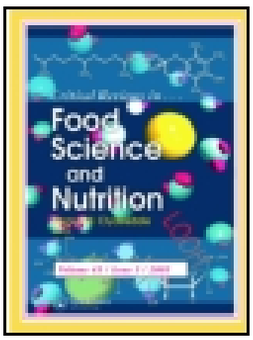

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Effect of pistachio on brachial artery diameter and flow-mediated dilatation: a systematic review and meta-analysis of randomized, controlled-feeding clinical studies

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Abstract

Background Results of previous clinical trials evaluating the effect of pistachio supplementation on endothelial reactivity (ER) are controversial.

Aims We aimed to assess the impact of pistachio on ER through systematic review of literature and meta-analysis of available randomized, controlled-feeding clinical studies (RCTs).

Methods The literature search included SCOPUS, PubMed-Medline, ISI Web of Science and Google Scholar databases up to 1st August 2017 to identify RCTs investigating the impact of

pistachio on ER. Two independent reviewers extracted data on study characteristics, methods and outcomes. Overall, the impact of pistachio on ER was reported in 4 trials.

Results The meta-analysis did not suggest a significant change in brachial artery flow-mediated dilatation (FMD) (WMD: +0.28%; 95%CI: -0.58, 1.13; p = 0.525) while brachial artery diameter (BAD) improved (WMD: +0.04%; 95%CI: 0.03, 0.06; p<0.001) following pistachios consumption.

Conclusion The present meta-analysis suggests a significant effect of pistachios on ER, affecting BAD but not FMD.

Keywords

pistachio; endothelial reactivity; flow mediated dilatation; brachial artery diameter; meta-analysis

Introduction

The health benefits of nuts, mainly in relation with cardiovascular disease (CVD) as well as to other chronic affections, have been largely demonstrated in both epidemiological and clinical studies.[Sabatè and Ang, 2009; Estruch et al., 2013; Bulló et al., 2015] For this reason, the American Heart Association,[Lloyd-Jones et al., 2010; Stone et al., 2014] the Canadian Cardiovascular Society [Anderson et al., 2013] and the US Food and Drug Administration [US Food and Drug Administration, 2003] recommended the regular consumption of nuts, in the context of a healthy diet, to prevent the risk of CVD. In fact, nuts have a healthy nutritional profile, that includes unsaturated fatty acids, protein, fibers, minerals, vitamins, γ-tocopherol, and a number of phytochemicals which contribute to promote cardiovascular health, when consumed with moderation and in the context of an overall balanced diet.[Bulló et al., 2015] Compare with other nuts, pistachios (*Pistacia vera*) have a lower content in fat (mostly from polyunsaturated and monounsaturated fatty acids) and energy, and higher levels of fibre (both soluble and insoluble), K^+, phytosterols, γ-tocopherol, vitamin K, and xanthophyll carotenoids.[U.S. Department of Agriculture ARS; Dreher, 2012] In addiction, they are the only nut containing significant amount of lutein and zeaxanthin.[U.S. Department of Agriculture ARS] Even for this reason, pistachios are listed among the top fifty food with a high antioxidant potential.[Halvorsen et al., 2006]

The European Food Safety Authority (EFSA) allowed an Article 13 claim that the daily consumption of 30 g of walnuts in the context of a balanced diet leads to improvement of endothelium-dependent vasodilation.[Alasalvar and Bolling, 2015] However, a growing body of clinical evidence suggests that also pistachios might be active on endothelium,

improving vascular function. In fact, they are a good source of L-arginine, which is a precursor of endogenous vasodilator nitric oxide.[Bath et al., 2017] Today, available studies are few and explorative and yield conflicting data. Therefore, we aimed to assess the impact of pistachios on endothelial reactivity (ER) through a systematic review of literature and meta-analysis of available RCTs.

