Echocardiographic assessment of aortic wall elasticity in apparently healthy individuals: the association with age and serum total cholesterol.

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Abstract

Background: The aortic elastic properties are relevant at several sites of cardiovascular. Increased arterial stiffness is an independent risk factor and predictor of cardiovascular mortality and an early predictor of coronary risk useful in screening. Therefore the evaluation of arterial stiffness may be important for clinical diagnosis and intervention in cardiovascular disease.

Aim: The purpose of this study was to show the effect of age and total serum cholesterol on the percent wall thickness change, after adjusting for stroke volume.

Methodology: A cross-sectional study using two-dimensional and Doppler of blood flow of aortic root echocardiography was preformed for a random sample of 60 apparently healthy males with an age ranging between 17 and 75 year. Aortic wall elasticity was assessed by percent wall thickness change.

Results: Using multivariate modelling it was shown that age, serum cholesterol and stroke volume were a statistically significant independent predictors of Aortic wall elasticity (assessed by percent wall thickness change), after adjusting for blood pressure and BMI. Age and serum total cholesterol had an average ROC area of round 0.7 when used to predict high rigidity of Aortic artery. An age of 68 years and above was 95% specific in detecting rigid artic artery with low sensitivity 30%. A serum total cholesterol of 199 mg/dl and above was associated with sensitivity of 50% and specificity of 85% in detecting rigid aortic artery.

Conclusion: Being in the sixth decade of life and having a serum cholesterol of >200 mg/dl will predict a rigid aorta with a reasonably high specificity. Measurements of aortic artery elasticity using Echocardiography is simple and may contribute to cardiovascular risk assessment.

Keywords: Echocardiography, stroke volume, aortic stiffness.

Introduction

The aortic elastic properties are relevant at several sites of cardiovascular function. Acting as an elastic buffering chamber behind the heart (the Wendkessel function), the aorta and some of the proximal large vessels store about 50% of the left ventricular stroke volume during systole. In diastole, the elastic forces of the aortic wall forward this 50% of the volume to the peripheral circulation, thus creating a continuous peripheral blood flow (1).

The stiffness of the aorta and other large arteries increases with age (2) . Beyond

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ageing, a further increase in arterial stiffness is observed in the presence of coronary artery disease (3) . This presumably reflects the wide spread nature of the atherosclerotic process (4,5) , thus conversely , an increase in arterial stiffness could be an early predictor of coronary risk useful in screening. An increase in pulse wave velocity (a consequence of increased large artery stiffness) has been shown to relate to outcome in a hypertensive population (6).

A number of studies have also examined the relation between plasma total or low-density lipoprotein (LDL) cholesterol and large artery stiffness in normotensive, asymptomatic patients. The effects of cholesterol in a hypertensive population are of particular interest because of their high risk for cardiovascular events and thus potential for screening(7-13).

The purpose of this study was to show the effect of age and total serum cholesterol on the percent wall thickness change, after adjusting for stroke volume.

Subjects and Methods

Study design: Cross-sectional study

Study setting: The examination was performed for normal people in outpatient department in Tikrit.

Study period: This study was performed for one year, from 2009-2010.

Study population: Apparently healthy adult males who accompanied ill subjects visiting the outpatient departments and volunteered to have the echocardiogram when were offered free of paying .

Study sample: a systematic random sample of every 3rd subject available in the waiting room of outpatient department. A total of 60 apparently healthy males were included in the sample with an age ranging between 17 and 75.

Examination and measurements:

All subjects underwent two-dimensional and Doppler of blood flow of aortic root. Echocardiography performed by an experienced echocardiographier. All echocardiograms were taken in the left lateral semi-decubitus position since this moves the heart away from the sternum and closure to the chest wall. Thus producing a better cardiac window. The transducer should be placed slightly left to the sternum in the third, forth or fifth intercostals space . Echocardiograms of abnormal aortic valve and aortic root show two parallel signals representing the anterior and the posterior wall move in anterior direction during systole and in posterior during diastole. The aortic cusp echo has a box like systolic

configuration indicating brisk opening and closure of the valve. The cusp produce a central linear echo during diastole . At aging , the aortic stenosis occur and so the signal pattern of valve motion will show thickened valve echoes during systole and diastole and distortion of the normal box-like pattern .The motion pattern through cardiac cycle of both wall of aortic root and aortic valve leaflets and the diameter of aorta is majorly influenced by homodynamic factors such as stroke volume and cardiac pressure.

