we used in a Chilean population-based stroke study.¹³ The MEDAS is a 14-point questionnaire validated and used in the PREDIMED study to assess adherence to a MeDi pattern (Supplement Material); higher scores are associated with higher adherence, where 14 points is the maximum score.¹⁴ This tool is valid for the rapid assessment of adherence to the MeDi and useful for time-limited clinical and research settings.¹⁵ In this questionnaire, 0 is given if the patient does not meet the item definition of adherence and 1 otherwise; the sum of all items is the total MEDAS score. From January 2017, a vascular neurology fellow or vascular neurology staff obtains in one session the MEDAS score of all patients admitted with a diagnosis of AIS before discharge. Adherence to the MeDi before the index stroke was assessed in the previous month with patient history obtained from either the patients (85%) or their next of kin (15%). Adherence was defined as low (06 points) or high (714 points) based on the median MEDAS score of our cohort, which is close to the score of 7 proposed by PREDIMED investigators.¹⁶

The local ethics committee and the institutional review board of the hospital approved the study registry protocol. Written informed consent was obtained from every patient, as requested by local regulatory law.

Statistical analyze

Sociodemographic characteristics, cardiovascular risk factors, lipid profile, and HbA1c were compared with MeDi adherence (the MEDAS score) using the Chi-squared test or Fisher's exact test for frequencies. The t-test was used for normally distributed continuous variables and Wilcoxon log-rank test for non-normally distributed continuous variables in univariate analyses, employed to compare the variables between those with high and low adherence to MeDi.

Binomial logistic regression was employed to investigate the independent association of pre-morbidity variables with the MEDAS scores. The following variables were included in this model as covariates or confounders: sex, age, less than 12 years of education, lifestyle, BMI, previous functional dependency, history of a previous stroke, mood disorder, diabetes, dyslipidemia, and hypertension. Only variables with a *p*-value of less than 0.25 or clinical importance (e.g., age, sex, and hypertension) were included in the model. Variables with collinearity were excluded. As alcohol consumption is part of the MEDAS score, it was omitted as a variable.

All statistical analyses were conducted using Epi Info 7.2.2.6 or Stata 14.0. An alpha error < 0.05 was considered significant. The paper is reported according to the STROBE guidelines.¹⁷

The data are available upon reasonable formal request to the corresponding author.

Results

From February 2017 to February 2020, a total of 413 AIS patients met the inclusion criteria. The mean age of the participants was 68.6 (17.4) years and 176 (42.6%) of them were female. The MEDAS was normally distributed with a median score of 6 (IQR 4–7) points (Fig. 1). Low adherence (MEDAS ≤ 6) was observed in 253 (61.2%) patients. Table 1 presents the baseline demographic, clinical, and laboratory characteristics of both high- and low-adherence groups. Those with low MEDAS scores had less years of education, more frequent diabetes mellitus, sedentarism, greater BMI, increased alcohol consumption, and higher LDLc.

Binomial regression analysis demonstrated that younger age, less education, greater extent of previous dependency, hypertension, sedentary lifestyle, and higher BMI were significantly associated with lower adherence to a MeDi (Table 2). Adherence to the individual components

of the MeDi was heterogeneous (Fig. 2). However, the lowest adherence was for items 2, 4, 8–10, and 12, suggesting that patients generally consume fewer servings of olive oil, wine, legumes, seafood, and nuts than recommended, according to the MEDAS.

Discussion

Our results indicated that, in a prospective cohort of AIS patients, patients that were younger and had less education, previous hypertension, sedentary lifestyle, higher BMI, and/or previous dependency were less likely to adhere to the Mediterranean style diet.

Moreover, we found that adherence to the individual components of the MeDi was very heterogeneous; fish and legume consumption had the lowest adherence, whereas appropriate weekly servings of red meat and chicken/turkey had the highest.

In this cohort, the mean MEDAS score was 6 (SD 2.3) points, comparable to the mean 5.7 (SD 1.6) reported in a validation study of the self-applicable questionnaire for the MeDi in 53,366 Chilean adults.¹⁸

Our main results agree with those of Grosso et al., who, in a random sample of 3090 adults from eastern Sicily, reported that older and more educated people were more likely to be in the highest tertile of the MeDi score in a multivariate analysis (OR1.90; 95% CI 1.39–2.59 and OR1.29; 95% CI 1.05–1.58, respectively). Other population-based studies have also demonstrated the association between a sedentary lifestyle and MeDi adherence.^{19,20}

Our results are similar to those of a large cross-sectional study of 4348 Chilean adults, evaluated using the Chilean Mediterranean Diet Index (Chilean MDI, a locally validated version of the 14-item MEDAS questionnaire), which reported that being overweight or obese was significantly and independently associated with moderate (OR = 1.58 and 1.54, respectively) or low (OR = 2.20 and 2.49, respectively) adherence to the Chilean-MDI scores.²¹

