Postural Changes in Measures of Arterial Stiffness in Hypertensive Subjects on Antihypertensive Drug Therapy: A Prospective, Pilot Study

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Abstract

Prospective study with a controlled arm to know if there are variations of measures of arterial stiffness with posture in subjects with hypertension on antihypertensive medications.

We studied postural variations of measures of arterial stiffness in 21 subjects with diagnosed hypertension on antihypertensive medications and compared them with 21 normotensive subjects. All subjects underwent pulse-wave analysis on Sphygmo-Cor in the morning between 8 AM to 10 AM initially in supine and then in sitting position after 3 minutes. Summary measures on demographics, and blood pressure characteristics at sitting and supine positions are obtained. Differences between characteristics at supine and sitting position are compared using nonparametric paired test of Wilcoxon signed-rank test. A value of $p < 0.05$ was accepted as statistically significant.

Antihypertensive medications decreased the supine aortic augmentation pressure (AAP) and augmentation index (AI) but not significantly. When subgroups of patients with antihypertensive treatment were analyzed, it was noted that angiotensin-converting enzyme inhibitor and angiotensin receptor blocker group (12) decreased AAP and AI significantly in supine position compared with patients on other antihypertensive medications (9) (p -value 0.034 and 0.038, respectively). There was no significant difference in other groups of calcium channel blockers, β -blockers, or diuretics. However, in normotensive control arm, there was an increase in AAP and AI in the supine position.

Keywords

- hypertension
- young
- posture
- arterial stiffness

In hypertensive subjects, on antihypertensive, there was reduction in AAP and AI in supine position compared with those of normotensives. The significance of the decrease in AAP and AI in supine position on antihypertensive needs to be studied further.

This is a prospective study with a controlled arm of normotensive subjects to know if there are variations of measures of arterial stiffness with posture in subjects with hypertension

on antihypertensive medications when compared with normotensive subjects. Postural variations of measures of arterial stiffness have not been described in the literature.

Methods

We studied postural variations of measures of arterial stiffness in 21 subjects with diagnosed hypertension on ambulatory blood pressure (BP) monitoring on antihypertensive medications and compared them with 21 normotensive subjects.

Normotensive subjects had clinic BP readings below 140/90 mm Hg and hypertensive subjects had clinic BP readings above 140/90 mm Hg on at least two separate occasions. All subjects underwent pulse-wave analysis on SphygmoCor in the morning between 8 AM to 10 AM initially in supine and then in sitting position after 3 minutes. These subjects were told to refrain from smoking, eating, or drinking beverages 3 hours before the test and to refrain from drinking alcohol 10 hours before the test (as per European Society of Hypertension guidelines). Ethics approval was taken before the start of the study. Informed consent was taken from all participants.

Statistical Methods

Summary measures on demographics, and BP characteristics at sitting and supine positions are obtained. Normality of the data is determined by constructing histograms and checking for normal distribution. Differences between characteristics at supine and sitting positions are compared using nonpara-

metric paired test of Wilcoxon signed-rank test. A p -value of $p < 0.05$ was accepted as statistically significant. Statistical analysis was performed using stata v10.1 (StataCorp, College Station, TX) and p -values < 0.05 is considered statistically significant.

Results

In normotensive control arm, there was increase in supine aortic augmentation pressure (AAP) and augmentation index (AI). There was statistically significant difference between supine (higher) and sitting (lower) AI (p -value 0.01) as well as AAP (p -value 0.04). In hypertensive patients on antihypertensive medications, there was no significant difference between supine and sitting parameters of arterial stiffness. Antihypertensive medications decreased the supine AAP and AI but not significantly (► **Table 1**).

When subgroups of patients on antihypertensive medications were analyzed, it was noted that angiotensin-converting enzyme (ACE) inhibitor and angiotensin receptor blockers (ARBs) group (12) decreased AAP and AI significantly in supine position compared with patients on other antihypertensive medications (9) (p -value 0.034 and 0.038, respectively). There was no significant difference in other groups of calcium channel blockers, β -blockers, or diuretics (► **Table 2**).

