

## Original Article

# Mediterranean diet adherence in patients with congenital heart disease

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**Abstract:** The Mediterranean diet, based on a rural life where people ate what they grew, has shown cardiovascular benefits. Cross-sectional study of congenital heart disease (CHD) patients recruited consecutively from a single hospital outpatient clinic with the aim of determining their adherence to the Mediterranean diet according to the PREDIMED questionnaire. CHD complexity was categorized as simple, moderate, or great and demographic, clinical and blood test data were recorded. 200 CHD patients, median age 28 (16-54) years old and 120 (60%) males were studied. 45 (22.5%), 122 (61%) and 33 (16.5%) CHD patients had simple, moderate, and great complexity defects respectively. PREDIMED score was classified as low (score 0-5), intermediate (6-9) or high (> 9). 146 (83%) CHD patients showed a suboptimal Mediterranean diet adherence (PREDIMED score < 9) with less than half of patients eating enough vegetables, fruits, legumes, fish or nuts but with a high intake of butter/margarine, commercial sweets and carbonated beverages. No significant differences were seen between sex, body mass index, cardiovascular risk factors, CHD complexity or the educational level and the PREDIMED scores. Only being married was associated with a significant lower Mediterranean diet adherence (P=0.019). Meanwhile, no statistical significance was observed between serum glucose, creatinine, uric acid, albumin, LDL cholesterol, HDL cholesterol or triglycerides levels according to the PREDIMED classification (low, intermediate or high adherence). Conclusions: CHD patients have a low adherence to the Mediterranean diet with a low intake of vegetables, fruits, legumes, and fish.

**Keywords:** Mediterranean diet, PREDIMED, congenital heart disease, lipids

### Introduction

The Mediterranean diet consists essentially of fruit, vegetables, dried fruit and nuts based on a rural life where people ate what they grew being widely recognised as one of the healthier nutrition habits in the world with a substantially reduced risk of cardiovascular disease [1, 2]. In the last decades, however, the composition of the Mediterranean diet has changed dramatically, and the quality and quantity of food people eat has led to the loss of the traditional Mediterranean diet pattern. Factors accounting for this shift include more poverty, sedentari-ness and increased intake of processed foods. Also, changing lifestyles and busy schedules have been having a huge impact on our eating habits. This is particularly relevant in Spain where diabetes exerts a great impact on public

health due to its high prevalence [3]. Similarly, trends in the prevalence of childhood obesity and overweight in Spain have continuously increased in the last decades [4].

Physical inactivity, obesity, diabetes, and acquired cardiovascular disease may be at least as prevalent in patients with congenital heart disease as in the general population [5]. As most patients with congenital heart disease (CHD) survive into adulthood due to the improvement in the medical and surgical treatment, knowing their dietary habits is crucial as reduction in excess calories and improvement in dietary composition may prevent many primary and secondary cardiovascular events [6].

The objective of this study is to examine demographic and clinical variables that favor a sub-

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optimal Mediterranean diet and the relationship between diet adherence and blood test in CHD patients.

## Material and methods

Cross-sectional study among consecutive CHD patients recruited from a single hospital outpatient clinic between October 2018 and April 2019. Inclusion criteria were patients 16 years or older with a structural CHD verified by cardiac imaging. Patients unable to answer the survey, who did not want to participate or with a life expectancy less than one year were excluded from the study. All patients or their parents gave their written informed consent for participation. The protocol of the study was approved by the Hospital's Ethics Committee (CEIc/CEIm 890) and in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

### Clinical data

Basic information collected included age, sex, BMI (weight (kg)/height (m<sup>2</sup>)), CHD complexity categorized as simple, moderate or of great complexity [7], and comorbidities such as cardiovascular risk factors [systemic arterial hypertension (blood pressure > 140/90 mmHg or with antihypertensive treatment), diabetes mellitus (fasting serum glucose > 126 mg/dL or under oral anti-diabetic agents or insulin medication), dyslipidaemia and smoking status] [8-10]. Educational level was categorized as none and primary vs. middle and university while marital status was classified as single, divorced, separated or widower vs. cohabit or married.

