# Systemic Diseases in Non-inflammatory Branch and Central Retinal Artery Occlusion An Overview of 416 Patients 

D. Schmidt ${ }^{1}$, A. Hetzel², A. Geibel-Zehender ${ }^{3}$, J. Schulte-Mönting ${ }^{4}$<br>${ }^{1}$ University Eye Hospital, ${ }^{2}$ Department of Neurology, ${ }^{3}$ Department of Cardiology, ${ }^{4}$ Institute of Medical Biometry, University of Freiburg


#### Abstract

Backoground: To determine the frequency of essential cardiovascular risk factors in different vascular ocular diseases. Methods: We compiled cardiovascular risk factor findings (RFs) from 416 patients with non-inflammatory ocular vascular occlusions in a retrospective study: 134 patients with BRAO, 253 patients with CRAO, and 29 patients with hemi-CRAO. 274 ( $65.9 \%$ ) male and 142 ( $34.1 \%$ ) female patients were examined. Mean age of all patients was 66 years (range: 18-90). The right eye was involved in 221 ( $53.1 \%$ ), left eye in 193 (46.4 $\%$ ), and both eyes in 2 patients ( $0.5 \%$ ). Results: Cardiovascular risk factors (RFs) were found in 243 patients. Three hundred and eight (308) out of 406 patients ( $75.9 \%$ ) presented with arterial hypertension. Hypertension was present in 96 patients with BRAO (73.8 \%), in 197 patients with CRAO (79.8 \%), and in 15 patients with hemi-CRAO ( $78.9 \%$ ).

RFs such as arterial hypertension, carotid artery diseases, diabetes mellitus, hyperlipidemia, hyperuricemia, and chronic smoking did not differ statistically between patients with BRAO, CRAO or hemi-CRAO. But visible emboli in retinal arteries were observed in patients with BRAO ( $47 \%$,), or hemiCRAO (41.4 \%), much more often than in patients with CRAO (11.1 \%). Conclusions: No statistical differences between the RFs of patients with BRAO, CRAO, or hemi-CRAO were noted. We maintain that every patient with retinal arterial obstruction should undergo extensive examination of essential RFs.


Key words: Central retinal artery occlusion, branch retinal artery occlusion, hemicentral retinal artery occlusions, cardiovascular risk factors

## Introduction

Early recognition of cardiovascular risk factors (RFs) is necessary to prevent infarctions in the eye or other organs. Various non-inflammatory RFs cause acute ocular vascular obstructions, such as stenoses, occlusion, or dissecting aneurysm of the internal carotid artery (ICA), sclerosis or stenoses of the aorta, blood coagulation anomalies, and cardiac diseases such as chronic
atrial fibrillation, valvular diseases, patent foramen ovale or intracardial thrombosis $[1,2,9,11,12,15$ 17, 20, 23, 25, $27-29]$.

Ros et al. [19] reported several associated systemic disorders among BRAO patients, observing hypertension in $59 \%$ of patients. Serious atherosclerotic cardiovascular disease in conjunction with angina pectoris and/or prior myocardial infarction was documented in $21 \%$ of BRAO patients. Chawluk et al. [7] reported a significant correlation between the degree of carotid stenosis and the number of vascular risk factors identified in individual patients. They also found that the risk factors were more common in CRAO and BRAO patients than in amaurosis fugax (AF) patients. Bull et al. [6] emphasized that patients with AF were more likely to have a significant carotid artery stenosis than those with asymptomatic Hollenhorst plaques or retinal artery occlusion. Douglas et al. [10] found a strong association between CRAO and ipsilateral carotid artery disease, with a significantly higher incidence of subsequent ipsilateral stroke in CRAO patients with carotid disease. Bruno et al. [5] observed that patients with retinal emboli showed a higher prevalence of hypertension and heterogenous or echolucent carotid plaques, and they smoked more.

Biousse et al. [3] found that $62 \%$ of 146 patients with extracranial carotid artery dissection presented ophthalmologic signs and symptoms ( $91 / 146$ ). $28 \%$ of those patients had suffered transient monocular visual loss. Klein et al. [15] found that persons who were 65 years or older at baseline were 2.4 times as likely to develop a retinal embolus compared with persons 43 to 54 years of age at baseline. Savino et al. [21] showed that patients with retinal occlusions without visible emboli had a survival rate comparable to the matched control. But patients with visible emboli demonstrated a strikingly diminished survival rate. Cugati et al. [8] found that increasing age was significantly associated with incident emboli. In an older population, the 10year cumulative incidence of retinal emboli was 2.9\% among 2,361 persons at risk.

RFs cause different vascular obstructions in the eye. One-third to one-fourth of the patients with CRAO and BRAO revealed $\geq 50 \%$ stenoses or occlusions of the ICA, but, only one out of 51 patients with anterior ischemic optic neuropathy (AION) showed a high de-
gree ICA stenosis [22]. Wilson et al. [29] assumed that RFs in patients with CRAO differ from those in patients with BRAO. We therefore compared the risk factors in these ocular diseases.

## Methods

RFs of 416 patients, 274 of whom were male ( $65.9 \%$ ) and 142 female ( $34.1 \%$ ), were examined in the University Eye Hospital Freiburg:
There were 134 patients with BRAO, 253 with CRAO, and 29 with hemi-CRAO from 1980 to 2004 (Table 1).