Table 1 Data showing postural changes in arterial stiffness parameters in normotensive and hypertensive subjects

Normotensive subjects			
Number	21		
Mean age in years (range)	33 (20–61)		
Mean body mass index	25.24 (17.85–37.89)		
Normotensive subjects			
Parameters	Supine	Sitting	<i>p</i> -Value
Mean CASP mm Hg (range)	100.5 (81–135)	102 (81–134)	0.79
Mean APP mm Hg (range)	36.5 (23–60)	35 (20–60)	0.13
Mean AAP mm Hg (range)	9.7 (1–30)	6.8 (–2 to +17)	0.04
Mean AI mm Hg (range)	23.5 (3–52)	16.42 (0–31)	0.01
Mean OI (range)	92 (83–100)	92 (80–100)	0.82
Hypertensive subjects			
Number	21		
Mean age in years (range)	47.33 (20–89)		
Mean body mass index	29.55 (18.34–42.33).		
Hypertensive subjects			
Parameters	Supine	Sitting	<i>p</i> -Value
Mean CASP mm Hg (range)	131 (100–180)	132 (100–180)	0.888
Mean APP mm Hg (range)	52 (28–89)	51 (27–77)	0.266
Mean AAP mm Hg (range)	11.9 (–5 to +29)	12.6 (–2 to +38)	0.448
Mean AI mm Hg (range)	18.85 (–14 to +40)	19.14 (–5 to +45)	0.870
Mean OI (range)	94 (82–100)	94 (85–100)	0.669

Abbreviations: AAP, aortic augmentation pressure; AI, augmentation index; APP, aortic pulse pressure; CASP, central aortic systolic pressure; OI, operator index.

Table 2 Data showing postural changes in arterial stiffness parameters in hypertensive subjects on ACE inhibitors/ARBs and other antihypertensive medications

ACE inhibitors/ARBs				Other antihypertensive drugs		
Number	12			9		
Age in years (range)	53.17 (23–89)			39.56 (20–80)		
BMI (range)	29.20 (18.34–40.35)			30.03 (18.87–42.33)		
	Supine	Sitting	<i>p</i> -Value	Supine	Sitting	<i>p</i> -Value
Mean CASP mm Hg (range)	135.42 (100–169)	133.42 (101–160)	0.583	126.89 (102–180)	130.44 (100–180)	0.407
Mean APP mm Hg (range)	57.42 (28–89)	53.92 (27–77)	0.123	46.78 (32–65)	46.67 (28–71)	0.973
Mean AAP mm Hg (range)	12.17 (–5 to +29)	14.33 (–2 to +38)	0.034	11.56 (5–21)	10.33 (0–27)	0.477
Mean AI mm Hg (range)	16.92 (–14 to +32)	20.58 (–3 to +45)	0.038	21.44 (9–40)	17.22 (–5 to +41)	0.184
Mean OI (range)	94.67 (85–100)	94.08 (82–100)	0.774	93.67 (87–100)	95.89 (89–100)	0.303

Abbreviations: AAP, aortic augmentation pressure; ACE, angiotensin-converting enzyme; APP, aortic pulse pressure; AI, augmentation index; ARBs, angiotensin receptor blockers; BMI, body mass index; CASP, central aortic systolic pressure; OI, operator index.

Discussion

Literature review showed that there are very few studies that mention variation of parameters of arterial stiffness with posture in patients with hypertension on antihypertensive medications. Some similar studies are highlighted that showed variation with body position and changes in parameters of arterial stiffness.

Hasegawa and Rodbard in 1979 had shown the importance of body position on aortic hemodynamic and changes in pressure in brachial and posterior malleoli arteries related to posture.¹ Vrachatis et al recently found that there was increase in AI and aortic pulse pressure in aorta in supine position compare with the sitting position, which is consistent with our findings in normotensive subjects but not in hypertensive subjects on medications.² Jaccoud et al showed body position has a major impact on the pattern of central aortic pressure augmentation by reflected waves in healthy young women examined either during third-trimester pregnancy or in the no-pregnant state. They studied applanation tonometry in sitting and supine positions in 24 young women (18–30 years) in the third trimester of normal pregnancy and in 20 healthy nonpregnant women of the same age group. Our group compares variation of parameters of arterial stiffness with posture in hypertensive subjects and normotensive subjects and the effect of antihypertensive.³ Wilkinson et al showed that with decreasing heart rate, and consequently increasing ejection duration, the reflected pressure waves have more opportunity to reach the ascending aorta in systole, leading to a higher AI if all other factors remain constant.⁴ Again, in our study, the AI was corrected for a heart rate of 75 beats per minute for calculation of AI. It is well known that parameters of arterial stiffness are related to cardiovascular outcomes^{5–15} (► **Table 3**). In the current study, we demonstrated postural variations of parameters of arterial stiffness in patients with hypertension on antihypertensive medications and

compared this cohort with normotensive cohort. Hypertensive subjects on antihypertensive medications had a decrease in AAP and AI in supine position but not significantly, but subgroups of patients on ACE inhibitors and ARBs had a significantly lower AAP and AI in supine position when compared with sitting position (*p* < 0.05), whereas normotensives had significantly higher AAP and AI in supine position than sitting position (*p* < 0.05). The significance of this blunting effect by antihypertensive medications in supine position needs to be studied further, especially ACE inhibitors.

