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ORIGINAL ARTICLE

Healthy and unhealthy dietary patterns and sperm quality from the Led-Fertyl study

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Abstract

Background: Dietary patterns may affect sperm quality, but the scientific evidence is limited.

Objective: To evaluate the association between adherence to different a-priori dietary patterns and sperm quality parameters in healthy reproductive-age men.

Materials and methods: A cross-sectional analysis was conducted using data from 200 young men enrolled in the Led-Fertyl study. Tertiles of six a-priori dietary patterns were estimated: four healthy dietary patterns [Mediterranean Diet Adherence Screener (MEDAS), Dietary Approaches to Stop Hypertension (DASH), Healthful Plant-Based Diet Index (hPDI) and EAT-Lancet Score], and two unhealthy dietary patterns [Western Diet and Unhealthful Plant-Based Diet Index (uPDI)]. Sperm quality parameters (count, concentration, vitality, total and progressive motility, and normal morphology) were considered the main outcomes.

Results: Compared with the lowest tertile, participants in the highest MEDAS tertile had higher total sperm count (β = 3.2;95%CI: 1.0, 5.5) and concentration (β = 1.8;95%CI: 0.6, 3.0), and total (β = 8.2;95%CI: 1.3, 15.1) and progressive

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motility ($\beta = 7.1$;95%CI: 0.2, 14.0). Similarly, participants in the highest hPDI tertile had higher total sperm count ($\beta = 3.4$;95%CI: 1.4, 5.5) and concentration ($\beta = 1.2$;95%CI: 0.0, 2.3) compared with those in the lowest tertile. When these dietary patterns were modelled as continuous variables (for each 1-point increment in the specific score), an inverse association was found between the uPDI and Western and total sperm count [($\beta = -2.7$;95%CI: −4.8, −0.7) and ($\beta = -3.8$;95%CI: −5.8, −1.7), respectively] and sperm concentration [($\beta = -1.2$;95%CI: −2.4, −0.1) and ($\beta = -1.7$;95%CI: −2.8, −0.5), respectively]. Compared with participants in the lowest tertile, those in the highest uPDI tertile presented higher odds of abnormal sperm concentration (OR: 4.6;95%CI: 1.0, 19.9) and one or more seminogram abnormalities (OR: 2.3;95%CI: 1.1, 5.0).

Conclusions: Our findings suggest that higher adherence to healthy dietary patterns (Mediterranean and healthful plant-based diet) was positively associated with better sperm quality parameters, in contrast, greater adherence to unhealthy dietary patterns was inversely associated.

KEYWORDS
dietary patterns, infertility, Mediterranean diet, sperm quality

1 | INTRODUCTION

Infertility is defined by the World Health Organization (WHO) as "a disease of the reproductive system leading to the failure to achieve pregnancy after 12 months or more of regular unprotected sexual intercourse".[1,2] Approximately one in six people globally are affected, which represents 17.5% of couples of reproductive age, and it has been recognized by the WHO as a worldwide public health problem.[3] Over the past 50 years, sperm count has drastically decreased (slope of -0.87 million/mL/year) globally,[4] and some evidence has shown that this decrease is more evident in Europe and the United States.[5] Environmental and lifestyle factors such as sedentary behavior,[6] cigarette smoking,[7] alcohol consumption,[8] pollution,[9] and unhealthy diets[8,10] have been recognized as the key factors associated with metabolic syndrome,[11] type 2 diabetes,[12] and obesity[13] explaining this reduction in semen quality parameters, impacting on fertility.

In the last few years, several studies have been focused on the role that specific foods or dietary compounds may have on semen quality and fertility outcomes. Specifically, it has been described that some foods such as fish,[14,15] nuts,[16] white meat,[15] whole grains, fruits and vegetables,[17,18] low-fat dairy products,[8] and micronutrients including omega-3 fatty acids,[19] some antioxidants and vitamins[19] are positively associated with semen quality. Conversely, processed meat,[15] full-fat dairy products,[20] soy-based products,[21] coffee,[22] alcohol,[22,23] and sugar-sweetened beverages[24,25] have been negatively associated with semen quality. Although this research is valuable, its approach has limitations, including the incapacity to consider the interactions among food or nutrients and the impracticality of examining the isolated effects of highly correlated dietary compounds.[26] Notwithstanding, dietary patterns research might be more relevant in the context of primary prevention of infertility than focusing on individual nutrients or foods.

Several healthy and unhealthy a-priori dietary patterns scores have been developed to assess dietary quality.[27] In this sense, healthy dietary patterns, characterized by a high intake of fruits, whole grains, legumes, vegetables, and low-fat dairy products such as the Mediterranean diet,[28–30] the Dietary Approaches to Stop Hypertension (DASH)[27,31,32] and the healthful plant-based diet index (hPDI)[33], have been associated with improved sperm quality parameters in some cohorts. In contrast, controversial evidence has shown that adherence to unhealthy diet characterized by a Western dietary pattern, including food high in salt and refined grains, is inversely associated with sperm concentration[34] and other testicular functions,[35] but other authors have found no associations.[9] In addition, an unhealthful plant-based diet[33] may have a negative association with semen quality, mainly by reducing sperm concentration and motility. However, most of the aforementioned studies were conducted in men from infertile couples, and the scope of the impact of dietary patterns on sperm quality in men from general populations is limited. Therefore, this study aims to comprehensively evaluate the association between several healthy and unhealthy a-priori dietary patterns with different sperm quality parameters in a cohort of healthy men of reproductive age.

