



“HISTOMORPHOLOGY EVALUATION OF MACULAR THICKNESS AS AN INDICATOR OF RETINAL MICROVASCULAR DAMAGE IN SYSTEMIC HYPERTENSION”

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ABSTRACT

Background: Microvascular damage is another significant effect of systemic hypertension, and the retina is a delicate piece of evidence of changes in the systemic vasculature. The retinal alterations should be observed early enough to avoid complications.

Objective: The objective was to assess the use of optical coherence tomography in measuring the degree of retinal microvascular injury in patients with systemic hypertension by measuring their macular thickness as a histomorphological parameter.

Methods: The cross-sectional study was done at the Al Ibrahim Eye Hospital between December 2023 and June 2024. The sample size was 120, 60 hypertensive patients and 60 healthy controls of the same age. A thorough ophthalmic examination and a macular thickness evaluation were done on all the people with spectral-domain optical coherence tomography. The values of the macular thickness were measured both at the center and the quadrant. The SPSS version 26 and the independent t-tests and Pearson correlation analysis were employed to carry out the statistical analysis.

Results: Hypertensive patients showed a significantly reduced central macular thickness ($238.4 \pm 18.6 \mu\text{m}$) compared to controls ($252.7 \pm 16.9 \mu\text{m}$). The difference between the average macular thickness was also significant with the hypertensive group favoring. Quadrant-wise results indicated that the superior and temporal areas were significantly thin. Systolic blood pressure and macular thickness were found to have a negative correlation ($r = -0.47$, $p < 0.01$), and so was the disease duration

and retinal thickness ($r = -0.52$, $p < 0.001$). It should be noted that despite the absence of clinical retinopathy, the thinning of the macula was noted.

Conclusion: Macular thickness is an accurate and delicate biomarker that can be used to identify early retinal microvascular damage in systemic hypertension. Diagnosis and clinical management can be enhanced with the help of optical coherence tomography.

Keywords: *Systemic hypertension, macular thickness, retinal microvasculature, optical coherence tomography, hypertensive retinopathy, retinal biomarkers*

INTRODUCTION

Systemic hypertension is a major health problem that affects the world and is a known risk factor of microvascular injury of the diverse organ systems such as the retina. The retinal microvasculature provides a noninvasive and unique vascular bed to study the systemic vascular alterations, which discloses the possible existence of hypertensive harm at an early phase. The recent advances in retinal imaging have enabled the possibility to measure capillary networks in details and proved that retinal vascular changes are strongly correlated with the cardiovascular remodeling in the whole body. Studies have revealed that myocardial remodelling is linked with changes in the density and structure of capillaries within the retina which indicates the interdependence of microvascular pathology in the process of hypertension (1). Chronic hypertension also leads to progressive vascular remodelling which causes structural and functional damage of retinal vessels (2). Thickness of the retina particularly in the macula region has proved to be a significant biomarker to detect the slightest microvascular alterations. Vascular compromise and neurodegenerative changes are manifested in retinal thickness changes. It is demonstrated that the changes in retinal thickness are not only hypertension-associated but also are also found in other conditions of systemic inflammation such as lupus that means that retinal imaging can be used in a broader range of application in the diagnosis of systemic diseases (3).

Macular changes in the microvasculature may also exist in individuals with hypertension who have no clinically evident retinopathy, and therefore the need to have structural assessment at an early age (4). As the central vision organ, the macula is the one that is especially susceptible to microvascular alterations because of the high metabolic activity. The morphological and the microcirculatory alterations of the macula have been extensively studied in disease conditions such as diabetic macular edema where the buildup of fluid and vascular leakage leads to increased thickness which is measurable (5). This may be the same processes at work in hypertension, where endothelial malfunction and increased vascular permeability is an etiological process in retina modification. In addition, other systemic factors such as aging and high blood pressure have also been reported to play a powerful influence on the microvascular integrity and this further places the systemic hemodynamics in the retinal health (6). There is recent research that has broadened the scope of retinal microvascular changes in different systemic diseases that supports the notion that retinal imaging may be used as a surrogate endpoint of systemic vascular health.

