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INTRODUCTION

References in the literature place increasing importance on risk factors and lifestyle in cardiovascular disease as accumulating valid data have demonstrated the link between these and the pathogenesis of heart disease.

Once the knowledge barrier was overcome, where genetic factors were considered to be the determinants in the onset and progression of the disease and drug treatment was the solution, modern approaches recognise the role of risk factors in both prevention and curative management of the disease...

Despite the sustained concerns in this field, cardiovascular diseases are the main cause of death worldwide, and Romania ranks first in Europe in terms of cardiovascular mortality (109 deaths/100,000 inhabitants and 57% of all deaths are caused by cardiovascular disease).

In the vast majority of cases, the occurrence and development of this pathology are closely linked to risk factors; consequently, risk prediction and assessment strategies have been developed and are continuously updated as evidence is validated.

I opted for this topic because I considered it an opportunity to be able to study and observe habits that are not only clinical but part of everyday life, to synthesize an ecological, population-based perspective, able to address a number of challenges without curative intervention.

This research has been a challenge, both in terms of identifying and consulting bibliographic references (only a first search in Pub Med including cardiovascular risk factors generates 27,219 results and for cardiovascular risk the search reveals 39,843 published articles - cardiovascular risk factors - Search Results - PubMed (nih.gov) accessed on 26.06.2022) and in terms of the multitude of specialists interested in the field.

I have proposed an approach to the topic from an epidemiological, population and applied to the territorial specificity of our country, so that the thesis is a useful tool for understanding from this perspective. With the conviction that the chosen topic is challenging, both for preventionists and clinicians, but also for each of us, I hope that I have succeeded at least in part to clarify relevant and useful aspects in an extremely vast and interesting field.

Carrying out this research at a time when we are all facing a pandemic has given me the opportunity to study and make humble considerations in a field related to cardiovascular risk factors of an infectious nature, a field that is still insufficiently elucidated and constantly being updated.

Without claiming that the results of this work are complete, I believe, however, that they can constitute elements that can generate new directions for the evaluation of this extremely interesting subject. I am at your disposal with great interest and gratitude for any suggestions, criticisms or opinions that you may have.

CHAPTER 2. EPIDEMIOLOGY

The impact of cardiovascular diseases at global, regional (European) and Romanian level is estimated/calculated using incidence and prevalence in the population, but other indicators are also used - the burden of disease is quantified by disability-adjusted life years (DALYs), representing the total years of life lost through premature death and years lived with disability due to the presence of disease or accidents, according to the severity of the disease (definition used by WHO).

Figure 1 shows the incidence and prevalence rates of cardiovascular diseases per 100,000 inhabitants for the year 2020, and our country is above the regional average, with an incidence of 776 cases per 100,000 inhabitants and a prevalence of 7141 per 100,000 inhabitants.

Corroborating these data with the mortality generated by cardiovascular diseases where we rank first in Europe, we can interpret the incidence and prevalence data as having a limitation generated by reporting (under-reporting) and difficult access of the population to health services.

CHAPTER 3. RISK FACTORS

3.1. Basic concepts: risk factors

A risk factor is considered to be a determinant that increases the likelihood of disease occurrence or favours its negative evolution.

Criteria for determining risk factors should include:

- biological plausibility;
- strength of association (the relative risk of individuals exposed to a particular risk factor is greater than that of unexposed individuals);
- exposure to risk factors must precede the onset of the condition;
- specificity (exposure is associated with a statistically increased risk of developing the disease);
- dose-dependent effect (risk increases with longer or higher dose exposure to risk factors);
- the "dose-dependent" effect (risk increases with longer exposure or higher dose exposure to risk factors);
- consistency or generalizability of results;
- study on different populations, multiple types of studies;
- potential reversibility if exposure to risk factors is stopped or reduced.

In the case of non-modifiable risk factors, an important role is played by risk factor control (role in prophylaxis), independence of association with the specific condition when other risk factors already known for the same condition are controlled.

If risk factors act systemically and persist over time, they can be transformed by quantitative accumulation so as to favour the onset of a disease or create a predisposition to the condition.

The practical utility of identifying, knowing the risk factors is to be able to prevent or delay the progression of a disease by identifying and stopping exposure to the action of risk factors known to be specific to the disease or other appropriate measures and to be able to predict the incidence of a disease in different populations exposed to the action of risk factors.

The ability of the risk to develop the disease or worsen its prognosis is considered to exist:

- major risk factors (responsible for more than 90% of the risk of developing or worsening a disease) - smoking, elevated BP values, elevated TC values (>190 mg/dl), elevated LDL-C values (>115 mg/dl), elevated HDL-C values (<40 mg/dl), presence of diabetes, advancing age;
- minor risk factors (contributory) that may influence disease and progression to a lesser extent - increased TG, low and dense LDL, homocysteine, clotting factors: fibrinogen, CRP;
- predisposing risk factors - obesity, physical inactivity, male gender, family history of premature BCI, insulin resistance, socio-economic factors, psychological and behavioural factors, inadequate response to stress;
- susceptibility factors - left ventricular hypertrophy (LVH) leading to hypertension, target organ damage, and
- factors with cardiovascular protective value - antioxidants, physical activity, HDL cholesterol, low alcohol consumption, hormones: oestrogens with replacement therapy.

Risk factors can act both individually and in groups (they can potentiate each other), so identifying them and determining the influence of each factor is part of both individual and population assessment and is part of cardiovascular risk management.

Another classification, based on the possibility of intervention through lifestyle or drug treatment, divides risk factors into modifiable (those that can be controlled by the strategies outlined above) and non-modifiable (e.g. age, gender or hereditary factors).

3.2. Risk factors: classification

The most common classification in the literature groups risk factors into categories that relate to their background, which I will summarise in the following list.

3.2.1. Biological factors

Sex/Gender. Men are at increased risk of cardiovascular disease, while in women the incidence increases after the onset of menopause. There are behavioural, social and economic factors dependent on the sex of the individual that influence health concern, disease perception, decision making, thus impacting on the occurrence and progression of CVD.

Possible causes for the higher prevalence in males are more frequent smoking and higher plasma lipid levels.

Age is the main risk factor influencing CVD. The major importance of this factor is that it is unchangeable and cannot be intervened upon. The risk of CVD increases with advancing age, the onset of the disease for women is considered likely after the age of 55 and for men from the age of 45.

Recommendations for intervention are expressed in terms of the overall risk level which increases with age, so that virtually all individuals and all populations over 70 have a very high cardiovascular risk (greater than 15%).

Family history - is a risk factor independent of other risk factors and is associated with the existence of cardiovascular disease in first-degree relatives (men under 55 and women under 65) with a risk ranging from 1.5 to 1.7.

Phenotypes -involved in the pathophysiology of cardiovascular disease (dyslipidaemia, hypertension, diabetes, cardiac and vascular hypertrophy, endothelial dysfunction and atherosclerosis) and may have clinical relevance, but also in prevention, as each phenotype has its own genetic and environmental determinants.

Genotypes - the relationship between gene and environment (their interaction) is important for understanding how genetic information can be used in risk assessment, and this finding will be important for future research. However, there is research that has shown that for the human population the genetic code changes very slowly (0.2% in 20,000 years) which means that genes can change over 250 generations and not from one generation to the next. However, other research suggests that under the influence of environmental factors the genetic structure can be modified relatively easily.

As epigenetic mechanisms (reversible changes in genes depending on the environment), DNA methylation, histone modification and the non-coding RNA mechanism have been identified. DNA methylation is a reversible process (demethylation) and the degree of DNA methylation is strongly influenced by lifestyle (some gene fragments are less methylated in smokers than in non-smokers). The DNA tests used for risk prediction do not provide more useful information for patient diagnosis at this time (11% prediction rate for 10-year follow-up of healthy male subjects in the UK) and are a time-consuming and expensive procedure.

3.2.2. Economic factors

- Economic status (income and expenditure/household);
- Gross earnings;
- Unemployment rate;
- Labour force;

- Length of public roads;
- Population with access to sewerage;
- Volume of drinking water distributed.

3.2.3. Social factors

- Level of education;
- Average life expectancy;
- Life expectancy at birth by sex;
- Family status;
- Occupational stress.

3.2.4. Psychological factors

Low socio-economic status. It is mentioned in many prospective studies that point out that the population of both sexes with low educational level, low income, representing the low status labour force and living in poor areas, is exposed to an increased risk for both general mortality and cardiovascular disease mortality. [relative risk (RR) is between 1.3 and 2.0].

Social isolation and low social recognition. Recent analyses and studies confirm that people who are isolated or do not interact with their peers have an increased risk of premature death from cardiovascular disease. Lack of social support also leads to decreased survival with a possible unfavourable prognosis among subjects with CVD symptoms (relative RR risk is between 1.5 and 3.0).

Occupational and family stress. Occupational stress, such as high demands, lack of social support and various constraints at work, is a cardiovascular risk factor for men [odds ratio (OR) 1.5]. For women, studies involving them are insufficient to draw firm conclusions. Litigation, crisis situations, stressful family environment are mentioned in various studies as potentially increasing the risk of cardiovascular disease [hazard ratio (HR) ranging from 2.7 to 4.0], especially among women (RR~2.9-4.0).

Depression. Results of meta-analyses highlight that clinical depression and clinical symptoms with depressive cough can predict cardiovascular events (RR between 1.6 and 1.9) and worsen their prognosis (Odds Ratio between 1.6 and 2.4). The provision of social support is likely to counteract the adverse effects of depression, whereas the absence of social support has been shown to potentiate the adverse effects of depression.