2 | MATERIAL AND METHODS

2.1 | Design and study population

The Led-Fertyl (Lifestyle and environmental determinants of seminogram and other male fertility related parameters) study is an observational study with the aim of identifying and quantifying dietary

TABLE 1 General characteristics of the study population.

Characteristics	All population ($n = 200$)
Age (years)	28.4 ± 5.5
BMI (kg/m^2)	24.4 ± 3.2
Waist circumference (cm)	83.2 ± 8.3
Systolic blood pressure (mmHg)	128 ± 10
Diastolic blood pressure (mmHg)	74 ± 9
Physical activity (METs min/week)	4087 ± 3093
Hours of sleep (hours/day)	7.4 ± 0.8
Weight status	
Normal weight/Thinness	119 (59.5)
Overweight/Obesity	81 (40.5)
Elevated waist circumference (≥102 cm)	7 (3.5)
Elevated triglycerides (≥ 150 mg/dL)	16 (8)
Reduced HDL-cholesterol (< 40 mg/dL)	18 (9)
Elevated blood pressure (≥ 130/85 mmHg)	21 (10.50)
Elevated fasting plasma glucose (≥ 100 mg/dL)	11 (5.50)
Smoking status	
Never smoker	137 (68.5)
Current smoker	25 (12.5)
Former smoker	26 (13.0)
No reported	12 (6.0)
Education	
High school or less	71 (35.5)
College or high education	129 (64.5)
Civil status	
Single	177 (88.5)
Married	20 (10.0)
Other	3 (1.5)
Ethnicity	
Hispanic	160 (80)
Caucasic	32 (16)
Other	8 (4)
Seminogram parameters	
Sexual abstinence (days)	4 [3–5]
pH	8.5 [8.0–8.5]
Volume (ml)	3.5 [2.5–4.5]
Volume < 1.5 mL	6 (3.0)
Total sperm count (× 10^6 spz)	158.6 [94.6–282.6]
Total sperm count < 39 × 10^6 spz	19 (9.5)
Sperm concentration (× 10^6 spz/mL)	48.5 [28.7–83.4]
Sperm concentration < 15 × 10^6 spz/mL	20 (10.0)
Vitality (%)	81.0 [75.0–88.5]
Vitality < 58%	12 (6.0)
Total motility (%)	59.3 ± 17.6
Total motility < 40% motile	25 (12.5)
Progressive motility (%)	43.2 ± 17.4
Progressive motility < 32% motile	56 (28.0)
Non-progressive motility (%)	16.5 ± 6.8
Normal sperm morphology (%)	8.5 [5.0–15.0]
Normal sperm morphology < 4%	29 (14.6)
Seminogram abnormality	83 (41.5)

Note: Metabolic syndrome components (elevated waist circumference, triglycerides, blood pressure, and fasting plasma glucose and reduced HDL-cholesterol) definition according to the updated harmonized International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute criteria. Continuous variables were presented as means ± SD or medians [25th–75th percentiles] and categorical variables are presented as number (*n*) and percentages (%).
Abbreviations: BMI, body mass index; METs, metabolic equivalents; n, number of subjects; spz, spermatozoa; SD, standard deviation.

determinants and other lifestyle factors associated with sperm quality. This cross-sectional analysis includes the first 200 participants of the Led-Fertyl study; recruited between February 2021 and April 2023. Healthy reproductive-age men from the general population aged between 18 and 40 years, who had previously provided both online and written informed consent, were included. The inclusion and exclusion criteria have been reported in more detail previously.[36] The sample size includes at least a total of 192 men based on a 43.5% proportion of sperm progressive motility, a 7% margin of error, and 95% confidence level taking into account subpopulations greater than 100.000 men.

This study was conducted according to the Declaration of Helsinki guidelines and the protocol was approved by the Ethics Committee of the Institut d'Investigació Sanitària Pere i Virgili (CEIm-IISPV, Ref. 181/2019).

2.2 | Exposure: Dietary patterns

Dietary intake was assessed through phone interview conducted by trained dietitians using a validated, semi-quantitative 143-item food frequency questionnaire (FFQ),[37] covering consumption over the previous year. The FFQ collected information on portion sizes and consumption frequencies (with nine possible answers, ranging from "never or almost never" to "≥6 times/day") for each assessed food item. Thereafter, responses for each food item were converted into daily grams using the standard portion size of each item. Energy and nutrient intake were estimated using the Spanish food composition tables[38,39] and the e-DietBase software.[40]

Adherence to a total of six a-priori dietary patterns were computed and used as exposures. The Mediterranean diet adherence screener (MEDAS), which is based on 14 items and has a potential range of 0 (minimum adherence) to 14 (maximum adherence).[41] The healthful and unhealthful plant-based dietary patterns were determined using the plant-based diets index (PDI), which is

characterized by a higher consumption of plant based-foods than animal origin foods. Healthful plant-based diet index (hPDI) contains plant based-foods (whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and tea/coffee) that received positive scores, while less healthy plant based-foods (fruit juices, sweetened beverages, refined grains, potatoes, sweets/desserts) and animal food groups received reverse scores.[42] Unhealthful plant-based diet index (uPDI) assigns a positive score to less healthy plant foods and a negative score to healthy plant foods and animal food groups.[42] These dietary patterns have a potential range of 18 (minimum adherence) to 90 (maximum adherence) points.[42] The Dietary Approaches to Stop Hypertension (DASH) 2008 is based on eight items, that are scored on a scale of 1 to 5, with a potential range of 8 (minimal adherence) to 40 (maximal adherence).[43] The EAT-Lancet diet score is based on 14 items and has a potential range of 0 (minimal adherence) to 14 (maximal adherence).[44] Finally, the Western diet score, is characterized by a high consumption of red meat and fast or fried foods and low consumption of fruit, vegetables and fish with a possible score ranging from 12 to 60 points.[45]

2.3 | Outcome: Sperm quality parameters

The main outcomes of this study were as follows: sperm count and concentration, sperm vitality, total and progressive sperm motility, and sperm morphology.