Calculation of percent wall change:

The thickness of aortic wall measuring during systole and diastole anteriorly and posteriorly from the outer to the inner surface of the wall (in millimeters) ,and the wall thickness change calculated from this formula :

$$\text{Wall thickness} = \frac{\text{systolic diameter} - \text{diastolic diameter}}{\text{diastolic diameter}}$$

Hoeks et al (1990) (14)

The aortic root diameter represent a distance between aortic root anterior inner wall to the posterior inner wall(in millimeters). The cholesterol test was measured in laboratory by 12 hours fasting blood sample for all subjects.

Ethical considerations: An informed consent was obtained from study participants. The anonymous and scientific research nature of the experiment was explained to study subjects.

Statistical analysis:

An expert statistical advice was sought for. Statistical analysis was computer aided using SPSS ver 13. The difference in mean of a quantitative normally distributed variable between 3 groups was assessed by ANOVA. Multiple linear regression model was used to study the net and independent effect of age and total serum cholesterol on percent wall thickness change, after adjusting for stroke volume, BMI and blood pressure. ROC analysis was used to study the validity parameters of age and serum total cholesterol in predicting a stiff aortic artery.

Results

The results were based on the analysis of a random sample of 60 apparently healthy males. The percent wall thickness change was the principal outcome variable in the present study. It was intended to quantify the elasticity of Aortic artery by classifying wall thickness change into tertiles, as follows: highest rigidity-first tertile <= 7%, average elasticity-second tertile (7.1-16.7%) and highest elasticity-third tertile (16.8+).

As shown in table 1, the mean age was significantly higher among subjects with highest rigidity. There was a statistically

significant weak direct linear correlation between age and wall thickness change. the mean serum cholesterol was also significantly higher among subjects with highest rigidity. A weak and statistically insignificant positive linear trend was observed between serum cholesterol and wall thickness change. No important or statistically significant differences in mean BMI, systolic and diastolic blood pressure was observed between the 3 grades of aortic wall elasticity.

To study the net and independent effect of age and total serum cholesterol on percent wall thickness change, after adjusting for stroke volume, BMI and blood pressure, a multiple linear regression model was used. Age, serum cholesterol and stroke volume were a statistically significant independent predictors of Aortic wall elasticity (assessed by percent wall thickness change). Age (40-59 years) is associated with a mean decrease in wall thickness change of 7.3%, while being 60 years of age and older is associated with a mean decrease in wall thickness change of 14.6% compared to youngest age group (<40 years) after adjusting for the remaining explanatory variables included in the model. For each 5 mg/dl increase in serum total cholesterol the mean wall thickness change is expected to decrease by 1.1% after adjusting for age and the remaining explanatory variables included in the model. Stroke volume was the strongest explanatory variable in predicting wall thickness change. The model was statistically significant and able to predict 70% of variation in the dependent variable, table 2.

As shown in table 3 and figure 1, the ROC analysis was used to assess the relative value of age and serum total cholesterol when used as a test to predict subjects with highest rigidity of aortic wall. Both parameters had an average ROC area of around 0.7, with age being a stronger predictor in this context. An age of 68 years and above is 95% specific in detecting rigid aortic artery, it was however of low sensitivity (30%). The age of 58 was the optimum cut-off value that best classify the subjects into those with highest rigidity of aortic wall and those without this undesirable criteria, since it was associated with a sensitivity of 70% and specificity of 75%, table 4. A serum cholesterol of 212 mg/dl and above is 92.5% specific in detecting rigid aortic artery, it was however of low sensitivity (5%). A serum cholesterol of 199 mg/dl was the optimum cut-off value that best classify the subjects into those with highest rigidity of aortic wall and those without this undesirable criteria, since it was

associated with a sensitivity of 50% and specificity of 85%, table 5.

