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The effects of pomegranate juice consumption on blood pressure and cardiovascular health

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A B S T R A C T

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Hypertension (HTN) is the most common disease found in patients in primary care [JNC-7 Guidelines. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hyper* 2003;**42**:1206.]. It eventually requires medication if lifestyle modifications are not initiated or do not control the blood pressure well enough. The majority of patients would prefer not to have to be medicated to manage their disease, and HTN can be found to be a comorbidity along with diabetes, CAD, and many other cardiovascular diseases. Adverse effects, forgetfulness and patient ignorance are multiple reasons for the hesitancy to begin drug management. Pomegranate juice is rich in tannins, possesses anti-atherosclerotic properties, has anti-aging effects, and potent anti-oxidative characteristics. As some antioxidants have been shown to reduce blood pressure, the purpose of this review was to discover the effect of pomegranate juice consumption on blood pressure and cardiovascular health. Pomegranate juice consumption may reduce systolic blood pressure, inhibits serum ACE activity, and is convincingly a heart-healthy fruit [Aviram M, Dornfeld L. Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure. *Athero* 2001;**158**:195–8.]. More clinical research is needed as a number of the studies discussed include small sample sizes and few studies seem to have been undertaken in the recent 5–10 years.

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Over 45 million adults in the United States are affected by hypertension.¹⁵ Hypertension is a major risk factor for other cardiovascular diseases, such as stroke, myocardial infarction and heart failure. In order to prevent these cardiovascular diseases from occurring, control of a patient's blood pressure is necessary, either by lifestyle modifications, medication(s) or both. It is a large public health issue as many Americans are unaware that they have high blood pressure or that it is uncontrolled because it is largely asymptomatic in the early stages.¹⁵ A study performed by the Centers for Disease Control and Prevention from 1999 to 2000 suggested that only 31.0% of people with diagnosed hypertension were considered to be under control.¹⁵

Healthy People 2010 was initiated in January of 2000 by the United States Department of Health and Human Services. It is a nationwide health promotion and disease prevention program with certain objectives to be reached by 2010. The objective for dealing with blood pressure stated a goal of increasing control of blood pressure to 68% of adults greater than 18 years old.¹² Medications are available to help control blood pressure in adults, but many adults are reluctant to start drug treatment.⁹ Numerous

patients have issues with tolerating the medications used for treating hypertension, along with problems remembering to take the pill(s).⁹

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) stated that the risk of cardiovascular disease (CVD) beginning at 115/75 mmHg doubles with each increment of 20/10 mmHg; individuals who are normotensive (defined as blood pressure at or below 115/75) at age 55 have a 90 percent lifetime risk for developing hypertension.¹³

Cardiovascular disease is the major cause of death and disability in the United States.¹³ All patients should therefore be encouraged to make changes to their health in the attempt to prevent hypertension. JNC-7 also reported that most patients with hypertension will require two or more anti-hypertensive medications to achieve goal blood pressure (<140/90 mmHg, or <130/80 mmHg for patients with diabetes or chronic kidney disease).¹³

JNC-7 classifies blood pressure into four stages: Normal, Pre-hypertension, Stage 1 Hypertension, and Stage 2 Hypertension. Stage 1 is the first classification that gives the treatment guidelines as initiating drug therapy. Stage 1 is defined as systolic blood pressure of 140–159 mmHg and/or diastolic blood pressure 90–99 mmHg.¹³

Pomegranate juice is known to be rich in antioxidants, and levels of antioxidants have been found to be higher than in other natural

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juices and even in red wine.⁷ Antioxidants have numerous positive properties, including protection against cholesterol oxidation, anti-aging effects and protection against atherosclerosis.⁷ It is reasonable then to ask if the antioxidant properties of pomegranate juice could be helpful in preventing cardiovascular disease risk.

