Rīga Stradiņš University
Faculty of Medicine

PREVALENCE AND MUTUAL CORRELATIONS OF TRADITIONAL AND NEW CARDIOVASCULAR DISEASE RISK FACTORS AND METABOLIC SYNDROME UNDER LATVIA'S POPULATION

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The doctoral thesis and its summary are available at the Library of the Rīga Stradinš University (Dzirciema street 16, Rīga).

Abbreviations

ABI	-	Antebrachial index
AH	-	Arterial hypertension
AHA/NHLBI	-	American Heart Association/ National Heart, Lung and Blood Institute
ApoB/ApoA-1	-	Apolipoprotein B and Apolipoprotein A ratio
ASSIGN	-	AS, Adding Social deprivation and family history to cardiovascular risk assessment; SIGN, Scottish Intercollegiate Guidelines Network
ATP III	-	Adult Treatment Panel III
BMI	-	Body mass index
Ca Score	-	Coronary artery calcium
CC	-	Correlation coefficient
CG	-	Control group
CHD	-	Coronary heart disease
CI	-	Confidence interval
CRP	-	C- reactive protein
CV	-	Cardiovascular
CVD	-	Cardiovascular disease
CVE	-	Cardiovascular event
CVR	-	Cardiovascular risk
DBP	-	Diastolic blood pressure
DM	-	Diabetes mellitus
EAS	-	European Atherosclerosis Society
ESC	-	European Society of Cardiology
ESH	-	European Society of Hypertension
EUROASPEAR III	-	A European Society of Cardiology survey of secondary prevention of coronary heart disease III
Exp (β)	-	Exponentiated regression coefficients
FRISC II	-	In the Fragmin and/or early vascularisation during instability in coronary artery disease
GFR	-	Glomerular filtration rate
GP	-	General Practitioner
HDLC	-	High density lipoprotein cholesterol
HHO	-	Heart Health Offices
HOMA-IR	-	Homeostasis model assessment of insulin resistance
hsCRP	-	High sensitivity C-reactive protein
IAF	-	Intra-abdominal fat
IDF	-	International Diabetes Federation
IL	-	Interleukin
INVEST	-	The International Verapamil SR/Trandolapril Study
IR	-	Insulin resistance
JNC7	-	The Seventh Report of the National Committee
LDL-C	-	Low density lipoprotein cholesterol
MCP-1	-	Monocyte chemoattractant protein 1
M-CSF	-	Macrophage colony stimulating factor

MESA	-	Multi-Ethnic Study of Atherosclerosis
MI	-	Myocardial infarction
MS	-	Metabolic syndrome
MSCT	-	Multi slice computer tomography
NCEP	-	National Cholesterol Education Program
NHBPEP	-	The National High Blood Pressure Education Program
NO	-	Nitric oxide
OR	-	Odds ratio
PAI-1	-	Plasminogen activator inhibitor -1
PROCAM	-	Prospective Cardiovascular Munster Study
QRISK	-	Cardiovascular disease risk calculator, based on the QRESEARCH® database of anonymised UK primary care patients
RF	-	Risk factor
SBP	-	Systolic blood pressure
SCORE	-	Systemic Coronary Risk Evaluation
SPSS	-	Statistical Package for the Social Sciences
TC	-	Total cholesterol
TG	-	Triglycerides
TNF-α	-	Tumor necrosis factor alpha
USPSTF	-	U.S. Preventive Services Task Force
VCAM-1	-	Vascular cell adhesion molecule 1
WC	-	Waist circumference
WHO	-	World Health Organisation

1. Introduction

Cardiovascular diseases (CVD) are the most frequent cause of death in the world. In 2004, around 17.1 million people died of CVD, which accounts for 29% of all deaths that year. The figure is forcast to reach 23.6 million by 2030 [WHO, 2009].

CVD are also critical in Latvia, which still faces one of the highest rates of CVD morbidity and CVD mortality in Europe, CVD being the main cause of death in our country (55.2% of all deaths in 2005) [Ērglis, 2007]. It can be explained with the widely spread CVD risk factors (RF) among both CVD patients and those who consider themselves to be healthy. It is assumed that CVD in latent asymptomatic forms could be recognized with many of the latter. So far the prevalence of risk factors (RF) in Latvia has been described only in some statistical studies, but information about RF crosscorrelations and an indepth analysis does not exist at all.

The importance of so called traditional RF (arterial hypertension (AH), Diabetes mellitus (DM), obesity, smoking, family history of early coronary heart disease (CHD), male sex, dyslipidemia) in development of clinical forms of CVD [European Society of Cardiology (ESC), the guidelines of CVD prophylaxis, 2007] is widely described in scientific papers. There is emphasis on multifactoral approach to evaluating the impact of RF on CVD and on early atherosclerosis emergence and development. Over the last years special attention has been devoted to so-called cardiometabolic risk which contains both cardiovascular and endocrine parameters, thus highlighting the close relationship of pathogenesis of these diseases [*International Chair on Cardiometabolic risk*, 2010]. In order to improve and simplify early diagnosis of RF and clinical CVD forms there is a need for new reliable and sensitive markers that would simultaneously describe the condition of all concerned organ systems.

As obesity has reached epidemic proportions globally [*Poirier*, 2006], its impact on the development of CVD is being investigated in more and more detail. Approximately 80% of all type 2 DM events, 35% of CHD, and 55% of hypertension events in Europe are associated with extra weight and obesity. Lately, closer attention has been paid not only to extra weight but also to distribution of adipose tissue in the body. Abdominal obesity, which includes subcutaneous obesity as well as excessive intra-abdominal or visceral fat, is most dangerous. Adipose tissue, especially visceral fat, is a metabolically active organ [*Bays*, 2008; *Fain*, 2006; *Xavier*, 2006] that produces a large amount of different biologically active substances: adiponectine, leptin, resistin, tumor necrosis factor alpha (TNF-α), interleukin (IL4, IL6 etc.), plasminogen activator inhibitor 1 (PAI-1), C- reactive protein (CRP) and others [*Garg*, 2006; *Lau*, 2005; *Han*, 2007]. A more detailed investigation of these biologically active substances would allow a better understanding of their role in the development of CVD. In this respect, research on metabolism, pathophisiology and clinical impact of adipokines and inflammatory markers holds potential. These biologically active substances, synthesized by abdominal adipose tissue, influence the metabolism of lipids and glucose as well as stimulate the inflammation and the chronic dysfunction of endothelium [*Calabro*, 2008; *Matsuzawa*, 2006; *Graham*, 2007]. Recently the obesity is characterised as a chronic low level inflammation [*Engstrom*, 2003] and exactly this inflammation may be the cause of insulin resistance and other diseases associated with obesity (e.g. hyperlipidemia and metabolic syndrome (MS)) [*Calabro*, 2008].

The important role of inflammation in the development of atherosclerosis and its clinical manifestation has been proven recently [*Ross*, 1999; *Libby*, 2000; Libby, 2002; *Stoll*, 2006; *Fan*, 2003; *Tracy*, 1998]. Inflammatory cells, inflammatory proteins and inflammatory processes in vascular wall all play the dominant role in pathogenesis

of all atherosclerosis development stages (in initiation of atherosclerotic process, in progression of an existing ateroma, in instability and rupture of the atherosclerotic plaque, in development of restenosis after angioplasty) [*Libby*, 2000; *Liao*, 2002; *Inoue*, 2003; *Libby*, 1999; *Plutzky*, 2001]. Circulating inflammatory markers can predict cardiovascular events before they make themselves known. [*Danesh*, 2004].

Adiponectin is one of the metabolically active proteins (adipocytokines), secreted only in adipose tissue. Unlike other hormones, adiponectin has the ability to protect cardiovascular and metabolic processes due to its insulin sensitivisation and anti-inflammatory, antiaterogenic, antithrombotic, and antiangiogenic qualities [*Linn*, 2005; *Kato*, 2006]. However, published literature offers contradictory data on the beneficial features of adiponectin. Recent studies have proven that increased level of adiponectin in persons with high risk of CV events, or already clinically evident CHD (e.g. chronic heart failure), chronic renal disease and elderly men can be associated with higher mortality rate regardless of RF and the stage of heart failure. [*Kistorp*, 2005; *George*, 2006; *Menon*, 2006; *Wannamethee*, 2007].

Leptin is a hormone secreted in adipocytes that crosses the hemato-encephalic barrier and joins to the receptors in hypotolamus when entering the bloodstream. The secretion of neyropeptides and neuromediators is stimulated through these receptors and thus assimilation of food is inhibited. Leptin ensures the reciprocal link between energy reserves of adipose tissue and central nervous system [*Schiling*, 2002], regulates intake of food and sense of satiety, decreases appetite, and increases energy consumption [*Matsuzawa*, 2006; *Gimeno*, 2005; *Lago*, 2007]. The level of leptin is directly proportional to the quantity of adipose tissue; therefore, if it increases (in the case of adiposity), so does the level of leptin [*Xavier*, 2006; *Haynes*, 2008].

In literature the calcification of coronary arteries is treated as a synonym for atherosclerosis, since its main cause is the atherosclerotical process, except for patients with renal failure [*Burke*, 2003; *Greenland*, 2007]. The coronary artery calcium correlates strongly with the prevalence of atherosclerotic plaque in coronary arteries [*Budoff*, 2005].

PAI-1 belongs to the family of serine protease inhibitors. It is secreted by endothelium cells, vascular smooth muscle cells, thrombocytes, as well as adipocytes. PAI-1 is the main fibrinolysis inhibitor inactivating plasminogen activator of both types: urocinase type and tissue type [*Pi-Sunyer*, 2006; *Kershaw*, 2004*; Binder*, 2002]. Decreased fibrinolyse brings to increased accumulation of fibrin in arteries, atherothrombosis and increased risk of CVD development, particularly in cases of adiposity, insulin resistance, metabolic syndrome or type 2 DM [*Gimeno*, 2005].

When starting work on this research in 2006, internationally quoted literature did not contain much information concerning the correlations between the traditional RF mentioned above and adipokines (adiponectin, leptin, etc.), inflammatory markers (CRP, IL, TNF-α), insulin resistance (IR) index HOMA-IR (homeostasis model assessment of insulin resistance), thrombogenesis index (PAI-1), markers of early atherosclerosis (coronary artery calcium (*Ca Score*) and antibrahial index (ABI)). There was no data at all about the correlations of these biological markers under Latvia's population. Such data about adipokines, inflammation markers and parameters of thrombogenesis as risk markers for CVD would be very necessary in order to improve early diagnosis of CVD as well to develop practical and exact recommendations for application of these potential CVD risk markers in doctors' daily practice.

Having evaluated the existing data in scientific literature, availability of laboratory and radiological methods and the financial resources, the following markers were chosen for analysis: adiponectin, leptin, IL-6, TNF-α, PAI-1, insulin, the HOMA-

IR index, homocysteine, CRP, *Ca Score*, amount of intraabdominal adipose tissue and the correlation of all these with traditional CVD RF. Taking into consideration the increasing prevalence of MS in the world, this work pays special attention to analysis of MS prevalence in Latvia's population and its correlation with adipokines, changes in glucose metabolism, markers of inflammation and early artherosclerosis.

2. The structure of doctoral thesis

The Doctoral Thesis is written in Latvian and contains 186 pages. The thesis is illustrated with 33 tables and 30 figures. There are 386 references to recent sources.

3. The aim, tasks and hypotheses of the work

3.1. The aim of the work

To evaluate the prevalence of CVD RF and metabolic syndrome in different groups of Latvia's population and to estimate their correlations with markers of adipokine, inflammation, changes in glucose metabolism and early atherosclerosis, in order to produce practical recommendations for evaluation of cardiometabolic risk and for prophylaxis of CVD.

3.2. The tasks of the work

1. Developing standardised and compatible questionnaires for surveying different patient groups.

2. Obtaining data about CVD RF prevalence in ~20 000 persons who have visited Heart Health Offices (HHO) across Latvia (interviews; estimation of glucose level, cholesterol fraction level and CRP in blood). Analysing this date for various patient subgroups: the whole group; separately by gender; older and younger persons.

3. Obtaining data about CVD RF prevalence in ~1200 patients of general practitioners (GPs) (interviews; estimation of glucose level, cholesterol fraction level and CRP in blood). Analysing this date for various patient subgroups: the whole group; separately by gender; older and younger persons; persons with and without MS.

4. Estimating the prevalence of components of MS in GP patients.

5. Examining ~150 hospitalised patients, selecting patients with MS and forming a control group. Interviewing them, estimation of glucose level, cholesterol fraction level, adipokines level(adiponectin and leptin), inflammatory markers (CRP, IL6, TNFα)level, and the marker of thrombogenesis PAI-1level in blood, assessing visceral fat and coronary artery calcium using computer tomography, and assessing antebrachial index. Comparing this data for the MS patient group and the control group.

6. Estimating the correlations of the new CVD RFs with traditional CVD RFs in the case of MS.

7. Producing recommendations for the application of indices of adiponectin, leptin, IL6, TNF-α, PAI-1, CRP, insulin resistance index (HOMA-IR), amount of coronary artery calcium and amount of visceral fat, in order to detect effectively persons with high CVD risk at the primary healthcare level.

3.3. The hypothesis of the work

1. Frequently persons who consider themselves healthy are under-diagnosed with CVD RF.

2. Adipokines and markers of inflammation and thrombogenesis can be considered as practical and feasible indices for characterisation of early atherogenesis.
3. The estimation of the amount of coronary artery calcium is a sensitive method for detection of early atherosclerosis.
4. A more detailed evaluation of cardiometabolic risk will allow creating diagnostic recommendations for latent CVD and early atherosclerosis.

4. Materials and methods

The study was done in the Internal Disease Clinic of Riga 1st Hospital from 2006 until 2009. A database containing data of 28 836 persons was set up during this period. Collaboration partners of this study were: State Agency for Health Promotion, the activities of which were taken over by Agency of Community Health (K. Zariņa); general practitioners in different regions of Latvia; Health Center ARS (dr. L. Zvaigzne); E. Gulbis Laboratory Ltd (dr. D. Gavars); The Institute of Experimental and Clinical Medicine of the University of Latvia (assoc. prof. P. Tretjakovs).

4.1. Subject groups and their characteristics

Persons who were included in the work were divided in three groups, depending on the the place of inclusion and the extent of the investigation:

1) visitors of Heart Health Offices (HHO);
2) GP patients;
3) hospitalised patients, subdivided into the control group and the group with metabolic syndrome.

In order to survey and examine all the subjects according to one scheme, standardised and compatible questionnaires were developed, which strongly contributed to the later comparison and analysis of the data obtained. The examples of all three questionnaires are attached.

Heart Health Offices visitors

This group contains 27 235 persons who chose to visit HHO on their own iniciative from 1 July, 2007 until 31 December, 2008, where they could gain information on CVD RF, have their individual risk assessed, and receive recommendations for decreasing the risk and favourable lifestyle.

Online system for the heart health evaluation

In order to ensure effectiveness of HHO for the purposes of this study, an online system for assessing CVD RF was set up in Latvia for the first time in 2007 by Riga Stradins University in cooperation with The State Agency of Health Promotion.

Data on cardiovascular health of all HHO visitors was regularly fed into the system, stored there and analysed.

The processes of the online system for assessing cardiovascular health fall into three stages:

1) Entering the data into the online system by HHO nurses;
2) Storage of the data on the server; the server and the online system are monitored by a system administrator;
3) Analysis of the data.

Since the launch of the program in the summer 2007, the HHO have been visited by 52 764 patients and their data has been obtained (as on 25.06.2010).

The collected data can be analysed in several levels. It is possible to analyse the data of each individual HHO, of a particular time period, of a particular city or the whole country.

The obtained data provides statistical indices of HHO work and allows analysis of qualitative parameters of the achieved results, namely, the prevalence of different RF under Latvia's population and their intercorrelations.

General Practitioners patients

During our study two three-day campaigns were organised in all regions of Latvia and in Riga. During the campaign all patients over 18 years of age, regardless of their initial purpose of the visit to their general practitioner, could take part in the study, if complying with the inclusion/exclusion criteria.

Inclusion criteria:

1) age ≥18 years;
2) the patient has been acquainted with and has signed the informed consent form, confirmed by the Ethics Committee for Clinical and Physiological Research, and Drug and Pharmaceutical Product Clinical Investigation of the Research Institute of Cardiology, the University of Latvia.

Exclusion criteria:

1) acute or decompensated serious liver disease with liver failure syndrome;
2) acute infections during the last month;
3) chronic inflammatory diseases;
4) serious renal disease with chronic renal failure (GFR <60 ml/min);
5) thyroid diseases with changes in the level of thyreotrop hormones;
6) active neoplastic process.

Data of 1400 patients was obtained and analysed during the study. These patients, like the HHO visitors, were surveyed to existence of CVD risk factors and had a physical check-up. Total cholesterol (TC), triglycerides (TG), high and low density lipoprotein cholesterol (HDL-C and LDL-C), CRP, and non-high density cholesterol (NonHDL-C) (NonHDL-C= TC-HDL-C) were analysed in E. Gulbis Laboratory Ltd.

Hospitalised patients

Ninety patients with metabolic syndrome and eighty-one persons in control group were recruited in Internal Disease Clinic of Riga 1th Hospital.

Inclusion criteria:

1) persons of both sexes aged 30 - 75 years;
2) metabolic syndrome components, established by International Diabetes Federation;
3) persons without MS admitted to hospital due to different reasons (included in control group)
4) persons have been acquinted with and have signed the informed consent form, confirmed by the Ethics Committee for Clinical and Physiological Research, and Drug and Pharmaceutical Product Clinical Investigation of the Research Institute of Cardiology, the University of Latvia.

Exclusion criteria:

1) acute or decompensated serious liver disease with hepatocellular failure syndrome;
2) acute infections during last month;
3) chronic inflammatory diseases;
4) serious renal disease with chronic renal failure (GFR<60ml/min);
5) thyroid diseases with changes in the level of thyreotrop hormones;
6) active neoplastic process.