Semen parameters were evaluated as described in the WHO report (2010)[46] with at least 3 days of sexual abstinence. All analyses were performed on fresh samples with a maximum of 60 min after collection. Semen volume and pH were measured after 20 min of liquefaction with a pipette and pH indicator strips (Fisherbrand™), respectively. The reference lower limit for semen volume is 1.5 mL. In the case of pH, 7.2 is used as the lower threshold value.

Sperm concentration, motility and morphology were assessed using the computer-assisted sperm analysis (CASA) SCA® system version 6.5.0.67 (Microptic) and an Olympus CX43 phase contrast microscope (EVIDENT Corporation). Sperm motility was classified as progressive, non-progressive, and immobile and was expressed as a percentage of progressive motility, and total motility (progressive motility + non-progressive motility), using the 10X phase contrast objective, and analyzed in 200 spermatozoa. The lower reference limit for total motility and progressive motility were 40% and 32%, respectively. Total sperm count (millions of spermatozoa per ejaculate) was calculated by multiplying the ejaculated volume by the sperm concentration. The lower reference limit for total sperm count was 39×10^6 spermatozoa per ejaculate and for sperm concentration was 15×10^6 spermatozoa per mL. Sperm vitality was estimated using the hypo-osmotic swelling test (HOS test), measured manually with a 60X lens, and the lower reference limit for vitality was 58%. Sperm morphology was assessed on semen smears stained with the Hemacolor® (Sigma-Aldrich) kit and evaluated with the 60X lens using the SCA® system and identifying normal sperm or defects in the head, midpieces, principal piece, or combined abnormality. Sperm morphology was expressed as the percentage of normal forms with a lower reference limit of 4%. Sperm motility, vitality, and morphology were analyzed in 200 spermatozoa. An abnormal seminogram was considered when one or more sperm parameters were outside the aforementioned reference limits, according to the WHO guidelines.[46]

2.4 | General and covariate assessment

Sociodemographic data, personal history and lifestyle characteristics were obtained by online and self-reported questionnaires, which were checked by trained personnel. Body composition (weight, height, and waist circumference) and blood pressure were determined by trained dietitians in a face-to-face visit. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and categorized according to the WHO criteria.[47] Waist circumference was measured to the nearest 0.5 cm midpoint between the lower rib and the iliac crest with an anthropometric tape. Blood pressure was measured in duplicate 5 min apart using a semiautomatic oscillometer. We categorized the components of the metabolic syndrome as dichotomous variables according to the updated harmonized International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute criteria as follows: (1) elevated waist circumference for European individuals (≥102 cm), (2) elevated triglycerides (≥150 mg/dL) or drug treatment for elevated triglycerides, (3) reduced concentrations of HDL-cholesterol (< 40 mg/dL) or drug treatment for low HDL-C, (4) elevated blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg) or antihypertensive drug treatment, and (5) elevated fasting glucose (100 mg/dL) or drug treatment for elevated glucose.[48] The validated REGICOR short physical activity questionnaire was used to assess physical activity.[49]

2.5 | Statistical analysis

The latest Led-Fertyl database (May 2023) was used. Continuous variables were presented as means ± standard deviation (SD) or medians [25th–75th percentiles], depending on normal distributions, or number (%) for categorical variables. Normal distribution of the variables was evaluated using the Kolmogorov–Smirnov test and non-normal variables were cubic root-transformed to approach normality. Adherence to the six dietary pattern adherence scores were categorized into tertiles using the lowest tertile as the reference (T1). One-way analysis of variance (ANOVA) or the Kruskal–Wallis test was used to evaluate differences across tertiles of dietary patterns adherence for normally and non-normally distributed continuous variables, respectively. Chi-squared test was used for comparisons between categorical variables. Multivariable linear regression models were fitted to assess the associations between tertiles of adherence to the different a-priori dietary patterns as exposures and sperm parameters as outcomes. For these associations, dietary pattern scores were also analyzed as continuous variables (for each 1-point increment), expressing β-coefficients and 95% confidence intervals (CIs), and adjusted for several potential confounders. Model 1 was adjusted by age (years), BMI (kg/m^2),

smoking (never smoker, current smoker and former smoker), education (high school or less and college or high education), physical activity (METs min/week), and sleeping time (hours/day); Model 2 (full-adjusted model) was additionally adjusted by energy intake (kcal/day), and days of sexual abstinence. Additionally, was adjusted for blood pressure (elevated blood pressure ≥ 130/85 mmHg blood pressure or normal blood pressure < 130/85 mmHg). We performed linear regression analysis using the square root transformed sperm count, and concentration, vitality and normal sperm morphology in all models. In addition, multivariable logistic regression models were used to estimate odds ratios (OR) and their 95% confidence intervals (CIs) for the associations between dietary pattern scores, abnormal sperm quality parameters and abnormal seminogram according to WHO 2010 normality thresholds,[46] adjusted for the aforementioned confounders. All *p*-values were two-tailed with a significant level at 0.05. Statistical analyses were performed using the IBM-SPSS statistical package (version 27.0, SPSS Inc.) and STATA (version 14.0, StataCorp LLC.).

