Journal of Hypertension: Open Access
ISSN: 2167-1095

Asklany et al., J Hypertens (Los Angel) 2018, 7:2
DOI: 10.4172/2167-1095.1000251

Research Article Open Access

Hypertensive Retinopathy can Predict Severity of Coronary Artery Disease in Hypertensive Patients Presenting with Angina

Hany T Asklany[1]*, Khaled S Mohamed[1], Mahmoud M Genidy[2] and Lamia Yassin[1]

[1]*Department of Cardiology and Ophthalmology, Minia University, Egypt*
[2]*Faculty of Medicine, Minia University, Egypt*

Abstract

Background: Hypertension cause injures to blood vessels, which may be macro vascular like coronary artery or micro vascular like retinal artery. Retina is the only place in the body where micro vascular damage can be observed directly. Retinal microvascular changes could be a suitable window to detect changes related to the pathophysiological changes that occurred in coronary artery disease as well as hypertension.

Objective: To assess the relationship between retinal micro vascular changes and angiographic findings in hypertensive patients presenting with angina.

Methods: A prospective study was done over one year including 80 patients known to be hypertensive for whom stress test was positive and or equivocal for angina diagnosis were referred to ophthalmology clinic to assess retinal atherosclerosis and its severity based on the Scheie classification after that the coronaries lesions and the extent of its severity was assessed by coronary angiography using Gensini and also the modified Gensini score.

Results: A totals of 80 patients (53 males and 27 females) their age range (38-76 years) with a mean of 53.3 ± 7.97, 31 out of the 80(38.8%) were smokers. The results show there was a significant correlation between the occurrence of retinal artery atherosclerosis and the severity of coronary artery disease (CAD) development with p=0.0001. Also when using the CAD severity (using modified Gensini scoring) as a dependent variable a significant association between it and retinal atherosclerosis scores by using the Scheie criteria, and hypertension, smoking, and left ventricular hypertrophy (LVH) was noticed.

Conclusions: Retinal hypertensive changes at any grade can predict CAD severity in any hypertensive patients presenting with anginal chest pain with a moderate to high accuracy. Therefore retinopathy has a predictive and good association with CAD in patients with hypertension. Hence by assessing the retinal micro vascular changes could be used as an early cost effective method to screen and to predict CAD.

Keywords: Coronary circulation; Ocular circulation; Hypertensive retinopathy; Retinal micro vascular

Introduction

Coronary artery disease (CAD) considers nowadays the first cause of cardiovascular mortality worldwide [1]. Although CAD is considered a macro vascular disease, microangiopathy has been observed to play a role in its pathogenesis [2]. Atherosclerosis is a systemic disease that affects many arterial beds in the body, such as the retinal vasculature [3]. Retina is the only place in the body where micro vascular damage can be observed directly [4]. Structural changes in the retinal vasculature are considered as main indicators of systemic hypertensive damage and life prognosis [5]. There was a relationship between retinal arteriolar abnormalities and the development of clinical manifestations of atherosclerosis for coronary artery diseases and other risk factors for vascular disease as shown in some studies [6].

The aim of this study is to detect and assess if there is any association between retinal microvascular changes and the extent also severity of coronary heart disease in hypertensive patients, and explore its potential implications and usefulness for use in our clinical practice.

Patients and Methods

A prospective comparative, randomized open label study which done by the cooperation between cardiology and ophthalmology departments at Minia University hospital Egypt from January 2016 to October 2017. 200 patients known to be hypertensive "Hypertension was defined using JNC VIII classification [7]" presented by anginal chest pain, were referred to do Stress Electrocardiography (ECG), 50 of them were negative test and excluded while the remaining 150 patients were positive or equivocal stress ECG. 70 patients were not willing to join the study, but the remaining 80 patients who gave informed consent were included. The included 80 patients referred for ophthalmoscopy examination before undergoing coronary angiography. Excluded patients were those with Diabetes mellitus, past history of ischemic heart disease, presence of nephropathy (creatinine more than 1.5 mg/dL), and previous coronary angiography.

