

What do Retinal Vessels Reveal about Systemic Disease? Retinal Vessels and Systemic Disease – Basic Findings

Hans-Jürgen Grein

University of Applied Sciences Lübeck, Fielmann Akademie Schloss Plön, Plön, Germany

ABSTRACT

A number of systemic disorders are attended by distinct changes in blood vessels. The retinal vessels can easily be inspected with an ophthalmoscope. Some changes in retinal vessels allow us to draw direct conclusions about the status of blood vessels in the entire body. Major systemic diseases, such as diabetes or hypertension, can lead to typical changes in the retinal vessels with the resulting retinal pathology. Changes in the retinal vessels can also be an indicator for some specific ocular diseases. Early diagnosis and treatment of such diseases often prevent long-term damage or even blindness. Therefore, the evaluation of retinal arteries and veins should be a crucial part of an eye examination. In the following some basic principles of retinal findings and their correlation with systemic disease shall be discussed.

Key words: *retinal vessels, diabetes, hypertension, ophthalmoscopy*

Introduction

Blood carries out a multitude of functions and is supplied to all areas of the organism via the vascular system. If we look at the retina with an ophthalmoscope, we can see the vessels of the retina's internal blood supply. The vessels spread out radially from the papilla into all four quadrants. The vessels lie directly on the retina and are therefore in an excellent position for inspection. The entire course of the arteries and veins can be seen on the retina. In no other part of the body is it possible to observe the blood vessels so directly without the use of complicated technical equipment.

The structure of the vessels in the retina closely resembles that found in other parts of the body. Systemic changes in the blood vessels can affect all regions of the body to the same extent. Findings on retinal vessels therefore often mirror the condition of the vessels in the brain or in the heart. Disorders in the vessels give rise to typical findings on the retina that allow us to draw conclusions about serious common diseases.

In this article some of the fundamental principles of retinal changes shall be explained. A comprehensive account can be found in current literature on the subject¹⁻⁵. For a clinical pictorial documentation of eye disease see for example www.atlasophthalmology.com.

Structure of the Vessels

Arteries and veins differ greatly in terms of their wall structure. This is due to the vastly differing pressure level in the two types of vessel. As oxygen-rich blood comes from the heart, it is fed via the aorta into finer and finer arteries and ultimately into arterioles. The pressure in the arteries and arterioles is generated by the action of the heart. As blood is ejected in thrusts from the left-hand chamber of the heart, fluctuations are created in the arteries which, for example, can be measured at the arm. Here, the typical pressure within the vessel lies between 120 and 80 mmHg. A strong layer of muscle and the elastic properties of the arterial walls allow the vessels to withstand this pressure. The blood pressure in the arterioles falls and the pressure fluctuations cease. The blood is transported through further ramifications and into the capillaries. These are hair-fine vessels that permeate the tissue. The blood flows slowly through the capillaries and releases the oxygen. Subsequently the blood collects in larger and larger venules and veins and is finally fed back to the heart. The blood pressure in the veins is considerably lower than in the arteries. The walls of the veins are therefore thinner and have a finer layer of muscle. Larger veins have »butterfly« valves to prevent blood from flowing back away from the heart.

Arteries are usually accompanied by veins. When looking at the retina, we see the central artery and the central vein that already branch off in the papilla. These and subsequent branches run along on the retina. They supply the inner retina, therefore the bipolar and ganglion cells. The receptors are supplied by the choroid.

The inside of the fine capillary vessels is lined with endothelial cells. They are encased with pericytes. The diameter of the capillaries is so small that only single red blood corpuscles can pass through. Oxygen from the blood has to diffuse through the capillary wall into the tissue. The capillaries of the retina are situated in the bipolar cell layer. In addition to the red and the white blood corpuscles, the blood also consists of the blood plasma. This contains not only a variety of proteins, but also lipids and water. The capillaries of the retina are non-fenestrated. Sealed junctions between the endothelial cells, the so-called »tight junctions«, prevent the uncontrolled leakage of substance into the tissue.

Tight junctions are also situated in the area of the retinal pigment epithelium among the receptors. There, they ensure that no fluid from the choriocapillaris infiltrates into the retina. In sealing off the capillaries and the pigment epithelial cells, the tight junctions act as a so-called internal and external blood-retina barrier. In healthy eyes they shield the retina against edemas. In the event of disease, the tight junctions can lose their function, which is accompanied by the increased escape of fluid into the retina. The pigment epithelial cells ensure that excess fluid is removed from the retina. If their capacity for transporting fluids is overstretched, this results in retinal edemas.

Pathologic Principles

Many retinal changes may be traced back to two principle vessel disorders. The resulting findings are identical for different diseases (Table 1).