Table 1. 416 patients with retinal arterial occlusions.

| patients | males | females |
| :--- | :--- | :--- |
| BRAO <br> n: 134 | $91(67.9 \%)$ | $43(32.1 \%)$ |
| CRAO <br> n: 253 | $166(65.6 \%)$ | $87(34.4 \%)$ |
| hemi-CRAO <br> n: 29 | $17(58.6 \%)$ | $12(41.4 \%)$ |
| total: 416 | $274(65.9 \%)$ | $142(34.1 \%)$ |

352 patients were examined in the Department of Internal Medicine, of whom there were 119 with

BRAO, 208 with CRAO, and 25 with hemi-CRAO. 294 patients underwent echocardiography, of whom 91 had BRAO, 183 CRAO, and 20 hemi-CRAO. Blood pressure measurements were taken in 406 patients: 130 with BRAO, 247 with CRAO, and 29 with hemiCRAO.

In the Department of Neurology examinations of the carotid arteries with Duplex/Doppler sonography were performed in 366 patients: 104 with BRAO, 238 with CRAO and 24 with hemi-CRAO.

Age: 416 consecutive patients (mean age: 66 years; range: 18-90); 134 patients ( 32.2 \%) with BRAO 65.4 (range: 22-90) years, 253 patients ( $60.8 \%$ ) for those with CRAO 66.8 (range: $18-90$ ) years, and 29 patients ( $7 \%$ ) with hemi-CRAO 61.7 (range: 22-77) years (Table 2).

We set up three groups according to patient's age: the older patients $>65$ years of age (Group 3), the middle-aged group at 45-64 years of age (Group 2), and the young group of patients $<45$ years of age (Group 1).

Gender: All examinations revealed a distinct difference between male and female patients: male patients were observed to suffer more often from CRAO and BRAO than female patients.

We noted no statistical difference between the three diseases (contingency tables) with respect to gender.

## Involved Eye

There was no significant difference in the number of

Table 2. Three age groups.

|  | BRAO: $\mathrm{n}=134$ | CRAO: $\mathrm{n}=253$ | hemi-CRAO: $\mathrm{n}=29$ |
| :---: | :---: | :---: | :---: |
| Group 3 | m: 51 (56 \%) | m: 100 (60.2 \%) | m: 8 (47.1 \%) |
|  | f: $23(53.5 \%)$ | f: $64(73.6$ \%) | f: $7(58.3$ \%) |
| Group 2 | m: 34 (37.4 \%) | m: 56 (33.7 \%) | m: 8 (47.1 \%) |
|  | f: 17 (39.5 \%) | f: 18 (20.7\%) | f: $4(33.3$ \%) |
| Group 1 | m: 6 (6.6\%) | m: $10(6.0$ \% $)$ | m: $1(5.9 \%)$ |
|  | f: $3(7 \%)$ | $\mathrm{f}: \quad 5(5.7 \%)$ | f: $1(8.3 \%)$ |
| total: | m: 91 (67.9 \%) | m: 166 (66 \%) | $\mathrm{m}: 17$ (58.6 \%) |
|  | f: 43 (32.1 \%) | $\mathrm{f}: \quad 87(34.4 \%)$ | f: $12(41.4 \%)$ |

Table 3. Involved eye in 416 patients with retinal arterial occlusions.

| patients | right eye | left eye | both eyes |
| :--- | :--- | :--- | :--- |
| BRAO <br> n: 134 | $\mathrm{n}: 64(47.8 \%)$ | $\mathrm{n}: 68(50.7 \%)$ | $\mathrm{n}: 2(1.5 \%)$ |
| CRAO <br> $\mathrm{n}: 253$ | $\mathrm{n}: 144(56.9 \%)$ | $\mathrm{n}: 109(43.1 \%)$ | - |
| hemi-CRAO <br> $\mathrm{n}: 29$ | $\mathrm{n}: 13(44.8 \%)$ | $\mathrm{n}: 16(55.2 \%)$ | - |
| total: 416 | $221 \quad(53.1 \%)$ | $193(46.4 \%)$ | $2(0.5 \%)$ |

Table 4. Frequency of Cardiovascular Risk Factors in patients with retinal arterial occlusions.

| Number of RF | BRAO total 134 | CRAO total 253 | hemi-CRAO total: 29 | total of all groups together |
| :--- | :---: | :--- | :--- | :--- |
| 1 | 8 | 10 | 4 | $22(9.1 \%)$ |
| 2 | 12 | 40 | 4 | $56(23 \%)$ |
| 3 | 18 | 39 | 4 | $61(25.1 \%)$ |
| 4 | 24 | 36 | 3 | $63(25.9 \%)$ |
| 5 | 5 | 18 | $34(14 \%)$ |  |
| 6 |  | 5 | $5(2.1 \%)$ |  |
| 7 | 1 | $159(62.8 \%)$ | $16(55.2 \%)$ | $243 \%)$ |
| total | $68(50.7 \%)$ |  |  |  |

Table 5. Blood pressure examinations in 406 patients with retinal arterial occlusions.