In addition to doing questionnaires, physical examination and estimation of cholesterol fractions, in this group also parameters of early atherosclerosis were estimated: the

amount of coronary artery calcium and intraabdominal adipose tissue detected by computertomography, antebrachial index, inflammatory markers – CRP, IL6, and TNF-α, adipocytokines – adiponectin, leptin, and PAI-1, as well as homocysteine, glucose, insulin and insulin resistance index HOMA-IR (*homeostasis model assessment* = glucose x insulin /22.5).

4.2. Statistical analysis

All statistical calculations were done with *SPSS* (*Statistical Package for the Social Sciences) for Windows)*, version 17.0 and 18.0, *MS Excel 2007*, *EpiInfo 2001* subprogram *StatCalc*. In compliance with generally accepted principle in medical statistics, the level of significance was $p<0.05$.

Characteristics of variables

Generally accepted statistical methods were used for the characterisation of person groups [Teibe U., 2007; *Dawson, B.*, 2001; *Altman, D.G.*, 1997]. Quantitative variables are described as arithmetic mean and standard deviation, but in cases when the distribution of data did not complete criteria for normal distribution, the median and the quartiles (I and III) were used. The distribution of data was checked using histograms and Kolmogorov-Smirnov test. Categorical or qualitative variables were characterised in percentage terms. In order to generalize the acquired data to the investigated population, 95% confidence interval (CI) was calculated.

Comparison of groups

Two independent groups were compared by using the t-test of independent sampling, if the variables completed criteria for normal distribution. If the variables did not complete these criteria, Mann-Whitney test was used. Categorical variables were compared using Pearson χ^2 test, and also the continuity correction according to method of Yates was performed and the odds ratio (OR) calculated.

Relationship of parameters

The correlations between parameters were calculated using Spearman's rank correlation coefficient *r* (rho). The following classification of correlations ranking were used [Teibe, U., 2007]: correlation is weak if the correlation coefficient $r \leq 0.25$, correlation is average if the correlation coefficient is $0.25 < r < 0.75$, and correlation is strong if the correlation coefficient is $r \geq 0.75$.

Multifactorial analysis

Multifactoral analyses were performed in order to estimate the impact of the new RF and markers on MS and traditional RF. For the analysis of quantitative variables the method of multiple linear regression was used. Categorical variables were analysed by logistic regression acquiring the value of Exp(β), which characterises the odds ratio (OR).

5. Results

5.1. Patient questionnaires

Intercompatible questionnaires for interviewing each of the three groups were developed at the beginning of the study. All three questionnaires share the following parts:

1) General data of the patients (number of registration, age, sex);
2) Anamnestical data (family history on early CHD, smoking, arterial hypertension, CVD, DM, eating habits, physical activities and used medicines);

3) Anthropometric measurements (weight, height, blood pressure, heart rate);
4) Cholesterol fractions and glucose measurements (in all HHO, except for Riga, where only TC and TG were estimated).

The questionnaires for GP patients contain an additional part for estimation of CRP and MS components.

The questionnaire for hospitalised patients was most detailed; in addition to the first two parts the following were included:

1) adipokines (adiponectin, leptin, IL-6, TNF-α, PAI-1, homocysteine);
2) radiological investigations (ABI and coronary artery calcium and intraabdominal adipose tissue detected by computertomography).

5.2. Results in the group of HHO visitors

All HHO visitors between 01.07.2007 and 31.12.2008 (n=27 285) were included in this group. The highest attendency rate was for the persons of age 46 - 75 years, but the lowest for young patients in the age group of 18 - 30 years.

Table 5.2.1. contains the group's anthropometric and biochemical parameters, mean values and prevalence of RF, and information about lifestyle habits.

Table 5.2.1.

Visitors of HHO: Mean values and prevalence of anthropometric and biochemical parameters, and RF

Risk factors	
Age (years)	57.9±16.4
Men (n (%))	7533 (27.6)
TC (mmol/L)	5.40±1.09
≥5 mmol/L (n (%))	16 428 (60.2)
TG* (mmol/L)	1.53 (1.05, 2.19)
≥1.7 mmol/L (n (%))	4932 (41.7)
Arterial hypertension (n (%))	11 029 (40.4)
SBP (mm Hg)	137±23
DBP (mm Hg)	84±12
Without AH, but SBP≥140 mmHg and/or DBP≥90 mmHg (n (%))	8767 (32.2)
Diabetes mellitus (n (%))	1298 (4.8)
Glucose (mmol/L)	5.27±1.29
≥5.6 mmol/L (n (%))	3283 (14.6)
BMI (kg/m^2)	28.29±5.41
BMI ≥30 kg/m^2 (n (%))	9243 (33.9)
WC (cm)	93.5±13.1
WC ≥102 cm for men and ≥88 cm for women (n (%))	3770 (50.5)
Smokers (n (%))	3871 (14.2)
Positive family history (n (%))	4835 (17.7)
Physical activity (n (%)):	
Intensive	3722 (13.6)
Moderate	17 905 (65.7)
Sedentary lifestyle	5658 (20.7)
Healthy food habits (n (%)):	
Always applied	2924 (10.7)
Sometimes applied	11685 (42.8)
Not applied	12676 (46.5)

Explanation for table 5.2.1.

Categorical variables are expressed as number of occurrence n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply with the normal distribution.

The glucose level was estimated for 22 482 persons, TG for 11 830 persons.

Mean BMI in HHO visitors was increased 28.29±5.41 kg/m^2 and 50.5% of all HHO visitors had increased WC. Increased BMI was detected in 70% of HHO visitors (36.9% were overweight and 33.9% had adiposity). Lifestyle analysis showed that 14.2% were active smokers, 20.7% had sedentary lifestyle, 46.5% did not consider principles of healthy diet at all. 17.7% of HHO visitors reported family history of early CHD. Increased level of blood TC was detected in 60.2%, increased level of TG in 41.7% and increased level of glucose in 14.6%. 40.4% of HHO visitors were aware of their arterial hypertension, and 32.1% had undiagnosed AH. Only 4.8% of the visitors knew that they had DM, but increased glycaemia was detected in 14.6% of the patients.

In order to obtain additional information, the HHO visitors were divided into subgroups by sex. Table 5.2.2. shows the summary of anthropometric and biochemical parameters, traditional CVD RF and their prevalence, lifestyle information, and the level of significance of the difference between both groups.

Table 5.2.2.

Visitors of HHO: Anthropometric and biochemical parameters, mean values of RF and its prevalence, mean values and prevalence of anamnetic data in subgroups of both genders and the significance level of differences between both groups p

RF	**Men (n=7533)**	**Women (n=19751)**	**p**
Age (years)	55.0±17.7	59.0±15.7	**<0.001**
TC (mmol/L)	5.14±1.02	5.50±1.10	**<0.001**
≥5 mmol/L (n (%))	4415 (58.6)	12013 (60.8)	**<0.001**
TG *(mmol/L)	1.53 (1.04, 2.20)	1.53 (1.05, 2.19)	0.875
≥1.7 mmol/L (n (%))	1261 (41.6)	3670 (41.7)	0.867
Arterial hypertension (n (%))	2594 (34.4)	8435 (42.7)	**<0.001**
SBP (mm Hg)	138±21	136±23	**<0.001**
DBP (mm Hg)	86±12	84±12	**<0.001**
Diabetes mellitus (n (%))	286 (3.8)	1012 (5.1)	**<0.001**
Glucose (mmol/L)	5.40±1.47	5.22±1.22	**<0.001**
≥6.1 mmol/L (n (%))	1042 (18.7)	2241 (13.3)	**<0.001**
BMI (kg/m^2)	27.46±4.54	28.61±5.67	**<0.001**
BMI ≥30 kg/m^2 (n (%))	1902 (25.2)	7342 (37.2)	**<0.001**
WC (cm)	97.2±12.7	92.1±13.1	**<0.001**
WC≥102cm for men and ≥88cm for women (n (%))	2158 (28.6)	11 612 (58.8)	**<0.001**
Smokers (n (%))	2288 (30.3)	1583 (8.0)	**<0.001**
Positive family history (n (%))	946 (12.6)	3889 (19.7)	**<0.001**
Physical activity (n (%)):			
Intensive	1315 (17.5)	2407 (12.2)	**<0.001**
Moderate	4957 (65.8)	12 948 (65.6)	0.700
Sendentary lifestyle	1261 (16.7)	4397 (22.2)	**<0.001**
Healthy food habits (n (%)):			
Always applied	435 (5.8)	2489 (12.6)	**<0.001**
Sometimes applied	2463 (32.7)	9222 (46.7)	**<0.001**
Not applied	4635 (61.5)	8041 (40.7)	**<0.001**

Explanation for table 5.2.2.

Categorical variables are expressed as number of occurrence n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply with the normal distribution

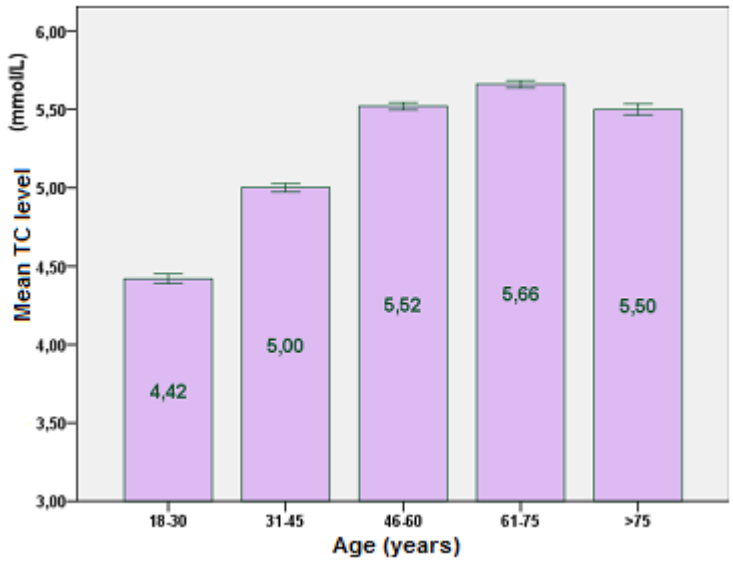
In case of quantitative variables significance level of distinctions between groups (p) is calculated using independent samples t-test (in case of normal distribution) or the *Mann-Whitney* test (if the data do not correspond to normal distribution). Categorical variables are compared using Pearson χ^2 test.

Women were 4 years older than men on average. In women enlarged WC was detected twice as aften as in men (58.8% vs. 28.6%, p<0.001). The weight of smokers was three times smaller in women (8% vs. 30.3%, p<0.001) than in men. Women had sedentary lifestyle significantly more often, while men more often did not consider healthy food recommendations (61.5% vs. 40.7% respectively), as well there were less men who considered them sometimes (resp. 32.7% vs. 46.7%), and men who considered them always (5.8% vs. 12.6%, respectively). Women significantly more often were informed to suffer from arterial hypertension (42.7% vs. 34.4%, respectively) and DM (5.1% vs. 3.8%, respectively). The lipid level analysis of the subgroups showed that in women mean TC level was by 0.36 mmol/L higher (p<0.001), but mean glucose level by 0.18 mmol/L lower (p<0.001).

In order to make a precise estimate of the prevalence of traditional RF under persons of different age, they were divided into five subgroups by age: 18–30; 31–45; 46–60; 61–75 and >75 years of age. The value of mean RF was estimated in each subgroup. The level of TC is shown in figure 5.2.1.

Figure 5.2.1.

The mean levels of TC in different age groups of HHO visitors with 95% CI

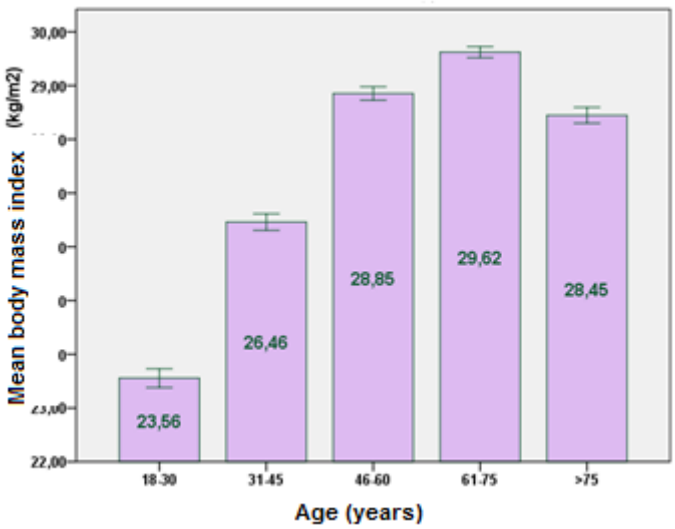


According to single factor analysis of variance (ANOVA), the mean TC indicators in age subgroups significantly differed (F (value of Fishers test) =820.061; p<0.001). The lowest mean TC level was estimated in the youngest group (18–30 years), and this was the only group where it did not exceeded 5 mmol/L (4.42 mmol/L). Up to the age of 61 years, the mean TC level statistically significantly increased (p<0.001) and reached 5.66 mmol/L, while in the oldest group (older than 75 years) level of TC once again decreased statistically significantly by 0.16 mmol/L.

In all age groups the changes of BMI as an obesity indicator were analysed. For these differences see figure 5.2.2.

Figure 5.2.2.

The mean BMI in different age groups of HHO visitors with 95% CI

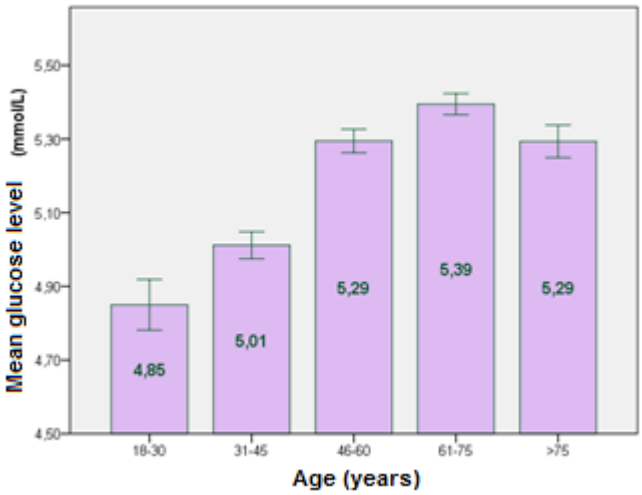


According to ANOVA mean BMI significantly differed in different age groups ($F=767.721$; $p<0.001$). As seen in figure 5.2.2., a normal mean BMI (23.56 kg/m^2) was detected only in the youngest group, but starting with the age of 31 years, mean BMI is over the normal range and it increases significantly with each next age group, reaching the maximum (29.63 kg/m^2) at the age of 61–75, but after the age of 75 years mean BMI once again significantly decreases to 28.45 kg/m^2.

Mean glucose level was assessed for each subgroup. The results are shown in figure 5.2.3.

Figure 5.2.3.

The mean glucose levels in different age groups of HHO visitors with 95% CI

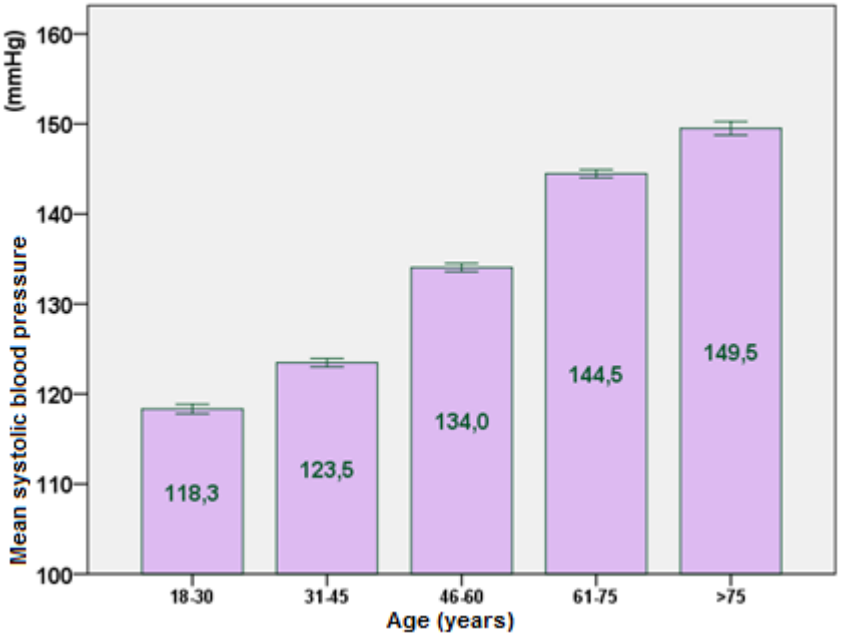


According to ANOVA mean glucose level correlates signicantly with age between different age ($F=87.873$; $p<0.001$). As seen in figure 5.2.3., the lowest glucose level was estimated in the age group of 18–30 years (4.85 mmol/L), and with each next age group mean glucose level significantly ($p<0.05$) increased reaching the maximum (5.39 mmol/L) in the age group of 61–75 years. After the age of 75 years, mean glucose level statistically significantly ($p<0.05$) decreased and fell back to the mean glucose level of age 46–60 years.

Changes of SBP and DBP were analysed in each age group separately. The results are shown in figures 5.2.4. and 5.2.5.

Figure 5.2.4.