Anxiety. Extensive epidemiological studies have indicated panic attacks as an appreciable risk in the occurrence of cardiovascular events (Hazard Ratio 1.7 and 4.2), noting that generalized phobic anxiety and panic attacks have the capacity to worsen the status of an established cardiovascular disease (odds ratio OD 1.01, respectively 2.0). In contradiction to the above findings, a large, prospective, cohort study analysed statistically post-hoc shows low all-cause overall mortality in patients with anxiety and cardiovascular disease (HR 0.7). In contrast, high mortality was identified in patients with myocardial infarction whose left ventricular function is reduced post-infarction (HR 1.3), suggesting diametrically opposite effects of anxiety status in different subgroups of patients with CVD.

Hostility and anger. Hostility is characterized by excessive feelings of mistrust, anger, rage along with the tendency of subjects to engage in aggressive social relationships. A recent meta-analysis associates both anger and hostility with increased risk of cardiovascular events in both healthy and cardiac subjects (HR 1.2). Failure to express anger may become important, so that suppression of anger in patients with CVD constitutes an increased risk of cardiac events (OR 2.9).

Personality type D. In contrast to isolated clinical manifestations of anxiety and depression, which frequently occur episodically, Type D ('distressed') personality requires a long-standing tendency to express a wide range of negative emotions (negative affect) and to inhibit self-expression in relation to others (social inhibition). This personality type (type D) has been shown to predict an unfavourable

course of illness in BCV patients (OR 3.7), including the postcorrection of depressive symptoms, stress and anger.

The effect of psychosocial risk factors is comparable to the effect that obesity or hypertension have.)

3.2.5. Clinical factors (comorbidities)

Hypertension is the most important preventable risk factor, with studies showing that mortality is directly proportional to increases in diastolic blood pressure. The prevalence of high blood pressure in the population places us in the list of countries with the highest number of hypertensives, with data published by the European Society of Cardiology claiming that 30% of the Romanian population has a BP value higher than 130/80 mmHg. Other studies, including national ones, place the prevalence of hypertension at higher values in the population.

Diabetes mellitus

Hyperglycaemia, insulin resistance and hyperinsulinaemia are pathophysiologically related to BCV. The diabetic population has a significantly higher cardiovascular risk than the general population. It is a risk factor that cannot be totally modified, it can only influence disease progression.

The prevalence in the population is 6.9%, above the average for the region.

Dyslipidaemia has a high prevalence, it is a modifiable factor to which great interest is attributed. The literature points out that reduced LDL-cholesterol is associated with lower cardiovascular mortality, while increased HDL-cholesterol is a protective factor.

Cholesterol

The causal relationship between elevated plasma cholesterol levels and atherosclerotic vascular disease is widely recognised. Lowering plasma cholesterol is recommended to reduce cardiovascular risk. Significantly, reducing total plasma cholesterol by 10% will induce a 25% decrease in overt coronary heart disease at 5 years, and a 40 mg/dl (about 1 mmol/l) decrease in LDL-cholesterol will be accompanied by a 20% reduction in coronary events.

Data from studies do not allow the identification of a target value for HDL-cholesterol.

Metabolic syndrome

The combination of three of these medical risk factors: diabetes, hypertension, obesity, increased triglycerides, decreased HDL-cholesterol defines the metabolic syndrome. The cardiovascular risk is categorically higher, but does not exceed that of the risk factors involved. It is a sensitive indicator for signalling the onset of cardiovascular disease.

Body mass index. In the general population obesity (chronic adipose disease) increases the risk of developing cardiovascular disease and is associated with an increased indicator of specific mortality due to CVD. But in patients with coronary artery disease the evidence takes on aspects. Studies involving patients with coronary artery disease or undergoing cardiac implant procedures (PCI) have evoked the presence of the "obesity paradox", in which BCA is a protective effect against a poor prognosis.

Other peculiarities related to body weight control are weight fluctuations: weight fluctuations of 5-15% and especially over 15% in the last 10 years increase the mortality rate from BCI by about 2-fold. For every kg reduction in body weight, LDL-cholesterol is reduced by 0.77 mg % and TC by 0.35 mg %. For obesity the European Society of Cardiology data indicates a prevalence of 22.5% in the population aged 15+ in 2020. Although the prevalence is low compared to other countries in the same geographical area, it is increasing at an accelerated rate compared to 2015, when we were recorded with an 8% prevalence of obesity (defined as BMI greater than 30 kg/mp).

Circulating markers of inflammatory activation and haemostasis - Inflammatory markers (CRP and fibrinogen) and Haemostasis markers (homocysteine and phospholipase) are linked to the occurrence of myocardial infarction (both fatal and non-fatal). Data provided by a meta-analysis generated from

national general (family) practice data, revealed that more frequently after recent respiratory or urinary tract infections first MI and stroke occur, with a maximum risk in the first 3 days after diagnosis (relative risk RR 5.0 and 3.2) that gradually decreases in the following weeks. The findings of the MONICA study, conducted under the auspices of the WHO, indicate that the population levels of various haemostatic factors are different when comparing results from centres in the participating countries, but there is also a highly significant association with the incidence of CVD recorded in those centres.

We report niche studies correlating markers of inflammation with the occurrence of type 2 diabetes mellitus and chronic heart failure correlated with interleukin-6 (IL-6). There are also a number of meta-analyses of observational epidemiological studies that reach the same results for CRP and fibrinogen.

Ankle-brachial index (ABI) - a relatively easy test recommended for screening asymptomatic atherosclerotic disease. A low IGB identifies higher risk of developing coronary artery disease. IGB is also implicated in predicting the likely development of angina pectoris, MI, congestive heart failure, cholesterol stones (CAGB), stroke or the need for carotid surgery. IGB and cardiovascular risk are inversely proportional.

Influenza and viral diseases with respiratory tropism. Seasonal influenza immunisation is recommended for patients with diagnosed cardiovascular disease, just as prophylactic vaccination measures are recommended for other respiratory viruses because outbreaks are proven to put cardiac patients at risk.

The recent pandemic (SARS CoV-2 infection and Covid disease) and its effects have revealed the magnitude of the cardiovascular effects on patients who have experienced the disease. (18, 10)

Chronic kidney disease. Both diabetes mellitus, dyslipidemia and hypertension are pathologies ultra-recognized as risk factors in chronic kidney disease and are ubiquitous in association. They act by favouring the progression of endothelial dysfunction as well as the progression of atherosclerosis, thus contributing to the development of renal failure. Vascular damage coexists in chronic kidney disease. The presence of microalbuminuria increases the cardiovascular risk by 2 to 4 times. A low glomerular filtration rate (GFR) is an indicator of cardiovascular disease and all-cause mortality. A study of a large cohort of patients identifies decreased GFR, anemia, and microalbuminuria as independently associated with BCV, and when all were reported together they reduced subjects' survival rates .

Sleep apnea syndrome. SAS is recognized as frequent obstruction (may be complete or only partial), of the upper airway during the time given to sleep. It is estimated to preferentially affect 24% of adult males versus 9% of adult females. Repetitive "stimulation" of sympathetic nervous system activity, increased blood pressure and oxidative stress due to pain, together with hypoxic episodes associated with increased levels of inflammatory markers, are considered as initiators for endothelial dysfunction and atherosclerosis. SAS is associated with 70% increased relative risk of cardiovascular mortality and morbidity. The risk of developing SAS is correlated in men aged 40-70 years with apnea-hypopnea index. Screening and treatment of sleep apnoea syndrome in patients with coronary artery disease and hypertension may reduce cardiac events and sudden cardiac death.

Erectile dysfunction. ED defined as the frequent and repeated inability of a male person to achieve and maintain a satisfactory erection for sexual intercourse, a condition found in 52% of male subjects in the age range 40-70 years. The determining causes may be psychological, neurological, hormonal, arterial or cavernous insufficiency, and combinations of these. ED prevalence is high in people with multiple cardiovascular risk factors as well as in those with established BCV. Lifestyle modification

and drug treatment of risk factors are known to be effective in improving sexual function in men with ED.

Psoriasis is considered an independent risk factor for MI. The pathophysiology of psoriasis is characterised by: increased antigen activity, activation of T cells and T helper cytokine type 1, resulting in the appearance of red scaly plaques with large circumference and diameter, and in some patients pathognomonic arthritis. Psoriasis is frequently associated with systemic inflammatory markers, such as elevated serum C-reactive protein (CRP) levels. The risk of psoriasis-associated MI is high in young patients with severe forms, but lessens with age. By controlling the classic risk factors of cardiovascular disease, the risk of psoriasis patients experiencing MI remains increased due to increased immunological activity. Patients with severe forms of psoriasis have a higher risk of developing MI than those with mild forms of the disease.

Rheumatoid arthritis. Subjects diagnosed with rheumatoid arthritis have double the risk of MI compared to the general population. Cardiovascular risk increases from the early stages of rheumatoid arthritis, possibly associated with systemic inflammation and prothrombotic status. By adopting a healthy lifestyle, including changes in patients' diet, smoking cessation, a daily exercise programme and appropriate medication treatment, modification of classic risk factors is important in reducing cardiovascular risk in patients diagnosed with rheumatoid arthritis. Observational studies support lower rates of cardiovascular events and cardiovascular mortality in patients with rheumatoid arthritis and psoriasis when treated with methotrexate (weekly, doses between 10 mg and 20 mg).

Lupus erythematosus. SLE is associated with endothelial dysfunction and increased risk of coronary heart disease, which is not explained by the classic risk factors for ischaemic heart disease. Systemic lupus erythematosus has microvascular dysfunction as its predividing manifestation, expressed in abnormalities of myocardial vascular flow and blood supply in the coronary circulation. Coronary microvascular dysfunction is an early indicator of accelerated coronary atherosclerosis, influencing increased cardiovascular morbidity and mortality in these patients.

Periodontitis is associated with endothelial dysfunction, atherosclerosis and increased risk of MI and stroke. Both economic factors and lifestyle habits such as low socioeconomic status and smoking play an important role. Periodontitis can be a risk factor contributing to impaired cardiovascular health and treatment is imperative along with the management of other cardiovascular risk factors.

