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The Effect of Plant-Based Nutrition Diets on Plasma Lipids Profile—A Study Case in Romania

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Abstract: Diet is an important tool in managing dyslipidemic disorders, thus contributing to the prophylaxis of cardiovascular morbidity. Research has shown that a plant-based diet could have positive effects through many pathways. We conducted a study on a group of 38 plant-based individuals from Romania who have adopted the diet for at least one year. The aim of the research was to evaluate eventual changes in their lipid profile. We analyzed to what extent the values of different markers significantly changed following the dietary transition. Improvements were obtained for body mass index (BMI) and all lipid markers, with the exception of high-density lipoprotein cholesterol (HDL-C). Results showed that 75.0% of persons with elevated TGs (triglycerides) succeeded in normalizing them, as well as individuals with high low-density lipoprotein cholesterol (LDL-C) levels, where 72.7% from the borderline elevated became optimal. The total cholesterol (TC)/HDL-C ratio shifted from elevated to optimum in 78.6% of cases. Results were poor in three participants with presumed familial hypercholesterolemia, which were later successfully managed by using lipid-lowering medication. In conclusion, although dyslipidemias are only a surrogate marker for cardiovascular morbidity, the actions by which a plant-based diet can influence cardiovascular diseases are multiple, and we consider that our study confirms its positive effect.

Keywords: plant-based; lipid profile; cardiovascular disease; vegan; dyslipidemia

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1. Introduction

Cardiovascular diseases are important causes of morbidity and mortality in the contemporary world. Primary and secondary prophylaxes are important targets, but measures are relatively difficult to be applied in current practice, due to the multifactorial etiology of this pathology. Mostly all prophylactic interventions also aim to improve the lipid profile, to reduce the level of lipoproteins that contain a high quantity of cholesterol (primarily LDL-C), and to increase the number of particles involved in the reverse transport of cholesterol, HDL-C. Oxidized LDL-C is absorbed by the subendothelial macrophages, after which the macrophages transform into foam cells and promote the expression of pro-inflammatory genes (e.g., nuclear factor kappa B-NFkB), initiating the inflammatory response. The lipid striae are formed initially, then, through structural and functional changes of the middle vascular tunic, the atheroma plaque is built, the vessel loses its

normal secretory properties (e.g., secretion of vasodilators, such as nitric oxide), suppleness, anticoagulant, and fibrinolytic properties. This creates the pathophysiological substrate for hypertension and thrombosis.

TGs are found in large quantities in chylomicrons (in the postprandial phase) and in very low-density lipoprotein cholesterol (VLDL-C) particles (in the interprandial phase); these plasma transporters are susceptible to the action of lipoprotein lipase, which cleaves TGs into fatty acids and glycerol, lipid components that can be taken up by cells, including the vascular endothelial cell and that can initiate inflammatory processes in the vascular intima. Although TGs are not components of the atheroma plaque, elevated levels are an indirect marker of high VLDL-C levels [1]. Both TG and TC levels are influenced by intake, especially the intake of carbohydrates and lipids in the diet, as well as alcohol consumption. Clinical studies have shown that improving the lipid profile has yielded results in terms of cardiovascular risk. Modifying the diet model is, in theory, a method available to every individual, correctly guided by specialists. Therefore, the approach to dyslipidemias can be successful through dietary changes, reduced hypertriglyceridemia and hypercholesterolemia being reported in many scientific studies. Moreover, current prevention guidelines state that the most important prevention measures are adherence to a healthy lifestyle, in which diet plays a central role [2].

Among the diets most often recommended for normalizing the plasma lipid profile, the most effective have been those based on plants. In these diets, most calories come from foods of plant origin, food of animal origin being present in small quantities. Lipid intake is usually variable but always is made mostly of unsaturated lipids, which largely replace saturated lipids, very abundant in the diet of the modern human. The presence of soluble fiber, antioxidant minerals, vitamins, phytonutrients, the low glycemic load, and the lack of cholesterol are some of the attributes of these diets. In addition, studies have shown that this kind of diet is associated with a lower incidence of high blood pressure and a lower BMI [3–9], factors involved in the prophylaxis of cardiovascular diseases. A classic example of a plant-based diet is the Mediterranean diet, even if the model used today is slightly different from the original type, much richer in vegetable oils [10].

In the last decade, more and more place was gained by diets mostly or completely based on plants (vegan, plant-based), in which foods of animal origin are completely excluded and all calories come from plant foods. This diet is based on cereals, legumes, pulses, including soy, which are completed with significant amounts of vegetables and fruits. Most dietary lipids are components of these food groups and are supplemented by others from oilseeds and oily fruits (olives, almonds, cashews, etc.). The addition of commercial oils is optional [11]. The reported action of the plant-based diet on the lipid profile has been favorable in many studies [12–16]. Of course, controlled clinical trials would be necessary to assess the direct effects on the associated pathology, but such studies are difficult, if not impossible to be performed when it comes to food and diets [17]. In addition, the diet effects are not always enough and must be supplemented by appropriate medication, taking into account that the lipid profile has a complex determinism, including a variety of gene polymorphisms [18–22]. Physical exertion also alters the transport of cholesterol between the central metabolic compartment (liver), physiological storage tissue (adipose tissue), and other peripheral tissues of the body, including vascular wall structures, thus reducing direct transport by reducing LDL-C and promoting reverse transport by increasing HDL-C [17].