Discussion

Measures of arterial elasticity have been proposed as surrogate markers for asymptomatic atherosclerosis(8). Therefore research in arterial elasticity has been given increased attention over the past few years. Increased arterial stiffness is an independent risk factor and predictor of cardiovascular mortality in a variety of diseases(15,16). It could be an early predictor of coronary risk useful in screening(6). Therefore the evaluation of arterial stiffness may be important for clinical diagnosis and intervention in cardiovascular disease. Currently a number of techniques are being used to assess arterial stiffness. Estimation of PWV (pulse wave velocity) is a simple, rapid and non-invasive method(17). The accuracy of this method, however is influenced by confounding factors like increased heart rate(18,19). Echo tracking techniques is a new method that may calculate real time displacement through radio frequency signal and phase zero crossing. Under the B/M mode, the technique can collect and analyze phase offsetting signal caused by vessel wall movement in the systolic and diastolic phases, track movements of vessel wall in real time and hence calculate the changes of arterial internal diameter (20).

The present study demonstrated clearly that Increasing age is an important and independent predictor for an increasing aortic artery wall stiffness (after adjusting for serum cholesterol, blood pressure and BMI). Being in the sixth decade of life will predict a rigid aorta with a reasonably high specificity. The Multi-ethnic Study of Atherosclerosis (MESA) on a cohort of 1053 reported that older age, higher blood pressure and smoking were independently (after adjustment in a multivariate analysis) associated with lower distensibility (elasticity) of the aortic artery(21). The MESA study used the Magnetic Resonance Imaging (MRI) double inversion recovery fast spin echo images of thoracic aorta to measure average and maximum wall thickness and calculate Airtic Distensibility (AD) using the formula:

AD= (Maximum area-Minimum area)/ minimum area X ΔP

ΔP=(systolic-diastolic blood pressure)

The present study showed that serum total cholesterol is an independent predictor for an increasing aortic artery wall stiffness (after adjusting for age, blood pressure and BMI). Having a serum cholesterol of >200 mg/dl will predict a rigid aorta with a reasonably high specificity. A number of

studies has examined the relation between plasma total cholesterol and large artery stiffness. Some studies reported no relation(7,8), others reported and inverse relation(9,10), while a third group agreed with the findings reported in the current study(11,12). In the largest and most recent cohort of elderly hypertensive subjects studied in a randomised controlled trial it was shown that plasma cholesterol perse was not associated with large artery stiffness(13). Such independence from cholesterol increases the potential for artery stiffness measurements to additionally contribute to cardiovascular risk assessment. The positive association between total cholesterol and aortic artery stiffness reported among apparently healthy individuals may fail to present itself among hypertensive subjects (who have a more stiff arteries in general).

The use of Atrovastatin, a blood lipid lowering drug in patients with hypertension and hypercholesterolaemia was associated with no changes in blood pressure and significant reduction in blood lipids and aortic stiffness. The increase in aortic wall elasticity correlated with the magnitude of reduction in total and LDL cholesterol(22). Another clinical trial on cholesterol lowering agent reached a similar conclusion(23). These findings strengthen the evidence in favor of a positive association between serum cholesterol and aortic wall stiffness.

The associations between age and aortic wall thickness and aortic distensibility have been reported in previous studies(24,25). Pathologic studies in animal models have shown that these changes can be attributed to structural modification of the arterial wall with increase in medial thickness, collagen content, and collagen/elastin ratio but decreases in elastin density. This is probably due to disintegration of orderly arrangement of elastic fibers and laminae with an increase in collagenous material and calcium deposition(26,27). Since increased aortic stiffness(28,29) and increased aortic wall thickness(30,31) have been proposed to be associated with increased incidence of cardiovascular events in rapidly growing number of older population, therefore burden of disease related to aortic stiffness and atherosclerosis would be expected to rise significantly in the future. Previous studies have shown that Aortic wall thickness(32) and Aortic distensibility(6) are associated with conventional risk factors of cardiovascular disorders.

Due to Wendkessel function, the measurements of aortic wall elasticity should be adjusted for ventricular stroke volume and blood pressure. Such an

adjustment was secured in the current study by the use of multiple linear regression.(1) The known confounding effect of gender on aortic elasticity(21) was adjusted for in the current study, by restricting the sample to males only. Such a limitation did not allow for studying the effect of gender in the population of Iraq. Further studies are needed to assess the confounding effect of smoking, gender, hypertension, diabetes and other cardiovascular risk factors on elastic property of aortic artery.