All included patients were subjected to:

1. Full data history, local cardiac and general examination.
2. 12-Lead surface ECG.

***Corresponding author:** Dr. Hany T Asklany, Department of Cardiology and Ophthalmology, Minia University, Egypt, Tel: 00201001180345; E-mail: hany_t_asklany@yahoo.com

Received August 17, 2018; **Accepted** September 17, 2018; **Published** September 25, 2018

Citation: Asklany HT, Mohamed KS, Genidy MM, Yassin L (2018) Hypertensive Retinopathy can Predict Severity of Coronary Artery Disease in Hypertensive Patients Presenting with Angina. J Hypertens (Los Angel) 7: 251. doi: 10.4172/2167-1095.1000251

3. Laboratory Investigation: Random blood sugar, serum creatinine, lipid profile.
4. Trans-thoracic Echocardiography (TTE): General Electric Vivid 3 was the echocardiographic machine that used for Echocardiographic examination and assessment of left ventricular ejection fraction (LVEF) by M-mode and for exclusion of valvular heart disease.
5. Stress Electrocardiogram using modified Bruce protocol.
6. Coronary angiography: Coronary angiograms were visually analysed and scored by two different and expert interventionist who did not know any knowledge of the patients either for their history nor their ophthalmoscope result. Gensini score measurement and assessment was those used by Tedeschi-Reiner et al. [8]. Coronary artery stenosis was described and classified as follows 1 for 1% to 25%; 2 for 26% to 50%; 4 for 51% to 75%; 8 for 76% to 90%; 16 for 91% to 99%, and 32 for complete occlusion using Gensini score. To obtain the modified Gensini score we multiply the result by a factor that indicates the importance of the lesion's position in the coronary vasculature.
7. Ophthalmoscopy: For all 80 patients, the direct ophthalmoscopy was used for the assessment of retinal microvascular changes after good preparation for each patient and the all 80 patients' examination done by the same ophthalmologist without knowing any data regarding their coronary artery status. The Scheie classification was used for the atherosclerotic vascular lesions in the retinal arteries (Table 1) [9].

Statistical analysis

Methods of statistical analysis:

a) Analytical statistics: Analysis of normally distributed variables (parametric) among study groups was done by the Student (t) test for quantitative variables, Chi-square (x^2), Fischer's exact test for qualitative data.

The p value ≥ 0.05 was interpreted as non-significant, p value <0.05 was interpreted as significant, p value <0.01 was interpreted as highly significant, p value <0.001 was interpreted as very high significant.

Results

This study included 27 females and 53 males (31 of males were smokers) (Table 2). All patients undergo stress Electrocardiogram (ECG), Echocardiography study and fundus examination. Stress ECG was divided into equivocal, low, intermediate and high risk. Left ventricular hypertrophy "LVH" was present in 24 patients (30%), and by using Echo the mean left ventricular ejection fraction (LVEF) was 59.68 ± 6.64 (Table 3). Fundus examination was normal in 41 patients and abnormal in 39 patients. The most common retinal micro vascular abnormality was broadening of light reflex and the less abnormality was silver wire (Table 3).

After fundus examination patients were classified according to Scheie score. The most common Scheie score was grade 2 in 20 patients, followed by grade 1 in 13 patients then grade 3 in 4 patients and grade 4 in 2 patients (Table 4). Also, after coronary angiography patients were classified according to Gensini and modified Gensini scores, the average Gensini score was 31.82 ± 30.54 and the average modified Gensini score was 63.65 ± 61.08 (Table 4).

When making correlation between the 3 different scores: Scheie score; Gensini and modified Gensini score there was a significant positive correlation between them (Table 5).

Grade 0	Normal
Grade 1	Barely detectable light reflex change
Grade 2	Obvious increased light reflex change
Grade 3	Copper-wire arterioles
Grade 4	Silver-wire arterioles

Table 1: The grading of the Scheie score in ophthalmoscopy examination.