Barrier disorders are a sign of the collapse of the tight junctions in the retinal vessels. The inner or outer blood-retina barrier is no longer able to function correctly. A typical consequence is the accumulation of fluid outside of the retinal cells, that is to say, an extracellular edema. In addition to aqueous blood components, red blood corpuscles also leak out and cause haemorrhages in the retina. The form of the haemorrhage depends on the layer in which the blood collects. Haemorrhages in the area of

the bipolar cells appear as spots or patches. Blood in the area of the ganglion cell fibres spreads out along the course of the fibres and has a flame-like appearance. Pre-retinal haemorrhages between the retina and the vitreous body often appear more extensive and may reveal a blood level as the blood descends according to gravity in a pouch like sheath. The haemorrhage is referred to as boat-shaped⁶.

Lipid-like substances also leak out of the blood vessels. These remain after reabsorption of the aqueous components as yellowish deposits, so-called hard exudates, in the retina. If fluid leaks from the choriocapillaris through the pigment epithelium into the retina, serous detachment of the receptors from the pigment epithelium can occur.

A second fundamental problem area in the retina is caused by circulatory disorders. In such cases, a lack of oxygen and nutrients occurs in the cell, e.g. in the event of arterial obstruction. Pumping mechanisms in the cell membrane become damaged and the cells react with an intracellular edema. The nerve fibres of the ganglion cells are also damaged by the lack of oxygen. Axoplasm comes out of the nerve cell axons and into the retinal tissue and creates the fluffy-looking cotton wool spots. The circulatory situation can be further exacerbated if arterio-venous shunt vessels are formed. The oxygen-rich blood then drains off into the venous system without having released any oxygen. These are referred to as intraretinal microvascular abnormalities. A later consequence of oxygen deficiency can be the growth of new vessels on the retina. These neovascularisations consist of inferior vessels that lead to further exsudations and haemorrhages. Ultimately, fibrovascular membranes can develop, which can lead to tractional detachment of the retina

Retinal Findings in Patients with Diabetes

Healthy retinal vessels have an even diameter and follow a slightly gyrose path. The vascular bifurcations are acute angled. A narrow light reflex can be seen on the vessels. The ratio of the width of arteries to their associated veins is 2:3. The A/V estimation should be made before the third bifurcation.

Among diabetics, many typical retinal changes can be observed that arise from the aforementioned pathological principles of disorders in the barrier and in the circulation. The disease is triggered by a microangiopathy. The endothelial cells and pericytes of the capillaries become damaged. The basal membrane thickens and the release of oxygen into the tissue is impeded. Small bulges, so-called microaneurysms, can occur on the capillaries. If the vessels rupture, then haemorrhages into the tissue can be observed. The venules show pathological changes, too. The diameter of the vessels fluctuates greatly and venous beading can occur. In the transition into proliferative diabeticretinopathy newly formed vessels are of inferior quality. Fibrous or fibrovascular tissue

TABLE 1
FINDINGS ON THE RETINA AND THEIR PATHOGENESIS³

Breakdown of the blood-retinal barrier	Ischemia
Extracellular edema	Intracellular edema
Haemorrhage	Cotton wool spots
Hard exudates	Intraretinal microvascular abnormalities
Leakage under the retina	Retinal neovascularisation

TABLE 2
CURRENT CLASSIFICATION OF DIABETIC RETINOPATHY⁹

Stadium	Findings
moderate non-proliferative DR (Background DR)	<ul style="list-style-type: none"> • Haemorrhages • Microaneurysms • Emergence hard exsudates
Severe non-proliferative DR	<ul style="list-style-type: none"> • Multiple retinal haemorrhages • Cotton wool spots • Venous beading • Intraretinal microvascular abnormalities
Diabetic Maculopathy	<ul style="list-style-type: none"> • Thickening of the macula in the centre • Hard exsudates around the macula • Macula edema (prob. cystoid)
Proliferative DR	<ul style="list-style-type: none"> • Neovascularisations • Fibrovascular membranes • Vitreous haemorrhage • Tractional retinal detachment

attaching to the sensory retina pulls it from the retinal pigment epithelium. Without therapy there is the danger of retinal detachment and finally blindness^{7,8}.

Retinal Findings in Patients with hypertension

Hypertension and arteriosclerosis often appear together. A focal or general arteriolar constriction and stretched vessels may be early findings. If the blood-retina barrier breaks down, haemorrhages, cotton wool spots and hard exsudates are possible. The hard exsudates can attach themselves around the macula and are referred to as macular star. In serious cases it is possible