3 | RESULTS

3.1 | Descriptive results

Table 1 shows general characteristics of the studied population. This analysis included 200 men participants with a mean (± SD) age of 28.4 (± 5.5) years, of whom 40.5% presented overweight or obesity. Most study population were single, non-smokers and had a college degree. In addition, 41.5% of them had at least one major seminogram parameter (volume, total sperm count, sperm concentration, vitality, total motility, progressive motility or normal sperm morphology) below the WHO 2010 reference values. The flowchart of the participants is displayed in Figure S1.

Those participants in the highest tertile to the MEDAS score were more likely to be physically active, to sleep more hours per day, have a lower waist circumference, and have a higher total sperm count, sperm concentration, and fewer seminogram abnormalities (Table S1). Those participants in the highest hPDI diet tertile the showed a higher age, lower diastolic blood pressure, and higher semen volume and total sperm count (Table S2). Men in the highest tertile to the DASH diet score were more likely to be physically active and have more total sperm count (Table S3). No significant differences in any general characteristic across tertiles of EAT-Lancet diet score (Table S4) were observed. Men in the lowest tertile to the uPDI diet score were more likely to be physically active and to have less seminogram abnormalities (Table S5), and those participants with the highest tertile to the Western diet score were more likely to be less physical active, to have lower education level and to present lower total sperm count (Table S6).

The study population showed a macronutrient distribution closer to the Mediterranean diet. However, a notable consumption of animal protein sources, mainly meats and derivates and eggs, was observed. Furthermore, there was an increased intake of saturated fats and a lower intake of polyunsaturated fats (Table 2).

TABLE 2 Dietary characteristics of the study population.

Variable	All population (*n* = 200)
Energy (kcal/day)	2647 ± 633
Macronutrients	
Total proteins (g/day)	107.2 ± 29.6
% Proteins from energy intake	16.2 ± 2.4
Total carbohydrates (g/day)	258.4 ± 80.3
% Carbohydrates from energy intake	38.8 ± 6.5
14 g fiber/1000 kcal	15 (7.5)
Total fats (g/day)	124.6 ± 33.9
% Fats from energy intake	42.5 ± 6.1
Monounsaturated FA (% of total kcal)	19.9 ± 4.0
Polyunsaturated FA (% of total kcal)	5.9 ± 1.4
Saturated FA (% of total kcal)	11.9 ± 2.7
Food groups consumption (g/day)	
Dairy	254.8 ± 189.6
Dairy products	28.0 ± 31.0
Eggs	43.3 ± 39.6
Meat and derivatives	168.3 ± 86.9
Fish and seafood	85.1 ± 46.2
Vegetables	251.0 ± 122.7
Tubers	73.8 ± 59.0
Fruits	196.4 ± 125.7
Oleaginous fruits	14.6 ± 14.5
Nuts	22.2 ± 23.0
Legumes	28.1 ± 21.0
Cereals	114.5 ± 78.3
Whole grains	36.2 ± 50.1
Oils and fats	36.8 ± 16.4
Pastry and bakery	41.0 ± 38.8
Sugars, cocoa and sweets	12.0 ± 15.1
Snacks	12.1 ± 10.0
Prepared foods	41.8 ± 31.6
Sauces and seasonings	4.0 ± 5.8
Sweetened beverage	117.5 ± 133.6
Alcoholic beverages	171.5 ± 209.7
PbA	5.8 ± 26.6
Coffee, tea and infusions	77.9 ± 75.3

Note: Categorical and continuous variables are presented as *n* (%) and means ± SD, respectively.
Abbreviations: SD, standard deviation; FA, fatty acids; g/day, grams per day; kcal/day, kilocalories per day; PbA, plant based alternative products.

3.2 | Dietary pattern scores and sperm quality parameters

Table 3 shows the associations (*β* coefficient; 95% CIs) between adherence to different a-priori dietary pattern scores and sperm quality

TABLE 3 Association (β coefficients and their 95% confidence interval) between tertiles of MEDAS, hPDI, DASH, EAT-Lancet diet score, uPDI and Western diet score and sperm quality parameters.