Vascular disease after radiotherapy. The incidence of stroke and ischaemic heart disease remains high for many years after completion of radiotherapy, signalling characteristic developments of atherosclerosis (including lipid accumulation), thrombosis and inflammatory changes. After radiotherapy it is advisable for oncological cases to optimise their risk factors.

Post-transplant vascular disease - Important risk factors (excluding immune factors) are dyslipidaemia, type II diabetes mellitus, hypertension. Consequent vascular injury significantly affects cardiac function.

3.2.6. Lifestyle factors

Smoking is a modifiable risk factor with a high prevalence in the population, especially in males. Cardiovascular risk increases the more the onset of smoking is before the age of 15. Even passive smoking increases cardiovascular risk.

The proven mechanisms by which smoking acts are arterial vasoconstriction, increased blood pressure, increased total cholesterol with decreased HDL-cholesterol fraction, platelet activation. In the European area, as a country we are at the top of the prevalence ranking in the general population (26.7% daily smokers), according to data centralised by the European Society of Cardiology.

Inadequate diet. High-calorie diets, high in saturated fats, excessive salt and sugar consumption contribute to an increased risk of cardiovascular disease.

Alcohol consumption. Excess alcohol negatively influences cardiovascular risk. However, there are also studies which conclude that moderate consumption (100–300 ml red wine) has a protective cardiovascular effect.

In the chart published by the European Society of Cardiology, we have an average consumption of 5.4 l of alcohol for women, but a high alcohol consumption of 18.6 l for men (for men we are ranked next to countries with a tradition of alcohol consumption such as Russia or Belarus, but we are outperformed by countries with a higher reported per capita alcohol consumption - France, Spain, Portugal - and a low prevalence of cardiovascular disease).

Sedentary lifestyles are associated with a doubling of cardiovascular risk compared to active people. Physical activity has beneficial effects by maintaining body weight, reducing blood pressure, improving lipid profile (cholesterol, triglycerides).

CHAPTER 4. CARDIOVASCULAR RISK

Cardiovascular risk is the likelihood that a person will at some point develop damage to the blood vessels and heart (fatal cardiovascular events - myocardial infarction and stroke - and non-fatal cardiovascular events) and is different from cardiovascular risk factors, being in fact the sum of their actions.

Cardiovascular risk estimation charts and algorithms are used to estimate cardiovascular risk taking into account the risk factors.

Cardiovascular risk levels can be established even in the absence of risk factors and there is no lower overall cardiovascular risk that excludes prevention or treatment of risk factors. Conversely, the presence of a risk factor does not automatically require its treatment.

Stratification of total cardiovascular risk is done in

- Low
- Moderate
- High
- Very high.

These estimates apply to both individuals and populations.

Low risk countries are Belgium, Denmark, France, Israel, Luxembourg, Norway, Spain, Switzerland, the Netherlands and the UK.

Moderate risk countries are Austria, Cyprus, Finland, Germany, Greece, Iceland, Ireland, Italy, Malta, Portugal, San Marino, Slovenia and Sweden.

High risk countries are Albania, Bosnia and Herzegovina, Croatia, Czech Republic, Estonia, Hungary, Kazakhstan, Poland, Slovakia and Turkey.

Very high risk countries are Algeria, Armenia, Azerbaijan, Belarus, Bulgaria, Egypt, Georgia, Kyrgyzstan, Latvia, Lebanon, Lithuania, Montenegro, Morocco, Republic of Moldova, Romania, Russian Federation, Serbia, Syria, Macedonia, Tunisia, Ukraine and Uzbekistan.

CHAPTER 5. PREVENTION METHODS

In cardiovascular prevention there are four prevention strategies, which are necessary and complementary.

1. Primary population-based prevention - aims to reduce risk factors at population level without the need for clinical examination of subjects and is important for reducing the overall incidence. In this type of prevention, the focus is on the incidence of disease in the population, not the disease of

the individual. The causes of the disease are different from the causes of the incidence and are achieved by establishing policies and interventions at community level (ecological strategy).

2. Primary prevention targets high-risk, healthy people who belong to the upper zone of risk distribution and differs from primary prevention in that it requires risk stratification to identify the upper samples.

3. Secondary prevention is aimed at patients with established, overt cardiovascular disease.

4. Tertiary prevention is applied when the patient has reached a more advanced stage of disease and aims at recovery.

In cardiovascular disease, there is no evidence that early detection is an effective way to prevent the disease, which is why community interventions (primary and primary prevention) remain the most effective in this case, with the greatest benefits in the population and the highest potential (for example, the Framingham study showed that a drop of only 10 mmHg in systolic blood pressure leads to a 30% decrease in mortality due to hypertension).

For the timely detection of biological or lifestyle risk factors (modifiable factors) aimed at identifying high-risk subjects, various tools are useful in line with the recommendations of the European Guidelines for the Prevention of Cardiovascular Disease in Medical Practice, respectively:

Availability of appropriate assessment systems

Real-time advice or treatment

Continuity

Patient access to treatment regardless of socio-economic status.

For the prevention of a single cardiovascular event it is useful to involve a large number of individuals without identifying an apparent benefit for them, which is the very paradox of prevention.

It is important the quality of the evidence (if it is strong, with low probability of bias, it can be extended) and what recommendations are supported by evidence. But not all evidence considered to be of high quality is worth recommending for implementation.

Using the method by which evidence can be prioritised requires valuable judgements that take into account the quality of the evidence and whether the objectives assessed were appropriate.

For population-based prevention programmes, results from observational epidemiological studies form the basis for the first level of recommendations.

Cardiovascular prevention has the overall objectives of reducing mortality and morbidity in high-risk individuals.

Even if it focuses only on the control of a (single) behavioural risk factor, group interventions on healthy lifestyle adoption often contain elements that influence multiple risk factors. Interventions involving psycho-educational and psychosocial behaviours can improve quality of life and significantly reduce risk factors.

The objectives of BCV prevention are to reduce their manifestations, impact on morbidity, quality of life and mortality generated, implement characteristics of individuals who aspire to remain healthy through promotion:

- Smoking cessation
- Adopting a healthy diet
- Moderate physical activity for 30 minutes daily
- Body mass index (BMI) below 25kg/m² and avoidance of central obesity
- Blood pressure below 140/90 mmHg
- Total cholesterol below 190 g/dl (5 mmol/l)
- LDL cholesterol below 115 mg/dl (3 mmol/l)
- Blood glucose below 110 mg/dl (6 mmol/l).

It also tends to achieve good control of risk factors in patients at high cardiovascular risk, primarily those with established CVD:

- Blood pressure below 130/80 mmHg if possible
- Total cholesterol below 175 mg/dl (4.5 mmol/l) or optionally 155 mg/dl (4 mmol/l) if possible
- LDL cholesterol below 100 mg/dl=2.5 mmol/l (optional below 80 mg/dl=2 mmol/l) if possible
- Blood glucose below 110 mg/dl (6 mmol/l) and HbA1c below 6.5% if possible.

according to the European Cardiovascular Prevention Guidelines implemented in Romania.

SPECIAL PART

CHAPTER 7. STUDY I. RESEARCH ON CARDIOVASCULAR RISK FACTORS IN A GROUP OF PATIENTS WITH DIAGNOSED BCV UNDERGOING TERTIARY PROPHYLAXIS

7.1. PURPOSE

Retrospective assessment of exposure of patients with diagnosed CVB to cardiovascular risk factors and Hierarchical assessment of cardiovascular risk factors identified in subjects included in the study group to highlight their existence, correlation and specificity, and territorial distribution.

7.2. STUDY OBJECTIVES

- To set up the study group consisting of patients with chronic cardiovascular disease, diagnosed with heart disease, admitted for tertiary prevention (cardiovascular recovery) in the Cardiovascular Recovery Hospital Dr Benedek Geza Covasna.
- Direct application of an extensive epidemiological survey on exposure to cardiovascular risk factors and corroboration of responses with medical data recorded in the General Clinical Observation Forms (GCOF)
- Study the particularities according to the regional distribution of cardiovascular risk factors
- Statistical processing of data from epidemiological assessment and medical records
- Comparison of data obtained in the study with existing data in the general population
- Formulation of conclusions.

7.3. MATERIAL AND METHOD

7.3.1. The research batch

The study is a descriptive, observational, epidemiological study conducted on a group of 499 chronic cardiovascular patients admitted for tertiary prevention procedures between January and April 2022. The selection of patients was made respecting the territorial distribution of the general population (starting from counties and grouped in regions) and the proportions of belonging to the environment of origin (urban/rural) and gender (male/female).

The epidemiological history data were obtained from direct examination by the epidemiologist (author of the present thesis) and the clinical data, and laboratory parameters as well as the medical history of identified comorbidities were taken from the General Clinical Observation Sheets (GCOS) of the patients in the Cardiovascular Recovery Hospital Dr. Benedek Géza Covasna.

Inclusion criteria

Inpatient

Subject diagnosed with chronic cardiovascular disease prior to inclusion in the study

Patient's agreement and willingness to provide information requested for the epidemiological investigation of cardiovascular risk factors.

Exclusion criteria

- Patient without a diagnosis of cardiovascular disease

- Acute patient
- Lack of consent to participate in the present research.

The selection of patients was done randomly, respecting only the criteria of belonging to the area, gender and environment of origin adjusted to those found in the general population of Romania. The confidence interval for patients selected for the study and the general population of the country is 99%.

The provisions of the national legislation on good practices concerning research on human subjects were respected, namely the Law on Patients' Rights (Law 46/2003) - Chapter IV - Right to confidentiality of information and right to privacy of the patient and Law 206/2004 on good conduct in scientific research, technological development and innovation.