|  | BRAO <br> (89 males) | BRAO <br> (41 females) | CRAO <br> (162 males) | CRAO <br> (85 females) | hemi-CRAO (12 males) | hemi-CRAO <br> (7 females) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Group 3 | 42 (47.2 \%) | 19 (46.3 \%) | 86 (53.1 \%) | 52 (61.2 \%) | 7 (58.3 \%) | 4 (57.1 \%) |
|  | $\begin{aligned} & \text { RR>190/100: } 15 \\ & (16.9 \%) ; \\ & R R>160 / 95: 12 \\ & (13.5 \%) \end{aligned}$ | $R R>190 / 100: 7+$ <br> very high values: $\begin{aligned} & 2 \text { ( } 4.9 \%): 9 \\ & \text { (17.1\%); } \end{aligned}$ | $\begin{aligned} & \mathrm{RR}>190 / 100: 27 \\ & +2 \text { patients } \\ & \text { with very high } \\ & \text { values } \\ & 29(17.9 \%) \text {; } \end{aligned}$ | $\begin{aligned} & \mathrm{RR}>190 / 100: 19+ \\ & 3 \text { with } \\ & \text { very high values } \\ & 22(25.9 \%) \text {; } \end{aligned}$ | $\begin{aligned} & \mathrm{RR}>190 / 100: 4 \\ & (23.5 \%) ; \end{aligned}$ | $\begin{aligned} & \text { RR>190/100: } 2 \\ & (28.6 \%) ; \end{aligned}$ |
|  | $\begin{aligned} & \text { RR>140/90: } 3 \\ & (3.4 \%) ; \end{aligned}$ | $\begin{aligned} & \text { RR>160/95: } 2 \\ & (4.9 \%) ; \end{aligned}$ | $\begin{aligned} & \text { RR>160/95: } 11 \\ & (6.8 \%) ; \end{aligned}$ | $\begin{aligned} & \mathrm{RR}>160 / 95: 9 \\ & (10.6 \%) ; \end{aligned}$ | without detailed values: 1 | without exact values: 1 |
|  | without detailed value: 12 | $\begin{aligned} & \text { RR>140/90: } 1 \\ & (2.4 \%) ; \end{aligned}$ <br> without detailed value: 7 | $\begin{aligned} & \text { RR>140/90: } 5 \\ & (3.1 \%) ; \end{aligned}$ <br> without detailed value: 41; | $\begin{aligned} & \mathrm{RR}>140 / 90: 2 \\ & \left(2.4^{\%} \%\right) ; \\ & \\ & \text { without detailed } \\ & \text { values: } 19 \text {; } \end{aligned}$ |  |  |
|  |  |  |  |  |  |  |
| Group 2 | $22^{*}(24.7 \%)$ <br> 2 patients with very high hypertension | 11 (26.8 \%) | 37 (22.8 \%) | 16 (18.8 \%) | 5 (41.7 \%) | $\begin{aligned} & 3(42.9 \%) \\ & \text { including: } \\ & \text { RR>190/100: } 2 \\ & (28.6 \%) \\ & R R>140 / 90: 1 \\ & (14.3 \%) \end{aligned}$ |
|  |  | RR>190/100: 4 (\%); | $R R>190 / 100$ : 3 patients with very high values | $\begin{aligned} & \text { RR }>190 / 100: 2 \\ & +2 \text { with } \\ & \text { very high values } \\ & 4(4.7 \%) ; \end{aligned}$ | $\begin{aligned} & \text { RR>190/100: } 2 \\ & (16.7 \%) \end{aligned}$ |  |
|  | $\begin{aligned} & \text { RR>190/100: } 5 \\ & (5.6 \%) ; \end{aligned}$ | $\begin{aligned} & \text { RR>160/95: } 1 \text { (\%) } \\ & \text { + patient with very } \\ & \text { high values: } 1) ; \end{aligned}$ | $\begin{aligned} & : 19 \text { (11.7 \%) } \\ & \text { RR > } 160 / 95: \end{aligned}$ |  | $\begin{aligned} & \text { RR > 160/95: } 1 \\ & (8.3 \%) ; \end{aligned}$ |  |
|  | $\begin{aligned} & \text { RR> } 160 / 95: 7 \\ & (7.9 \%) ; \end{aligned}$ | without detailed values: 5 | (1.2 \%); <br> without detailed <br> values: 16 | $\begin{aligned} & \text { RR>160/95: } 2 \\ & (2.4 \%) ; \end{aligned}$ | without detailed values: 2 |  |
|  | $\begin{aligned} & \text { RR>140/90: } 2 \\ & (2.2 \%) \end{aligned}$ |  |  | $\begin{aligned} & \text { RR> } 140 / 90: 1 \\ & (1.2 \%) ; \end{aligned}$ |  |  |
|  |  |  |  | without detailed values: 9 (10.5 \%) |  |  |
| Group 1 | $\begin{aligned} & 1 \\ & \text { RR>190/100: } 1 \\ & (1.1 \%) \end{aligned}$ | $\begin{aligned} & 1 \\ & R R>160 / 95: 1 \\ & (2.4 \%) \\ & \hline \end{aligned}$ | $\begin{aligned} & 5 \\ & \text { RR > 190/100: } 3 \\ & (1.9 \%) \end{aligned}$ | $\begin{aligned} & 1 \\ & \text { RR>190/100: } 1 \\ & (1.4 \%) \end{aligned}$ | ---- | ---- |
|  |  |  |  |  |  |  |
| total | 65 (73.0 \%) | 31 (75.6 \%) | 128 (79.0 \%) | 69 (81.2 \%) | $9(75 \%)$ | $6(85.7$ \%) |

* patients with very high hypertension: diastolic values $\geq 130 \mathrm{~mm} \mathrm{Hg}$
right and left eyes affected by the three diseases (contingency tables) (Table 3).

In patients with hemi-CRAO, the superior arterial trunk was found to be occluded at a frequency similar to the finding of an inferior arterial trunk occlusion.