		MEDAS			hPDI			DASH		
Sperm quality parameters		**T1**	**T3**	***P*-trend**	**T1**	**T3**	***P*-trend**	**T1**	**T3**	***P*-trend**
Total sperm count ($\times 10^6$ spz.)[a]	Crude model	Ref	**3.0 (0.9, 5.1)**	**0.005**	Ref	**3.2 (1.3, 5.2)**	**0.001**	Ref	1.0 (−1.0, 2.9)	0.305
	Model 1	Ref	**3.6 (1.4, 5.9)**	**0.002**	Ref	**3.2 (1.2, 5.2)**	**0.002**	Ref	1.4 (−0.6, 3.4)	0.154
	Model 2	Ref	**3.2 (1.0, 5.5)**	**0.005**	Ref	**3.4 (1.4, 5.5)**	**0.001**	Ref	1.8 (−0.6, 4.2)	0.119
Sperm concentration ($\times 10^6$ spz./mL)[a]	Crude model	Ref	**1.5 (0.4, 2.6)**	**0.009**	Ref	1.0 (−0.1, 2.1)	0.060	Ref	0.2 (−0.9, 1.2)	0.752
	Model 1	Ref	**1.9 (0.7, 3.1)**	**0.002**	Ref	1.1 (−0.0, 2.1)	0.057	Ref	0.4 (−0.6, 1.5)	0.385
	Model 2	Ref	**1.8 (0.6, 3.0)**	**0.005**	Ref	**1.2 (0.0, 2.3)**	**0.048**	Ref	0.5 (−0.8, 1.8)	0.389
Sperm vitality (%)[a]	Crude model	Ref	0.2 (−0.2, 0.6)	0.306	Ref	−0.1 (−0.4, 0.3)	0.770	Ref	−0.1 (−0.4, 0.3)	0.820
	Model 1	Ref	0.3 (−0.1, 0.7)	0.184	Ref	−0.0 (−0.4, 0.4)	0.976	Ref	0.0 (−0.4, 0.4)	0.847
	Model 2	Ref	0.3 (−0.2, 0.7)	0.230	Ref	0.0 (−0.4, 0.4)	0.947	Ref	−0.0 (−0.5, 0.4)	0.942
Total motility (%)	Crude model	Ref	5.7 (−0.7, 12.1)	0.079	Ref	1.4 (−4.6, 7.5)	0.638	Ref	−1.7 (−7.6, 4.3)	0.597
	Model 1	Ref	**8.2 (1.5, 15.0)**	**0.016**	Ref	3.7 (−2.4, 9.8)	0.228	Ref	−0.5 (−6.6, 5.5)	0.901
	Model 2	Ref	**8.2 (1.3, 15.1)**	**0.019**	Ref	3.8 (−2.7, 10.3)	0.246	Ref	−0.4 (−7.8, 6.9)	0.940
Progressive motility (%)	Crude model	Ref	5.4 (−1.0, 11.7)	0.099	Ref	2.8 (−3.2, 8.7)	0.353	Ref	−2.6 (−8.4, 3.3)	0.408
	Model 1	Ref	**7.0 (0.2, 13.8)**	**0.046**	Ref	4.3 (−1.8, 10.4)	0.169	Ref	−1.7 (−7.7, 4.4)	0.629
	Model 2	Ref	**7.1 (0.2, 14.0)**	**0.046**	Ref	4.3 (−2.2, 10.8)	0.194	Ref	−1.6 (−9.0, 5.8)	0.708
Non-progressive motility (%)	Crude model	Ref	−0.6 (−3.1, 1.9)	0.664	Ref	−2.1 (−4.4, 0.2)	0.074	Ref	−0.1 (−2.4, 2.2)	0.916
	Model 1	Ref	−0.0 (−2.6, 2.6)	0.990	Ref	−1.3 (−3.7, 1.0)	0.262	Ref	−0.0 (−2.4, 2.3)	0.966
	Model 2	Ref	−0.1 (−2.8, 2.6)	0.947	Ref	−1.4 (−3.9 1.1)	0.258	Ref	−0.3 (−3.1, 2.6)	0.830
Normal sperm morphology (%)[a]	Crude model	Ref	0.2 (−0.2, 0.7)	0.295	Ref	0.1 (−0.3, 0.5)	0.636	Ref	0.0 (−0.4, 0.4)	0.962
	Model 1	Ref	0.2 (−0.3, 0.7)	0.394	Ref	0.1 (−0.3, 0.5)	0.711	Ref	−0.0 (−0.4, 0.4)	0.967
	Model 2	Ref	0.2 (−0.2, 0.7)	0.324	Ref	0.1 (−0.4, 0.5)	0.683	Ref	0.0 (−0.5, 0.5)	0.961

(Continues)

TABLE 3 (Continued)

