

# STULONG – Longitudinal Study of Atherosclerosis Risk Factors

## 1 Introduction

In the early seventies of the twentieth century, a project of extensive epidemiological study of atherosclerosis primary prevention was developed in the then Czechoslovakia. It was entitled National Preventive Multifactor Study of Hard Attacks and Strokes. Institute of Clinical and Experimental Medicine (IKEM) in Prague 4 was the co-ordinating centre. The study was planned over a long period of time including six sites in the Czech and Slovak Republics. In the end, only two sites participated in the several years of observations, namely IKEM (managed by clinicians Mr Widimský and Ms Geizerová) and Medical Faculty of the Charles University in Plzen (managed by clinicians Mr Simon and Ms Rosolova). After several years, the study was concluded at both sites.

A truly longitudinal study was performed only at the 2<sup>nd</sup> internal clinic of the 1<sup>st</sup> Medical Faculty of the Charles University and General Faculty Hospital in Prague 2 (initially General Medicine Faculty of the Charles University and Faculty Hospital I) – managed by clinicians Mr Boudik, Ms Tomeckova-Suntychova and Mr Bultas. The study covered more than 20 years. From the original primary prevention, part of the male subjects, who contracted an atherosclerotic cardiovascular disease (KVO) in the course of the study, continued to be observed within the secondary prevention at the clinic.

Most of the data was transferred into electronic form by EuroMISE (European Centre for Medical Informatics, Statistics and Epidemiology) with the support of European project.

We include general information on study aims, methods of data collection and their principal processing.

## 2 Study Aims

1. Identify atherosclerosis risk factors prevalence in a population generally considered to be the most endangered by possible atherosclerosis complications, i.e. middle aged men.
2. Follow the development of these risk factors and their impact on the examined men health, especially with respect to atherosclerotic cardiovascular diseases.
3. Study the impact of complex risk factors intervention on their development and cardiovascular morbidity and mortality.
4. 10–12 years into the study, compare risk factors profile and health of the selected men, who originally did not show any atherosclerosis risk factors with a group of men showing risk factors from the beginning of the study.

### 3 Target Group Selection

Men born between 1926–1937 and living in health zones No. 1, 2, 14–47 in Prague 2 were selected from the Prague 2 election lists in year 1975.

The invitation for examination included a short explanation of the first examination purpose, procedure and later observations and asked for co-operation. At that time, no informed signature of the respondent was required. Should the man react to the first invitation for examination, we considered that a sufficient agreement with the examination itself, observation and results processing.

At the time of the first examination we answered possible questions.

Should the man fail to react to the first invitation, we would send minimum two more invitations. Entry examinations were performed in years 1976–1979.

### 4 Study Protocol

STULONG (Longitudinal Study) started as part of a multicenter study co-ordinated by the Institute of Clinical and Experimental Medicine in Prague 4 see Introduction.

First examination, definition of individual risk, their classification into groups for further observation and the observation itself followed a precise protocol of IKEM defined ahead of time. We have followed this protocol throughout the study.

### 5 Risk Factors (RF) Definition

- arterial hypertension – BP  $\geq$  160/95 mm Hg, men with the risk of hypertension were also those, who at the time of the first examination had both blood pressure values within the standard limits, who however were treated by medicaments,
- cholesterol – cholesterol level  $\geq$  260mg% (6.7 mmol/l).....hypercholesterolemia,
- triglycerides – triglycerides level  $\geq$  200mg% (2.2 mmol/l).....hypertriglyceridemia,
- smoking –  $\geq$  15 cig./day currently or smoking of the same number of cigarettes within 1 year prior to the study commencement (pipe or cigar smokers were considered non-smokers),
- Overweight – Brocka index  $>$  115 % (Brocka index: height in cm minus 100 = 100 %),
- Positive family case history: death of father or mother from ischemic disease, heart or vascular stroke before reaching 65 years of age.

Later, we included further laboratory examinations (see their limit values below):

- glycemie – blood sugar level  $\geq$  than 6.3 and less than 8 mmol/l ..... disturbed gluc. tolerance  $\geq$  8 mmol/l diabetes mellitus,
- HDL cholesterol (cholesterol ester of high density) – normal level over 1.2 mmol/l,
- LDL cholesterol (cholesterol ester of low density) – normal level up to 4.0 mmol/l,
- Uric Acid – normal level up to 420 micromol/l.

### **Definition of Hypertension or Hyperlipoproteinemia Risk:**

*High BP* had to be demonstrated in minimum two out of three measurements (2 measurements were taken during the first examination, possible third measurement took place 3–6 weeks later). Similarly, lipids had to exceed the top values in two cases to be included among the risk factors: should high value of lipids be detected during the first examination, the man was invited for a control check 6–12 weeks later. In case of only one value exceeding the top values, the man was invited for control check 3–6 weeks later. The risk of hypertriglyceridemia was not being identified during the first examination, however it also required repeated blood examination.

## **6 First Examination Methodology**

1 419 out of 2 370 invited men came for the first examination.

