

Significant measurement of mean carotid intima-media thickness in sustained essential hypertension

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ABSTRACT

الأهداف: تقييم التقدم المعتد إحصائياً للتصلب العصيدي والمقدر بوساطة مفرسة تشخّن باطن ووسط الشرايين السباتية الشائع والباطني في كلا الجانبين في المرضى المصابين بارتفاع ضغط الدم الشرياني عديم الأعراض، والمستديم المصاحب منها أو غير المصاحب للسكتة الإقفارية للدماغ.

الطريقة: تم إجراء الفحص على المرضى المراجعين لوحدة دوبلر الوعائية - مستشفى بغداد التعليمي - بغداد - العراق، خلال عام 2005م. وقد استطاق 119 مريضاً (61 أنثى و 58 ذكر) ممن تراوح أعمارهم ما بين 40-70 عاماً، من إكمال متطلبات الدراسة. تم تقسيم المرضى إلى مجاميع: المجموعة (I) أشخاص سليمين مع وجود ضغط الدم، المجموعة (II) فرط ضغط الدم عديم الأعراض، المجموعة الثالثة (III) فرط ضغط الدم المستديم من دون السكتة الإقفارية للدماغ، والمجموعة الرابعة (IV) فرط ضغط الدم المستديم المصاحب للسكتة الإقفارية للدماغ. تم إجراء قياسات انثروبومترية، فحوصات الشحوم والبروتينات الشحمية، وتفريس الشرايين السباتية الشائعة والباطنية.

النتائج: كان المعدل الحسابي لقطر وتشخّن باطن ووسط الشرايين السباتية الشائع والباطني في المجموعة (IV) أكبر من المجموعة (III)، والمجموعة (III) أكبر من المجموعة (II)، والمجموعة (II) أكبر من المجموعة (I). وقد صاحب هذه التغيرات المعتدة إحصائياً فرط في مستويات الكوليسترول والبروتين الشحمي منخفض الكثافة وتدني مستوى البروتين الشحمي عالي الكثافة باعتداد إحصائي. بلغت نسبة أرجحية تشخّن باطن ووسط الشرايين السباتية الشائع والباطني (Imm) في المجموعة (1.37).

خاتمة: تدعم هذه النتائج أهمية تفريس فرط ضغط الدم عديم الأعراض والمستديم للشرايين السباتية بوساطة دوبلر.

Objectives: To assess the significant association of atherosclerosis quantified by screening intima media thickness of bilateral common and internal carotid arteries in patients with asymptomatic and persistent hypertension with and without ischemic stroke.

Methods: Subjects in this investigation were recruited from the vascular Doppler unit at Baghdad Teaching

Hospital in Baghdad, Iraq during 2005. A total number of 119 (61 females and 58 males), with ages ranging from 40-70 years, were able to comply with the observational comparative study protocol. They are grouped into healthy normotensive (I), asymptomatic (preclinical) hypertension (II), sustained hypertension without (III) and with ischemic stroke (IV). Anthropometric measurements, lipids and lipoproteins biochemical tests, and B-mode image of high-resolution ultrasound scanning of common and internal carotid arteries were carried out.

Results: The mean diameter as well as intima media thickness of common and internal carotid arteries was significantly higher in group IV than group III, II, and group I. These changes were associated with significant increased fasting serum cholesterol, low-density lipoprotein, and decreased high-density lipoprotein. Intima media thickness above one mm was significantly observed in hypertension with ischemic stroke (odd ratio 1.37).

Conclusion: The results support the importance of screening asymptomatic as well as sustained treated hypertension by carotid ultrasound Doppler.

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Intima media thickness (IMT) is a validated and accepted marker for generalized atherosclerosis burden and cardiovascular risk.¹ Increasing total maximum IMT has been related to increasing age, male gender, recurrent ischemic stroke, coronary atherosclerosis,² peripheral atherosclerosis,³ smoking,⁴ hypertension, and diabetes mellitus.⁵ In an asymptomatic person, carotid IMT predicts future myocardial infarction and stroke.^{6,7} There is an association between increment baseline