In this paper, we conducted a preliminary study on a group of 38 vegans from Romania who have adopted this diet for at least one year and from which we could obtain data on test reports performed before and after the transition to veganism in terms of lipid profile. Our aim was to evaluate eventual changes, in a nonsmoking population, with moderate physical activity, after starting a plant-based diet. Even though a plant-based diet can theoretically influence circulating lipids by many pathways, not many real-life studies in this area have been carried out, especially in South-Eastern Europe. We analyzed

to what extent the values significantly changed as a result of dietary changes, considering the results as a starting point for the development of specific dietary counseling measures.

2. Materials and Methods

The formation of the working group took place within the CORE project, an ongoing project financed by the Romanian Ministry of Research, which aims to evaluate the food intake of different population groups with specific nutritional needs (pregnant women, seniors, obese, plant-based). The analysis of these data will provide arguments for drawing corrective nutritional measures, whenever the risk of developing deficiencies is found. The project included, among others, a group of people with exclusively plant-based (vegan) nutrition (n = 120), to whom an extensive nutritional interview was performed. After one year of the initial interview, members of the plant-based group were contacted by phone. They were informed about the objectives of the current study (evaluation of variation of circulating lipids under a vegan diet) and asked to what extent they have test reports covering their lipid profile before and after becoming vegan. Out of the total number of people in the group, 75 agreed to participate, but 37 of them failed to find the requested documents and could not be included in the analysis. Finally, 38 persons were able to provide laboratory tests from ISO certified laboratories which included the circulating lipids profile before and after becoming plant-based. These 38 persons are the subjects of the present analysis, designated hereafter as the study group (Figure 1).

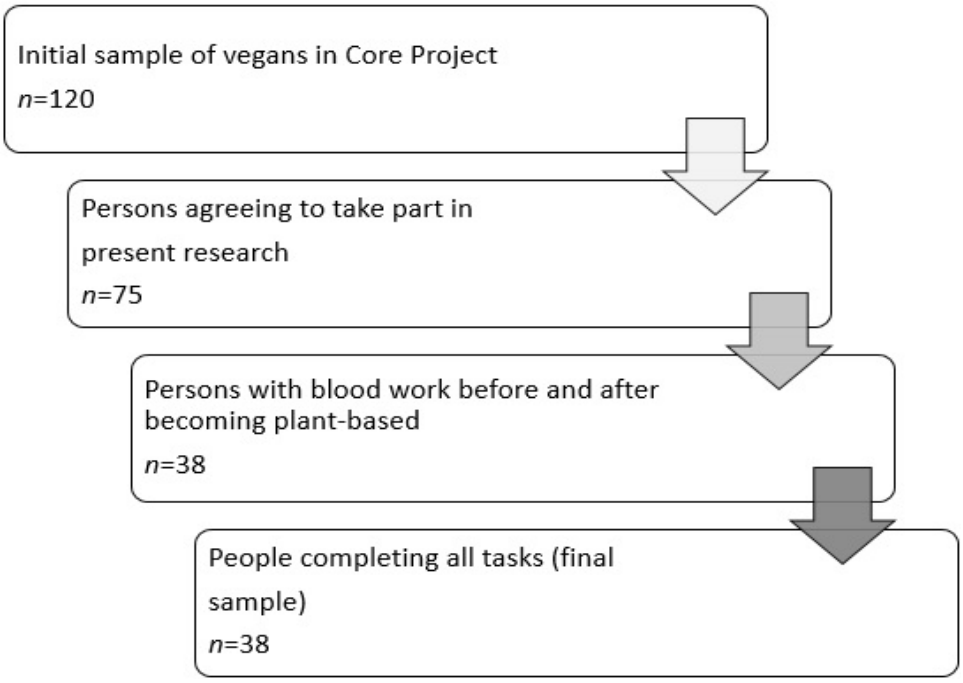


Figure 1. Selection of the group taking part in the research.

The method for the collection of data for the study was CATI (computer-assisted telephone interviewing). The questionnaire included general demographic items, year of the start of the plant-based diet, items about daily behavior (smoking, alcohol consumption, physical activity), self-reported somatic parameters (weight (W) before being vegan and at the moment of the interview and height (H)), chronic diseases diagnosed by a medical doctor (year of diagnosis, treatment). In subjects receiving lipid-lowering treatment, supplementary questions were posed on the duration of treatment, and lab tests before and after starting this treatment. Somatometric data allowed the calculation of current and previous BMI.

All members of the group were gathered at a vegan fair and a qualitative evaluation of their diets was carried out by interview by the principal investigator of this study.

Afterward, the participants were asked to send scanned copies of the required pairs of tests (lipid blood profile before and after becoming vegan). For persons who declared being treated for dyslipidemia, we took into consideration the values prior to the beginning of the drug treatment, in order to exclude the bias introduced by the effect of statins.

1. Lipid profile was defined based on the serum lipoproteins, considering the following as reference values:
   - TGs: optimal < 150 mg/dL (0); borderline elevated 150–199 mg/dL (1), elevated 200–499 mg/dL (2), very elevated $\geq$ 500 mg/dL (3)
   - TC: optimal < 200 mg/dL (0), borderline elevated 200–240 mg/dL (1), elevated $\geq$ 240 mg/dL (2)
   - HDL-C: low $\leq$ 40 mg/dL (2), normal > 40 mg/dL (1), protective > 60 mg/dL (0)
   - LDL-C: optimal < 100 mg/dL (0), optimal at the limit = 100–129 mg/dL (1), borderline elevated = 130–159 mg/dL (2), elevated = 160–189 mg/dL (3), very high $\geq$ 190 mg/dL (4)

Continuous variables were used for direct comparison of the lipoproteins before and after a plant-based diet. Categorical variables of the lipoproteins were used to define the major changes (switch from a category of risk to another) in the lipid profile.