TABLE 3
STAGES OF HYPERTENSIVE RETINOPATHY ON THE BASIS OF KEITH, WAGENER AND BARKER¹⁰

Hypertensive retinopathy	
Stage 1	<ul style="list-style-type: none"> • Arteriolar constriction • Mild venous tortuosity • Arteriosclerosis
Stage 2	<ul style="list-style-type: none"> • AV nicking • Crossing signs • Corkscrew tortuosity • Copper wire arterioles
Stage 3	<ul style="list-style-type: none"> • Cotton wool spots • Hard exsudates • Haemorrhages • Silver wire arterioles • Macular edema
Stage 4	<ul style="list-style-type: none"> • Papilledema

to see the macula and papillar edemas. The arterioles display a wide intensive light reflex (copper wire or silver wire) and variations in calibre. The arteries cross the veins in the form of an S and at an obtuse angle (Salus' sign). At the point where the artery crosses the vein, the latter often displays an hourglass-like constriction (Gunn's sign). This is caused by the thickening of the conjoint adventitia in the presence of arteriosclerosis. Another indication of high blood pressure is the radial pattern of corkscrew-like venules wrapped around the macula (Guist's sign). They are produced by a throttled blood flow in the area of arteriovenous crossing changes. Blood stasis causes a thickening of the veins distally of a crossing sign (Bonnet's sign). The vascular bifurcations can also become conspicuous under high blood pressure. Obtuse-angled bifurcations are formed that are reminiscent of the Greek omega (Omega sign).

The objective of clinical classifications of the hypertensive retinopathy is to assign retinal changes to the stage of hypertension^{6,9,10}. Findings at stage 1 and 2 in particular can be detected even if high blood pressure is not ascertainable.

Findings in Retinal Vascular Inflammations

Retinal vasculitis can be a consequence of local or systemic diseases. The most common systemic diseases associated with retinal vasculitis are Behçet's disease, sarcoidosis, and multiple sclerosis. A number of other rheumatologic conditions can also cause retinal vasculitis. Bacteria (e.g. borrelia), viruses (e.g. herpes family viruses) and parasites (e.g. toxoplasma) are potential infectious agents. There are also primary ocular causes of retinal vasculitis (e.g. Eales disease, posterior uveitis).

It is typical for inflamed retinal vessels to display vascular sheathing. In this case, the vessels are encased in a whitish material as a consequence of a disorder in the blood-retina barrier. There are often inflammatory cells present in the posterior vitreous cavity. In addition to retinal haemorrhaging, neovascularisation can occur. Typical symptoms of those affected include blurred vision, altered colour perception, floaters, metamorphopsia and scotomas. In some cases subjective symptoms can also be completely absent.

Conclusion

Retinal vascular changes and the direct morphological consequences can be easily detected during an ophthalmoscopic examination. These findings can provide us with information about serious systemic or localized diseases. In such cases, a thorough diagnosis should be carried out by an ophthalmologist and possibly an internist without delay.

REFERENCES

1. YANOFF M, DUKER S, Ophthalmology (Mosby; 3rd Edition 2008). — 2. KANSKY JJ, BOWLING B, Clinical Ophthalmology: A Systematic Approach (Butterworth Heinemann; 7th edition, 2011). — 3. KAMPIK A, GARNDORFER A, ULBIG MW, Erkrankungen der Retina – Aktuelle Aspekte der Diagnostik und Therapie (UNI-MED Verlag Bremen, 2002). — 4. KELLNER U, WACHTLIN J, Retina – Diagnostik und Therapie der Erkrankungen des hinteren Augenabschnitts (Georg Thieme Verlag Stuttgart 2008). — 5. REIM M, KIRCHHOF B, WOLF S, Diagnostik am Augenhintergrund (Thieme Verlag Stuttgart 2004). — 6. CHATTERJEE S, CHATTOPADHYA S, HOPE-ROSS M, LIP PL, Journal of Human Hypertension, 16 (2002) 667. — 7. CHEUNG N, MITCHELL P, WONG TY, Lancet, 376 (2010) 124. — 8. GROSSO A, CHEUNG N, VEGLIO F, WONG TY, J Hypertens, 29 (2011) 1667. — 9. WONG TY, MITCHELL P, N Engl J Med, 351 (2004) 2310. — 10. KEITH NM, WAGENER HP, BARKER NW, Am J Med, Sci 268 (1974) 336.

H.-J. Grein

University of Applied Sciences Lübeck, Fielmann Akademie Schloss Plön, Course of Optometry, Schloss, 24306 Plön, Germany

e-mail: grein@fh-luebeck.de

KAKO KRVNE ŽILE MREŽNICE MOGU OTKRITI SUSTAVNE BOLESTI? KRVNE ŽILE MREŽNICE I SUSTAVNE BOLESTI-TEMELJNA OTKRIĆA

SAŽETAK

Brojni sustavni poremećaji mogu uzrokovati različite promjene na krvnim žilama. Krvne žile mrežnice mogu se pomoću oftalmoskopa lako pregledati. Neke promjene na njima omogućuju postavljanje direktnih zaključaka o statusu krvnih žila cijeloga tijela. Učestale sustavne bolesti kao primjerice dijabetes ili hipertenzija dovode do tipičnih promjena krvnih žila mrežnice koje rezultiraju patološkim stanjima mrežnice. Promjene na krvnim žilama mrežnice mogu također biti indikator za neke specifične očne bolesti. Rana dijagnoza i tretman takvih bolesti često prevenira dugoročna oštećenja ili čak sljepoću. Dakle, procjena stanja arterija i vena mrežnice ključni su dio pregleda oka.