right common carotid artery IMT and progression of atherosclerosis.⁸ Humans who display exaggerated blood pressure reactivity to behavioral stressors are more likely to have increased carotid IMT than those who display attenuated blood pressure reactivity.⁹ High values of mean and maximal IMT were present in most common and internal carotid segments of borderline hypertensives compared with controls.¹⁰ In masked hypertension (namely, low office, high ambulatory blood pressure), the maximal IMT was significantly higher than in controlled-hypertension.¹¹ Moreover, the maximal IMT among patients with persistent hypertension were significantly greater than normotensive subjects.¹² Also, a high prevalence of IMT more than 1.3 mm was found in asymptomatic hypertensive subjects attending a vascular unit for routine ultrasound screening of the carotid arteries.¹³ The study aimed to assess the significant progression of atherosclerosis quantified by screening intima media thickness of bilateral common and internal carotid arteries in patients with persistent hypertension attending a vascular Doppler unit at Baghdad Hospital in Baghdad, Iraq.

Methods. Subjects in this investigation were recruited from the vascular Doppler unit at Baghdad Teaching Hospital in Baghdad, Iraq during 2005. An independent scientific committee revised and approved the study protocol and the information was provided to the patients. Subject's written consent was obtained prior to the enrollment in the study. The criteria of inclusion were patients of both genders, no age limitation, presenting with persistent-treated hypertension with/or without history of once not recurrent ischemic stroke (diagnosed by MRI). Also, untreated hypertensives (diagnosed at the time of the study) and healthy normotensive subjects as negative control were included in the study. Patients were excluded if they have secondary hypertension, diabetes mellitus, familial hyperlipidemia, previous or recent history of angina pectoris, myocardial infarction, angioplasty, congestive heart failure, valvular heart disease, atrial fibrillation, coronary bypass, carotid or peripheral vascular surgery, renal insufficiency, or they had received glucocorticosteroids or psychotropic drugs. Patients receiving antihypertensive, lipid lowering agents, or antiplatelets were not excluded from the study. A total number of 119 patients (61 females and 58 males), with ages ranging from 40-70 years, could comply with the study protocol and who had provided written consent. The subjects were divided into 4 groups: Group I (n=17): healthy normotensive subjects with blood pressure (BP) <140/90 mm Hg. Group II (n=24): asymptomatic subjects with BP ≥140/90 mm Hg. This group represented newly diagnosed untreated essential hypertension. Group III (n=52): patients with

sustained-treated essential hypertension (BP ≥ 140/90 mm Hg) without evidence of ischemic stroke. Group IV (n=26): patients with sustained-treated essential hypertension (BP ≥140/90 mm Hg) with clinical and radiological image evidence of ischemic stroke. Each subject admitted to the study was clinically examined. Three blood pressure measurements were taken in right arm, with the subject in the seated position, by appropriate size cuff. The second and third blood pressure readings were averaged. Subjects were considered to have hypertension if they had elevated systolic blood pressure ≥ 140 mm Hg and/or elevated diastolic blood pressure ≥ 90 mm Hg. The anthropometric measurements including body weight (kg) and height (m) were carried out. The body mass index was calculated as weight/height². Biochemical analysis included lipid profile (fasting lipids and lipoproteins) measurements. The ratio of triglycerides (TG) to high density lipoprotein (HDL) was calculated to determine atherogenic index as well as the particle size of atherogenic low density lipoprotein (LDL).^{14,15} Ultrasound screenings were performed with B-mode image of high resolution ultrasound scanner equipped with a 7 MHz linear array transducer. Anterior, antero-lateral, and postero-lateral projections were used to image the left and right common (CCA) and internal carotid arteries (ICA). The arterial diameters as well as the IMT measurements were carried out 3 times for each artery in each side. The average of 3 measurements of each diameter or IMT of carotid artery was taken.

Statistical analysis was carried out using Microsoft Excel 2003. The results are presented as absolute number, percent, median, range, odds ratio, and mean ± SD. The data are analyzed using unpaired two-tailed Student 't' test and difference between percentage tests, taking $p \leq 0.05$ as the lowest limit of significance.

Results. Table 1 shows the characteristics of the study. The median age of healthy normotensive subjects was less than corresponding hypertensives in groups II, III, IV. The levels of systolic and diastolic blood pressures in groups II, III, and IV were approximated to each other and they were significantly higher than group I ($p=0.0003$). The mean value of hypertension duration was not significantly ($p>0.05$) higher in group IV compared with group III (12.84 ± 6.05 versus 11.4 ± 4.68 years). The anthropometric measurements revealed that groups III and IV had higher values than groups I and II. Variable numbers of active smokers were found in all studied groups. Lipids (serum cholesterol) and lipoproteins (serum LDL) measurements were significantly increased with transition from group II (newly hypertensives) towards group IV (hypertensives with ischemic stroke) (Table 2). Significant decrease of

Table 1 - Characteristics of the study.