Demographic data	Descriptive statistics (n=80)
Age	
Range	(38-76)
Mean ± SD	53.3 ± 7.97
Sex	
Male	53 (66.2%)
Female	27 (33.8%)
Smoker	
No	49 (61.2%)
Yes	31 (38.8%)

Table 2: Demographic data of the patients.

Investigations	Descriptive statistics (No=80)
Stress ECG	
Equivocal	17 (21.2%)
Low risk	38 (47.5%)
Intermediate risk	18 (22.5%)
High risk	7 (8.8%)
EF	
Range	(50-80)
Mean ± SD	59.68 ± 6.64
LVH	
No	56 (70%)
Yes	24 (30%)
Fundus	
Normal	41 (51.3%)
Abnormal	39 (48.7%)
Fundus finding	
Normal	41 (51.3%)
Broadening of light reflex	13 (16.2%)
Narrowing	9 (11.3%)
Tortuosity	7 (8.8%)
Branchy angel abnormalities	4 (5%)
Copper wire	4 (5%)
Sliver wire	2 (2.5%)

Table 3: Data of stress ECG, Echocardiography and fundus examination in patients.

Different Scores	Descriptive statistics (No.=80)
Scheie score	
Grade 0 (Normal)	41 (51.2%)
Grade 1	13 (16.2%)
Grade 2	20 (25%)
Grade 3	4 (5%)
Grade 4	2 (2.5%)
Gensini score	
Range	(0-133)
Mean ± SD	31.82 ± 30.54
Modified Gensini score	
Range	(0-266)
Mean ± SD	63.65 ± 61.08

Table 4: Grading of different retinal artery atherosclerosis based on ophthalmoscope examination using the Scheie criteria and the range of Gensini and modified Gensini score.

There is a significant increase in modified Gensini score in patients with fundus examination that had tortuosity, branchy angel abnormalities, broadening of light reflex, narrowing, sliver wire and copper wire comparing with normal fundus (Table 6).

Also there is significant increase in Scheie, Gensini, and Modified Gensini scores in uncontrolled hypertension (HTN) comparing with controlled hypertension (HTN) (Table 7). Also there is significant increase in Scheie, Gensini, and Modified Gensini scores in uncontrolled hypertension (HTN) comparing with controlled hypertension (HTN) (Table 7).

Discussion

Hypertension cause injuries to blood vessels, which may be macro vascular like coronary artery or micro vascular like retinal artery. This study was designed to show the effect of hypertension on coronary artery and retinal artery and we tried to ascertain if a correlation and relation between both coronary and retinal artery diseases is present or not in hypertensive patients.

We intentionally exclude patients with history of neither diabetes mellitus, nor coronary heart disease from the study to steer clear of their effect on retinal circulation; we included 80 patients known to be hypertensive with anginal chest pain candidate for elective coronary angiography and fundus examination.

	Scheie score	
	r	P value
Gensini score	0.807	<0.001
Modified Gensini score	0.807	<0.001

Table 5: Correlation between Scheie score and Gensini and modified Gensini score.

Fundus finding	N	Modified Gensini score Mean ± SD	P value
Tortuosity			
-	41	9.7 ± 16	**<0.001**
+	7	125.1 ± 21.8	
Branchy angel abnormalities			
-	41	9.7 ± 16	**0.001**
+	4	127.5 ± 18.4	
Broadening of light reflex			
-	41	9.7 ± 16	**<0.001**
+	13	120.6 ± 8.1	
Narrowing			
-	41	9.7 ± 16	**<0.001**
+	9	95 ± 13.6	
Sliver wire			
-	41	9.7 ± 16	**0.012**
+	2	229 ± 52.3	
Copper wire			
-	41	9.7 ± 16	**0.001**
+	4	107 ± 8.9	

Table 6: Comparison between fundus finding and modified Gensini score.

