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Source / Izvornik: **Wiener Klinische Wochenschrift, 2008, 120, 684 - 692**

Journal article, Accepted version
Rad u časopisu, Završna verzija rukopisa prihvaćena za objavljivanje (postprint)

https://doi.org/10.1007/s00508-008-1065-7

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:604883

Differences in risk factors for coronary heart disease in patients from continental and Mediterranean regions of Croatia

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Text word count:	3385 words
Structured abstract word count:	287 words
Number of figures:	1
Number of tables:	5

This study was supported by an unrestricted scientific grant from Merck Sharp & Dohme IDEA, Inc., Croatia.

Abstract

Background. There are few data on differences in exposure to risk factors for coronary heart disease (CHD) in relation to geographic areas, especially areas with large differences in terms of continental and Mediterranean climates. To study these differences in Croatia, we analyzed data from the Treatment and Secondary Prevention of Ischemic Coronary Events in Croatia V (TASPIC-CRO V) study, which recruited Croatian CHD patients in two principal regions (Mediterranean and continental) of the country.

Methods. A total of 31 Croatian research centers participated in the study. We collected information on personal details, demographic characteristics and risk factor exposure from the hospital medical records of 3054 CHD patients. Risk factors included history of cigarette smoking, hypertension, hyperlipidemia (total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol) and diabetes type II.

Results. Both univariate and multivariate analyses showed that the prevalence of hypertension in examined CHD patients was significantly higher in the continental part of Croatia than in the Mediterranean part (univariate analysis: P <0.001; multivariate analysis: P=0.003). Multivariate analysis revealed a higher prevalence of decreased HDL-cholesterol in continental Croatia (P=0.006) and a higher prevalence of smokers in coastal Mediterranean Croatia (P=0.007). A significant difference in total cholesterol levels was noted between hospitalized CHD patients in two Mediterranean subregions (P<0.001). No significant differences between continental and coastal Mediterranean parts of Croatia were found for other CHD risk factors.

Conclusions. Higher prevalences of both hypertension and decreased HDL-cholesterol were recorded in hospitalized CHD patients in the continental part of Croatia, but in coastal Mediterranean Croatia there was higher prevalence of smokers. Differences in total cholesterol, LDL-cholesterol and triglycerides between hospitalized CHD patients in

continental and coastal Mediterranean Croatia did not follow the expected continental–Mediterranean pattern.

Key words: coronary heart disease, cardiovascular risk factors, diet, Mediterranean life style, hypertension, cholesterol

Introduction

Recent data for Croatia show that cardiovascular diseases caused 52.8% of all deaths in 2003 [1]. This classifies Croatia among the European countries with very high rates of mortality from cardiovascular disease [2]. Risk factors for ischemic heart disease, the most frequent form of cardiovascular disease, are widely recognized: they include lifestyle, habits, diet, environment, and genetic and other factors [3–5].

Studies conducted more than four decades ago showed that Mediterranean countries have lower mortality from cardiovascular diseases than continental countries [4]. The observed differences were explained by the lifestyles and diet in Mediterranean regions in comparison with other European regions [4, 6–17].

However, in more recent literature, the true extent of the effect of Mediterranean lifestyle and diet on the development of cardiovascular disease is more controversial. Most of the studies have shown that regional and lifestyle differences can have dramatic effects on development of cardiovascular disease [6–9, 18] and, in particular, the beneficial effects of a Mediterranean diet rich in vegetables, olive oil and fish, as well as the lifestyle, are especially highlighted [10–17, 19–21]; other authors, however, dispute these findings [22].

Croatia's history, climate and geographical shape provide an excellent example of a country with significant differences between its continental and Mediterranean parts, thus presenting a unique opportunity to study differences in the population, particularly at the subregion level.

This report explores differences in exposure to risk factors for coronary heart disease (CHD) in two principal regions of Croatia, continental and Mediterranean, by analyzing data from a study of CHD patients —the Treatment and Secondary Prevention of Ischemic Coronary Events in Croatia V (TASPIC-CRO V) study. The aim of our analysis was to resolve some of the controversies related to differences between Mediterranean and other parts of Europe in mortality rates for ischemic heart disease.

Materials and methods

A total of 31 research centers (7 university hospitals, 24 general hospitals) spanning the entire geographical area of Croatia took part in the TASPIC-CRO V study. Investigators in the research centers were asked to report consecutive patients of both sexes with the following diagnoses: acute myocardial infarction (Q and non-Q), angina pectoris (stable and non-stable) and post-infarction angina pectoris (stable and non-stable). Sources of data were diagnostic registers, patients' records, hospital discharge lists and other medical documents. The criteria for diagnosis and procedures were similar to those described in EUROASPIRE II [23] and TASPIC-CRO I-V [24].

Using the above criteria, we analyzed data from 3054 patients in TASPIC-CRO V who were consecutively hospitalized between September 30th 2002 and March 31st 2003. A modification to the EUROASPIRE methodology was used, permitting recruitment of patients over the age of 70. We divided the research centers into two main categories: continental (4 university hospitals, 19 general hospitals) and coastal Mediterranean (3 university hospitals, 5 general hospitals); these were further divided into traditional geographic regions: City of Zagreb, Central Croatia, Northern Croatia and Slavonia as parts of continental Croatia and Primorje/Istria and Dalmatia as parts of coastal Mediterranean Croatia (Fig. 1).