Method

Data from the epidemiological survey were uploaded into a centralising Excel Worksheet for mathematical processing. The information was recorded numerically or subsequently transformed into numerical values No= 0 and Yes=1 for interpretation.

Data analysis was done

- Through tables and graphs using Microsoft Excel
- Statistical mathematical processing using SPSS (Statistical Package for the Social Sciences).
- Discrete variables were presented as percentages, comparisons were made with the chi-square test
- Continuous variables were presented as mean or median according to distribution, comparisons were made with t-student or Pearson

7.4. RESULTS AND DISCUSSION

In the group formed during the research, we followed the following categories for cardiovascular risk factors:

1. Medical risk factors
 - 1.1. Hypertension (hypertension)
 - 1.2. diabetes mellitus (DZ)
 - 1.3. obesity (chronic adipose disease)
 - 1.4. vascular disease
 - 1.5. stroke
 - 1.6. myocardial infarction (MI)
 - 1.7. dyslipidaemia
 - 1.8. chronic kidney disease (CKD)
 - 1.9. sleep apnea
 - 1.10. erectile dysfunction
 - 1.11. psoriasis
 - 1.12. rheumatoid aortitis
 - 1.13. systemic lupus erythematosus (SLE)
 - 1.14. periodontosis
 - 1.15. depression
 - 1.16. anxiety
 - 1.17. radiotherapy
 - 1.18. transplantation
2. Hereditary history (genetic factors)

3. Social risk factors
 - 3.1. Educational level (education)
Occupation
Family status
 - 3.4. Existence of children
 - 3.5. Housing (environment)
 - 3.6. Number of people living with
 - 3.7. Access to drinking water
 - 3.8. Access to heating
 - 3.9. Access to sewage system
 - 3.10. Assessment of living conditions
4. Lifestyle factors
 - 4.1. Smoking
 - 4.2. Drinking alcoholic beverages
 - 4.3. Physical activity
 - 4.4. Sleep
 - 4.5. Stress
 - 4.6. Nutrition
 - 4.6.1. Type of diet
 - 4.6.2. Meat consumption
 - 4.6.3. Fruit and vegetable consumption
 - 4.6.4. Consumption of bread
 - 4.6.5. Consumption of soft drinks
 - 4.6.6. Sugar consumption restrictions
 - 4.6.7. Salt consumption restrictions.
5. Access to health services.
6. Passing through SARS CoV-2 infection.

For the current research we considered the division of the territory into the 8 current administrative regions corresponding to the historical regions of Romania, regions that have different lifestyle characteristics and habits and could provide data on cardiovascular risk factors.

7.4.1. Medical risk factors

Considering cardiovascular risk factors in the medical category, 99% of the patients in the study group have hypertension, 56% are obese and for 45% of them diabetes and vascular disease diagnoses are recorded.

The next comorbidities in order of incidence are periodontitis mentioned for 28% of cases, dyslipidemia present in 27% of subjects and anxiety present in 15% of patients.

In the hierarchy of risk factors follows fatal cardiovascular incidences present stroke in 11% and MI present in 10% of the study population.

The ranking of medical risk factors for the studied group indicates:

- Presence at the top of the hierarchy in all regions of hypertension. Given that the population evaluated is diagnosed with chronic cardiovascular disease and middle age predisposes to this pathology (vascular resistance increases with advancing age), the increased prevalence (in 6 areas 100%) of this comorbidity is noted. The sensitivity and importance of this observation I believe is represented by the fact that hypertension in most cases does not

have noisy symptoms although the effects are significant and disabling over time, but also that there is an adaptation of the body so that the minimization of symptoms is doubled by pathophysiological mechanisms. This observation overlaps with existing data both in the literature and in statistical processing of the general population where the first place as a cause of premature death and disability (assessed using DALYs) is still hypertension (for Romania with a decrease in incidence in the general population of 3.67% for the period 2009-2019). A 10 mmHg drop in blood pressure decreases the risk of death from CVD by 30% according to the Framingham study, making this risk factor a target for prophylactic interventions.

- The next RF in the medical category is BCA (chronic adipocyte disease = obesity), a risk factor that is absolutely influenced by lifestyle. Although in theory doctors, patients and their entourage are aware of the recommendations, the adoption of a lifestyle that allows body weight reduction is frequently difficult to implement and comply with. The only region in which BCA is ranked second in this hierarchy is Bucharest-Ilfov, where circulatory pathology (vascular diseases) is placed before this pathology, without the prevalence of BCA being low. For this pathology (which is an indicator of the health status of the population) the incidence trend is increasing (+2.67%) in the general population, which indicates the need for early and sustained interventions to optimize the body mass index. Weight loss by 10% decreases the risk of death by fatal events in BCV (MI and stroke) by 20%. Weight loss also prevents the onset and progression of hypertension, diabetes and dyslipidaemia. In the studied group the prevalence is 56%, higher than the prevalence in the general adult population (20-79 years) where it is 31.4% (PREDATOR study).
- Diabetes mellitus affects 45% of the subjects in the studied population, while the prevalence in the general population, according to INSP data, PREDATOR study (to assess the prevalence of diabetes in the adult population of Romania) is 11%, and in the SEPHAR III study is 12.2% which allows the interpretation of the results obtained in this population as dependent on the age of patients, the existence of risk factors for diabetes (hypertension, BCA and dyslipidemia). In territorial profile, diabetes cases are not evenly distributed being in close relation with the accessibility of specialized medical services and the addressability of the population. The prevalence of diabetes in the Romanian population, of epidemic proportions, is a cause for concern as it increased by 17.5% between 2009 and 2019.
- Vascular diseases are present in 45% of the studied population, their critical importance being linked to the possibility of fatal events (MI and stroke) whose consequences are primarily represented by mortality.
- Periodontosis, present in 27.66% of the subjects of this study, is significantly equal to the prevalence of dyslipidemia (present in 27.05% of the study population), the mention I would like to make is strictly related to the investigation of this risk factor in the general population. Dyslipidemia is thoroughly researched and mentioned as a risk factor (important also due to its increasing prevalence in the general population), used in the total cardiovascular risk assessment scores and tools, while periodontitis is neglected (probably due to its diagnosis in the dental services network for which the patient in our country has no inclination).
- For dyslipidemia in our study a prevalence of 27.05% is recorded, being the only classical medical risk factor known and assessed in BCV for which a lower prevalence is found than in the general population of Romania (the PREDATOR study mentions 38.5% of the general population affected by dyslipidemia).

- Another specific result is recorded for anxiety, which is identified as a risk factor for 15% of the patients evaluated, with increased prevalence of MI and stroke. I interpret the explanation for the placement of this pathology before the classic ones as being less investigated by clinicians and also the devastating effects of MI and stroke (which translate into mortality).
- Stroke is prevalent in the general population characteristic of the age groups, i.e. 0.1% under 40 years, 1.8% for the age group 40-55 years, 4.3% for those between 55-70 years and 13.9% for those over 70 years. For this risk factor the prevalence in the study group (adjusted for age of subjects) is superimposable with the results in the general population. I emphasize the importance to be given to this risk factor, as the generated mortality is 21%, and among stroke survivors only 30% have access to rehabilitation therapies.
- MI has been encountered in the studied population in 10% of patients, with the same caveats as for stroke (increased mortality) but also a caveat about the lower age at which this incident occurs (which in survivors becomes a negative prognostic factor).
- Erectile dysfunction has been assessed using the MHS (Men's Health Survey)2 in Romania, which found a prevalence of 25% in the male population over 35 years of age. According to the results of this survey 82% of men over 35 years old in Romania smoke and/or suffer from at least one of the following diseases: hypertension, hypercholesterolemia, diabetes mellitus, depression, benign prostatic hyperplasia, heart disease, stress. In our sample 30 (1.18%) of the 254 men documented a medical diagnosis of erectile dysfunction. Mention is that there is a marked reluctance of the subjects to address this risk factor (141).
- Depression is present in 5% of the general population, in our study it is identified in 9.62% of the evaluated subjects, having a link with presentation to specialist services.
- CKD in the general population is around 5%, in our study the prevalence recorded is double-10%, directly related to the age of the subjects.
- For sleep apnea, the literature reports a prevalence in the general population of 4%, with a higher prevalence in the study group (7.21%) due to the presence of obesity, hypertension and diabetes mellitus - known risk factors for the development of apnea.
- Rheumatoid arthritis, with a prevalence of 1% in the general population, is recorded as a risk factor in 2% of the study population.
- Psoriasis was found in 1.2% of the patients studied, a lower percentage than in the general population, where 5% of people are affected by this pathology.
- Radiotherapy, systemic lupus erythematosus and transplantation are risk factors identified in the study in a very small number of patients, so I cannot consider the influences significant at the research level (at the individual level, however, the influence of these risk factors is certainly important).

On average, each subject investigated in the study has an average number of 3.73 medical RFs, ranging from no medical RFs (1 patient) to a maximum of 8 medical RFs present in 7 patients. There is a statistically significant correlation (validated with chi-square test) between the presence and the number of RF for:

- arterial hypertension (hypertension)
- diabetes mellitus
- obesity
- stroke
- myocardial infarction
- dyslipidaemia



- chronic kidney disease
- sleep apnea
- rheumatoid arthritis
- systemic lupus erythematosus
- periodontosis
- depression
- anxiety
- transplant
- And there is no statistical correlation between the number of cardiovascular risk factors and
 - - erectile dysfunction
 - - radiotherapy
 - - psoriasis

Highly significant statistical correlations were also found for the following associations:

- passive smoking status and obesity
- hereditary history and region of origin of subjects, presence of vascular disease, stroke, myocardial infarction and dyslipidaemia
- deaths due to cardiovascular disease in first-degree relatives and the presence of vascular disease, myocardial infarction, chronic kidney disease, rheumatoid arthritis and radiotherapy
- meat consumption (predominantly pork) and residence environment, occurrence of myocardial infarction and radiotherapy

7.4.2. Risk factors - hereditary and collateral history

Although it is a non-influential factor, the existence of a hereditary-collateral history has a definite negative prognosis in cardiovascular disease, which is why it is given great importance.