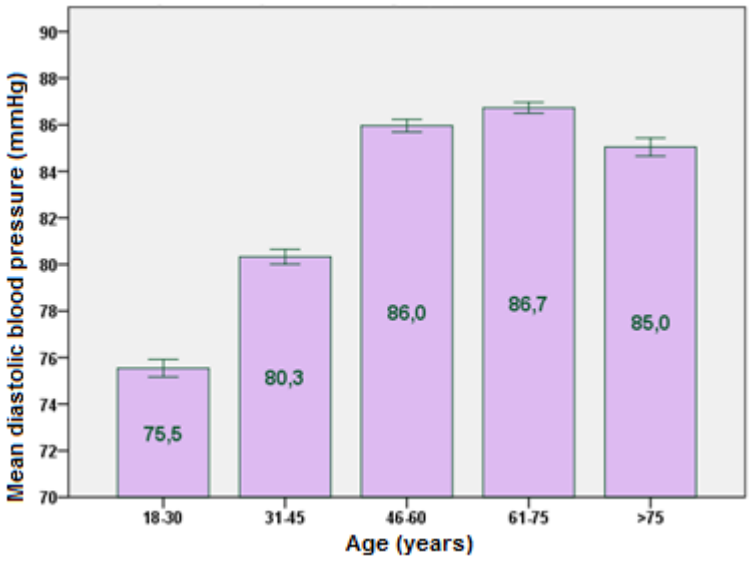
The mean levels of SBP of HHO visitors in different age groups with 95% CI



According to ANOVA, the mean level of SBP under different age groups of HHO visitors differed statistically significantly (F=1592.820; p<0.001). As seen in figure 5.2.4., mean SBP level increased with each next group of age.

Figure 5.2.5.

The mean levels of DBP of HHO visitors in different age groups with 95% CI

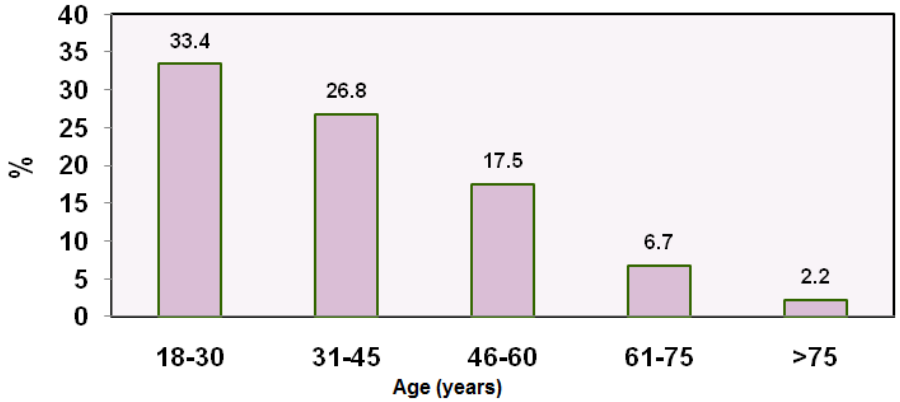


According to ANOVA mean indicator of DBP differed significantly (F=579.319; p<0.001) in different age groups. As seen in figure 5.2.5, persons under 30 years had the lowest mean DBP and it increased with each next age group reaching its maximum at the age of 61–75 years, but after 75 years, mean DBP decreased.

The same as traditional CVD RF, also the prevalence of smokers under different age groups of HHO visitors was analysed (figure5.2.6.).

Figure 5.2.6.

The prevalence of smokers in different age groups of HHO visitors



The highest percentage of smokers was detected in the youngest group – 33.4%, (95% CI 31.4–35.5%). The number of smokers decreased with each next age group. In the group 31–45 years it was only 26.8% (95% CI 25.5–28.2%), in the group 46–60 years – 17.5% (95% CI 16.6–18.4%), in the group 61–75 years - 6.7% (95% CI 6.2–7.2%), but under persons older than 75 years, only 2.2% (95% CI 1.8–2.8%) of the HHO visitors were smokers.

Summary of results in group of HHO visitors:

- The prevalence of CVD RF under the visitors of HHO was very high:
  60.2% had increased level of TC; 41.7% had increased level of TG; 40.4% had arterial hypertension; 14.6% had increased glycaemia.
- A big proportion of HHC visitors, i.e. 32%, had undiagnosed AH.
- In more than one third of the HHO visitors at least one of the obesity indicators exceeded the range of normal:
  36.9% were overweight, but 33.9% had a significant obesity. Women more often than men were obese and overweight.
- More than 40% did not follow the recommendations of a healthy life style:
  14.2% were smokers; 20.7% practised sedentary life style; 46.5% did not apply the basic principles of a healthy diet.
- It was observed that BMI, the level of TC, glucose, SBP and DBP increased with age, reaching their maximum values at the age of 61–75 years, but after the age of 75 the level of these indicators started to drop. The level of SBP was an exception, reaching its maximum value over the age of 75 years.
- The most unfavourable CVS RF profile with their most rapid increase was observed in males aged below 45 (higher mean TC, BMI, glucose, SBP and DBP) and females aged above 45 (SBP and DBP mean levels increased rapidly reaching the mean level of the same indices in males, while the mean TC and BMI indicators even exceeded those of males in the corresponding age group).

5.3. Results of the GP patient group

Table 5.2.1. contains anthropometric and biochemical parameters, mean values and prevalence of RF, as well as the information about lifestyle habits for the group (n= 1400).

Table 5.3.1.

Patients of general practitioners: Anthropometric and biochemical parameters, mean values of RF and its prevalence, mean values and prevalence of anamnestic data

Risk factors	
Age (years)	55.2±14.4
Men (n (%))	379 (27.1)
TC (mmol/L)	5.64±1.22
≥5 mmol/L (n (%))	959 (68.5)
LDL-C (mmol/L)	3.49±1.05
≥ 3mmol/L (n (%))	949 (67.8)
HDL-C (mmol/L)	1.41±0.38
<1.03 mmol/L for men and <1.29 mmol/L for women (n (%))	450 (32.1)
TG *(mmol/L)	1.52 (1.24, 2.37)
≥1.7 mmol/L (n (%))	477 (34.1)
NonHDL-C (mmol/L)	4.22±1.23
≥3.8 mmol/L (n (%))	857 (61.2)
CRP* (mg/L)	1.5 (0.7, 3.3)
CRP>3 mg/L (n (%))	370 (24.4)
Arterial hypertension (n (%))	736 (52.6)
SBP (mm Hg)	135±19
≥140 mm Hg (n (%))	629 (44.9)
DBP (mm Hg)	82±10
≥90 mm Hg (n (%))	420 (30.0)
Without AH, but SBP≥140 and/or DBP≥90 mm Hg (n (%))	121 (18.2)
Metabolic syndrome (n (%))	715 (51.1)
Diabetes mellitus (n (%))	129 (9.2)
Glucose (mmol/L)	5.64±1.45
≥6.1 mmol/L (n (%))	293 (20.9)
BMI (kg/m^2)	28.76±5.48
BMI ≥30 kg/m^2 (n (%))	508 (36.3)
WC (cm)	94.1±14.8
WC ≥102 cm for men and ≥88cm for women (n (%))	780 (55.7)
Smokers (n (%))	275 (19.7)
Positive family history (n (%))	328 (23.4)
Physical activity (n (%)):	
Intensive	113 (8.1)
Moderate	756 (54.0)
Sedentary lifestyle	531 (37.9)
Healthy food habits (n (%)):	
Always applied	231 (16.5)
Sometimes applied	549 (39.2)
Not applied	620 (44.3)

Categorical variables are expressed as number of occurrences n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply with the normal distribution.

Lifestyle analysis showed that 19.7% were active smokers, 37.9% had sedentary lifestyle, 44.3% did not consider healthy diet recommendations, 39.2% did it episodically, while 16.5% did not consider them at all. 55.7% of the group had increased WC, while 36.3% had increased BMI. The analysis of lipid parameters showed increased TC level with 68.5% of the patients, increased LDL-C level with 67.8%, increased TG level with 34.1% and decreased HDL-C level with 32.1% of the patients. 18.1% of the GP patients appeared to have atherogenic dislipidemia, 52.6% had arterial hypertension, 44.9% had increased SBP, 37.1% had increased DBP. Among the patients who had not been diagnosed with arterial hypertension so far, 18.2% were estimated to have increased level of SBP and/or DBP. Metabolic syndrome was

detected in 51.1% of the patients, DM in 9.2%, and increased glucose level in 20.9% of the patients.

GP visitors were also divided into subgroups by sex. Table 5.3.2. shows the summary of anthropometric and biochemical parameters, traditional CVD RF and their prevalence, lifestyle information, and the level of significance of the difference between both groups.

Table 5.3.2.

Patients of general practitioners: anthropometric and biochemical parameters, mean values of RF and their prevalence, mean values and prevalence of anamnetic data in subgroups of genders and the significance of differences between both groups p

RF	**Man (n=379)**	**Women (n=1021)**	**p**
Age (years	55.0±14.8	55.3±14.2	0.671
TC (mmol/L)	5.42±1.25	5.72±1.20	**<0.001**
≥5 mmol/L (n (%))	235 (62.0)	724 (70.9)	**<0.001**
LDL-C (mmol/L)	3.36±1.00	3.54±1.06	**0.006**
≥3 mmol/L (n (%))	248 (65.4)	701 (67.7)	0.760
HDL-C (mmol/L)	1.23±0.34	1.48±0.37	**<0.001**
<1.03 for men and <1.29mmol/L for women. (n (%))	119 (31.4)	331 (32.4)	0.716
TG *(mmol/L)	1.85(1.53,2.32)	1.56(1.21,2.08)	**<0.001**
≥1.7 mmol/L (n (%))	148 (39.1)	329 (32.2)	**0.017**
CRP *(mg/L)	1.7 (0.90,3.40)	1,5 (0.70, 3.10)	**0.037**
CRP>3 mg/L	107 (28.2)	263 (25.8)	0.314
NonHDL-C (mmol/L)	4.19±1.25	4.24±1.22	0.451
NonHDL-C >3.8 mmol/L	232 (61.2)	625 (61.2)	0.989
Atherogenic dysplipidemia (n (%))	71 (18.7)	182 (17.8)	0.763
Arterial hypertension (n (%))	211 (55.7)	525 (51.4)	0.157
SBP (mm Hg)	137±18	136±20	0.111
≥140 mm Hg (n (%))	177 (46.4)	453 (44.3)	0.435
DBP (mm Hg)	83±9	81±10	**0.002**
≥90 mm Hg (n (%))	126 (33.0)	294 (28.8)	0.106
Without AH, but AT≥140/90 mm Hg (n (%))	40 (23.8)	81 (16.3)	**0.030**
Metabolic syndrome (n (%))	157 (41.4)	558(54.7)	**0.015**
Diabetes mellitus (n (%))	36 (9.5)	93 (9.1)	0.823
Glucose (mmol/L)	5.81±1.59	5.57±1.39	**0.006**
≥6.1 mmol/L (n (%))	108 (28.5)	185 (18.1)	**<0.001**
BMI (kg/m^2)	28.53±4.91	28.85±5.68	0.338
BMI ≥30 kg/m^2 (n (%))	126 (33.2)	382 (37.4)	0.149
WC (cm)	99.1±14.0	92.2±14.7	**<0.001**
WC ≥102cm for men ≥88 cm for women (n (%))	159 (42.0)	621 (60.8)	**<0.001**
Smokers (n (%))	126 (33.2)	149 (14.6)	**<0.001**
Positive family history (n (%))	78 (20.6)	250 (24.5)	**0.018**
Physical activity (n (%)): Intensive	50 (13.2)	63 (6.2)	**<0.001**
Moderate	196 (51.7)	560 (54.8)	0.296
Sedentary lifestyle	133 (35.1)	398 (39.0)	0.183
Healthy food habits (n (%)):			
Always applied	41 (10.8)	190 (18.6)	**<0.001**
Sometimes applied	135 (35.6)	414 (40.5)	0.093
Not applied	203 (54.6)	417 (40.9)	**<0.001**

Categorical variables are expressed as number of occurrence n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply the normal distribution.

In case of quantitative variables significance level of distinctions between groups (p) is calculated using independent samples t-test (in case of normal distribution) or the *Mann-Whitney* test (if the data do not correspond to normal distribution). Categorical variables are compared using Pearson χ^2 test.

In this subgroup mean age did not differ by sex. Smoking men outnumbered smoking women two to one (33.2% vs. 14.6% respectively, p<0.001), women

significantly more often reported family history of early CHD (24.5% vs. 20.6% respectively, p=0.018), while men more often did not consider healthy food recommendations (54.6% vs. 40.9% respectively, p<0.001). Women significantly more often had increased WC (60.8% vs. 42.0% respectively, p<0.001) and increased BMI, but the latter difference was not statistically significant. The analysis of mean lipid levels showed significantly higher mean TC level in women, as well as significantly more occurrences of increased TC in women (70.9% vs. 62.0% respectively, p<0.001). Women also has significantly higher level of LDL-C and HDL-C, but the differences in the frequency of their prevalence were not significant. Men showed significantly higher mean level of TG and hypertriglyceridemia more frequently than women (39.1% vs. 32.2% respectively, p=0.017). Aterogenic dislipidemia was met equally frequently in both sexes. Analysis of arterial hypertension prevalence and mean blood pressure showed, that only mean DBP value exhibited significant differences, which was higher in men (83±9 vs. 81±10mmHg respectively, p=0.002); and increased blood pressure was more often detected in men without arterial hypertension in anamnesis (23.8% vs. 16.3% respectively, p=0.030). Women statistically significantly more often had metabolic syndrome (54.7% vs. 41.4% respectively, p=0.015), while men had statistically significantly higher glucose level, were more frequently diagnosed with hyperglyceamia, and had higher level of CRP.

Patients with and without metabolic syndrome were analysed separately. Mean indicators, their prevalence and significance level of differences between both groups p is summarised in table 5.3.3.

Table 5.3.3.

Patients of general practitioners: Anthropometric and biochemical parameters, mean values of RF and their prevalence, mean values and prevalence of anamnetic data for patients with and without MS and the significance of differences between both groups p

Risk Factor	Without MS (n=685)	With MS (n=715)	p
TC (mmol/L)	5.42±1.14	5.80±1.26	**<0.001**
≥5 mmol/L (n (%))	440 (64.2)	505 (70.6)	**<0.001**
LDL-C (mmol/L)	3.32±0.99	3.63±1.06	**<0.001**
≥3 mmol/L (n (%))	437 (63.7)	512 (71.6)	**<0.001**
HDL-C (mmol/L)	1.57±0.39	1.29±0.34	**<0.001**
<1.03 for men and <1,29mmol/L for women (n (%))	105 (15.3)	345 (48.3)	**<0.001**
TG* (mmol/L)	1.03 (0.79, 1.4)	1.73(1.21, 2.33)	**<0.001**
≥1.7 mmol/L (n (%))	84 (12.3)	349 (48.8)	**<0.001**
Non HDL-C (mmol/L)	3.85±1.12	4.51±1.23	**<0.001**
NonHDL-C >3.8 mmol/L (n (%))	361 (52.7)	496 (69.4)	**<0.001**
Atherogenic dyslipidemia (n (%))	29 (4.2)	223 (31.2)	**<0.001**
CRP *(mg/L)	1.04 (0.50, 2.50)	2.00 (1.00, 3.78)	**<0.001**
CRP>3 mg/L (n (%))	129 (18.8)	259 (36.2)	**<0.001**
Arterial hypertension (n (%))	303 (44.2)	413 (57.8)	**<0.001**
SBP (mm Hg)	129±18	141±19	**<0.001**
≥140 mm Hg (n (%))	222 (32.4)	379 (53.0)	**<0.001**
DBP (mm Hg)	79±10	84±9	**<0.001**
≥90 mm Hg (n (%))	146 (21.3)	255 (35.7)	**<0.001**
Diabetes mellitus (n (%))	19 (2.8)	97 (13.6)	**<0.001**
Glucose (mmol/L)	5.18±0.91	5.99±1.67	**<0.001**
≥6.1 mmol/L (n (%))	53 (7.7)	214 (29.9)	**<0.001**
BMI (kg/m^2)	26.02±4.72	30.83±5.09	**<0.001**
BMI ≥30 kg/m^2 (n (%))	127 (18.5)	345 (48.3)	**<0.001**
WC (cm)	85.4±12.9	100.6±12.7	**0.005**
WC ≥102cm for men and ≥88cm for women (n (%))	190 (27.7)	497 (69.5)	**<0.001**
Smokers (n (%))	171 (25.0)	112 (15.7)	**<0.001**
Positive family history (n (%))	142 (20.7)	179 (25.0)	**0.007**

Contiuation of table 5.3.3.

Risk Factor	Without MS (n=685)	With MS (n=715)	p
Physical activity (n (%)):			
Intensive	87 (12.7)	40 (5.5)	**<0.001**
Moderate	420 (61.3)	373 (52.2)	**0.002**
Sedentary lifestyle	178 (26.0)	302 (42.3)	**<0.001**
Healthy food habits (n (%)):			
Always applied	156 (22.8)	104 (14.5)	**<0.001**
Sometimes applied	263 (38.5)	316 (44.2)	**0.036**
Not applied	266 (39.7)	295 (41.3)	0.354

Categorical variables are expressed as number of occurrences n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply the normal distribution

In case of quantitative variables significance level of distinctions between groups (p) is calculated using independent samples t-test (in case of normal distribution) or the *Mann-Whitney* test (if the data do not correspond to normal distribution). Categorical variables are compared using Pearson χ^2 test.

Patients with MS smoked statistically significantly more rarely, but more often admitted sedentary lifestyle. Among these subgroups all MS diagnostic criteria exhibited statistically significant changes, namely, larger WC, higher TG and glucose levels, lower HDL-C, higher SBP and DBP, and these alterations were met statistically significantly more often. Patients with MS showed significantly higher mean TC and levels of nonHDL-C and LDL-C, and these alterations were met more often. Also aterogenic dislipidemia was significantly more often detected in patients with MS.

All five MS diagnostic criteria were detected in 8.8% of all GP patients, four criteria in 17.1%, and three criteria, which is the minimum for MS diagnosis, in 25.3%. Only in 8.6 % of GP patients none of MS diagnostic criteria were detected, one criterion was detected in 14.6% and two criteria in 25.6%.

