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DIAGNOSTIC CHANGES IN THE EYE AS A CRITERION FOR METABOLIC SYNDROME

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Annotation. Metabolic syndrome has emerged as a worldwide health hazard to modern lifestyles, representing a range of metabolic disorders and a risk factor for cardiovascular disease. Although interesting and compelling evidence is being collected, it raises awareness of the need for further research in this area to continue to strengthen these associations and uncover the pathological processes that support them. Ultimately, it targets patients with metabolic syndrome as a group of individuals at increased risk of developing age-related eye disease and vision loss.

Key words: metabolic syndrome, retinopathy, changes in retinal vessels.

Relevance. Metabolic syndrome has emerged as a worldwide health hazard to modern lifestyles, representing a range of metabolic disorders and a risk factor for cardiovascular disease. Although interesting and compelling evidence is being collected, it raises awareness of the need for further research in this area to continue to strengthen these associations and uncover the pathological processes that support them. Ultimately, it targets patients with metabolic syndrome as a group of individuals at increased risk of developing age-related eye disease and vision loss.

Purpose of the study. This review aims to collect published evidence supporting the association between visual changes and metabolic syndrome, and to examine the associated physiopathological processes that accompany this syndrome and lead to these diseases.

Material and methods. Both retinal imaging and digital image analysis provide non-invasive assessment of retinal microvascular caliber in vivo. Retinal microvascular abnormalities predict an increased risk of diabetes, hypertension, coronary heart disease, stroke, and mortality.

Results and discussions. Metabolic syndrome is characterized by multifactorial pathological changes such as obesity, hyperglycemia, hypertension and dyslipidemia. Abdominal obesity and insulin resistance are considered the main factors in the development of the syndrome. In medical practice, it is recommended to establish MS in a patient with a combination of abdominal obesity and two of four factors: an increase in the level of triglycerides in the blood (TG) (more than 1.7 mmol/l), a decrease in the level of high-density lipoproteins (HDL) (less than 1.3 mmol /l in men and less than 1.29 mmol/l in women), an increase in blood pressure by more than 130 and 85 mmHg. Art., an increase in

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fasting plasma glucose levels by more than 5.6 mmol/l. Eye diseases such as diabetic retinopathy, central retinal artery occlusion, cataracts, age-related macular degeneration, glaucoma, and dry eye syndrome are associated with many components of metabolic syndrome. However, their relationship with metabolic syndrome has become a topic of research in its own right.

Several studies also show an association between metabolic syndrome and the retinal microvasculature. A study of atherosclerosis risk in communities found that metabolic syndrome was associated with microvascular changes in the retina. The Australian Heart Eye Study found that metabolic syndrome was associated with narrower retinal arterioles but not wider retinal venules in individuals at high risk of coronary heart disease.
Most of these studies were population-based or included patients at high risk of developing diabetes or heart disease[1]. Studies have reported associations between components of metabolic syndrome and eye diseases such as dry eye syndrome. And tear function was studied in patients with metabolic syndrome. The authors found dysfunction of the lacrimal gland and the volume of tear fluid in these patients. The Schirmer test, tear breakup time, and ocular surface fluorescein staining index are the most commonly used tests in the diagnosis and follow-up of dry eye syndrome. Tear osmolarity is a valuable method for identifying dry eye syndrome [2]. In Wang's study S. B examined cross-sectional associations between metabolic syndrome and retinal vascular caliber in adults at high risk for cardiovascular disease. They reported
that individuals with metabolic syndrome were more likely to have narrowing
of the caliber of retinal arterioles, regardless of age, gender,
smoking status, and the caliber of associated vessels. This association
persisted in patients without diabetes. In contrast, in participants without CAD
and without hypertension, there was no association between metabolic
syndrome and retinal arteriolar caliber. Blood pressure,
waist circumference, and serum triglyceride levels were distinct components of metabolic syndrome that showed inverse associations with retinal arteriolar caliber, suggesting that the association is likely driven primarily by higher blood pressure, as well as obesity and dyslipidemia. They found no significant association between metabolic syndrome and retinal vein caliber.
Other studies, such as the ARIC, Funagata, and Handan
Eye studies, have reported narrowing of retinal arteriolar caliber in association with metabolic syndrome. The magnitude of the difference in adjusted
mean retinal arteriolar caliber between patients with
and without metabolic syndrome was slightly larger in our cohort (4.30 mm) compared
with that observed in Funagata (2.95 mm) and the
Handan Eye Study (3 ,60mm). These results indicate that in patients at high risk for cardiovascular disease, narrowing of retinal arteriolar caliber is more closely associated with common metabolic syndrome than widening of retinal vein caliber. Also, a study in Japan suggests that retinal arteriolar narrowing is also associated with the occurrence of metabolic syndrome. However, some
previous studies of metabolic syndrome have shown an association
between metabolic syndrome and retinal arteriolar narrowing and
venous dilatation, while others have identified associations
with only one or other of these vascular signs. In the Funagata study, metabolic syndrome was associated with wider venous diameter, while the ARIC study demonstrated an