The weight of the maternal lineage in terms of both cardiovascular suffering and deaths in the family due to it is noted.

In the regional distribution of the risk factors listed, Bucharest-Ilfov and Banat stand out with a high prevalence of maternal hereditary history.

The hereditary-collateral antecedents are correlated (with statistical significance)

- Amount of AHC with number of medical RF
- AHC sum with region
- AHC sum with residence environment
- AHC sum and vascular diseases
- AHC sum and stroke
- Sum AHC and MI
- AHC sum and dyslipidaemia

7.4.3. Risk factors – social

Education

7.4.3. Risk factors - social

The most common levels of education are high school (35%) followed by vocational school (31%) according to the training period of the subjects.

Lack of education is considered a risk factor, while higher education (university studies) is a protective factor.

Within the regions, high school education predominates, followed by vocational school, except for the Bucharest-Ilfov region where most of the people in the study group have graduated from university and the Oltenia region where the majority of people without education are included in the study.

Occupation

Several categories were used for occupation, but due to age and disabilities acquired due to illness the subjects fell into only 2 (employed or retired with a clear variation in favour of the latter category).

Social status

For the social status categories, married people benefit from protection (lack of alienation, existence of a purpose, sense of belonging), while single people (unmarried, divorced or widowed) have an additional risk factor.

The existence of children is a protective factor, while the absence of children is considered a risk factor.

In the regional analysis, married people are predominant in all regions, with the highest proportions of divorced people in Oltenia and widowed people in Bucharest-Ilfov.

According to the presence of children in the subjects' families, the areas with the highest proportion of people with children are Transylvania and Muntenia, while Dobrogea is the region where we find the highest proportion of people without children.

Living conditions

94% of the respondents consider that they have adequate housing conditions (regardless of the quantification of the other variables). I consider this aspect to be of greater importance than external assessments of the subject.

Only 7.62% of the people surveyed live alone which is a risk factor.

On average, a subject lives with 2 other people.

Access to the water network is ensured for 92% of the subjects of the study, access to the heating network for 42% and access to the sewage system for 59%.

In all regions, the population living in urban areas is 100% satisfied with the housing conditions, while in the population living in rural areas there are variations, with the highest percentage of dissatisfaction with the housing conditions being in the Muntenia region, while in the Bucharest-Ilfov region and the entire rural population is satisfied with the housing conditions.

7.4.4. Lifestyle

Smoking

In the research group 56.31% of the subjects are smokers, while 17.43% are former smokers.

Compared to the prevalence in the general population (44% of the adult population) the proportion is significantly higher.

At the same time there is a high percentage of subjects who are passive smokers (they belong approximately equally to the non-smokers category - 109 persons and smokers - 117 persons).

The period during which smokers have consumed toxic substances is impressive - the average duration is 45.65 years.

Also for former smokers the data obtained in the present research support that they smoked on average 35.87 years before quitting, and the period without tobacco use in this category is 10.08 years, significantly shorter than the period of exposure.

The average age for the onset of this habit is low at 21 years, which makes me emphasize the need for prevention primarily in young communities.

In terms of territorial distribution, the highest percentage of active smokers is found in Banat and Transylvania, while the prevalence of smoking (active and former smokers) is highest in Muntenia and Transylvania, with Muntenia also recording the highest percentage of smoking cessation (highest percentage of former smokers).

Active smokers have the longest exposure period (average time since smoking) in Banat (46.79 years) and the shortest in Oltenia (41 years).

As for the populations who quit smoking, the longest period since quitting is found in the Muntenia region with 14.23 years average period, and the shortest is found in Bucharest-Ilfov with an average period of 8 years.

Exercise

Only 11% of the subjects of this research consider that they are sedentary and that for medical reasons (difficulties in moving, pain) they do not have enough physical activity.

For 51% of them physical activity is carried out for a period between 30 min daily and 60 min daily. Sedentary lifestyles and reduced physical activity (more than 30 min/day but less than 60 min) are considered risk factors, while physical activity of more than 60 min/day is considered a protective factor as it is part of cardiovascular disease prevention.

In all regions physical activity falls predominantly in the range of over 30 min, under 60 min daily. The highest proportion of sedentary people is identified among subjects in Muntenia, while the highest proportion of active people (who perform physical activity over 60 min daily) is in Bucharest-Ilfov.

Sleep duration

The quality and duration of rest time was assessed in the study, with inadequate sleep duration (less than 7 hours daily average) experienced by 37% of subjects) and sleep disorders (present in 18%) of patients being included in the risk factors category, while adequate sleep duration (more than 7 hours daily, without disorders) is considered a protective factor.

The region with inadequate sleep duration (less than 7 hours/day) is Moldova, while the percentage of patients with sleep disorders is highest in Muntenia.

Stress

A special category in the present survey is stress, with only 4.21% of CVD patients not recognising a source of stress.

The low percentage of positive responses regarding stress at work can be explained by the high percentage of retired people (in line with age).

More than 95% of the subjects recognise several categories of stress, the most important cause being economic worries (recognised by 98.2% of patients), followed by social worries (97.8%) and family causes of stress (95.71%).

Stress is recognized with multiple sources by the entire population of the Bucharest-Ilfov region, with regional variations being minimal, with values exceeding 90%.

Nutrition

The predominant type of diet is mixed, found in 86% of the study population, followed by 7% of ovo-lacto-vegetarian diet.

As the type of diet in itself is not a risk factor (the risk consists mainly in the quantity and quality of the food), this indicator will be considered as an enabling factor, not as a risk or protective factor. On the other hand, the habit of restricting animal protein in the diet (fasting) is cited in the literature as a protective factor, so we will consider people who fast (weekly, occasional or black fasting) as protected categories, and people who do not fast (15% of the study group) as risk factors. The predominant type of diet is the mixed one, animal protein restriction is the most common in Muntenia (ovo-lacto-vegetarian diet), Bucharest-Ilfov (vegetarian) and Moldova (vegan). The habit of restricting the ingestion of animal protein (fasting), with beneficial effects, is practised in weekly stages, periodically and fasting when no solid food is eaten. Most people observing this pattern (rooted in religious customs) are in Transylvania for the cohorts studied.

Meat consumption

The vast majority (431 people out of 499 studied) consume meat and 13.63% of the study population do not eat this type of food.

Consumption assessed by the predominant amount in the diet by type of meat is divided into pork, red meat (beef, game), white meat (chicken) and fish.

As the first 2 categories are high in fat they will be included in the risk factor category, while the last 2 categories, low in fat and easy to digest, will be included in the protective factor category (it is worth noting that for only 1% fish is the preferred choice in the diet).

Consumption of semi-prepared foods is a risk factor due to the presence of excess amounts of salt, fat and stabilisers, exposure being 5 times higher in the study group (semi-prepared food consumers vs. non-consumers).

Fruit and vegetable consumption

In Romania, the percentage of people not consuming fruit and vegetables is the highest in Europe according to data provided by Eurostat.

In the group of patients investigated, the percentages of those consuming fruit and vegetables are clearly higher than reported and we consider the consumption of raw fruit and vegetables on a daily basis as a protective factor and their consumption on a weekly basis as a risk factor (since the food ration will most likely be supplemented by carbohydrates).

A small proportion of the cohort consumes raw fruit daily, 10% in Oltenia and Transylvania, while insufficient portions of raw vegetables consumed daily we have mainly in Bucharest-Ilfov.

Bread consumption

The risk factor in this food category is the excess quantity and consumption of white bread (found in 82.16% of subjects).

Elimination of bread from the regular diet, consumption of black bread or bread with seeds are considered protective factors.

For bread consumption, most subjects consume white bread in Bucharest-Ilfov and Banat, while black bread is consumed most in Moldova and Crişana.

Consumption of non-alcoholic beverages

Carbonated drinks are a risk factor due to their high sugar content. Regardless of the frequency of consumption we quantify the risk factor, in the case of the 38% of subjects who do not consume carbonated drinks we quantify the protective factor.

Moderate coffee consumption may have beneficial effects on blood pressure values, but excess is a risk factor through cardiostimulant effects. More than half of the patients in the study consume coffee daily, which is a predisposing (favouring) factor for hypertension and rhythm and conduction disorders.

Tea consumption is a protective factor, it is recognised as a blood pressure regulator through its diuretic effect, digestive aid which helps to maintain an optimal body weight, useful in excretion. The percentage of the study population not consuming tea (17%) will be quantified as a risk factor. Carbonated beverages are consumed by a large proportion of the population with CVD in Bucharest, Ilfov and Muntenia, while the highest proportions of people who do not consume carbonated beverages are found in Banat and Crişana.

Consumption of alcoholic beverages

The type and frequency of alcoholic beverages consumed has different impacts on cardiovascular health.

Existing data provide arguments for and against the consumption of beer (which would favour diuresis but increase body weight by ingested calories and by favouring hepatic steatosis) and wine (a small defined amount up to 300 ml consumed daily would show beneficial effects in some studies, while in others alcohol intake is a risk factor). For spirits there is a congruent opinion of studies classifying this habit as bringing additional risks in cardiovascular disease.

In this research the only protected category will be those who do not consume alcoholic beverages (34.47%).

According to the type of alcoholic beverages consumed by the patients in the study group, in Transylvania they drink the most beer, in Moldova they are the most consumers of wine, and in Bucharest-Ilfov they are the most consumers of refined alcohol (spirits).