Sperm quality parameters		EAT-Lancet			uPDI			Western		
		T1	T3	*P-trend*	T1	T3	*P-trend*	T1	T3	*P-trend*
Total sperm count (× 10^6 spz.)[a]	Crude model	Ref	1.1 (−0.9, 3.1)	0.228	Ref	**−2.5 (−4.5, −0.5)**	**0.013**	Ref	**−3.1 (−5.1, −1.1)**	**0.002**
	Model 1	Ref	1.0 (−1.1, 3.0)	0.286	Ref	**−2.9 (−4.9, −0.9)**	**0.005**	Ref	**−4.0 (−6.1, −1.9)**	**0.000**
	Model 2	Ref	1.2 (−1.0, 3.3)	0.249	Ref	**−2.7 (−4.8, −0.7)**	**0.010**	Ref	**−3.8 (−5.8, −1.7)**	**0.000**
Sperm concentration (× 10^6 spz./mL)[a]	Crude model	Ref	0.4 (−0.6, 1.5)	0.341	Ref	−1.1 (−2.1, 0.0)	0.051	Ref	**−1.3 (−2.3, −0.2)**	**0.019**
	Model 1	Ref	0.4 (−0.7, 1.5)	0.393	Ref	**−1.3 (−2.3, −0.2)**	**0.020**	Ref	**−1.7 (−2.9, −0.6)**	**0.003**
	Model 2	Ref	0.5 (−0.7, 1.7)	0.336	Ref	**−1.2 (−2.4, −0.1)**	**0.030**	Ref	**−1.7 (−2.8, −0.5)**	**0.004**
Sperm vitality (%)[a]	Crude model	Ref	−0.1 (−0.5, 0.3)	0.630	Ref	−0.2 (−0.6, 0.2)	0.258	Ref	0.0 (−0.4, 0.4)	0.895
	Model 1	Ref	−0.1 (−0.5, 0.3)	0.771	Ref	−0.2 (−0.6, 0.2)	0.227	Ref	−0.0 (−0.4, 0.4)	0.913
	Model 2	Ref	−0.0 (−0.5, 0.4)	0.876	Ref	−0.2 (−0.6, 0.2)	0.287	Ref	−0.0 (−0.4, 0.4)	0.919
Total motility (%)	Crude model	Ref	1.2 (−4.8, 7.3)	0.644	Ref	−3.7 (−9.7, 2.4)	0.228	Ref	−0.3 (−6.4, 5.8)	0.878
	Model 1	Ref	2.4 (−3.7, 8.5)	0.413	Ref	−5.4 (−11.5, 0.6)	0.071	Ref	−2.7 (−9.1, 3.8)	0.374
	Model 2	Ref	2.6 (−4.1, 9.2)	0.428	Ref	−5.7 (−12.0, 0.6)	0.069	Ref	−2.5 (−9.0, 4.0)	0.414
Progressive motility (%)	Crude model	Ref	1.6 (−4.4, 7.6)	0.564	Ref	−0.9 (−6.9, 5.1)	0.731	Ref	0.4 (−5.6, 6.4)	0.927
	Model 1	Ref	2.1 (−4.0, 8.2)	0.459	Ref	−2.1 (−8.2, 4.0)	0.435	Ref	−1.2 (−7.7, 5.3)	0.680
	Model 2	Ref	2.0 (−4.7, 8.7)	0.523	Ref	−2.4 (−8.8, 4.0)	0.402	Ref	−1.0 (−7.5, 5.6)	0.732
Non-progressive motility (%)	Crude model	Ref	−0.7 (−3.0, 1.7)	0.611	Ref	−1.7 (−4.1, 0.6)	0.167	Ref	−0.2 (−2.5, 2.1)	0.882
	Model 1	Ref	−0.2 (−2.5, 2.2)	0.943	Ref	−2.1 (−4.4, 0.2)	0.091	Ref	−0.8 (−3.3, 1.7)	0.532
	Model 2	Ref	−0.1 (−2.6, 2.5)	0.994	Ref	−2.2 (−4.6, 0.3)	0.099	Ref	−0.8 (−3.4, 1.7)	0.534
Normal sperm morphology (%)[a]	Crude model	Ref	−0.2 (−0.6, 0.2)	0.304	Ref	−0.3 (−0.7, 0.1)	0.156	Ref	−0.2 (−0.6, 0.3)	0.436
	Model 1	Ref	−0.2 (−0.7, 0.2)	0.279	Ref	−0.3 (−0.7, 0.1)	0.194	Ref	−0.2 (−0.6, 0.3)	0.469
	Model 2	Ref	−0.3 (−0.8, 0.2)	0.230	Ref	−0.4 (−0.8, 0.1)	0.142	Ref	−0.2 (−0.6, 0.3)	0.441

Abbreviations: BMI, body mass index; DASH, dietary approaches to stop hypertension; EAT-Lancet, EAT-Lancet diet score; hPDI, healthful plant-based diet index; MEDAS, Mediterranean diet adherence screener; spz, spermatozoa; T, tertile; uPDI, unhealthful plant-based diet index and Western, Western diet score. β coefficients were estimated using multivariable linear regression models. Model 1 adjusted by age (years), smoking status (current, former, never), education (high school or less, college or high education), BMI (kg/m^2), physical activity (METs min/week) and sleeping hours (hours/day). Model 2 was additionally adjusted by energy intake (kcal/day) and sexual abstinence (days).

Bold indicates p-value < 0.05.

[a]Total sperm count, sperm concentration, sperm vitality and normal sperm morphology were root-square transformed to approximate a normal distribution.

parameters. The full-adjusted model showed significantly higher total sperm count (β = 3.2; 95% CI: 1.0, 5.5), sperm concentration (β = 1.8; 95% CI: 0.6, 3.0), total motility (β = 8.2; 95% CI: 1.3, 15.1) and progressive motility (β = 7.1; 95% CI: 0.2, 14.0) in the highest tertile of the MEDAS, compared to those participants in the lowest tertile. In addition, compared to those participants in the lowest tertile of the hPDI score, those in the highest tertile have higher total sperm count (β = 3.4; 95% CI: 1.4, 5.5) and sperm concentration (β = 1.2; 95% CI: 0.0, 2.3). These results remained essentially unchanged even adjusting for blood pressure (Table S7). No significant associations between DASH or EAT-Lancet diet scores and sperm quality parameters were found. Compared to participants allocated in the lowest tertile of the uPDI and Western dietary patterns, those in the highest tertile of adherence have lower total sperm count ((β = -2.7; 95% CI: -4.8, -0.7) and (β = -3.8; 95% CI: -5.8, -1.7), respectively) and sperm concentration ((β = -1.2; 95% CI: -2.4, -0.1) and (β = -1.7; 95% CI: -2.8, -0.5), respectively).

When these dietary patterns were modeled as continuous variables (for each 1-point increment in the specific score), similar positive associations were found with total sperm count (β = 0.6; 95% CI: 0.2, 1.1), sperm concentration (β = 0.3; 95% CI: 0.1, 0.6) and total motility (β = 1.6; 95% CI: 0.2, 3.0) for MEDAS; total sperm count (β = 0.1; 95% CI: 0.0, 0.2) for hPDI score. For the Western diet score, inverse associations were found with total sperm count (β = -0.2; 95% CI: -0.3, -0.1) and sperm concentration (β = -0.1; 95% CI: -0.2, -0.0), and normal sperm morphology (β = -0.2; 95% CI: -0.3, -0.0) for EAT-Lancet diet score (Figure 1).