### Questionnaires

Adherence to the Mediterranean diet was measured using a validated 14-item questionnaire (PREDIMED) [11]. Each item scored 1 or 0 and the PREDIMED score was calculated as follows: score 0-5, low adherence; score 6-9, intermediate adherence; score  $\geq 10$ , high adherence. The questions of the survey are specified in **Table 2**. The questionnaire was recorded during a face-to-face interview with a physician during the patient consultation. In CHD patients with reading or comprehension difficulties the test was performed with the parent's help.

### Blood test

The blood test was carried out on the following days of the survey. After an overnight fast of at least 10 hours blood samples were drawn for the measurements by spectrophotometric methods of plasma glucose, serum creatinine, albumin, uric acid, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (TG) (in milligrams per decilitre) using an Olympus AU 2700 (Olympus Diagnostic, Hamburg, Germany).

### Statistical analysis

Quantitative variables were expressed as mean  $\pm$  standard deviation or median and percentiles (5-95). Qualitative variables were expressed in percentages. A normal distribution was tested using the Kolmogorov-Smirnov test. Possible associations between categorical variables were evaluated by using the Pearson chi-square test. Continuous data were compared by Student's t-test or Mann-Whitney test for variables with or without normal distribution, respectively. A One-Way Analysis of Variance (ANOVA) was used to test the equality of three or more means at one time by using variances. The Kruskal-Wallis test was used as a backup method for ANOVA when the dependent variable was not normally distributed. A *p* values less than 0.05 was considered statically significant. Data analysis was carried out using SPSS 24.0 (SPSS, Chicago, IL).

## Results

### CHD population

Two hundred out of 204 patients with CHD, median age 28 (17-58) years old and 102 (60%) males were included in the study. 4 patients with Down syndrome unable to answer the questionnaire were excluded. No patient was ruled out due to a life expectancy less than one year and no patient refused to participate in the study. According to CHD complexity patients were classified as having simple (45 patients), moderate (122 patients) and great (33 patients) defects. **Table 1** shows the different types of CHD depending on the anatomical classification.

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**Table 1.** Congenital heart disease (CHD) anatomical Classification

Types of congenital heart disease	CHD Anatomy complexity (n)
Simple defects	45
Isolated small ASD	1
Isolated small VSD	20
Mild isolated pulmonary stenosis	2
Mild repaired conditions	1
Previously ligated or occluded ductus arteriosus	2
Repaired secundum ASD or sinus venous defect without significant shunt	10
Repaired VSD without significant shunt	9
Defects of moderate complexity	122
Repaired or unrepaired conditions	
Aorto-left unrepaired conditions	1
Anomalous pulmonary venous connection	1
AVSD partial or complete	21
Congenital aortic stenosis	16
Congenital mitral valve disease	1
Coarctation of the aorta	22
Ebstein anomaly (spectrum from mild to severe)	2
Pulmonary valve regurgitation (moderate or greater)	21
Peripheral pulmonary stenosis	2
Subvalvular aortic stenosis	7
Repaired tetralogy of Fallot	27
VSD with a great shunt	1
Defects of great complexity	33
Cyanotic CHD (unrepaired or palliated, all forms)	1
Double outlet right ventricle	4
Fontan procedures	1
Single ventricle	2
Pulmonary atresia	6
Dextro and Levo transposition of the great arteries	18
Truncus arteriosus	1
<b>Total of CHD patients</b>	<b>200</b>

n: number of patients, CHD: congenital heart disease, ASD: Atrial septal defect, VSD: Ventricular septal defect, AVSD: atrioventricular septal defect.

### *PREDIMED questionnaire according to anatomical complexity*

**Table 2** shows demographic and clinical data and the results of the 14-items of the PREDIMED questionnaire grouped by CHD complexity. Patients with great CHD complexity had significantly higher educational level and used significantly less olive oil and sofrito (sauce made with tomato and onion, leek, or garlic and simmered with olive oil) than CHD patients in the simple and moderate groups. On the other hand no significant differences were seen between CHD complexity (mild, moderate or great

and gender, marital status and the rest of items of the Mediterranean diet adherence survey (questions 3 to 13).