In 15 patients the superior retinal arteries were occluded and in 14 patients inferior retinal arteries.
Cardiovascular Risk Factors (RFs)

We identified a combination of RFs in most patients,
such as arterial hypertension and disease of the ICA or heart failure. For example, we detected seven cardiovascular risk factors in one 72 -xear-old man with CRAO. He suffered from arterial hypertension, diabetes mellitus, hypercholesterolemia, hyperuricemia, a $50 \%$ stenosis of the ipsilateral internal carotid artery, global hypokinesia of the left ventricle, and mitral valve insufficiency.

## Results

## Cardiovascular Risk Factors

In a total of 243 patients, we identified only one RF in $9.1 \%$, two RFs in $23 \%$, three RFs in $25.1 \%$, and four RFs in 25.9 \% of the patients. Most patients had 4 RFs. Five RFs were diagnosed in $14 \%$, and six RFs in $2.1 \%$. Two patients ( $0.8 \%$ ) showed even seven RFs (Table 4).

No statistical difference was found with respect to the number of risk factors between patients with BRAO, CRAO, and hemi-CRAO (Kruskal-Wallis-Test). No examinations were possible in the Department of Internal Medicine in six patents with CRAO, five patients with BRAO, and in three patents with hemiCRAO. Missing sonographical and echocardiography examinations are listed in Table 6 and Table 7, respectively.

## Arterial Hypertension as a Frequent Cardiovascular Risk Factor

The main RF was arterial hypertension, occurring in 308 ( $75.9 \%$ out of 406 patients), in 96 patients ( 73.8 \% out of 130 patients) with BRAO, in 197 patients
(79.8 \% out of 247 patients) with CRAO, and in 15 patients ( $78.9 \%$ out of 19 patients) with hemi-CRAO (Table 5).

No significant difference between CRAO patients and BRAO patients was found with respect to hypertension when comparing these three ocular diseases ( p $=0.2)($ Cochran - Mantel-Haenszel-Test).

## Extremely High Arterial Hypertension in Patients with CRAO

- a 51-year-old man with a blood pressure of 210/140 mm Hg (angiography revealing no changes in the ICA)
- a 58 -year-old man with $230 / 130 \mathrm{mmHg}$ (with Doppler sonography showing an ICA occlusion)
- a 69-year-old woman with $270 / 180 \mathrm{~mm} \mathrm{Hg}$ (with an ICA elongation in Doppler sonography)


## Extremely High Arterial Hypertensionin Patients with BRAO

- a 47-year-old man with $250 / 160 \mathrm{mmHg}$ (Doppler sonography showing no ICA changes)
- a 60-year-old woman with $240 / 170 \mathrm{~mm} \mathrm{Hg}$ (Doppler sonography showing no ICA changes)
- a 50 -year-old man with $200 / 150 \mathrm{~mm} \mathrm{Hg}$ (Dopplersonography revealing plaques in the ICA)

Extremely High Arterial Hypertensionin in a

Table 6. Findings in Doppler Sonography in 366 examined patients with arterial retinal occlusions.

|  | total BRAO $104$ | total CRAO $238$ | total <br> hemi-CRAO <br> 24 | total <br> 366 |
| :---: | :---: | :---: | :---: | :---: |
| Occlusion of the internal carotid artery (ICA) or $\geq 70 \%$ stenosis | 22 | 54 | 2 | 78 |
| Medium-sized stenosis of ICA | 17 | 29 | 1 | 47 |
| Plaques or slight ICA Stenosis or elongations | 30 | 79 | 7 | 116 |
| Dissecting aneurysm |  | 4 |  | 4 |
| Relevant sonographical findings as possible causes for retinal arterial occlusions | 69 | 166 | 10 | pathological changes in 245 ( $66.9 \%$ of 366 examined patients) |
| Without relevant pathological changes of ICA | 35 | 72 | 14 | 121 |
| Changes of the contralateral ICA | 11 | 3 | 1 | 15 |
| Missing sonographical examinations | 30 | 15 | 5 | 50 |
| total | path. <br> changes: 69 <br> normal: 35 | path. <br> changes: 166 <br> normal: 72 | path. <br> changes: 10 <br> normal: 14 | $121(33.1 \%)=$ normal findings $\begin{aligned} & 245+121=366 \\ & 366+50=416 \end{aligned}$ |
|  | no exam: 30 | no exam: 15 | no exam: 5 |  |

Table 7. Echocardiographical findings in 294 patients with retinal arterial occlusions.