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association with focal arteriolar narrowing. In the Multi-Ethnic Study of Atherosclerosis, venous dilation was associated with obesity, hypertriglyceridemia, low HDL, and hyperglycemia, and arteriolar narrowing was associated with hypertension. Narrowing of retinal arteriolar caliber is thought to indicate changes in endothelial function associated with hypertension and aging, including intimal thickening, medial hyperplasia, hyalinization, and arteriolar sclerosis. Generalized constriction of retinal arterioles may also reflect abnormalities of vasomotor constriction affecting vascular smooth muscle cells and neuromuscular junctions. Research has previously shown that in children, obesity is associated with arteriolar narrowing, possibly due to endothelial dysfunction. Previously, the Blue Mountains Eye Study also showed that dyslipidemia is associated with arteriolar narrowing. On the other hand, wider retinal vein caliber is widely associated with systemic inflammation and related conditions, including atherosclerosis, smoking, and hypercholesterolemia. Retinal vein dilatation also appears to be associated with biomarkers of malnutrition, especially albumin and transthyretin [3-6]. Ocular complications reported to be associated with metabolic syndrome include retinopathy, high intraocular pressure, cataracts, macular degeneration, and exophthalmitis. The alarming increase in the prevalence of obesity or metabolic syndrome is likely to further exacerbate the risk of obesity-related ophthalmic changes. Retinal diseases, including age-related macular degeneration (AMD), retinitis pigmentosa (RP), and diabetic retinopathy (DR), represent a leading cause of irreversible blindness in developed and developing countries. While AMD is characterized by loss of central vision, RP is typically characterized by rod and cone dystrophy, resulting in loss of rod and cone photoreceptors and predominantly degeneration of rod photoreceptors. In some populations, obesity is a major component of metabolic syndrome, which is associated with microvascular changes in the retina. In addition, retinal degeneration has been reported as a component of obesity [7–10].

The results of the study by Matthias Huber et al may indicate that features of metabolic syndrome are exacerbated by microvascular changes. However, they only looked at one aspect
of microangiopathy in a limited area of the rat retina. Moreover, other aspects of microangiopathy, as they can be studied in humans throughout the fundus using more sophisticated methods, were not determined in the rat model studied. Taken together, these data indicate the presence of underlying microangiopathy in the retina of obese animals. As a consequence of discrete morphological damage to the retina in obese animals, we next asked whether functional deficits could be observed in this setting of microangiopathy in the absence of major structural changes in the retina. The electroretinograms of obese rats were normal, indicating that the processing of light signals of varying intensities was essentially intact. Therefore, it can
be concluded that the obese rats retained their visual ability, indicating that neural networks and complex interactions with glial cells were not fundamentally disrupted by metabolic changes in obese animals. In this regard, the above-described morphology with intact retinal integrity correlated well with overall good ERG function. However, several individual tests, such as scotopic and photopic ERG, 30 Hz flicker ERG, may be associated with impaired bipolar or Müllerian glial cell function. Since further sensory bipolar cell activity remained unchanged on electroretinograms, Müller cells were the most likely cause of b wave reduction. Thus, Müller cells may be a critical cell type in the initial pathogenesis of early retinopathy in type 2 diabetes with metabolic syndrome. They may be responsible for the modulation of many key functions in retinopathy, as they are involved, for example, in