The difference in the parameters of the macular and peripapillary microvascular parameters in patients with lupus nephritis is an example of that (7). On the same note, connective tissue diseases have been linked with a marked microvascular alteration in the ocular surface and retina, which underscores the systemic effect of the vascular dysfunction (8). The impact of systemic disease on retinal vasculature has also been highlighted by the fact that the changes in the diameter of retinal vessels and the choroidal thickness were dramatic in the patients during the COVID-19 pandemic (9). These results indicate that retinal structure can be directly affected by systemic inflammation and vascular damage. Besides, the choroidal vascularity index has become a valuable parameter of measurement of vascular changes in different systemic diseases that offers supplementary information regarding the correlation between the systemic and ocular microcirculation (10).

The increased knowledge of retinal imaging biomarkers has led to the incorporation of these biomarkers in cardiovascular risk assessment models. The retinal imaging tools are standardized to

allow their use in clinical practice to allow the early detection and monitoring of microvascular damage in systemic diseases like hypertension (11). Histopathological studies that have demonstrated the vascularity change, inflammation, and gliosis in retinal tissues have also supported imaging to bridge the gap in the research between imaging and tissue-based pathology (12). Along with the hypertension, numerous inflammatory and autoimmune diseases have been demonstrated to have high rates of macular and choroidal thickness change. The example of changes in Behcet's disease is foveal and choroidal thickness, which can be measured and altered, which is a symptom of vascular inflammation (13). Likewise, the retinal alterations detected by optical coherence tomography in the preclinical phase of systemic lupus erythematosus can be used to emphasize the possibility of retinal imaging to identify the disease at an early stage (14).

This is further supported by studies on systemic sclerosis, which show that alterations in vascularity and macular choroidal thickness are strongly correlated with the extent of the disease and the implication in vascularity (15). These results confirm the hypothesis that systemic vascular diseases have some common pathogenic processes that are reflected in the retina. Also, studies on pathologies like keratoconus have shown that there are major variations in retinal neurovascular parameters, indicating that even non-vascular baseline ailments may potentially affect retinal microcirculation (16). The choroidal implication of the systemic vasculitis also demonstrates the vulnerability of the ocular microvasculature to systemic inflammation.

Systematic review has been used to explain the quantity of choroidal and retinal vascular change in vasculitis in support of the fact that the eye is a delicate indicator of systemic vascular pathology (17). On the basis of these results, histomorphological analysis of the macular thickness could have a potential in measuring the retinal microvascular injury in hypertension in the systemic disease. Overall, sophisticated retina scans coupled with histomorphology provide a holistic approach to the alterations in microvasculature in the hypertension scenario. This research is expected to make a contribution to the emerging amount of literature that confirms the utility of retinal biomarkers in the early diagnosis and treatment of vascular diseases in the body in general and the macular thickness in particular.

Objective: To determine the alterations of the macular thickness as a histomorphological index of retinal microvascular damage in patients with systemic hypertension, and to determine its diagnostic value using optical coherence tomography images.

.MATERIALS AND METHODS

Study Design: A cross-sectional observational study.

Study Setting: Department of Ophthalmology, Al Ibrahim Eye Hospital.

Duration of Study: December 2023 – June 2024

Sample Size: One hundred and twenty (120) were used (60 hypertensive patients and 60 age matches healthy controls) based on a 95% confidence interval and 80% power in the study.

Inclusion Criteria: Inclusion criteria consisted of patients aged 30 to 65 years who had systemic hypertension as diagnosis at least one-year-old. Participants who had controlled or uncontrolled blood pressure regardless of gender were recruited. The patients who had a clear ocular media and had no previous history of ocular surgery were only chosen so as to have reliable imaging results.

Exclusion Criteria: Patients who had diabetes mellitus, retinal diseases, glaucoma or ocular trauma in the past were excluded. Patients with systemic inflammatory or autoimmune conditions that involve microvasculature were also eliminated. Patients whose OCT images were of low quality or had severe refractive errors were excluded.

Methods: Every player underwent an in-depth ophthalmic examination which involved a visual acuity examination, slit-lamp examination as well as fundoscopic examination. The measurement of blood pressure was done by the use of a calibrated sphygmomanometer. Spectral-domain optical coherence tomography (SD-OCT) was used to measure macular thickness. The central foveae thickness, average macular thickness and quadrant value of thickness were derived. These people were divided into hypertensive and control groups. The OCT scans were done at controlled conditions by a trained technician to minimize the inter-observer variability. The scans of each eye were analyzed by scanning the eyes three times and taking the average. The SPSS version 26 was used to analyze data. Independent sample t-tests were the ones used in the comparison of the macular thickness between groups. The analysis of the relationship between the level of blood pressure and retinal thickness was done through Pearson correlation analysis. The p-value of less than 0.05 was considered significant.

