The effects of cashew nut intake on lipid profile and blood pressure: a systematic review and meta-analysis of randomized controlled trials

Article (Accepted Version)

Jalali, Mohammad, Karamizadeh, Maliheh, Ferns, Gordon A, Zare, Morteza, Moosavian, Seyedeh Parisa and Akbarzadeh, Marzieh (2020) The effects of cashew nut intake on lipid profile and blood pressure: a systematic review and meta-analysis of randomized controlled trials. *Complementary Therapies in Medicine*, 50. a102387. ISSN 0965-2299

This version is available from Sussex Research Online: <http://sro.sussex.ac.uk/id/eprint/91205/>

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher's version. Please see the URL above for details on accessing the published version.

Copyright and reuse:

Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

The Effects of Cashew Nut Intake on Lipid Profile and Blood Pressure: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Mohammad Jalali^{1,2}, Maliheh Karamizadeh^{1,2}, Gordon A Ferns³, Seyedeh Parisa Moosavian⁴,

Morteza Zare², Marzieh Akbarzadeh²

¹ Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.

² Nutrition Research Center, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran.

³ Brighton & Sussex Medical School, Division of Medical Education, Falmer, Brighton, Sussex, UK

⁴ Department of Clinical Nutrition, School of Nutrition and Food Science, Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

***Corresponding author:** Marzieh Akbarzadeh,

Nutrition research center,

School of Nutrition and Food Sciences,

Shiraz University of Medical Sciences,

Razi Ave, Shiraz, Iran.

Post Code: 7153675541,

Tel: +98 7137251005,

Fax: +98 37257288

E-mail: M_akbarzadeh@sums.ac.ir

Abstract:

Background: Dyslipidemia and hypertension are important risk factors for cardiovascular disease (CVD). Some studies have suggested that the consumption of nuts may reduce CVD risk.

Objective: The present systematic review and meta-analysis was conducted to investigate the efficacy of cashew nut consumption on lipid profile and blood pressure.

Methods: PubMed, Embase, Scopus, Web of Science and Cochrane Library were systematically searched to identify randomized control trials (RCTs) examining the effects of cashew nut intake on serum triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), serum total cholesterol (TC), systolic blood pressure (SBP) or diastolic blood pressure (DBP) until 15 November 2019. Random-effects or fixed-effects models were used to pool weighted mean difference (WMD) and 95% confidence intervals (CI). Potential publication bias was assessed using Egger's test. Sensitivity analysis was performed to assess the impact of each individual study on the pooled results.

Results: A meta-analysis on 392 participants showed that cashew consumption had no significant effects on lipid profile and DBP. However, there was a significant reduction in SBP (WMD = -3.39, 95% CI = [-6.13, -0.65], $P = 0.01$, $I^2 = 0.0\%$) in the group receiving an increased cashew nut intake compared to the controls. There was no significant publication bias in the meta-analysis. A sensitivity analysis, omitting single trials in turn, did not have a significant effect on the pooled results.

Conclusion: This meta-analysis demonstrated that cashew nut consumption might reduce SBP but has no effects on lipid profile and DBP.

Keywords: Cashew nut, Lipid profile, Blood pressure, Review, Meta-analysis

1 Introduction:

Cardiovascular disease (CVD) is a major cause of death worldwide, leading to more than 4 million deaths in Europe and nearly 930,000 in the US annually [1]. CVD is not only a problem in high-income countries; low- and middle-income countries (LMIC) also have a high prevalence and mortality rate attributable to CVD; almost 80% of CVD deaths occur in LMICs, and close to 40% of these are defined as premature [2]. In 2017, the global deaths attributable to CVD was reported to be ~ 17.8 million. And the rate of CVD death was ~ 3 times higher in lower- and middle-income countries compared to those with high-incomes [3]. Diet plays an important role in preventing CVD [4]. It has been suggested that adherence to a healthy diet reduces the risk of cardiovascular disease by 80-90% [5]. A daily intake of nuts can improve CVD risk [6]. Nuts are rich in antioxidants, and have a favorable fat content, which can account for their enhanced health benefits [7, 8]. The Dietary Guidelines Advisory Committee (DGAC), has proposed that the consumption of nuts is associated with reducing CVD risk and American's dietary guidelines emphasize nuts as part of a healthy diet. In these guidelines, 5 servings of nuts/seeds/soy products are recommended per week as part of a 2000 calorie diet [9, 10]. The FDA have indicated that eating 1.5 ounces of tree nuts per day as part of a cholesterol- and saturated fat-restricted diet might reduce the risk of CVD [11].