Summary of results of GP patients group:

- The prevalence of CVD RF under GP patients is very high:
  68.5% of the patients had an increased level of TC; 67.8% had an increased level of LDL-C; 34.1% had an increased level of TG; 52.6% had arterial hypertension; 9.2% had DM; 20.9% had a hyperglycemia.
- The prevalence of MS in these patients is very high (51.1%) and only in 8.6% of GP patients none of MS criteria were detected.
- Also in this group many patients did not follow healthy lifestyle recommendations:
  19.7% were smokers; 37.9% practised sedentary lifestyle; 44.3% did not apply the basic principles of a healthy diet.

5.4. Results of the group of hospitalised patients with MS and in the control group

Hospitalised patients were divided into two groups: 90 patients with MS and 81 persons in the control group.

Table 5.4.1. contains characteristics of both groups: demographic and risk factors, traditional and new biochemical risk factors, inflammatory markers and other characteristics of new risk factors, as well as information about lifestyle habits (smoking, diet and physical activity).

Table 5.4.1.

Hospitalised patients: Anthropometric and biochemical parameters, mean values of new and traditional RF and their prevalence, mean values and prevalence of anamnetic data and radiological parameters in patients with MS and control group and the significance of differences between both groups p

Risk factors	**Control group (n=81)**	**With MS (n=90)**	**p**
Age (years)	47.7±11.0	54.2±11.1	**<0.001**
Men (n (%))	22 (27.2)	41 (45.6)	**0.017**
TC (mmol/L)	5.68±0.97	5.88±1.37	0.233
≥5 mmol/L (n (%))	56 (69.1)	61 (71.8)	0.710
HDL-C (mmol/L)	1.83±0.44	1.25±0.36	**<0.001**
<1.03for men /<1.29 for women (n (%))	2 (2,5)	38 (44.7)	**<0.001**
TG* (mmol/L)	1.10 (0.92, 1.43)	2,33 (1.87, 2.88)	**<0.001**
≥1.7 mmol/L (n (%))	9 (11.1)	65 (76.5)	**<0.001**
LDL-C (mmol/L)	3,33±0,91	3,69±1,21	**0.025**
≥3 mmol/L (n (%))	53 (65.4)	64 (75.3)	0.164
NonHDL-C (mmol/L)	3.85±0.96	4.63±1.24	**<0.001**
CRP* (mg/L)	0.82 (0.40, 1.61)	1.75 (0.91, 5.54)	**<0.001**
>3 mg/L (n (%))	7 (8.6)	34 (37.8)	**<0.001**
Adiponectin *(mg/L)	50.65 (33.05. 74.60)	32.20 (18.20. 50.55)	**<0.001**
LepTIn* (ng/ml)	7.17 (3.13, 13.33)	15.90 (7.26, 25.45)	**0.002**
IL6* (pg/ml)	0.12 (0.12, 0.67)	0.12 (0.12, 0.64)	0.869
PAI-1* (ng/ml)	36.35 (26.09, 45.20)	58.82 (34.60, 86.73)	**<0.001**
TNF-α* (pg/ml)	3.16 (1.60, 4.73)	3.73 (1.58, 5.91)	0.233
Homocystein (μmol/L)	11.38±3.35	11.75±4.35	0.703
SPB (mm Hg)	123.6±21.1	137.9±22.4	**<0.001**
DBP (mm Hg)	78.7±12.7	86.0±14.2	**<0.001**
Glucose (mmol/L	4.95±0.45	6.19±2.34	**<0.001**
Insulin (μIV/L)	6.62±4.42	14.41±8.58	**<0.001**
HOMA-IR* index	1.12 (0.66, 1.93)	3.28 (2.12, 5.36)	**<0.001**
>2 (n (%))	19 (27.7)	65 (76.5)	**<0.001**
BMI (kg/m^2)	26.63±4.36	32.57±5.79	**<0.001**
BMI >30 kg/m^2	11 (13.6)	48 (56.5)	**<0.001**
WC (cm)	97.7±11.8	110.5±13.2	**<0.001**
WC >102 cm for men and >88 cm for women	52 (64.2)	74 (87.1)	**<0.001**
Smokers (n (%))	15 (18.5)	18 (20.0)	0.956
Positive family history (n (%))	13 (16.0)	25 (27.8)	0.167
Physical activity (n (%)): Intensive	8 (9.9)	2 (2.2)	0.067
Moderate	44 (54.3)	46 (51.1)	0.860
Sedentary lifestyle	29 (35.8)	42 (46.7)	0.069
Healthy food habits (n (%)):			
Always applied	5 (6.2)	11 (12.2)	0.325
Sometimes applied	46 (56.8)	51 (56.7)	0.978
Not applied	30 (37.0)	28 (31.1)	0.765
ABI	1.00±0.13	0.97±0.14	0.265
Ca Score*	0 (0, 2.5)	13 (0, 141)	**<0.001**
IAF (cm^3)	55±33	114±52	**<0.001**
CVR (*SCORE*)	1 (0, 3)	4 (2, 8)	**<0.001**

Categorical variables are expressed as number of occurrences n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply the normal distribution

In case of quantitative variables significance level of distinctions between groups (p) is calculated using independent samples t-test (in case of normal distribution) or the *Mann-Whitney* test (if the data do not correspond to normal distribution). Categorical variables are compared using Pearson χ^2 test.

Patients with MS, in comparison to the control group, statistically significantly (p<0,001) differed in all MS diagnostic criteria parameters, namely, larger WC, higher levels of TG and glucose, lower level of HDL-C, higher SBP and DBP were detected.

Along the differences in traditional RF differences in new risk factors were also observed. MS patients, in comparison to the control group, had statistically significantly (p=0.002) higher levels of leptin, PAI-1 (p<0.001), CRP (p<0.001) and lower level of adiponectin (p<0.001), remarkable insulin resistance (higher level of insulin and the HOMA-IR index), and statistically significantly (p<0.001) higher amount of coronary artery calcium, IAF and higher fatal CVE risk within 10 years (according to *SCORE*) was detected.

In patients with MS not only higher values of above mentioned parameters were detected, but statistically significantly more often (p<0.001) unfavorable alterations were observed. Only 2.5% of the control group had decreased level of HDL-C, while in 44.7% of MS such alterations were detected. Similar alterations were also observed in cases of increased TG level; in 11.1% of the control group and in 76.5% of MS patients. In MS patients significantly more frequently increased levels of CRP (37.8% vs. 8.6%, respectively) and glucose (29.4% vs. 0%, respectively) and the HOMA-IR index (76.5% vs. 27.7%, respectively) were observed.

Statistically significant alterations of TC, IL-6, TNF-α, homocysteine level and ABI were not detected in these groups.

Table 5.4.2. contains anthropometric and biochemical indices, mean values of the new and traditional RF, anamnetic and radiological parameters as well as the information about lifestyle habits depending on the sex.

Table 5.4.2.

Hospitalised patients with MS: Anthropometric and biochemical parameters, mean values of new and traditional RF and their prevalence, mean values and prevalence of anamnetic and radiologic data for subgroups of sexes and the significance of differences between both groups p

Risk Factors	**Men (n=41)**	**Women (n=49)**	**p**
Age (years)	52.6±11.4	55.9±10.7	0.158
TC (mmol/L)	5.48±1.47	6.22±1.20	**0.012**
≥5 mmol/L (n (%))	23 (56.1)	41 (83.7)	**0.005**
LDL-C (mmol/L)	3,16±1,20	4,09±1,07	**0.002**
≥ 3 mmol/L (n (%))	15 (51.7)	32 (82.1)	**0.009**
HDL-C (mmol/L)	1.09±0.24	1.38±0.39	**<0.001**
<1.03 vīr. un <1.29 siev. (n (%))	19 (46.3)	23 (46.9)	0.562
TG* (mmol/L)	2.13 (1.22, 2.52)	1.93 (0.81, 1.88)	**0.023**
≥1.7 mmol/L (n (%))	31 (75.6)	36 (73.5)	0.506
NonHDL-C (mmol/L)	4.38±1.39	4.83±1.08	0.094
NonHDL-C>3.8 mmol/L (n(%))	23 (56.1)	40 (81.5)	**0.008**
CRP* (mg/L)	1,.62 (0.79, 3.26)	2.11 (0.95, 4.31)	0.445
CRP>3 mg/L (n (%))	13 (36.1)	10 (25.6)	0.453
AdiponecTIn* (ng/ml)	23.40 (14,.20; 42.25)	39.60 (25.70; 47.40)	0.056
Leptin* (ng/ml)	7,75 (4,68, 18.28)	23.65 (11.85, 28,.52)	**<0.001**
IL6* (pg/ml)	0,64 (0,12; 1,04)	0,64 (0,12; 0,64)	0.196
PAI-1* (ng/ml)	61.75 (42.93, 85,76)	58,90 (38,60; 87,70)	0.610
TNF-α* (pg/ml)	2.97 (1.61, 5.58)	4.61 (1.87, 6. 36)	0.369
Homocystein (μmol/L)	12.05±3.70	11.51±4.84	0.580
Arterial hypertension (n (%))	34 (82.9)	40 (81.6)	0.874
SBP (mm Hg)	138.6±21.1	137.4±23.6	0.797
DBP (mm Hg)	86.1±13.9	85.8±14.6	0.925
Diabetes mellitus (n (%))	7 (17.1)	8 (16.3)	0.937
Glucose (mmol/L)	6.15±1.91	6.23±2.67	0.864
≥ 6.1 mmol/L (n (%))	22 (53.7)	27 (55.1)	0.891
Insulin* (μIV/L)	12.90 (7.76, 19.00)	13.10 (8.42, 19.97)	0.547
HOMA-IR index*	3.25 (2.03, 4.82)	3.28 (1.99, 5.68)	0.778
HOMA-IR index>2	28 (75.7)	35 (74.5)	0.900

Continuation of table 5.4.2.

Risk Factors	Men (n=41)	Women (n=49)	p
BMI (kg/m^2)	31.98±4.24	33.06±6.84	0.364
BMI ≥30 kg/m^2 (n (%))	24 (58.5)	28 (57.1)	0.894
WC (cm)	111.8±11.4	109.4±14.5	0.374
WC >102 cm men, >88 cm women (n (%))	41 (100.0)	49 (100.0)	1.000
ABI	1.00±0.13	0.96±0.15	0.336
Ca Score	11 (0, 213)	4 (0, 122)	0.573
IAF (cm^3)	140±51	96±45	**0.005**
Smokers (n (%))	8 (20.5)	9 (19.6)	0.348
Positive family history (n (%))	29 (74.4)	28 (60.9)	0.219
Physical activity (n (%)): Intensive	1 (2.6)	1 (2.2)	0.951
Moderate	22 (56.4)	21 (45.7)	0.483
Sedentary lifestyle	16 (41.0)	24 (52.2)	0.331
Healthy food habits (n (%)):			
Always applied	0 (0)	8 (17.4)	**0.004**
Sometimes applied	23 (59.0)	27 (58.7)	0.869
Not applied	16 (41.0)	11 (23.9)	**0.001**
CVR (*SCORE*)	4 (1, 10)	3 (1, 4)	**0.012**

Categorical variables are expressed as number of occurrences n (%); Quantitative variables as arithmetic mean ±SD in case of normal distribution or *median (I and III quartile), if data do not comply the normal distribution

In case of quantitative variables significance level of distinctions between groups (p) is calculated using independent samples t-test (in case of normal distribution) or the *Mann-Whitney* test (if the data do not correspond to normal distribution). Categorical variables are compared using Pearson χ^2 test.

The age did not statistically significantly differ for the sexes. Men statistically significantly (p=0.001) more often did not considered healthy food recommendations. In women statistically significantly higher levels of TC (6.22 mmol/L vs. 5.48 mmol/L, respectively) and LDL-C (4.09 mmol/L vs. 3.16 mmol/L, respectively) were observed, and these values were frequently above normal. Also mean HDL-C level was statistically significantly higher in women than in men (1.38 mmol/L vs. 1.09 mmol/L, respectively), but the prevalence of decreased level of HDL-C did not differ (p=0.562). In men statistically significantly higher mean level of TG (2.13 mmol/L vs. 1.93 mmol/L, respectively) was observed, but increased level of TG was equally freaquently observed in both sexes. Women had statistically significantly higher mean leptin level (23.65 ng/ml vs. 7.75 ng/ml, respectively). Although mean adiponectine level was higher in women (39.6 ng/ml vs. 23.40 ng/ml, respectively), the difference was not statistically significant (p=0.056). In men statistically significantly higher potential fatal CVE risk within next 10 years (according to *SCORE)* was estimated .

Like in GP patient group, prevalence of MS diagnostic criteria was analysed.

All five MS diagnostic criteria were detected in 22.3% of patients, four criteria in 26.7%, and three criteria in 51.1%.

Comparing the patients breakdown depending on the relevance of fatal CVE risk (*SCORE)*, statistically significant differences in the control group and MS patients were observed (according to chi-squarred tests χ^2=26.047; p<0.001). In MS patient group two times fewer patients with low fatal CVE risk were detected compared to the control group (38% v. 77% respectively), 2.8 times more patients with average risk (28% vs. 10% respectively) and 2.5 times more patients with high risk assessment (34% vs. 14% respectively).

Similarly the patient breakdown in control and MS groups depending on the amount of coronary artery calcium was analysed. During the study the investigation of 96 persons (48 in the control group and 48 MS patients) was completed. In MS patients statistically significantly more often (according to chi-squarred tests χ^2=8.649; p=0.003)

increased *Ca Score* was detected (29% (n=14) vs. 6% (n=3) respectively) compared to control group.

The prevalence of different RF and markers were analysed depending on fatal CVE risk within next 10 years (*SCORE*). Depending on *SCORE* patients were divided into two groups, namely, with *SCORE* <5% and *SCORE* ≥5%. In patients with increased *SCORE*, statistically significantly more often (p<0.001) MS was observed. In patients with high fatal CVE risk within next 10 years (≥5%) (according *SCORE*) increased level of CRP was detected in 21% of cases, but in patients with fatal CVE risk <5% increased level of CPR was detected in 18% of cases; however, this difference was not statistically significant (p=0.572). The same tendency was observed in cases of unfavourable heredity. Unfavourable heredity was estimated for 22.6% of patients with fatal CVE risk <5% and for 21.3% of patients with risk ≥5%; yet, this difference was not statistically significant (p=0.865). In patients with increased fatal CVE risk (≥5%) 62% had increased level of PAI-1, while in other patients increased level of PAI-1 was detected in 53% of cases, yet this difference was not statistically significant (p=0.249). Similar coherence was observed also in cases of decreased level of adiponectin and increased level of leptin. Decrease of adiponectin level was detected in 70% of patients with fatal CVE risk ≥5% and in 66% of the rest of the group; and increase of leptin level was detected in 68% of patients with fatal CVE risk ≥5% and in 65% of the rest of the group; however, these differences were not statistically significant (p=0.547 in case of adiponectin and p=0.878 in case of leptin). All patients with fatal CVE risk ≥5% had increased *Ca Score*, while in patients with fatal CVE risk <5% nobody had increased *Ca Score*.

Summary of results within the group of hospitalised patients with MS and control group:

- Patients with MS had higher levels of CRP, adiponectin, leptin, PAI-1, insulin and the HOMA-IR index.
- Patients with MS had bigger amount of coronary artery calcium and it was observed statistically significantly (p=0.003) more frequently than in control group.
- Patients with MS had higher fatal CVE risk (*SCORE*) and patients with increased fatal CVE risk more frequently had MS.
- Also in case of MS the difference in sex is valid for CVD RF:
  Women had higher level of TC, LDL-C, HDL-C.
- More than 20% of MS patients had all five criteria for MS diagnosis.
- Patients with MS had 2.5 times higher risk of CVE.
- All patients with increased fatal CVE risk had increased Ca Score.

5.5. The relationship between new and traditional risk factors in case of metabolic syndrome

5.5.1. Analysis of correlation

Using Spearman's correlations coefficient, the relationship between new and traditional risk factors in case of MS was analysed.

Tables 5.5.1. and 5.5.2. show coefficients of these correlations, their significance levels p, and 95% CI for statistically significant coefficients of correlations.

Table 5.5.1.

