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Abstract. A cross-sectional survey was conducted in Hungary using the Cerberus system which includes: 1) a questionnaire addressing the risk factors for stroke/cardiovascular disease; 2) amplifiers to record the pulse waves of cerebral arteries (rheoencephalography) and peripheral arteries, electrocardiogram and electroencephalogram. Additionally, subjects were measured for carotid stenosis by Doppler ultrasound and 12-lead electrocardiogram; subjects were also screened for blood cholesterol, glucose, and triglyceride levels. Prevalence of the following stroke risk factors was identified: overweight, 63.25%; sclerotic brain arteries (by rheoencephalogram), 54.29%; heart disease, 37.92%; pathologic carotid flow, 34.24%; smoking, 30.55%; high blood cholesterol, 28.70%; hypertension, 27.83%; high triglyceride, 24.35%; abnormality in electrocardiogram, 20%; high glucose, 15.95%; symptoms of transient ischemic attack, 16.07%; alcohol abuse, 6.74%; and diabetes, 4.53%. The study demonstrates a possible model for primary cardiovascular disease/stroke prevention. This method offers a standardizable, cost effective, practical technique for mass screenings by identifying the population at high risk for cardiovascular disturbances, especially cerebrovascular disease (primary prevention). In this model, the rheoencephalogram can detect cerebrovascular arteriosclerosis in the susceptibility/presymptomatic phase, earlier than the Doppler ultrasound technique. The method also provides a model for storing analog physiological signals in a computer-based medical record and is a first step in applying an expert system to stroke prevention.

1.Introduction

A multi-faceted survey was conducted in 1992–94 to ascertain the somatic, mental and socio-economic conditions of the residents of a village in eastern Hungary. Here we report data on prevalence of somatic disorders from the survey. Objectives were: a) To collect and compare prevalence of known cardiovascular disease, including stroke risk factors, in a specific population (a Hungarian village); b) to test a computer-based mass screening device ("Cerberus") designed to identify individuals in the test population at high risk for stroke; c) to compare results obtained with Cerberus with known stroke risk/cardiovascular disease factors and traditional medical records.

2.Methods

A sample of 546 non-symptomatic volunteers ranging in age from 14 to 83 years participated in the study. The sample was evaluated according to the full protocol, which included blood chemistry, electrocardiogram (ECG), Doppler control, and Cerberus testing. The analyzed REG sample involved 457 subjects, 309 female and 148 male. For 252 subjects, Doppler ultrasonography (B mode or duplex scan, Ultramark 4 and Apogee, ATL, USA) was used to measure carotid stenosis of internal carotid

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artery. Doppler B images were obtained for 184 of the 252 subjects. Mean velocity for "out of normal range" (pathological blood flow) was considered as above 40 cm/sec. Psychological tests were performed and reported elsewhere together with other somatic data [2,3].

2.1 Cerberus measurement

The Cerberus system (Quintlab Ltd, Budapest, Hungary) was described in detail elsewhere [1]. Briefly, it is a computer-based inquiry employing Magic, previously Gral software. The examination requires about 20 minutes and can be administered by a technician. A professional trained in vascular neurology interprets the results, contained in a graphically illustrated summary. It is possible to give each subject a report at the conclusion of the examination, indicating 1. healthy, 2. cerebral blood flow disturbance, 3. peripheral blood flow disturbance, 4. neurological or internal medical disturbance, 5. other. First, a questionnaire was administered; blood pressure was measured; and vegetative balance was calculated from blood pressure and heart rate. The questionnaire addressed demographics (12 items), stress (8 items) and anxiety (STAI), stroke risk factors (5 items), and neurological symptoms indicating a possible past transient ischemic attack (21 items). Then, multichannel polygraphic recordings (16 items) were made as follows: 1. ECG; 2. EEG from T5-O1, T6-O2 according to 10/20 system of EEG with ECI System (Electro-Cap Int'l, Eaton, OH); 3. bio-impedance pulses of the head (REG) derived from Fp1-F7 and Fp2-F8 (according to electrode localization in international 10/20 EEG system) and of limbs (both sides) with circumferential electrodes (Rheoscreen, Medis GmbH, Ilmenau, Germany). Following a one minute polygraphic recording, blood pressure was re-measured, and the STAI was repeated. Custom software was developed for Cerberus to perform the following signal processing procedures: analog – digital conversion (275 Hz) and display of analog physiological signals; calculation of fast Fourier transform from EEG; averaging of pulse curves; determination of dominant frequency peak for EEG and of minimum/maximum values for REG and peripheral pulse waves. REG was considered arteriosclerotic if its anacrotic (rising) portion was above the 180 ms threshold, modified after Jenkner [4]. From data collected by measuring blood pressure and heart rate, Cerberus software calculated the ergotrop/trophotrop ratio; modified vegetative (autonomic nervous system) balance by Kerdo and Sipos [1]: $1-(\text{diastolic blood pressure/HR})\times100$. Body Mass Index (BMI) was calculated as weight (kg) /height (m^2). Overweight was defined as BMI>25 for male and BMI>23.8 for female, respectively.

