Original Research Article

Effect of Hypertension on Vascular Age

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Abstract

Background: Cardiovascular disease which is an outcome measure have several conventional risk factors which include older age, hypertension, diabetes mellitus, alcohol intake, smoking, decreased physical activity, abdominal obesity, high risk diet and psychosocial stress. Stiffening of large arteries known as arterial stiffness (arteriosclerosis) has been shown to be an important risk marker for future cardiovascular events and mortality beyond well-known cardiovascular risk factors.
Aim of study: To determine the effect of Hypertension on arterial stiffness and so the cardiovascular disease. Therefore in this study, we attempted to find the effect of hypertension on vascular stiffness.
Material and methods: A cross sectional study was conducted at Department of Medicine, Dhiraj Hospital affiliated with SBKS MI & RC Sumandeep Vidyapeeth University to measure and analyse the vascular age in hypertensive patients. Total of 90 hypertensive patients were enrolled for the study after taking informed written consent. Vascular age is calculated in all patients using MOBILO-O-GRAPH, after taking into consideration the various vascular parameters.
Results: Vascular aging become faster in older patients (>60 years) than in younger patients (p=0.011). Also Male hypertensives had worse vessels compared to their female counterpart (p=0.001). Also the presence of dyslipidaemia had highly significant effect on vascular age of hypertensive patients (p<0.001). We had also seen that greater the duration of hypertension, more the effect on arterial stiffness.
Conclusion: Though prediction of exact cardiovascular risk is not possible by measuring vascular age of the hypertensive patients but such information is very useful for mass sensitization and education.

Key words

Vascular age, Arterial stiffness, Hypertension, Risk factors.

Introduction

The vascular age of a patient with Cardio vascular risk factors is defined as the age that an individual of the same sex as our patient would have if he or she were to have the same absolute risk but controlled risk factors [1]. It simply means, how old are your arteries?, regardless of how old are you which suggests the biological age.

Arterial aging starts early in life and is a process that span from normal aging to pathological aging and the profound changes related to atherosclerosis. This aging process involves all three layers of the arterial wall [2]. Furthermore, this aging process involve not only the large elastic arteries (with their elastic content of the media), but also other parts of the entire vascular system, for example, remodelling of small arteries due to an increase in blood pressure [3]. There is also a negative impact on the microvasculature of stiff large arteries when pulse wave energy is transmitted to the microcirculation, causing damage [4].

Arterial aging was first named and systematically studied in Italy by Taddei, et al. [5] and in the united states by Lakatta, et al. in the BISLA study (Baltimore Longitudinal study of Aging) [6]. During the same period, and having already begun in the 1980s, researchers in Maastricht (Struijker-Bourdier, Stehouwer, et al.) [7], Ghent (Van Bortel, Rietzchel, Segers, et al.) [8], and Paris (Safar, London, Laurent, Benetos, Boutouyrie, Bla-cher, et al.) [9-11] contributed important findings to describe arterial stiffness and changes in central wave reflections shaping the hemodynamics of aging, as well as changes in microcirculation. In recent years, Dzau, Safar, and O'Rourke coined the term "the cardiovascular aging continuum" to describe the long road from risk factors to cardiovascular events and post-event complication [12].

In subject with hypertension, the principal structural modification of vessel wall is hypertrophy of the medial layer [22, 23]. In younger hypertensive subjects, the alterations of the mechanical properties results mainly from the elevated BP itself, as reduced carotid compliance and distensibility disappear in isobaric conditions [24]. However, in some other territories such as the femoral artery or even the thoracic aorta, intrinsic changes in stiffness (i.e., increased stiffness in isobaric condition) may be observed [25]. In subjects with hypertension, active mechanisms within the arterial wall are certainly involved because, at the site of peripheral muscular arteries such as the radial artery, diameter is unchanged despite the elevated BP, whereas in central arteries, the diameter is increased in proportion with the level of BP [23].