Regarding the frequency of consumption for all types of alcoholic beverages, the habit of daily consumption is most frequent in Muntenia, weekly consumption of alcoholic beverages is most frequent in Transylvania and occasional consumption in Moldova.

Most people who consume alcoholic beverages are found in the study in the region of Moldova, and most people who do not consume alcoholic beverages in Banat.

Salt restriction

Excess salt intake negatively influences blood pressure control, with cardiac patients recommended to restrict salt intake. For the 97% who restrict salt intake as a preventive (tertiary) measure I will consider protective factor, and the exposure of the 3% without restriction will be considered risk behaviour.

In the region of Moldova we find in the research most patients who do not have a sodium (salt) restriction regime, in contrast in Dobrogea and Muntenia all the study population controls the amount of salt.

Sugar restriction

Carbohydrate intake has a negative influence on diabetes control, weight maintenance and metabolic syndrome. In the research population, more than half of the people do not consume sugar (protective factor).

Without sugar restriction in the diet we find the highest proportion of people in Bucharest-Ilfov, while in Oltenia are the most people who do not consume sugar.

7.4.5. Access to health services

Although it is a characteristic of the research subjects that they have a concern for their own health, which is also based on addressability to health services but also on accessibility, in the studied group there is the greatest difficulty in accessing ambulatory services (1 out of 3 subjects does not have access to this type of services). A percentage of 6.21% of the subjects claim that they do not have access to any type of health service, while 57% declare that all types of care are accessible. I consider as a risk factor the population that does not have access to health services (regardless of category - family doctor, outpatient, hospital) and as a protective factor the category that has access to all the services listed.

Access to health services is possible in an increased proportion for the studied cohort (given that it is a characteristic of this group that they attach importance to care), the most difficult access to the family doctor is recorded in Crişana and the most difficult access to the specialist outpatient clinic and hospital is recorded in Muntenia.

We ranked the top 20 cardiovascular risk factors for each region according to their prevalence in the population with cardiovascular disease we studied .

Risk factors are not the same in all regions.

For those risk factors present in all territories, there are regional variations.

The medical risk factors included in this classification are limited in number - there are 4 major risk factors plus possibly up to 2 more medical risk factors.

The share is represented by lifestyle risk factors, modifiable risk factors. It is important to point out that in a group of patients with long-standing cardiovascular disease, lifestyle habits have not undergone appropriate modifications for prevention.

The weights in the study population of all RF included in the hierarchy affect more than 1 in 3 subjects.

For the whole country, almost in the whole population the presence of stress (family, economic and social) and increased blood pressure values are detected.

The next places in the hierarchy are occupied by harmful eating habits - consumption of semi-prepared foods, white bread, pork, consumption of alcohol and carbonated drinks, insufficient consumption of raw vegetables, lack of sugar consumption restrictions, smoking - both active and passive smoking are present in the hierarchy, insufficient physical activity, insufficient sleep duration (less than 7 hours of sleep in 24 hours), female sex (which is a predisposing factor according to the age of the lot and postmenopausal hormonal status), maternal AHC among genetic factors, housing conditions - wood heating, education level - high school education.

The ranges of variation for risk factors in the studied cohort are small for female prevalence and large for housing conditions - wood heating insufficient consumption of raw vegetables.

Variation intervals for risk factors

Rank	Risk factor	Median	Lower quartile	Upper quartile	Variation%
1	HTA	99	93,88	100	6,52
2	stress	98,2	91,38	100	9,43
3	semiprepared	82,77	77,59	85,39	10,05
4	white bread	82,66	77,53	87,53	12,90
5	pork	70,33	65,52	73,44	12,09
6	alcohol consumption	65,23	55,1	71,11	29,06
7	active smoker	56,31	50,77	64,44	26,93

8	low physical activity	56,8	53,45	64,44	20,56
9	obesity	56,11	52,11	67,35	29,25
10	insufficient raw vegetables	53,64	27,58	69,23	151,02
11	female gender	50,9	50,94	52,96	3,97
12	consumption of carbo drinks	46,92	39,66	53,45	34,77
13	passive smoker	45,29	35,21	57,11	62,20
14	insufficient sleep duration	44,92	39,66	50,56	27,48
15	maternal AHC	45,47	30,77	53,33	73,32
16	vascular disease	45,09	30,77	58,62	90,51
17	DZ	45,09	35,21	57,14	62,28
18	wood heating	39,55	10,34	56,34	444,87
19	no sugar restriction	39,68	34,69	46,55	34,19
20	education - high school	34,85	25,84	44,83	73,49

Hierarchizing each category of risk factors and protective factors, the characterization of the BCV patient in the study group is outlined to be:

Female aged 67.26 years (mean age in the study group), urban resident.

Mother suffered from cardiovascular disease

High school education

Retired

Married with children

Lives with family, with 2 other persons

Has an average of 4 medical conditions (comorbidities) in order of likelihood these are hypertension (99%), obesity (56%), diabetes (45%) and vascular disease (45%), followed by periodontitis, dyslipidemia and anxiety

Have access to drinking water, communal heating (mains), sewage system and consider their living conditions adequate

Is a smoker, has been smoking for 46 years (on average)

She does physical activity more than 30 min/day, less than 60 min/day

Has an adequate sleep duration (7 hours)

Has sources of stress in the family, is burdened by economic and social worries

As for diet, it is mixed, fasts regularly, consumes mainly pork, consumes semi-prepared meat, raw fruit daily, prepared fruit weekly, raw vegetables weekly, prepared vegetables daily, white bread, does not consume carbonated beverages, coffee daily, tea daily, no sugar, restricted salt intake, consumes wine weekly, and occasionally liquor

Has access to medical services - family doctor, outpatient clinic, hospital

Is vaccinated against Covid, had Covid before vaccination and had cardiovascular events after Covid.

7.5 CONCLUSIONS

1. The present research was done in a group of chronic patients, with the particularity of the impact of risk factors over a long period of time
2. As a limitation for the extension of the results, I mention the overrepresentation of cases with a long-term evolution.

3. If in studies on cardiovascular risk factors, subjects are part of the general population (not selected by chronic cardiovascular disease criteria as in the present cohort) and risk factors are investigated in order to use the data in the development of tools for calculating total cardiovascular risk, in my study, regardless of the existing cardiovascular risk, risk factors were retrospectively identified with a bias towards prevention. Exposure and effect were investigated concurrently.
4. Evidence that these patients require more intensive measures than the general population lies in the detected prevalences, with values significantly higher than those described in the literature for the general population groups.
5. The patient was not investigated as an individual but as part of the population. Therefore protective measures may remain at population level.
6. For hypertension we found a prevalence of 99%, while in the general population it is around 40%.
7. There are 2 medical risk factors for which the recorded prevalences are lower than those described in the literature, dyslipidaemia and SLE.
8. For the medical risk factors, the number and strength of association is also important.
9. Data analysis was done regionally as the patient's area of origin can significantly influence the patient's lifestyle.
10. In the ranking of risk factors for cardiovascular disease, in the top 20 factors that negatively influence the occurrence and prognosis of the disease, only 20% are medical RF.
11. The most risk factors in accordance with the prevalence obtained are those related to lifestyle - diet, exercise, ingestion of toxicants - tobacco, alcohol, excess sugar and salt, rest time, lifestyle. Their importance lies primarily in the fact that it is easier to intervene on them.
12. In contrast, the protective factors ranked reveal that simple actions (such as salt restriction) are effective in preventing (at any level) cardiovascular disease. Here social factors play a primary role, followed by diet.
13. We can conclude that even in patients with proven cardiac morbidity, the application of preventive measures is only a desideratum because in fact exposure continues consciously (or unconsciously).
14. Preventive measures can change the quality of life without changing the individual.
15. Since the average age of the subjects is high, we recall that there is a systematic selective survival error in this group.

CHAPTER 8. STUDY II - RESEARCH ON THE IMPACT OF INFECTION WITH SARS VIRUS CoV-2 IN A COHORT OF PATIENTS WITH CHRONIC CARDIOVASCULAR DISEASE

With the investigation through epidemiological anamnesis of the cohort of patients with cardiovascular disease admitted for tertiary prevention of the disease in the middle of the pandemic episode generated by the SARS Cov-2 virus, in the framework of the assessment of risk factors in the segment of viral infections, I had the opportunity to describe the aspects generated by Covid disease on this particular category of subjects.

The fulminating evolution of viral infections worldwide (where 550 million cases have been recorded since the onset - 2 years ago), with devastating effects in terms of mortality generated (6.34 million deaths_ data obtained by electronic consultation of CSSE data - Center for Systems Science and Engineering at Johns Hopkins University at systems.jhu.edu/research/public-health/ncov/ accessed on 04.07.2022) has called for health systems to assess these cases.

Romania recorded 2.93 million cases resulting in 67,000 deaths.

The literature indicates that in the case of pre-existing conditions (chronic heart disease, diabetes, hypertension or obesity) there is a correlation with the development of severe forms of Covid-19 and a significant increase in mortality due to COVID-19. Infection induces cardiac manifestations (67,95,156)

The concerns of cardiologists refer to the fact that the cardiovascular system is affected due to pathophysiological mechanisms that are still insufficiently understood (62,96,181). During this period we have all read that cardiovascular disease is a risk factor for SARS CoV-2 infection.

During this period we all learned that cardiovascular disease is a risk factor for SARS CoV-2 infection, with the publication of an impressive body of research insisting on this pre-existing BCV sequence - Covid-19 infection - worsened outcome and prognosis.

Reviewing the classification of cardiovascular risk factors in which viral infection is distinctly mentioned, I was struck by the mentions of the virus being the risk factor in the reverse sequence viral infection-enhanced cardiac manifestations during evolution.

From this point of view I approached my research.

8.1. PURPOSE OF THE STUDY

Retrospective evaluation of exposure of patients with diagnosed BCV to cardiovascular risk factors - specific status of passing through SARS CoV-2 infection.