A variable consisting of the TC/HDL-C ratio (TC/HDL-C) was also constituted, due to its prognostic value in terms of cardiovascular morbidity. Results of this ratio were interpreted as Ideal <3.5 (0); optimum = below 5 (2); increased >5, based on the previously communicated data (3).

2. The BMI was analyzed as a categorical variable, using four categories: Underweight (0) if BMI < 18.5, normal weight (1) if BMI = 18.5–24.9, overweight (pre-obese) (2) if BMI = 25–29.9, and obese (3) if BMI $\geq$ 30.

All working variables (BMI, lipid panel, TC/HDL-C) were identified with "1", for values before plant-based dieting and with "2", for values under "plant-based" dieting.

Results were statistically processed using SPSS 14.0 software. All data were considered either as continuous variables or as ordinal in the categories described above. We used descriptive tests; as for data analysis, *t*-tests, and Pearson for correlations tests were applied for continuous variables, since the Kolmogorov–Smirnoff normality test could reject the hypothesis of a non-normal distribution of data (p in all cases >0.05). The Wilcoxon signed-rank test was used for ordinal variables, allowing to calculate individuals "migrating" from a category of lipids value, to another. The statistical significance threshold for all statistical tests was 0.05.

Consent to participate in the study was requested from each participant. The Ethics Committee of the National Institute of Research and Development for Food Bioresearches, Bucharest, Romania assessed and approved the study (nr. 714/17.06.2019).

3. Results

The group included 20 women and 18 men. The average age was 36 years. The youngest respondent was 21 years old and the oldest 65. The level of education was high, with 27 being college graduates, 6 had postgraduate studies, and 5 had high school education. The most common duration of plant-based adherence was 2 years (in 29% of members).

All participants were never smokers. Alcohol consumption was scarce, all of the respondents stating that they drink 1–2 glasses of alcoholic beverages once a month or less. In the qualitative evaluation of food intake, all participants reported following a whole food plant-based diet, which included less than one portion per week of vegan fast food (mock meat, mock cheese, sweets, etc.).

The whole group declared themselves physically active, with at least half an hour of strenuous physical activity per day. When asked about weight loss, 14 persons answered that they had lost weight since the adoption of the plant-based diet, which was not con-

firmed by the comparison of BMI, showing that only seven people lost weight since the adoption of this particular diet.

Regarding the presence of associated chronic diseases, five people were diagnosed with allergies during their lifetime and two with immunological disorders (rheumatoid arthritis). All of them had extensive medical documents to confirm these conditions. No cardiovascular disease could be documented in any of the participants. Out of the whole group, three people were currently under treatment with hypocholesterolemic medication (statins). In all of them, the onset of the treatment was subsequent to the beginning of the vegan diet.

Along with lipid values, documents sent by participants included other values of blood parameters (glycaemia, proteinemia, calcemia, etc.) that have been analyzed and no statistical differences were noticed for any of them when comparing values from the pre-vegan period with the vegan one. Table 1 shows mean values of BMI and circulating lipids, before and after adopting a vegan diet, in women and men (*t*-test was applied for statistical significance evaluation).

Table 1. BMI and lipid profile before (1) and after (2) dieting.

Variable	Men (Mean Value)	Women (Mean Value)
BMI 1 (kg/m^2)	22.3	23.0
BMI 2 (kg/m^2)	21.2	22.2
p	0.001	0.006
TG 1 (mg/dL)	117.6	117.9
TG 2 (mg/dL)	104.3	102.6
p	0.003	0.005
TC 1(mg/dL)	0.186.5	203.4
TC 2 (mg/dL)	152.9	168.3
p	0.000	0.000
HDL-C 1(mg/dL)	45.0	48.2
HDL-C 2(mg/dL)	43.7	47.4
	0.338	0.530
LDL-C 1 (mg/dL)	133.3	143.5
LDL-C 2 (mg/dL)	99.0	108.9
p	0.000	0.000
TC/HDL-C 1	4.1	4.2
TC/HDL-C 2	3.5	3.5
p	0.000	0.000

BMI—body mass index, TG—triglycerides, TC—total cholesterol, HDL-C—high-density lipoprotein cholesterol, LDL-C—low-density lipoprotein cholesterol, TC/HDL-C—total cholesterol to high-density lipoprotein cholesterol ratio.

Decreases in the mean values can be observed in all parameters. Results were in all cases statistically significant, with the exception of HDL-C. Indeed, HDL-C shows a variation found in other studies performed on vegans and vegetarians (Table 2), with 82.4% of those with low values (below 40 mg/dL) failing to reach higher normal and protective categories.

Table 2. Percent of persons (%) "migrating" between categories of cardiovascular risk related to the HDL-C.

		HDL-C 2 Category		
		Normal	**Low**	**Protective**
HDL-C 1 category	normal	17.6%	82.4%	-
	low	93.8%	6.2%	-
	protective	50.0%	-	50.0%

HDL-C 1—high-density lipoprotein cholesterol before plant-based diet; HDL-C 2—high-density lipoprotein cholesterol after plant-based diet.

