Risk factor control and adherence to treatment in patients
with coronary heart disease in the Republic of Srpska,
Bosnia and Herzegovina in 2005-2006

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Abstract

Introduction: European treatment guidelines in persons with known coronary heart disease (CHD) focus on adherence to antiplatelet therapy, β-blockers, ACE/ARBs, and lipid-lowering agents, with goals for blood pressure (BP) of < 140/90 mm Hg and LDL cholesterol of < 3.0 mmol/l. Data on adherence to these measures in Eastern Europe are limited.

Material and methods: The Third Republic of Srpska, Bosnia and Herzegovina, Coronary Prevention Study (ROSCOPS III) was conducted in 2005-2006 at 10 primary heath care centres in 601 patients (36% female, mean age 55 years) with CHD including acute myocardial infarction or ischaemia, coronary artery bypass graft, or angioplasty who were examined and interviewed at least 6 months after the event. We examined the proportion of subjects on recommended treatments and at goal for BP, LDL-C, and non-smoking.

Results: The proportion of subjects on recommended treatments included 61% for β-blockers, 79% for ACE/ARBs, 63% for lipid-lowering agents and 74% for antiplatelet therapy. Only 30% of subjects were on all four of these treatments. 59% of subjects had BP at goal of < 140/90 mm Hg and 33% were controlled to < 130/80 mm Hg, 41% for LDL-C, and 88% were non-smokers. Improvements were seen in lipid-lowering and ACE/ARB drug use and non-smoking status from an earlier survey (ROSCOPS II) in 2002-2003.

Conclusions: Our data show, despite improvement over recent years, that many persons with CHD in the Republic of Srpska, Bosnia and Herzegovina are neither on recommended treatments nor at target for BP and/or LDL-C. Improved efforts targeted at both physicians and patients to address these issues are needed.

Key words: treatment, risk factors, coronary heart disease, secondary prevention.
disease mortality rates decreased by 2% in Western countries and increased 6% in the East and parts of Central Europe. In the former Yugoslavia and Republic of Srpska/Bosnia and Herzegovina, after a period of decreased CVD mortality from 1980 to 1990, there have been increases in mortality due to CVD.

Risk factor control and lifestyle changes are the foundation of secondary prevention efforts. Over the past 11 years, guideline panels, including those from the European Society of Cardiology [1], American Heart Association, and American College of Cardiology [2], have developed a series of recommendations for therapy and clinical management of risk factors in persons with CHD. Previous studies have shown that cardiovascular risk factors among CHD patients are poorly controlled [3] and often remain above target levels, despite improvements over recent years [4]. Lifestyle, goal values of risk factors, and therapeutic goals set by recommendations of the Joint European Societies for coronary disease prevention in clinical practice are not achieved by most patients throughout Europe [1, 5]. Many national multicentre studies have shown results similar to those in EUROASPIRE I (1995/96), EUROASPIRE II (1999/2000), and EUROASPIRE III (2006/2007) [3, 6, 7].

Data are lacking regarding the recent status of adherence to recommended treatments and risk factor goal attainment among CHD patients, particularly in Eastern and Southeastern European countries. We assessed the extent of CHD risk factor control, goal attainment, and adherence to recommended treatments in adults of the Republic of Srpska, Bosnia and Herzegovina with known CHD from a recent examination following diagnosis of CHD.

Material and methods

We identified 601 adults (36% female) 18 years and older with known CHD between December 2005 and December 2006 in 10 primary health centres in selected areas of the Republic of Srpska, a state entity comprising 1.4 million people and encompassing the northern part of Bosnia and Herzegovina. General practitioners performed interviews and examinations at least 6 months after the event. Coronary heart disease was verified by medical records based on diagnosis including acute myocardial infarction (ST elevation and non-ST elevation MI) (47%, n = 283), elective or emergency coronary artery bypass graft (CABG) (24%, n = 144), acute myocardial ischaemia but no evidence of infarction (troponin negative) (21%, n = 126) or elective or emergency percutaneous transluminal coronary angioplasty (PTCA) (8%, n = 48). We examined overall goal attainment for blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C), as defined by the European Society of Cardiology Third Joint Task Force of European and other societies on Cardiovascular Disease Prevention in Clinical Practice. Goal attainment included BP below 140/90 mm Hg (although results are also presented according to recently released recommendations for a lower goal of below 130/80 mm Hg) [8], LDL-C less than < 3 mmol/l (115 mg/dl) and non-smoking status. Treatment for β-blockers, renin-angiotensin blockade (ACE/ARBs) medications, antiplatelets, and lipid-lowering agents were identified by visual inspection of medications brought in by subjects or from chart review.