To identify the particularities of the subjects included in the study group in terms of the infectious vector and the prophylaxis measures applied in order to highlight their existence, correlation and specificity, as well as their territorial distribution.

8.2. STUDY OBJECTIVES

1. To set up the study group made up of patients with chronic cardiovascular suffering, with heart disease, admitted for tertiary prevention (cardiovascular recovery) in the Cardiovascular Recovery Hospital Dr Benedek Géza Covasna.
2. Direct application of an extensive epidemiological survey on exposure to SARS CoV-2 and corroboration of responses with medical data recorded in the General Clinical Observation Forms (GCOF).
3. Study the particularities according to regional distribution
4. Statistical processing of data from epidemiological assessment and medical records
5. Comparison of the data obtained in the study with the existing data in the general population
6. Formulation of conclusions.

8.3. MATERIAL AND METHOD

8.3.1. Research group

The study is a descriptive, observational epidemiological study conducted on a group of 499 chronic cardiovascular patients from all over the country (national representation) admitted for tertiary prevention procedures during the period January - April 2022.

The selection of patients was made respecting the territorial distribution of the general population (starting from counties and grouped in regions) and the proportions of belonging to the environment of origin (urban/rural) and gender (male/female).

Data on epidemiological history were obtained from direct examination by the epidemiologist (author of the present thesis) and clinical data on vaccination and infection were confirmed in the national reporting system Coronaforms. Medical history of identified comorbidities were taken from the General Clinical Observation Sheets (GCOS) of patients in the Cardiovascular Recovery Hospital Dr. Benedek Géza Covasna.

Inclusion criteria:

Inpatient

Subject diagnosed with chronic cardiovascular disease prior to inclusion in the study
Patient's agreement and willingness to provide information requested for epidemiological investigation of viral vector exposure

Exclusion criteria:

- Patient without a diagnosis of cardiovascular disease
- Acute patient
- Lack of consent to participate in the present research.

The selection of patients was done randomly, respecting only the criteria of belonging to the area, gender and environment of origin adjusted to those found in the general population of Romania. The confidence interval (confidence) for patients selected for the study and the general population of the country is 99% for both gender and background.

Method

Data from the epidemiological survey were loaded into a centralising Excel worksheet for mathematical processing. The information was recorded numerically or subsequently transformed into numerical values No= 0 and Yes=1 for interpretation.

Data analysis was done

- Through tables and graphs using Microsoft Excel
- Statistical mathematical processing using SPSS (Statistical Package for the Social Sciences) - F-tests for variance, t-student tests
- The main methods of analysis were odds ratio, risk ratio, hazard ratio

8.4. RESULTS AND DISCUSSION

As the study group is the same used in the previous research in this PhD thesis, we insisted on some aspects that are specifically related to SARS CoV-2 exposure, Covid-19 disease status, primary prophylaxis approach (vaccine) as we have this protective maneuver available from 2021.

The majority of patients are vaccinated (469 out of 499 patients studied). The explanation lies in the fact that at the time of the research, vaccination status was the prioritisation criterion for access to hospital rehabilitation services (so as to minimise the possibility of developing an eventual severe form of the disease).

The lowest proportion of vaccinated patients is found in Muntenia.

There is no statistical correlation between sex/gender and vaccination status ($p=0.855$). For the vaccinated there is a slight shift in the weight of the group towards the male sex (without statistical significance however).

Vaccinated/unvaccinated status is not correlated with the background (rural/urban) (chi-square test $p=0.086$), but percentage wise we have a higher percentage of vaccinated patients from urban background.

The cohort of patients passed through the disease in a proportion of 78.4%, the highest proportion of subjects from Bucharest-Ilfov, the lowest proportion of subjects from Transylvania. There was no correlation between regions and illnesses in the studied group.

More rural women experienced the disease in the study group, but there was no correlation between illness and gender or environment of origin ($p=0.274$ for gender and $p=0.185$ for environment of residence).

Timing of illness passage according to vaccination is important because most patients who experienced an illness episode did so before vaccination.

Territorial distributions, by gender and by environment of residence did not statistically correlate with the time of disease onset by vaccination (before or after) for environment of residence $p=0.264$, for gender $p=0.378$, for region $p=0.644$).

Percentage most patients who had disease before vaccination were from Transylvania, female and urban.

Of the study group 78.35% (n=391) experienced Covid infection and 21.65% (n=108) had no disease. Using the contingency table, we calculate the prevalence of disease in the vaccinated group which is 78.46% (R1) while in the unvaccinated group it is 76.66% (R2).

The RR (relative risk) = $R1/R2$ is 1.02, the value close to 1 meaning that vaccination would have had no real influence on the occurrence of the disease.

However, if we also take into account the time of disease onset (before or after vaccination in the vaccinated group), the real situation is that unvaccinated patients at the time of disease onset in our group had a risk 15.31 times higher than vaccinated patients, R1 93.86% - risk of disease onset in the group of patients who had the disease before vaccination (n=367) and R2 6.13% risk of disease onset in the group of those who had the disease after vaccination (n=24).

The RR (attributable risk) is 0.065 (subunit value) which shows that the vaccine was in fact protective. Of the 391 patients who experienced Covid-19 disease (recall that all have pre-existing chronic cardiovascular disease), 198 (50.63%) report that after the infectious episode they experienced unusual cardiovascular events (which they had not experienced before or whose manifestations exceed the usual symptomatology).

The distribution of those who experienced cardiovascular events after the illness, according to environment of origin and sex/gender reveals that a higher proportion of urban men experienced these complications, without statistically demonstrating a correlation. ($p=0.407$ for gender variation and $p=0.685$ for variation between means of origin).

The regional distribution of post Covid cardiovascular events shows that most events reported in the population were reported in Moldova while the fewest were in Banat.

Validation tests do not indicate a statistical association between the region of origin of patients and the rate of occurrence of unusual cardiovascular events ($p=0.975$).

The occurrence of cardiovascular events post Covid-19 and the number of cardiovascular risk factors in the medical category (comorbidities) that the patient has has a highly significant statistical association ($p<0.001$ with a 99.9% confidence interval).

While there is no statistical correlation between smoking and the occurrence of cardiovascular events ($p=0.926$), there is a highly significant correlation between the occurrence of cardiovascular events post SARS CoV-2 infection and passive smoking status ($p<0.001$ with a 99.9% confidence interval).

The relative risk of occurrence of post Covid cardiovascular events in the cardiac population is 50.6%, double the risk described in the large American and Western European cohorts followed in the general population (where in the literature we find values between 10% and 30%, with a mean of 25%).

CONCLUSIONS

1. The study group has predominantly vaccinated patients (93.99%), with no statistically significant differences between rural and urban populations or between genders and with homogeneous regional distribution.
2. 93% of subjects in the study group are vaccinated, the vaccine being a protective factor against the disease. The relative risk of disease of the unvaccinated is 15 times higher than that of the vaccinated population in this sample.
3. Women in urban areas and in the Crişana region are predominantly vaccinated
4. Unvaccinated in the same proportion (50%-50%) are women and men in rural areas, especially in the Muntenia region
5. In the study group, more women in rural areas and in the Bucharest-Ilfov region were affected. The least number of men in the urban area of Transylvania experienced the disease.

6. Most cases of the disease occurred before vaccination, predominantly in women from urban areas and Transylvania. After vaccination, most cases of the disease occurred in men from rural areas and in the Banat region.
7. More than one third of the study population experienced unusual cardiovascular events, 50.63% of the infected patients. In the study the prevalence of post Covid cardiovascular symptoms in patients with pre-existing cardiovascular disease is higher (50%) than the prevalence in international studies for the general population (25%).
8. Cardiovascular symptomatology occurring post Covid-19 is heterogeneous, ranging from extreme fatigability and hypertensive episodes to fatal cardiovascular events - MI and stroke. The relative risk of developing supra-adjuvant cardiovascular events ranges from 0.75% to 13.55% in the group.
9. There is a highly significant statistical correlation between the occurrence of post Covid-19 cardiovascular events and the number of medical risk factors (comorbidities) a patient has.
10. There is a highly significant statistical correlation between the occurrence of post Covid-19 cardiovascular events and passive smokers (no evidence of a link with smokers in the batch).
11. Clinicians should also consider Covid-19 history when assessing cardiovascular risks.
12. These observations may provide additional rationale for countering natural immunization as the long-term solution against viral disease, given the complications.

CHAPTER 9. FINAL CONCLUSIONS

Cardiovascular disease is a public health problem both globally, regionally and especially nationally as we have the highest mortality in Europe (62%) due to heart disease.

In this context, of alarming increase in incidents and prevalence of cases, correlated with increasing life expectancy (which translates into increasing age of patients needing medical care in this area), as well as the association of a marked number of comorbidities (in our study the average was 4 medical risk factors present per patient), indicate the need for multidisciplinary care for this category of patients, with the support of cardiologists and the expertise of other medical specialties (family doctor, internist, diabetologist, nephrologist, endocrinologist, neurologist, psychiatrist), related specialties (psychologist, nutritionist, physiotherapist) and, last but not least, the support of preventionists.

Epidemiological assessment of lifestyle, medical risk factors, hereditary and collateral history, socio-economic status of patients, access to health services and their regional distribution allows the identification of distinct vulnerable groups with tailored prevention needs.

Extrapolation of prevalences of associated diseases obtained in large cohorts of the general population (SEPHAR, PREDATORR studies) indicates millions of inhabitants affected by the burden of chronic diseases with disabling and long-lasting evolution. Our study indicates in the population with pre-existing cardiovascular diseases higher prevalence rates than in the general population which are reasons to approach this category with much more determination and specificity due to the much higher attributable risks.