Changes in the TG categories are presented in Table 3. We noticed that 75% of people with high TG values managed to normalize them. Regarding TC, data are presented in Table 4. All borderline values decreased within normal limits and only 30% of the increased values did not change.

Table 3. Percent of persons (%) "migrating" between categories of cardiovascular risk related to TGs.

		TG 2 Category	
		Normal	**Borderline Elevated**
TG 1 category	normal	100%	-
	borderline elevated	75%	25%

TG 1—triglycerides before plant-based diet; TG 2—triglycerides after plant-based diet.

Table 4. Percent of persons (%) "migrating" from a category to another of TC after becoming plant-based, where TC 1 are % before plant-based and TC 2 after.

		TC 2 Category		
		Optimal	**Borderline Elevated**	**Elevated**
TC 1 category	optimal	100%	-	-
	borderline elevated	100%	-	-
	elevated	30%	40%	30%

TC 1—total cholesterol before plant-based diet; TC 2—total cholesterol after plant-based diet.

Of all the lipid markers, LDL-C was the most influenced. Only 9.1% of those with optimal showed an increase (up to the elevated borderline category) and 22.2% of those with high values remained in the same category (Table 5).

Table 5. Percent of persons (%) "migrating" from a category to another of LDL-C after becoming plant-based, where LDL-C 1 is % before plant-based and LDL-C 2 after.

		LDL-C 2 Category				
		Optimal	**Borderline Optimal**	**Borderline Elevated**	**Elevated**	**Very Elevated**
LDL-C 1 category	optimal	100%	-	-	-	-
	borderline optimal	83.8%	16.2%	-	-	-
	borderline elevated	72.7%	18.2%	-	9.1%	-
	elevated	-	66.7%	33.3%	-	-
	very elevated	-	-	66.7%	11.1%	22.2%

LDL-C 1—low-density lipoprotein cholesterol before plant-based diet; LDL-C 2—low-density lipoprotein cholesterol after plant-based.

Finally, from the analysis of the TC/HDL-C ratio, "migrations" could be observed towards higher-risk categories in only 12.5% of participants, the rest remained in the initial category or decreased their ratio, which led to a decreased potential risk of cardiovascular disease (Table 6).

Table 6. Percent of persons (%) "migrating" from a category to another of TC/HDL-C ratio after becoming plant-based, where TC/HDL-C 1 is % before plant-based, and TC/HDL-C 2 after.

		TC/HDL-C 2		
		Ideal	**Optimum**	**Increased**
TC/HDL-C 1	Ideal	100%	-	-
	Optimum	62.5%	25.0%	12.5%
	increased	7.1%	78.6%	14.3%

TC/HDL-C 1—total cholesterol/high-density lipoprotein cholesterol before plant-based diet; TC/HDL-C 2—total cholesterol/high-density lipoprotein cholesterol after plant-based diet.

In the next step, we applied a Wilcoxon signed-rank test for circulating lipid values, considered as categorical (ordinal) values as described in the methods section, before and after becoming plant-based. In all cases we confirmed results from *t*-tests: for TC ($Z = -3.35$; $p = 0.001$), LDL-C ($Z = -4.47$; $p = 0.000$), and TC/HDL-C ($Z = 4.04$; $p = 0.000$). The only non-significant change was of HDL-C ($Z = 3.78$; $p = 0.705$). These changes converged for a positive evolution of the lipid profile, with subjects expressing a shift from a higher category of risk to a lower one.

Regarding BMI, several changes were noted: 13% ($n = 3$) of normal-weight individuals ($n = 23$) became underweight, 20% ($n = 2$) of overweight ($n = 10$) became normal weighted, and all obese ($n = 2$) became overweight. As mentioned above (Table 1), the mean differences in BMI both in men and in women were statistically significant.

The Wilcoxon signed-rank test applied to the BMI changes showed a significant difference ($Z = 2.64$; $p = 0.008$) after the introduction of the plant-based diet.

Additionally, in order to outline the possible reciprocal influences between variables, we applied the Pearson correlation test. This test highlighted a significant positive correlation only between the BMI variation and the TC variation (correlation coefficient: 0.34, $p = 0.045$). The statistical significance is maintained even in partial correlation, with age as a covariate The duration of the plant-based regimen did not correlate with any of the above variables.

4. Discussion

Circulating lipids are closely connected with food intake. In the present study, we showed a better lipid profile after changing the omnivore diet to a plant-based diet for the majority of lipoproteins, namely TC, TG, LDL-C, and TC/HDL-C. Though it seems that a plant-based diet has no positive consequences regarding HDL-C values. There are studies in which a plant-based diet could be associated with a reduction of HDL-C, a phenomenon that is undesirable, HDL-C being considered a cardiovascular protective factor [23]. However, other research did not find this decrease in value. In fact, the cardiovascular risk associated with HDL-C levels does not seem to be linear, but a "U" type; levels <40 mg/dL for men and <50 mg/dL for women or >97 mg/dL for men and >116 mg/dL for women are associated with a higher risk [24].

Pharmacological molecules aimed at increasing HDL-C such as those with cholesteryl ester transfer protein (CETP) inhibitors or niacin, even if achieving this goal, did not reduce the cardiovascular risk [6,25]. The explanation for the results lies probably in the lack of homogeneity of HDL-C particles and the fact that direct methods for determining HDL-C measure only the TC loading of high-density lipoprotein particles and not the distribution of cholesterol between different HDL-C subtypes, which would reflect perhaps

more appropriately the reverse transport properties of cholesterol beneficial in reducing cardiovascular risk [26].