The data were collected from the patients' hospital medical records for any time prior to the date of acute hospital admission or procedure, and at the discharge. Data included personal and demographic details, together with risk factors: history of cigarette smoking, hypertension, hyperlipidemia (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol) and diabetes type II [3–5]. All the equipment used was standardized for use in daily clinical work with patients, with certificates from the State Office for Metrology; all laboratories in Croatia have certificates of quality issued by the Ministry of Health, thus ensuring standardized measuring of biochemical variables. All blood samples were fasting

and drawn during first 24 hours of admission to the hospital. The research centers recorded risk factors in uniform predefined ways, with criteria valid in 2003 according to the guidelines in use in everyday clinical practice at that time. Hypertension was defined as all values of RR ≥140 mmHg systolic and ≥90 mmHg diastolic. Total cholesterol >5.00 mmol/l and LDL-cholesterol >3.00 mmol/l (Friedewald equation) were considered elevated, HDL-cholesterol <1.00 mmol/l was considered lowered and triglycerides >2.00 mmol/l were considered elevated. Diabetes was diagnosed if the fasting plasma glucose level was ≥7.0 mmol/l, or ≥11.1 mmol/l at any other time.

Statistical analysis

Statistical methods used in this analysis were cross-tabulations of 2x2 contingency tables analyzed using Fisher's exact test. For higher order contingency tables, the χ^2 test with the Monte Carlo test of statistical significance was used. Binary logistic regression analysis was used to produce unadjusted and adjusted odds ratios, which indicated the likelihood of living in the coastal Mediterranean region for respondents with certain characteristics relative to the reference group (those living in the continental region). P levels of 0.05 or less were accepted as statistically significant.

Informed consent was obtained from every patient and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Results

A total of 3054 patients were recruited: 1969 (64.5%) in the continental region of Croatia and 1085 (35.5%) in the coastal Mediterranean region (Table 1). The mean age was 64.2±11.3 years (range 23–102). Analysis of relation of age to sex showed that 63.9% of the patients were men (mean age 61.7±11.2 years) and 36.1% women (mean age 68.5±10.1 years), the

difference being significant (P <0.001). The difference in mean age of patients in the continental and Mediterranean parts was not significant (P=0.387).

Analysis of diagnoses by region (continental and coastal) showed more Q-wave myocardial infarctions in the coastal region than in the continental region, but this reached only borderline significance (41.1% and 37.5%, P=0.052). Unstable angina and stable post-infarction angina were significantly more frequent in the continental region than in the coastal region (16.2% and 12.4%, P=0.007; 6.0% and 3.7%, P=0.006).

Regional and subregional distribution of risk factors were analyzed (Table 2). Regional differences showed significantly more hypertension in the continental region (72.4% and 62.1%, P <0.001) and also a borderline significance of lower HDL-cholesterol values (37.9% and 33.8%, P=0.071). At the subregion level, there were significant differences in frequency of elevated total cholesterol (53.4% of patients in Primorje/Istria; 79.5% in Slavonia, P <0.001), elevated LDL-cholesterol (54.7% of patients in Primorje/Istria; 79.7% in Slavonia, P <0.001), elevated triglycerides (28.8% of patients in Primorje/Istria; 43.1% in Dalmatia, P <0.001) and **presence of hypertension (61.8% of patients in Primorje/Istria; 79.1% in Central Croatia, P <0.001).**

In analysis by traditional region (Table 2), prevalences of diabetes (ranging from 29.2% in Slavonia to 34.5% in Central Croatia) and smoking (ranging from 29.8% in the City of Zagreb to 36.4% in Northern Croatia) did not show any significant differences (P=0.385 and P=0.133). There was significant difference in prevalence of hypertension (P<0.001) in hospitalized CHD patients, with Slavonia (61.9%), Primorje/Istria (61.8%) and Dalmatia (62.5%) having the lowest prevalence, and Central Croatia (79.1%) having the highest.

Table 3 shows mean values for four risk factors (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides), comparing regional and subregional differences.

Total cholesterol levels were highest in Slavonia (average 6.08±1.37 mmol/l), Dalmatia (5.95±1.33 mmol/l), Central Croatia (5.78±1.36 mmol/l), the City of Zagreb (5.58±1.41 mmol/l) and Northern Croatia (5.56±1.31 mmol/l) and lowest in Primorje/Istria (5.28±1.25 mmol/l), with these differences being statistically significant (P <0.001). Pairwise comparisons of total cholesterol by region (with Bonferroni correction), showed that levels in the City of Zagreb were significantly lower than in Dalmatia (P <0.001) but significantly higher than in Primorje/Istria (P=0.002), levels in Central Croatia were significantly higher than in Primorje/Istria (P <0.001), levels in Northern Croatia were significantly lower than in Dalmatia (P <0.001) but significantly higher than in Primorje/Istria (P=0.003), and levels in Slavonia were significantly higher than in Primorje/Istria (P <0.001).

LDL-cholesterol levels were highest in Slavonia (4.10±2.49 mmol/l), Dalmatia (3.82±1.21 mmol/l), Central Croatia (3.80±2.41 mmol/l), City of Zagreb (3.65±2.71 mmol/l), Northern Croatia (3.63±1.17 mmol/l) and lowest in Primorje/Istria (3.28±0.95 mmol/l), with these differences being statistically significant (P <0.001). Pairwise comparisons of LDL-cholesterol by region (with Bonferroni correction) showed that levels were borderline significantly higher in Central Croatia than in Primorje/Istria (P=0.067) and levels in Slavonia were significantly higher than in Primorje/Istria (P <0.001).

HDL-cholesterol levels were lowest in Primorje/Istria (1.09±0.58 mmol/l), Central Croatia (1.17±0.36 mmol/l), City of Zagreb (1.17±0.53 mmol/l), Northern Croatia (1.18±0.49 mmol/l), Dalmatia (1.21±0.35 mmol/l) and highest in Slavonia (1.25±0.42 mmol/l), with these differences being statistically significant (P=0.008). Pairwise comparisons of HDL-cholesterol by region (with Bonferroni correction) showed that levels were significantly lower in Primorje/Istria than in Slavonia (P=0.005).

