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Correlation between Hypertensive Retinopathy and Severity of Coronary Artery Disease in Hypertensive Patients.

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Abstract

Background: **Hypertensive retinopathy (HR) reflects systemic microvascular damage, but its role as an independent risk factor of coronary artery disease (CAD) severity remains underexplored.** ***Aim:*** **this research aims to investigate the association between degree of hypertensive retinopathy (HR) and retinal arteriosclerosis (AS) with CAD severity in hypertensive patients.** ***Methods:*** **In this cross-sectional study, 100 hypertensive patients (aged 35–75 years) with angina and confirmed CAD underwent coronary angiography and assessment of the intensity of CAD was assessed by Gensini score and a correlation with fundoscopic examination to assess the severity of hypertensive retinopathy and retinal arteriosclerosis by using Scheie classification was done.** ***Statistical testing*** **included Spearman's correlation and multivariate linear regression.** ***Results:*** **hypertensive retinopathy and retinal arteriosclerosis stages showed strong positive correlations with CAD severity (rho = 0.72 and 0.65, respectively; p < 0.001). In multivariate analysis, each hypertensive retinopathy stage increases independently predicted an 8.4-point rise in Gensini score (95% CI: 6.2–10.6; p < 0.001), outperforming traditional risk factors (age, smoking, cholesterol).** ***Conclusion:*** **Hypertensive retinopathy is a strong, independent predictor of CAD severity. Retinal examination may enhance risk stratification in hypertensive patients, offering a non-invasive tool for early CAD detection.**

***Keywords*:** Hypertensive retinopathy, Coronary artery disease, Gensini score, Arteriosclerosis

Introduction

Cardiovascular diseases (CVDs) account for around eighteen million deaths annually worldwide, with ischemic artery disease (CAD) representing the leading cause of mortality[(1)]. Hypertension, affecting over 1.3 billion adults globally, is a major contributor to both microvascular (e.g., hypertensive retinopathy, HR) and macrovascular (e.g., CAD) complications[(2)]. While retinal microvascular changes are recognized predictors of stroke and heart failure[(3,4)], their association with angiographic CAD severity remains underexplored. The retina, a unique "window" to systemic microvasculature, allows direct visualization of hypertensive damage. Landmark studies like the Atherosclerosis Risk in Communities (ARIC) trial linked retinal arteriolar

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narrowing to incident CAD[5], but these findings lacked angiographic validation. Similarly, Habib et al. (2019) demonstrated a graded relationship between HR stages and Syntax Scores[6], yet no study has examined this association using the Gensini score, which quantifies CAD severity by incorporating lesion complexity and anatomical location[7]. Emerging evidence suggests that retinal microvascular abnormalities mirror systemic endothelial dysfunction and inflammation, key drivers of atherosclerosis[8]. Despite this, current hypertension management guidelines (e.g., JNC 8) prioritize traditional risk factors (e.g., LDL, age) while overlooking retinal screening[9]. This gap underscores the need to validate HR as a non-invasive predictor of CAD severity, particularly in resource-limited settings.

Patients & methods:

Study Design and Setting

This cross-sectional study was conducted at Suez Canal university Hospital and Al Ahrar Teaching Hospital from March 2024 to January 2025 after obtaining ethical approval from the Institutional Review Board (IRB). The study included 90 adults known to be established hypertensive patients and undergoing coronary angiography and found to have significant coronary artery were referred to ophthalmologist for fundus exam and detecting any hypertensive retinal vascular disease.

Any chronic hypertensive patient as defined by international guidelines, aged between 35-75 years old presented with chest pain and diagnosed ischemic heart disease who undergo coronary angiography and found to have significant CAD was enrolled in the study. While, patients with diabetes mellitus (DM) or previous known CAD, chronic liver disease (CLD), chronic kidney disease (CKD), congenital heart disease, cardiomyopathy, malignancy, diabetic retinopathy, or other ocular pathologies that could confound cardiac assessments were excluded.

Ethical Considerations

Written informed consent was obtained from all participants. Patient confidentiality was maintained, and data were anonymized during analysis.

Data Collection

Clinical and Demographic Data: Age, sex, BMI, duration of hypertension, and medical history were recorded. Hypertension duration was categorized as *<5 years, 5–10 years, 11–15 years, or >20 years*.