The cashew is a tree nut that seems to have a beneficial effect on CVD risk factors. *Anacardium occidentale* L is the formal name of the cashew tree, which is widely growing up in Central America, the tropical regions of South America, and in tropical countries such as Thailand, Vietnam, and India. [12, 13]. After almond, walnut, and pistachios, cashew is the world's fourth-most-produced nut and the third-most-consumed nut in the US after almond and walnut. Each unit of cashew (28 grams of cashew) contains 4.3 grams of protein, 74 mg of magnesium (19 percent of the body's daily requirement) and 160 mg of potassium (5 percent of the body's daily requirement). 60 and 18 percent of the fats in cashew are MUFA and PUFA, respectively. Although there are more than 4 grams of saturated fat per 50 grams of cashew, it should have borne in mind that about 40-50% of the saturated fats in cashew are as stearic acid that has no effect on plasma LDL cholesterol (LDL-C) concentrations. [1, 14].

A number of studies have examined the effects of consumption of cashew on lipid profile and blood pressure. However, randomized controlled trials (RCTs) have reported conflicting results, and therefore do not provide clear information for dietary recommendations. The discrepancy in the results may be explained by differences in study design, study duration, study populations, study conditions, and the dose of substance used.

To date, no systematic reviews have been published specifically on the effects of cashew consumption on lipid profile and blood pressure. In the present study, a systematic review and meta-analysis of RCTs was conducted to summarize the evidence on the effects of cashew consumption on lipid profile and blood pressure in subjects over the age of 18 years.

2 Methods:

2.1 Protocol:

The present meta-analysis is based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (*PRISMA*) guidelines [15].

2.2 Systematic search:

The systematic search was undertaken using international online databases including PubMed, Embase, Scopus, Web of Science and Cochrane Library for all potential relevant literature investigating the effects of cashew intake on blood lipid profile and blood pressure without any restriction from inception up to 15 November 2019. The following search design was planned for the systematic search in titles and abstracts: [keywords for cashew] AND [keywords for blood lipid profile OR keywords for blood pressure] AND [keywords for type of study]. The wild-card term “*” was applied in some cases to increase the sensitivity of the search strategy. Additionally, to find further eligible evidences and prevent missing relevant publications, the reference lists of included records and review articles and Google Scholar were hand-searched. EndNote X9 was used to simplify the literature screening process.

2.3 Inclusion and Exclusion criteria:

Original articles were included in the present meta-analysis if they: 1) were RCTs, 2) administered cashew as intervention in adults (≥ 18 years old), 3) reported a sufficient data for

lipid profile (TG, TC, HDL-C, LDL-C) or blood pressure (SBP, DBP), 3) published in English language. In the other hand, exclusion criteria were: 1) being not original research (reviews, book chapters, conference abstracts, editorials and letters), 2) papers with combined supplement of nutrients, nuts or drugs, 3) animal studies, 4) studies with lack of any essential information including non-extractable or unconvertable data and 5) papers without suitable control group.