Characteristics	Group I (n=17)	Group II (n=24)	Group III (n=52)	Group IV (n=26)
<i>Gender</i>				
Male	8	11	28	11
Female	9	13	24	15
<i>Age (years)</i>				
Male	46 (42-50)	55 (47-62)	55 (44-78)	56 (45-75)
Female	50 (48-61)	59 (44-64)	58 (49-75)	55 (42-66)
<i>Duration of high BP (years)</i>				
Male	-	-	9.0 (5-23)	13.0 (5-30)
Female	-	-	11.5 (6-20)	12.0 (5-20)
Total	-	-	9.5 (5-23)	12.5 (5-30)
<i>SBP (mm Hg)</i>				
Male	130 (120-135)	155 (140-165)	150 (130-170)	145 (130-170)
Female	130 (125-135)	160 (140-170)	155 (135-180)	150 (135-175)
Total	130 (120-135)	160 (140-170)	155 (130-180)	150 (130-175)
<i>DBP (mm Hg)</i>				
Male	80 (60-85)	95 (90-100)	95 (70-110)	95 (70-110)
Female	80 (60-85)	95 (90-100)	95 (70-105)	95 (70-110)
Total	80 (60-85)	95 (90-100)	95 (70-110)	95 (70-110)
<i>BMI (kg/m²)</i>				
Male	27.8 (24.2-32.2)	26.9 (22.8-35.0)	31.3 (23.3-38.8)	29.4 (25.0-33.7)
Female	30.4 (25.9-35.4)	29.0 (22.2-33.3)	31.3 (22.0-36.1)	29.5 (25.3-33.2)
Total	28.0 (24.2-35.4)	27.6 (22.2-35.0)	31.3 (22.0-38.8)	29.5 (25.0-33.7)
<i>Active smoking (No.)</i>				
Male	4	6	14	5
Female	2	3	10	5
Total	6	9	24	10

The results are expressed as median (range), BP - blood pressure, SBP - systolic blood pressure, DBP - diastolic blood pressure, BMI - body mass index

Table 2 - Fasting serum lipids and lipoprotein levels profile.

Lipid/lipoprotein level	Group I (n=17)	Group II (n=24)	Group III (n=52)	P-value	Group IV (n=26)	P-value
<i>Cholesterol (mg%)</i>						
Male	211.8±36.9	186.1±35.7	230.0±40.4		242.5±33.0	
Female	198.4±32.3	207.0±43.8	235.4±48.6	(p=0.019)	239.7±36.8	(p=0.009)
Total	204.7±34.2	197.4±40.8	232.5±44.0	(p=0.010)	240.8±34.6	(p=0.002)
<i>Triglycerides (mg%)</i>						
Male	176.9±66.4	131.4±28.6	164.8±56.8		155.4±58.5	
Female	147.3±31.9	134.6±47.8	162.3±42.6		128.9±31.6	
Total	161.2±51.7	133.1±39.3	163.6±50.3		140.1±45.9	
<i>LDL (mg%)</i>						
Male	129.8±25.8	121.5±29.5	158.9±41.3	(p=0.025)	183.1±33.0	(p=0.001)
Female	116.2±38.9	135.8±43.9	164.5±44.8	(p=0.007)	180.0±38.5	(p=0.001)
Total	122.6±33.1	129.3±37.9	161.5±42.6	(p=0.0004)	181.3±35.6	(p=3x10 ⁻⁶)
<i>HDL (mg%)</i>						
Male	42.8±8.7	39.0±6.6	38.3±9.6		34.4±9.4	
Female	48.1±10.1	45.5±10.4	37.7±9.0	(p=0.017)	32.9±8.5	(p=0.001)
Total	45.6±9.6	42.5±9.3	38.0±9.2	(p=0.008)	33.5±8.7	(p=0.0002)
<i>TG/HDL ratio</i>						
Male	4.104±1.125	3.432±0.841	4.680±2.510		4.680±1.670	
Female	3.220±1.062	3.177±1.661	4.615±1.945	(p=0.015)	4.120±1.352	
Total	3.639±1.15	3.294±1.328	4.650±2.245	(p=0.018)	4.357±1.490	

The results are expressed as mean ± SD, probability values are compared with Group I
LDL - low density lipoprotein, HDL - high density lipoprotein, TG - triglycerides

Table 3 - Mean diameter (mm) of common and internal carotid arteries measurement.