Initial examination started through an interview and a form completion by a doctor. The form included all general administrative data on the examined man, the level of education reached, data on function and responsibility at the workplace, general habits – movement, smoking, alcohol drinking. Data on family and personal case history focused around cardio-vascular diseases, pain in the chest and legs and breathlessness stating its level. Of course, the initial examination included also general physical check up including blood pressure measuring, basic anthropometric examination – weight, height, skin folds over the triceps and subscapularis muscles. An ECG was made, blood taken for the purpose of general laboratory examination and the urine was tested using paper method. Were it had proven as necessary, further tests were performed, e.g. bicycle ergometry test to identify pain in the chest.

244 attributes were identified for all of them. Here you can find details on the various attributes.

## **7 Men Classification for Long-Term Observation**

Men division for further observation was based on the presence of RF, overall health condition and ECG result. These criteria divided men into 3 groups designated as NG (normal group), RG (risk group), PG (pathologic group):

**NG** = a group of men showing no RF defined above, showing no manifestation cardio-vascular disease or other serious illness making their ten-year-long observation impossible and without and ECG diagnosis.

**RG** = group of men with at least one RF defined above, showing no manifestation cardio-vascular illness or other serious illness making their ten-year-long observation impossible and without and ECG diagnosis.

**PG** = group of men with a manifested cardio-vascular disease or other serious disease making their ten-year-long observation impossible (e.g. malignant illness, advanced failure of liver or kidneys, serious nerve or psychological problem). The pathologic group included also men with diabetes treated with orally administered anti-diabetics or insulin and men with pathologic ECG diagnosis – Minnesota evaluation, codes:

**1–1,2** – oscillation  $Q \geq 0,04$  vt. In one of the outputs I, II, V1–6; **4–1** – horizontal or declining depression of section  $ST \geq 1$  mm in one of the outputs I, II, VL, V1–6; **5–1** – negative  $T = 5$  mm in one of the outputs I, II, V2–6, or in output VL, if it is  $R = 5$ mm or in output VF, should QRS be low; **6–1** – chamber blockade of the 3rd level; **7–1** – blockade of the left Tawarov shoulder; **8–1** – several polytope chamber ES (more than 10% of registered cycles), **8–3** – chamber fibrillation or flutter.

Risk group – **RG** – was further subjected to random division into two sub-groups designated as **RGI** (intervened risk group) and **RGC** (control risk group). The division was based on the number of medical circuit the men lived in: even numbers belonged to RGI, odd numbers to RGC (in the 7-ies, Czechoslovak health system was strictly divided into circuits according to the permanent address and the change to a different circuit was allowed only in very special cases. At the first examination, no significant difference in age, socio-economic factors or RF occurrence was demonstrated between the original RGI and RGC.

## 8 Long-term Observation Methodology

Further observation was based on their division into groups, as stated above:

**NG** – 10 % of this group was examined minimum 1 time per year just as the risk group – see designation MGS. In this group of men, similarly to the risk group, intervention was initiated as soon as a RF was identified and confirmed (hyperlipemy, arterial hypertensio). The remaining men of the NG ere invited for a control check up 10–12 years later.

**RGI** – Intense complex intervention of RF took place at the 2<sup>nd</sup> internal clinic of the 1<sup>st</sup> Medical Faculty of Charles University and VFN. These men were invited for check up minimum twice yearly. Following pharmacological intervention, they were invited as necessary.

**RGC** – Following the initial examination, the men in this group received a short written notice including their laboratory results and ECG description and a recommendation to take these results to their doctor. Possible intervention of RF was left to the decision of these doctors (for ethical reasons, it was impossible to create a pure control group being left without any help also in case of identified RF).

**PG** – men in this group were excluded from further observation.

The control form was filled in for men of both RG and NG, who were observed (NGO) once a year. It included data similar to the first examination (see above) and changes compared to the previous form. Data on current medication focused around anti-hypertension and hypolipidemy substances. Any other medications were included in the comment. Skin folds measurements were not taken after 2–3 years from the study commencement.

We recorded or serious illnesses and operations from the last form. In case of cardio-vascular disease, we asked the relevant medical institutions to send us a report copy to confirm or negate the disease as reported by the man. Should an atherosclerotic cardio-vascular disease (ICHS, CMP, ICHDK) have been identified in one of the RG or NGO members in a certain year of the study, the men was excluded from the original group and transferred into the care of a clinic

within the secondary prevention of atherosclerotic diseases. In the following years, no more control forms were filled in with such men. Controlled KVO are coded 410–414, 426–428, 431, 433–436 and 440 in the International Diseases Classification (9th version – 1978), or I20–I25, I61, I63–I67 and 170 in the 10th version (1992).

Details on the various attributes are to be found here.

## 9 Intervention of atherosclerosis Risk Factors

Intervention was the key problem of the study. We tried to optimise and modify influencable RF. Intervention was based on non-pharmacological influence. Pharmacological intervention may be mostly used only in the last years.

*1. non-pharmacological intervention:* interviews on lifestyle, .e. diet, physical activity, suitability or necessity to stop smoking and reduce weight. The interviews were repeated during each stay and except for general instructions, they focused also around specific RF of a given man.

*2. pharmacological intervention:* treatment of arterial hypertension and hyperlipoproteinemy – was very limited in the initial stages of the study. Pharmacological therapy was recommended with respect to the overall risk of a given man and his possible other diseases.

The regular visits of a doctor themselves could represent an intervention, provided the patient new the reason of the visit, parameters to be followed and desirable parameter values.