2.4 Data selection:

Eligible articles were reviewed by two independent investigators and the following information were abstracted: 1) first author name, 2) country, 3) type of trial, 4) participants health status, 5) mean age, 6) sample size, 7) treatment duration, 8) cashew dosage, 9) quality and 10) change and standard deviation (SD) of outcomes (calculated up to 2 decimals). Net changes in TG, TC, HDL-C, LDL-C, SBP and DBP were calculated by subtracting the value at baseline from that after intervention in the active-treated groups and in the control ones. SDs of the mean difference were obtained as the following procedure: $SD = \text{square root } [((SD \text{ pre})^2 + (SD \text{ post})^2) - (2r \times SD \text{ pre} \times SD \text{ post})]$, considering a correlation coefficient (r) = 0.5 for both pre-test / post-test (parallel groups) and crossover designed studies [16]. Given reporting IQR, SD was determined using $(\text{third quartile} - \text{first quartile}) / 1.35$ [17]. In the case of those studies that reported standard error (SE), SD was obtained using this formula: $(SD = SE \times \sqrt{n})$. Mean changes and relevant SDs were extracted for the first step of the Cross-over designed study. The reported concentration of lipid profile in all papers were converted into the usual unit (mg/dl). Also, any doubts were resolved through a discussion between the mentioned authors.

2.5 Risk of bias appraisal:

The Cochrane Risk of Bias Tool was used by two independent reviewers to qualify the included RCTs and explore potential risk of bias for the following categories: sequence generation, allocation concealment, blinding, blinding of outcome assessment, incomplete outcome data, selective reporting and other biases. “Low”, “High” or “Unclear” terms were used to judge each item. Additionally, any disagreement was resolved by the corresponding author. RevMan v5.3 software was executed to draw a proper figure.

2.6 Statistical analyses:

A random-effects model was applied to pool weighted mean difference (WMD) and 95% confidence intervals (CI). Statistical heterogeneity [18] was assessed using I^2 (high $\geq 50\%$, low $< 50\%$) for chi-square [19]. In addition, meta-regression were conducted by potential moderators including mean age of participants and treatment duration to seek the source of statistical heterogeneity. Potential publication bias was assessed using Egger’s test for outcomes with more than 2 effect sizes [20]. To evaluate the impact of each study on the pooled results, sensitivity analysis (removing one study at a time) was executed. A P -value < 0.05 was considered as statistically significant. Stata v13 was used to analyze all data.

3 Results:

3.1 Flow and demographic characteristics of included studies:

The study selection process is shown in Figure 1. Briefly, 437 records were identified by systematic search of the online databases (PubMed: 55, Embase: 48, Scopus: 178 and Web of Science: 156). One hundred and eighty six papers were omitted because they were duplicates. Of

the remaining records, 241 did not meet the inclusion criteria by screening titles and abstracts and were also excluded. Thus, 9 studies were assessed for eligibility and screened by full-text. Finally, 3 full-text articles were included in the present systematic review and meta-analysis [1, 6, 21].

Table 1 shows some demographic characteristics of the included RCTs. The timeframe of publication was between 2007 and 2019. One study was conducted in South Africa [21], two others in the USA [1] and India [6]. Two RCTs were designed as parallel [6, 21] and one trial was designed as crossover [1]. The range of mean age of the total participants was between 45 and 56.8 years old. In total, 190 and 202 subjects in the intervention group and control group were pooled in this meta-analysis, respectively. Minimum and maximum intervention duration was 4 weeks and 12 weeks, respectively. Although, one study reported no data for dosage of cashew [21], dosage of the two other studies was 30 [6] and 42 [1] gram per day. The methodological quality assessment of the included trials is shown in Figure 2.

3.2 The effects of cashew intake on the lipid profile:

As shown in Figure 3A, B, C, D, serum TG (WMD = 1.12 mg/dl, 95% CI = [-7.51, 9.74], $P = 0.80$, $I^2 = 0.0\%$), HDL-C (WMD = 0.29 mg/dl, 95% CI = [-2.52, 3.10], $P = 0.84$, $I^2 = 65.3\%$), TC (WMD = 0.86 mg/dl, 95% CI = [-4.47, 6.18], $P = 0.75$, $I^2 = 44.0\%$) and LDL-C (WMD = -0.93 mg/dl, 95% CI = [-4.83, 2.96], $P = 0.63$, $I^2 = 33.1\%$) were not significantly affected by cashew consumption as compared to the control group.