Differential effects of antihypertensive medications on AI and central aortic systolic pressure (CASP) are well known.¹⁶ Previous studies have proved that ACE inhibitors could effectively reduce CASP and AI, whereas other antihypertensive medications showed various effects on arterial stiffness markers: calcium channel blockers were as effective a therapy as ACE inhibitors in reducing arterial stiffness markers; however, diuretics had minimal effect on reflection wave and central BP, which might be even increased by some of the β -blockers.¹⁶ However, the effects of different antihypertensive medications on postural variations of arterial stiffness have not been studied yet. Our study further demonstrated that ACE inhibitor might reduce more significant AI and AAP from sitting to supine position in hypertensive patients, which were not displayed in the counterparts on calcium channel blockers, β -blockers, and diuretics even though all the drugs reduce the supine AAP and AI but not significantly.

The limitations of the study include the following.

- Older patients were not studied although such variations in AAP and AI with the medications may be relevant in the elderly hypertensive population.
- There was no placebo used in the normotensive control group.

Table 3 Relationship between parameters of arterial stiffness and cardiovascular outcomes

Study and number	Mean age	Population	Parameters assessed	Posture	Follow-up (mean, y)	Hazard ratio for cardiovascular outcomes
Verwoert et al ⁵ 2849	71.9 ± 6.9	Elderly population	PWV	Supine	7.9	1.94 (CI, 1.32–2.85)
Sutton-Tyrrell et al ⁶ 2488	73.7 ± 2.9	Random population (age 70–79 y)	PWV	Not documented	4.6	1.6 (CI, 1.2–2.2)
Chirinos et al ⁷ 297	63.8 ± 10.3	Males going for coronary angiography	AI	Invasively during angiography (supine)	3.5	1.2 (CI, 1.08–1.34)
Weber et al ⁸ 465	CAD 63.8 ± 10.3 No CAD 53.7 ± 11.7	Symptomatic males undergoing coronary angiography	AI AP	Sitting	–	6.91 (CI, 1.41–33.70)
Laurent et al ⁹ 1715	51 ± 13	Essential hypertensive patients	PWV	Not documented	7.9	1.71 (CI, 1.48–1.96)
Boutouyrie et al ¹⁰ 1045	51	Hypertensive patients	PWV	Not documented	5.7	(i) 1.42 (CI, 1.10–1.82) (ii) 1.41 (CI, 1.17–1.70)
Safar et al ¹¹ 180	51.5 ± 16.3	End-stage renal disease patients	(1) Central pressure (2) PWV	Not documented	4.3 ± 3	(i) 1.4 (CI, 1.1–1.8) (ii) 1.3 (CI, 1.0–1.7)
Meaume et al ¹² 141	87.1 ± 6.6	>70 y of age	PWV	Supine	2.5	1.19 (CI, 1.03–1.37)
Laurent et al ¹³ 1980	50 ± 13	Essential hypertensive patients	PWV	Not documented	9.3 ± 4.4	(i) 2.14 (CI, 1.71–2.67) (ii) 2.35 (CI, 1.76–3.14)
Roman et al ¹⁴ 3520	58 ± 14	American Indians	Central pressure	Not documented	7	1.15 (CI, 1.07–1.24)
Mitchell et al ¹⁵ 2232	63 ± 12	Framingham study	PWV	Supine	7.8	1.48 (CI, 1.61–1.91)

Abbreviations: AI, augmentation index; AP, augmentation pressure; CI, confidence interval; PWV, pulse wave velocity.

The strengths of this study include the following.

- Novel data on variation of parameters of arterial stiffness with posture in hypertensive on antihypertensive medications and a controlled arm of normotensive. This is the first Asian data to the best of our knowledge.
- Tonometry done using SphygmoCor by specialized dedicated nursing staff.
- The study had high median operator index (>90%), which makes our findings very reliable.

From here on, further studies are needed to explore the variation of AI and AAP with posture in different groups of patients on antihypertensive medications especially elderly and end-stage renal failure patients.

Conclusion

In hypertensive subjects, on antihypertensive medications, there was reduction in AAP and AI in supine position but not significantly. ACE inhibitors and ARBs reduced supine AAP and AI significantly. However, normotensive subjects had significantly high supine AAP and AI compared with those in sitting posture. The significance of decrease in AAP and AI in supine position on antihypertensive medications needs to be studied further.

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