### *Demographic, clinical and blood test data according to the PREDIMED score adherence*

Meanwhile, **Table 3** shows demographic, clinical and blood test data according to the PREDIMED score. 41 (20.5%), 125 (62.5%) and 34 (17%) patients showed a low, intermediate, and high PREDIMED score respectively. No significant differences were seen according to age, sex, BMI, cardiovascular risk factors, Down syn-

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**Table 2.** Demographic data and the PREDIMED questionnaire in CHD patients according to the anatomical complexity

	CHD anatomical complexity			p	All CHD
	Mild	Moderate	Great		
Number of patients	45	122	33		
Age, years	23 (16-70)	30 (16-55)	28 (17-48)	0.185	28 (16-54)
Sex (male), n	30 (67)	69 (57)	21 (63)	0.445	120 (60)
Educational levels, n				0.006	
None and primary	19 (42)	39 (32)	3 (9)		61 (30)
Medium and university	26 (58)	83 (68)	30 (90)		139 (65)
Marital status, n				0.643	
Single, divorced, separated & widower	36 (80)	89 (73)	25 (76)		150 (75)
Cohabit & married	9 (20)	33 (27)	8 (24)		50 (25)
PREDIMED questionnaire					
1. Do you use olive oil as main culinary fat? (yes), n	40 (89)	106 (87)	23 (70)	0.035	169 (84)
2. How much olive oil do you consume in a given day? ( $\geq 4$ tablespoons), n	24 (53)	76 (65)	12 (36)	0.011	112 (56)
3. How many vegetable servings do you consume per day? ( $\geq 2$ ), n	15 (33)	53 (43)	15 (45)	0.411	83 (41)
4. How many fruit units do you consume per day? ( $\geq 3$ ), n	15 (33)	46 (38)	10 (30)	0.691	71 (35)
5. How many servings of red meat, hamburger, or meat products do you consume per day? ( $< 1$ ), n	28 (62)	72 (59)	21 (46)	0.859	121 (60)
6. How many servings of butter, margarine, or cream do you consume per day? ( $< 1$ ), n	37 (82)	93 (76)	26 (79)	0.704	156 (78)
7. How many sweet or carbonated beverages do you drink per day? ( $< 1$ ), n	27 (60)	71 (58)	23 (70)	0.486	121 (60)
8. How much wine do you drink per week? ( $\geq 7$ glasses), n	1 (2)	8 (7)	0 (0)	0.192	9 (4)
9. How many servings of legumes do you consume per week? ( $\geq 3$ ), n	20 (44)	50 (41)	17 (51)	0.551	87 (43)
10. How many servings of fish or shellfish do you consume per week? ( $\geq 3$ ), n	10 (22)	37 (30)	8 (24)	0.524	55 (27)
11. How many times per week do you consume commercial sweets or pastries? ( $< 3$ ), n	22 (49)	65 (53)	19 (58)	0.746	106 (53)
12. How many servings of nuts (including peanuts) do you consume per week? ( $\geq 3$ ), n	15 (33)	42 (34)	10 (30)	0.905	67 (33)
13. Do you consume chicken, turkey, or rabbit meat instead of pork, hamburger, or sausage? (yes), n	34 (76)	102 (84)	28 (85)	0.436	164 (82)
14. How many times per week do you consume vegetables, pasta, rice, with sofrito? ( $\geq 2$ ), n	40 (89)	105 (86)	20 (60)	0.003	165 (82)

n: number of patients, CHD: congenital heart disease. The data are expressed as number and percentages.

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**Table 3.** Demographic, clinical and blood test data according to the PREDIMED score adherence in CHD patients