2.2 Data analysis

Artifact contaminated recordings were excluded from further processing (REG, ECG). For statistical treatment and analysis, Framework, GraphPad Prism, Excel and SAS software were used. In most cases, results for male and female subjects were calculated separately (for REG data, where hemispherical differences were less than 5%, female and male groups were analyzed together). After the automatic measurement of REG, a second REG calculation was made off-line to calculate the first derivative parameter (n=390). $P<0.05$ was considered significant.

3. Results

Dominant risk factors, listed by incidence, were as follows: obesity, smoking, heart disease, and hypertension. There were slight differences between male and female groups. Significant correlations with age were observed for overweight, hypertension, total risk, vegetative balance and sclerotic brain arteries. Blood serum values had no significant correlation to age. Mean vegetative balance was 88.05 (m), 93.54 (f), but these differences were not significant; however, age dependency was significant for females in the youngest and oldest groups, decreasing from 109 (16–25 y) to 83 (over 65 y). Smoking was more frequent among males (39.08%) than females (22.07%). Less than 1% of females and more than 12% of males declared themselves as a "regular drinker". The proportion females and more than 12% of males declared themselves as a "regular drinker". The proportion of "hypertonics" (systolic blood pressure above 135 mmHg) in the self-report questionnaires equaled 22.90% for males and 32.68% for females. Heart disease was mentioned by every third male subject (35.64%) and by

40.22% of females. Less than 5% of both sexes were aware of the presence of diabetes mellitus. For further details see [2,5].

3.1. REG

REG anacrotic time was significantly correlated with age and vegetative balance; there were no gender differences. REG was significantly correlated to systemic arterial pressure in females. The most significant observation in regard to REG anacrotic time was related to age: both REG anacrotic time and the time interval between ECG R peak and peak of REG first derivative increased with age. Lateral differences in REG amplitude and REG anacrotic time were found more frequently in middle aged groups (age 40 to 60) than in younger or older groups. In the whole sample, 70% of the subjects over 60 years of age could be considered as cerebrovascular patients, according to the mentioned 180 ms criteria. For 52.78% (male) and 55.8% (female), a sclerotic REG curve was observed. The slope of regression function for REG vs. age was 3.195±0.45 for females, 2.96±0.62 for males 41. The age dependency of sclerotic brain arteries by REG was highly significant, above all other risk factors. Significant correlations were observed between somatic and psychological variables – for details see [3]. In all subjects who were found arteriosclerotic by REG measurement, the REG pulse wave was altered; however, for most of these patients, the EEG spectral parameters were in the normal range, and the Doppler control showed no pathological alteration. The regression line of the REG anacrotic time vs. age had a slope 10 times sharper than that of Doppler systolic velocity (figure 1).