	Controlled HTN (No.=60)	Uncontrolled (No.=20)	P value
	Mean ± SD	Mean ± SD	
Scheie score	0.56 ± 0.85	1.95 ± 1.1	<0.001
Gensini score	21.53 ± 23.97	62.7 ± 27.51	<0.001
Modified Gensini score	43.07 ± 47.94	125.4 ± 55.02	<0.001

Table 7: Comparison between uncontrolled and controlled hypertension (HTN) regarding different scores.

In the current study we showed that there is strong correlation between atherosclerotic retinal vessels changes and those atherosclerotic changes in coronary arteries in hypertensive patients and these changes were much more in patients with uncontrolled hypertension when compared with controlled hypertensive patients. In a similar study by Tabatabaee et al., who involved 168 hypertensive patients (aged 40-70 years) underwent coronary angiogram-phy. He found that the degree of retinal arterial atherosclerosis was strongly correlated with that of coronary artery disease (CAD) in its severity as well as its extension in coronaries without exclusion of any other risk factors [10].

In contrast to the present study another study by Tedeschi-Reiner et al., which include 109 patients (aged 40-80 years) with suspected CAD underwent coronary angiography a strong correlation was detected and confirmed between retinal atherosclerosis and CAD lesion severity but after exclusion of hypertensive patients [8].

In the present study we included middle aged and elderly hypertensive patients and we observe that there is no correlation between gender and other finding of significance in retinal circulation while in a another study by Wang et al., who focused on the arteriolar narrowing in retinal circulation and CAD, he showed a relation between retinal arterial narrowing and risk of CAD more in women than in men. The predominance of micro vascular mechanisms as a cause of CAD in women could be a good explanation for this observation in that study. The important difference between these studies and the present one is that their study cohort involved middle-aged men and women, whereas our study patients were middle-aged and elderly persons with hypertension. Hence, it is difficult to conclude that a similar hypothesis will hold true for our elderly patients with hypertension [11].

Also in another study by Wang et al., who used the diameter as a value in measuring smaller retinal arterioles as well as that of larger venules as a predictor of assessment of severity CAD and stroke mortality. This study concluded that the diameter of retinal vessel could be used as a predictor of CAD risk and stroke-related mortality in middle-aged persons, but unfortunately we can't use that value of vessel caliber changes in the present study [12,13].

In the current study we found a significant relationship in retinopathy grades in hypertensive patients which was much more in uncontrolled hypertensive patients compared to controlled ones the same result was found in a study by Wong et al., who find found that retinopathy is significantly more frequent in hypertensive compared with normotensive subjects. Further, in this group without diabetes, higher or less-well controlled blood pressure is associated with a higher frequency and severity of retinopathy, independent of blood glucose level [14]. Also in another study by Kolman et al., who found that multiple retinal changes such as arteriovenous nicking, arteriolar narrowing, and other different stages of retinopathy, were more frequent and obvious in uncontrolled hypertensive patients despite using antihypertensive medications when compared to those with controlled hypertensive patients and also those who were normotensives [15].

Also in our study we found that in uncontrolled hypertensive the severity of development of coronary heart disease increased in a significant manner with a significant correlation which is the same results found in a study by Smith et al., who compared the effect of resistant hypertension (res-HTN) on CAD severity and he concluded

that res-HTN is associated with the risk of cardiovascular severity events when compared with nonresistant HTN [16].

Our findings of the relationship between CAD and that of retinal vessel changes support the concept that retinal vessel changes may reflect lifetime cumulative effects of various vascular processes on the microvasculature and may be used as a novel biomarker of CHD risk in hypertensive patients.

Conclusion

Hypertension cause injures to blood vessels, which may be macro vascular like coronary artery or micro vascular like retinal artery, important observations from our study are that retinopathy has a strong association with CAD in patients with hypertension. Also, any grade of hypertensive retinopathy could predict CAD in hypertensive patients with angina with an accepted moderate accuracy and hence could be used as a cost effective screening tool to predict CAD early in the disease course especially in a resource-poor setting. However, the observations of our study need validation in larger population studies before its application in clinical practice.