We analysed the attainment of goals and adherence to treatment across gender. We compared treatment patterns and control of BP and LDL-C to ROSCOPS II, a study of similar methodology conducted in 363 patients (21% female, mean age 52 years) among 7 primary health centres in 2002-2003 [9, 10].

Measurements

Blood pressure was measured using a mercury sphygmomanometer and taking the average of two readings from the examination. Total cholesterol and triglycerides were measured enzymatically. How density lipoprotein cholesterol was measured directly in the serum, and LDL-C levels were calculated using the Friedewald formula.

Statistical analysis

The Chi-square test of proportions was used to compare proportions of those on the different treatments or at goal for LDL-C, BP, and non-smoking status across gender, and for each of these measures between ROSCOPS II and ROSCOPS III.

Results

The proportions on recommended treatments for ROSCOPS III were 61% for β-blockers, 79% for ACE/ARBs, 63% for lipid-lowering agents, and 74% for antiplatelet therapy (Table I). Only 30% of subjects were on all four of these treatments. Significantly greater proportions of men were on lipid-lowering and antiplatelet therapy than women. The proportions on recommended treatments for ROSCOPS II were 59% for β-blockers, 53% for ACE/ARBs, 28% for lipid-lowering agents, and 70% for antiplatelet therapy. Only about 9% were on all four recommended treatments (Table I). Overall, treatment rates with lipid-lowering agents (p < 0.01), ACE/ARBs (p < 0.01) and antiplatelets (p < 0.05 in males) as well as for all four recommended treatments (p < 0.01) were greater in ROSCOPS III than in ROSCOPS II. Similar results
were observed when analyses were stratified by gender (Table I).

Overall, in ROSCOPS III the proportion of CHD participants at goal was 59% for BP (33% based on SBP/DBP 130/80 mm Hg goal), 41% for LDL-C, and 88% were not smoking (Table II). Compared to ROSCOPS II, there was similar control for BP (58 vs. 59%) and LDL-C (42 vs. 41%), but the proportion of non-smokers was improved (88 vs. 72%) due to dramatically less smoking in men. There was also better LDL-C control in females ($p < 0.01$) in ROSCOPS II and better BP control in males in ROSCOPS III. While two-thirds to three-fourths of patients were on recommended BP and statin therapies, with recent increases in lipid-lowering medication and ACE/ARB use, 41 and 59% of the population remain inadequately controlled for BP and LDL-C, respectively.

**Discussion**

Our study is unique in being among the most recent studies of treatment adherence and risk factor control in CHD patients in Southeastern Europe. In the Republic of Srpska, Bosnia and Herzegovina, we report that many persons with CHD in 2005-2006 fall short of the European Guidelines’ recommended goals for BP and lipids. However, our reported treatment rates for cardioprotective drugs (ACE/ARBs, β-blockers, lipid-lowering agents, and antiplatelets) are higher than reports from previous investigations in European clinical populations that have examined CHD patients [1, 11]. We also report significant improvement in ROSCOPS III since ROSCOPS II for ACE/ARBs, lipid-lowering agents, antiplatelets and all four despite no improvement in β-blocker use. Also, there were more persons on recommended treatments when comparing our study to ROSCOPS I, a study done in 2001 where 430 CHD patients were surveyed and only 45% of subjects were on antiplatelets, 23% on β-blockers, 5% on lipid-lowering agents, and 62% on ACE/ARBs [10]. However, the proportion at goal for BP has not improved in ROSCOPS III and for LDL-C has actually

**Table I. Proportions of patients with coronary heart disease on recommended therapies**

| Proportions (%) | ROSCOPS II# | ROSCOPS III# |
|-----------------|------------|-------------|
|                 | Male | Female | Total | Male | Female | Total |
| β-Blockers      | 59.2 | 57.9  | 59.0  | 62.8 | 59.0  | 61.4  |
|                 | (287) | (76)  | (363) | (384) | (217) | (601) |
| Lipid-lowering agents | 28.6 | 26.3  | 28.1  | 68.5**†† | 52.1** | 62.6** |
|                 | (287) | (76)  | (363) | (384) | (217) | (601) |
| Antiplatelets   | 71.8 | 65.8  | 70.0  | 77.9**†† | 66.4  | 73.7  |
|                 | (287) | (76)  | (363) | (384) | (217) | (601) |
| ACE/ARBs        | 51.9 | 56.6  | 52.9  | 78.1** | 80.6** | 79.0** |
|                 | (287) | (76)  | (363) | (384) | (217) | (601) |
| All four        | 8.7  | 7.9   | 8.5   | 32.8** | 26.6** | 30.4** |