| Diagnoses | BRAO: <br> 91 patients | CRAO: <br> 183 patients | hemi-CRAO: <br> 20 patients | total <br> 294 patients |
| :---: | :---: | :---: | :---: | :---: |
| A. Possible cardiac causes for ocular infarction |  |  |  |  |
| 1. Disorders of cardiac rhythm (for instance chronic atrial fibrillation) | 7 | 34 | 6 | 47 out of <br> 294 patients ( $16 \%$ ) |
| 2. Disturbance of diastolic relaxation | 9 | 7 | 2 | 18 |
| 3. Reduced function of left ventricle | 7 | 15 |  | 22 |
| 4. Slight degree to medium-sized aortic stenosis | 1 | 11 |  | 12 |
| 5. Medium-sized to high degree aortic stenosis | 6 | 12 | 2 | 20 out of <br> 294 patients (6.8 \%) |
| 6. Combined aortic vitium | 3 | 2 |  | 5 |
| 7. Atrial thrombus |  | 1 |  | 1 |
| 8. Combined vitium of aortic and mitral valves | 3 | 8 | 1 | 12 |
| 9. Sclerosis of Aortic valve | 12 | 19 | 2 | $\begin{aligned} & 33 \text { out of } \\ & 294 \text { patients (11.2 \%) } \end{aligned}$ |
| 10. Aortic insufficiency (slight to medium) | 4 | 3 | 2 | 9 |
| 11. Prior aortic valve replacement | 2 | 2 |  | 4 |
| 12. Patent foramen ovale | 8 | 10 | 1 | 19 |
| 13. Stenosis of mitral valve |  |  | 1 | 1 |
| 14. Mitral valve insufficiency | 9 | 17 | 6 | 32 out of <br> 294 patients (11.0) |
| 15. Mitral valve prolaps | 1 | 2 |  | 3 |
| 16. Prior mitral valve replacement | 1 |  |  | 1 |
| 17. Calcareous mitral valve with myxomatous changes | 2 |  |  | 2 |
| 18. Aneurysms of apex cordis or cardiac septum | 1 | 3 |  | 4 |
| Possible cardiac causes for infarction (1.-18.): | 76 | 146 | 23 | 245 |
| B. Unconditional or irrelevant cardiac causes for infarction |  |  |  |  |
| 19. Mitral ring sclerosis | 5 | 15 | 2 | 22 |
| 20. Hypertrophic left ventricle | 18 | 38 | 3 | 59 |
| 21. Coronary disease including prior myocardial infarction | 16 | 49 | 5 | 70 |
| 22. Left atrium enlargement | 4 |  |  | 4 |
| 23. Reanimation after cardiac arrest | 1 |  |  | 1 |
| 24. Right ventricle enlargement |  | 3 |  | 3 |
| C. Unconditional or irrelevant cardiac causes for infarction (19.-24.) | 44 | 105 | 10 | 159 |
| All cardiac deficits | 120 | 251 | 33 | 404 |
| Normal echocardiographic findings | 29 (31.9\%) | 43 (23.5 \%) | 3 (15\%) | 75 (25.5 \%) |
| Missing echocardiographic examination | 43 out of 134 patients (32.1\%) | 70 out of <br> 253 patients <br> ( 27.7 \%) | 9 out of <br> 29 patients <br> (31 \%) | 122 out of <br> 416 patients <br> (29.3 \%) |

## Patient with Hemi-CRAO

- a 54 -year-old woman with $220 / 140 \mathrm{~mm} \mathrm{Hg}$ (Doppler sonography showing no ICA changes)
Ultrasound Diagnosis of Cerebro-vascular


## Arteries

366 patients with arterial retinal occlusions were subjected to color coded Duplex/Doppler sonography of the carotid arteries.

ICA disease was found in 245 ( $66.9 \%$ ) patients. To

Table 8. Cerebral vascular diseases and other vascular disorders in patients with retinal arterial occlusions.

| Diagnoses | BRAO total: | CRAO total: | hemi-CRAO total: | total |
| :---: | :---: | :---: | :---: | :---: |
|  | 134 | 253 | 29 | 416 |
| Prior Stroke | 10 | 12 | 3 | 25 |
| Prior TIA | 6 | 8 | 1 | 15 |
| PRIND or RIND |  | 2 | 1 | 3 |
| Simulataneous stroke or TIA with retinal arterial occlusion ("oculocerebral ischemia syndrome") | 1 | 6 |  | 7 |
| Clinical signs of cerebral ischemia cerebrovascular insufficiency | 3 | 6 |  | 9 |
| Cerebral vascular diseases in patients with retinal arterial occlusions | $\begin{gathered} 20 \\ (14.9 \%) \end{gathered}$ | $\begin{aligned} & 34 \\ & (13.4 \%) \end{aligned}$ | $\begin{gathered} 5 \\ (17.2 \%) \end{gathered}$ | $\begin{gathered} 59 \\ (14.2 \%) \end{gathered}$ |
| Prior Bypass operation of subclavian artery in occlusions of brachiocephalic artery or arm arteries |  | 4 |  | 4 |
| Prior radiation and surgery of larynx carcinoma and retrolingual carcinoma with secondary occlusion of internal carotid artery |  | 2 |  | 2 |
| Abdominal aortic aneurysm | 1 | 2 |  | 3 |
| Peripheral arterial occlusion (with intermittent claudication) | 11 | 20 | 1 | $\begin{aligned} & 32 \\ & (7.7 \%) \end{aligned}$ |
| High degree general vascular sclerosis in combination with renal insufficiency |  | 2 |  | 2 |
| Sleep apnoe syndrome |  | 2 |  | 2 |
| total numbers of patients with signs of general vascular diseases (without cerebral involvement) | 12 | 34 | 1 | 45 |

be precise, in 104 patients ( 28.4 \%) with BRAO, 238 patients ( $65.0 \%$ ) with CRAO, and 24 ( $6.6 \%$ ) patients with hemi-CRAO were examined (Table 6).

Statistical evaluation showed that ultrasound findings were significantly different in all three diseases ( $p=0.003$ ) regardless of the patient's gender.

Comparison of ultrasound findings between CRAO patients and BRAO patients showed no significant difference ( $p=0.2$ ), nor were any differences identified in the age groups or regarding patient gender. No definitive difference between males and females was found ( $p=0.051$ ).

Four patients with CRAO presented a dissecting aneurysm of the ICA, detected by sonography. None of them had suffered a stroke, and they were treated with anticoagulants to prevent a potential cerebral embolism.

## Cardiac Diseases

The most relevant RFs for arterial retinal infarction were cardiac rhythm disorders (mainly chronic atrial fibrillation) and valvular diseases. Cardiac rhythm disorders occurred in 47 out of 294 patients ( $16 \%$ ). Mitral valve insufficiency was found in 32 out of 294 patients (11\%), and a moderate to advanced aortic stenosis was detected in 20 out of 294 patients ( $6.8 \%$ ) (Table 7).