Results

The study involved 120 participants that consisted of 60 patients who were diagnosed with systemic hypertension and 60 healthy controls. The two groups were similar in terms of demographics and no statistically significant deviation in terms of age or gender distribution (p The mean age of the hypertensive patients was 49.2/8.7 years and controls was 47.9/9.5 years. The thickness of the macula measured using spectral-domain optical coherence tomography (SD-OCT) showed that there were significant differences in the two groups. The mean central macular thickness (CMT) of hypertensive patients ($238.4 \pm 18.6 \mu\text{m}$) was statistically lower than that of controls ($252.7 \pm 16.9 \mu\text{m}$) indicating structural retinal thinning. In the same vein, average macular thickness had statistically significant decrease in hypertensive patients ($276.3 \pm 20.4 \mu\text{m}$) in comparison to the control group ($289.8 \pm 19.7 \mu\text{m}$).

Table 1: Demographic Characteristics of Participants (n=120)

Variable	Hypertensive Group (n=60)	Control Group (n=60)
Mean Age (years)	49.2 $\pm$ 8.7	47.9 $\pm$ 9.5
Male (%)	33 (55%)	32 (53.3%)
Female (%)	27 (45%)	28 (46.7%)

The superior quadrant thickness was 281.5 22.1 μg in hypertensive and 298.6 21.3 μg in controls ($p < 0.001$). The temporal quadrant also had a lot of thinning ($p < 0.01$) with nasal and inferior quadrants also having moderate but statistically significant thinning.

Table 2: Comparison of Central and Average Macular Thickness

Parameter	Hypertensive Group	Control Group	p-value
Central Macular Thickness	238.4 $\pm$ 18.6 μm	252.7 $\pm$ 16.9 μm	<0.001
Average Macular Thickness	276.3 $\pm$ 20.4 μm	289.8 $\pm$ 19.7 μm	<0.001

There was quadrant-wise analysis which revealed that there was no locality of the macular region spared and the superior and temporal quadrants exhibited the greatest thinning.

Table 3: Quadrant-wise Macular Thickness Comparison

Quadrant	Hypertensive Group (μm)	Control Group (μm)	p-value
Superior	281.5 $\pm$ 22.1	298.6 $\pm$ 21.3	<0.001
Inferior	274.2 $\pm$ 19.5	286.7 $\pm$ 18.9	<0.01
Nasal	269.8 $\pm$ 18.7	281.4 $\pm$ 17.6	<0.01

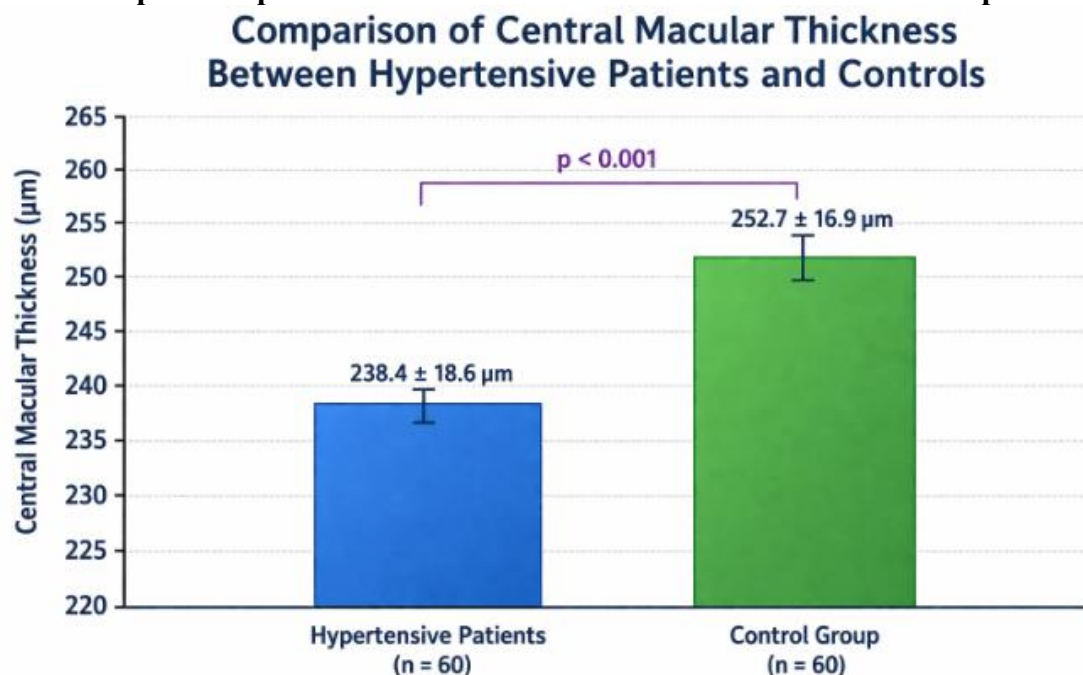
Quadrant	Hypertensive Group (μm)	Control Group (μm)	p-value
Temporal	260.6 ± 17.9	275.3 ± 16.8	<0.01