Methods

Search Strategy

The study was designed according to guidelines of the 2009 preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement.[Moher et al., 2009] PubMed-Medline, SCOPUS Google Scholar and ISI Web of Science databases were searched using the following search items in titles and abstracts: ("pistachio" OR "pistachios" OR "Pistacia vera nut" OR "Pistacia vera nuts") AND ("Endothelium" OR "FMD" OR "F M D" OR "Flow Mediated Dilatation" OR "BAD" OR "B A D" OR "Brachial Artery Diameter" OR "Endothelial Reactivity" OR "ER" OR "E R"). The wild-card term "*" was used to increase the sensitivity of the search strategy. The reference lists of identified papers were checked manually for additional relevant article. No language restriction was used in literature search. The search was limited to studied in human. The literature was searched from inception to August 1st, 2017.

Study Selection

Original studies were included if they met the following inclusion criteria: (i) being a randomized controlled trial with either parallel or cross-over design, (ii) investigating the impact of chronic pistachios dietetic supplementation on BAD and FMD, (iii) presentation

of sufficient information on ER at baseline and at the end of follow-up in each group. Exclusion criteria were: (i) non-interventional trials, (ii) lack of a control group for pistachios dietetic supplementation, (iii) observational studies with case-control, cross-sectional or cohort design, (iv) testing acute effect of pistachios dietetic intake, and (v) lack of sufficient information on baseline or follow-up BAD or FMD.

Data Extraction

Eligible studies were reviewed and following data were abstracted: 1) first author's name; 2) year of publication; 3) study location; 4) study design; 5) dose and duration of pistachios supplementation; 6) inclusion criteria and underlying disease; 7) number of participants in the active and control group; 8) age, gender and body mass index (BMI) of study participants; 9) baseline plasma concentrations of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG); 10) baseline systolic (SBP) and diastolic blood pressure (DBP) measurements at rest; and 11) baseline BAD and FMD.

Quality Assessment

A systematic assessment of bias in the included study was performed using the Cochrane criteria.[Higgins and Green, 2010] The items utilized for the assessment of each study were as follows: adequacy of sequence generation, allocation concealment, blinding addressing of dropouts (incomplete outcome data), selective outcome reporting, and other probable sources of bias. Based on the recommendations of the Cochrane Handbook, a decision of "yes" characterized low risk of bias, while "no" indicated high risk of bias. Labelling an item as "unclear" suggested an unclear or unknown risk of bias.

Quantitative Data Synthesis

Meta-analysis was conducted using Comprehensive Meta-Analysis (CMA) V3 software (Biostat, NJ).[Borenstein et al., 2005] For parallel-group trials, difference in means (the effect size) in BAD and FMD were calculated by subtracting the value after intervention in the control group from the value in the active-treated one. For cross-over studies, changes in BAD and FMD were calculated by subtracting the value after control intervention from the reported after treatment. The standardized mean differences in BAD and FMD were obtained by dividing the differences in means by the relative standard deviations (computed within groups and pooled). In order to avoid double-counting problem in trials comparing multiple treatment arms versus a single control group, the number of subjects in the control group was divided by the number of treatment arms. The results of the selected studies were combined using the generic inverse variance method and a fixed- and random-effects model depending on the presence of high (≥50%) or low-to-moderate (<50%) heterogeneity, respectively. Heterogeneity was quantitatively assessed using I^2 index. Effect sizes were indicated as weighted mean difference (WMD) and 95% confidence interval (CI). In order to examine the influence of each study on the overall effect size, sensitivity analysis was executed using leave-one-out method, i.e. removing one study each time and repeating the analysis.

Publication bias

Potential publication bias was explored using visual inspection of Begg's funnel plot asymmetry, Begg's rank correlation test and Egger's weighted regression test. Duval &

Tweedie “trim and fill” method was used to adjust the analysis for the effects of publication bias.[Duval and Tweedie, 2000]

Results

Flow and characteristics of the included study

In summary, after several database searches 44 published studies were identified and the abstracts reviewed. Of these, 19 were non-original article and were excluded. Then, other 15 studies were eliminated because they did not meet the inclusion criteria. Thus, 10 full text articles were careful assessed and reviewed. Afterwards, 6 studies (list available as supplementary file) were excluded because: acute intervention studies (n = 3), and uncontrolled studies (n = 3). Finally, 4 studies were eligible and included in the meta-analysis.[Kasliwal et al., 2015; Sauder et al., 2015; West et al., 2012; Sari et al., 2010] The study selection process is shown in **Figure 1**.