Trigycerides levels by region were highest in Dalmatia (2.16±1.65 mmol/l), Central Croatia (2.15±1.44 mmol/l), City of Zagreb (2.09±1.64 mmol/l), Slavonia (2.06±1.24 mmol/l), Primorje/Istria (1.90±1.32 mmol/l) and lowest in Northern Croatia (1.83±1.30 mmol/l), with

these differences being statistically significant ($P<0.001$). Pairwise comparisons of triglycerides by region (with Bonferroni correction) showed that levels were significantly lower in Northern Croatia than in Dalmatia ($P<0.001$).

As shown in Table 4, decreased HDL-cholesterol, hypertension, smoking and the patient's sex are risk factors that significantly change the odds for patients to live in the coastal region. Thus, patients with hypertension have 27% smaller odds for living in coastal Croatia (OR 0.73, CI 0.59–0.89, $P=0.003$) than non-hypertensive patients; patients with decreased HDL-cholesterol have 26% smaller odds (OR 0.74, CI=0.60–0.92, $P=0.006$) than patients with normal HDL-cholesterol; patients who smoke have 33% higher odds (OR 1.33, CI=1.08–1.64, $P=0.007$) than non-smokers; and female CHD patients have 25% smaller odds (OR 0.75, CI=0.60–0.93, $P=0.009$) than male CHD patients.

Discussion

The TASPIC-CRO V study, which recruited and investigated hospitalized CHD patients, showed that the prevalences of most cardiovascular risk factors do not differ between the continental and Mediterranean areas of Croatia. Using simple univariate analysis we showed that in TASPIC-CRO V the only significant difference between these two parts of Croatia was the higher prevalence of hypertension in the continental part. In addition, the use of multivariate analysis showed that patients with hypertension have 27% smaller odds for living in costal-Mediterranean Croatia.

As Croatia's continental part could be considered as "north" and its coastal-Mediterranean part "south", it is interesting to compare our results with those of a similar study published in 1998 by Park et al [9]. They investigated geographic differences in the characteristics of coronary artery disease in India and found a lower frequency of unstable angina in the south (coastal part) of India (the opposite from what we observed) and a higher prevalence of hypertension in northern (continental) India (which is in accordance with our results).

It is well known that morbidity and mortality from cardiovascular diseases are much lower in the countries of the Mediterranean region than in continental parts of Europe [25]. Cardiovascular mortality rates (both male and female) in Croatia seem to show a similar pattern in 2003: these were highest for Northern Croatia and Slavonia (continental part), and lowest for Dalmatia and Primorje/Istria (Mediterranean part), with rates for Central Croatia and City of Zagreb lying in between [1].

The majority of the literature, corroborated by general public consensus, claims that the reasons for lower rates of ischemic heart disease and cardiovascular disease mortality in Mediterranean regions in relation to other parts of Europe lie in different prevalences and incidences of risk factors for those diseases and different lifestyles and habits [4, 13, 15].

In our study, analysis of the prevalence of elevated total cholesterol levels in hospitalized CHD patients in traditional geographic regions of Croatia showed the lowest prevalence in the coastal subregion Primorje/Istria (53.4%). This could be expected if one assumes that coastal parts of Croatia are characterized by Mediterranean diet. However, the difference between the two coastal subregions Primorje/Istria and Dalmatia in patients' total cholesterol levels was found to be significant, with higher levels measured in Dalmatia ($P < 0.001$). The reason for the difference between these two Mediterranean parts of Croatia remains unclear.

Based on currently available research data, three possible explanations for the observed differences in cardiovascular risk factors in hospitalized CHD patients can be offered. One is based upon the effects of war (1991–1995) and postwar stress in Croatia on acute and chronic CHD [26, 27], and the influence of war and the post-war period on the changes throughout the country of traditional lifestyles of people who developed CHD. The second explanation could be the extensive migrations of the population during the war and the post-war period; these caused dramatic differences in the habits, diets and lifestyles of the migrated populations compared with the traditional lifestyles in each region [28]. If this is the case, exposure to stress, social deprivation and unhealthy lifestyles might have overcome any possible

protective effects of the Mediterranean diet and lifestyle in patients affected with CHD. The third explanation could be that for some reason the diet has changed in at least one of these two traditional Croatian geographic regions; for example, a trend toward consumption of 'fast food' and an increase in consumption of animal fat from dairy products [29, 30]. In this context it is also interesting to note that multivariate analysis showed that patients with decreased HDL-cholesterol have 26% smaller odds for living in coastal-Mediterranean Croatia, but at the same time patients who smoke have 33% higher odds. Although the odds for decreased HDL-cholesterol could be explained by Mediterranean diet (although it is not clear why this beneficial effect is not observed in other lipid variables investigated), it is difficult to explain why patients who smoke have higher odds of living in coastal Croatia. The common characteristic of all the mentioned confounding factors is that currently there are insufficient data to allow exact quantification of the influence of each one on cardiovascular risk factors. Research projects currently underway in Croatia offer hope that quantification for some of the confounding factors will soon be possible.

Analysis of mean levels of total cholesterol in hospitalized CHD patients in traditional geographic regions showed that mean levels were lowest in Primorje/Istria (5.28±1.25 mmol/l) and highest in Slavonia (6.08±1.37 mmol/l), but nevertheless above an acceptable 5.0 mmol/l everywhere. This was not a completely unexpected finding, because this survey examined a population of hospitalized CHD patients who would be expected to have one or more cardiovascular risk factors. However, the fact that there are such profound differences between traditional geographic regions in prevalence and occurrence of cardiovascular risk factors requires further analysis.