	PREDIMED score adherence			p
	Low score 0-5	Intermediate score 6-9	High score $\geq$ 10	
Number of patients, n	41	125	34	
Age, years	30 (18-53)	24 (17-35)	34 (16-62)	0.115
Sex (male), n	29 (71)	71 (57)	20 (59)	0.284
BMI, Kg/m <sup>2</sup>	25 (19-38)	24 (17-35)	24 (18-33)	0.290
Arterial hypertension, n	4 (10)	8 (6)	5 (15)	0.290
Diabetes mellitus, n	2 (5)	4 (3)	1 (3)	0.863
Dyslipidemia, n	5 (12)	13 (10)	7 (21)	0.281
Smoking, n	4 (10)	4 (3)	4 (12)	0.092
Down's syndrome, n	0 (0)	11 (9)	3 (9)	0.144
CHD complexity, n				0.189
Mild	7 (17)	32 (26)	6 (18)	
Moderate	26 (63)	70 (56)	26 (76)	
Great	8 (20)	23 (18)	2 (6)	
Educational level, n				0.530
None and primary	11 (27)	37 (30)	13 (38)	
Medium and university	30 (73)	88 (70)	21 (62)	
Marital status, n				0.019
Single, divorced, separated & widower	27 (66)	102 (81)	21 (62)	
Cohabit & married	14 (34)	23 (18)	13 (38)	
Blood analytical data				
Serum glucose, mg/dL	96 $\pm$ 11	95 $\pm$ 13	99 $\pm$ 14	0.384
Serum creatinine, mg/dL	0.8 $\pm$ 0.2	0.8 $\pm$ 0.2	0.8 $\pm$ 0.2	0.477
Serum albumin, g/dL	4 (4-6)	4 (4-5)	4 (4-5)	0.596
Serum uric acid, mg/dL	5 (4-9)	6 (3-9)	5 (2-9)	0.362
Total cholesterol, mg/dL	160 $\pm$ 32	157 $\pm$ 38	175 $\pm$ 38	0.083
LDL cholesterol, mg/dL	90 $\pm$ 26	90 $\pm$ 31	101 $\pm$ 31	0.115
HDL cholesterol, mg/dL	47 $\pm$ 10	50 $\pm$ 11	51 $\pm$ 11	0.180
Triglycerides, mg/dL	103 (37-273)	84 (37-208)	83 (46-305)	0.788

n: number of patients, CHD: congenital heart disease, BMI: body mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein. The data are expressed as median and percentages (5-95), mean  $\pm$  standard deviation and number and percentages in parenthesis.

drome, CHD complexity or educational level according to the Mediterranean diet adherence level. Similarly, no significant differences were seen between the PREDIMED score and total or LDL cholesterol concentrations. On the other hand, cohabiting and being married was associated with a higher adherence to the Mediterranean diet than single, divorced, separated or widower CHD patients (P=0.019).

### Discussion

Cardiovascular disease is the most important threat to the health of today's population [11]

affecting also to CHD patients [12]. Numerous studies have shown that the adherence to the Mediterranean diet is associated with a decrease in cardiovascular risk [13-15] and with a higher life expectancy and quality of life [4]. During the last decades, a quick and important modification of the dietary habits has been observed in the Mediterranean countries, especially among young people [16]. For instance, in Spain [17] up to 69% of the child and adolescent population has been found to have suboptimal adherence to the Mediterranean diet as also occurs in countries such as Greece [18] or Italy where the percentage

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may be even higher [19]. Similarly, Durá Travé T. et al. [20], in a college population aged 18-25 years to whom a dietary survey was performed, found that 9%, 62% and 28% had a low, intermediate, and high adherence to the Mediterranean diet respectively. Likewise García Cabrera et al. [21], after evaluating 18 cross-sectional studies, found a low adherence to the Mediterranean diet among children and adolescents by using the KIDMED test (21% of the surveyed population had low adherence versus a 10% with high adherence) as also seen in our series with less than half of our CHD patients consuming sufficient amounts of vegetables, fruits, legumes, fish or nuts and with a high intake of butter/margarine, commercial sweets and carbonated beverages.

Adult CHD are at equal risk as their matched peers to be overweight and obese [5]. Nonetheless metabolic syndrome, a constellation of risk factors for cardiovascular disease including obesity, dyslipidemia, insulin resistance, and hypertension, is more common among adult CHD than in the general population [22, 23]. Unfortunately, there are no studies on dietary habits in adult patients with CHD. As dietary patterns close to the Mediterranean diet (rich in fruit and vegetables and high in monounsaturated fats) are negatively associated with features of the metabolic syndrome [24] and chronic inflammation [25] special attention should be paid to CHD patients, a population with a higher risk of cardiovascular complications in the medium long term.