Data were pooled from 4 RCTs comprising 9 treatment arms, which included 178 subjects, with 119 in the pistachio arm and 117 in the control arm. Included studies were published between 2010 and 2015, and were conducted in USA (2), India and Turkey. Clinical trials used different quantities of pistachios and the intervention period ranged between 4 and 12 weeks. Selected trials were designed cross-over,[Sauder et al., 2015; West et al., 2012] or per parallel groups.[Kasliwal et al., 2015; Sari et al., 2010] Enrolled subjects were normolipidemic adults, [Sari et al., 2010] adults with mild dyslipidaemia,[West et al., 2012; Sari et al., 2010] and well-controlled type 2 diabetes.[Sauder et al., 2015] Anthropometric and biochemical characteristics of the evaluated studies are presented in **Table 1**.

BAD and FMD measurements methods

Non-invasive ultrasound was used for the measurement of BAD and brachial artery FMD in all the included studies.

Risk of bias assessment

Almost all included studies were characterized by insufficient information about the sequence generation, allocation concealment, personnel and outcome assessors. All evaluated studies showed low risk of bias according to incomplete outcome data and selective outcome reporting. Details of the quality of bias assessment are shown in **Table 2**.

Effect of pistachio on BAD

The impact of pistachio on BAD was reported in 9 treatment arms. Meta-analysis suggested a significant increase of BAD following pistachio diet supplementation (WMD: +0.04%; 95%CI: 0.03, 0.06;p<0.001) (**Figure 2**). This result was robust in the leave-one-out sensitivity analysis (**Figure 2**).

Effect of pistachio on FMD

The impact of pistachio on FMD was reported in 9 treatment arms. Meta-analysis did not suggest any significant increase of FMD following pistachio diet supplementation (WMD: +0.28%; 95%CI: -0.58, 1.13; p = 0.525) (**Figure 3**). This result was robust in the leave-one-out sensitivity analysis (**Figure 3**).

Publication bias regarding pistachio's effect on BAD

The funnel plot of standard error by effect size (WMD) was asymmetric (**Figure 4**), suggesting potential publication bias in the meta-analysis of pistachio's effect on BAD. The presence of publication bias was confirmed by Egger's linear regression (intercept = -1.2; standard error = 0.31; 95%CI: -2.18, 0.23; t = 3.93, df = 3; two-tailed p-value = 0.03) and

Begg's rank correlation (Kendall's Tau with continuity correction = -0.2; z = 0.49; two-tailed p-value = 0.62). Correction of this asymmetry using Duval & Tweedie "trim and fill" method yielded 3 potentially missing study on the right-side of the funnel plot, and an adjusted effect size of 0.05% (95%CI: 0.03, 0.07) (**Figure 4**).

Publication bias regarding pistachio's effect on FMD

The funnel plot of the study standard error by WMD was asymmetric, suggesting potential publication bias in the meta-analysis of pistachio's effect on FMD (**Figure 5**). This observation was confirmed by the marginally significant results of Begg's rank correlation test (Kendall's Tau with continuity correction = 0.3; z = 0.73; two-tailed p-value = 0.46) and Egger's linear regression test (intercept = 1.9; standard error = 1.43; 95%CI: -2.66, 6.46; t = 1.33, df = 3; two-tailed p-value = 0.28). Correction of this asymmetry using Duval & Tweedie "trim and fill" method yielded one potentially missing study on the left-side of the funnel plot, and an adjusted effect size of -0.25% (95%CI: -1.24, 0.74) (**Figure 5**).