Additionally, the cardio-protective properties of HDL-C particles are not only limited to cholesterol but also the ability to anti-inflammatory, antioxidant, and vasodilation effects. Therefore, a probably more appropriate assessment of cardiovascular risk should be made taking into account all these elements, i.e., the functional properties of HDL-C particles. In this regard, the analysis of cholesterol efflux capacity in a cohort of 8592 subjects showed a negative correlation with cardiovascular events that the measurement by classical methods of HDL-C in the same cohort was not able to determine [27].

Many participants lost weight as vegans. Other studies have shown similar results [28,29] and it is well known that especially in some groups of overweight/obese patients, with associated metabolic syndrome, a whole food plant-based diet induces a lowering of BMI and a positive trend of the value of different circulating markers of heart disease and diabetes [30]. Improving weight status may be one of the explanations for the amelioration of the lipid profile, as it improves insulin sensitivity, reduces the atherogenic subfractions of lipoprotein particles (LDL 5, HDL 3b, and HDL 3c) [30], or may act by lipid-independent mechanisms such as decreased trimethylamine (TMA) production whose metabolite obtained by oxidation in the liver is closely correlated with cardiovascular risk [31]. However, in our study, the BMI variation was significantly correlated just with the TC values. Thus, we can state that lowering of some circulating lipids can be achieved under a plant-based diet independent of weight loss. We also noticed a false perception of weight loss in some of the participants. The misperception of actual body weight is common in modern society, drawing attention to the need for proper education on how to assess normal weight status.

The link between elevated TGs and cardiovascular disease is well documented. TGs of intermediate-sized lipoprotein particles are able to reach the intima of the vascular wall, even if the penetration rate is lower than that of LDL-C particles [32], from where they are either degraded to gaseous acids and glycerol and initiating inflammatory processes or are directly taken up by macrophages which they turn into foam cells [1]. Diet is an essential tool of reducing them directly, as well as indirectly, through the effect on weight loss. A meta-analysis from 2017 [33] showed that plant-based diets are associated with decreased total values of cholesterol, LDL-C, and HDL-C, but not with decreased TG, perhaps because not all included studies have discussed the BMI variation over time. However, this meta-analysis cumulated data from studies with subjects on vegan diets and on egg-milk-vegetarian diets, therefore the results were not entirely comparable with our results based on an exclusively vegan diet. When comparing vegan and vegetarian diets, the article points out that in randomized studies, the decrease in LDL-C is higher in vegans than in vegetarians. The lowering of the LDL-C values was also an expected finding of our study, as well as the reduced values of the TC/HDL-C ratio in 87.5% of the participants. The TC/HDL-C ratio is a well-known predictor for heart disease risk and lower values are a signal of better cardiovascular health.

This is the first study following the lipid profile evolution in a vegan group in Romania. Even though the vegan diet has gained terrain in recent years, the number of Romanian vegans is quite low and has been previously evaluated as being around 27,000 (data not published). Comparing this figure with the Romanian population of nearly 19 million people, we can ascertain that just a very small number of Romanians embraced this diet, in spite of its health benefits. Even more, anecdotal reports show that doctors generally discourage patients to adopt a plant-based diet, perceived as unhealthy and generating nutritional deficiencies [34].

Studies on vegans are relatively few because the number of individuals who follow this diet for a long enough period to be associated with changes in physical or biochemical parameters is quite small. There is a low number of international studies that provide consistent data, often groups of vegans or vegetarians being separated from large population cohorts. However, results obtained from these major cohorts (European Prospective

Investigation into Cancer and Nutrition Study, Adventists Health Study) show a reduction in lipid parameters that are traditionally associated with cardiovascular morbidity [35–37].

However, a plant-based diet can also be followed without being considered an advantage for health. There is no homogenous plant-based diet, many variants being possible. There are many examples of foods that do not contain ingredients of animal origin and are caloric dense and nutritionally poor (pastries, French fries, sweets, etc.). The lack of a detailed investigation of the types of food consumed can lead to different conclusions, biasing the general conception of a plant-based diet as being sanogenic. Thus, studies can arrive at conclusions that do not associate plant-based diets with a prophylactic action on cardiovascular diseases. A recent study indicated positive effects in preventing dyslipidemia only in a plant-based diet rich in nutritionally dense and low in processed foods (healthful plant-based diets) [38]. Studies that have considered a whole plant-based diet have always reported positive health results [39].

In our group, preliminary investigations of the types of food consumed (unpublished data) indicated a preponderance of eating little or no processed food, food that frequently was eaten raw or sprouted, and avoiding foods with high levels of sugar and fat. The diet of vegans in Romania is not so much diversified, since specialized products, rich in saturated fats and salt (like mock meats or cheeses), are scarce and very expensive. Thus, the vegan diet consists mainly of locally grown products, cereals, and legumes, with some added soy products. In this respect, the positive findings of our study should not extrapolate to vegetarian diets rich in processed vegetarian foods.

A recent meta-analysis showed multiple advantages of plant-based diets [40]. On one hand, the reduction of the intake of saturated fats and monounsaturated fatty acids (MUFA), in parallel with the increase of polyunsaturated fatty acids (PUFA) led to a better lipid profile. On the other hand, this meta-analysis also pointed out that although the lipid profile is improved, the nutritional deficiencies that can occur in vegans (B12, iron, zinc, omega3) [41], if not avoided, can cancel out the positive effects of a whole food plant-based diet.