Among the elderly hypertensive, medial hypertrophy is associated with a considerable development of the extracellular matrix of the media and even of the adventitia. This histomorphometric pattern is associated with reduced compliance and distensibility independent of BP level [26]. Again, these changes are observed at the site of central, but not peripheral arteries. The level of nitric oxide (NO) production or release contribute to arterial aging and hypertensive. The renin-angiotensin-aldosterone system (RAAS) activity may also play a key role in the regulation of arterial stiffness in hypertensive. In hypertensive but not in normotensives, the angiotensin II type 1 receptor [27] and aldosterone synthase gene variants [28] are significant determinants of arterial stiffness.

Tools to assess vascular age

A) Pulse wave velocity

Each heartbeat sends a wave of blood through the body's network of arteries. The stiffer the arteries, the faster this wave travels. Measuring the speed of the pulse wave provides information about how stiff or flexible the arteries are. The speed of the wave can be converted into vascular age.

B) Carotid intima-media thickness

The innermost layer of an artery's wall is called the intima and it provides a smooth surface for blood to flow through. The media is the middle

layer and its muscle and elastic fibres let the vessel expand and contract with each heart beat. The thicker the intima and the media, the more likely the artery is choked with cholesterol-filled atherosclerotic plaque. It can be measured by ultrasound. This measurement can be used to estimate vascular age.

C) Framingham score

It is used to determine 10 years cardiovascular risk. The sex-specific risk factors considered were age, HDL-C, total cholesterol, SBP, DM and smoking status. Each variables received a weighted score; the sum of the score for each variable was then translated to the risk for a CV event in 10 years and the VA.

Materials and methods

Cross sectional study was conducted at Department of Medicine, Dhiraj Hospital affiliated with SBKS MI & RC Sumandeep Vidyapeeth University to measure and analyse the vascular age in hypertensive patients. Total of 90 hypertensive patients were enrolled for the study after taking informed written content. Detailed demographic profile, clinical features, detailed history related to hypertension including duration of diagnosis, drug treatment compliance, complications was also recorded. Details of other cardiovascular risk factors were also noted in CRF. Thorough clinical examination including anthropometric measurements was performed. Necessary investigations were done. Framingham risk score was calculated for all patients.

The following vascular parameters were measured to calculate vascular age in all patients using MOBIL-O-GRAPH, the parameters were:

Brachial blood pressure (systolic plus diastolic), Central blood pressure (systolic plus diastolic), Stroke volume, Cardiac output, Total vascular resistance, Cardiac index, Augmentation pressure, Reflection magnitude, Pulse wave velocity. Vascular age was calculated by using MOBIL-O-GRAPH by measuring above parameters. Collected data was analysed and interpreted by use of appropriate statistical methods.

Framingham risk score was also calculated by taking in consideration various parameters like, Total cholesterol, HDL cholesterol, Smoking, Sex, Systolic blood pressure, Diabetes, Age.

Results

Total of 90 hypertensive patients were enrolled in the study. The mean biological age of the study group of 90 hypertensive patients was 48 +/- 13.17 years. The vascular age measured by MOBILO-O-GRAPH was further divided into three subgroups.

- Older than biological age
- Same as biological age
- Less than biological age

Out of total 90 hypertensive patients, vascular age of 34(37.77%) patients was more than their biological age, 50(55.55%) had similar vascular age, while 6(6.66%) had better vascular age than their current biological age. In further age sub group analysis, we noted that, as biological age increases, vascular aging become faster and more number of older patients has worse arteries. 65.22% of elderly patients were having more vascular age than their biological age.

Almost two-third 63(70%) of study group was consist of male hypertensive patients. M:F ratio being 2.5:1. **Table - 1** shows the difference in vascular age in both genders and as per age.

Male hypertensives were having worse vessels compared to their female counterparts. Little less than half of males were having more vascular age, while only 22.22% females were having vascular age more than their biological age. And this gender differences was statistically significant (p value=0.001).