Discussion

At the best of our knowledge, the current systematic review and meta-analysis is the first one to comprehensively analyse evidences from RCTs on the efficacy of supplementation with pistachios on ER. Results did not show any significant increase of FMD following supplementation with pistachios, while BAD significantly improved.

As regards FMD, our findings substantially resumed what was just concluded by Xiao et al, [Xiao et al., 2017] who did not report – except for walnuts – any beneficial effect associated with nuts consumption, as far as our meta-analysis is more comprehensive by the inclusion

of a greater number of RCTs. However, BAD improvement suggests that pistachio consumption promotes NO-dependent vasodilatation.

All the studies included in the present meta-analysis enrolled normolipidemic subjects or subjects with mild dyslipidemia.[Kasliwal et al., 2015; Sauder et al., 2015; West et al., 2012; Sari et al., 2010] In 2 out of these, FMD significantly improved after pistachio supplementation.[Kasliwal et al., 2015; Sari et al., 2010] In the other ones, subjects with impaired fasting plasma glucose (FPG≤124 mg/dL) and well-controlled type 2 diabetes (T2DM) were included.[Sauder et al., 2015; West et al., 2012] Previously, Ma et al. reported a significant improvement in FMD in T2DM adults after 8 weeks of walnut-enriched diet.[Ma et al., 2010] These discrepant findings could be explained by the type of nut studied. In fact, walnuts contain a greater amount of polyunsaturated fatty acids than pistachios (47,2 g vs 13,5 g per 100 g of nuts) which have been shown to improve insulin responsiveness in T2DM subjects and decrease blood glucose level.[Ros et al., 2006; 2010 Dietary Guidelines Advisory Committee (DGAC) NEL Systematic Reviews; 2010] Therefore, walnuts effect on FMD in T2DM could be mediated by an insulin-dependent action. Conversely, pistachios are richer in flavonoids (14 mg vs 3 mg per 100 g of nuts), procyanidins (237 mg vs 67 mg per 100 g of nuts), tocopherols (7 mg vs 6 mg per 100 g of nuts), lutein and zeaxanthin (1405 μg vs 9 μg per 100 g of nuts), and phytosterols (214 mg vs 108 mg per 100 g of nuts) than walnuts and also contain a greater amount of carotenoids (332 μg per 100 g of pistachios). All of these compounds are reported to have direct vascular effect, modulating endothelial function potentially by increasing NO synthesis, or enhancing NO bioavailability and acting on voltage-gated ion

channels.[Edwards et al., 2015; Upadhyay et al., 2015] Moreover, pistachios are a great source of essential amino acids, with a lysine/arginine ratio of 0.55 which is higher than all the others nuts and legume.[Souza et al., 2015] Consequently, their vasoactive effect is also manifested without affecting other conditions which per se damage the vessel and is exalted by a healthy endothelium.

Pistachio's effect of BAD – as emerges from our meta-analysis – endorsed what already stated. It did not appear in any single study because individually unpowered: hence, the importance of the present meta-analysis.

Certainly, our meta-analysis has some limitations. Firstly, among the 4 eligible RCTs was found a moderate and marginally significant heterogeneity which may be due to differences in the intervention duration, sample size, type (if salted or unsalted) and daily dose of pistachios. For this reason, we performed the random effects analysis, which is a suitable method in the presence of heterogeneity studies. Remarkably, the significance of estimated pooled effect size on BAD was not biased by any single study.

Secondly, almost all the included studies had short periods of pistachio supplementation, whilst most of the previous clinical trials showing advantages of nut consumption on FMD had longer interventional period.[Ma et al., 2010; Njike et al., 2015; West et al., 2010; Katz et al., 2012] In this regard, it is worth noting that among the 4 studies included in the meta-analysis, the study by Kasliwal et al. was the only one which lasted for more than 4 weeks.[Kasliwal et al., 2015] Moreover, since no dose-escalation study has yet been carried out to determine the optimal dose of pistachios to improve the endothelial function, it is

unclear if the doses used in the included trials are sufficient to elicit a sizable effect in FMD in clinical setting, even if they certainly are enough to improve BAD.