Correlation between new RF and age, obesity indicators, blood pressure; correlation significance level p and 95% confidence intervals for statistically significant correlation

		Age		WC		BMI		SBP		DBP	
		CG	**MS**	**CG**	**MS**	**CG**	**MS**	**CG**	**MS**	**CG**	**MS**
ABI	CC *P* CI	-0.018 *0.877*	-0.133 *0.288*	0.172 *0.129*	-0.083 *0.509*	0.151 *0.183*	-0.076 *0.544*	0.129 *0.257*	**-0.270** ***0.028*** -0.504--0.027	0.028 *0.809*	-0.056 *0.656*
CRP	CC *P* CI	0.043 *0.704*	-0.081 *0.488*	**0.238** ***0.033*** 0.012-0.432	**0.367** ***0.001*** 0.138-0.550	**0.251** ***0.024*** 0.023-0.455	**0.326** ***0.004*** 0.034-0.520	0.110 *0.328*	-0.103 *0.379*	0.181 *0.106*	-0.048 *0.680*
Adipo-nectin	CC *P* CI	-0.009 *0.933*	0.178 *0.093*	-0.135 *0.230*	**-0.279** ***0.009*** -0.429--0.087	-0.152 *0.176*	**-0.275** ***0.010*** -0.431--0.026	-0.217 *0.052*	**0.274** ***0.009*** 0.011-0.475	-0.157 *0.161*	0.202 *0.056*
Homo-cystein	CC *P* CI	**0.356** ***0.002*** 0.137-0.532	**0.245** ***0.032*** 0.002-0.437	0.200 *0.092*	-0.040 *0.733*	0.117 *0.326*	-0.136 *0.237*	0.080 *0.504*	**0.239** ***0.035*** 0.025-0.421	0.001 *0.996*	0.177 *0.124*
Leptin	CC *P* CI	0.172 *0.127*	0.048 *0.659*	**0.563** ***<0.001*** 0.371-0.714	**0.340** ***0.001*** 0.077-0.492	**0.584** ***<0.001*** 0.344-0.741	**0.442** ***<0.001*** 0.205-0.595	0.120 *0.289*	-0.094 *0.386*	0.099 *0.381*	-0.092 *0.395*
IL6	CC *p*	-0.161 *0.151*	-0.083 *0.448*	0.132 *0.241*	0.079 *0.470*	0.112 *0.322*	0.105 *0.334*	0.131 *0.245*	0.015 *0.890*	0.121 *0.284*	0.073 *0.507*
PAI-1	CC *P* CI	0.016 *0.890*	-0.141 *0.191*	0.166 *0.145*	**0.406** ***<0.001*** 0.193-0.564	**0.319** ***0.004*** 0.069-0.531	**0.524** ***<0.001*** 0.345-0.663	0.098 *0.390*	0.123 *0.252*	0.111 *0.329*	0.162 *0.131*
TNF-α	CC *p*	0.041 *0.713*	0.112 *0.308*	0.064 *0.572*	-0.103 *0.349*	0.100 *0.376*	-0.111 *0.314*	-0.040 *0.720*	-0.022 *0.843*	-0.053 *0.641*	-0.132 *0.227*
Insulin	CC *P* CI	-0.089 *0.434*	-0.081 *0.461*	**0.413** ***<0.001*** 0.188-0.582	**0.431** ***<0.001*** 0.236-0.614	**0.491** ***<0.001*** 0.282-0.622	**0.490** ***<0.001*** 0.267-0.660	**0.234** ***0.037*** 0.051-0.418	-0.029 *0.794*	0.217 *0.053*	0.014 *0.897*
HOMA-IR index	CC *P* CI	-0.085 *0.453*	-0.030 *0.784*	**0.414** ***<0.001*** 0.174-0.590	**0.459** ***<0.001*** 0.269-0.641	**0.486** ***<0.001*** 0.284-0.618	**0.510** ***0.001*** 0.326-0.673	**0.267** ***0.017*** 0.021-0.440	-0.036 *0.742*	**0.239** ***0.033*** 0.004-0.426	-0.016 *0.884*
CaScore	CC *P* CI	**0.468** ***0.001*** 0.149-0.664	**0.285** ***0.049*** 0.088-0.550	**0.385** ***0.007*** 0.063-0.599	**0.482** ***<0.001*** 0.153-0.696	0.132 *0.369*	**0.375** ***0.009*** 0.087-0.624	0.207 *0.159*	-0.008 *0.954*	-0.067 *0.651*	-0.106 *0.471*
Intra-abdomi-nal fat	CC *P* CI	**0.464** ***0.001*** 0.174-0.663	0.121 *0.425*	**0.665** ***<0.001*** 0.448-0.694	**0.621** ***<0.001*** 0.346-0.814	**0.692** ***<0.001*** 0.487-0.820	**0.508** ***<0.001*** 0.202-0.742	**0.410** ***0.004*** 0.104-0.610	-0.032 *0.833*	0.206 *0.164*	-0.024 *0.874*

As seen in table 5.5.1. ABI has a statistically significantly (p=0.028) negative correlation only with SBP in case of MS, but with other parameters statistically significant correlations were not found.

The levels of CRP, leptin, and insulin and the HOMA-IR index statistically significantly positively correleated with the obesity indices (WC and BMI) in MS patients as well as in control group, while the level of adiponectin statistically significantly negatively correlated with obesity indices only in group of MS patients.

The level of homocysteine statistically significantly positively correlated with age in both groups but with SBP only in patients with MS.

The level of PAI-1 statistically significantly positively correlated with BMI in both groups and with WC only in group of MS patients.

A statistically significantly positive correlation between insuline level and SBP as well as positive correlation between HOMA-IR index and SBP and DBP were found in patients of control group.

The amount of coronary artery calcium statistically significantly positively correlated with age and WC in both groups, while with BMI only in case of metabolic syndrome.

The levels of IL6 and TNF-α did not statistically significantly correlate with any of the traditional RF refered to this table in any of the groups.

Taking into account the controversial data in literature about the most precise antropometric indicator of adiposity, the relationship of WC and BMI with visceral adiposity was analysed. Both WC and BMI statistically significantly ($p<0.001$) positively correlated with amount of intraabdominal fat, but in MS patients the correlation was stronger with WC (correlation coefficient 0.621 with 95% CI 0.346–0.814) and in the control group the correlation was stronger with BMI (correlation coefficient =0.692 with 95% CI 0.487–0.820). In the control group statistically significant positive correlation between amount of intraabdominal (visceral) fat and the age and SBP was observed.

Table 5.5.2.

Correlation between new RF and cholesterol parameters, total fatal CVE risk (according SCORE) and the level of glucose, correlations significance level p and 95% CI for statistically significant correlation

		LDL-C		TG		HDL-C		CVR		Glucose	
		CG	**MS**	**CG**	**MS**	**CG**	**MS**	**CG**	**MS**	**CG**	**MS**
ABI	CC	0.170	0.184	0.142	-0.015	-0.130	0.070	0.125	0.030	0.017	-0.113
	p	*0.136*	*0.196*	*0.213*	*0.908*	*0.252*	*0.578*	*0.271*	*0.808*	*0.884*	*0.367*
CRP	CC	0.113	-0.027	0.184	0.128	**-0.264**	**-0.340**	0.027	-0.107	-0.006	0.058
	P	*0.317*	*0.839*	*0.099*	*0.273*	***0.017***	***0.003***	*0.808*	*0.362*	*0.955*	*0.618*
	CI					-0.451--0.051	-0.451--0.093				
Adipo-nectin	CC	0.026	0.136	**-0.262**	-0.195	**0.475**	**0.356**	**-0.288**	0.078	**-0.289**	-0.144
	P	*0.816*	*0.270*	***0.020***	*0.066*	***<0.001***	***<0.001***	***0.009***	*0.467*	***0.009***	*0.175*
	CI			-0.473--0.027		0.278-0.642	0.117-0.513	0.022-0.479		0.018-0.480	
Homo-cystein	CC	**0.233**	0.088	0.216	-0.065	-0.168	-0.079	**0.422**	**0.343**	-0.057	0.061
	P	***0.049***	*0.517*	*0.068*	*0.572*	*0.157*	*0.496*	***<0.001***	***0.002***	*0.632*	*0.595*
	CI	0.038-0.504						0.203-0.615	0.105-0.540		
Leptin	CC	0.160	-0.011	0.050	0.039	-0.114	0.050	-0.039	-0.128	0.021	0.154
	p	*0.158*	*0.929*	*0.657*	*0.718*	*0.316*	*0.647*	*0.733*	*0.236*	*0.856*	*0.153*
IL6	CC	0.047	-0.210	-0.151	0.124	-0.058	0.044	-0.108	-0.172	0.047	0.077
	p	*0.677*	*0.091*	*0.179*	*0.254*	*0.606*	*0.687*	*0.337*	*0.113*	*0.677*	*0.482*
PAI-1	CC	0.168	**-0.249**	**0.248**	**0.273**	-0.197	-0.137	0.071	-0.064	-0.077	**0.336**
	P	*0.142*	***0.042***	***0.028***	***0.010***	*0.081*	*0.204*	*0.533*	*0.556*	*0.500*	***0.001***
	CI		-0.505-0.040	0.044-0.514	0.035-0.469						0.109-0.533
TNF-a	CC	0.139	0.086	-0.009	-0.047	-0.063	0.077	-0.047	-0.052	-0.063	0.027
	p	*0.217*	*0.498*	*0.936*	*0.672*	*0.574*	*0.483*	*0.676*	*0.635*	*0.579*	*0.805*
Insulin	CC	0.068	-0.128	**0.368**	**0.297**	**-0.271**	**-0.235**	0.071	0.029	**0.326**	0.196
	P	*0.552*	*0.317*	***0.001***	***0.006***	***0.015***	***0.031***	*0.529*	*0.791*	***0.003***	*0.073*
	CI			0.151-0.557	0.087-0.458	-0.468--0.055	0.022-0.412			0.105-0.533	
HOMA-IR	CC	0.082	-0.141	**0.387**	**0.294**	**-0.271**	**-0.262**	0.093	0.079	**0.430**	**0.406**
	P	*0.472*	*0.272*	***<0.001***	***0.006***	***0.015***	***0.016***	*0.410*	*0.470*	***<0.001***	***<0.001***
index	CI			0.161-0.599	0.100-0.449	0.161-0.599	-0.441-0.014			0.211-0.621	0.139-0.597
CaScore	CC	0.041	-0.299	**0.389**	0.093	**-0.313**	-0.212	**0.475**	**0.323**	0.089	**0.451**
	P	*0.781*	*0.081*	***0.006***	*0.530*	***0.030***	*0.148*	***0.001***	***0.025***	*0.549*	***0.002***
	CI			0.045-0.591		-0.494-0.051		0.154-0.699	0.035-0.571		0.063-0.715
Intra-abdomi-nal fat	CC	0.206	**-0.434**	**0.441**	**0.328**	**-0.506**	**-0.425**	**0.574**	**0.330**	**0.296**	0.246
	P	*0.166*	***0.010***	***0.002***	***0.026***	***<0.001***	***0.003***	***<0.001***	***0.025***	***0.043***	*0.099*
	CI		-0.645--0.128	0.188-0.657	0.053-0.587	-0.691--0.285	-0.711--0.123	0.334-0.734	0.078-0.584	0.038-0.553	

As seen in table 5.5.2 the levels of CRP and insulin, the HOMA-IR index, amount of coronary artery calcium and intraabdominal (visceral) fat statistically significantly negatively and the level of adiponectin positively correlated with HDL-C.

Statistically significant negative correlations of adiponectin with levels of TG and glucose and total fatal CVE risk within next 10 years (according *SCORE*) were observed in control group.

The level of homocysteine statistically significantly positively correlated with LDL-C in control group and with total fatal CVE risk within next 10 years (according *SCORE*) in both groups.

Level of PAI-1 statistically significantly negatively correlated with level of LDL-C and positively with glucose in MS patients, but statistically significantly positively with TG level in both groups.

The level of insulin, the HOMA-IR index and amount of intraabdominal (visceral) fat statistically significantly positively correlated with the level of TG in both groups, but with amount of coronary artery calcium only in control group.

The HOMA-IR index statistically significantly positively correlated with the level of glucose in both groups, but with the level of insulin only in control group.

In addition to the correlations mentioned above, the amount of coronary artery calcium positively correlated also with total fatal CVE risk within next 10 years (*SCORE*) in both groups but with level of glucose only in group of MS patients.

In addition to the correlations mentioned above, intraabdominal (visceral) fat statistically significantly negatively correlated with LDL-C in MS patients, positively with total fatal CVE risk within next 10 years (*SCORE*) in both groups and with level of glucose in control group.

No statistically significant correlations of level of PBI, leptin, IL6 and TNF-α with the considered traditional RF risks were observed. TC was not included under the table of traditional RF because none of the markers showed statistically significant correlations with this RF.

Summary of correlations analysis:

Analysing the relationship of the traditional and new RF by correlation analysis, the closest statistically significant correlations were observed between the following parameters:

- Leptin and obesity indices (WC and BMI), particularly in control group.
- PAI-1 and obesity indices (WC and BMI). For WC and PAI-1 statistically significant correlations were observed only in MS patients, but BMI correlated with PAI-1 statistically significantly in both MS patients and control group.
- Insulin and obesity indices (in MS patients as well as in control group) and SBP (control group).
- The HOMA-IR index and obesity indices (in both MS patients and control group) as well as SBP and DBP (in control group).
- *Ca Score* and age, and WC also in both groups, and with glucose in MS patients, and with TG and HDL-C in control group.
- Amount of visceral fat and obesity indices (WC and BMI) in both groups and with fatal CVE risk in control group.
- Homocysteine and CVE risk.
- Adiponectin and HDL-C.
- The HOMA-IR index and glucose.

5.5.2. Regression analysis

Since not only each separate RF influences the development of CVD and MS but they influence each other, in order to evaluate this influence the method of

multifactoral analysis was used. In case of quantitative parameters was used the multiple linear regression, but in case of binary parameters the binary logistic analysis was used.

The relationship between new RF and metabolic syndrome

1) Relationship of PAI-1 and MS.

Since in case of MS the level of PAI-1 was statistically significantly higher compared to control group (58.82 (34.60, 86.73) vs. 36.35 (26.09, 45.20) ng/ml; p<0.001), in order to verify this relationship a regression model was created, shown in table 5.5.3.

Table 5.5.3.

Regression model for relationship of PAI-1 and MS

	B	S.E.	Significance	Exp(B)	95% CI EXP(B)	
					Lower	Upper
PAI-1	1.300	0.311	<0.001	3.668	1.995	6.743
Constant	-0.975	0.245	<0.001	0.377		

B – Regression coefficient; S.E. – Standard error; Exp (B) – OR; 95% CI –95% Confidence interval

As seen in table 5.5.3. the odds ratio (OR) of a patient with increased level of PAI-1 will having MS or a patient with MS having increased level of PAI-1, is 3.7 with 95% CI 2.0–6.7.

2) Relationship of adiponectin and MS.

Evaluating the level of adiponectin in MS patients and patients in control group was a statistically significant decrease of the level value in case of MS (32.20 (18.20, 50.55) vs. 50.65 (33.05, 74.60) mg/L; p<0.001) was observed. In order to verify this relationship a regression model was created, shown in table 5.5.4.

Table 5.5.4.

Regression model for relationship between adiponectin and MS

	B	S.E.	Significance	Exp(B)	95% C.I. EXP(B)	
					Lower	Upper
Adiponectin	1.164	0.331	<0.001	3.204	1.674	6.131
Constant	-1.017	0.283	<0.001	0.362		

B – Regression coefficient; S.E. – Standard error; Exp (B) – OR; 95% CI –95% Confidence interval

As seen in table 5.5.4. the odds ratio of patient with decresed level of adiponectin having MS or a patient with MS having decresed level of adiponectin is 3.2 with 95% CI 1.7–6.1.

3) Relationship between CRP and MS

Differences of CRP level for in patients with and without MS were observed. In case of MS the level of CRP was statistically significantly higher (1.75 (0.91, 5.54) vs. 0.82 (0.40, 1.61) mg/L; p<0.001). In orer to evaluate this relationship a regression model was created, shown in table 5.5.5.

Table 5.5.5.

Regression model for relationship between CRP and MS

	B	S.E.	Significance	Exp(B)	95% C.I. EXP(B)	
					Lower	Upper
CRP	1.264	0.396	0.001	3,.538	1.630	7.683
Constant	-0.613	0.172	<0.001	0.542		

B – Regression coefficient; S.E. – Standard error; Exp (B) – OR; 95% CI –95% Confidence interval.

As seen in table 5.5.5., the OR of a patient with increased level of CRP having MS or a patient with MS having increased level of CRP is 3.5 with 95% CI 1.6–7.7.

4) Relationship between amount of coronary artery calcium and MS.

In patients with MS a larger amount of coronary artery calcium (13 (0, 141) vs. 0 (0, 2.5); p <0.001) was detected. In order to evaluate its relationship with MS the regression model was created, shown in table 5.5.6.

Table 5.5.6.

Regression model for relationship between amount of coronary artery calcium and MS

	B	S.E.	Significance	Exp(B)	95% C.I. EXP(B)	
					Lower	Upper
Ca Score	2.092	0.672	0.002	8.098	2.171	30.206
Constant	-0.551	0.215	0.010	0.576		

B – Regression coefficient; S.E. – Standard error; Exp (B) – OR; 95% CI –95% Confidence interval

As seen in table 5.5.6. the odds ratio of a patient with larger amount of coronary artery calcium having MS or a patient with MS having larger amount of coronary artery calcium is 8.1 with 95% CI 2.2–30.2.

5) Relationship between fatal CVE risk within next 10 years (according to *SCORE*) and MS.

Higher fatal CVE risk within next 10 years (according to *SCORE*) in MS patients than in control group (resp. 4 (2, 8) vs. 1 (0, 3), p<0,001) was observed. In order to evaluate this relationship a regression model was created, shown in table 5.5.7.

Table 5.5.7.

Regression model for relationship between fatal CVE risk and MS

	B	S.E.	Significance	Exp(B)	95% C.I. EXP(B)	
					Lower	Upper
CVE risk	1.138	0.296	<0.001	3.121	1.748	5.572
Constant	-0.750	0.208	<0.001	0.472		

B – Regression coefficient; S.E. – Standard error; Exp (B) – OR; 95% CI –95% Confidence interval

As seen in the table 5.5.7, the OR, that a patient with a increased fatal CVE risk within next 10 years (according to *SCORE*) will have MS or a MS patient will have an increased fatal CVE risk within next 10 years (according to *SCORE*) is 3.1 with 95% CI 1.7–5.6.

The association of new risk factors with traditional risk factors

In order to evaluate the association of new risk factors with traditional risk factors along the correlation analysis the multifactoral linear regression was used.

1) The association of PAI-1 with TG and glucose.

Since the distribution of PAI-1 and TG data did not comply with the norm, a logarithmic transformation was done, which allowed to obtain a distribution approximated to the normal one.

The summary of the regression model calculations is visualised in table 5.5.8.

Table 5.5.8.

Summary of regression model for association of PAI-1 with TG and glucose

	B	S.E.	Beta	t	Significance
Constant	3,410	0,113		30,124	<0,001
Log TG	0,400	0,063	0,418	6,397	<0,001
Glucose	0,047	0,020	0,151	2,318	0,022

B – Regression coefficient; S.E. – Standard error; Beta – standardized coefficient, t – t-test value

As seen in the table 5.5.8. the level of PAI-1 is statistically significantly influenced by both glucose and TG levels. The determination coefficient of this linear regression model is r^2= 0.228.

2) The association of CVE risk (*SCORE*) with new RF.

To verify the relationship adiponectin, homocysteine, *Ca Score*, CRP were used.

Parameters whose distribution did not comply with the norm where transformed (CVE risk, adiponectin, CRP, *Ca Score*). The summary of the regression calculations is visualised in table 5.5.9.