In further sub group analysis, we have compared effect of presence of modifiable cardio-metabolic risk factors on vascular age of participants. Presence of dyslipidaemia had highly significant

effect on vascular age of hypertensive patients (p value:<0.001). More than three fourth (79.7%) study participants having dyslipidaemia along with hypertension were having older vessels than their biological age. The other modifiable cardio-metabolic risk factors showing effect on vessels was obesity. Out of 56 hypertensive patients having BMI >24.9, 44.64% had bad vessels, difference vascular age between obese and non-obese being statistically significant (p value: 0.006). Surprisingly, we could not be able to find statistically significant effect of smoking and diabetes on vascular age in our study (**Table - 2**).

Table – 1: Comparison of vascular age with biological age in non-modifiable risk factors.

Age Group (Years)	Total	More Vascular Age	%	Same Vascular Age	%	Younger Vascular Age	%	Chi Square Value	p value
≤ 40	31	8	25.81	18	58.06	5	16.13	12.99	**0.011**
40 to 60	36	11	30.56	24	66.67	1	2.78		
≥60	23	15	65.22	8	34.78	0	0.00		

Gender	Total	More Vascular Age	%	Same Vascular Age	%	Younger Vascular Age	%	Chi Square Value	p value
Male	63	28	44.44	32	50.79	3	4.76	23.52	0.001
Female	27	6	22.22	18	66.67	3	11.11	14.00	0.001

Table - 2: Comparison of Vascular vs Biological age in patients with modifiable cardio-vascular risk factors.

Risk Factor	Presence	Total	More Vascular Age	%	Same Vascular Age	%	Younger Vascular Age	%	Chi Square Value	p value
Smoking	Yes	40	18	45.00	19	47.50	3	7.50	1.91	0.385
	No	50	16	32.00	31	62.00	3	6.00		
Diabetes	Yes	11	6	54.55	5	45.45	0	0.00	1.04	0.593
	No	79	28	35.44	45	56.96	6	7.59		
Dyslipidemia	Yes	43	34	79.07	9	20.93	0	0.00	55.09	0.001
	No	47	0	0.00	41	87.23	6	12.77		
Obesity	Yes	56	25	44.64	29	51.79	2	3.57	10.22	0.006
	No	34	9	26.47	21	61.76	4	11.76		

Table - 3: Effect of duration of hypertension on vascular age.

Duration of HTN	Total	More Vascular Age	%	Same Vascular Age	%	Younger Vascular Age	%	Chi Square Value	p value
Up to 5 Years	15	4	26.67%	9	60.00%	2	13.33%	16.07	0.002
5 to 10 Years	54	29	53.70%	21	38.89%	4	7.41%		
> 10 Years	21	17	80.95%	4	19.05%	0	0.00%		

Effect of duration of hypertension on vascular age was analysed in table no:3. As the duration of hypertension increases, the number of patients having older vessels than their biological age, increases. 80% of patients diagnosed having hypertension since more than 10 years were older by their biological vessel age. The worrisome results was almost one-fourth (26.64%) of participants having diagnosed hypertension since less than 5 years were also having abnormal vascular parameter and so vascular age (**Table – 3**).

Table – 4: Age vs Framingham score and MOBILO-O-Graph.

Age group	Number of pt	EVA by MOBIL-O-GRAPH	EVA by Framingham score
>40	32	7	9
40-60	32	14	13
>60	26	16	16

Comparison to Framingham risk score

In our study, mean biological age of the study group was 48+/-13.17 years. Mean vascular age measured using Framingham score for the study group was 61+/-16.05 years. We tried compare the Early vascular age (EVA) measured by MOBIL-O-GRAPH with gold standard Framingham score in different biological age groups. Almost similar percentage of hypertensive patients in all three groups were having early vascular aging by MOBILO-O-GRAPH.