The prevalence of elevated LDL-cholesterol in hospitalized CHD patients in different traditional regions followed the same pattern as that for total cholesterol, again with the lowest mean levels of LDL-cholesterol (Primorje/Istria, 3.28±0.95 mmol/l) being above acceptable levels.

Analysis of the prevalence of decreased HDL-cholesterol in hospitalized CHD patients showed a somewhat different pattern: the highest prevalence was in Northern Croatia (39.3%) and the lowest in Dalmatia (32.2%). But when we analyzed the mean levels of HDL-cholesterol, a pattern identical to those described for mean levels of total cholesterol and LDL-cholesterol was found: the lowest mean levels of HDL-cholesterol were measured in Primorje/Istria (1.09±0.58 mmol/l) and the highest in Slavonia (1.25±0.42 mmol/l). Multivariate analysis showed a higher prevalence of decreased HDL-cholesterol in continental Croatia than in coastal-Mediterranean Croatia (P=0.006).

The inconsistency became even greater when we analyzed the prevalence of elevated triglycerides in hospitalized CHD patients in traditional regions: the lowest prevalence was in Primorje/Istria (28.8%) and the highest in Dalmatia (43.1%), both coastal regions with Mediterranean diet. Only two traditional regions showed mean levels of triglycerides that were not elevated: Northern Croatia (1.83±1.30 mmol/l) and Primorje/Istria (1.90±1.32 mmol/l). The highest mean level of triglycerides was in the Mediterranean region of Dalmatia (2.16±1.65 mmol/l), a significant difference in comparison with Primorje/Istria (P=0.045).

Since these differences are not in line with “a priori” expectations, a question should be asked: are any beneficial effects of a Mediterranean lifestyle really observed in Croatia? If not, is it because the diet habits have changed? Apparently, this cannot be answered as there are no firm data to provide any information that would enable us to draw a conclusion.

Regardless of the diet issues, the prevalence of risk factors for CHD is extremely high in Croatia [1, 30]. This will not lead to favorable trends in prevalence and future incidence of CHD unless action is taken to reduce those risks, which includes not just effective treatment of CHD patients but also effective prevention [31]. Furthermore, although there are differences between regions, they are concentrated in traditional geographic regions (subregions), and in most cases do not follow the expected continental-Mediterranean pattern. Also, in most cases there seem to be no clear beneficial effects of the Mediterranean diet; it

appears that there are no consistent differences between the continental and Mediterranean parts of Croatia in cardiovascular risk factors in the studied CHD population.

Although in our study there were no data on education level and habitation status of the patients (native/immigrants), an interesting example from Austria shows the need for intensifying the care of less well educated people and people of non-national origin concerning prevention of CHD risk factors, which were higher in those groups [32].

We also compared our data on prevalence of risk factors in CHD patients with data from the First Croatian Health project, conducted on the general population almost 10 years ago (Table 5). Results from that project found no significant differences between continental and coastal-Mediterranean parts of Croatia concerning the majority of risk factors for cardiovascular diseases (smoking, hypertension, total and LDL-cholesterol, triglycerides) [29]. The most unexpected difference between the two studies was the lower level of total cholesterol in the CHD patients compared with the general population; however, taking into account the time difference between the two studies, the explanation may be that standards of living and healthcare have increased in the meanwhile and may be expected to result in lower total cholesterol levels. Nevertheless, this does not explain another observed difference – that CHD patients have higher triglyceride levels. Other differences in comparison with the general population include, as expected, a higher prevalence of hypertension in CHD patients and a higher rate of smoking in male patients, but also, surprisingly, a lower rate of smoking in female CHD patients.

In the context of these differences, one should bear in mind that for several reasons it is very difficult to compare these two surveyed populations, and Table 5 is presented to show approximate comparisons only for the purpose of giving a clearer picture of the available data on this topic in Croatia. One of the main difficulties is that, although there have been many recent studies in Croatia, at present there are no universally accepted results on the exact prevalence of risk factors. There is only a general public consensus that the prevalence of

these factors is high, indicating a strong need for an evidence-based survey that would yield objective and universally acceptable results. In that respect, an application for a scientific grant has been successfully submitted to the Croatian Ministry of Science, Education and Sports to support a program of projects investigating these risk factors in several types of population: general, adolescents, hospitalized CHD patients, families of killed war soldiers, and patients who already have risk factors but have not developed CHD symptoms.