Limitations

Although this is a single centre trial and the number is relatively small, yet statistical analysis was valid for the conclusions taken. However, a large number might be needed for firmer conclusions. Another limitation was the fact that only coronary artery disease patients were included without a using a control group. Studies with a larger number of patients including a control group are needed to evaluate retinal vascular changes more comprehensively in patients with coronary artery disease.

References

1. Okrainec K, Banerjee DK, Eisenberg MJ (2004) Coronary artery disease in the developing world. Am Heart J 148: 7-15.
2. Hiller R, Sperduto RD, Podgor MJ, Ferris FL, Wilson PW (1988) Diabetic retinopathy and cardiovascular disease in type II diabetics. The Framingham Heart Study and the Framingham Eye Study. Am J Epidemiol 128: 402-409.
3. Hansson GK (2005) Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 352: 1685-1695.
4. Shantha GP, Srinivasan Y, Kumar AA, Salim S, Prabakhar S, et al. (2010) Can retinal changes predict coronary artery disease in elderly hypertensive patients presenting with angina? Am J Emergency Med 28: 617-621.
5. Dodson PM1, Lip GY, Eames SM, Gibson JM, Beevers DG (1996) Hypertensive retinopathy: a review of existing classification systems and a suggestion for a simplified grading system. J Hum Hypertens 10: 93-98.
6. Wong TY, Islam FM, Klein R, Klein BE, Cotch MF, et al. (2006) Retinal Vascular Caliber, Cardiovascular Risk Factors and Inflammation: The Multi-Ethnic Study of Atherosclerosis (MESA). Invest Ophthalmol Vis Sci 47: 2341-2350.
7. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, et al. (2014) 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). Jama 311: 507-520.
8. Tedeschi-Reiner E, Strozzi M, Skoric B, Reiner Z (2005) Relation of atherosclerotic changes in retinal arteries to the extent of coronary artery disease. Am J Cardiol 96: 1107-1109.
9. Scheie HG (1953) Evaluation of ophthalmoscopic changes of hypertension and arteriolar sclerosis. AMA Arch Ophthalmol 49: 117-138.
10. Tabatabaee A, Asharin MR, Dehghan MH, Pourbehi MR, Nasiri-Ahmadabadi M, et al. (2013) Retinal vessel abnormalities predict coronary artery diseases. Perfusion 28: 232-237.
11. Wang JJ, Liew G, Wong TY, Smith W, Klein R, et al. (2006) Retinal vascular calibre and the risk of coronary heart disease-related death. Heart 92: 1583-1587.
12. Wang JJ, Liew G, Klein R, Rochtchina E, Knudtson MD, et al. (2007) Retinal vessel diameter and cardiovascular mortality: pooled data analysis from two older populations. Eur Heart J 28: 1984-1992.
13. Wu HQ, Wu H, Shi LL, Yu LY, Wang LY, et al. (2017) The association between retinal vasculature changes and stroke: a literature review and Meta-analysis. Int J Ophthalmol 10: 109-114.
14. Wong TY, Klein R, Klein BE, Tielsch JM, Hubbard L, et al. (2001) Retinal microvascular abnormalities and their relationship with hypertension, cardiovascular disease, and mortality. Surv Ophthalmol 46: 59-80.
15. Kolman SA, van Sijl AM, van der Sluijs FA, van de Ree MA (2017) Consideration of hypertensive retinopathy as an important end-organ damage in patients with hypertension. J Hum Hypertens 31: 121-125.
16. Smith SM, Gong Y, Handberg E, Messerli FH, Bakris GL, et al. (2014) Predictors and outcomes of resistant hypertension among patients with coronary artery disease and hypertension. J Hypertens 32: 635-643.