In conclusion, the favourable effect of pistachios emerging from the current meta-analysis suggests the possible use of this nut as functional food in order to promote the vascular health. However, further well-designed trials are needed to confirm whether longer-term pistachio supplementation might significantly improve ER by increasing FMD other than BAD.

Disclosure statement

The authors have no affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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- ACUTE POSTPRANDIAL STUDIES (EXCLUDED FROM THE META-ANALYSIS)

1. Kendall CW, West SG, Augustin LS, Esfahani A, Vidgen E, Bashyam B, Sauder KA, Campbell J, Chiavaroli L, Jenkins AL, Jenkins DJ. Acute effects of pistachio consumption on glucose and insulin, satiety hormones and endothelial function in the metabolic syndrome. Eur J Clin Nutr. 2014 Mar;68(3):370-5. doi:10.1038/ejcn.2013.275.
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glycemia. Eur J Clin Nutr. 2011 Jun;65(6):696-702. doi: 10.1038/ejcn.2011.12.

3. Nieman DC, Scherr J, Luo B, Meaney MP, Dréau D, Sha W, Dew DA, Henson DA, Pappan KL. Influence of pistachios on performance and exercise-induced inflammation, oxidative stress, immune dysfunction, and metabolite shifts in cyclists: a randomized, crossover trial. PLoS One. 2014 Nov 19;9(11):e113725. doi: 10.1371/journal.pone.0113725.

- UNCONTROLLED STUDIES (EXCLUDED FROM THE META-ANALYSIS)

1. Honselman CS, Painter JE, Kennedy-Hagan KJ, Halvorson A, Rhodes K, Brooks TL, Skwir K. In-shell pistachio nuts reduce caloric intake compared to shelled nuts. Appetite. 2011 Oct;57(2):414-7. doi: 10.1016/j.appet.2011.02.022.
2. Kennedy-Hagan K, Painter JE, Honselman C, Halvorson A, Rhodes K, Skwir K. The effect of pistachio shells as a visual cue in reducing caloric consumption. Appetite. 2011 Oct;57(2):418-20. doi: 10.1016/j.appet.2011.06.003.
3. Aldemir M, Okulu E, Neşelioğlu S, Erel O, Kayıgil O. Pistachio diet improves erectile function parameters and serum lipid profiles in patients with erectile dysfunction. Int J Impot Res. 2011 Jan-Feb;23(1):32-8. doi: 10.1038/ijir.2010.33.

- ELIGIBLE STUDIES (INCLUDED IN THE META-ANALYSIS)

1. Kasliwal RR, Bansal M, Mehrotra R, Yeptho KP, Trehan N. Effect of pistachio nut consumption on endothelial function and arterial stiffness. Nutrition. 2015 May;31(5):678-85. doi: 10.1016/j.nut.2014.10.019.

2. Sauder KA, McCrea CE, Ulbrecht JS, Kris-Etherton PM, West SG. Effects of pistachios on the lipid/lipoprotein profile, glycemic control, inflammation, and endothelial function in type 2 diabetes: A randomized trial. Metabolism. 2015 Nov;64(11):1521-9. doi: 10.1016/j.metabol.2015.07.021.
3. Sari I, Baltaci Y, Bagci C, Davutoglu V, Erel O, Celik H, Ozer O, Aksoy N, Aksoy M. Effect of pistachio diet on lipid parameters, endothelial function, inflammation, and oxidative status: a prospective study. Nutrition. 2010 Apr;26(4):399-404. doi: 10.1016/j.nut.2009.05.023.
4. West SG, Gebauer SK, Kay CD, Bagshaw DM, Savastano DM, Diefenbach C, Kris-Etherton PM. Diets containing pistachios reduce systolic blood pressure and peripheral vascular responses to stress in adults with dyslipidemia. Hypertension. 2012 Jul;60(1):58-63. doi: 10.1161/HYPERTENSIONAHA.111.182147.