Acknowledgements

TASPIC-CRO coordinator: Professor Šime Mihatov, MD, PhD

TASPIC-CRO investigators: Marija Agostini, Zagreb; Vladimir Ambrož, Pakrac; Debora Anić Kasuto, Krapinske Toplice; Zdravko Babić, Zagreb; Franjo Baborski, Krapinske Toplice; Anica Badanjak, Popovača; Željka Bakliža, Koprivnica; Ljiljana Banfić, Zagreb; Armida Barbić Bonassin, Pula; Mijo Bergovec, Zagreb; Branko Bilić, Sisak; Stanko Biočić, Zagreb; Mirko Blašković, Ogulin; Ivo Božić, Split; Vojtjeh Brida, Zagreb; Irena Bruketa, Opatija; Antun Car, Dubrovnik; Duško Cerovec, Krapinske Toplice; Nedeljko Ciglenečki, Krapinske Toplice; Dalibor Cukon, Pula; Dubravka Čaržavec, Zabok; Katja Čatipović, Osijek; Zlatko Čubranić, Rijeka; Ćepić Nedjeljko, Nova Gradiška; Dijana Delić Brkljačić, Zagreb; Željka Diklić, Rijeka; Dubravko Dobrović, Rijeka; Nikša Drinković, Zagreb; Dražen Duplančić, Split; Vesna Emih-Pajalić, Opatija; Damir Fabijanić, Split; Jasna Fabijanić, Opatija; Milica Gabor, Čakovec; Darko Gabrić, Zagreb; Duška Glavaš, Split; Mladen Gostović, Zagreb; Janko Grman, Karlovac; Robert Grubišić-Čabo, Šibenik; Mirela Gunjević-Delišimunović, Pakrac; Marina Halapir, Krapinske Toplice; Josip Halle, Zagreb; Davor Horvat, Karlovac; Nevenka Horvat, Zagreb; Bachir Hoteit, Duga Resa; Rudolf Hranilović, Čakovec; Neven Ištvanović, Krapinske Toplice; Suzy Ivančić-Vagaja, Opatija; Mario Ivanuša, Bjelovar; Hrvoje Iveković, Zagreb; Marijan Jakić, Osijek; Damir Japundžić, Nova Gradiška; Ivan Jelić, Sisak; Jasna Jelić, Knin; Vesna Jelić, Karlovac; Mirjana Jembrek Gostović, Zagreb; Melita Jerić, Varaždin; Vladimir Jonke, Zagreb; Nediljko Jukić, Pula; Mario Jurin, Šibenik; Silvija Juzbašić, Vinkovci; Aleksandar Knežević, Zadar; Marijana Knežević-Praveček, Slavonski Brod; Slavica Kojundžić, Šibenik; Mladen Komadina, Zagreb; Branko Krajinović, Popovača; Dragica Kramarić, Koprivnica; Stjepan Kranjčević, Zagreb; Goran Krstačić, Zagreb; Željko Kupanovac, Rijeka; Ante Kuzmanić, Split; Maja Lopac, Zagreb; Martina Lovrić Benčić, Zagreb; Petar Lozo, Split; Josip Lukenda, Zagreb; Tanja Lukenda, Zagreb; Ajvor Lukin, Split; Ksenija Lukin Eškinja, Opatija; Mladen Makitan,

Varaždin; Eduard Margetić, Zagreb; Andreja Marić, Čakovec; Marina Marin, Vinkovci; Branimir Marković, Split; Richard Matasić, Zagreb; Ivanka Mihajlović, Vukovar; Bernarda Mihaliček Rubeš, Krapinske Toplice; Krešimir Milas, Pula; Davor Miličić, Zagreb; Jure Mirat, Zagreb; Dinko Mirić, Split; Rajko Miškulin, Rijeka; Marija Mlinarić, Vukovar; Berislav Mostovac, Virovitica; Katarina Novak, Split; Ljerka Nuić, Popovača; Branko Ostrički, Čakovec; Marjan Padovan, Rijeka; Vesna Pehar-Pejčinović, Požega; Ružica Perković-Avelini, Split; Ksenija Pešek, Zabok; Ruža Petras, Sisak; Davorin Pezerović, Vinkovci; Karmela Piljak-Altabas, Zagreb; Hrvoje Pintarić, Zagreb; Miroslav Plažanin, Našice; Ljiljana Pleskalt, Bjelovar; Darko Počanić, Zagreb; Željko Popović, Virovitica; Marija Puharić-Harašlić, Opatija; Davor Puljević, Zagreb; Krešimir Putarek, Zagreb; Miroslav Raguž, Zagreb; Drago Rakić, Split; Tahir Ramqaj, Krapinske Toplice; Vjekoslava Raos, Zagreb; Ile Raštegorac, Požega; Davor Richter, Zagreb; Josip Rubes, Krapinske Toplice; Ljerka Rukavina-Prpić, Opatija; Pejo Samardžić, Slavonski Brod; Bosiljka Siuc-Paro, Rijeka; Boško Skorić, Zagreb; Dragan Slunjski, Varaždin; Ivan Sokol, Zagreb; Dražen Šebetić, Bjelovar; Jadranka Šeparović Hanževački, Zagreb; Aljoša Šikić, Zadar; Anton Šmalcelj, Zagreb; Krešimir Štambuk, Zagreb; Zorislav Šušak, Biograd; Krešimir Šutalo, Koprivnica; Dragan Trivanović, Pula; Dubravko Tršinski, Varaždin; Ljudevit Ulaković, Zabok; Roman Urek, Zagreb; Krešimir Vidović, Popovača; Josip Vincelj, Dubrava; Slobodanka Vučković-Rapaić, Opatija; Marija Vujičić, Split; Đuro Vukosavić, Zagreb; Tea Zaninović Jurjević, Rijeka; Luka Zaputović, Rijeka; Josip Zorko, Ogulin; Davorka Žagar, Rijeka.

This study was supported by an unrestricted scientific grant from Merck Sharp & Dohme IDEA Inc., Croatia. We thank Mr. Žarko Bajić from Biometrika Healthcare Research for his technical help and statistical analysis of the survey data.

References

1. Croatian National Institute of Public Health (2004) Croatian Health Service Yearbook. Croatian National Institute of Public Health, Zagreb, p. 7, 66–68
2. World Health Organization (2003) The World Health Report 2003 – Shaping the Future. World Health Organization, Geneva
3. Kannel WB, Dawber TR, Kagan A, Revotskie N, Stokes J (1961) Factors of risk in the development of coronary heart disease — six-year follow up experience: The Framingham study. Ann Intern Med 55: 33–50
4. Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, et al (1986) The diet and 15-year death rate in the seven countries study. Am J Epid 124: 903–915
5. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al (2004) Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 364: 937–952
6. Iestra JA, Kromhout D, van der Schouw YT, Grobbee DE, Boshuizen HC, van Staveren WA (2005) Effect size estimates of lifestyle and dietary changes on all-cause mortality in coronary artery disease patients: a systematic review. Circulation 112: 924–934
7. Tucker KL, Hallfrisch J, Qiao N, Muller D, Andres R, Fleg JL (2005) Baltimore Longitudinal Study of Aging. The combination of high fruit and vegetable and low saturated fat intakes is more protective against mortality in aging men than is either alone: the Baltimore Longitudinal Study of Aging. J Nutr 135: 556–561
8. Dauchet L, Ferrières J, Arveiler D, Yarnell JW, Gey F, Ducimetière P, et al (2004) Frequency of fruit and vegetable consumption and coronary heart disease in France and Northern Ireland: the PRIME study. Br J Nutr 92: 963–972
9. Park D, Desai P, Aiyengar J, Balladur A (1998) Geographic differences in the characteristics of coronary artery disease in India. Int J Cardiol 67: 187–189