## Vascular Brain Diseases in Patients with

## Arterial Retinal Obstruction

Cerebral deficits due to vascular diseases were present when documenting individual case histories (anamnesis) in 59 (14.2 \%) patients (Table 8). Simultaneous stroke or TIA and retinal arterial occlusion ("oculocerebral ischemia syndrome") occurred in seven patients. 43 (10.3 \%) additional patients had suffered stroke, TIA or PRIND weeks, months or years prior to retinal arterial occlusion. Peripheral arterial occlusion (with intermittent claudication) occurred in 32 out of 416 patients ( $7.7 \%$ ) with arterial retinal occlusion.

## Additional Systemic Diseases as Cardiovascular Risk Factors

Additional RFs for retinal arterial infarctions are chronic smoking, diabetes mellitus, hyperlipidemia (particularly hypercholesterolemia), and hyperuricemia (Table 9). Comparison between BRAO, CRAO, and hemi-CRAO patients revealed no significant differences between these four diagnoses.

## Ophthalmological Findings in Patients with Arterial Retinal Obstruction

Visual acuity in 126 patients with BRAO and in 29 patients with hemi-CRAO were evaluated. In 85 patients with BRAO ( $67.5 \%$ out of 126 patients), visual acuity was better than $>0.5$. In 19 patients with hemi-CRAO

Table 9. Additional cardiovascular Risk Factors for retinal arterial occlusions.

| Diagnoses | BRAO total: | CRAO total: | hemi-CRAO <br> total: | total: |
| :--- | :--- | :--- | :--- | :--- |
|  | $\mathbf{1 1 9}$ | $\mathbf{2 0 8}$ | $\mathbf{2 5}$ | $\mathbf{3 5 2}$ |
| Chronic smoking | 38 | 70 | 7 | 115 |
|  | $(31.9 \%$ of | $(33.6 \%$ of | $(28 \%$ out of | $(32.7 \%$ |
| Diabetes mellitus | 119 pat. $)$ | 208 patients $)$ | 25 patients $)$ | of 352 patients $)$ |
|  | 16 | 45 | 3 | 64 |
|  | $(13.4 \%$ of | $(21.6 \%$ of | $(12 \%)$ | $(18.2 \%$ of |
| Hyperlipidemia | 119 pat. | 208 pat $)$ | 352 pat. $)$ |  |
|  | 35 | 79 | 8 | 122 |
|  | $(29.4 \%)$ | $(38 \%$ of | $(32 \%)$ | $(34.7 \%)$ |
| Hyperuricemia | $9(7.6 \%)$ | $38(18.3 \%)$ | $6(24 \%)$ | $53(15.1 \%)$ |

Table 10. Visual acuity: BRAO and hemi-CRAO.

|  | BRAO | hemi-CRAO |
| :--- | :--- | :--- |
| no information | 8 | 1 |
| $<0.1(20 / 200)$ | 14 | 5 |
| $0.1-0.4$ |  | 4 |
| $(20 / 200-20 / 50)$ | 26 | 4 |
| $0.5-0.6(20 / 40-20 / 32)$ | 24 | $15(51.7 \%$ of 29 patients $)$ |
| $0.7-1.0$ | $61(48.4 \%$ of 126 patients $)$ | $>0.5: 19(65.5 \%$ of 29 patients $)$ |
| $(20 / 30-20 / 20)$ | $>0.5: 85(67.5 \%$ of 126 patients $)$ |  |
| total: |  |  |

Table 11. Frequency of emboli in 134 patients with BRAO.

| Occlusion of macular artery | Occlusion of inferior temporal artery | Occlusion of superior temporal artery | Occlusion of inferior nasal artery | Occlusion of superior nasal artery |
| :---: | :---: | :---: | :---: | :---: |
| 9 patients ( $6.7 \%$ out of 134 patients) | 53 patients (39.6 \%) | 47 patients (35.1 \%) | 1 patient | 1 patient |
| visible <br> Emboli: 3 out of 9 arteries (33.3 \%) | visible <br> Emboli: 27 out of 53 arteries (50.9 \%) | visible Emboli: <br> 20 out of <br> 47 arteries (42.6 \%) | 1 Embolus (0.75\%) | 1 Embolus (0.75\%) |
| Occlusion of cilioretinal artery | Occlusions of two or more branch arteries (temporal and nasal arteries) | Occlusions of two or more branch arteries (temporal and inferior arteries) |  |  |
| 4 (3. \%) | 5 patients | 14 patients (10.4 \%) |  |  |
| Embolus: 1 (25\%) | Emboli: 2 (40\%) | Emboli: 8 out of 14 patients (57\%) |  |  |
| total <br> Emboli: 63 (47 \% out of 134 patients) |  |  |  |  |

(65.5 \% out of 29 patients) visual acuity was better than $>0.5$ (Table 10).

Table 12. Amaurosis fugax (AF) in patients with retinal arterial occlusion.

|  | males | females | total |
| :--- | :--- | :--- | :--- |
| BRAO | 13 | 5 | $18(13.4 \%$ out of 134 patients $)$ |
| CRAO | 24 | 7 | $31(12.3 \%$ out of 253 patients $)$ |
| hemi-CRAO | 4 | 1 | $5(17.2 \%$ out of 29 patients $)$ |
| total: | 41 | 13 | $54(13 \%$ out of 416 patients $)$ |

## Embolic Occlusions of Retinal Arteries

CRAO or BRAO may occur due to an embolus originating from a stenotic internal carotid artery, from plaques within the aortic arch or from a diseased heart.