3.2 Doppler ultrasound

For subjects measured by Doppler ultrasound, pathologic flow (mean systolic velocity) was found in 29.41% of the males and 39.06% of the females; pathological flow values appeared in younger as well as older age groups. Although moderate stenosis (less than 50%) was detected in more than 20% of this group (right side, 35.32%; left side, 25.54%), the differences were not significant. Severe stenosis (higher than 50%) was observed in 3.8% of the measured population, without laterality. Maximum "out of normal range" patients appeared in the 55–65 age group. The slope of regression for IC systolic flow vs. age was –0.45±0.11 (f) and –0.346±0.15 (m).
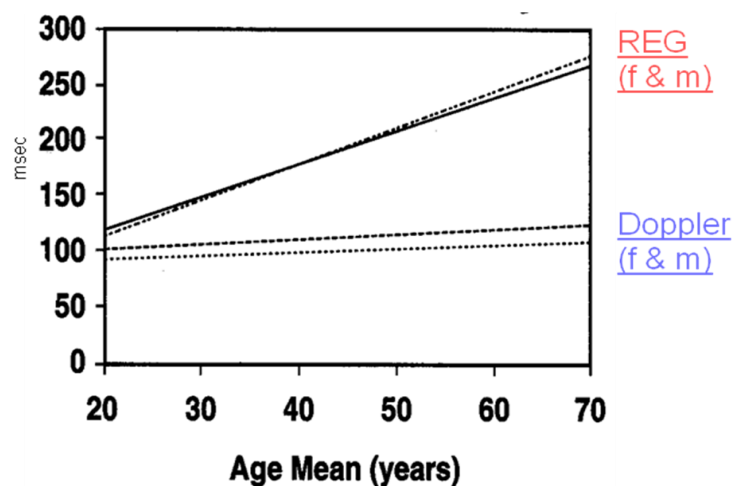

Figure 1. Comparison of slope of age regression lines (REG anacrotic time and Doppler systolic velocity). REG anacrotic time (Y axis in ms: REG anacrotic time) and Doppler systolic flow velocity (Y axis not shown) of internal carotid artery are plotted as a function of age (X axis). The regression lines of male and female groups are similar, but the slope of REG is about ten times steeper than that of the Doppler curve. f: female, m: male. Reprinted courtesy of Health Quest Publications Anti-Aging Medical Therapeutics, Vol. II [5].

4. Discussion

Stroke is unique among neurological diseases, since it has a high prevalence and burden of illness, high economic cost, and is preventable [6]. Epidemiological approaches to stroke prevention include the "high risk" and "mass" approaches. The prevention of stroke can be accomplished by the high-risk or mass approach or a combination of these approaches. The high-risk approach prevents strokes but is also expensive. The mass approach may be more cost-effective, which could lead to substantial savings, but further research is needed to investigate these possible benefits. In this study we introduced a mass approach: REG measurements revealed symptoms of arteriosclerosis in 54.26% of our subjects; within the identical population, the Doppler ultrasound measurements showed 30.43% with arteriosclerosis. The difference of slope of regression lines between REG anacrotic time and Doppler systolic velocity was ten to one, which can be interpreted as increased sensitivity of REG to detect cerebrovascular arteriosclerotic alteration. The present study validated our initial hypothesis – that Cerberus (REG measurement) would predict the presence of cerebral arteriosclerosis in the susceptibility/ pre-symptomatic or "upstream phase", earlier than Doppler ultrasound measurements. The explanation of this difference can be based upon the nature of the development of arteriosclerosis and upon differences between REG and Doppler methods.

5. Conclusion

In summary, our results showed that the earliest manifestation of cerebral arteriosclerosis is the lost elasticity of cerebral arteries, which can be detected by the bioimpedance method (REG). This information is even more practical and more important than the presence and prevalence of a single stroke risk factor. The present study demonstrated the usefulness of the new, multifactorial screening tool, Cerberus, which offers the potential for primary prevention of a general population both for stroke and cardiovascular disorders [7]. People found to be at high risk for stroke would be referred to physicians for further treatment and control of the disease. We propose screening individuals every five years, beginning at age 40, to detect and control the progression of arteriosclerosis.

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