10. Trichopoulou A, Bamia C, Trichopoulos D (2005) Mediterranean diet and survival among patients with coronary heart disease in Greece. Arch Intern Med 165: 929–935
11. Fidanza F, Alberti A, Lanti M, Menotti A (2004) Mediterranean diet score: correlation with 25-year mortality from coronary heart disease in the Seven Countries Study. Nutr Metab Cardiovasc Dis 14: 397
12. Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, et al (2004) Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA 292: 1433–1439
13. Panagiotakos DB, Pitsavos C, Polychronopoulos E, Chrysohoou C, Zampelas A, Trichopoulou A (2004) Can a Mediterranean diet moderate the development and clinical progression of coronary heart disease? A systematic review. Med Sci Monit 10: RA193–198
14. Leonhauser IU, Dorandt S, Willmund E, Honsel J (2004) The benefit of the Mediterranean diet — considerations to modify German food patterns. Eur J Nutr 43 Suppl 1: I/31–38
15. Kok FJ, Kromhout D (2004) Atherosclerosis—epidemiological studies on the health effects of a Mediterranean diet. Eur J Nutr 43 Suppl 1: I/2–5
16. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D (2003) Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med 348: 2599–2608
17. Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C, Toutouzas P (2002) Primary prevention of acute coronary events through the adoption of a Mediterranean-style diet. East Mediterr Health J 8: 593–602
18. Menon V, Rumsfeld JS, Roe MT, Cohen MG, Peterson ED, Brindis RG, et al (2006) Regional outcomes after admission for high-risk non-ST-segment elevation acute coronary syndromes. Am J Med 119: 584–590

19. Pitsavos C, Panagiotakos DB, Chrysohoou C, Skoumas J, Papaioannou I, Stefanadis C, et al (2002) The effect of Mediterranean diet on the risk of the development of acute coronary syndromes in hypercholesterolemic people: a case-control study (CARDIO2000). Coron Artery Dis 13: 295–300
20. Pitsavos C, Panagiotakos DB, Chrysohoou C, Kokkinos PF, Skoumas J, Papaioannou I, et al (2002) The effect of the combination of Mediterranean diet and leisure time physical activity on the risk of developing acute coronary syndromes, in hypertensive subjects. J Hum Hypertens 16: 517–524
21. Giugliano D, Esposito K (2008) Mediterranean diet and metabolic diseases. Curr Opin Lipidol 19: 63–68
22. Gillum RF, Mussolino M, Madans JH (2000) The relation between fish consumption, death from all causes, and incidence of coronary heart disease. The NHANES I Epidemiologic Follow-up Study. J Clin Epidemiol 53: 237–244
23. EUROASPIRE II Group (2001) Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries: Principal results from EUROASPIRE II Euro Heart Survey Programme. Eur Heart J 22: 554–572
24. Reiner Z, Mihatov S, Milicic D, Bergovec M, Planinc D (2006) Treatment and secondary prevention of ischemic coronary events in Croatia. Eur J Cardiovasc Prev Rehabil 13: 646–654
25. Uemura K, Pisa Z (1988) Trends in cardiovascular disease mortality in industrialized countries since 1950. World Health Stat Q 41: 155–178
26. Bergovec M, Mihatov S, Prpic H, Rogan S, Batarelo V, Sjerobabski V (1992) Acute myocardial infarction among civilians in Zagreb city area. Lancet 339: 303
27. Bergovec M, Heim I, Vasilj I, Jembrek-Gostović M, Bergovec M, Strnad M (2005) Acute coronary syndromes and the 1992–1995 War in Bosnia and Herzegovina: a 10-year retrospective study. Mil Med 170: 431–434

28. Babic-Banaszak A, Kovacic L, Kovacevic L, Vuletic G, Mujkic A, Ebling Z (2002) Impact of war on health related quality of life in Croatia: population study. Croat Med J 43: 396–402
29. Turek S, Rudan I, Smolej-Narancic N, Szirovicza L, Cubrilo-Turek M, Zerjavic-Hrabak V, et al (2001) A large cross-sectional study of health attitudes, knowledge, behaviour and risks in the post-war Croatian population (The first Croatian Health Project). Coll Antropol 25: 77–96
30. Reiner Z (2003) Kardiovaskulare Risikofaktoren in Kroatien. In: Schwandt P, Haas GM (eds) Prevention von Herzinfarkt und Schlaganfal. Stiftung zur Pravention der Arterioskleroze, Muenchen, pp 68–70
31. Reiner Z, Tedeschi-Reiner E (2006) Atherosclerosis – a paradox of eastern European countries. Atherosclerosis 7: 461
32. Ulmer H, Diem G, Bischof HP, Ruttmann E, Concin H (2001) Recent trends and sociodemographic distribution of cardiovascular risk factors: results from two population surveys in the Austrian WHO CINDI demonstration area. Wien Klin Wochenschr 113: 573–579

Legend to Figure 1.