Framingham score in different biological age groups. Almost similar percentage of hypertensive patients in all three groups were having early vascular aging by MOBILO-O-GRAPH (**Table – 4**).

Discussion

Stiffening of large arteries known as arterial stiffness (arteriosclerosis) has been shown to be an important risk marker for future cardiovascular events and mortality beyond well-known cardiovascular risk factors, based on two updated meta-analysis [13, 14]. The prediction of total mortality hints that arterial stiffness could be a marker of aging and frailty in general, including increased risk of many causes of mortality. Measurement of arterial stiffness is preferably performed by use of c-f PWV [15] with a risk threshold of 10 m/s according to an updated consensus document from 2012 published in the Journal of Hypertension [16]. This can be achieved by both direct and indirect methods, which are reasonably well correlated with each other in most cases, even if the direct measurement (c-f PWV) is preferred. Arterial stiffness is known to be strongly associated with age and hypertension [17], findings also confirmed in a longitudinal study from United States [18]. The arterial aging is tightly inter-correlated with blood pressure and causes the increase in pulse pressure seen in aged individuals. In some individuals, the arterial stiffening seen with increasing age is more pronounced and occur earlier in life, a marker of early vascular age (EVA). In fact, a number of non-hemodynamic components are thought to affect arterial aging, such as hyperglycaemia and dyslipidaemia. Several cross-sectional studies have shown an association between arterial stiffness and diabetes as well as with markers of impaired glucose metabolism [19, 20]. This is also evident in subjects with end-stage renal disease (ESRD) with an increased central arterial stiffness. Arteriosclerosis, stiffness of large arteries is most evident sequel of hypertension as discussed above. More than one third of hypertensive patients had more vascular age than their biological age suggesting having bad arterial condition.

Non modifiable risk factors for coronary artery disease like increasing age and male gender also has detrimental effect on vessel age, as suggested by the findings of our studies that frequency of increased vascular age is more in elderly& male hypertensive. Study done by O. Ostroumova, et al. showed that Vascular age was higher in naive middle-age hypertensive patients compared to

control. Both in hypertensive patients and in control group the highest values of vascular age were obtained using a Framingham Heart study risk tables, which takes into account the largest amount of clinical and laboratory data [30]. Study done by Carlos Bermudez et al shows that patients with metabolic syndrome and hypertension have poorer endothelial function than patients with metabolic syndrome and normotension. This explain a worse cardiovascular outcome in patients with metabolic syndrome and hypertension and usefulness of measures to improve endothelial function [29].

Our study also had demonstrated detrimental effect of obesity and dyslipidaemia, major components of the metabolic syndrome and coronary artery disease risk factors on vascular age in hypertensive patients. Statistically significant number of hypertensive patients having these risk factors had more vascular age compared to their biological age.

In EXERDIET-HTA study by IIargiGorostegi-Anduaga, et al. shows that
a) Cardio-vascular risk is significantly higher in men than in women despite them having the same CVR values and this is not affected by age.
b) Predicted VA is significantly higher than chronological age in obese or overweight people with primary hypertension with no sex related differences [31].

Framingham scoring system is well established and widely used non-invasive risk stratification system for cardiovascular disease which is based on multiple parameters. The early vascular age measured by MOBILO-O-GRAPH showing almost similar prediction as Framingham score. It is also non-invasive, less time consuming, portable method to predict early vascular aging (EVA) so can be used as first screening tool for hypertensive patients.

Limitation

MOBILO-O-GRAPH only predict about presence of EVA but cannot exactly grade the severity of vascular damage or else directly predict the cardiovascular risk.

Conclusion

Though prediction of exact cardiovascular risk is not possible by measuring vascular age of the hypertensive patients but such information is very useful for mass sensitization and education. Vascular age measurement by instruments like MOBILO-O-GRAPH can be utilised as screening and educating patients regarding Cardiovascular risk factors and also to motivate them to start with life style modification and regular treatment.

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