Table 5.5.9.

Summary of regression model calculations of associations between CVE risk and adiponectin, CRP, homocysteine and Ca Score

	B	S.E.	Beta	t	Significance
Constant	-0.398	0.542		-0.735	0.046
Log adiponectin	0.068	0.122	0.050	0.560	0.577
Homocystein	0.041	0.019	0.171	2.184	0.031
Log *Ca Score*	0.089	0.036	0.225	2.479	0.015
Intra-abdominal fat	0.008	0.002	0.491	4.940	<0.001

B – Regression coefficient; S.E. – Standard error; Beta – standardized coefficient, t – t-test value

As seen in table 5.5.9 the fatal CVE risk is statistically significantly influenced by the amount of *Ca Score*, visceral fat and level of homocysteine. According to the data of multiple linear regression, adiponectin does not influence the fatal CVE risk. The determination coefficient of this linear regression model is r^2=0.437.

3) The association of HDL-C with new CVD RF.

To verify the relationship the following parameters were used: adiponectin, CRP, the HOMA-IR index, amount of visceral fat. Parameters whose distribution did not comply with the norm were transformed. The summary of the regression calculations is visualised in table 5.5.10.

Table 5.5.10

Summary of regression model calculations for association of HDL-C with adiponectin, CRP, HOMA-IR index and amount of visceral fat

	B	S.E.	Beta	t	Significance
Constant	1.244	0.284		4.387	<0.001
Log CRP	-0.031	0.035	-0.073	-0.873	0.385
Log adiponectin	0.179	0.066	0.244	2.703	0.008
Log HOMA-IR index	-0.150	0.052	-0.283	-2.877	0.005
Intra-abdominal fat	-0.003	0.001	-0.318	-3.286	0.001

B – Regression coefficient; S.E. – Standard error; Beta – standardized coefficient, t – t-test value

As seen in table 5.5.10 HDL-C is statistically significantly influenced by the level of adiponectin, the HOMA-IR index and amount of visceral fat. According to the

data of multiple linear regression, CRP does not influence the level of HDL-C. The determination coefficient of the linear regression model is r^2=0,520.

Summary of regression analysis

- The analysis of binar logistic regression confirmed the correlation of MS and increased level of PAI-1, adiponectin and CRP, incresed amount of coronary artery calcium and increased fatal CVE risk (*SCORE*).
- The analysis of multiple linear regression confirmed the following correlations of new and traditional RF:

  CVE risk with coronary artery calcium, visceral fat and homocysteine;
  PAI-1 with TG and glucose;
  HDL-C with the level of adiponectin, the HOMA-IR index and amount of visceral fat.

6. Discussion

The aim of the doctoral thesis was to evaluate the prevalence of CVD RF and metabolic syndrome in differenat groups of Latvia's population and to estimate their correlations with markers of adipokine, inflammation, changes in glucose metabolism and early atherosclerosis, in order to produce practical recommendations for evaluation of cardiometabolic risk and for prophylaxis of CVD.

6.1. Prevalence of the traditional cardiovascular risk factors and metabolic syndrome diagnostic criteria among various contingents of the Latvian residents

The data obtained in the process of review of more than 27 thousand of HHO (the Heart Health Office) visitors and 1,400 patients of GP confirmed the seriousness of the situation in our country as the CVD RF prevalence among the residents is very high.

Prevalence of Dislipidemia

Having analyzed the prevalence of the dislipidemia we identified the increased TC level for 60% of the HHO visitors and 69% of the patients of the GP. It should be added that the data of other studies conducted in Latvia within the recent years show even higher occurrence of the TC level (76% in the National Heart Disease and their Risk Factors Cross-Section Study (NHDRFCS) in 2009 [Dzērve, 2010]). The average TC level in our observation was 5.4 mmol/L for HHO visitors and 5.6 mmol/L for the patients of the GP. The average TC showing in the both groups was lower than in NHDRFCS (5.9 mmol/L) [Dzērve, 2010] and in the data acquired during the Cholesterol Days (6.0 mmol/L) [Bahs, 2004]; however, higher than in the data provided by the WHO about Latvia in 2005 (5.3 mmol/L) [WHO, 2005]. Having analyzed the TC level sex differences, both among visitors of the HHO and patients of GP the statistically significant ($p<0.001$) higher average TC level for women was observed (5.5 mmol/L vs. 5.1 mmol/L in the HHO group and 5.7 mmol/L vs. 5.4 mmol/L in the group of the GP' patients). Our data differed from the data provided by the WHO for 2005 where the TC level was equal for the both sexes – 5.3 mmol/L [WHO, 2005]. One of the possible explanations of the different data could be the higher average age of the female subgroup among the HHO visitors (59.0 vs. 55.0 years respectively). However, in the group of the patients of the GP the average TC level remained higher for women though the average age of the both sexes did not differ in terms of statistical significance ($p=0.671$).

According to the WHO data, the average TC level in Europe varies from 4.8 mmol/L in Greece and 4.9 mmol/L in Netherlands to 6.1 mmol/L in Luxembourg and

6.2 mmol/L in Serbia and Montenegro [WHO, 2005]. Hence, despite the high CV death rate in our country the Latvian average TC level is not higher than in Europe.

Having analyzed the changes of the average TC level in terms of the age we observed its increase with the age. The maximum TC level for male was reached at the age of 46-75, and for female – at the age of 61–75 but after the age of 75 the average TC level reduced for the both sexes. The acquired results conform to the data mentioned in the literature – the TC level increases with the age for men till the age of ~65, women – till the age of 75 and start reducing later [*Ferrara*, 1997; *Schaefer*, 1994].

We identified the increased LDL-C for 67.8% of the GP' patients compared with 74% according to the NHDRFCS data [Dzērve, 2010]. In the group of patients of the GP (LDL-C level was not determined for HHO patients) we also identified the statistically significant ($p=0.006$) higher LDL-C level for women although the increased LDL-C occurrence was equally high for the both sex representatives (65.4% for men and 67.7% for women, $p=0.760$).

Having analyzed the HDL-C among the patients of the GP (HDL-C level was not determined for HHO patients), it was statistically significantly ($p<0.001$) higher for women. The low HDL-C occurrence does not differ among the both sexes ($p=0.716$), it was present in 31.4% of men and 32.4% of women. The data acquired in our study about the low HDL-C level occurrence significantly exceeds the NHDRFCS data where it was present only in 17% of men and 16% of women [Dzērve, 2010]. Comparing the obtained results with the data of the study conducted in 11 European countries "Pan-European Survey on HDL-C", the low HDL-C spread in Latvia is equal to the countries with a comparatively little occurrence of the low HDL-C level (the occurrence of the low HDL-C in this study ranged from 30% in France to 49% in Netherlands [*Bruckert*, 2006]). Also the average HDL-C level, according to our observation data, (1.41 mmol/L in the GP'patients group) was higher than in any of 11 European countries participating in the mentioned study. The average HDL-C level in this study ranged from1.22 mmol/L in Netherlands to 1.36 mmol/L in Belgium [*Bruckert*, 2006].

The average TG level in the both studied groups of persons was 1.5 mmol/L which also conforms to the NHDRFCS data [Dzērve, 2010]. In terms of percentage the highest share of the increased TG level was present in the HHO visitors – 42%. In the group of the patients of the family doctors the increased TG level occurrence was 34% and in the NHDRFCS - 24% [Dzērve, 2010]. The increased TG level occurrence among the HHO visitors is the most conforming to the result of the "Pan-European Survey on HDL-C" where the increased TG level was present in 49% of men and 45% of women. Having analyzed the sex peculiarities both among the visitors of HHO and patients of GP the statistically significant ($p<0.001$) higher average TG level was present in men. It conforms also to the data described in the literature that men have higher TG level till the age of 50, at the age of 50-60 this difference evens out but after the age of 50 the higher level is present in women [*Carroll*, 2005].

Prevalence of Arterial Hypertension

The high prevalence of the arterial hypertension was present in the both studied groups of persons – 40% in the HHO visitors and 53% in the patients of the GP. The observed difference between the studied groups could be explained by differences in completion of a questionnaire. The AH data in the group of the GP' patients was provided by the consulting physician basing on the previous medical documentation records and objective visits but as regards the HHO patients, this information was based only on the information provided by the patient itself. The NHDRFCS identified the AH for 45% of the patients [Dzērve, 2010] but according to the IMMIDIET (The impact of migration as a model of gene-environment interaction) research data, the AH spread in

Europe is 24% [*Costanzo*, 2008]. The observation that the increased SBP and/or DBP was present in 54% of the HHO visitors which considered that they did not have AH also proves the fact that residents are not sufficiently informed about AH as CVD RF and do not recognize and estimate it sufficiently.

Having analyzed the blood pressure level in terms of the age the SBP and DBP increase with the age was identified. SBP continued increasing also in the age group above 75 but DBP reached the maximum level at the age of 61–75 and reduced after the age of 75. Such SBP and DBP interrelation with the age is described also in the literature – the SBP continues increasing during the entire life but DBP does not increase anymore in the last life decades and may even reduce [*Franclin*, 1997]. The higher average SBP level in the age group till 61-75 was identified for men but after the age of 75 the average SBP level is higher for women. The average DBP is higher for men till the age of 75 but after the age of 75 statistically significant differences of the averages DBP levels for sexes was not observed.

Obesity

The thought expressed in the scientific literature that the obesity has reached the range of epidemic is confirmed also in our observation. The overweight was present in 78% and the obesity – in 34% of the HHO visitors. Similar data was acquired also among the patients of the GP – the obesity was identified with 36% of patients and the increased WC– for 56% among the patients of this group. The obtained overweight and adiposity prevalence showings significantly exceed the WHO data published in 2006 (45% – overweight and 16% - adiposity) and are similar to NHDRFCS data (31% adiposity) [Dzērve, 2010]. The sex differences were observed as well. The increased WC was statistically significantly ($p<0.001$) more frequently present in women in the both studied groups. BMI increased with the age and already starting from the age of 31 the average BMI exceeds the normal level and even reaches the obesity level among women (30 kg/m^2) after the age of 61. The average BMI in the both reviewed groups of patients was similar (28 kg/m^2 – HHO visitors, 29 kg/m^2 – for the patients of the GP). The obtained results match with the results acquired during the Cholesterol Days in 2004 (28 kg/m^2 [Bahs, 2004]) though they significantly exceed "International Obesity TaskForce" (IOTF) data according to which Latvia belongs to the European countries with comparatively low obesity spread and average BMI 25.1 kg/m^2 [*IOTF*, 2002; *EuroBarometer*, 2006]. The data on the obesity prevalence also prove the opinion that the Latvian residents are not sufficiently informed about the CVD RF, among other also about the obesity and underestimate it. According to the *IOTF* data, only 12% of women residing in Latvia and 18% of men admit having the obesity an 32% of women and 28% of men admit that they are overweight [*IOTF*, 2006].

Sedentary Lifestyle

The prevalence of the sedentary lifestyle is closely related with the prevalence of the obesity as the sedentary lifestyle is in particular more present in obese persons compared to the persons having normal weight [*Varo*, 2003]. As regards our observation, 21% of the HHO visitors and 38% of the patients of the family doctors admitted leading a sedentary lifestyle. These showings are significantly lower than the results obtained in the study conducted in more than 15 European Union member states. This study revealed the lowest sedentary lifestyle prevalence in Sweden (43%) and the highest – in Portugal (88%) [*Varo*, 2003]. Latvia was not included in the research. Our observed significantly lower showing of the sedentary lifestyle may be explained with the biased evaluation of respondents regarding their own level of physical activities compared to the metabolic equivalent calculation of physical activities in the aforementioned study.

Smoking

The share of smokers in the studied groups of persons was 14% among the HHO visitors and 20% among the patients of the GP. These data are significantly lower than the data of "*EuroBarometer*" in 2009 and WHO in 2008. According to "*EuroBarometer*" data, the regular smokers in Latvia comprise 30% and 7% more smoke occasionally [*EuroBarometer*, 2009] and Latvia ranks 3rd in terms of the number of smoking residents. According to WHO data, 53% of men and 19% of women smoke in Latvia (46% of men and 14% of women smoke on a regular basis) [WHO, 2008].

Having analyzed the share of smokers in terms of the age it was identified that 30% of men and 8% of women smoked among the HHO visitors and 33% of men and 15% of women smoked among the patients of the GP.

Having analyzed the share of smokers among the HHO visitors in terms of the age the biggest percentage of smokers was observed in the youngest age group of 18–30 where 49% of men and 22% of women smoked. The percentage of smokers reduced with every following age group and after the age of 75 only 7% of men and 0.6% of women smoked.

Increased Glucose Level and Diabetes Mellitus

Within our observation the diabetes mellitus was present in 4.8% of the HHO visitors and 9.2% of the patients of the GP and the increased glucose level – in 14.6% of the HHO visitors and 20.9% of the patients of the family doctors. DM spread in the world according to the WHO data varies from 3% to 8% depending on the region and in Europe 3–5% on average [WHO, 2000]. According to the DIA-screen (the diabetes mellitus screening program in Latvia for residents with the increased DM risk) study results it is concluded that the DM spread in Latvia may be ~3.8% [Pīrāgs, 2003].

Prevalence of Metabolic Syndrome Diagnostic Criteria

The prevalence of the metabolic syndrome and its criteria was analyzed among the patients of the GP. Out of 1,400 examined patients MeS was present in 51.1% of cases (54.7% in women and 41.4% in men, p=0.015) which is significantly more than in the National Health Statistics Report (NHSR). 3,423 persons aged above 20 were studied in this report, out of which MeS was identified for 34% - equal for female and male representatives [Ervin, 2009]. Both in our study and NHSR the MeS prevalence increased with the age.

The reason of the difference of the metabolic syndrome prevalence in these studies may be different criteria of the obesity anthropometric parameters. NCEP/ATP III recommended waist measurement thresholds were used in the NHSR study (102 cm for men and 88 cm for women) and the IDF recommended thresholds were used in our study (94 cm for men and 80 cm for women). In the both studies the abdominal obesity was the most frequent MeS diagnosis criteria (in 56% of cases in our study and in 53% of cases in NHSR study) followed by AH (in 53% of cases in our study and 40% of cases in NHSR study) and glycemia ≥5.6 mmol/L (35% in our study and 39% in NHSR study). The MeS prevalence observed in our study significantly exceeds also the MeS prevalence in Europe which according to data of various authors ranges from 7-36% [*Balkau*, 2005].

Out of 1,400 examined patients in this group all five MeS criteria was present in 8.8% of the patients, 4 criteria - 17.1% , 3 criteria – 25.3%, 2 criteria – 25.6%, 1 criterion – 14.6% and only 8.6% of patients did not have any of the MeS criteria. The most common MeS criteria combinations were the abdominal obesity + AH + glucose metabolism changes different from the observation data in the Riga cardiology offices where the most common MeS criteria combination was AH + increased TG level + low HDL-C level. [Bahs, 2004].

6.2. Peculiarities of the new risk factors and markers for patients with and without the metabolic syndrome

In our observation we analyzed the peculiarities of the following new CVD RF and markers for MeS patients and control group persons – adiponectin, leptin, IL-6, TNF-α, PAI-1, CRP, homocysteine, HOMA-IR index, insulin, the amount of calcium in coronary arteries and the intra-abdominal fat amount.

Adiponectin

The statistically significant ($p<0.001$) lower average adiponectin level was present in MeS patients than in the control group (32.20 mg/L vs. 50.65 mg/L, respectively). Having analyzed the differences of the adiponectin level among sex the tendency of the higher adiponectin level for women was identified; however, this difference was not statistically significant ($p=0.056$). Also the study results described in the literature presents similar tendencies – lower adiponectin level in case of the MeS [*Shaibi*, 2004, *Gannage-Yared*, 2006; *Wang* 2010; *Lara-Castro*, 2007].

Leptin

The average leptin level of the MeS patients was statistically significantly ($p=0.002$) higher (15.90 ng/ml vs. 7.17 ng/ml, respectively) than of the control group persons. In the female subgroup as well the statistically significant ($p<0.001$) considerably higher average leptin level was observed (23.65 ng/ml vs. 7.75 ng/ml, respectively). Also data available in the literature confirm our observation of the higher average leptin level for women [*Samara*, 2010; *Murphy*, 2010] and in case of the MeS [*Ji*, 2010].

Inflammation markers

The quoted literature contains data about TNF-α and IL-6 level increase for the obese patients [*Moon*, 2004], which is one of the principle MeS components and for this reason also in our observation we compared TNF-α and IL-6 level differences for MeS patients and in the control group. Within our observation statistically significant TNF-α and IL-6 level differences in these groups were not identified. Having analyzed the average TNF-α and IL-6 levels separately for the both sexes, statistically significant differences were not observed. Data available in the published literature are controversial – there are studies, in which higher average TNF-α and IL-6 level is observed for the MeS patients [*Van Guilder*, 2006; *Gurrola-Diaz*, 2009] as well as there are studies where these changes depend not on the MeS but in particular on the obesity.

Out of all evaluated inflammation markers only the statistically significant ($p<0.001$) increased CRP level was identified for MeS patients. This observation matches also with the CRP changes in case of MeS described in the literature [*Pischon*, 2008] and taking into account the CRP role in the CVD risk prediction proven in the extensive studies conducted within the recent years [*Colabro*, 2007; *Ridker*, 2004; *Pearson*, 2003, *BoeTHoldt*, 2006; *Danesh*, 2004] it also indicates of a higher CV event risk for MeS patients.

PAI-1

Having analyzed the PAI-1 average level differences for the MeS patients and control group patients, the statistically significant ($p<0.001$) higher level thereof was observed (58.82 ng/ml vs. 36.35 ng/ml respectively). Having analyzed separately the PAI-1 level in the subgroups of the both sexes, the statistically significant differences were not observed ($p=0.610$). This observation conforms also with the data available in the literature about the PAI-1 level increase for patients with MeS and obesity [*Alessi*, 2006; *Chou*, 2009].