Conclusions

1. Increasing age and serum total cholesterol are important and independent predictors for an increasing aortic artery wall stiffness. Being in the sixth decade of life and having a serum cholesterol of > 200 mg/dl will predict a rigid aorta with a reasonably high specificity.
2. A high stroke volume is the most important and independent parameter associated with increased wall thickness change.
3. Measurements of aortic artery elasticity using Echocardiography is simple and may contribute to cardiovascular risk assessment.

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Table 1: The mean of selected independent variables by ordered categories of aortic artery elasticity.

	Aortic artery elasticity			
	Highest rigidity (n=20)	Average elasticity (n=20)	Highest elasticity (n=20)	P
Age in years				**0.015**
Range	(19 - 72)	(20 - 68)	(20 - 75)	
Mean+/-SE	59.7+/-2.95	47.8+/-3	47.4+/-3.82	
r=-0.273 P=0.035				
Serum total cholesterol (mg/dl)				**0.032**
Range	(158 - 215)	(155 - 226)	(116 - 220)	
Mean+/-SE	192.6+/-3.41	181.5+/-4.41	173.8+/-6.5	
r=-0.173 P=0.19[NS]				
Body mass index (BMI Kg/m2)				**0.63[NS]**
Range	(21.1 - 33.7)	(19.9 - 35.6)	(16.9 - 35.1)	
Mean+/-SE	26.5+/-0.78	26.6+/-0.97	25.4+/-1.17	
r=0.091 P=0.49[NS]				
Systolic blood pressure (mmHg)				**0.08[NS]**
Range	(120 - 135)	(115 - 140)	(115 - 140)	
Mean+/-SE	129.5+/-1.2	124.8+/-1.68	126.5+/-1.54	
r=-0.107 P=0.42[NS]				
Diastolic blood pressure (mmHg)				**0.41[NS]**
Range	(70 - 75)	(70 - 75)	(65 - 80)	
Mean+/-SE	74+/-0.46	73.5+/-0.53	75+/-1.2	
r=0.191 P=0.15[NS]				
Stroke volume (cm3/beat)				**<0.001**
Range	(128.3 - 281)	(80.2 - 308.7)	(108.1 - 395.3)	
Mean+/-SE	191.4+/-10.02	182.2+/-12.64	257.8+/-14.95	
r=0.587 P<0.001				

Table 2: Multiple linear regression model with percent wall thickness change as the dependent (response) variable and selected independent variables.

	Unstandardized Coefficients	P	Standardized Coefficients
Age group (years)		0.01	-0.399
40-59 years of age compared to <40	-7.3		
60+ years of age compared to < 40	-14.6		
Serum total cholesterol (mg/dl)	-0.23	0.022	-0.371
Stroke volume (cm3/beat)	0.14	<0.001	0.617

Note: The model was also adjusted for BMI in addition to systolic and diastolic blood pressure.
R^2=0.70 P (Model)<0.001