In our study, the evolution of the lipid panel was generally favorable. It is also important to underline that all the participants were never smokers, even if smoking status was not a selection criterion. Most probably this reflects more concern about health aspects in general, which made them have a lipid profile checking even before starting the plant-based diet. Therefore, we cannot extend our conclusions to smokers.

We also found three "outliers", two women and one man, in whom the values of cholesterol, LDL-C, and HDL-C were not those expected under the plant-based diet. The attending physician prescribed atorvastatin in these cases (at doses of 5 and 10 mg/day, respectively), which led to a significant decrease in cholesterol and LDL-C. In these cases, it could be stated that there was probably familial hypercholesterolemia, although no one has shown associated clinical signs (xanthomas, xanthelasmas, etc.) or a history of such disease in close relatives. The two females presented laboratory determinations of Apolipoprotein B that were within normal limits, but more detailed investigations were not available. The conclusion resulting from the analysis of these cases was that the plant-based diet has its limits and even if it succeeds in cases of inherited hypercholesterolemia to lower cholesterol and LDL-C levels, the extent of this effect is not enough for sound management of the problem. As such, customizing the approach is always strictly necessary.

Limitations: The group of people included in the study was small and composed of cardiovascular healthy people with a relatively young average age. These biases could not be avoided, since the Romanian vegans form a small group, relative to the general population and because not many vegans can afford or are interested in carrying out expansive blood work. The group's lifestyle, evaluated by a qualitative approach, was healthy, at least by self-reported information about daily habits. We do not have information about the family history of the participants. We relied on self-reported intake of foods. Additionally, other unreported lifestyle factors might have acted as confounders for the

final results (e.g., level of stress management), but we were not able to evaluate them at the moment of the study.

5. Conclusions

Although dyslipidemias are only a surrogate marker for cardiovascular morbidity and the actions by which the plant-based diet can influence cardiovascular diseases are multiple, we consider that the results of our study did confirm a positive effect. After a minimum of one year of plant-based regimen, low in any processed vegetarian foods, nonsmokers had favorable effects in terms of markers such as TG, TC, and LDL-C. However, such diets had limited benefits in familial hypercholesterolemia, which requires specialized investigations and drug treatment.

Author Contributions: C.A.Z., R.E.B., and C.G. collected, analyzed, and interpreted the patient data. C.A.Z., T.S., and M.R.O. collected the data and had substantial contributions to the conception of the study and statistical analysis, the interpretation of the data, and the writing of the manuscript. R.E.B., R.V., and C.G. contributed to the literature retrieval and manuscript modifications. C.A.Z., F.A.M., R.E.B., and T.S. supervised and designed the present study and contributed to the approval of the final version of the manuscript. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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References

1. Nordestgaard, B.G. Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease. *Circ. Res.* **2016**, *118*, 547–563. [CrossRef]
2. Arnett, D.K.; Blumenthal, R.S.; Albert, M.A.; Buroker, A.B.; Goldberger, Z.D.; Hahn, E.J.; Himmelfarb, C.D.; Khera, A.; Lloyd-Jones, D.; McEvoy, J.W.; et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* **2019**, *140*, e596–e646. [CrossRef] [PubMed]
3. Bohîlțea, R.E.; Zugravu, C.A.; Neacsu, A.; Navolan, D.; Berceanu, C.; Nemescu, D.; Bodean, O.; Turcan, N.; Baros, A.; Cîrstoiu, M.M. The prevalence of Vitamin D deficiency and its obstetrical effects. A prospective study on Romanian patients. *Rev. Chim.* **2019**, *70*, 1228–1233. [CrossRef]
4. Bohiltea, R.E.; Zugravu, C.A.; Nemescu, D.; Turcan, N.; Paulet, F.; Gherghiceanu, F.; Ducu, I.; Cirstoiu, M.M. Impact of obesity on the prognosis of hypertensive disorders in pregnancy. *Exp. Ther. Med.* **2020**, *20*, 2423–2428. [CrossRef] [PubMed]
5. Grigoriu, C.; Furtunescu, F.; Gaman, L.E.; Balaceanu, A.L.; Buzatu, R.; Grigoriu, M.A. Biochemical Marker of Preeclampsia—Hypertriglyceridemia—And the Impact of Secondary Prevention Therapy. *Rev. Chim.* **2018**, *69*, 2740–2743. [CrossRef]
6. Iordachescu, A.C.; Cirstoiu, M.M.; Zugravu, C.A.; Teodor, O.M.; Turcan, N.; Ducu, I.; Bohiltea, R.E. Dietary Behavior during Pregnancy. *Exp. Ther. Med.* **2020**, *20*, 2460–2464. [CrossRef] [PubMed]
7. Key, T.; Davey, G. Prevalence of obesity is low in people who do not eat meat. *BMJ* **1996**, *313*, 816–817. [CrossRef]
8. Pettersen, B.J.; Anousheh, R.; Fan, J.; Jaceldo-Siegl, K.; Fraser, G.E. Vegetarian diets and blood pressure among white subjects: Results from the Adventist Health Study-2 (AHS-2). *Public Health Nutr.* **2012**, *15*, 1909–1916. [CrossRef] [PubMed]
9. Sandu, C.; Bica, C.; Salmen, T.; Stoica, R.; Bohiltea, R.; Gherghiceanu, F.; Pacu, I.; Stefan, S.; Serafinceanu, C.; Stoian, A.P. Gestational diabetes-modern management and therapeutic approach (Review). *Exp. Ther. Med.* **2021**, *21*, 81–86. [CrossRef] [PubMed]