Homocysteine

In our observation the statistically significant differences of the average homocysteine level for MeS patients were not identified, also the sex differences for the average homocysteine level were not present. Our observation does not conform to the data of the published studies related to the higher average homocysteine level for MeS patients [*Guven*, 2004, *Yoon*, 2008] as well as to the fact that the increase of this level is not connected with the increase of the CV events [*Hajer*, 2007].

HOMA-IR index and insulin level

In our observation we determined also the IR showing HOMA-IR index and insulin both for the MeS patients and control group. The interconnection of IR and MeS is commonly recognized and also our observation data confirmed it. More than twice as high HOMA-IR index was observed for MeS patients (3.28 vs. 1.12, respectively; $p<0.001$) compared to the persons in the control group. Also the increased HOMA-IR level was observed for MeS patients significantly more frequently (>2) compared to the control group (27.7% vs. 76.5%, respectively).

Amount of coronary arteries calcium

The statistically significant ($p<0.001$) higher Ca Score was present in MeS patients as well as more frequently than for patients of the control group the increased Ca Score level was observed. Interpretation of our study results was limited by a comparatively small number of patients with the increased Ca Score (n=17) which did not allow to analyze these data in various patient subgroups. Also data published in the world quoted literature reflect Ca Score as a perspective showing for identification of the persons with the higher CV events risk among the MeS patients [*Malik*, 2009].

Visceral or intra-abdominal adiposity

The visceral adiposity is one of the principle MeS criteria, our study results prove it as well because the MeS patients have the statistically significant ($p<0.001$) higher amount of the visceral adipose tissues. The increased amount of the visceral adipose tissues also corresponds with the increased cytokine (leptin, PAI-1) and low adiponectin level because, as known, in particular the adipose tissues are the source of these biologically active substances [*Garg*, 2006; *Lau*, 2005; *Han*, 2007]. Determination of the visceral adiposity may help the patients not having the MeS; however, having the adiposity to identify the CVD risk.

6.3. Association of the new risk factors and markers with the traditional risk factors

Interrelation of the leptin level with the obesity (as one of the independent CVD RF) and its anthropometric showings has been already previously proven in the studies [*Xavier*, 2006; *Haynes*, 2008] and our observation data confirmed it as well – WC and BMI statistically significantly positively correlated with the leptin in the both groups (for MeS patients and in the control group). We identified also the statistically significant ($p=0.047$) leptin relation with the Ca Score level – the early atherosclerosis showing. These data as well as relation of the leptin level with the insulin resistance and CRP described in the literature (inflammation markers and independent various CVD RF) [*Colabro*, 2007; *Ridker*, 2004; *Pearson*, 2003] allow considering the leptin to be one of the CVD markers.

PAI-1 is the main fibrinolysis inhibitor; the increase of level thereof leads to the intense fibrin deposits in the arterial wall and enables formation of the atherothrombosis [*Gimeno*, 2005]. The obtained data indicate of the increased PAI-1 level as an independent MeS showing while in the MeS case the considerably increased CVD risk has been proven [*Arnlov*, 2010]. Taking into account the data about the role

of PAI-1 in development of the atherosclerosis in the arterial wall and its relation with MeS, the increased PAI-1 level may be considered as one of the increased CVD risk markers.

The insulin level and HOMA-IR index statistically significantly positively correlate with the obesity showings in the both groups which prove the relation of the insulin resistance with the obesity and metabolic syndrome and according to the literature data IR in particular is considered to be the link between the glucose metabolic disorders and CVD [*Libby*, 2007].

The amount of calcium deposited in the coronary arteries is the subclinic atherosclerosis marker and increase of the Ca Score level is related with the increased CVD risk [*Pletcher*, 2004]. We observed the statistically significant positive correlation of the Ca Score level with the age and relation thereof with the increased fatal CVD risk (according to *SCORE*). Determination of Ca Score provides information about the atherosclerosis process development and can be used in the CVD risk screening.

The correlation of the visceral adipose tissues with the anthropometric adiposity parameters is well known and widely described in the literature. However, the published studies contain controversial data on which of the indicators (BMI or WC) reflects the visceral obesity better [*Moore*, 2009]. Our results show that for the persons of the control group the visceral adiposity is better reflected by BMI and for the MeS patients – by WC.

Homocysteine as an independent CVD RF has been already described in the previous studies [*Mateztzky*, 2003; *Soinio*, 2004; *Stubbs*, 2000; *Virtanen*, 2005]. Also in our observation the homocysteine level statistically significantly positively correlated with the fatal risk of the CV events in the both groups of patients. Determination of the homocysteine level is recommended for the CVD risk screening in order to evaluate the possible risk level though should not be used for the risk monitoring as within the repeated studies in which the CV event number and death rate showings of the patients following the reduction of the homocysteine level (receiving B group vitamins and folic acid in the course of treatment) did not reduce [*Ebbing*, 2008; *Toole*, 2004; *Lonn*, 2008].

The observed statistically significant positive correlation of the adiponectin level with HDL-cholesterol which has been previously described also by authors of other studies [*Wolk*, 2007] allows equaling the adiponectin role to the HDL-C role in CVD risk determination.

7. Conclusions

1) When analysing the results of currently the most extensive study of CVD RF prevalence in Latvia (with 27 285 participants), high prevalence of all traditional CVD RF was recognized. Among the study participants, 60.2% had increased TC, 40.4% had arterial hypertension (AH), in 32.1% it was undiagnosed previously, 14.6% had increased levels of blood glucose, 33.9% were obese, and 14.2% were smokers. More than 20% had sedentary lifestyle, while only 10.7% followed healthy diet recommendations on a daily basis.

   The most unfavourable CVS RF profile with the most rapid increase of RF components was observed in males aged below 45 (higher levels of TC, body mass index (BMI), glucose, systolic and diastolic blood pressure (SBP and DBP) and females aged above 45 (SBP and DBP mean levels increased rapidly reaching the mean level of the same indices in males, while the mean TC and BMI indicators exceeded those of males in the corresponding age group). After the age of 75, CVD

RFs (all except SBP) were less pronounced in both sexes. SBP continued to increase in both sexes after the age of 75.

2) Among both Heart Health Clinic visitors and general practitioners' patients CVD RF prevalence was very high: elevated level of TC was detected in 68.5%, low-density lipoprotein-cholesterol (LDL-C) in 67.8%, triglycerides (TG) in 34.1%, 52.6% had AH, 9.2% had diabetes mellitus, 19.7% were smokers, 37.9% had sedentary lifestyle, and 44.3% did not obey the principles of healthy diet.
   Statistically significantly higher mean TC level ($p<0.001$), higher mean low-density lipoprotein-cholesterol (LDL-C) level ($p=0.006$) and higher mean high-density lipoprotein-cholesterol (HDL-C) level ($p<0.001$) were detected in women, while men showed higher mean TC level ($p<0.001$), higher mean DBP level ($p=0.002$) and higher mean glucose level ($p=0.006$).

3) Prevalence of metabolic syndrome (MS) and its diagnostic criteria was very high among the subjects of the study and significantly exceeded the European average. MS was detected in 51.1% of the general practitioners' group; among other subjects, in 26 % two MS criteria were detected while in 15% one MS criterion.

4) In addition to traditional MS criteria, MS patients also had increased levels of C-reactive protein (CRP), leptin, Plasminogen activator inhibitor -1 (PAI-1), and insulin, higher HOMA-IR index, decreased level of adiponectin, a larger amount of coronary artery calcium, and higher fatal cardiovascular event (CVE) risk (according to *SCORE*). All the patients with increased *Ca Score* also had increased fatal CVE risk (according to *SCORE*).
   MS assessment provides valuable supplementary information in addition to traditional CVD assessment according to *SCORE*, since 66% of the patients with MS were associated with low or moderate KVD risk.

5) Binary logistic regression analysis confirmed association between MS and increased levels of Plasminogen activator inhibitor -1 (PAI-1), adiponectin, CRP, a larger amount of coronary artery calcium, and higher fatal cardiovascular event (CVE) risk (according to *SCORE*). Whereas multiple linear regression analysis confirmed the association between increased fatal CVE risk and increased *Ca Score*, increased intra-abdominal fat (IAF), increased homocysteine level; the association between increased level of PAI-1 and increased levels of TG and glucose; as well as the association between decreased level of HDL-C, decreased level of adiponectin, and increased HOMA-IR and increased IAF.
6) The decrease in the adiponectin level, the increase in the level of leptin and PAI-1, as well as the increase in the amount of coronary artery calcium and homocysteine can be considered equal to the traditional CVD risk factors and can be similarly used for assessing cardiovascular risk.
7) On the basis of the obtained results, practical recommendations have been produced for early identification of persons with high CVD risk (see page 123).
8) This study confirms not only the necessity for MS detection but also the importance of new, valuable, additional criteria along the traditional CVD risk assessment scheme *SCORE*.

8. Practical recommendations

1) To introduce methods for assessing *Ca Score*, adiponectin, PAI-1, leptin and the HOMA-IR index in clinical practice in order to identify high risk CVD patients more effectively.
2) On the basis of the results of the current study, practical recommendations for early identification of persons with high CVD risk have been produced, since these persons need intensive CVD RFs reduction.
   These recommendations are applicable with men aged >40 and women aged >50.

   Step I

   Obtaining anamnesis data and carrying out basic examination.

   Age, sex, unfavorable family history, smoking, diabetes mellitus and presence of arterial hypertension.
   Blood pressure, waist circumference, BMI, tests for lipids and glucose.

   Step II

   Identification of high CVD risk persons

   Persons belonging to **high risk CVD group**

   1. patients with existing CVD and/or DM (type 2 or type 1 with microalbuminuria)
   2. their fatal CVE risk according to *SCORE* is ≥5% (currently or in a long term future)
   3. patients with metabolic syndrome
   4. patients:
      a. whose moderate fatal CVE risk according to *SCORE* is 3-4%;
      b. with two MS criteria;
      c. with unfavourable family history

      and

      Ca *Score* >100 or at least two of the following changes:↓ adiponectin, ↑ leptin, ↑ PAI-1 levels, ↑ HOMA-IR index.

   Persons who do not comply with any of the above criteria do not have high CVD risk.
3) Raising patients' awareness of CVD RF should be continued and expanded; patients should be taught to recognise them.
4) The network of HHO should be expanded and promoted, thus giving patients the opportunity to be consulted on CVD RF by a trained nurse who would estimate the CVD RF, calculate the total CVD risk, inform about the possibilities to correct CVD RF and refer the patient to the General Practitioner, if needed.
5) The public health online monitoring system should be continued and developed by extending the scope of the data included, thus gaining exhaustive information not only about prevalence of CVD RF under Latvia's population, but also about other topical problems of public health.
6) To advance introduction of methods for assessing *Ca Score*, adiponectin, PAI-1, leptin and the HOMA-IR index in physicians' daily practice, in order to identify high risk CVD patients more effectively.

Novelty of the study

1) Within the scope of this study the first online heart health monitoring system was launched in Latvia. It stores information on cardiovascular health of Latvia's population. Since the launch in July 2007, data of more than 50 000 patient has been collected.
2) This is the first study in Latvia that analysed the prevalence of new CVD RF and their relationship with traditional CVD RF, estimated visceral adipose tissue and amount of coronary artery calcium with computer-tomography, and estimated cytokines in daily clinical practice.

Practical application

The evaluation of *Ca Score*, adiponectin, PAI-1 and leptin in clinical practice and invention of a new, a two-step only scheme for CVD risk assessment in GP, internist and cardiologist daily practice will improve the identification of high risk cardiovascular patients.

Approbation of the dissertation themes

Publication

- 12 articles in journals:

1) A.Kalvelis, **I.Stuķēna**, G.Bahs, A.Lejnieks.
Do We Correctly Assess the Risk of Cardiovascular Disease? Characteristics of Risk Factors for Cardiovascular Disease Depending on the Sex and Age of Patients in Latvia. The European Journal of Cardiovascular Medicine, apstiprināts publikācijai 2011.gadā.
2) G.Bahs, A.Kalvelis, **I.Stuķēna**, M.Auziņš, P.Tretjakovs, A.Lejnieks.
Levels of inflammatory mediators in people with rheumatoid arthritis or cardiovascular disease. Do they differ? Scientific Proceedings of Riga Stradiņš University, 2010, apstiprinats publikācijai.
3) P.Tretjakovs, A.Jurka, I.Bormane, I.Miķelsone, D.Reihmane, L.Balode, V.Mackēvicš, **I.Stuķēna**, G.Bahs, J.I.Aivars, V.Pīrāgs.
Relation of inflammatory chemokines to insulin resistance and hypoadiponectinemia in coronary artery disease patients. European Journal of Internal Medicine, 2009; 20: 712-717.
4) **I.Stuķēna**, A.Kalvelis, G.Bahs, U.Teibe, P.Tretjakovs, A.Lejnieks.
Association between Inflammatory Markers and Clinical and Metabolic Risk Factors for Cardiovascular Diseases. Proceedings of the Latvian Acadamy of Sciences. Section B, Vol. 63 (2009), No. 4/5 (663/664), pp. 211–216
5) **I.Stuķēna**, A.Kalvelis, G.Bahs, U.Teibe, P.Tretjakovs, A.Lejnieks.
Characteristics of cardiovascular RFs and their correlation with the sex and age of patients in the Latvian population. Proceedings of the Latvian Acadamy of Sciences. Section B, Vol. 63 (2009), No. 4/5 (663/664), pp. 147–152.
6) P.Tretjakovs, A.Jurka, I.Bormane, I.Miķelsone, D.Reihmane, L.Balode, I.Jaunalksne, V.Mackēvicš, **I.Stuķēna**, G.Bahs, A.Lejnieks, J.I.Aivars, V.Pīrāgs.
Relation of endothelial dysfunction and adipokines levels to insulin resistance in metabolic syndrome patients. Proceedings of the Latvian Acadamy of Sciences. Section B, Vol. 63 (2009), No. 4/5 (663/664), pp. 222–227.
7) **I.Stuķēna**, G.Bahs, A.Lejnieks, A.Kalvelis, U.Teibe, L.Zvaigzne.

The Correlation between Various Indicators of Obesity and Age, Indicators of Lipids, Carbonhydrates Metabolism and Inflammation. RSU Collection of Scientific Papers 2008; 17-22.

8) Bormane I., Tretjakovs P., Jurka A., Mikelsone I., Reihmane D., Balode L., Aivars J. I., **Stukena I**., Cirule K., Bahs G., Pirags V.

Alterations of serum adhesion molecules and cutaneus endothelium-dependent vasodilatation in insulin resistant obese patients

Acta Universitatis Latviensis, Biology 2009; 753: 107-116.

9) P.Tretjakovs, A.Jurka, I.Bormane, I.Miķelsone, D.Reihmane, L.Balode, J.I.Aivars, **I.Stukēna**, G.Bahs.

Changes of plasminogen activator inhibitor-1, adhesion molecules, and endothelium-dependent vasodilatation and their relationship to insulin resistance in metabolic syndrome patients. Scientific Proceedings of Riga Stradiņš University, 2009: 35-43.

10) P**.**Tretjakovs, A.Jurka, I.Bormane, I.Miķelsone, D.Reihmane, L.Balode, J.I.Aivars, **I.Stukēna**, G.Bahs, A.Lejnieks.

Alterations of tumor necrosis factor-alpha, endothelin-1 and vasomotor activity in patients with insulin resistance. Scientific Proceedings of Riga Stradiņš University, 2008: 27-34.

11) A.Lejnieks, **I.Stuķēna**, G.Bahs, A.Kalvelis, U.Teibe.

Triglicerīdu un augsta blīvuma lipoproteīnu holesterīna saistība ar citiem kardiovaskulāro slimību riska faktoriem. RSU Zinātniskie raksti 2008;87-92.

12) A.Kalvelis, G.Bahs, **I.Stuķēna**, J.Verbovenko.

C-reaktīvā olbaktuma asociācijas ar kardiovaskulāro slimību riska faktoriem. RSU Zinātniskie raksti 2007; 44-47.

- 8 thesis published in journals

1) A.Kalvelis, A.Lejnieks, G.Bahs**, I.Stukena**, U.Teibe.

Correlaton between blood preasure and lipids

Atherosclerosis.suppl.Abstracts 77-th Congress of EAS, April 26-29, 2008, Istambul, Turkey p.260

2) A.Kalvelis, A.Lejnieks, G.Bahs, **I.Stukena**, U.Teibe.

Assotiation between waist circumference and other cardiovascular risk factors.

Atherosclerosis.suppl.Abstracts 77-th Congress of EAS, April 26-29, 2008, Istambul, Turkey p.17l.

3) Kalvelis, G.Bahs, **I.Stukena**, A.Lejnieks, U.Teibe.

Correlation of heart rate with cardiovascular risk factors. Circulation Vol 117, No19, May 13, 2008, p156.

4) A.Kalvelis, **I.Stukena**, G.Bahs, A.Lejnieks, U.Teibe, A.V.Putnina.

Physical activity is more effective at reducing cardiovascular disease risk than diet. EJCP&R, 2009; Volume16, Supplement 1, S45

5) G.Bahs, I.Stukena, A.Kalvelis, U.Teibe, A.V.Putnina, A.Lejnieks

Markers of inflammation and adipokines in the case of metabolic syndrome. Journal of Diabetes 2009; April, Volume 1 Issue s1; A168

6) G.Bahs, **I.Stukena**, A.Kalvelis, U.Teibe, A.V.Putnina, A.Lejnieks.

Correlations of glucose metabolism with adipokines and markers of inflammation. Journal of Diabetes, 2009, April, Volume 1 Issue s1; A170.

7) Lejnieks, G.Bahs, A.Kalvelis**, I.Stukena**, U.Teibe, A.V.Putnina.

Correlation of obesity indicators with other cardiovascular risk factors. Journal of Clin Lipidol.2008, Volume2, Number 5S, S42

8) A.Lejnieks, G.Bahs, A.Kalvelis, **I.Stukena**, U.Teibe, A.V.Putnina.