Table 1 – Baseline characteristics of the studies included in the meta-analysis.

FIRST AUTHOR (year)	STUDY LOCATION	DESIGN	TARGET POPULATION	TREATMENT DURATION	PARTICIPANTS	STUDY GROUP	AGE (years)	BMI (Kg/m²)	MALE (n, %)	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Glucose (mg/dL)	SBP (mm Hg)	DBP (mm Hg)	ENDOTHELIAL REACTIVITY	
																	BRACHIAL ARTERY DIAMETER (mm)	BRACHIAL ARTERY FMD (%)
Kasliwal, RR (2014) [20]	India	Open label, randomized, parallel-group, controlled-feeding clinical study	Adult subjects with mild dyslipidemia	12 weeks	27	Lifestyle modification	40.4±8.2	27.8±4.7	20 (74.1%)	212.2±30.7	161.2±63.6	43.4±11.1	141.7±22.3	87.3±8.0	124±11	76±9	4.21±0.56	7.84±4.66
					29	Lifestyle modification with consumption of 80 g (in-shell) pistachios	37.7±7.6	26.1±2.9	26 (89.7%)	196.5±41.6	139.1±64.7	39.2±14.1	133.9±38.1	87.7±7.3	128±13	76±9	4.21±0.47	5.6±4.67
Sauder, KA (2015) [18]	USA	Randomized, crossover, controlled-feeding clinical study	Adult subjects with well-controlled type 2 diabetes	4 weeks	30	Pistachio-free control diet	56.1±7.8	31.2±3.1	15 (50%)	162±2	62±2	43±1	98±2	106±11	116.2±13.6	71.0±5.4	4.49±0.15	5.28±0.41
					30	Diet containing 20% of daily energy from pistachios												
Sari, I (2010) [19]	Turkey	Prospective, parallel-group, controlled-feeding clinical study	Normolipidemic healthy young men	4 weeks	32	Mediterranean pistachio-free diet	22 (21-24)	NA	32 (100%)	199.6±41.8	91.2±39.7	43.3±9.7	142.0±37.4	91±8	117±8	73±8	3.22±0.23	7.19±1.65
					32	Diet containing ~20% of daily caloric intake from pistachios												
West, SG (2012) [17]	USA	Randomized, cross-over, controlled-feeding clinical study	Adult subjects with mild dyslipidemia	4 weeks	28	Low-fat pistachio-free control diet	NA	21-35	10 (35.7%)	≥111	<349	NA	NA	≤124	111.9±2.5	69.5±1.2	3.9±0.1	5.7±0.6
					28	Diet containing 10% of energy from pistachios												
					28	Diet containing 20% of energy from												