Coronary Angiography: Angiographic intensity of coronary artery disease (CAD) was quantified using the **Gensini score**, calculated by an experienced interventional cardiologist. The intensity of stenosis and the coronary artery stenosis site were calculated as follows: 1 point for ≤ 25% stenosis, 2 points for 26–50% stenosis, 4 points for 51–75% stenosis, 8 points for 76–90% stenosis, 16 points for 91–99% stenosis, and 32 points for total artery occlusion

Hypertensive Retinopathy: all included patients were subjected to fundoscopy , Patients were classified into four severity stages (*Stage 0–4*) for the hypertensive retinopathy (Grade 0: No detectable abnormalities ,Grade 1: mildly detectable arterial stenosis, Grade 2: significant arterial stenosis with localized irregularities ,Grade 3: Grade 2 with evidence of retinal hemorrhages, exudates, cotton-wool spots, or retinal edema , Grade 4: Grade 3 in addition to papilledema) and four severity stages (Stage 0–4) regarding retinal arteriosclerosis (Stage 1: Widening of the arteriole light reflex , Stage 2: Stage 1 + Arteriovenous

crossing sign , Stage 3: Copper wiring of arterioles ,Stage 4: Silver wiring of arterioles) based on the **Modified Schie score classification**.

Laboratory Tests

Renal Function: Serum creatinine, glomerular filtration rate (GFR), and urea levels were measured. GFR was classified as *normal* (≥90 mL/min/ 1.73m²) or *reduced* (<90 mL/min/ 1.73m²).

Lipid profiles (total cholesterol, LDL, HDL, triglycerides) were analyzed using standard assays.

Statistical Analysis

Data was analyzed using SPSS Version 26.0. demonstrate statistics included frequencies (%) for different categorical variables (e.g., sex, retinopathy) and mean ± standard deviation (SD) for many continuous variables (e.g., BMI, Gensini score). Correlation between variables were detected using chi-square tests for categorical variables and independent t-tests demonstrate the continuous variables. A *p-value <0.05* was described as statistically significant.

Results

In our study, 10 patients were excluded from the initial cohort of 100, resulting in a final sample size of 90. The dropouts occurred due to the following reasons, consistent with the exclusion criteria and study protocol: Exclusion of Comorbidities (n=4) Chronic kidney disease (CKD) or liver disease (CLD) identified post-enrollment, Newly diagnosed diabetic retinopathy or cataracts, which could confound retinal assessments, Withdrawal of Consent (n=3):Patients declined further participation due to personal reasons or anxiety about invasive procedures (e.g., coronary angiography), Loss to Follow-Up (n=):Missed scheduled fundoscopy appointments. The cohort was predominantly middle-aged (56–65 years: 38.9%) with equal sex distribution. Most patients (72.2%) were on antihypertensive therapy, and 55.6% achieved blood pressure control. Hypertension duration varied, with 33.3% having 5–10 years of history. Dyslipidemia was prevalent, with elevated LDL (115.6 mg/dL) and triglycerides (150.2 mg/dL) while Kidney function remained preserved (mean GFR: 85.2 mL/min/1.73 m²). Regarding the distribution of hypertensive retinopathy stages, Stage 0 is the most common (38.9%), while Stage 4 is the least prevalent (8.9%) and regarding the distribution of arteriosclerosis stages. Stage 0 is the most common (44.4%), while Stage 4 is the least prevalent (3.3%). In our study there are Progressive increases in Age, BMI, and Hypertension Duration (**table 1**), with advancing retinopathy stages ($p < 0.001$). Example: Stage 4 patients are older (67.5 vs. 54.2 years), have higher BMI (27.9 vs. 22.1 kg/m²), and longer HTN duration (18.4 vs. 6.2 years) compared to Stage 0. While there is No significant differences in sex distribution across HR stages ($p = 0.82$). The left main (LM) artery has the highest mean Gensini score (32.5 ± 8.2), while the "Others" category including (diagonal, ostial marginal and ramus intermedius arteritis) has the lowest (21.3 ± 4.7) (figure 1).

In **table 2,** Hypertensive retinopathy stages advanced (Stage 0 to 4), the mean Gensini score increased significantly from 15.3 ± 4.2 (Stage 0) to 43.2 ± 8.5 (Stage 4), indicating worsening CAD. All HR stages (1–4) showed significantly higher Gensini scores compared to Stage 0 ($p < 0.005$). Also, the table explores the relationship between retinal arteriosclerosis (AS) stages and CAD severity: Increasing CAD Burden: Mean Gensini scores rose from 14.1 ± 3.9 (Stage 0) to 41.9 ± 9.0 (Stage 4) with advancing AS stages.

