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Effects of pomegranate juice on blood pressure: A systematic review and meta-analysis of randomized controlled trials

Amirhossein Sahebkar[a,b,**], Claudio Ferri[c], Paolo Giorgini[c], Simona Bo[d], Petr Nachtigal[e], Davide Grassi[c,*]

[a] Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[b] Metabolic Research Centre, Royal Perth Hospital, School of Medicine and Pharmacology, University of Western Australia, Perth, Australia
[c] Department of Life, Health & Environmental Sciences, University of L'Aquila, Italy
[d] Department of Medical Sciences, University of Turin, Turin, Italy
[e] Charles University in Prague, Faculty of Pharmacy in Hradec Kralove, Department of Biological and Medical Sciences, Hradec Kralove, Czechia

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ABSTRACT

Punica granatum L. (Pomegranate) has been claimed to provide several health benefits. Pomegranate juice is a polyphenol-rich fruit juice with high antioxidant capacity. Several studies suggested that pomegranate juice can exert antiatherogenic, antioxidant, antihypertensive, and anti-inflammatory effects. Nevertheless, the potential cardioprotective benefits of pomegranate juice deserve further clinical investigation. To systematically review and meta-analyze available evidence from randomized placebo-controlled trials (RCTs) investigating the effects of pomegranate juice consumption and blood pressure (BP). A comprehensive literature search in Medline and Scopus was carried out to identify eligible RCTs. A meta-analysis of eligible studies was performed using a random-effects model. Quality assessment, sensitivity analysisand publication bias evaluations were conducted using standard methods. Quantitative data synthesis from 8 RCTs showed significant reductions in both systolic [weighed mean difference (WMD): −4.96 mmHg, 95% CI: −7.67 to −2.25, p < 0.001) and diastolic BP (WMD: −2.01 mmHg, 95% CI: −3.71 to −0.31, p = 0.021) after pomegranate juice consumption. Effects on SBP remained stable to sensitivity analyses. Pomegranate juice reduced SBP regardless of the duration (>12 wks: WMD = −4.36 mmHg, 95% CI: −7.89 to −0.82, p = 0.016) and <12 wks: WMD = −5.83 mmHg, 95% CI: −10.05 to −1.61, p = 0.007) and dose consumed (>240 cc: WMD = −3.62 mmHg, 95% CI: −6.62 to −0.63, p = 0.018) and <240 cc: WMD = −11.01 mmHg, 95% CI: −17.38 to −4.65, p = 0.001, pomegranate juice per day) whereas doses >240 cc provided a borderline significant effect in reducing DBP. The present meta-analysis suggests consistent benefits of pomegranate juice consumption on BP. This evidence suggests it may be prudent to include this fruit juice in a heart-healthy diet.

1. Introduction

Cardiovascular disease is the number one cause of mortality and morbidity worldwide. Hypertension is a leading risk factor for cardiovascular disease [1,2]. It has been demonstrated a linear relationship between blood pressure levels and the risk of cardiovascular disease and also the state of pre-hypertension (not clinically expressed hypertension) is considered a cardiovascular risk for a large part of the population [2]. Therefore, lowering blood pressure, even in the normal range, through dietary modifications may decrease the risk of end-organ damage caused by hypertension [1,2]. Lifestyle modifications, including adherence to a heart-healthy diet, have substantial effects on cardiovascular risk factors such as hypertension [2]. Mounting evidence from epidemiological studies suggests that there is an association between diets rich in fruits and vegetables and a reduction in the incidence of cardiovascular disease [3]. Fruits and vegetables contain a wide range of potentially cardioprotective components including fibre, folate, anti-oxidants, vitamins and a large number of non-nutrient phytochemicals such as carotenoids and polyphenols [3–5]. Epi-

Abbreviations: ACE, angiotensin-converting enzyme; BMI, body mass index; BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; NO, nitric oxide; NOS, nityric oxide synthase; RCTs, randomized placebo-controlled trials; RRR, reduction in relative risk; SBP, systolic blood pressure; WMD, weighed mean difference.