We constituted a study group of 499 patients from all 8 regions of the country (with national representativeness), distributed according to criteria of gender (female/male), living environment (rural/urban) and proportional to the regional distribution of the Romanian population according to INS data from 2020.

Prevalence of hypertension determined in the study group is 99% while in the general population the SEPHAR study determines 44%, for chronic adipose disease (obesity) in our study 56.11% vs. 31.40%

in the PREDATORR study cohort, diabetes mellitus 45.29% vs. 11.60% in PREDATORR and 12.20% in SEPHAR, vascular diseases 45.09% in the study group, periodontitis 27.66%, dyslipidemia 27.05% in the study group vs. 38.50% in the general population (PREDATORR study), anxiety 14.63%, stroke 10.82%, myocardial infarction 10.22%, depression 9.62%, chronic kidney disease 9.42% vs. 5% in the general population, apnea 7.21%, erectile dysfunction 6.01% in the study group vs. 25% in the general population, rheumatoid arthritis 2.00%, radiotherapy 1.40%, psoriasis 1.20%, systemic lupus erythematosus 0.60%, transplantation 0.20%. (113)

Conducting research during the pandemic period generated by the SARS CoV-2 virus allowed us to follow the exposure of patients with chronic cardiovascular disease installed prior to viral exposure and the attitude towards immunization by vaccination. While 93.99% of the study subjects were vaccinated at the time of examination (this was a condition to facilitate access to the hospital unit for health care), 78.36% experienced the disease. Risk analysis in vaccinated and unvaccinated indicated that the vaccinated population had a 15 times lower risk of getting the disease than the unvaccinated population (the vast majority of patients got the disease when they were not yet vaccinated, i.e. 2/3). If in large group researches, the occurrence of post Covid-19 cardiovascular effects (in the long-term course of the disease) has been observed in patients from the general population ranging from 10.00% to 30.00%, for the subjects in our study, unusual cardiovascular events occurred in 39.69%. The relative risk of occurrence of unusual cardiovascular events is 50% in the population with pre-existing heart disease in the study vs. 25% that for the general population.

Cardiovascular events were considered to be all new-onset or exacerbated long-term manifestations, i.e. hypertensive episodes, extreme fatigue, precordial pain with anginal character, arrhythmias and major, fatal cardiovascular events- stroke and myocardial infarction.

This extended observation of a group of patients with special characteristics of age (mean in the group is 67.26 years) and history of chronic cardiovascular disease, exposure to heterogeneous risk factors and grouping of characteristics according to the geographic region where the patient comes from allowed both the prioritization of the catalogued risk factors, the identification from the same survey of protective factors, and their processing.

We obtained highly statistically significant correlations (considered negative prognostic factors by the strength of the association) between

- the number of risk factors present in each patient (variations between 0 risk factors for 1 patient and 8 risk factors present for 7 patients, with a mean of 3.65) and sleep duration ($p=0.008$), passive smoking status ($p<0.001$), hereditary history, presence of hypertension ($p<0.001$), obesity ($p<0.001$), diabetes mellitus ($p<0.001$), myocardial infarction ($p<0.001$), vascular disease ($p<0.001$), stroke ($p<0.001$), dyslipidemia ($p<0.001$), chronic kidney disease ($p=0.001$), sleep apnea syndrome ($p=0.009$), rheumatoid arthritis ($p=0.003$), systemic lupus erythematosus ($p=0.001$), periodontitis ($p<0.001$), depression ($p<0.001$), anxiety ($p<0.001$) and transplantation ($p=0.001$), as well as for the occurrence of unusual cardiovascular events post-Covid ($p<0.001$ with 99.99% confidence interval), while for erectile dysfunction ($p=0.166$), psoriasis ($p=0.166$) and radiotherapy ($p=0.535$), as well as for smoking status in this group we did not find statistically significant correlation
- passive smoking status and obesity
- subjects' hereditary history and region of origin, presence of vascular disease, stroke, myocardial infarction and dyslipidemia
- deaths due to cardiovascular disease in first-degree relatives and the presence of vascular disease, myocardial infarction, chronic kidney disease, rheumatoid arthritis and radiotherapy
- meat consumption (predominantly pork) and residence environment, occurrence of myocardial infarction and radiotherapy

As identified medical risk factors, regardless of region, gender or background, the top 4 positions are occupied by hypertension, obesity, diabetes mellitus and vascular disease, followed by periodontitis (a top position in the hierarchy), dyslipidaemia and anxiety.

In the large group of risk factors, in the top 20 positions at national level we find only 4 medical risk factors, mainly psychological factors (stress in the second position after hypertension) and lifestyle factors (inadequate nutrition - consumption of semi-prepared foods, white bread, pork, insufficient raw vegetables, sugar, carbonated drinks, lack of physical activity, alcohol consumption, smoking, insufficient sleep).

This ranking would allow effective preventive action if we could implement the recommendations. However, the present study shows that it is not easy for patients to give up harmful habits (e.g. 56.31% in the group are smokers, plus 17.43% ex-smokers, which is higher than the average prevalence in the general population in subjects who are aware of the cardiovascular risk they are exposed to through smoking. The average period of exposure to risk is 45.56 years for smokers and 35.87 years for ex-smokers, while for ex-smokers the average period since quitting is 10.08 years). In the category of protective factors the first position in the hierarchy is occupied by salt restriction, followed by not living alone and not having sleep disorders.

The characterisation of the subjects in the study reveals a general representative profile along the following lines, but without this profile being adapted to specific subcategories

- Female aged 67.26 years, urban resident
- Mother suffered from cardiovascular disease
- High school education
- Retired
- Married with children
- Lives with her family, with 2 other people
- Has an average of 4 medical conditions (comorbidities) in order of likelihood these are hypertension (99%), obesity (56%), diabetes mellitus (45%) and vascular disease (45%), followed by periodontitis, dyslipidemia and anxiety
- Have access to drinking water, communal heating (mains), sewage system and consider their living conditions adequate
- Is a smoker, has been smoking for 46.26 years (on average)
- Does physical activity more than 30 min/day, less than 60 min/day
- Has an adequate sleep duration (7 hours)
- Has sources of stress in the family, is burdened by economic and social worries
- As for diet, it is mixed, fasts regularly, consumes mainly pork, consumes semi-prepared meat, raw fruit daily, prepared fruit weekly, raw vegetables weekly, prepared vegetables daily, white bread, does not consume carbonated beverages, coffee daily, tea daily, no sugar, restricted salt intake, consumes wine weekly, and occasionally liquor
- Has access to medical services - family doctor, outpatient clinic, hospital
- Is vaccinated against Covid, had Covid before vaccination and had cardiovascular events after Covid

STUDY LIMITATIONS

1. Subjects with cardiovascular disease in the study are older than the general population averages (the cardiac population has undergone a degree of selection)

2. The patients are admitted to a hospital for tertiary prevention of the underlying disease, they are patients who attach importance to their health status, this fact limiting the degree of representativeness for the Romanian population
3. Cases with long term chronic evolution are overrepresented in the group and there is a systematic error of selective survival
4. The same category of patients was not included in the study if they were admitted before 2022
5. As the study group has a uniform distribution we used in the data processing the mean (not the median which is characteristic for non-uniform distribution and not sensitive to higher values)
6. Using variable mean data are characteristic for populations, we do not attribute characteristics to members of a group that they do not possess as individuals. Preventive measures will be addressed accordingly to that population.
7. We obtained the catagraph of cardiovascular risk factors and protective factors, but not the weight of each, and did not investigate the strength of the association

CHAPTER 10. ORIGINAL CONTRIBUTIONS. DISSEMINATION OF RESULTS. FUTURE RESEARCH DIRECTIONS

10.1 ORIGINAL CONTRIBUTIONS

- In the general part the scientometric study reviewing national and international literature.
- The study group was made up of patients with a long history of cardiovascular disease, patients on whom risk factors and protective factors had a long period of action.
- The subgroups of the group were constituted respecting the criteria of gender and environment of origin, respecting the proportions of the general population of the 8 administrative areas (corresponding to the historical regions of the country). This is the factor to which the subject has had the longest exposure and can confer specific information. There are no national studies addressed to this category of patients (heart patients for the investigation of cardiovascular risk factors) and no reports on historical territories covering the whole area of Romania.
- We used risk factors for population characterization, not for aggregation into tools to assess total cardiovascular risk (as is the trend in large cohort studies since Framingham)
- The data processing was done to be able to develop prevention strategies in the interest of the specific individual, not to standardize population characteristics and translate them to the individual thus decreasing their appropriateness.
- Cardiac patient exposure to SARS CoV-2 virus and the superadded cardiovascular effects of chronic disease also constitute a different approach in research on a viral infectious disease that has generated a pandemic

10.2 FUTURE RESEARCH DIRECTIONS

- The study of known cardiovascular risk factors can be a starting point for the development of effective public prevention policies, since in this disease, once the disease is established, exposure to risk factors does not cease.
- The study can be continued either by following the same patients over time or by including new patients in the study to make it nationally representative.
Data processing can be continued so that we can make specific associations of risk factors, which through targeted actions can be minimized
- Covid-19 pathology research on the patient with cardiovascular disease can be a starting point for further research to clarify the importance of this risk factor and its impact on subjects affected by cardiac pathology.

CHAPTER 11. EXPLOITATION OF RESEARCH RESULTS

The exploitation of the research results was done by

- 3 articles (2 of which in ISI listed journals) published as first author,
- participation in 2 external exchange of experience in centres with tradition in cardiovascular disease prevention (in Italy under the guidance of the national cardiovascular prevention coordinator and in Spain in a national research centre on cardiovascular risk factors)
- participation with 2 posters at international cardiology congresses and author of a paper also at an international cardiology congress
- research reports and dissertations in the doctoral training programme
- elaboration and defence of the doctoral thesis