Republic of Croatia: surveyed research centers were divided into two principal regions (continental and coastal-Mediterranean) and into traditional geographic regions/subregions (City of Zagreb, Central Croatia, Northern Croatia and Slavonia as parts of continental Croatia; Primorje/Istria and Dalmatia as parts of coastal-Mediterranean Croatia)

Table 1. TASPIC-CRO V* study: distribution of 3054 CHD patients** by sex, mean age and Croatian region

	No. (%) of patients				Mean age ± std. dev. (years)			
	Total	**Male**	**Female**	***P***	**Total**	**Male**	**Female**	***P***
Continental	1969 (64.5)	1136 (61.2)	721 (38.8)	< 0.001	64.2±11.2	61.5±11.0	68.4±10.1	< 0.001
Mediterranean	1085 (35.5)	696 (68.9)	314 (31.1)	<0.001	64.1±11.4	62.1±11.3	68.6±10.1	<0.001
Total	3054 (100)	1832 (63.9)	1035 (36.1)	<0.001	64.2±11.3	61.7±11.2	68.5±10.1	<0.001

*Treatment and Secondary Prevention of Ischemic Coronary Events in Croatia V;

**coronary heart disease patients hospitalized between September 30th 2002 and March 31st 2003

Table 2. TASPIC-CRO V* study: regional and subregional distribution of risk factors of 3054 CHD patients**

No. (%) with risk factors	Continental	Mediterranean	χ^2	df	*P*	City of Zagreb	Central Croatia	Northern Croatia	Slavonia
Elevated total cholesterol (>5.00 mmol/l)	1257 (65.6)	673 (64.7)	0.238	1	0.628	384 (63.2)	242 (67.8)	457 (62.4)	174 (79.5)
Elevated LDL (>3.00 mmol/l)	949 (68.7)	460 (67.6)	0.220	1	0.651	337 (65.1)	118 (68.6)	349 (68.4)	145 (79.7)
Decreased HDL (<1.00 mmol/l)	579 (37.9)	235 (33.8)	3.386	1	0.071	218 (39.2)	59 (33.9)	241 (39.3)	61 (33.0)
Elevated triglycerides (>2.00 mmol/l)	693 (36.2)	370 (35.9)	0.037	1	0.872	244 (40.3)	132 (37.1)	229 (31.3)	88 (40.2)
Diabetes	602 (30.6)	324 (29.9)	0.168	1	0.711	187 (29.8)	127 (34.5)	222 (29.7)	66 (29.2)
Hypertension	1425 (72.4)	674 (62.1)	34.209	1	<0.001	434 (69.1)	291 (79.1)	560 (75.0)	140 (61.9)
Smoking	657 (33.4)	381 (35.1)	0.953	1	0.338	187 (29.8)	127 (34.5)	272 (36.4)	71 (31.4)

*Treatment and Secondary Prevention of Ischemic Coronary Events in Croatia V; **coronary heart disease patients hospitalized between September 30th 2002 and March 31st 2003

Table 3. TASPIC-CRO V* study: regional and subregional mean values of risk factors of 3054 CHD patients**

Mean values of risk factors (in mmol/l) ± std. dev.	**Continental**	**Mediterranean**	***P***	**City of Zagreb**	**Central Croatia**	**Northern Croatia**	**Slavonia**	**Primorje and Istria**	**I**
Total cholesterol	5.67±1.37	5.61±1.33	0.309	5.58±1.41	5.78±1.36	5.56±1.31	6.08±1.37	5.28±1.25	5
P	/	/	/	<0.001 =0.002	<0.001	<0.001 =0.003	<0.001	=0.002 <0.001 =0.003 <0.001	<
LDL-cholesterol	3.72±2.19	3.61±1.14	0.227	3.65±2.71	3.80±2.41	3.63±1.17	4.10±2.49	3.28±0.95	3
P	/	/	/		=0.067		<0.001	=0.067 <0.001	
HDL-cholesterol	1.18±0.49	1.17±0.46	0.376	1.17±0.53	1.17±0.36	1.18±0.49	1.25±0.42	1.09±0.58	1
P	/	/	/				=0.005	=0.005	
Triglycerides	2.00±1.44	2.03±1.50	0.579	2.09±1.64	2.15±1.44	1.83±1.30	2.06±1.24	1.90±1.32	2
P						<0.001			<

*Treatment and Secondary Prevention of Ischemic Coronary Events in Croatia V; ** coronary heart disease patients hospitalized between September 30th 2002 and March 31st 2003

Table 4. TASPIC-CRO V* study: binary logistic regression (univariate and multivariate, adjusted solution) for CVD risk factors by geographic region

		Region			
		N (%)		OR (95% CI**) p†	
		Continental	Coastal	Univariate analysis	Multivariate analysis
Elevated total cholesterol (>5.00 mmol/l)	No	771 (40.2)	423 (40.7)	1	1
	Yes	1145 (59.8)	617 (59.3)	0.98 (0.84-1.14) 0.819	0.90(0.68- 1.20) 0.484
	Total	1916 (100.0)	1040 (100.0)		
Elevated LDL (>3.00 mmol/l)	No	433 (31.3)	220 (33.7)	1	1
	Yes	949 (68.7)	460 (32.6)	0.95 (0.78-1.16) 0.639	0.96 (0.72-1.29) 0.796
	Total	1382 (100.0)	680 (100.0)		
Decreased HDL (<1.00 mmol/l)	No	950 (62.1)	460 (66.2)	1	1
	Yes	579 (39.7)	235 (33.8)	0.84 (0.69-1.01) 0.066	0.74 (0.60-0.92) 0.006
	Total	1529 (100.0)	695 (100.0)		
Elevated triglycerides (>2.00 mmol/l)	No	1219 (63.8)	661 (64.1)	1	1
	Yes	693 (36.2)	370 (35.9)	0.99 (0.84-1.15) 0.847	1.01 (0.81-1.25) 0.943
	Total	1912 (100.0)	1031 (100.0)		
Diabetes	No	1367 (69.4)	761 (70.1)	1	1
	Yes	602 (30.6)	324 (29.9)	1.16 (0.94-1.44) 0.161	1.86 (0.69-1.06) 0.161
	Total	1969 (100.0)	1085 (100.0)		
Hypertension	No	544 (27.6)	411 (37.9)	1	1
	Yes	1425 (72.4)	674 (62.1)	0.63 (0.54-0.73) 0.000	0.73 (0.59-0.89) 0.003
	Total	1969 (100.0)	1085 (100.0)		
Smoking	No	1312 (66.6)	704 (64.9)	1	1
	Yes	657 (33.4)	381 (35.1)	1.08 (0.92-1.26) 0.329	1.33 (1.08-1.64) 0.007
	Total	1969 (100.0)	1085 (100.0)		
Sex	Male	1136 (61.2)	696 (68.9)	1	1