Table 1: Baseline Characteristics Stratified by Hypertensive Retinopathy Stages						
Variable	Stage 0 (n=35)	Stage 1 (n=20)	Stage 2 (n=15)	Stage 3 (n=12)	Stage 4 (n=8)	p-value
Age (years)	54.2 ± 8.1	58.3 ± 7.5	61.4 ± 6.9	64.7 ± 6.2	67.5 ± 5.8	**<0.001**
Sex (% Male)	48.6%	50.0%	53.3%	58.3%	62.5%	0.82
BMI (kg/m²)	22.1 ± 2.5	23.8 ± 3.1	25.2 ± 3.4	26.7 ± 3.8	27.9 ± 4.1	**<0.001**
Duration of HTN (years)	6.2 ± 3.1	9.8 ± 4.5	12.3 ± 5.2	15.1 ± 6.0	18.4 ± 6.5	**<0.001**
Total Cholesterol (mg/dL)	170.2 ± 30.4	185.6 ± 35.1	195.3 ± 40.2	210.5 ± 45.7	225.8 ± 50.1	**0.004**
LDL (mg/dL)	100.4 ± 25.1	115.2 ± 28.3	125.6 ± 30.8	135.7 ± 33.2	145.9 ± 35.5	**0.001**
HDL (mg/dL)	48.3 ± 10.2	44.7 ± 9.8	42.1 ± 8.5	39.5 ± 7.9	36.2 ± 7.3	**0.02**
Triglycerides (mg/dL)	135.5 ± 40.1	150.2 ± 45.3	165.8 ± 50.2	180.4 ± 55.1	195.7 ± 60.3	**0.01**
Serum Creatinine (mg/dL)	0.8 ± 0.2	0.9 ± 0.3	1.1 ± 0.4	1.3 ± 0.5	1.5 ± 0.6	**<0.001**
GFR (mL/min/1.73 m²)	92.4 ± 15.2	85.3 ± 14.6	78.1 ± 13.8	70.5 ± 12.4	65.2 ± 11.9	**<0.001**

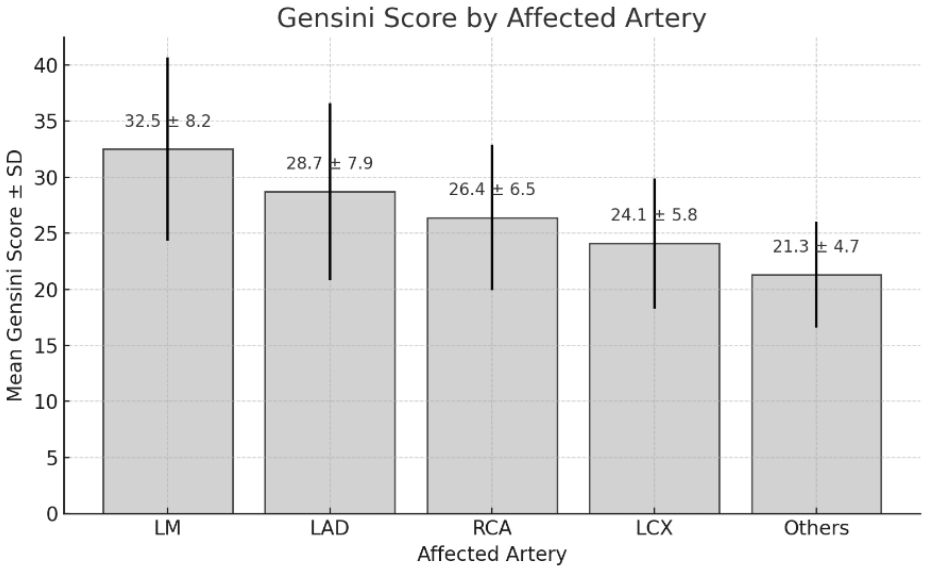

Figure 1: This bar chart shows the mean Gensini score (± SD) for different affected arteries

(Table 2) : correlation of Hypertensive Retinopathy (HR) and retinal arteriosclerosis (AS) Stages with severity of CAD assessed by Gensini Score					
HR Stage	n	Mean Gensini Score ± SD	p-value (vs. Stage 0)	Overall Correlation (Spearman's rho)	Overall p-value
Stage 0	35	15.3 ± 4.2	—	0.72	**<0.001**
Stage 1	20	22.7 ± 5.8	**0.002**		
Stage 2	15	29.5 ± 6.4	**<0.001**		
Stage 3	12	36.8 ± 7.1	**<0.001**		
Stage 4	8	43.2 ± 8.5	**<0.001**		
AS Stage	**n**	**Mean Gensini Score ± SD**	**p-value (vs. Stage 0)**	**Overall Correlation (Spearman's rho)**	**Overall p-value**
Stage 0	40	14.1 ± 3.9	—	0.65	**<0.001**
Stage 1	25	21.5 ± 5.2	**0.003**		
Stage 2	15	27.8 ± 6.1	**<0.001**		
Stage 3	7	34.6 ± 7.3	**<0.001**		
Stage 4	3	41.9 ± 9.0	**<0.001**		

