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Static retinal vessel analysis in a cohort study - correlation with cardiovascular risk factors and diseases

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Considering the increasing case numbers of cardiovascular diseases and events, the establishment of new parameters of risk stratification, diagnosis and progress monitoring is necessary. Changes in retinal vascular structures reflect the damage caused by aging, cardiovascular diseases, inflammatory processes and endothelial dysfunction in the human body. Other cohort studies in the USA, the Netherlands or Australia have already examined the parameters of retinal vessel analysis for their connection with the presence of cardio- or cerebrovascular diseases or risk factors.
Now it was necessary to collect corresponding data from a large Central European cohort and to show their connections. We aimed to establish retinal vascular analysis as a non-invasive examination in the context of cardiovascular risk stratification.
In this study, the first 5,000 of a total of approximately 15,000 subjects of the Gutenberg health study were examined for a statistical relationship between changes in retinal vessel diameter and the presence of cardiovascular risk factors or secondary diseases.
The Gutenberg Health Study is a monocentric, population-based prospective cohort study with subjects aged between 35 and 74 from the Mainz-Bingen area.
For data collection by means of static retinal vessel analysis, digital retinal images were generated with the help of a non-mydriatic fundus camera from Imedos. AVR, CRAE and CRVE values were determined by computer-assisted software analysis according to the formula by Hubbard and Parr. This was accomplished with 4313 subjects.
The retinal vessel analysis was performed by two examiners. Their interclass correlation coefficient for their interobserver variability was 0.896 showing a high degree of agreement.
We considered cardiovascular risk parameters and diseases as age (binary and categories), gender, systemic hypertension, diabetes mellitus (binary and HbA1c), dyslipidemia, obesity, smoking, the presence of peripheral artery occlusive disease, medicated heart failure and a history or family history for stroke or myocardial infarction. Systemic hypertension was in addition to a binary categorization classified into 3 subgroups: controlled, screening detected (during GHS examination) and uncontrolled hypertension. The collection of the health data occurred by means of computer-assisted personal interviews, venous blood withdrawal and repeated measurements of resting blood pressure. The presence or absence of these risk factors and cardiovascular diseases divides the collective into cardiovascular "HEALTHY" and "ILL" participants.
Correlating AVR, CRAE and CRVE with the individual cardiovascular parameters, a univariable analysis was performed using the Mann-Whitney-U test or T-test for the binary variables. The Kruskall-Wallis test or a linear regression was used for the univariate analysis of the categorically classified variables with more than two values. In addition, a multivariable analysis using logistic regression for CRAE, CRVE and AVR was performed binary above and below the 5% percentiles for age, systemic hypertension, diabetes mellitus, smoking, dyslipidaemia, history or family history for stroke or myocardial infarction, PAOD and medicated heart failure.
In the univariable analysis, significantly lower AVR values were found in subjects with systemic hypertension, HbA1c values >6.5 %, dyslipidaemia, obesity, PAOD and also in patients defined as cardiovascular "ILL", male participants and those with a history of myocardial infarction. AVR values decreased with increasing age. Lower AVR values were also found in diabetics, but no statistical significance could be demonstrated. Increased AV ratios were present in smokers. In family history for myocardial infarction and history or family history for stroke there was no correlation to changes in the AVR.

Significantly lower CRAE values were found in the group defined as cardiovascular “ILL", with increasing age, in men compared to women, with systemic hypertension and with HbA1c values >6.5%. Higher CRAE values were found in smokers.
No correlation with changes in CRAE values were found for diabetes mellitus, dyslipidemia, obesity, PAOD, medicated heart failure and for stroke or myocardial infarction neither in history nor family history.
Significantly higher CRVE values were found in the group of subjects defined as cardiovascular "ILL". Compared to men, women had elevated CRVE values. Similarly, increased CRVE values were found in dyslipidemia, smokers, obesity and stroke in the family history. Lower CRVE values could be found in categorical classification with increasing age, but not in binary classification. There was no change in CRVE values with systemic hypertension, diabetes mellitus, PAOD, medicated heart failure, for history for stroke and myocardial infarction neither in history nor family history.
In the multivariable analysis, the results were significant for a correlation between reduced AVR value in old age and in women with a history of stroke.
In addition, the multivariable analysis confirmed the relationship between reduction of AVR in arterial hypertension in both women and men already shown in the univariable analysis. Men with arterial hypertension had a 2-fold increased chance, women with arterial hypertension had a 3-fold increased chance of having AVR values below the 5th percentile. Similarly, multivariable analysis provided significant evidence of a reduction in CRAE values with increasing age and in the presence of arterial hypertension in both women and men. In addition, women who smoke had significantly higher CRVE values. The multivariable evaluation for changes in CRVE values showed a significant reduction in age with men and an increase in CRVE in smokers and in the presence of PAOD.
The correlations found in our Central European cohort thus correspond largely with the existing data from Australia and the USA. Especially the reduction of AVR and CRAE values in cases with arterial hypertension could be confirmed.
The predictive connection between narrowing of the retinal arterioles and development of an art. hypertension is known as well.
The newly demonstrated relationship between the degree of reduction of the AVR and the CRAE value in dependence of the degree of control of arterial hypertension goes beyond the already found correlations. In our study, subjects with an inadequately treated art. hypertension had lower AVR and CRAE values than study participants with well adjusted controlled arterial hypertension. This observation suggests retinal vessel analysis not only as a variable or screening parameter in cardiovascular risk assessment, but also as a possible control and progress parameter in the assessment of antihypertensive therapy. A non-invasive examination of the occular fundus could be used to estimate the risk of developing arterial hypertension and at the same time assess the quality of the therapy.
Based on this initial examination, the predictive value of the AV ratio in individual disease prediction should be examined by means of follow-up examinations. Do patients with conspicuously high or low AVR, CRAE or CRVE values in the initial examination over time develop an arterial hypertension, diabetes mellitus or suffer a stroke or heart attack? For this purpose, cut-offs should and could be defined for when AVR or CRAE/CRVE values are to be considered pathological.
The available and future data from the Gutenberg health study provide an outlook on the application of retinal vascular analysis in individual cardiovascular risk assessment.