Compared to participants allocated in the lowest tertile of adherence to the MEDAS score, those in the highest tertile have 80% lower odds of having abnormal total motility (OR: 0.2; 95% CI: 0.1, 1.0) and 60% lower risk of presenting seminogram abnormalities (OR: 0.4; 95% CI: 0.2, 0.9). Those participants in the highest tertile to the hPDI score showed a lower prevalence risk of abnormal sperm count (OR: 0.2; 95% CI: 0.1, 0.9). Moreover, men in the highest tertile of adherence to uPDI had 4.6 (95% CI: 1.0, 19.9) and 2.3 (95% CI: 1.1, 5.0) higher odds of presenting an abnormal sperm concentration diagnosis and seminogram abnormalities, respectively (Table S8 and Figure S2).

4 | DISCUSSION

An in-depth analysis of various healthy (MEDAS, DASH, hPDI, and EAT-Lancet), and unhealthy (uPDI and Western diet) a-priori dietary patterns and their potential association with sperm quality in men from the general population was conducted. The results of this study showed that higher adherence to MEDAS and hPDI was positively associated with sperm count and concentration. In addition, higher MEDAS adherence was positively associated with total and progressive motility. In contrast, higher adherence to uPDI and Western diet was inversely associated with sperm count and concentration.

The positive associations observed in our study between men's adherence to the healthy MEDAS and hPDI dietary patterns and higher sperm count are consistent with the inverse relationship observed between men's adherence to the unhealthy Western diet and uPDI and sperm count. These findings are aligned with the results reported in the systematic review and meta-analysis by Cao et al. (2022), which suggested the beneficial effects of adopting healthy dietary patterns and, conversely, the detrimental impact of unhealthy dietary patterns on sperm count.[50] Furthermore, these findings are in line with an expanding scientific literature showing several associations between the consumption of different specific foods and semen quality parameters. For example, it has been reported that higher consumption of nuts,[16] fish,[15,51] vegetables and fruits,[52] all components of the healthy a-priori dietary patterns assessed in our study, is positively associated with sperm quality. In addition, other foods and nutrients typically found in unhealthy dietary patterns, such as saturated and trans fatty acids,[53] animal products,[15] or simple carbohydrates[54] have been inversely associated with sperm quality. Furthermore, unhealthy patterns that have been already associated with a higher prevalence of metabolic syndrome,[55] in turn, could negatively affect sperm quality.[11]

We also found that a higher adherence to unhealthy dietary patterns increases the risk of having oligozoospermia (abnormal sperm count or/and concentration) or other combined seminogram abnormalities (oligo-, astheno-, teratozoospermia). This could be explained by the low consumption of olive oil, nuts and fish, which mainly contain monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs), polyphenols and antioxidants, and a high consumption of saturated fats.[56] According to the evidence, supplementation with MUFAs and PUFAs could modify the composition of the sperm plasma membrane, reduce the deoxyribonucleic acid (DNA) damage caused by oxidative stress, and/or modulate the enzymatic activities involved in energy metabolism and sperm function.[16,51] Furthermore, it has been shown that the intake of vitamins, antioxidants and carotenoids is related with higher sperm counts.[33,57] This could be explained by the fact that mature sperm are highly susceptible to abnormal levels of reactive oxygen species (ROS), which could lead to a reduced sperm count and motility and increased morphological abnormalities. Antioxidants found in fruits and vegetables could regulate the required equilibrium of seminal ROS, improving semen quality and reducing alterations in sperm DNA.[58] This is supported by the study by Eskenazi B et al. (2005), which evaluated healthy non-smoking men from a non-clinical setting and concluded that higher antioxidant intake (vitamins C and E) was associated with higher sperm count, concentration and progressive motility in healthy men.[59]

Our study has limitations that deserve to be mentioned. Firstly, the cross-sectional observational design, which does not allow to establish cause-effect relationships. Second, even though this study used a validated FFQ administered by a trained dietitian via phone interview, it is not possible to exclude measurement errors and recall bias. Third, although we adjusted our models by several potential confounders, residual confounding cannot be dismissed. Fourth, the sample size of our study is relatively small, although was sufficient to achieve the proposed objectives. Fifthly, no hormonal data or glycolipid parameters, both potential impact semen quality, were available in the population studied to be considered as covariates. In addition, andrological physical examination such as testicular volume and potential other