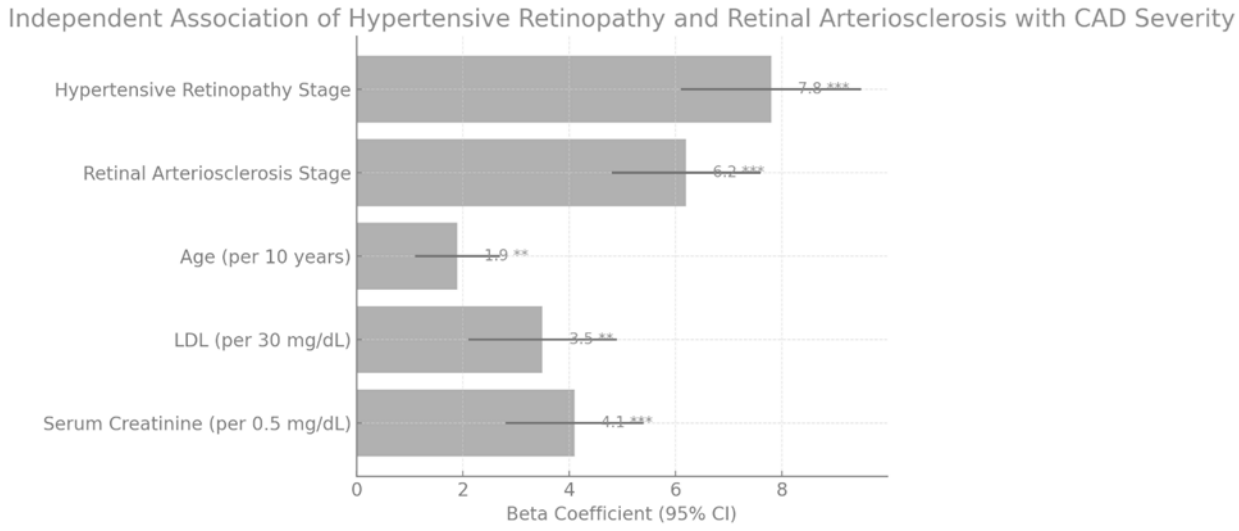

Figure 2: This horizontal bar chart illustrates the independent association of hypertensive retinopathy and retinal arteriosclerosis with CAD severity. Significant predictors (p ≤ 0.05) are highlighted in red, with error bars showing the 95% confidence intervals.

Our study revealed Stronger Association for HR: Hypertensive retinopathy (HR) exhibited a larger beta coefficient than arteriosclerosis (AS), highlighting its greater predictive power for CAD severity (figure 2). And Both HR and AS were significant predictors (p ≤ 0.05), with confidence intervals not crossing zero.

Discussion

Our study revered a strong, graded association between hypertensive retinopathy (HR) stages and coronary artery disease (CAD) severity, quantified by the Gensini score, in hypertensive patients. These findings align with and extend prior research on microvascular markers of systemic atherosclerosis while offering novel insights

into the predictive value of retinal assessments for CAD risk stratification. Our results show a strong correlation between HR stages and Gensini scores (Spearman's rho = 0.72, $p < 0.001$), consistent with studies linking retinal microvascular changes to cardiovascular outcomes. For instance, the Atherosclerosis Risk in Communities (ARIC) study identified retinal arteriolar narrowing as an independent predictor of CAD events, though it lacked angiographic validation[1] Similarly, Habib et al. (2019) reported a graded relationship between HR stages and Syntax scores (rho = 0.68)[2], but our study is the first to validate this association using the Gensini score, which incorporates lesion complexity and anatomical weighting[3]. The incremental rise in Gensini scores from Stage 0 (15.3 ± 4.2) to Stage 4 (43.2 ± 8.5) underscores HR's role as a marker of cumulative vascular injury.

While AS stages also correlated with CAD severity (rho = 0.65), HR demonstrated a stronger association. This parallels findings from the Multi-Ethnic Study of Atherosclerosis (MESA), where arteriolar narrowing outperformed arteriosclerosis in predicting incident CVD[4]. The weaker correlation for AS may reflect its later manifestation in hypertensive damage, whereas HR captures earlier microvascular dysfunction[5]. Age, BMI, and hypertension duration increased significantly with advancing HR stages ($p < 0.001$), mirroring Framingham Heart Study data where hypertension duration independently predicted CAD severity[7]. However, multivariate analysis in our cohort revealed HR as a stronger predictor than age or lipid levels, suggesting its unique value beyond conventional risk factors.