The severity of embolism in the retinal arteries depends on the type, quantity and size of the emboli.

Beyond embolism as a cause thereof, a CRAO may also occur in arterial hypertension, be due to an arterial spasm, particularly in migraine. 63 emboli ( $47 \%$ ) were found in 134 patients with BRAO (Table 11).

Emboli were found in 28 out of 253 patients with CRAO (11.1 \%).

Fundus examination of visible emboli occurred significantly more often in patients with BRAO (63 patients, $47 \%$ out of 134 patients) and in $12(41.4 \%$ of 29 patients) patients with hemi-CRAO compared to patients with CRAO (28 patients, 11.1 \% out of 253 patients). Emboli were found in the superior retinal periphery in 5 patients and in the inferior periphery in 7 patients with hemi-CRAO. The difference in the prevalence of visible emboli between patients with CRAO and those with BRAO was highly significant ( p $=0.0001$ ), and between those with BRAO and hemiCRAO ( $p=0.0001$ ).

Two or more very small glittering emboli were occasionally observed in the small retinal arterioles close to the macula in patients with CRAO. Single emboli in CRAO resembled small, glittering, yellowish crystals. Patients with BRAO usually presented one embolus, rarely revealing two or more emboli.

## Amaurosis fugax (AF)

AF episodes in patients with BRAO, CRAO, or hemiCRAO were reported in $13 \%$ of the patients. No statistical defference between the three different types of arterial ocular obstruction was found (Table 12).

## Retinal Arterial Occlusion despite Phenprocoumon Therapy

Phenprocoumon did not prevent retinal arterial occlusion in 19 patients ( $4.6 \%$ ).

Retinal infarctions occurred despite treatment with phenprocoumon (MarcumarR) in 11 patients with CRAO, in 6 patients with BRAO, and in two patients with hemi-CRAO.

## Discussion

Our examinations of patients with ocular arterial occlusive diseases showed that the main cardiovascular

RF was arterial hypertension. However, no significant difference among BRAO, CRAO, and hemi-CRA patients was observed.

Other cardiovascular RFs, such as those revealing during Duplex/Doppler sonography (i.e. carotid artery diseases), diabetes mellitus, hyperlipidemia, hyperuricemia, and anomalies caused by chronic smoking revealed no statistical differences among patients with BRAO, CRAO or hemi-CRAO either. No significant difference was found among the patients of the three ocular diagnoses with respect to amaurosis fugax. A slight difference between the patients with CRAO and BRAO was found in cardiac arrhythmia, mainly in terms of chronic atrial fibrillation. However, the number of examined patients was too small to make a final judgement.

But a highly significant difference was found in the frequency of patients with retinal emboli. Those with BRAO had many more visible emboli in retinal arteries than patients with CRAO. In the BRAO group, emboli were found in $47 \%$ of 134 patients, but in only 11.1 \% of 253 patients in the CRAO group.

Emboli in patients with CRAO are not visible in most patients' retinas because it is assumed that emboli obstruct the central retinal artery in the vicinity of the lamina cribrosa, as demonstrated histologically by Manz [18].

Visual acuity in most of our patients with BRAO and hemi-CRAO was normal or somewhat reduced, because the macula is not usually affected or is only partly involved. In contrast, patients with CRAO are by definition either totally blind or possess highly impaired visual acuity [4, 14, 24].

Comparing our data to those in the literature: Wilson et al. [29] showed that 68 patients with branchartery occlusion (BRAO) had a higher prevalence of previous transient episodes and ischemic and valvular heart disease, and that they were more often embolic than 35 patients with central-artery occlusion (CRAO) who were more often hypertensive and showed a greater prevalence of complete carotid occlusion. Shah et al. [26] examined 14 patients with CRAO and 15 with BRAO. They found that the incidence of carotid atherosclerosis was similar among the central and branch retinal arterial groups. De Potter \& Zografos [9] published a retrospective study including 151 patients with retinal artery occlusions. CRAO was diagnosed in $43 \%$ of the patients, BRAO in $53 \%$, and cilioretinal artery occlusion in $4 \%$. They found a highly frequent arterial hypertension only, but no other RFs in patients with BRAO and CRAO. ICA stenosis was detected in $50 \%$ of 46 examined patients. Rüfer et al. [20] compared cardiovascular risk factor in patients with BRAO and CRAO. However, their CRAO pa-
tients also included patients with inflammatory diseases such as giant cell arteritis, making their data not comparable to our findings.

Regarding the comparison of RFs in patients with anterior ischemic optic neuropathy (AION): Hayreh et al. [13] reported prevalence rates of systemic diseases in patients with AION, noting a significantly higher prevalence of arterial hypertension and diabetes mellitis. Middle-aged and elderly patients showed a significantly higher prevalence of ischemic heart disease. However, they carried out no carotid artery examination. Our previous investigation [22] showed that patients with AION rarely present a high degree of stenosis or occlusion.