Correlation analysis showed that systolic blood pressure and central macular thickness had a strong negative correlation ($r = -0.47$, $p < 0.01$). In addition, the duration of hypertension was strongly associated with the macular thinning ($r = -0.52$, $p < 0.001$) which was a progressive microvascular damage. Money revealed that 40 percent of hypertensive patients suffered mild hypertensive retinopathy and 60 percent of them did not show any retinal changes. However, surprisingly, OCT revealed the presence of macular thinning in patient who was not having clinical retinopathy, which is sensitive in detecting early microvascular damage.

Table 4: Correlation of Blood Pressure and Duration with Macular Thickness

Variable	Correlation Coefficient (r)	p-value
Systolic Blood Pressure	-0.47	<0.01
Duration of Hypertension	-0.52	<0.001

Graph: Comparison of Central Macular Thickness Between Groups



Discussion

The research under consideration demonstrates the significance of the role of the macular thickness as the indicator of retinal microvascular damage because it demonstrates that the macular thickness is significantly reduced in patients with the systemic hypertension rendering it a sensitive measure of the histomorphologic alterations. These findings are in line with the current emerging data indicating that retinal microcirculation is a marker of the health of the vascular system, and may provide early signals of hypertensive damage to end-organs. Previous researchers have indicated that retinal capillary network alterations are closely related to systemic cardiovascular remodelling, suggesting that retinal alterations are more similar to more general microvascular pathology in hypertension (1). Moreover, structural retinal damage is said to be dissimilar in chronic hypertension and clinically apparent hypertensive retinopathy, indicating that subclinical changes are manifested prior to the occurrence of observable changes (2). The decrease in central and average macular thickness as was

evident in this study underscores how the retinal microvasculature is susceptible to continued high blood pressure. The same has been noted in systemic diseases like lupus where microvascular changes are in tandem with quantifiable changes in retinal thickness (3).

Additionally, the study that has compared the hypertensive effects on the macular microvasculature of individuals with diabetes without retinopathy has revealed an early vascular impairment, which justifies the autonomous role of hypertension on the retinal architecture (4). The high capillary density in Macula makes it very susceptible to ischemic damage due to high metabolic requirements. Macular morphology and microcirculation alteration have been extensively reported in disease conditions such as diabetic macular edema and the structural changes have been explained by the increased vascular permeability (5). Nevertheless, although hypertension does not always seem to be accompanied by apparent edema, chronic endothelial dysfunction and capillary dropout may cause retinal pallor. Moreover, there are systemic elements that were demonstrated to have a negative impact on microvascular integrity as aging and long-term effects of high blood pressure (6). The imaging modalities of the retina, as well as the optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA), have enhanced the ability of detecting subtle microvascular alteration.