3.3 The effects of cashew intake on the improvement of blood pressure:

As presented in Figure 3E, cashew composition significantly lowered SBP (WMD = -3.39, 95% CI = [-6.13, -0.65], $P = 0.01$, $I^2 = 0.0\%$). However, DBP (Figure 3F) was not significantly affected by cashew intake (WMD = -1.45, 95% CI = [-3.16, 0.26], $P = 0.97$, $I^2 = 0.0\%$).

3.4 Meta-regression:

Meta-regression analysis did not find the sources of statistical heterogeneity for HDL-C based on mean age (coefficient = 0.30, 95% CI = [-3.86, 4.47], $P = 0.52$) and treatment duration (coefficient = 0.22, 95% CI = [-6.70, 7.14], $P = 0.75$).

3.5 Publication bias and sensitivity analysis:

No significant publication bias was found in the meta-analyses (P for TG = 0.24, HDL-C = 0.38, LDL-C = 0.73 and TC = 0.84). Also, sensitivity analysis revealed that pooled results were not affected by each of the included trial (Figure 5).

4 Discussion:

In this systematic review and meta-analysis on RCTs, cashew nut consumption reduced SBP significantly but had no effects on lipid profile and DBP.

With increasing the prevalence of CVD, researchers have focused on dietary approaches that can lower CVD risk factors. In this regard, healthy dietary patterns such as DASH diet or Mediterranean diet and some functional foods such as tree nuts have been under more study [21]. Tree nuts which are an important component of DASH diet are low glycemic food items which are high in protein, PUFA, MUFA dietary fiber vitamins and minerals which are all in line with

dietary recommendations for CVD prevention and control [21]. Also, previous research has confirmed their role in preventing cardiovascular events [8].

Previous meta-analyses have revealed positive effects of tree nuts on lowering LDL cholesterol and total-cholesterol level [8, 22-24]. But there remain some unresolved questions in this field. For instance, it is not clear if some nuts are more effective in lowering cardiovascular risk factors than others.

In the present meta-analysis, cashew nut consumption had no significant effect on blood lipids. Cashew nuts have a high content of MUFA (37.9%), and PUFA (11.97%) [25]. Besides the hypocholesterolemic effects of PUFAs, MUFAs are effective in cholesterol-lowering, but less than PUFAs and their effects on lowering cholesterol level depends on the saturated fatty acids other than stearic acid. When the intakes of hypercholesterolemic SFAs (C12:0-C16:0) are low, MUFA can lower LDL-C [26]. Also, based on the regression equations developed by Yu et.al., for predicting the effects of dietary fatty acids on blood lipids, MUFA and PUFA are negatively correlated to LDL-C [26]. Saturated fatty acids comprise 13.47% of cashew nut fats [25]. Saturated fatty acids have been shown to increase LDL-C, but in cashew, the predominant SFA (6.13%) is stearic acid (C18:0) [25]. Unlike other SFAs (C12:0-C16:0), which are hypercholesterolemic, stearic acid is neutral and it is not related to increased LDL-C and CVD risk [1, 26].

The high content of MUFA (37.9%) and PUFA (11.97%) [25], and low levels of hypercholesterolemic SFAs in cashew have previously been related to LDL-lowering effects of cashew nut [1, 21]. But in the present meta-analysis, we did not find this effects.

In a meta-analysis on the effects of tree nuts on cardiovascular risk factors, nut consumption lowered total cholesterol, LDL cholesterol, and ApoB. In dose-response analysis, it was shown that daily intake of 60 g (about 2 oz, or 2 servings) of nuts had stronger effects on lowering LDL-C, and providing 100 g nuts per day reduced LDL-C by up to 35 mg/dL [27]. In the trials included in the present study, doses of cashew was remarkably less than the mentioned amounts. Additional trials on the effects of higher doses of cashew on lipid profile are needed.