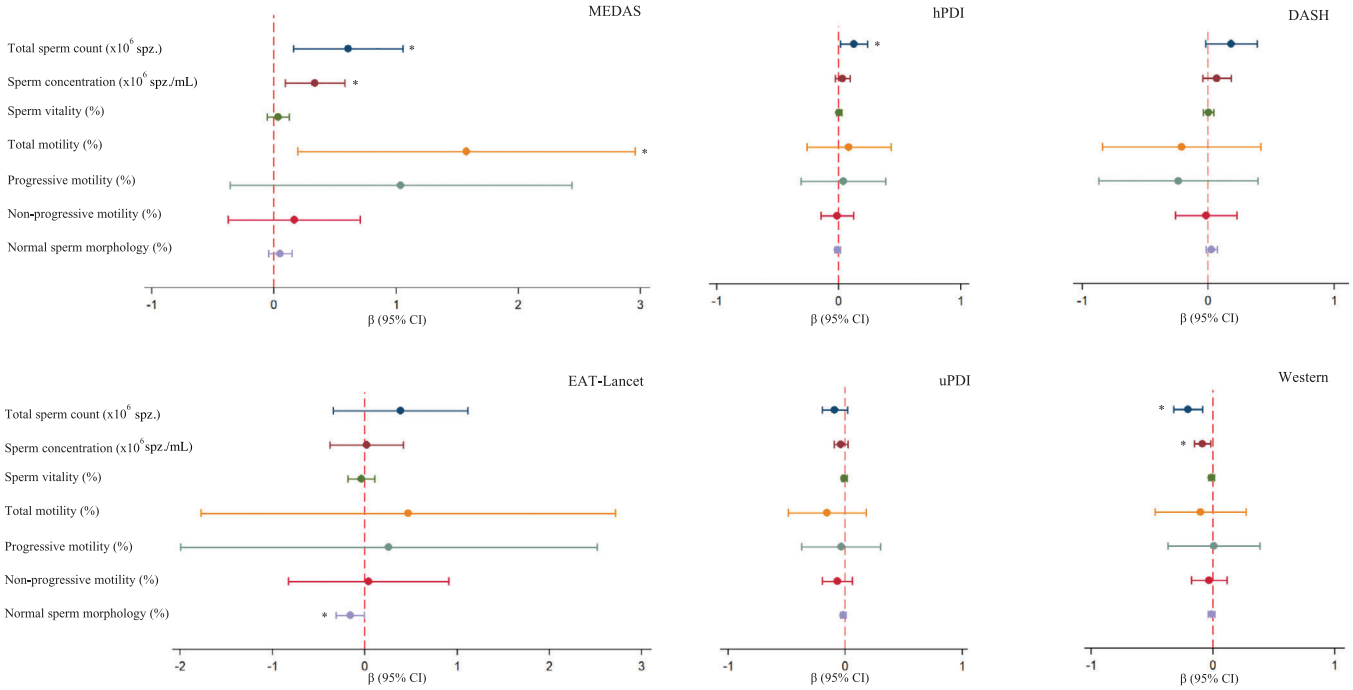

FIGURE 1 Associations (β coefficients and their 95% confidence interval) between one-point increment in each a-priori dietary pattern score and sperm quality parameters. β coefficients were estimated using multivariable linear regression models. Models were adjusted by age (years), smoking status (current, former, never), education (high school or less, college or high education), BMI (kg/m^2), physical activity (METs min/week), sleeping hours (hours/day), energy intake (kcal/day) and sexual abstinence (days). DASH, dietary approaches to stop hypertension; EAT-Lancet, EAT-Lancet diet score; hPDI, healthful plant-based diet index; MEDAS, Mediterranean diet adherence screener; uPDI, unhealthful plant-based diet index; Western, Western diet score. *Asterisks show statistical differences.

clinical information relevant to sperm quality was not available in our study cohort to discard some rare infertility causes. Finally, a notable limitation of our study is the absence of fertility status evaluation among participants. Future research should include a subgroup of proven fertile men to provide more comprehensive insights, particularly considering strict criteria for fertility. Although our associations are statistically significant, we acknowledge that we cannot affirm that are clinically relevant. Randomized clinical trials with fertility as an endpoint are warranted in the future for this purpose.

The primary strength of our study lies in conducting a comprehensive analysis of several a-priori healthy and unhealthy dietary patterns among well-phenotyped men of reproductive age from the general population. A rigorous protocol was adhered for sample handling, processing, and analysis utilizing the CASA SCA® system, all conducted by a single researcher. It is important to emphasize that although our cohort is from a general population and healthy reproductive-age men, we cannot rule out whether our healthy population is fertile or infertile. In fact, compared with another cohort of fertile and healthy men, the percentage of seminogram abnormalities (20.4%) is lower than in our results (41.5%).[60]

In conclusion, our findings suggest a relationship between men's dietary patterns and sperm quality parameters. Specifically, higher adherence to healthy dietary patterns was associated with better sperm quality parameters, while adherence to unhealthy dietary patterns was associated with poorer sperm quality. However, it is important to note that our study did not assess fertility potential, and therefore, no conclusions regarding fertility can be drawn from these results. Further research is needed to replicate our findings, including additional analysis such as hormonal levels and complementary sperm function tests, like DNA fragmentation and semen ROS test, to extend their applicability to other populations, and to determine whether these results hold true in proven fertile men. In particular, conducting long-term and well-controlled clinical trials in fertile men where unhealthy patterns are replaced by healthier ones would be especially valuable.

AUTHOR CONTRIBUTIONS

Estefanía Davila-Cordova, Albert Salas-Huetos, Jordi Salas-Salvadó, and Nancy Babio: Designed and conducted the research. Estefanía Davila-Cordova, Albert Salas-Huetos, Cristina Valle-Hita, and Nancy Babio: Analyzed the data. Estefanía Davila-Cordova, Albert Salas-Huetos, and Nancy Babio: Wrote the article. Estefanía Davila-Cordova, Albert Salas-Huetos, Cristina Valle-Hita, María Fernández de la Puente, María Ángeles Martínez, Antoni Palau-Galindo, Claudia Del Egido-González, José María Manzanares, Elena Sánchez-Resino, Jordi Salas-Salvadó, and Nancy Babio: Conducted the research and revised the manuscript for important intellectual content and read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. Estefanía Davila-Cordova, Albert

Salas-Huetos, Jordi Salas-Salvadó, and Nancy Babio are the guarantors of this work, and as such, they had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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