* Corresponding author at: University of L'Aquila, Department of Life, Health and Environmental Sciences, Viale S Salvatore, Delta 6 Medicina, 67100 Coppito, L'Aquila, Italy.
** Corresponding author at: Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
E-mail address: davide.grassi@cc.univaq.it (D. Grassi).

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demiological evidence suggests that polyphenols, at least in part, might explain the cardiovascular benefits from increased fruit and vegetable intake [5].

A growing evidence suggests putative beneficial effects of various polyphenol subclasses on biological systems [5]. Accordingly, some clinical intervention studies support the hypothesis of cardiovascular benefits from polyphenol-rich beverages including tea, cocoa and red wine [5–8]. Furthermore, consumption flavonoid-rich fruits and vegetables has been proposed to lower blood pressure and confer cardiovascular protection [3–5].

Punica granatum L. (Pomegranate) has been widely investigated in relation to its cardioproetctive and anti-hypertensive effects. Pomegranate has been claimed to provide several health benefits. Pomegranate juice is a polyphenol-rich fruit juice with a high antioxidant capacity. Pomegranate can help preventing or treating several cardiovascular risk factors including hypertension, hypercholesterolemia, oxidative stress, hyperglycemia, and inflammation [3,9]. Nevertheless, studies investigating the anti-hypertensive effects of pomegrnate juice have produced different results. An explanation for these discrepant results could be differences in the source and polyphenolic content of juice that was used, and also differences in demographic characteristics of the populations studied in clinical trials. Furthermore, extrapolation of experimental data to the human is fraught with problems, predominantly regarding the bioavailability and metabolism of the different classes of polyphenols [6–9]. Finally individual studies assessing the anti-hypertensive effects of pomegranate juice have been mainly performed with limited number of participants, thereby making generalization of results difficult. The impact of fruit polyphenols on cardiovascular mortality is of considerable public health importance and would help to inform policy on recommendations of the types of fruits to be consumed for cardiovascular protection. Thus, we aimed to perform an up-to-date systematic review and meta-analysis of randomized controlled trials (RCTs) investigating the effects of pomegranate juice consumption on blood pressure.

2. Methods

2.1. Search strategy

This study was designed according to the guidelines of the 2009 preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement guidelines [10]. SCOPUS (http://www.scopus.com) and Medline (http://www.ncbi.nlm.nih.gov/pubmed) and two Iranian bibliographic databases namely MagIran (www.magiran.com) and Scientific Information Database (www.SID.ir) were searched using the following search terms in titles and abstracts (also in combination with MESH terms): ("randomized controlled trial" OR randomized OR placebo) and ("blood pressure" OR hypertension OR anti-hypertensive OR hypotension OR hypotensive) and (pomegranate OR *Punica*). The wild-card term "*" was used to increase the sensitivity of the search strategy. No language restriction was used in the literature search. The search was limited to studies in human. The literature was searched from inception to December 12th, 2014.

2.2. Study selection

Original studies were included if they met the following inclusion criteria: (i) be a randomized clinical case-control or case-cross-over trial, (ii) investigated the impact of pomegranate juice on blood pressure, (iii) presentation of sufficient information on baseline and at the end of study in both pomegranate and control groups, and (iv) administering pomegranate for a period of

Table 1
Characteristics of studies included in the meta-analysis.