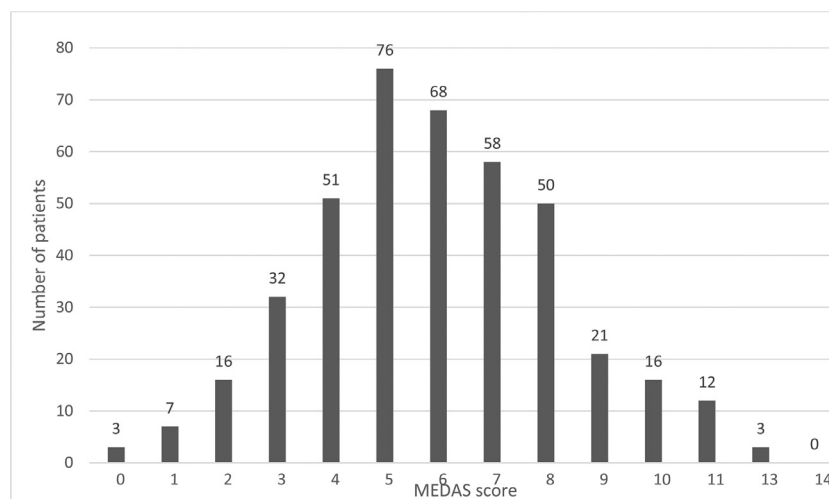


Fig. 1. Distribution of MEDAS scores in the total cohort.

Table 1. Baseline characteristics of ischemic stroke patients by adherence to a Mediterranean diet using Mediterranean diet adherence screener (MEDAS) score.

Variable	High adherence N (%) 160 (38.7)	Low adherence N (%) 253 (61.2)	P value
Age (years)	69.7 (16.0)	67.9 (18.2)	0.3
Female	70 (43.7)	106 (41.9)	0.7
Education \leq 12 years	27 (18.8)	96 (37.9)	< 0.001
Hypertension	92 (57.5)	159 (62.8)	0.3
Diabetes mellitus	19 (11.9)	52 (20.6)	0.02
Insulin resistance	15 (9.4)	23 (9.1)	0.9
Dyslipidemia	62 (38.7)	90 (35.7)	0.7
Prior stroke	29 (18.1)	44 (17.4)	0.9
Coronary artery disease	21 (13.1)	34 (13.4)	0.9
Mood disorder	20 (12.5)	36 (14.2)	0.7
Sleep apnea/hypopnea syndrome	13 (8.1)	17 (6.9)	0.7
Current smoker	48 (30.0)	51 (20.2)	0.2
Alcohol consumption	81 (50.6)	90 (35.6)	0.003
Sedentary lifestyle	95 (59.4)	198 (78.3)	< 0.001
Overweigh	95 (59.4)	181 (71.4)	0.01
Previous dependency	12 (7.5)	29 (11.5)	0.2
BMI*	25.2 (3.4)	26.7 (4.3)	< 0.001
Total cholesterol, mg/dL	157.1 (45.0)	167.9 (48.1)	0.03
LDL \dagger cholesterol, mg/dL	99.4 (38.1)	110.6 (44.1)	0.01
HDL \ddagger cholesterol, mg/dL	48.9 (14.9)	48.1 (14.8)	0.5
Triglycerides, mg/dL	130.6 (109.7)	137.9 (81.3)	0.2
HbA1c \S	6.2 (4.5)	6.1 (1.3)	0.2

Data a mean (SD) and n (%). *BMI: Body mass index. \dagger LDL: low-density lipoprotein. \ddagger HDL: high-density lipoprotein, \S HbA1c: glycosylated hemoglobin A1c.

Table 2. Pre-stroke comorbidities and factors that are significantly associated with lower adherence to a Mediterranean diet (MEDAS scores \leq 6).

Variable	Odds Ratio	95% CI*	P value
Younger age	1.01	1.00–1.01	< 0.001
Education \leq 12 years	1.35	1.17–1.54	< 0.001
Previous disability	1.06	1.01–1.12	0.03
Greater BMI \dagger	1.03	1.01–1.04	0.003
Sedentary lifestyle	1.35	1.19–1.53	< 0.001
Hypertension	1.16	1.02–1.33	0.03

*CI: confidence interval. \dagger BMI: body mass index.

Our findings are also in agreement with those of a recent systematic review and meta-analysis of 59001 participants from 16 observational studies has shown that the odds of developing hypertension was 13% lower with higher adherence to MeDi (95% CI 0.78–0.98, $p = 0.017$).²² Although we did not ascertain the cause of premorbid dependency, this factor may have been related to greater cardiovascular morbidities and cognitive decline, influencing lower adherence to MeDi. A study of 7430 AIS patients treated with intravenous thrombolysis showed that prior stroke, dementia, heart, and bone diseases were the most common causes of a pre-existing dependency.²³ An other study of AIS patients treated with thrombectomy, those with a previous dependency were older and more often female, with a history of previous stroke, and

greater vascular risk factors than the previously independent patients²⁴ Furthermore, cognitive decline and dementia have been shown to be associated with lower adherence to MeDi.^{25,26}