In the present study, cashew nuts appeared to lower systolic blood pressure. The potentially positive effects of nuts on blood pressure are likely to be effective because of their fatty acid composition. It was previously shown that α -linolenic acid in walnut was related to decreased blood pressure [28], and also high MUFA intake was documented to lower blood pressure [29], decrease inflammation and prevent cardiovascular events [21]. Previous studies have also revealed that substitution of carbohydrates with MUFA can lower blood pressure [30]. Schutte et.al., found that consumption of unsalted cashew for 20% of energy for 8 weeks could improve baroreflex sensitivity, which is a key mechanism for blood pressure control [31]. Baroreceptor sensitivity is an important factor in development of cardiovascular diseases and metabolic syndrome [31]. It is well documented that lipid profile abnormalities can lead to increased blood pressure and increased risk for CVD events, by impairing baro-receptor sensitivity (BRS), and impaired BRS is tightly associated with hypertension and increased inflammatory markers [31]. BRS is highly affected by dietary components [31], and studies have confirmed that diet can affect BRS. And it was revealed by Schutte et.al., that cashew consumption which is high in PUFA can increase BRS sensitivity. Also, dietary fats are effective on the density and function of cardiac adreno-receptors [31].

Beside the fatty acid composition of the nuts, other components of nuts may be responsible for cardioprotective effects. Nuts are high in plant sterols, dietary fiber, folic acid, antioxidants, arginine that have positive effects on endothelial function. Cashew nuts contain large amounts of arginine. Thirty grams of cashew contains 2.9 g arginine [6]. Arginine is the precursor of nitric oxide, an endogenous vasodilator [32], which can be responsible for blood pressure lowering effects of cashew. Results of a meta-analysis confirmed that arginine supplementation (6-63 g/day) can improve flow mediated dilation and cardiovascular health [33]. Therefore, cashew can control blood pressure via several mechanisms.

To the best of our knowledge, the present study is the first meta-analysis on the effects of cashew nut on cardiovascular risk factors. As a strong point to the present study, our systematic search minimized the probability of missing studies in this field. Also, the duration of the interventions were logical to see changes in blood lipids [34]. The limitation of the present study is the small number of included studies, due to the limited published papers. Also, in the studies included, the fatty acid and macronutrient proportion of the diets of cashew and control group were not identical, and cashew inclusion in the diet led to differences between the two group's diets. Therefore, it is suggested that future studies apply identical diets to both intervention and control groups so that the seen effects could be related to the nuts. Moreover, the included participants were not restricted to a special disease. In addition, the included trials reported insufficient data for undertaking meta-regression based on the other heterogeneous covariates.

Conclusion: This meta-analysis demonstrated that cashew nut consumption might reduce SBP but has no effects on lipid profile and DBP.

Funding and conflict of interest:

None to declare.

Author contribution:

MJ and MA contributed to study concept and design. MJ, SPM and MZ contributed to literature search and data selection. MJ contributed to data analysis. MJ, MK, GAF and MA contributed to drafting and reviewing the final manuscript. All authors read and approved the final version.

References:

1. Baer, D.J. and J.A. Novotny, *Consumption of cashew nuts does not influence blood lipids or other markers of cardiovascular disease in humans: a randomized controlled trial*. Am J Clin Nutr, 2019. **109**(2): p. 269-275.
2. Anand, S., C. Bradshaw, and D. Prabhakaran, *Prevention and management of CVD in LMICs: why do ethnicity, culture, and context matter?* BMC Medicine, 2020. **18**(1): p. 7.
3. Jagannathan, R., et al., *Global updates on cardiovascular disease mortality trends and attribution of traditional risk factors*. 2019. **19**(7): p. 44.
4. Sun, Q., et al., *Associations between dietary patterns and 10-year cardiovascular disease risk score levels among Chinese coal miners--a cross-sectional study*. BMC Public Health, 2019. **19**(1): p. 1704.
5. Garcia-Rios, A., et al., *New diet trials and cardiovascular risk*. Curr Opin Cardiol, 2018. **33**(4): p. 423-428.
6. Mohan, V., et al., *Cashew Nut Consumption Increases HDL Cholesterol and Reduces Systolic Blood Pressure in Asian Indians with Type 2 Diabetes: A 12-Week Randomized Controlled Trial*. J Nutr, 2018. **148**(1): p. 63-69.
7. Pieters, M., et al., *Clustering of haemostatic variables and the effect of high cashew and walnut diets on these variables in metabolic syndrome patients*. Blood Coagul Fibrinolysis, 2005. **16**(6): p. 429-37.
8. Del Gobbo, L.C., et al., *Effects of tree nuts on blood lipids, apolipoproteins, and blood pressure: systematic review, meta-analysis, and dose-response of 61 controlled intervention trials*. Am J Clin Nutr, 2015. **102**(6): p. 1347-56.
9. McGuire, S.J.A.i.n., *Scientific report of the 2015 dietary guidelines advisory committee. Washington, dc: Us departments of agriculture and health and human services, 2015*. 2016. **7**(1): p. 202-204.
10. Committee, U.S.D.G.A., *Dietary guidelines for Americans, 2010*. 2010: US Department of Health and Human Services, US Department of Agriculture.
11. Ternus, M., et al., *Qualified health claim for nuts and heart disease prevention: development of consumer-friendly language*. 2006. **41**(2): p. 62-66.

12. Giovannini, P., M.J. Howes, and S.E. Edwards, *Medicinal plants used in the traditional management of diabetes and its sequelae in Central America: A review*. J Ethnopharmacol, 2016. **184**: p. 58-71.
13. Kaewbutra, S., et al., *Cashew Apple Juice Improves Physical Fitness and Oxidative Stress Status in the Middle-Aged and Elderly Volunteers*. J Med Assoc Thai, 2016. **99 Suppl 5**: p. S161-72.
14. Mah, E., et al., *Cashew consumption reduces total and LDL cholesterol: a randomized, crossover, controlled-feeding trial*. Am J Clin Nutr, 2017. **105**(5): p. 1070-1078.
15. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement*. 2009. **151**(4): p. 264-269.
16. Follmann, D., et al., *Variance imputation for overviews of clinical trials with continuous response*. 1992. **45**(7): p. 769-773.
17. Wan, X., et al., *Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range*. BMC Medical Research Methodology, 2014. **14**(1): p. 135.
18. Sedgwick, P., *Meta-analyses: what is heterogeneity?* BMJ, 2015. **350**: p. h1435.
19. Higgins, J.P., et al., *Measuring inconsistency in meta-analyses*. BMJ, 2003. **327**(7414): p. 557-60.
20. Egger, M., et al., *Bias in meta-analysis detected by a simple, graphical test*. BMJ, 1997. **315**(7109): p. 629-34.
21. Mukuddem-Petersen, J., et al., *Effects of a high walnut and high cashew nut diet on selected markers of the metabolic syndrome: a controlled feeding trial*. Br J Nutr, 2007. **97**(6): p. 1144-53.
22. Demonty, I., et al., *Continuous dose-response relationship of the LDL-cholesterol-lowering effect of phytosterol intake*. J Nutr, 2009. **139**(2): p. 271-84.
23. Phung, O.J., et al., *Almonds have a neutral effect on serum lipid profiles: a meta-analysis of randomized trials*. J Am Diet Assoc, 2009. **109**(5): p. 865-73.
24. Banel, D.K. and F.B. Hu, *Effects of walnut consumption on blood lipids and other cardiovascular risk factors: a meta-analysis and systematic review*. Am J Clin Nutr, 2009. **90**(1): p. 56-63.
25. O'Neil, C.E., V.L. Fulgoni, 3rd, and T.A. Nicklas, *Tree Nut consumption is associated with better adiposity measures and cardiovascular and metabolic syndrome health risk factors in U.S. Adults: NHANES 2005-2010*. Nutr J, 2015. **14**(1): p. 64.
26. Yu, S., et al., *Plasma cholesterol-predictive equations demonstrate that stearic acid is neutral and monounsaturated fatty acids are hypocholesterolemic*. The American Journal of Clinical Nutrition, 1995. **61**(5): p. 1129-1139.
27. Del Gobbo, L.C., et al., *Effects of tree nuts on blood lipids, apolipoproteins, and blood pressure: Systematic review, meta-analysis, and dose-response of 61 controlled intervention trials*. American Journal of Clinical Nutrition, 2015. **102**(6): p. 1347-1356.
28. Ferrara, L.A., et al., *Olive oil and reduced need for antihypertensive medications*. Arch Intern Med, 2000. **160**(6): p. 837-42.
29. Roche, H.M., et al., *Effect of long-term olive oil dietary intervention on postprandial triacylglycerol and factor VII metabolism*. Am J Clin Nutr, 1998. **68**(3): p. 552-60.
30. Appel, L.J., et al., *Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial*. JAMA, 2005. **294**(19): p. 2455-64.
31. Schutte, A.E., et al., *Modulation of baroreflex sensitivity by walnuts versus cashew nuts in subjects with metabolic syndrome*. Am J Hypertens, 2006. **19**(6): p. 629-36.
32. Huynh, N. and J. Chin-Dusting, *Amino acids, arginase and nitric oxide in vascular health*. Clinical and experimental pharmacology & physiology, 2006. **33**: p. 1-8.
33. Schwingshackl, L., B. Strasser, and G. Hoffmann, *Effects of monounsaturated fatty acids on glycaemic control in patients with abnormal glucose metabolism: a systematic review and meta-analysis*. Ann Nutr Metab, 2011. **58**(4): p. 290-6.
34. Kris-Etherton, P.M. and J. Dietschy, *Design criteria for studies examining individual fatty acid effects on cardiovascular disease risk factors: human and animal studies*. Am J Clin Nutr, 1997. **65**(5 Suppl): p. 1590S-1596S.