A review article evaluated the heart-healthy benefits of pomegranate juice.⁵ In the included studies reviewed, pomegranate juice (PJ) decreased systolic blood pressure in one clinical trial and appeared to offer many other cardiovascular benefits, including a decrease on the progression of atherosclerosis. These claims have also been supported by Aviram and Dornfeld, who suggested a positive cardiovascular effect from pomegranate juice with reference to a reduction in cholesterol and atherosclerotic levels.³ It would appear that, PJ produced statistically significant results in patients on various medications, suggesting the juice may also be an effective adjunct in patients at risk of serious heart disease.⁵

There are over 50 million adults in the United States with hypertension and cardiovascular issues today therefore this issue is relevant to all nurse practitioners and health care workers.³ In the USA, nurse practitioners manage a large percentage of the population's primary care and since hypertension is so highly prevalent, are at the forefront of this condition.⁸ Nurse practitioners who include non-pharmacological methods of managing hypertension in their patients tend to see better clinical outcomes.⁸ This paper discusses the effects of pomegranate juice on blood pressure and cardiovascular health.

1. Search criteria

PubMed, Cochrane Review, CINAHL, and Google Scholar were searched for research and review relevant literature. Inclusion criteria for the search were articles dated 2009 or earlier which included information regarding pomegranate juice and cardiovascular health. A total of one hundred and thirty articles were found after entering the keywords, with five papers meeting criteria for inclusion. It was also felt important to recognize the cardiovascular effects of hypertension and include studies addressing cardiovascular issues with pomegranate juice.

2. State of the science

A study by Aviram & Dornfeld demonstrated a 5% decline in systolic blood pressure with daily consumption of 50 ml of pomegranate juice for two weeks. Both males and females were studied, with each participant on anti-hypertensive pharmacological therapy. Lowered blood pressure may have resulted from a direct interaction of the PJ with serum angiotensin converting enzyme (ACE), but there was no significant reduction in serum ACE activity.³

An *in vitro* study was performed, as well as a clinical study with 15 healthy male volunteers. It was a randomized, single-dose, 5-way crossover study, with 1 week elapsing between trials. Results indicated that unlike grapefruit juice, pomegranate juice does not significantly affect the cytochrome P450-3A pathway, therefore making it safe for patients on other medications that interact poorly with grapefruit juice to use¹⁰; however, the study involved a small sample size and thus limited generalizability. This study is one of two showing clear clinical evidence of PJ's rapid effect on systolic blood pressure in the past ten years.

Another study demonstrated lowered blood pressure in patients with carotid artery stenosis who had consumed pomegranate juice for 3 years.⁴ Ten patients were given PJ for 1 year with five patients continuing up to 3 years. Systolic blood pressure was reduced by 21% after 1 year of PJ consumption and was not further reduced during the 3 years of PJ consumption. The results of this again, small scale study, suggest that PJ consumption by patients with carotid artery stenosis appears to decrease systolic blood pressure. These effects could be

related to the potent antioxidant characteristics of PJ polyphenols but it is clear further research is required. This study demonstrates both the long and short term effects of PJ on blood pressure.

In 2006, pomegranate juice was noted to reduce the oxidized low-density lipoprotein downregulation of endothelial nitric oxide synthase (NOSIII) in human coronary endothelial cells.⁷ Data suggested that PJ can exert beneficial effects on the evolution of clinical vascular complications, coronary heart disease, and atherogenesis in humans by enhancing the NOSIII bioactivity. This relates to the positive effects of lowering blood pressure in hypertensive patients. This was an *in vitro* study, thus it cannot be assumed clinically relevant in human subjects. Nevertheless the study does have important implications for further clinical research in human subjects. Another study discussed the role of pomegranate seed oil in reducing weight gain and lowering type² diabetes mellitus risk in CD-1 mice on high-fat diets.² While the clinical question deals with cardiovascular health, it has been well documented that patients who are overweight are at a higher risk for type² diabetes mellitus and HTN.¹⁴ This study examined the seed oil rather than the juice, as the authors feel that the juice and/or fruit consumption has been scientifically proven to reduce the risk of CVD. The limitation of this study is that animal studies cannot be assumed to be clinically relevant in human subjects, but it still provides data to help answer some of the questions that have been placed forward.