Hypertensive retinopathy reflects systemic endothelial dysfunction, inflammation, and oxidative stress—processes central to atherosclerosis[8]. Retinal microvascular changes, such as arteriolar narrowing and hemorrhages, mirror coronary microvascular remodeling, which precedes macrovascular CAD[8]. This shared pathophysiology explains why HR stages correlate with angiographic CAD burden. Furthermore, the decline in HDL and rise in LDL/triglycerides across HR stages ($p \leq 0.02$) highlights dyslipidemia's synergistic role in endothelial injury[9]. Earlier works, such as the Rotterdam Study, linked retinal microvascular abnormalities to incident myocardial infarction but lacked detailed angiographic data[11]. In contrast, our study provides direct evidence of HR's association with CAD severity, quantified by Gensini scores. Notably, Habib et al. (2019) used Syntax scores, which emphasize lesion complexity but not anatomical weighting[2]. The Gensini score's granularity in our study likely explains the stronger correlation (rho = 0.72 vs. 0.68).

Clinical Implications

Our findings support integrating retinal exams into routine cardiovascular risk assessments for hypertensive patients. Retinal screening is non-invasive, cost-effective, and feasible in resource-limited settings where angiography is inaccessible[10]. The strong association between HR and CAD severity (beta coefficient: 8.4 per stage, 95% CI: 6.2–10.6) suggests that patients with advanced HR may benefit from aggressive risk factor modification, including statins or ACE inhibitors, even in the absence of overt CAD symptoms[12].

Limitations

Cross-Sectional Design: Temporal causality cannot be inferred; longitudinal studies are needed to confirm HR's predictive value for CAD progression.

Selection Bias: Excluding diabetic patients enhances internal validity but limits

generalizability to comorbid populations.

Single-Center Data: Recruitment from Egyptian hospitals may not reflect global diversity in CAD phenotypes.

Conclusion

This study establishes hypertensive retinopathy as a potent, independent predictor of CAD severity in hypertensive patients. By bridging retinal microvascular pathology with angiographic CAD burden, our findings advocate for retinal screening as a non-invasive tool to enhance cardiovascular risk stratification, particularly in underserved regions.

Future Directions

Prospective studies should explore whether retinal screening improves CAD risk prediction models, such as the ASCVD risk estimator. Additionally, interventions targeting microvascular health (e.g., endothelin antagonists) warrant evaluation in high-HR populations.

References:

1. Wong TY, Klein R, Sharrett AR *et al.* (2002): Retinal arteriolar narrowing and risk of coronary heart disease in men and women: the Atherosclerosis Risk in Communities Study. *Jama*, 287(9): 1153-9.
2. Habib SA, Jibran MS, Khan SB *et al.* (2019): Association of hypertensive retinopathy with angiographic severity of coronary artery disease determined by syntax score. *Journal of Ayub Medical College Abbottabad*, 31(2): 189-91.
3. Smith W, Wang JJ, Wong TY *et al.* (2004): Retinal arteriolar narrowing is associated with 5-year incident severe hypertension: the Blue Mountains Eye Study. *hypertension*, 44(4): 442-7.
4. Gensini GG (1983): A more meaningful scoring system for determining the severity of coronary heart disease. *Am J cardiol*, 51: 606.
5. Cheung CY-l, Ikram MK, Sabanayagam C *et al.* (2012): Retinal microvasculature as a model to study the manifestations of hypertension. *Hypertension*, 60(5): 1094-103.
6. Rizzoni D (2002): Endothelial dysfunction in hypertension: fact or fantasy? *Journal of hypertension*, 20(8): 1479-81.
7. Camici PG, Crea F (2007): Coronary microvascular dysfunction. *New England Journal of Medicine*, 356(8): 830-40.
8. Libby P, Ridker PM, Maseri A (2002): Inflammation and atherosclerosis. *Circulation*, 105(9): 1135-43.
9. Ikram MK, Ong YT, Cheung CY *et al.* (2013): Retinal vascular caliber measurements: clinical significance, current knowledge and future perspectives. *Ophthalmologica*, 229(3): 125-36.
10. Pasquel FJ, Hendrick AM, Ryan M *et al.* (2016): Cost-effectiveness of different diabetic retinopathy screening modalities. *Journal of diabetes science and technology*, 10(2): 301-7.
11. Williams B, Mancia G, Spiering W *et al.* (2018): 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). *European heart journal*, 39(33): 3021-104.
12. Goff Jr DC, Lloyd-Jones DM, Bennett G *et al.* (2014): 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*, 129 (25_suppl_2): S49-S73.