The limitation of this observational study were the cross-sectional nature and the possibility of recall bias, but we have no indication that patients with higher or lower adherence would have a differential recall of their diet patterns. Another possible source of bias is that we obtained data on dietary intake from the next of kin for approximately 15% of the patients. Previous studies have reported a high agreement between the mean intake of foods reported by interviewing subjects and their surrogates, indicating that surrogate data may be useful in descriptive studies and provide an unbiased estimate of mean consumption by a group. However, these studies have included a few elderly subjects and were dependent on the frequency of food consumption, gender of the index subject, relationship of the surrogate to the index subject, and data collection method.²⁷ Another consideration is that we chose the MEDAS score for its practicality and international validation, but there are other 28 scoring systems that evaluate the degree of adherence to the MeDi.^{15,28} A recent systematic review suggested that three of these demonstrated the highest level of evidence for conceptual suitability, applicability, and psychometric properties.²⁹ We did not use the Chilean version of the Mediterranean diet (Chilean MDI) which has been

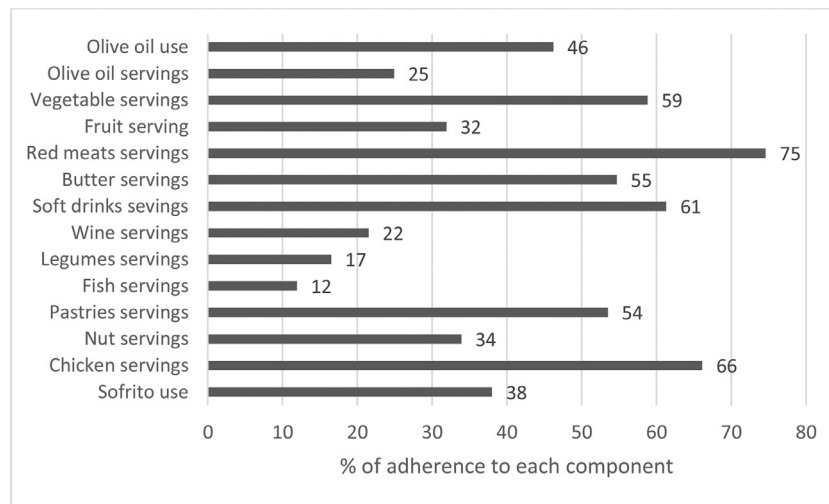


Fig. 2. Adherence to the Mediterranean diet for each component of the MEDAS score.

validated as a self-administered questionnaire because we administered the score ourselves.^{18,30} Another limitation is that this was a single-center study and included a relatively small sample size, which limits external validity.

Lower adherence to particular components of the MeDi pattern in this cohort is concerning, as these are the positively weighted components in most scores and contribute the most to the potential beneficial effects of the diet.^{8,31} Furthermore, these components primarily contribute to unsaturated fat content, an appropriate MUFA/SFA ratio, polyphenol content, and phytochemical, micronutrient flavonoid, and fiber contents. These foods not only constitute the backbone of the MeDi biological effect substrate but also are nutritionally adequate for meeting dietary nutritional goals, as demonstrated by Maillot.³² In particular, low consumption of fish, fruit, vegetable, and olive oil is associated with a significant increase in the risk of stroke and could become the target of specific interventions to decrease the burden of stroke.³³ In the same direction). Similarly, the PURE study found that high consumption of fruit, vegetable, and legume is associated with a low risk of stroke; the maximum benefits can be obtained by consuming three to four servings per day.³⁴ Our data may help develop diet prevention interventions for these described populations by focusing on the specific MeDi components with lower adherence and higher nutritional value.

Conclusion

In summary we have shown that in this cohort of patients with AIS, adherence to Medi was lower in those with a younger age and less education, as well as in patients with hypertension, sedentary lifestyle, higher BMI, and/or a previous dependency. The key aspects of MeDi components with particular deficiency were low consumption of seafood, wine, legumes, and olive oil servings. These data provide a benchmark for planning tailored dietary interventions of preventive strategies in practice and research for these populations.

Declaration of Competing Interest

Verónica V. Olavarría reports receiving research grants from Clínica Alemana de Santiago, Boehringer–Ingelheim and Conicyt.

Victor H. Navia received a travel grant from Boehringer Ingelheim.

Dr. Alejandro M. Brunser received a research grant from Clínica Alemana for the RECCA registry.

Pablo M. Lavados reports research support from Clínica Alemana and Boehringer Ingelheim. Research grants from The George Institute and Clínica Alemana de Santiago during the conduct of the study; unrestricted research grants from Lundbeck and Boehringer Ingelheim; personal fees from AstraZeneca and Bayer as SOC-RATES and ESUS NAVIGATE trials national leader and a Chilean Government research grant for the ÑANDU project outside the submitted work.

Enrico Mazzon and Alexis Rojo report no conflicts of interest.

Funding

The RECCA cohort has been funded by unconditional research grants from Clínica Alemana de Santiago and Boehringer Ingelheim.

Acknowledgments: We thank the English edition of our paper by Professor Craig S. Anderson and Enago.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.jstrokecerebrovasdis.2021.106154](https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.106154).

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