10. Tricopoulou, A.; Vasipoulou, E. Mediterran diet and longevity. *Br. J. Nutr.* **2000**, *84*, 205–209. [CrossRef]
11. Patti, A.M.; Carruba, G.; Cicero, A.F.G.; Banach, M.; Nikolic, D.; Giglio, R.V.; Terranova, A.; Soresi, M.; Giannitrapani, L.; Montalto, G.; et al. Daily Use of Extra Virgin Olive Oil with High Oleocanthal Concentration Reduced Body Weight, Waist Circumference, Alanine Transaminase, Inflammatory Cytokines and Hepatic Steatosis in Subjects with the Metabolic Syndrome: A 2-Month Intervention Study. *Metabolites* **2020**, *10*, 392. [CrossRef] [PubMed]
12. Barnard, N.D.; Scialli, A.R.; Bertron, P.; Hurlock, D.; Edmonds, K.; Talev, L. Effectiveness of a low-fat vegetarian diet in altering serum lipids in healthy premenopausal woman. *Am. J. Cardiol* **2000**, *85*, 969–972. [CrossRef]
13. Cooper, R.S.; Goldberg, R.B.; Trevisan, M.; Tsong, Y.; Liu, K.; Stamler, J.; Rubenstein, A.; Scanu, A.M. The selective lipid-lowering effect of vegetarianism on low-density lipoproteins in a crossover experiment. *Atherosclerosis* **1982**, *44*, 293–305. [CrossRef]
14. Dinu, M.; Pagliai, G.; Angelino, D.; Rosi, A.; Dall'Asta, M.; Bresciani, L.; Ferraris, C.; Guglielmetti, M.; Godos, J.; Del Bo', C.; et al. Effects of Popular Diets on Anthropometric and Cardiometabolic Parameters: An Umbrella Review of Meta-Analyses of Randomized Controlled Trials. *Adv. Nutr.* **2020**, *11*, 815–833. [CrossRef] [PubMed]
15. Harman, S.K.; Parnell, W.R. The nutritional health of New Zealand vegetarian and non-vegetarian Seventh-day Adventists: Selected vitamin, mineral and lipid levels. *N. Z. Med. J.* **1998**, *111*, 91–94. [PubMed]
16. Key, T.J.; Davey, G.K.; Appleby, P.N. Health benefits of a vegetarian diet. *Proc. Nutr. Soc.* **1999**, *58*, 271–275. [CrossRef]
17. Freeman, A.; Morris, P.; Barnard, N.; Esselstyn, C.; Ros, E.; Agatston, A.; Devries, S.; O'Keefe, J.; Miller, M.; Ornish, D.; et al. Trending Cardiovascular Nutrition Controversies. *J. Am. Coll. Cardiol.* **2017**, *69*, 1172–1187. [CrossRef] [PubMed]
18. Cicero, A.F.G.; Fogacci, F.; Stoian, A.P.; Vrablik, M.; Al Rasadi, K.; Banach, M.; Toth, P.P.; Rizzo, M. Nutraceuticals in the Management of Dyslipidemia: Which, When, and for Whom? Could Nutraceuticals Help Low-Risk Individuals with Non-optimal Lipid Levels? *Curr. Atheroscler. Rep.* **2021**, *23*, 57. [CrossRef]
19. Crismaru, I.; Stoian, A.P.; Bratu, O.G.; Gaman, M.A.; Stanescu, A.M.A.; Bacalbasa, N.; Diaconu, C.C. Low-density lipoprotein cholesterol lowering treatment: The current approach. *Lipids Health Dis.* **2020**, *19*, 85. [CrossRef]
20. Gheorghe, G.; Toth, P.P.; Bungau, S.; Behl, T.; Ilie, M.; Pantea Stoian, A.; Bratu, O.G.; Bacalbasa, N.; Rus, M.; Diaconu, C.C. Cardiovascular Risk and Statin Therapy Considerations in Women. *Diagnostics* **2020**, *10*, 483. [CrossRef]
21. Giglio, R.V.; Carruba, G.; Cicero, A.F.G.; Banach, M.; Patti, A.M.; Nikolic, D.; Cocciadiferro, L.; Zarcone, M.; Montalto, G.; Stoian, A.P.; et al. Pasta Supplemented with Opuntia ficus-indica Extract Improves Metabolic Parameters and Reduces Atherogenic Small Dense Low-Density Lipoproteins in Patients with Risk Factors for the Metabolic Syndrome: A Four-Week Intervention Study. *Metabolites* **2020**, *10*, 428. [CrossRef]
22. Grigore-Gurgu, L. Genomics Era in the Nutrition Field. In *The Annals of the University Dunarea De Jos of Galati. Fascicle VI—Food Technology*; Galati University Press: Galati, Romania, 2018; Volume 42, pp. 168–174.
23. Chang, S.L.; Lee, K.J.; Nfor, O.N.; Chen, P.H.; Lu, W.Y.; Ho, C.C.; Lung, C.C.; Chou, M.C.; Liaw, Y.P. Vegetarian Diets along with Regular Exercise: Impact on High-Density Lipoprotein Cholesterol Levels among Taiwanese Adults. *Medicina* **2020**, *56*, 74. [CrossRef]
24. Allard-Ratick, P.; Sandesara, P.; Quyyumi, A.; Sperling, L. Everything in Moderation: Investigating the U-Shaped Link Between HDL Cholesterol and Adverse Outcomes. *US Cardiol. Rev.* **2019**, *13*, 49–53. [CrossRef]
25. Keene, D.; Price, C.; Shun-Shin, M.J.; Francis, D.P. Effect on cardiovascular risk of high-density lipoprotein targeted drug treatments niacin, fibrates, and CETP inhibitors: Meta-analysis of randomized controlled trials including 117,411 patients. *BMJ* **2014**, *349*, 4379. [CrossRef]
26. Hafiane, A.l.; Genest, J. High density lipoproteins: Measurement techniques and potential biomarkers of cardiovascular risk. *BBA Clin.* **2015**, *3*, 175–188. [CrossRef]
27. Ebtehaj, S.; Gruppen, E.G.; Bakker, S.J.L.; Dullaart, R.P.F.; Tietge, U.J.F. HDL (High-Density Lipoprotein) Cholesterol Efflux Capacity Is Associated with Incident Cardiovascular Disease in the General Population. *Arterioscler. Thromb. Vasc.* **2019**, *39*, 1874–1883. [CrossRef]
28. Turner-McGrievy, G.M.; Davidson, C.R.; Wingard, E.E.; Wilcox, S.; Frongillo, E.A. Comparative effectiveness of plant-based diets for weight loss: A randomized controlled trial of five different diets. *Nutrition* **2015**, *31*, 350–358. [CrossRef] [PubMed]
29. Tran, E.; Dale, H.F.; Jensen, C.; Lied, G.A. Effects of Plant-Based Diets on Weight Status: A Systematic Review. *Diabetes Metab. Syndr. Obes.* **2020**, *13*, 3433–3448. [CrossRef]
30. Pedersen, L.R.; Olsen, R.H.; Anholm, C.; Walzem, R.L.; Fenger, M.; Eugen-Olsen, J.; Haugaard, S.B.; Prescott, E. Weight loss is superior to exercise in improving the atherogenic lipid profile in a sedentary, overweight population with stable coronary artery disease: A randomized trial. *Atherosclerosis* **2016**, *246*, 221–228. [CrossRef]
31. Koeth, R.A.; Wang, Z.; Levison, B.S.; Buffa, J.A.; Org, E.; Sheehy, B.T.; Britt, E.B.; Fu, X.; Wu, Y.; Li, L.; et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nat. Med.* **2013**, *19*, 576–585. [CrossRef]
32. Nordestgaard, B.G.; Tybjaerg-Hansen, A.; Lewis, B. Influx in vivo of low density, intermediate density, and very low-density lipoproteins into aortic intimas of genetically hyperlipidemic rabbits. Roles of plasma concentrations, extent of aortic lesion, and lipoprotein particle size as determinants. *Arterioscler. Thromb.* **1992**, *12*, 6–18. [CrossRef]
33. Yokoyama, Y.; Levin, S.M.; Barnard, N.D. Association between plant-based diets and plasma lipids: A systematic review and meta-analysis. *Nutr. Rev.* **2017**, *75*, 683–698. [CrossRef] [PubMed]
34. Storz, M.A. Is There a Lack of Support for Whole-Food, Plant-Based Diets in the Medical Community? *Perm J.* **2018**, *23*, 18–068. [CrossRef] [PubMed]