Author	Study design	Target Population	Treatment duration	N	Study groups	Age, years	Female (n, %)	BMI, (kg/m^2)	SBP (mmHg)	DBP (mmHg)	Fasting glucose (mg/dl)	Total cholesterol (mg/dl)	LDL cholesterol (mg/dl)	HDL cholesterol (mg/dl)	Triglycerides (mg/dl)
Aviram et al. [17]	Randomized, placebo-controlled	Carotid artery stenosis (hypertension and hyperlipidemia)	1 year	10	PJ 50 ml/day	ND	ND	ND	174 ± 8	81 ± 3	123 ± 9	184 ± 7	113 ± 6	47 ± 4	118 ± 16
				9	Control	ND	ND	ND	160 ± 7	88 ± 4	ND	ND	ND	ND	ND
Sumner et al. [18]	Randomized, double-blind, placebo-controlled	Ischemic coronary heart disease	3 months	26	PJ 240 ml/day	69 ± 11	4 (15.0)	28 ± 6	130 ± 15	72 ± 12	116 ± 31	170 ± 42	91 ± 33	48 ± 11	149 ± 107
				19	Control	69 ± 9	1 (5.0)	29 ± 5	126 ± 25	72 ± 11	121 ± 63	157 ± 32	80 ± 35	46 ± 12	155 ± 102
Davidson et al. [19]	Randomized, double-blind, placebo-controlled	At least 1 cardiovascular risk factor and high CIMT	18 months	146	PJ 240 ml/day	60.8 ± 7.3	61 (42.0)	28.6 ± 4.8	127.7 ± 18.7	70.9 ± 10.5	94.6 ± 10.0	224.3 ± 37.8	138.8 ± 33.5	55.1 ± 15.4	152.8 ± 75.4
				143	Control	60.5 ± 7.8	64 (45.0)	28.7 ± 4.5	129.3 ± 18.4	71.5 ± 11.0	94.7 ± 8.9	227.2 ± 35.7	142.3 ± 29.6	56.1 ± 13.9	144.3 ± 65.4
Lynn et al. [20]	Randomized parallel single-blind, placebo-controlled	Healthy subjects	4 weeks	24	PJ 330 ml/day	39.0 ± 1.24	16 (66.6)	24.99 ± 1.26	115.2 ± 2.4	72.1 ± 1.7	ND	ND	ND	ND	ND
				24	Control	36.1 ± 0.92	16 (66.6)	24.99 ± 1.06	111.7 ± 2.1	69.6 ± 1.6	ND	ND	ND	ND	ND
Tsang et al. [21]	Randomized, placebo-controlled, cross-over	Healthy volunteers	4 weeks	28	PJ 500 ml/day	50.4 ± 6.1	16 (57.1)	26.7 ± 3.3	128.9 ± 5.1	76.2 ± 4.8	86.7 ± 9.5	210.8 ± 38.7	128.0 ± 28.2	58.8 ± 17.0	101.6 ± 34.5
					Control				133.8 ± 16.3	80.9 ± 10.9	85.4 ± 4.9	174.4 ± 19.7	98.2 ± 30.5	56.5 ± 21.7	101.0 ± 45.2
Sohrab et al. [22]	randomized, double-blind, placebo-controlled	patients with type 2 diabetes	12 weeks	22	PJ 250 ml/day	55 ± 6.7	11 (50.0)	29.4 ± 3.9	ND	ND	160.3 ± 47.8	ND	ND	ND	ND
				22	control	56.9 ± 3.2	10 (45.5)	28.6 ± 4.2	ND	ND	148.7 ± 42.1	ND	ND	ND	ND
Asgary et al. [23]	Single-blind, placebo-controlled	Hypertension	2 weeks	11	PJ 150 ml/day	58.9 ± 5.0	8 (72.7)	26.7 ± 3.4	124.5 ± 15.7	76.3 ± 6.7	90.6 ± 7.0	218.7 ± 42.8	127.2 ± 24.2	49.2 ± 8.0	171.1 ± 78.9
				10	Control	46.9 ± 12.3	7 (70.0)	27.9 ± 4.1	128.0 ± 13.1	85.0 ± 8.0	89.1 ± 11.3	187.0 ± 30.2	109.4 ± 25.8	40.4 ± 6.9	165.6 ± 124.3
Shema-Didi et al. [24]	Randomized, double-blind, placebo-controlled	Hemodialysis patients	1 year	66	PJ 100 cc 3 times/week	ND	ND	ND	135.7 ± 21.3	67.7 ± 13.8	ND	167.3 ± 43.5	100.0 ± 33.1	36.8 ± 10.8	167.3 ± 86.3
				35	Control	ND	ND	ND	135.6 ± 27.7	63.8 ± 20.4	ND	165.1 ± 35.8	94.3 ± 27.2	34.3 ± 15.4	206.1 ± 109.4

Values are expressed as mean ± SD.
Abbreviations: PJ, pomegranate juice; ND, no data; BMI, body mass index.