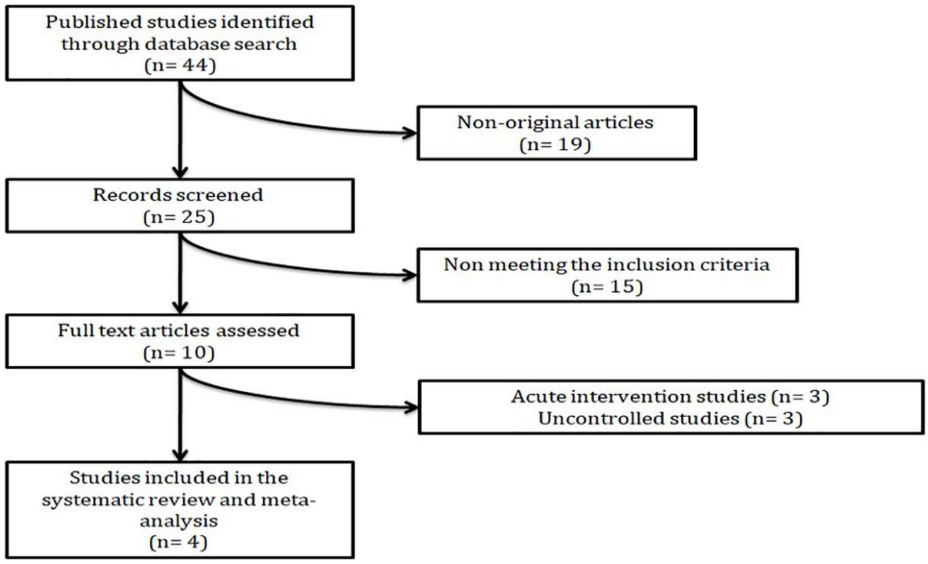
						pistachios												

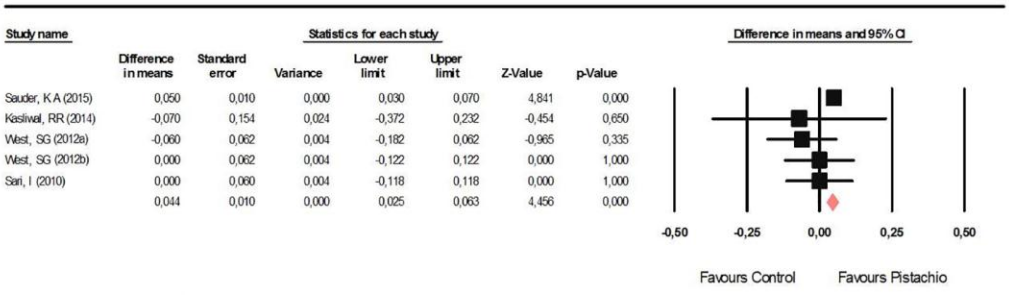
BMI: Body Mass Index; DBP: Diastolic Blood Pressure; FMD: Flow-Mediated Dilatation; HDL-C: High Density Lipoprotein Cholesterol; LDL-C: Low Density Lipoprotein Cholesterol; NA: Not Available; SBP: Systolic Blood Pressure; TC: Total Cholesterol; TG: Triglycerides.

Table 2 – Quality of bias assessment of the included studies according to Cochrane guidelines.

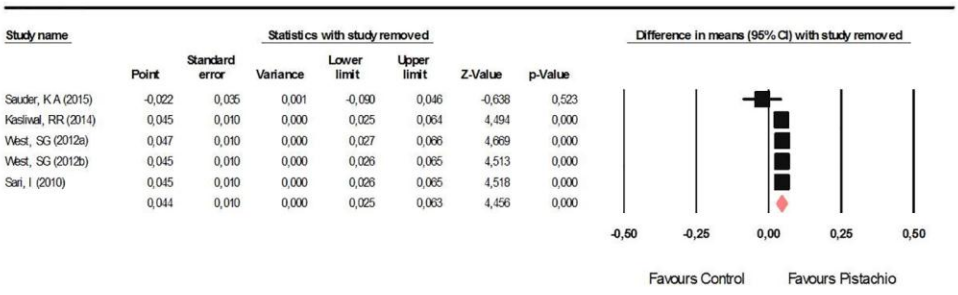
AUTHOR	SEQUENCE GENERATION	ALLOCATION CONCEALMENT	BLINDING OF PARTICIPANTS, PERSONNEL AND OUTCOME ASSESSMENT	INCOMPLETE OUTCOME DATA	SELECTIVE OUTCOME REPORTING	OTHER POTENTIAL THREATS TO VALIDITY
Sauder, K A (2015) [18]	L	L	U	L	L	U
Kasliwal, RR (2014) [20]	L	L	U	L	L	L
West, SG (2012) [17]	U	U	U	L	L	U
Sari, I (2010) [19]	L	U	U	L	L	U

L = low risk of bias; H = high risk of bias; U = unclear risk of bias.