Assotiation of total cholesterol and other cardiovascular risk factors. Journal of Clin Lipidol.2008, Volume 2, Number 5S, S42

Presentations

- 2 oral presentations

1) Jaunie kardiovaskulāro slimību riska faktori
RSU, scientific conference at Faculty of Internal medicine on 27.08.2008.
2) Kardiovaskulārie riska faktori Latvijā – bieži izplatīti un nekontrolēti.
Meeting of Latvian Endocrinology society 10.12.2010.

- 20 poster presentations

Year 2010

1) **I.Stukena**, A.Kalvelis, G.Bahs, A.Lejnieks.
Clinical and biochemical associations of non-high density lipoprotein cholesterol.
World Cardiology Congress 2010, 14.-19.06., Beijing, China
2) **I.Stukena**, A.Kalvelis, G.Bahs, A.Lejnieks.
Glucose metabolism changes promote subclinical atherosclerosis.
World Cardiology Congress 2010, 14.-19.06., Beijing, China
3) **I.Stukena**, G.Bahs, A.Kalvelis, A.Lejnieks
Coronary artery calcium score is a more sensitive indicator of subclinical atherosclerosis than ankle-brachial index.
Europien Atherosclerosis Society Congress 2010, 20-23.06., Hamburg, Germany
4) P.Tretjakovs, A.Jurka, I.Bormane,G.Bahs, D.Reihmane, I.Mikelsone, K.Elksne, D.Krievina, **I.Stukena**, K.Cirule, J. Verbovenko, V.Pirags
Plasminogen activator inhibitor-1, myeloperoxiDBPe and matrix metallopreteinase-9 in coronary artery disease patients with and without type 2 diabetes mellitus
Controversies to Consensus in diabetes, Obesity and Hypertension, 2010, 11.-14.03., Buenos Aires, Argentine
5) **I.Stukena**, A.Kalvelis, G.Bahs, U.Teibe, A.Lejnieks.
Vēdera apkārtmēra korelācijas ar lipīdu, glikozes un C-reaktīvā olbaltuma līmeņiem.
RSU Scientific Conference 18.-19.03.2010.
6) **I.Stukena**, A.Kalvelis, G.Bahs, U.Teibe, A.Lejnieks.
Homocisteīns-neatkarīgs kardiovaskulāro slimību riska faktors.
RSU Scientific Conference 8.-19.03.2010.

Year 2009

7) A.Kalvelis, **I.Stukena**, G.Bahs, A.Lejnieks.
Gender and adiposity influences association between blood pressure and cardiovascular diseases risk factors.
World Hypertensive Congress 2009, 29.10.-01.11., Beijing, China
8) G.Bahs, **I.Stukena**, A.Kalvelis, U.Teibe, A.V.Putnina, A.Lejnieks
Markers of inflammation and adipokines in the case of metabolic syndrome.
The 3rd International Congress on Prediabetes and the Metabolic Syndrome 02.04, Nice, France
9) G.Bahs, **I.Stukena**, A.Kalvelis, U.Teibe, A.V.Putnina, A.Lejnieks
Correlations of glucose metabolism with adipokines and markers of inflammation.
The 3rd International Congress on Prediabetes and the Metabolic Syndrome 02.04., Nice, France
10) A.Kalvelis, **I.Stukena**, G.Bahs, A.Lejnieks, U.Teibe, A.V.Putnina.
Physical activity is more effective at reducing cardiovascular disease risk than diet.
EuroPrevent 06.–09.05. 2009, Stockholm, Sweden

11) A.Kalvelis, **I.Stukena**, G.Bahs, U.Teibe, A.Lejnieks.
Correlation of heart frequency with other cardiovascular disease risk factors in the case of adiposity.
Mediterranear Cardiology Meeting, 26.-28.04., Taormina, Sicilly

12) **I.Stukena**, A.Kalvelis, G.Bahs, A.Lejnieks, U.Teibe.
Triglicerīdu, augsta blīvuma lipoproteīnu holesterīna un glikozes korelācija pacientiem ar metabolo sindromu un bez tā.
RSU Scientific Conference 2009; 03.04, Riga

13) **I.Stukena**, G.Bahs, A.Kalvelis, A.Lejnieks, U.Teibe.
-reaktīvā olbaltuma korelācija ar lipīdiem aptaukošanās gadījumā.
RSU Scientific Conference 2009; 03.04, Riga

Year 2008

A.Kalvelis, A.Lejnieks, G.Bahs, **I.Stukena**, U.Teibe.
Relationship of inflammatory indicators and metabolic syndrome lipid alteration.
RSU Scientific Conference

14) A.Kalvelis, A.Lejnieks, G.Bahs, **I.Stukena**, U.Teibe.
Relationship of obesity and age, lipide, carbohydrates metabolism and inflammatory indicators. RSU Scientific Conference

15) Lejnieks, G.Bahs, A.Kalvelis, **I.Stukena**, U.Teibe, A.V.Putnina.
Correlation of obesity indicators with other cardiovascular risk factors.
7th International Symposium „Multiple Risk Factors in Cardiovascular Diseases", 22.-25.10., Venezia, Italy

16) A.Lejnieks, G.Bahs, A.Kalvelis, **I.Stukena**, U.Teibe, A.V.Putnina.
Assotiation of total cholesterol and other cardiovascular risk factors.
7th International Symposium „Multiple Risk Factors in Cardiovascular Diseases", 22.-25.10., Venezia, Italy

17) Kalvelis, G.Bahs, **I.Stukena**, A.Lejnieks, U.Teibe.
Correlation of heart rate with cardiovascular risk factors.
World Congress of Cardiology, 2008, BuenosAires, Argentine

18) A.Kalvelis, G.Bahs, **I.Stukena**, A.Lejnieks, U.Teibe
Assesment of cardiovascular risk factors in accordance to gender.
International forum „Evaluation of Cardivascular Care", Monte Carlo, 27.-29.02.

Year 2007

19) A.Kalvelis, G.Bahs, **I.Stukena**, J.Verbovenko
C-reaktīvā olbaltuma asociācijas ar kardiovaskulāro slimību riska faktoriem.RSU scientific conference

Supplement

Patients questionares

I Questionare for Heart Health Offices visitors

Sirds veselības kabinets: _____ **SVK anketa**

SIRDS SLIMĪBU RISKA FAKTORU NOVĒRTĒJUMA ANKETA

Pacienta ID ☐☐☐☐ **Datums** ☐☐/☐☐/ **200_** **Protokola Nr.** ☐☐☐☐

S **V**

Vecums ☐☐ **Dzimums** ☐ ☐

Izglītība
- ☐ **pamatizglītība**
- ☐ **vispārējā vidējā**
- ☐ **vidējā speciālā**
- ☐ **augstākā**

Dzīvesvieta
- ☐ **Rīga**
- ☐ **cita pilsēta**
- ☐ **lauki**

Svars ☐☐☐ **kg** **Augums** ☐☐☐ **cm** **ĶMI** ☐☐, ☐ **kg/m2**

Vidukļa apkārtmērs ☐☐☐ **cm**

Nelabvēlīga iedzimtība 1. pakāpes radiniekiem:	**Jā**	**Nē**	**Nezin**
Siev.<65g.,vīr.<55g. MI, insults, pēkšņa kardiāla nāve	☐	☐	☐
Aptaukošanās	☐	☐	☐
Cukura diabēts	☐	☐	☐
Arteriālā hipertensija	☐	☐	☐

Smēķēšana: **Nesmēķē** ☐ **Smēķē pa laikam** ☐☐ **cik cigaretes dienā** **Smēķē ik dienas** ☐

Agrāk smēķējis ik dienas ☐ **kopumā** ☐☐ **gadus**

Fiziskā aktivitāte:

intensīva* ☐

*nodarbojas ar aktīvu sportu vai intensīvām fiziskām aktivitātēm vismaz 30min un 3-4x nedēļā

mērena* ☐

*pastaigas, braukšana ar divriteni vai citas vieglas fiziskās nodarbības vismaz 4 stundas nedēļā

mazkustīgs ☐

Veselīga uztura ieteikumi: **Ievēro lielāko daļu** ☐ **Ievēro dažus** ☐ **Neievēro** ☐

Esošās slimības:

	Jā	**Nē**	**Nezin**
Arteriāla hipertenzija	☐	☐	☐
Cukura diabēts	☐	☐	☐
Mirdzaritmija	☐	☐	☐
Sirds mazspēja	☐	☐	☐
Stenokardija	☐	☐	☐
Agrāk pārciests miokarda infarkts	☐	☐	☐
Agrāk pārciests insults	☐	☐	☐

Vai ir mērīts holesterīns Jā ☐ Nē ☐ Nezin ☐

Zin savu holesterīnu Jā ☐ Nē ☐ **Ja, jā tas ir:** Paaugstināts ☐ Normāls ☐

Vai lieto holesterīnu pazeminošus medikamentus(statīnus) Jā ☐ Nē ☐ Nezin ☐

Papildus izmeklējumi:

Asins spiediens (apmeklējuma laikā) ☐☐☐/☐☐☐ **mmHgst.**

Pulss (apmeklējuma laikā) ☐☐☐ **xmin**

Pacients ir tukšā dūšā* Jā ☐ Nē ☐

*8 stundas pirms vizītes nav ēdis

Veicamās analīzes:

	Ja pacients tukšā dūšā:	**Ja nav tukšā dūšā:**
Kopējais HOL	☐☐, ☐☐ **mmol/l**	**Kopējais HOL** ☐☐, ☐☐ **mmol/l**
ZBLH	☐☐, ☐☐ **mmol/l**	**TG** ☐☐, ☐☐ **mmol/l**
ABLH	☐☐, ☐☐ **mmol/l**	
TG	☐☐, ☐☐ **mmol/l**	
Glikoze	☐☐, ☐☐ **mmol/l**	

II Questionare for general practitionare patients

Ģimenes ārstu pac. Anketa

SIRDS SLIMĪBU RISKA FAKTORU NOVĒRTĒJUMA ANKETA

Pacienta iniciāļi ☐☐ **Datums** ☐☐/☐☐/ 200_ **Protokola Nr.** ☐☐☐☐

Vizītes iemesls: _____

Vecums ☐☐ **Dzimums** **S** ☐ **V** ☐

Izglītība
- ☐ pamtizglītība
- ☐ vispārējā vidējā
- ☐ vidējā speciālā
- ☐ augstākā

Dzīves vieta
- ☐ Rīga
- ☐ cita pilsēta
- ☐ lauki

Svars ☐☐☐ **kg** **Augums** ☐☐☐ **cm** **ĶMI** ☐☐, ☐ **kg/cm2**

Vēdera apkārtmērs ☐☐☐ **cm**

Nelabvēlīga iedzimtība 1. pakāpes radiniekiem:	**Jā**	**Nē**	**Nezin**
Siev.<65g.,vīr.<55g. MI, insults, pēkšņa kardiāla nāve	☐	☐	☐
Aptaukošanās	☐	☐	☐
Cukura diabēts	☐	☐	☐
Arteriāla hipertenzija	☐	☐	☐

Smēķēšana: **Nesmēķē** ☐ **Smēķē pa laikam** ☐ **Smēķē ik dienas** ☐

Cik cigaretes dienā ☐☐

Agrāk smēķējis ik dienas ☐ **kopumā cik gadus** ☐☐

Fiziskā aktivitāte:

intensīva* ☐

*nodarbojas ar aktīvu sportu vai intensīvām fiziskām aktivitātēm vismaz 30min un 3-4x nedēļā

mērena* ☐

*pastaigas, braukšana ar divriteni vai citas vieglas fiziskās nodarbības vismaz 4 stundas nedēļā

mazkustīgs ☐

Veselīga uztura ieteikumi: **Ievēro lielāko daļu** ☐ **Ievēro dažus** ☐ **Neievēro** ☐

Esošās slimības:

	Jā					**Nē**
AH	☐	(pakāpe)	**1.** ☐	**2.** ☐	**3.** ☐	☐
CD	☐	(tips)	**1.** ☐	**2.** ☐		☐
MA	☐	☐ Pastāvīga	☐ Paroksismi			☐
		I	**II**	**III**	**IV**	**(NYHA)**
SM	☐	☐	☐	☐	☐	☐
		I	**II**	**III**	**IV**	**(FK)**
Stenokardija	☐	☐	☐	☐	☐	☐
Vecs MI	☐					☐
Insults	☐					☐
Kāju IS	☐					☐

Citas _____

	Jā	Nē			
Zin savu holesterīnu	☐	☐	**Ja, jā tas ir:**	**Paaugstināts** ☐	**Normāls** ☐

	Jā	Nē	
Saņem Hol pazeminošu Th	☐	☐	
Simvastatīns	☐		* _____
			* ilgums un deva
Atorvastatīns	☐		* _____
Cits statīns	☐		* _____
Fibrāti	☐		* _____

	Jā	Nē
Saņem AKFI	☐	☐
Saņem A II AR	☐	☐
Saņem Glitazonus	☐	☐
Saņem Metformīnu	☐	☐

Papildus izmeklējumi:

Asins spiediens (apmeklējuma laikā) ☐☐☐/☐☐☐ **mmHgst.**

Pulss (apmeklējuma laikā) ☐☐☐ **xmin**

	Jā	Nē
Pacients ir tukšā dūšā*	☐	☐

*8 stundas pirms vizītes nav ēdis

Veicamās analīzes, ja pacients tukšā dūšā:

Glikoze ☐☐, ☐☐ **mmol/l**

Kopējais HOL ☐☐, ☐☐ **mmol/l**

ABLH ☐☐, ☐☐ **mmol/l**

TG ☐☐, ☐☐ **mmol/l**

CRO ☐☐, ☐☐ **mg/l**

III Questionare for hospitalised patients

Stacionāra pacientu anketa

SIRDS SLIMĪBU RISKA FAKTORU NOVĒRTĒJMA ANKETA

Pacienta iniciāļi ☐☐ **Datums** ☐☐/☐☐/ .200_ **Protokola Nr** ☐☐☐☐

S V

Vecums ☐☐ **Dzimums** ☐ ☐

Stacionēšanas iemesls_____

Svars ☐☐☐ **kg** **Augums** ☐☐☐ **cm** **ĶMI** ☐☐, ☐ **kg/m2**

Vidukļa apkārtmērs ☐☐☐ **cm**

Nelabvēlīga iedzimtība 1. pakāpes radiniekiem:	**Jā**	**Nē**	**Nezin**
Siev.<65.g.,vīr.,55g. MI, insults, pēkšņa kardiāla nāve	☐	☐	☐
Aptaukošanās	☐	☐	☐
Cukura diabēts	☐	☐	☐
Arteriāla hipertenzija	☐	☐	☐

Smēķēšana: **Nesmēķē** ☐ **Smēķē pa laikam** ☐ **Smēķē ik dienas** ☐

Cik cigaretes dienā ☐☐

Agrāk smēķējis ik dienas ☐ **kopumā cik** ☐☐ **gadus**

Fiziskā aktivitāte:

intensīva* ☐

* nodarbojas ar aktīvu sportu vai intensīvām fiziskām aktivitātēm vismaz 30min un 3-4x nedēļā

mērena* ☐

*pastaigas, braukšana ar divriteni vai citas vieglas fiziskās nodarbības vismaz 4 stundas nedēļā

mazkustīgs ☐

Veselīga uztura ieteikumi: **Ievēro lielāko daļu** ☐ **Ievēro dažus** ☐ **Neievēro** ☐

Esošās slimības:

	Jā						**Nē**
AH	☐	(pakāpe)	**1.** ☐	**2.** ☐	**3.** ☐		☐
CD	☐	(tips)	**1.** ☐	**2.** ☐			☐
		Pastāvīga	**Paroksismi**				
MA	☐	☐	☐				☐
		I	**II**	**III**	**IV**	**(NYHA)**	
SM	☐	☐	☐	☐	☐		☐
		I	**II**	**III**	**IV**	**(FK)**	
Stenokardija	☐	☐	☐	☐	☐		☐
Vecs MI	☐						☐
Insults	☐						☐
Kāju IS	☐						☐
Citas							

	Jā	**Nē**		**Paaugstināts**	**Normāls**
Zin savu holesterīnu:	☐	☐	**Ja, jā tas ir:**	☐	☐

	Jā	Nē
Saņem Hol pazeminošu Th	☐	☐
Simvastatīns	☐	* _____
Atorvastatīns	☐	* _____
Cits statīns	☐	* _____
Fibrāti	☐	* _____

* ilgums un deva

	Jā	Nē
Saņem AKFI	☐	☐
Saņem A II AR	☐	☐
Saņem Glitazonus	☐	☐
Saņem Metformīnu	☐	☐

Sirds frekvence ☐☐☐ x/min AT Sistoliskais ☐☐☐ / Diastoliskais ☐☐☐ mmHg st.

Potītes/brahiālais In ☐☐,☐☐

Kopējais Hol.	☐☐,☐☐ mmol/L	CRO	☐☐,☐☐ mg/l
ABLH	☐☐,☐☐ mmol/L	Adiponektīns	☐☐,☐☐ mg/l
ZBLH	☐☐,☐☐ mmol/L	Homocisteīns	☐☐,☐☐ µmol/L
TG	☐☐,☐☐ mmol/L	Leptīns	☐☐,☐☐ ng/ml
Glikoze	☐☐,☐☐ mmol/L	IL-6	☐☐,☐☐ pg/ml
Insulīns	☐☐,☐☐ µIV/L	PAI-1	☐☐,☐☐ ng/ml
HOMA-IR In	☐☐,☐☐	TNF-α	☐☐,☐☐ pg/ml

DT atradne

Ca Score ☐☐☐☐

I/abdomin. tauku daudzums ☐☐☐☐ cm^3

Kopējais kardiovaskulārais risks

Pēc SCORE	Augsts	Mērens	Zems
	☐	☐	☐
	>5%	2-4%	<1%