Pomegranate juice contains antioxidants shown to possess anti-atherosclerotic properties. In 2005, forty-five patients with stable coronary heart disease (CHD), with confirmed stress-induced ischemia that was documented by at least one reversible myocardial perfusion defect on computed tomography (CT) and confirmed by an independent observer.¹⁷ The study employed rigorous exclusion criteria. Methodology included a randomized double-blind controlled trial with an intervention group and a placebo group. The results demonstrated for the first time, that daily consumption of PJ for 3 months may decrease myocardial ischemia and improve myocardial perfusion in patients who have ischemic CHD.¹⁶ There were no statistically significant effects on blood pressure. Although the sample size in this study was relatively small, the authors pointed out the strength of the design and the clinically significant and statistically significant improvements in myocardial perfusion observed in the experimental group over a short period suggesting that daily consumption of PJ could have important clinical benefits.¹⁶

Davidson et al. performed a randomized, double-blind parallel trial to assess the influence of PJ consumption on anterior and posterior carotid intima-media thickness (CIMT) progression rates in subjects at moderate risk for coronary heart disease.⁶ Subjects were men, from 45 to 74 years of age, and women, from 55 to 74 years of age, with more than one coronary heart disease risk factor and baseline posterior wall CIMT 0.7–2.0 mm, without significant stenosis. Participants consumed 240 ml/day of PJ or a control beverage for up to 18 months. There were no statistically significant results in overall CIMT progression. The authors feel that based on the results, subjects at moderate coronary heart disease risk, PJ consumption had no significant effect on overall CIMT progression rate but may have slowed down CIMT progression in subjects with increased oxidative stress and disturbances in the triglyceride-rich lipoprotein/HDL axis.⁶

The final article identified in the literature search addressed nonpharmacological approaches in the management of hypertension by DeSimone and Crowe who concluded from their extensive literature review that nonpharmacological strategies are to be recommended as successful primary and adjunctive treatment options for lowering blood pressure. The benefits of many of these approaches extend to and promote overall health and well being.⁸ The limitations of this review include some conflicts of interest with the authors and the funding source, but the literature review is extensive.

3. Conclusion

This review suggests that pomegranate juice has shown considerable anti-atherosclerotic, anti-hypertensive, antioxidant, and anti-inflammatory effects in human subjects and mouse models. The principal mechanisms of action of pomegranate juice may include decreased systolic blood pressure, thus causing an overall positive effect on the progression of atherosclerosis and the ensuing potential development of coronary heart disease. Based on the data reviewed, pomegranate juice supplementation does not exert beneficial effects in subjects with type 2 diabetes and CVD.⁵ But with only two clinical trials showing a decrease in blood pressure, we cannot say with certainty that PJ should be prescribed for cardiovascular health. Pomegranate juice awaits additional clinical research to further verify its cardiovascular effects.

Upon searching the National Institute of Health's Complementary and Alternative Medicine's current research (2005–2008), there were no ongoing studies or previous research discussing the use of pomegranate juice in HTN. There was a study about the use of pomegranate fruit extract to treat osteoarthritis,¹¹ and a study regarding the use of pomegranate juice extract for skin cancer chemoprevention.¹ These studies indicate that the historical use of pomegranate juice as an alternative for traditional medications for many conditions is worth further discussion and study.

Hypertension remains an important public health challenge, and current rates are still far below the Healthy People 2010 goal of 50%.⁸ By integrating nonpharmacological approaches and lifestyle changes into blood pressure-lowering regimens, health care practitioners can help to improve clinical outcomes as well as decrease the economic burden of hypertension.⁸

Author	Summary of article
Basu & Penugonda Aviram & Dornfeld	↓ SBP, ↓ progression of atherosclerosis ↓ cholesterol and atherosclerotic levels; effective adjunct in patients at risk of serious heart disease
Farkas, Oleson, Zhao, et al. Aviram, Rosenblat, Gaitini, et al. De Nigris, Williams-Ignarro, Botti, et al.	No effect on cytochrome P450-3A pathway ↓ BP in patients with carotid artery stenosis ↓ oxidized low-density lipoprotein downregulation of endothelial nitric oxide synthase
Sumner, Elliott-Eller, Weidner, et al.	Consumption of PJ may ↓ myocardial ischemia and improve myocardial perfusion; no statistical effects on BP
DeSimone & Crowe	Nonpharmacological strategies recommended as successful primary and adjunct treatment for ↓ blood pressure.
Davidson, Maki, Dicklin, et al. Search engines: PubMed, CINAHL, Cochrane Review, Google Scholar	No statistically significant results on CIMT Keywords: pomegranate juice, cardiovascular health, blood pressure, hypertension, pomegranate juice therapy, antioxidant pomegranate juice
McFarlin, Strohacker, Kueht	↓ weight gain, ↓ type 2 DM risk in high-fat diets in mice

Conflict of interest

None to report.

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