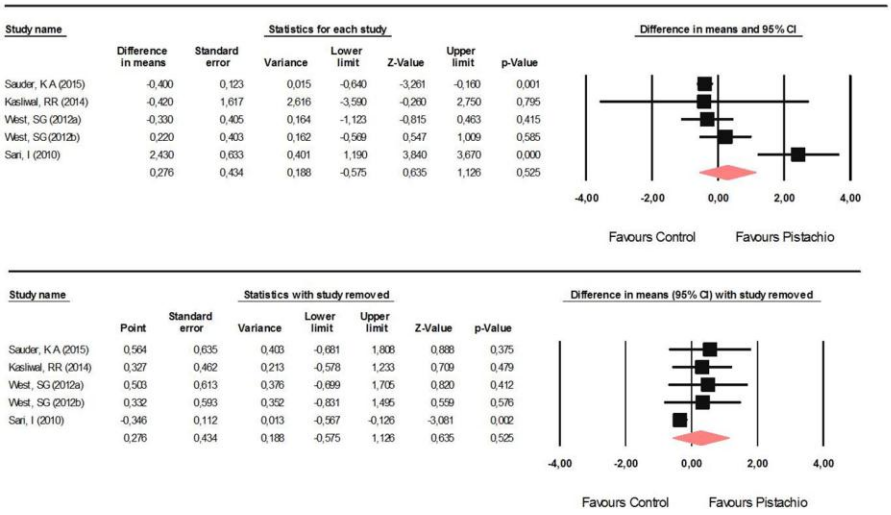




Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Sauder, K A (2015)	0,050	0,010	0,000	0,030	0,070	4,841	0,000
Kasliwal, RR (2014)	-0,070	0,154	0,024	-0,372	0,232	-0,454	0,650
West, SG (2012a)	-0,060	0,062	0,004	-0,182	0,062	-0,965	0,335
West, SG (2012b)	0,000	0,062	0,004	-0,122	0,122	0,000	1,000
Sari, I (2010)	0,000	0,060	0,004	-0,118	0,118	0,000	1,000
	0,044	0,010	0,000	0,025	0,063	4,456	0,000



Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Sauder, K A (2015)	-0,022	0,035	0,001	-0,090	0,046	-0,638	0,523
Kasliwal, RR (2014)	0,045	0,010	0,000	0,025	0,064	4,494	0,000
West, SG (2012a)	0,047	0,010	0,000	0,027	0,066	4,669	0,000
West, SG (2012b)	0,045	0,010	0,000	0,026	0,065	4,513	0,000
Sari, I (2010)	0,045	0,010	0,000	0,026	0,065	4,518	0,000
	0,044	0,010	0,000	0,025	0,063	4,456	0,000



Study name	Difference in means	Standard error	Variance	Lower limit	Z-Value	Upper limit	p-Value
Sauder, K A (2015)	-0,400	0,123	0,015	-0,640	-3,261	-0,160	0,001
Kasliwal, RR (2014)	-0,420	1,617	2,616	-3,590	-0,260	2,750	0,795
West, SG (2012a)	-0,330	0,405	0,164	-1,123	-0,815	0,463	0,415
West, SG (2012b)	0,220	0,403	0,162	-0,569	0,547	1,009	0,585
Sari, I (2010)	2,430	0,633	0,401	1,190	3,840	3,670	0,000
	0,276	0,434	0,188	-0,575	0,635	1,126	0,525

Study name	Point	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Sauder, K A (2015)	0,564	0,635	0,403	-0,681	1,808	0,888	0,375
Kasliwal, RR (2014)	0,327	0,462	0,213	-0,578	1,233	0,709	0,479
West, SG (2012a)	0,503	0,613	0,376	-0,699	1,705	0,820	0,412
West, SG (2012b)	0,332	0,593	0,352	-0,831	1,495	0,559	0,576
Sari, I (2010)	-0,346	0,112	0,013	-0,567	-0,126	-3,081	0,002
	0,276	0,434	0,188	-0,575	1,126	0,635	0,525