In relation to age and gender, although previous studies in the general population have found that older and male patients may have a higher Mediterranean diet adherence, probably due to the fact that older patients have better dietary habits acquired in childhood in addition to having more time to cook and eat, and men consume a greater amount of alcohol, which scores positively in the PREDIMED survey, no significant differences were seen in age and sex in our series probably due to the young age of our CHD patients. Similarly, no significant difference was seen according to the education status despite the Mediterranean diet adherence seems to increase based on the academic and income levels [26]. This could be explained because the majority of our young adult CHD patients lived with their parents

regardless of the educational level. In fact, according to the latest Spanish National Statistics Institute (INE) survey, 53% of young people (between 25 and 29 years old) and 25% of adults (between 30 and 34 years old) still lived with their parents irrespective of their study levels, weighed down by unemployment and the precariousness and instability of the labour market [27]. On the other hand, our married CHD people scored lower in the Mediterranean diet adherence survey than single, widowed, separated, or divorced [28] probably because our patients, most of them young, lived at home with their parents and therefore ate better. On the contrary, although it might be thought that patients with more complex CHD could eat better to avoid added long-term complications, no significant differences were observed in our series between the different complexities.

In relation to glycemic and lipid levels it has been shown that the Mediterranean diet is effective in reducing the metabolic syndrome. However, previous randomised controlled trials in healthy adults and adults at high risk of CVD, have found only small reductions in total cholesterol and LDL cholesterol concentrations in patients with a Mediterranean dietary pattern in comparison with other groups who received either no intervention or minimal intervention [29]. On the other hand, other studies have found no significant association between the Mediterranean diet adherence and LDL cholesterol concentrations [30-32] as also seen in our series. This lack of significance, seen in cholesterol levels, may be in relation to the young age of our CHD patients as cholesterol levels in healthy patients gradually increases up from 40 years of age [33]. The same would apply to the lack of significance in serum glucose concentration according to the Mediterranean diet adherence as aging is by far the strongest known risk factor of diabetes mellitus [34].

There are, however, limitations in our study that may impact our findings. Firstly, unmeasured incomes as families with low income generally eat a less nutritious diet than those with a higher income, either because they cannot afford enough food or because they eat foods that are nutritionally poor. Secondly, responses on self-rated eating habits may lead understanding and recall bias and finally our reliance on



cross-sectional data does not allow for causal inferences.

In conclusion in our study, to our knowledge the first one conducted in CHD patients, we found a suboptimal adherence to the Mediterranean diet. Because adult CHD patients have other abnormalities that may make their heart more vulnerable, to both the development of atherosclerosis and adverse sequelae of a cardiovascular event, it seems reasonable to insist on healthy dietary habits in this group of patients.

### Disclosure of conflict of interest

None.