Table 1. Demographic characteristics of the included RCTs

First author (Publication year)	Country	Type of trial	Participants health status	Mean age (year)	Sample size (Intervention group / Control group)	Treatment duration (week)	Dose of Cashew (gram / day)	Included outcomes
Mukuddem-Petersen (2007)	South Africa	Parallel	Metabolic syndrome	45	21 / 22	8 w	NR ϕ	SBP, SBP, TG, TC, HDL-C, LDL-C
Mohan (2018)	India	Parallel	T2DM	51.3	129 / 140	12 w	30	SBP, SBP, TG, TC, HDL-C, LDL-C
Baer (2019)	The USA	Crossover	Healthy adults	56.8	40 / 40	4 w	42	TG, TC, HDL-C, LDL-C

ϕ not clearly reported

Figure 1. Flow diagram of data selection process

Mukuddem-Petersen (2007)	Mohan (2018)	Baer (2019)	
			Random sequence generation (selection bias)
			Allocation concealment (selection bias)
			Blinding of participants and personnel (performance bias)
			Blinding of outcome assessment (detection bias)
			Incomplete outcome data addressed (attrition bias)
			Selective reporting (reporting bias)
			other sources of bias(e.g. bias of study design, trial stoppedearly, extreme baseline imbalance, and fraudulent trial)

Figure 2. Risk of bias assessment of the included studies according to the Cochrane guidelines

Figure 3. Forest plot detailing WMDs and 95% CIs for the meta-analyses of serum TG (A), HDL-C (B), LDL-C (C), TC (D), SBP (E) and DBP (F)

Figure 4. Meta-regression of HDL-C with treatment duration (A) and mean age of participants (B)

Figure 5. Sensitivity analysis for TG (A), HDL-C (B), LDL-C (C) and TC (D)