Arteries	Group I (n=17)	Group II (n=24)	Group III (n=52)	P-value	Group IV (n=26)	P-value
Right CCA	5.523±0.613	5.540±0.359	7.401±0.856	($p=5 \times 10^{-12}$)	7.692±0.794	($p=1.7 \times 10^{-12}$)
Left CCA	5.782±0.658	5.733±0.554	6.926±0.666	($p=1.1 \times 10^{-6}$)	7.300±0.705	($p=1.9 \times 10^{-8}$)
Right ICA	3.811±0.441	3.895±0.566	4.478±0.630	($p=2.2 \times 10^{-5}$)	5.080±1.028	($p=2.6 \times 10^{-6}$)
Left ICA	3.888±0.358	3.820±0.579	4.417±0.763	($p=0.0003$)	4.673±0.771	($p=6.3 \times 10^{-3}$)

The results are expressed as mean ± SD, probability values are compared with Group I
CCA - common carotid artery, ICA - internal carotid artery

Table 4 - Mean intima-media thickness (mm) of common and internal carotid arteries measurement.

Arteries	Group I (n=17)	Group II (n=24)	P-value	Group III (n=52)	P-value	Group IV (n=26)	P-value
Right CCA	0.541±0.050	0.612±0.115	($p=0.01$)	0.789±0.147	($p=1.5 \times 10^{-15}$)	0.811±0.190	($p=1.2 \times 10^{-7}$)
Left CCA	0.602±0.083	0.670±0.112	($p=0.03$)	0.802±0.142	($p=7 \times 10^{-9}$)	0.861±0.168	($p=5.7 \times 10^{-8}$)
Right ICA	0.364±0.049	0.412±0.115	($p=0.05$)	0.515±0.152	($p=4 \times 10^{-8}$)	0.611±0.167	($p=6.5 \times 10^{-8}$)
Left ICA	0.405±0.074	0.447±0.085		0.523±0.162	($p=0.00015$)	0.603±0.161	($p=3.5 \times 10^{-6}$)

The results are expressed as mean ± SD, probability values are compared with Group I
CCA - common carotid artery, ICA - internal carotid artery

Table 5 - Number (percent) of cases with raised lesion intima media thickness (> 1.0 mm).

Arteries	Group I (n=17)	Group II (n=24)	Group III (n=52)	Group IV (n=26)
Right CCA	0	0	6 (11.5)	4 (15.4)
Left CCA	0	0	1 (1.9)	0
Right ICA	0	0	5 (9.6)	3 (11.5)
Left ICA	0	0	2 (3.8)	0

CCA - common carotid artery, ICA - internal carotid artery

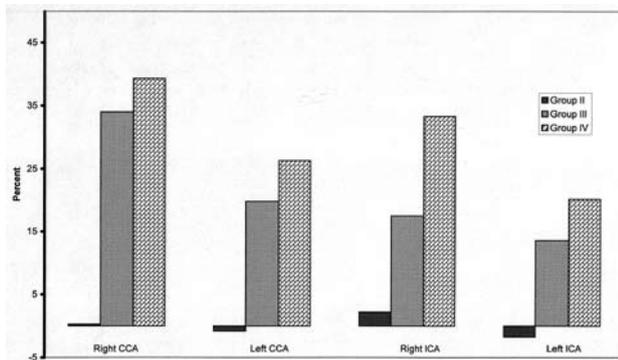


Figure 1 - The percent increment in carotid artery diameter in hypertensive patients in reference to normotensives. CCA - common carotid artery, ICA - internal carotid artery.