Studies on systemic lupus erythematosus have also revealed that strong alterations in the macular and papillary microvasculature and patients who experienced vascular alterations in the disease exhibited disease specific vascular patterns (7). Also in the same vein, the correlation of connective tissue diseases with the general microvascular aberration of the retina and ocular surface have contributed to the overall validation of the systemic reaction of such changes (8). These findings indicate the increased generality of retinal imaging in hypertension. Retinal vascular parameters also have been demonstrated to be affected by systemic inflammatory conditions. Indicatively, severe cases of COVID-19 patients have exhibited a promising change in retinal vessel diameter and choroidal thickness, which is an expression of inflammation in the systemic vascularity and vascular endothelia destruction (9). Choroidal vascularity index now is a significant parameter, which is applied in quantifying vascularity in normal individuals and systemic illnesses as well as provides additional information on the relationship between systemic and ocular circulations (10). Retinal imaging biomarker have increasingly gained recognition as being of clinical use in cardiovascular medicine. Standardization of techniques has enabled the application of imaging techniques in clinical practice as it has made it possible to detect and monitor microvascular damage in systemic diseases such as hypertension at an early stage (11).

The histopathological research has also supported the imaging evidence that has demonstrated the changes in the retinal vascularity, inflammation and gliosis, which substantiate the structural changes that are exhibited in the OCT research (12). In addition to hypertension, several systemic inflammatory and autoimmune diseases have demonstrated that there are extensive changes in the choroidal thickness and the macular thickness. One such example is that patients with Behets disease experience alterations in the foveal and choroidal thickness which are symptoms of inflammation in the vessels (13). Similarly, preclinical retinal changes in OCT in systemic lupus erythematosus are an indication that the disease can be diagnosed at a tender age before it can develop any clinical signs (14). These findings underscore the fact that retinal examination plays a critical role in tracking systemic conditions. Besides this concept, studies in the field of systemic sclerosis have pointed out that the change in the macular choroidal thickness, choroidal volume and the vascularity index involved significant changes according to the severity of the disease and the vascularity (15). Also, in the new investigations of keratoconus, retinal neurovascular parameters have altered greatly implying that primary conditions that are non-vascular can affect retinal microcirculation (16).

The ocular tissue sensitivity to systemic vascular pathology is further underscored by the fact that choroid is involved in systemic vasculitis. A systematic review revealed extensive choroidal and retinal changes in the vasculitis and establishes the importance of ocular imaging in the disease activity identification procedure (17). The results are in line with the present study that indicated high levels of macular thinning in hypertensive patients indicating early microvascular damage. The

current relationship between systolic blood pressure, time and macular thickness hypertension also gives credence to the progressive nature of the hypertensive retinal damage. As the blood pressure increases and the disease is extended, a cumulative micro vascular damage is caused which leads to structural changes in the retina. Interestingly, the sensitivity of OCT in revealing subclinical changes is manifested by the observation that the macular thinning is observed in patients without any clinical manifestations of hypertensive retinopathy (15). Clinical implications of this are substantial since timely intervention can be achieved by early diagnosis and avoid retinal damage that cannot be reversed.

This is because cross-sectional design is not causal and longitudinal studies are needed to establish how the macular thickness varies with time. In addition, the disparity in the management of antihypertension and lifestyle change may also have an impact on the retinal outcomes and should be included in the future studies (14). This research has come up with great evidence to show that the macular thickness is reliable and sensitive parameter to indicate retinal microvascular damage in systemic hypertension. The implementation of the OCT-based assessment in the everyday clinical practice may assist in enhancing the early diagnosing, risk assessment, and the introduction of therapeutic measures intended to prevent the development of vision-endangering complications and pathological changes in the vascular system.

Conclusion

The paper concludes that in patients with systemic hypertension, the macular thickness would be a useful histomorphological variable that reflects retinal microvascular damage. The mentioned reduction of the central and average macular thickness in hypertensive individuals is a marker of early structural alterations in retinal microcirculation even though no hypertensive retinopathy is observed. These findings illustrate optical coherence tomography as a non-invasive diagnostic tool to detect subclinical retinal changes in its sensitivity. The close association between the level of blood pressure and macular thinning and the length of hypertension also serves as the confirmation that the microvascular damage is progressive in relation to chronic hypertension. The point is that these changes must be noticed at the early stage so that some intervention and preventing of complications which can lead to the loss of a vision can be made. The retinal imaging as the component of the routine check-up of hypertensive patients can contribute to the enhancement of the clinical decision-making and risk evaluation. It is recommended that longitudinal studies should be conducted in the future to validate these findings and to establish whether or not the macular thickness is prognostic in systemic vascular diseases.

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