	Female	721	(38.8)	314	(36.1)	0.71 (0.60-0.84) 0.000	0.75 (0.60-0.93) 0.009
	Total	1857	(100.0)	1010	(100.0)		

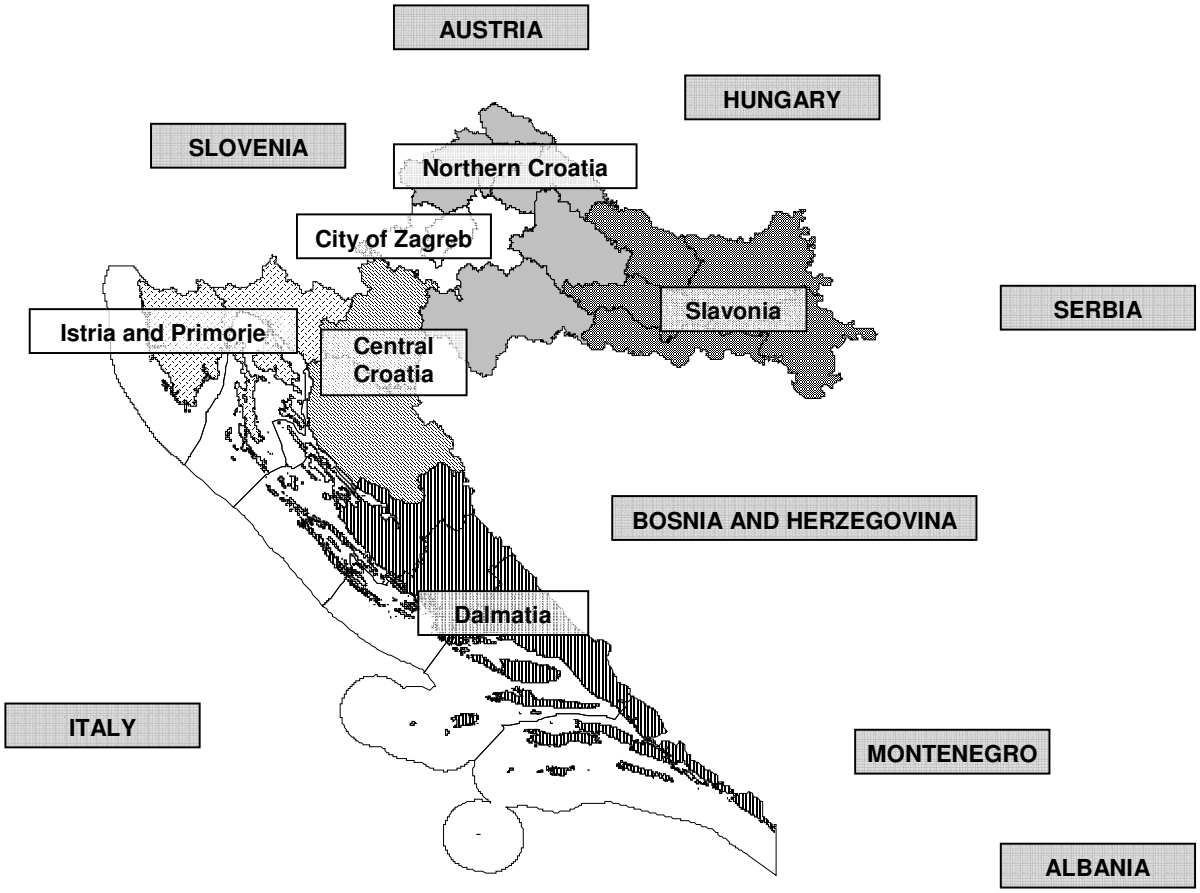
*Treatment and Secondary Prevention of Ischemic Coronary events in Croatia V; CVD coronary vascular disease; **Odds ratio 95% confidence interval; † OR = odds ratio; first category of each independent variable was the referent; continental region was the reference category of dependent variable

Table 5. Comparison of data on prevalence of CHD* risk factors in the Croatian general population [29] and the Croatian CHD population (3054 patients**)

	First Croatian Health Project [29] (1995–1997) General population	**TASPIC-CRO V*** (2002–2003) CHD patient population**
Total cholesterol (mmol/l)	5.74±1.33	5.65±1.35
LDL-cholesterol (mmol/l)	3.76±1.18	3.68±1.91
HDL-cholesterol (mmol/l)	1.18±0.37	1.18±0.48
Triglycerides (mmol/l)	1.76±1.41	2.01±1.46
Diabetes (%)	no data	30.3
Hypertension (%)	27.7	68.7
Smoking – males (%)	34.1	44.1
Smoking – females (%)	26.6	17.0

*coronary heart disease; ** hospitalized between September 30th 2002 and March 31st 2003; ***Treatment and Secondary Prevention of Ischemic Coronary Events in Croatia V

Figure 1.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