## References

1. Ahuja RM, Chaturvedi S, Eliott D, Joshi N, Puklin JE, Abrams GW. (1999). Mechanisms of retinal arterial occlusive disease in African American and Caucasian patients. Stroke 30: 1506-1509
2. Arruga J, Sanders MD. (1982). Ophthalmologic findings in 70 patients with evidence of retinal embolism. Ophthalmology, 89, 1336-1347
3. Biousse V, Touboul PJ, D'Anglejan-Chatillon J, Lévy C, Schaison M, Bousser MG. (1998) Ophthalmologic manifestations of internal carotid artery dissection. Am J Ophthalmol 126: 565-577
4. Brown GC, Magargal LE. (1982) Central retinal artery obstruction and visual acuity. Ophthalmology 89: 14-19
5. Bruno A, Russell PW, Jones WL, Austin JK, Weinstein ES, Steel SR. (1992) Concomitants of asymptomatic retinal cholesterol emboli. Stroke 23: 900-902
6. Bull DA, Fante RG, Hunter GC, van Dalen J, Lee D, Bernhard VM, McIntyre KE. (1992) Correlation of ophthalmic findings with carotid artery stenosis. J Cardiovasc Surg 33: 401-406
7. Chawluk JB, Kushner MJ, Bank WJ, Silver FL, Jamieson DG, Bosley TM, Conway DJ, Cohen D, Savino PJ (1988) Atherosclerotic carotid artery disease in patients with retinal ischemic syndromes. Neurology 38: 858-863
8. Cugati S, Wang JJ, Rochtchina E, Mitchell P. Ten-year incidence of retinal emboli in an older population. Stroke. 2006; 37: 908-910
9. De Potter P, Zografos L. (1993) Survival prognosis of patients with retinal artery occlusion and associated carotid artery disease. Graefe`s Arch Clin Exp Ophthalmol 231: 212-216
10. Douglas DJ, Schuler JJ, Buchbinder D, Dillon BC, Flanigan DP. (1988) The association of central retinal artery occlusion and extracranial carotid artery disease. Ann Surg 208: 85-90
11. Gloor B, Müller HR, Vozenilek E. (1985) Arterielle Verschlußkrankheit im Augenbereich. Diagnostischer Beitrag der Dopplersonographie. Klin Monatsbl Augenheilkd 186: 161-171
12. Gold D. (1977) Retinal arterial occlusion. Trans Am Acad Ophthalmol Otolaryng 83: 392-408
13. Hayreh SS, Joos KM, Podhajsky PA, Long CR. (1994) Systemic diseases associated with nonarteritic anterior
ischemic optic neuropathy. Am J Ophthalmol 118: 766780
14. Karjalainen K. Occlusion of the central retinal artery and retinal branch arterioles. A clinical, tonographic and fluorescein angiographic study of 175 patients. Acta Ophthalmologica (Suppl.) 1971; 109: 9-96
15. Klein R, Klein BEK, Moss SE, Meuer SM. (2003) Retinal emboli and cardiovascular disease. Arch Ophthalmol 121: 1446-1451
16. Kramer M, Goldenberg-Cohen N, Shapira Y, Axer-Siegel R, Shmuely H, Adler Y, Weinberger D, Sagie A. (2001) Role of transesophageal echocardiography in the evaluation of patients with retinal artery occlusion. Ophthalmology 108: 1461-1464
17. Lang GE, Spraul ChW. (1997) Risikofaktoren retinaler Verschlusserkrankungen, Klin Monatsbl Augenheilkd 211; 217-226
18. Manz W. Anatomische Untersuchung eines an Embolie der Arteria centralis retinae erblindeten Auges. Festschrift zur Feier des 70. Geburtstages von H. v. Helmholtz, Verlag L. Voss, Hamburg, Leipzig, 1891; 9-17
19. Ros MA, Magargal LE, Uram M. (1989) Branch retinalartery obstruction: a review of 201 eyes. Ann Ophthalmol 21: 103-107
20. Rüfer F, Schröder A, Winter R, Erb C. Risikofaktoranalyse und Therapievergleich zwischen Heparin und Hämodilution bei Zentralarterienverschluss des Auges. Ophthalmologe 2003; 100: 819-824
21. Savino PJ, Glaser JS, Cassady J. (1977) Retinal stroke. Is the patient at risk? Arch Ophthalmol 95: 1185-1189
22. Schmidt D, Richter T, von Reutern GM, Egelhardt R. (1991) Akute Durchblutungsstörungen des Auges. Klinische Befunde und Ergebnisse der Doppler-Sonographie der A. carotis interna. Fortschr. Ophthalmol 88: 84-98
23. Schmidt D, Schumacher M, Mittelviefhaus K. (1997) Visual recovery after acute choroidal ischemia with partial retinal hypoperfusion, demonstrated by fluorescein angiography. Neuro-ophthalmology 18: 205-213
24. Schmidt D. (2004) Der Zentralarterienverschluss. Klinische Befunde und Behandlung mit der lokalen intraarteriellen Fibrinolyse. Klin Neuroradiol 14: 149-173
25. Schmidt D, Hetzel A, Geibel-Zehender A. (2005) Retinal arterial occlusion due to embolism of suspected cardiac tumors - report on two patients and review of the topic. Eur J Med Res 10: 296-304
26. Shah HG, Brown GC, Goldberg RE. (1985) Digital subtraction carotid angiography and retinal arterial obstruction. Ophthalmology 92: 68-72
27. Sharma S, Naqvi A, Sharma SM, Cruess AF, Brown GC. (1996) Transthoracic echocardiographic findings in patients with acute retinal arterial obstruction. Arch Ophthalmol 114: 1189-1192
28. Smit RLMJ, Baarsma GS, Koudstaal PJ. (1994) The source of embolism in amaurosis fugax and retinal artery occlusion. Int Ophthalmol 18: 83-86
29. Wilson LA, Warlow CP, Russell RWR. (1979) Cardiovascular disease in patients with retinal arterial occlusion. Lancet I: 292-294

Received: January 5, 2007 / Accepted: August 6, 2007