| Proportions (%) | ROSCOPS II# | ROSCOPS III# |
|-----------------|------------|-------------|
|                 | Male | Female | Total | Male | Female | Total |
| Non-smokers     | 67.9†† | 85.5  | 71.6  | 90.4***†† | 82.5  | 87.6** |
|                 | (287) | (76)  | (363) | (376) | (212) | (588) |
| BP < 140/90 mm Hg | 57.5 | 57.9  | 57.6  | 63.9 | 50.5  | 59.1  |
|                 | (287) | (76)  | (363) | (324) | (182) | (506) |
| LDL-C < 3.0 mmol/l (115 mg/dl) | 37.6†† | 57.9  | 41.9  | 44.1 | 35.6** | 41.0 |
|                 | (287) | (76)  | (363) | (161) | (90)  | (251) |

ROSCOPS – Republic of Srpska Coronary Prevention Study, ACE/ARBs – angiotensin receptor blockade medications, †total sample sizes available for each measure are indicated in parentheses, *p < 0.05, **p < 0.01 when compared to ROSCOPS II, ††p < 0.01 comparing males and females
worsened in women compared to ROSCOPS II. The fact that many patients are not at goal for BP and LDL-C indicates the need for adequate dosing and/or combination therapy of lipid and BP control in such individuals from the onset of therapeutic intervention and working with patients on adherence to treatment.

Our rates of lipid control indicate improvement from earlier reports in CHD patients. The American College of Cardiology Evaluation of Preventive Therapeutics (ACCEPT) study in 1998 showed that only about 24% of CHD patients in the USA had LDL-C treated to a target value less than < 3 mmol/l [12]. Our BP control rate of 59.1% can be compared to the lower rates of control of 41, 41.2, and 38.7% reported earlier in the EUROASPIRE I, II, and III studies, respectively [11-13]. However, based on the newly released recommended targets of < 130/80 mm Hg for patients with CHD in a recent statement from the American Heart Association [8], only 33% would be considered to be at goal, indicating the further need for use of combination or intensive therapeutic approaches. From the EUROASPIRE I, II, and III studies, there has been an increased use of antiplatelets (80, 84 and 93%, respectively), β-blockers (56, 69, and 85%, respectively), ACE/ARBs (31, 49, and 75%, respectively) and lipid-lowering medication (18, 57, and 87%, respectively) in participants with a history of CHD [3, 6, 7]. There was no change in BP control despite increased use of anti-hypertensive medication and there was continued improvement in lipid control with increased use of statins. However, preventive cardiology practice can be improved, as was shown in the PREVESE studies. The first PREVESE study was conducted in Spain in 1994, and then in 1998, in patients after an event of myocardial infarction. Significant changes in the use of medications were shown in a one-year time span since discharge from hospital; there was increased use of β-blockers from 38 to 42% and significant increase in use of statins from 29 to 57% during this period. At the end of the one-year follow-up, only 3.6% of CHD patients smoked and 90% of them reached the BP goals [13]. Our study as well as EUROASPIRE I, II, and III among persons with CHD shows improvements in the use of cardioprotective drugs from earlier reports; however, many persons still remain inadequately controlled. In addition, our study shows an increasing number of CHD patients who are non-smokers from ROSCOPS II to ROSCOPS III (72 vs. 88%, respectively). EUROASPIRE I, II, and III also showed a small increase in the number of non-smokers (80, 79, and 83% respectively) [3, 6, 7]. These studies demonstrate that under conventionally guided management, a large number of CHD patients are left untreated by cardioprotective drugs, despite an increase in use. In comparison to recent reports, the majority of patients are still not achieving BP and cholesterol targets [14, 15]. The findings of EUROACTION investigators suggest that multidisciplinary efforts can effectively alter patient behaviour and modify risk factors [16].

Our study has several strengths and limitations. While we standardized procedures for measurement of risk factors and evaluations of medical history, not all participants had risk factor measurements available; hence estimates could be biased if those with missing information for risk factors were not representative of the cohort at large. Also, the time from the CHD event to the time of follow-up examination visit was variable and compliance may vary with time, possibly being lower the longer the time that has passed since the event. Importantly, however, CHD event status was verified by a physician medical record review.