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### References

- [1] Aguilà Q, Ramón MÀ, Matesanz S, Vilatimó R, Del Moral I, Brotons C and Ulied À. Assessment study of the nutritional status, eating habits and physical activity of the schooled population of Centelles, Hostalets de Balenyà and Sant Martí de Centelles (ALIN 2014 Study). *Endocrinol Diabetes Nutr* 2017; 64: 138-145.
- [2] Martínez-González MA, Gea A and Ruiz-Canela M. The mediterranean diet and cardiovascular health. *Circ Res* 2019; 124: 779-798.
- [3] Lopez-Bastida J, Boronat M, Moreno JO and Schurer W. Costs, outcomes and challenges for diabetes care in Spain. *Global Health* 2013; 9: 17.
- [4] Franco M, Sanz B, Otero L, Domínguez-Vila A and Caballero B. Prevention of childhood obesity in Spain: a focus on policies outside the health sector. *SESPAS report 2010. Gac Sanit* 2010; 24 Suppl 1: 49-55.
- [5] Lerman JB, Parness IA and Shenoy RU. Body weights in adults with congenital heart disease and the obesity frequency. *Am J Cardiol* 2017; 119: 638-642.
- [6] Yu E, Malik VS and Hu FB. Cardiovascular disease prevention by diet modification: JACC Health promotion series. *J Am Coll Cardiol* 2018; 72: 914-926.
- [7] Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, Khairy P, Landzberg MJ, Saidi A, Valente AM and Van Hare GF. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019; 139: e637-e697.
- [8] Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V and Desormais I; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* 2018; 39: 3021-3104.
- [9] Authors/Task Force Members, Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, Deaton C, Escaned J, Hammes HP, Huikuri H, Marre M, Marx N, Mellbin L, Ostergren J, Patrono C, Seferovic P, Uva MS, Taskinen MR, Tendera M, Tuomilehto J, Valensi P, Zamorano JL; ESC Committee for Practice Guidelines (CPG), Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, De Backer G, Sirnes PA, Ezquerro EA, Avogaro A, Badimon L, Baranova E, Baumgartner H, Betteridge J, Ceriello A, Fagard R, Funck-Brentano C, Gulba DC, Hasdai D, Hoes AW, Kjekshus JK, Knuuti J, Kolh P, Lev E, Mueller C, Neyses L, Nilsson PM, Perk J, Ponikowski P, Reiner Z, Sattar N, Schächinger V, Scheen A, Schirmer H, Strömberg A, Sudzhaeva S, Tamargo JL, Viigimaa M, Vlachopoulos C and Xuereb RG. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2013; 34: 3035-3087.
- [10] Martínez-Quintana E, Rodríguez-Hernández JL, Rodríguez-González F, Riaño-Ruiz M, Fraguera-Medina C, Girolimetti A and Jiménez-Rodríguez S. Cardiovascular risk factors and arterial thrombotic events in congenital heart disease patients. *Int J Clin Pract* 2019; 73: 1-8.
- [11] Yusuf S, Joseph P, Rangarajan S, Islam S, Mentz A, Hystad P, Brauer M, Kutty VR, Gupta R, Wielgosz A, AlHabib KF, Dans A, Lopez-Jaramillo P, Avezum A, Lanas F, Oguz A, Kruger IM, Diaz R, Yusuf K, Mony P, Chifamba J, Yeates K, Kelishadi R, Yusufali A, Khatib R, Rahman O,