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angiogenesis. In the maintenance of blood-retinal barriers, in the metabolism of neurotransmitters and in the homeostasis of retinal fluid. This suggests that the pathogenesis associated with Müller cells
is characteristic of type 2 diabetes with obesity and metabolic syndrome,
since in STZ-induced diabetic rats, the reduction of b-waves usually occurs not before, but simultaneously with changes in the amplitudes of oscillatory potentials. However, changes in oscillatory potentials in obese animals were limited by a small but significant increase in latency. This characteristic of oscillatory potentials
precedes leakage on fluorescein angiography and is therefore consistent with the mild microangiopathy found in the morphological analysis of this study. In humans, this ERG pattern is typical of diabetic patients with discrete microangiopathy, but not with more profound fundus changes such as hard exudates that represent later stages of diabetic retinopathy. Related to this is increased latency of oscillatory potentials without decreased amplitude in obese rats in combination with early microangiopathy is similar to early diabetic retinopathy in humans. The findings in obese animals are complemented by subtle photoreceptor dysfunction indicated by altered wave parameters such
as decreased amplitude, increased latency, and higher
wave values. Notably, altered photoreceptor function has also been described in a rat model of induced diabetes based on varying findings. In addition, disturbances in a- and b-wave parameters may be a consequence of circulatory disorders characteristic of diabetic retinopathy, and therefore may correlate with morphologically described microangiopathy

Microvascular density is defined as the number of microvessels per unit volume of tissue or, more commonly, per cross-sectional area of tissue. A decrease in microvascular density is called microvascular rarefaction and often precedes diagnosable symptoms associated with certain cardiovascular diseases. In particular, rarefaction is closely associated with cases of mild hypertension and type 2 diabetes mellitus (T2DM). Microvascular rarefaction is often found in multiple tissue types after initial onset due to the migratory nature of endothelial inflammation. This is evident in cortical tissue from obese rats, where a depression of 20% relative to controls developed in parallel with a depression in skeletal muscle. The results of this study suggest that reduced bioavailability of the vasodilator nitric oxide (NO) corresponds to rarefaction and may be the underlying mechanistic cause of this vascular outcome in metabolic dysfunction. Other vasodilatory factors such as endothelial hyperpolarizing factor of mental origin may also play a significant role in maintaining vascular tone. Clinical studies in patients with hypertension have shown that individuals with primary hypertension exhibit microvascular rarefaction in the skin tissue, whereas previous theories mainly were focused on reducing arteriolar diameter. The observed rarefaction usually occurs first as a structural abnormality, suggesting that vascular rarefaction is likely a factor in hypertension rather than an outcome, although it is certainly possible that they act in a feedback fashion. This is further supported by animal studies, where it was observed that antihypertensive drugs attenuate microvascular rarefaction if taken before the development of hypertension. The vacuum can be classified as functional (the vessel receives little or no blood flow) or structural (the vessel physically wears away until it becomes anatomically absent). Under functional rarefaction, nonperfused vessels at rest can still participate in perfusion in response to increased metabolic demands. Compared to anatomical vacuum, functional vacuum provides flexibility and adaptation to increased
demands, which may be a key factor in cardiovascular endurance. The relatively permanent

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loss of functional vasculature associated with structural rarefaction reduces the upper limit of the metabolic demands that the tissue can support. Under conditions of increased demand, the remaining functioning vessels may be overperfused to compensate for the lost vessels, subjecting them to increased pressure according to Darcy's law of blood flow. Mathematical models suggest that arteriolar rarefaction can increase peripheral resistance by approximately 20% in the vascular bed. However, the actual rarefaction in vivo may be greater if excess perfusion activates the myogenic contraction response, where vessels actively constrict in response to increased blood pressure. Decreased functional microvasculature reduces the overall efficiency of oxygen and nutrient delivery, resulting in unmet metabolic needs in certain local tissues. In this case, the organs become deficient in functional units, increasing the risk of hypoxia, as can be seen in cases of hypertensive end-organ damage and diabetic limb amputations. Increased heterogeneous perfusion due to microvascular rarefaction also limits the delivery and therefore the function of most signaling molecules, including insulin. Microvascular rarefaction is associated with insulin resistance due to Although microvascular remodeling may indicate impending disease, there is considerable uncertainty given vascular differences among species, sex, organ type, genetic predisposition, and experimental conditions. Moreover, most tissue layers in vivo do not correspond to simple models in which all vascular units have the same properties and perfusion behavior. Models may also not account for angiogenesis, where new vessels are created by proangiogenic factors that alter vascular perfusion and pathways [14].