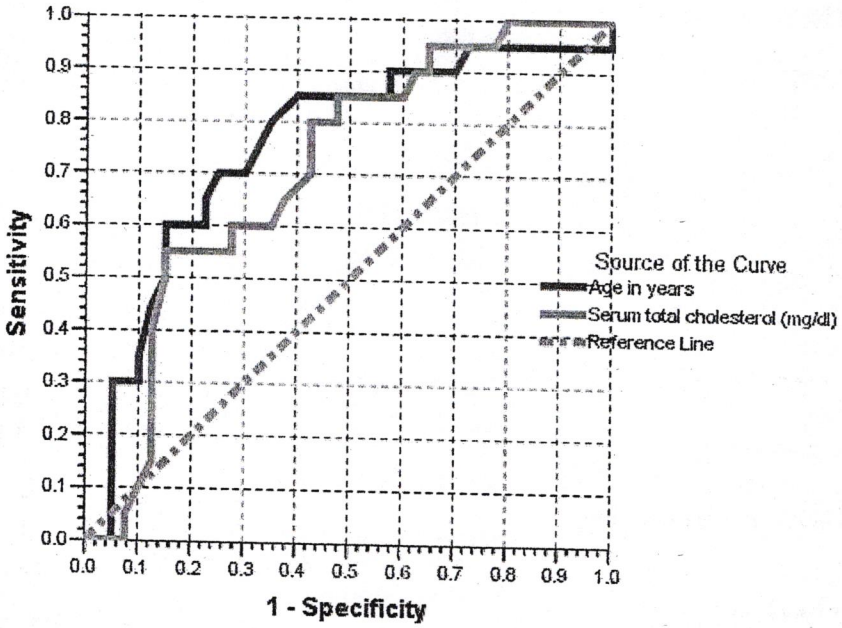

Figure 1: ROC curve for age and serum total cholesterol when used to predict subjects with highest rigidity of aortic artery differentiating them from those with less rigid arteries.

Table 3: ROC area for age and serum total cholesterol when used to predict subjects with highest rigidity of aortic artery differentiating them from those with less rigid arteries.

	ROC area	P
Age in years	0.758	0.001
Serum total cholesterol (mg/dl)	0.713	0.008

Table 4: The validity parameters of age when used to predict subjects with highest rigidity of aortic artery differentiating them from those with less rigid arteries.

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	False -ve	False +ve
≥ 34 (Highest sensitivity)	95	27.5	50	5	72.5
≥ 58 (Optimum)	70	75	73.3	30	25
≥ 68 (Highest specificity)	30	95	73.3	70	5

Table 5: The validity parameters of serum total cholesterol (mg/dl) when used to predict subjects with highest rigidity of aortic artery differentiating them from those with less rigid arteries.

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	False -ve	False +ve
≥ 156 (Highest sensitivity)	100	20	46.7	0	80
≥ 199 (Optimum)	50	85	73.3	50	15
≥ 212 (Highest specificity)	5	92.5	63.3	95	7.5

الخلاصة

الخلفية الأساسية : مطاطية الشريان الابهر ذات أهمية في عدة مواضع في الجهاز الوعائي القلبي. إن زيادة تصلب الشرايين عامل خطورة مهم ومستقل ومؤشر على توقع الوفاة القلبية وكذلك كمؤشر مبكر على خطورة الإصابة بمرض الشرايين التاجية عند عمليات المسح المرضي. ولهذا فإن تقويم التصلب الشرياني ذو أهمية في التشخيص السريري والتداخل عند علاج أمراض القلب والأوعية الدموية.

الهدف: إن الغاية من هذا البحث هو لبيان مدى تأثير العمر وكمية الكولسترول في الدم على نسبة التغيير في سماكة جدار الشرايين بعد ضبط الحجم الانقباضي للدم.

الطرائق: هو إجراء بحث مقطعي لاستخدام الدوبلر والايكو لقياس كمية الدم الذي يمر من خلال جذع الشريان الابهر في 60 شخص سالم من الامراض ويتراوح اعمارهم بين 17-75 سنة. إن مطاطية جدار الشريان الابهر تم تقييمها إستنادا الى نسبة التغيرات في السماكة الجدارية للشريان الابهر.

النتائج: استخدام النموذج عديد الاختلافات اظهر ان العمر ، وكمية الكولسترول في الدم وكمية الدم المدفوع بضربة قلبية واحدة ذي قيمة احصائية غير معتمدة على توقع على مطاطية جدار الشريان الابهر بعد ضبط ضغط الدم و BMI باستخدام التقييم الاحصائي ROC واظهرت النتائج ان عمر 68 سنة فأكثر كان 95% نوعيا في كشف التصلب الشرياني وقليل الحساسية 30% ، وكمية كولسترول 199 ملغم/ dl فاكثر يتناغم مع حساسية 50% ونوعيا 85% في كشف تصلب الشريان الابهر.

الاستنتاج: كون الشخص في العقد السادس من عمره مع كمية كولسترول اكثر من (200ملغم) تشير الى ان توقع الاصابة بتصلب الشريان الابهر عالية نوعيا. قياس مطاطية الشريان الابهر باستخدام الايكو عملية سهلة وبسيطة لتقويم مخاطر الاصابة بأمراض الاوعية الدموية والقلبية.