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- Zatonska K, Iqbal R, Wei L, Bo H, Rosengren A, Kaur M, Mohan V, Lear SA, Teo KK, Leong D, O'Donnell M, McKee M and Dagenais G. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet* 2020; 395: 795-808.
- [12] Bigras JL. Cardiovascular risk factors in patients with congenital heart disease. *Can J Cardiol* 2020; 36: 1458-1466.
- [13] Martínez-González MA, García-Arellano A, Toledo E, Salas-Salvadó J, Buil-Cosiales P, Corella D, Covas MI, Schröder H, Arós F, Gómez-Gracia E, Fiol M, Ruiz-Gutiérrez V, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Muñoz MA, Wärnberg J, Ros E and Estruch R; PREDIMED Study Investigators. A 14-item Mediterranean diet assessment tool and obesity indexes among high-risk subjects: the PREDIMED trial. *PLoS One* 2012; 7: e43134.
- [14] Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. *Circulation* 2016; 133: 187-225.
- [15] Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA and Martínez-González MA. Retraction and republication: primary prevention of cardiovascular disease with a mediterranean diet. *N Engl J Med* 2013; 368: 1279-1290. *N Engl J Med* 2018; 378: 2441-2442.
- [16] Olmedo-Requena R, González-Donquiles C, Dávila-Batista V, Romaguera D, Castelló A, Molina de la Torre AJ, Amiano P, Dierssen-Sotos T, Guevara M, Fernández-Tardón G, Lozano-Lorca M, Alguacil J, Peiró R, Huerta JM, Gracia-Lavedan E, Aragonés N, Fernández-Villa T, Solans M, Gómez-Acebo I, Castaño-Vinyals G, Kogevinas M, Pollán M and Martín V. Agreement among mediterranean diet pattern adherence indexes: MCC-spain study. *Nutrients* 2019; 11: 488.
- [17] León-Muñoz LM, Guallar-Castillón P, Graciani A, López-García E, Mesas AE, Aguilera MT, Banegas JR and Rodríguez-Artalejo F. Adherence to the Mediterranean diet pattern has declined in Spanish adults. *J Nutr* 2012; 142: 1843-1850.
- [18] Papadaki S and Mavrikaki E. Greek adolescents and the Mediterranean diet: factors affecting quality and adherence. *Nutrition* 2015; 31: 345-349.
- [19] Archero F, Ricotti R, Solito A, Carrera D, Civello F, Di Bella R, Bellone S and Prodam F. Adherence to the mediterranean diet among school children and adolescents living in northern Italy and unhealthy food behaviors associated to overweight. *Nutrients* 2018; 10: 1322.
- [20] Durá Travé T and Castroviejo Gandarias A. Adherence to a Mediterranean diet in a college population. *Nutr Hosp* 2011; 26: 602-608.
- [21] García Cabrera S, Herrera Fernández N, Rodríguez Hernández C, Nissensohn M, Román-Viñas B and Serra-Majem L. Kidmed test; prevalence of low adherence to the mediterranean diet in children and young; a systematic review. *Nutr Hosp* 2015; 32: 2390-2399.
- [22] Niwa K. Metabolic syndrome in adult congenital heart disease. *Korean Circ J* 2019; 49: 691-708.
- [23] Deen JF, Krieger EV, Slee AE, Arslan A, Arterburn D, Stout KK and Portman MA. Metabolic syndrome in adults with congenital heart disease. *J Am Heart Assoc* 2016; 5: e001132.
- [24] Esposito K, Ciotola M and Giugliano D. Mediterranean diet and the metabolic syndrome. *Mol Nutr Food Res* 2007; 51: 1268-1274.
- [25] Giugliano D and Esposito K. Mediterranean diet and metabolic diseases. *Curr Opin Lipidol* 2008; 19: 63-68.
- [26] León-Muñoz LM, Guallar-Castillón P, Graciani A, López-García E, Mesas AE, Aguilera MT, Banegas JR and Rodríguez-Artalejo F. Adherence to the Mediterranean diet pattern has declined in Spanish adults. *J Nutr* 2012; 142: 1843-1850.
- [27] Instituto Nacional de Estadística. Encuesta Continua de Hogares. Metodología. Madrid: Instituto Nacional de Estadística, 2016; pp. 8.
- [28] Jurado D, Burgos-Garrido E, Diaz FJ, Martínez-Ortega JM and Gurpegui M. Adherence to the mediterranean dietary pattern and personality in patients attending a primary health center. *J Acad Nutr Diet* 2012; 112: 887-891.
- [29] Ros E, Martínez-González MA, Estruch R, Salas-Salvadó J, Fitó M, Martínez JA and Corella D. Mediterranean diet and cardiovascular health: teachings of the PREDIMED study. *Adv Nutr* 2014; 5: 330S-336S.
- [30] Razquin C, Liang L, Toledo E, Clish CB, Ruiz-Canela M, Zheng Y, Wang DD, Corella D, Castaner O, Ros E, Aros F, Gomez-Gracia E, Fiol M, Santos-Lozano JM, Guasch-Ferre M, Serra-Majem L, Sala-Vila A, Buil-Cosiales P, Bullo M, Fito M, Portoles O, Estruch R, Salas-Salvado J, Hu FB and Martinez-Gonzalez MA. Plasma lipiome patterns associated with cardiovascular risk in the PREDIMED trial: a case-cohort study. *Int J Cardiol* 2018; 253: 126-132.
- [31] Rees K, Takeda A, Martin N, Ellis L, Wijesekera D, Vepa A, Das A, Hartley L and Stranges S. Mediterranean-style diet for the primary and secondary prevention of cardiovascular dis-



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- ease. *Cochrane Database Syst Rev* 2019; 3: CD009825.
- [32] Dinu M, Pagliai G, Casini A and Sofi F. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials. *Eur J Clin Nutr* 2018; 72: 30-43.
- [33] Rao PN and Sastry NS. Serum cholesterol levels of males and females in different age groups in South India. *Am J Clin Nutr* 1980; 33: 181-182.
- [34] Savji N, Rockman CB, Skolnick AH, Guo Y, Adelman MA, Riles T and Berger JS. Association between advanced age and vascular disease in different arterial territories: a population database of over 3.6 million subjects. *J Am Coll Cardiol* 2013; 61: 1736-1743.