Conclusion. In conclusion, this review suggests that microvascular narrowing of retinal arterioles is associated with metabolic syndrome in individuals .
This may reflect the influence of high blood pressure, obesity and dyslipidemia, a process that may be mediated by endothelial dysfunction.

LITERATURE/ REFERENCES

1. American Heart Association (AHA). About Metabolic Syndrome. Available at: https://www.heart.org/en/health-topics/metabolic-syndrome/about-metabolic-syndrome. Accessed June 25,2021
2. Sevil Karaman Erdur, Rukiye Aydin, Mustafa Ozsutcu, Oktay Olmuscelik, Mustafa Eliacik, Goktug Demirci & Mehmet Selim Kocabora (2017): The Relationship between Metabolic Syndrome, Its Components, and Dry Eye: A Cross-Sectional Study, Current Eye Research, DOI :10.1080/02713683.2017.1280511
3. Wang SB, Mitchell P, Plant AJH, et al . Br J Ophthalmol 2016; 100 : 1041–1046 .
4. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome — a new world-wide defi nition . A Consensus Statement from the International Diabetes Federation. Diabet Med 2006;23:469 – 80
5. Jongh RT, Serne EH, RG IJ, et al . Impaired microvascular function in obesity: implications for obesity-associated microangiopathy, hypertension, and insulin resistance. Circulation 2004;109:2529 – 35.

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

6. Wong TY, Duncan BB, Golden SH, et al . Associations between the metabolic syndrome and retinal microvascular signs: the Atherosclerosis Risk in Communities study. Invest Ophthalmol Vis Sci 2004;45:2949 – 54.
7. Kishore Kumar Godisela, Singareddy Sreenivasa Reddy, Chekkilla Uday Kumar, Natarajan Saravanan, Paduru Yadagiri Reddy, Monica M. Jablonski, Radha Ayyagari, Geereddy Bhanuprakash Reddy: Impact of obesity with impaired glucose tolerance on retinal degeneration in a rat model of metabolic syndrome/Molecular Vision 2017; 23:263-274 <http://www.molvis.org/molvis/v23/263> Received 3 December 2016 | Accepted 12 April 2017 | Published April 14, 2017
8. Bohlman H. Communicating the ocular and systemic complications of obesity to patients. Optometry 2005; 76:701-12. [PMID: 16361032] .
9. Cheung N, Wong TY. Obesity and eye diseases. Surv Ophthalmol 2007; 52:180-95. [PMID: 17355856] .
10. Klein R, Peto T, Bird A, Vannewkirk MR. The epidemiology of age-related macular degeneration. Am J Ophthalmol 2004;137:486-95. [PMID: 15013873] .
11. Matthias Huber, Peter Heiduschka, Focke Ziemssen, Juliane Bolbrinker and Reinhold Kreutz: Microangiopathy and visual deficits characterize the retinopathy of a spontaneously hypertensive rat model with type 2 diabetes and metabolic syndrome/Hypertension Research (2011) 34, 103–112; doi:10.1038/hr.2010.168; published online 7 October 2010.
12. Cheung N, Wong TY. Diabetic retinopathy and systemic vascular complications. Prog Retin Eye Res 2008; 27 : 161–176.
13. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, Matthews DR. UKPDS 50: risk factors for incidence and progression of retinopathy in Type II diabetes over 6 years from diagnosis. Diabetologia 2001; 44 : 156–163.
14. Angelina Wong Shu Qing Chen Brayden D. Halvorson Jefferson C. Frisbee/Microvessel Density: Integrating Sex-Based Differences and Elevated Cardiovascular Risks in Metabolic Syndrome; J Vasc Res 2022;59:1–15