In conclusion, a substantial majority of CHD patients in the Republic of Srpska, Bosnia and Herzegovina still are not optimally treated for BP or LDL-C; however, there have been recent improvements in treatment, particularly lipid-lowering medication and ACE inhibitors/ARBs. Further education of patients and providers in the appropriate use (including effective dosages and use of combination therapies) of cardioprotective drugs is needed. There is a need for uniform surveillance of coronary patients who need the support of hospitals, rehabilitation centres and general practitioners for the purpose of appropriate implementation of secondary prevention measures.

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References
1. De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice: third joint task force of European and other societies on cardiovascular disease prevention in clinical practice. Eur J Cardiovasc Prev Rehabil 2003; 2 (Suppl 1): 2-63.
2. Smith SC Jr, Allen J, Blair SN, et al. National Heart, Lung, and Blood Institute. AHA/ACC Guidelines for Secondary Prevention Patients with Coronary and other Atherosclerotic Vascular Disease: 2006 update. Circulation 2006; 113: 2363-72.
3. EUROASPIRE I and II Group. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. Lancet 2001; 357: 995-1001.
4. Wong ND, Cupples LA, Ostfeld AM, Levy D, Kannel WB. Risk factors for long-term coronary prognosis after initial myocardial infarction: the Framingham Study. Am J Epidemiol 1989; 130: 469-80.
5. Davigius ML, Lloyd-Jones DM, Pirzada A. Preventing cardiovascular disease in the 21st century: therapeutic and preventive implications of current evidence. Am J Cardiovasc Drugs 2006; 6: 87-101.

6. Kotseva K, Wood D, De Backer G, et al. EUROASPIRE III: A survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from twenty-two European countries. Eur J Cardiovasc Prev Rehabil 2009; 16: 121-37.

7. Kotseva K, Wood D, De Backer G, et al. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, III surveys in eight European countries. Lancet 2009; 373: 929-40.

8. Rosendorff C, Black HR, Cannon CP, et al. American Heart Association Council for High Blood Pressure Research; American Heart Association Council on Clinical Cardiology; American Heart Association Council on Epidemiology and Prevention. Treatment of hypertension in the prevention and management of ischemic heart disease; a scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. Circulation 2007; 115: 2761-88.

9. Vulic D, Krneta M, Lazarevic A, et al. Results of Coronary Prevention Study in Republika Srpska (ROSCOPS I & II) changing therapeutic aproach in CHD patients. 75th Congress of the European Society of Atherosclerosis. Prague, April 2005 [abstract T02-P-021].

10. Vulic D, Kerotic Tj, Vulic B, Krneta M, Pavic Z. Trend risk factors of Coronary Prevention Study in Republika Srpska-Bosnia and Herzegovina (ROSCOPS). In: Kostner MG, Kostner MK (eds). Atherosclerosis: risk factors, diagnosis and treatment. Bologna: Manduzi Editore 2002; 97-100.

11. Graham I, Atar D, Borch-Johnsen K, et al. European Guidelines on Cardiovascular Disease Prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other Societies on Cardiovascular Disease prevention in clinical practice. Eur J Cardiovasc Prev Rehabil 2007; 14 (Suppl. 2): S1-113.

12. Pearson TA, Peters TD, Feury D. The American College of Cardiology Evaluation of Preventive Therapeutics (ACCEPT) study: attainment of goals for comprehensive risk reduction in patients with coronary disease in the US. J Am Coll Cardiol 1998; 31: 186A.

13. De Velasco JA, Rodriguez JA, Ridocci F, Aznar J. Action to improve secondary prevention in coronary heart disease patients: one-year follow-up of shared care program. Eur Heart J 2004; 6 (Suppl. 1): 27-32.

14. Brekke M, Gjelsvik B. Secondary cardiovascular risk prevention — we can do better. Lancet 2009; 373: 873-974.

15. Brook RD, Greenland P. Secondary prevention. In: Wong ND, Black HR, Gardin JM (eds). Textbook of preventive cardiology: a practical approach. USA: McGraw-Hill Companies 2005; 583-99.

16. Wood DA, Kotseva K, Connoly S, et al. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: a paired, cluster-randomised controlled trial. Lancet 2008; 371: 1999-2012.