35. Fraser, G.E. Vegetarian diets: What do we know of their effects on common chronic diseases? *Am. J. Clin. Nutr.* **2009**, *89*, 1607S–1612S. [CrossRef] [PubMed]
36. Matsumoto, S.; Beeson, W.L.; Shavlik, D.J.; Siapco, G.; Jalcedo-Siegl, K.; Fraser, G.; Knutsen, S. Association between vegetarian diets and cardiovascular risk factors in non-Hispanic white participants of the Adventist Health Study-2. *J. Nutr. Sci.* **2019**, *8*, e6. [CrossRef] [PubMed]
37. Glenn Andrea, J.; Viguiliouk, E.; Seider, M.; Boucher, B.A.; Khan Tauseef, A.; Blanco, M.S.; Jenkins, D.J.A.; Kahleová, H.; Rahelić, D.; Salas-Salvadó, J.; et al. Relation of Vegetarian Dietary Patterns with Major Cardiovascular Outcomes: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. *Front. Nutr.* **2019**, *6*, 80. [CrossRef] [PubMed]
38. Campbell, E.K.; Fidahusain, M.; Campbell, T.M. Evaluation of an Eight-Week Whole-Food Plant-Based Lifestyle Modification Program. *Nutrients* **2019**, *11*, 2068. [CrossRef]
39. Jingxuan, Q.; Grace, L.; Hui, L.M.; Han, N.; Zheng, S.W.; Jonathan, T. The Association of Plant-Based Diet with Cardiovascular Disease and Mortality: A Meta-Analysis and Systematic Review of Prospect Cohort Studies. *Front. Cardiovasc. Med.* **2021**, *8*, 1389.
40. Benatar, J.R.; Stewart, R.A.H. Cardiometabolic risk factors in vegans; A meta-analysis of observational studies. *PLoS ONE* **2018**, *13*, e0209086.
41. Zugravu, C.; Macri, A.; Belc, N.; Bohiltea, R. Efficacy of supplementation with methylcobalamin and cyancobalamin in maintaining the level of serum holotranscobalamin in a group of plant-based diet (vegan) adults. *Exp. Ther. Med.* **2021**, *22*, 993. [CrossRef]