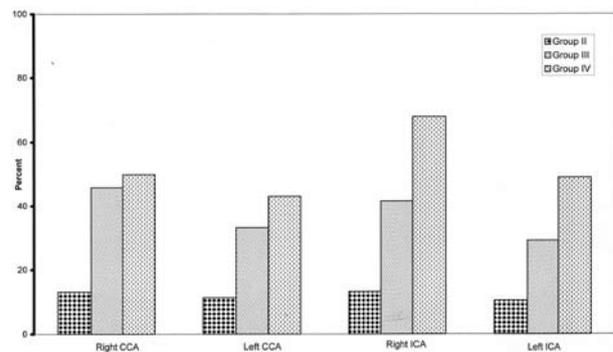


Figure 2 - The percent increment in intima medial thickness in hypertensive patients in reference to normotensives. CCA - common carotid artery, ICA - internal carotid artery.

HDL was also observed in a similar pattern (Table 2). Although triglycerides to HDL ratio was significantly higher in groups III and IV compared with groups I and II, it did not significantly differ between groups III and IV (Table 2). The mean value of bilateral carotid arteries diameter, common, or internal, was significantly higher in groups III and IV compared with groups I and II, it did not significantly differ between groups III and IV (Table 3, Figure 1). Remodeling of carotid blood vessels was well seen in groups II and III and it was negligible in group II compared with normotensives (Figure 1). The mean IMT was significantly increased with transition from group II (newly hypertensives) towards group IV (hypertensives with ischemic stroke) (Table 4, Figure 2). Moreover, hypertensive patients with history of ischemic stroke have a significant high value of mean IMT compared with those without stroke (Table 4). The increment in the right carotid arteries was higher than the corresponding left side in groups II, III and IV (Table 4, Figure 2). The percent of raised lesion IMT (>1.0 mm) was not significantly higher in CCA (bilaterally) in group IV compared with group III (Table 5). The estimated odds ratio was 1.37 in group IV compared with group III.

Discussion. This study shows the sequences of clinical essential hypertension (asymptomatic, sustained without and with ischemic stroke) associated with atherosclerosis, quantified by the mean IMT in carotid arteries. The present study also shows carotid IMT above 1.0 mm was significantly found in hypertensives with stroke (odds ratio 1.37). Asymptomatic (preclinical) hypertensives have significantly increased mean IMT by 10.4-13.2% compared with normotensives. This percent is less than that reported by Hoshide et al¹⁶ who found an 18.8% increment in masked hypertension. Our findings are similar to those reported by Puota et al¹⁷ who found that an increased mean IMT in sustained treated hypertension was significantly higher than grade-1 untreated hypertension and the later was higher than normotensive subjects. Both the age and body mass index were not additively influenced by IMT measurement in hypertension.^{17,18} Lipid and lipoprotein measurements showed interesting findings. The significant increment in fasting serum cholesterol and LDL was associated with a significant increase in mean IMT in each hypertensive group. The increment in lipids and lipoproteins was associated with progressive atherosclerosis.^{17,19} Previous studies showed the association between LDL particle and IMT in familial hyperlipidemia members,²⁰ and even in healthy middle aged healthy subjects.²¹ In this study, we demonstrate the association of LDL atherogenic particles with progressive atherosclerosis in 3 different groups of hypertension. There is evidence

that the low level of HDL as a criterion of metabolic syndrome in diabetics is accompanied with high carotid IMT value.²²

The study does not show any significant differences in IMT measurement between common and internal carotids as well as right and left. A significant increase in carotid diameter reflecting blood vessel remodeling is well observed in sustained hypertensive, but not in asymptomatic hypertensives. A previous study carried out on normotensive, untreated hypertensives, and treated hypertensives showed a positive correlation between progressive atherosclerosis and carotid remodeling, but with a difference in slope for each studied group.²³ In this study, the test of correlation statistical analysis was not carried out because of small sample size. The significant high IMT in hypertension, whether asymptomatic or symptomatic or complicated with stroke, as well as the detection of significant percent of IMT >1 mm give us a hint to recommend medical intervention at the level above that of sustained hypertension without stroke for the purpose to prevent further atherosclerosis. In this study, patients receiving lipid lowering agents as part of their medication were not excluded, therefore, this may have contributed as one of the limitations in assessment of IMT.

We conclude that the results support the importance of screening asymptomatic as well as sustained treated hypertensives by carotid ultrasound Doppler to assess the risk of atherosclerosis burden. Further study is recommended to evaluate the role of antihypertensive agents in remodeling the carotid blood vessels.

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Related topics

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