Over time changes in the prevention of recurrent coronary artery disease in everyday practice

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Short title: Prevention of recurrent coronary artery disease

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WHAT’S NEW?

We found a significant increase in the proportion of patients with high blood pressure (49.7% vs. 59.3%, \( P < 0.01 \)) and high LDL cholesterol (28.1% vs. 39.7%, \( P < 0.001 \)) at goal between 2011–2013 and 2016–2017 in patients aged ≤80 years. On the other hand, there was no significant change in the control of other risk factors (smoking, glycemia, body mass index). Despite an increase in the uptake of blood-pressure lowering drugs, a considerable proportion of patients with coronary artery disease (CAD) still have uncontrolled blood pressure. In addition, the high proportion of both patients with elevated LDL cholesterol despite the wide use of lipid-lowering drugs as well as patients who are overweight or obese suggests there is a great potential for lifestyle modification and adherence improvement. Our results likewise point to the need for further reduction in cardiovascular risk in CAD patients and that a revision of state funded cardiac prevention programs is justified.
ABSTRACT

Introduction: Patients with coronary artery disease (CAD) are at high risk of recurrent cardiovascular events and control of their risk factors is crucial.

Objectives: To compare the implementation of the ESC guidelines regarding prevention of recurrent CAD in 2016–2017 with their implementation in 2011–2013.

Patients and methods: Five hospitals with cardiology departments serving the city of Krakow and its surrounding districts participated in the study. Consecutive patients with established CAD were interviewed 6–18 months after hospitalization: in 2011–2013 and 2016–2017.

Results: We examined 616 patients in 2011–2013 and 388 in 2016–2017 (age: 64.7 (8.8) vs. 66.4 (8.4), P <0.01). After adjusting for covariates the proportion of patients with high blood pressure decreased by 8.9% [95% confidence intervals: (-15.6%; -2.1%)] and the proportion of patients with high LDL cholesterol declined by 9.5% (-16.7%; -2.2%) in 2016/2017 compared with 2011/2013, whereas the proportion of smoking patients [-0.2% (-6.0%; 5.5%)] and those with high glucose levels [3.9% (-2.2%; 10.0%)] and a body mass index ≥25 kg/m² [3.8% (-3.9%; 11.6%)] did not change significantly. The proportion of patients prescribed antiplatelets, β-blockers, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, calcium antagonists and anticoagulants increased significantly.

Conclusions: Between 2011–2013 and 2016–2017 we observed an increase in the proportion of CAD patients prescribed with cardiovascular drugs and consequently a slight improvement in the control of their blood pressure and LDL cholesterol. No significant changes were found in the case of the other main risk factors.
INTRODUCTION

Cardiovascular diseases are the leading cause of deaths in most developed countries [1-3]. Many scientific societies, including the European Society of Cardiology (ESC) and numerous national medical associations have emphasized the importance of cardiovascular prevention [4-7].

The control of cardiovascular risk factors in patients with coronary artery disease (CAD) only slightly improved in Poland between 1997–98 and 2011–2013 [8]. There is potential for more effective implementation of the ESC guidelines on CAD prevention [8]. Indeed, one of the suggested major causes of high mortality rates following hospitalization for CAD is insufficient quality of medical care in the field of recurrent CAD prevention [9-11]. The implementation of guidelines on recurrent CAD prevention in day-to-day clinical practice was assessed every few years beginning from 1997–1998 [8]. The aim of the present analysis was to compare the implementation of the ESC guidelines regarding recurrent CAD prevention in 2016–2017 with their implementation in 2011–2013.

PATIENTS AND METHODS

We analyzed the data of participants from two surveys appraising cardiovascular prevention in patients with established CAD in 2011–2013 and 2016–2017 [12-14]. The same five hospitals providing cardiological care in the city and surrounding districts participated in each survey. The participating hospitals serve a population of approximately 1,200,000 inhabitants. The methods used in the surveys had been published previously and were similar on each occasion [12-14]. Briefly, patients aged ≤80 years and hospitalized for an acute coronary syndrome or a myocardial revascularization procedure were interviewed 6–18 months following their discharge from hospital. Centrally trained research staff collected data using standardized methods and the same instruments.
A patient’s personal medical history, lifestyle and medication regimen were evaluated using a standard data collection form. Smoking status was verified by assessing the concentration of breath carbon monoxide with a smokerlyzer (Bedfont Scientific, Ltd., UK). Height and weight were measured in a standing position without shoes and heavy outwear on standard scales with a vertical ruler (SECA). Body mass index (BMI) was calculated according to the following formula: \( \text{BMI} = \frac{\text{weight [kg]}}{\text{height [m]}^2} \). Blood pressure was measured twice, on the right arm in a sitting position after at least five minutes of rest using an automatic device. The mean of two readings was used for the present analysis. A fasting venous blood sample was taken to measure plasma lipid and glucose levels. The blood samples were analyzed in the central laboratory, which was the same in both surveys. The present report took into account the results of analyses performed no later than 12 hours after blood collection.

We analyzed the proportions of patients with risk factors not meeting the recommended goals: current smoking, low-density lipoprotein (LDL) cholesterol level ≥1.8 mmol/l, fasting glucose level ≥7.0 mmol/l, BMI ≥25 kg/m². In the case of blood pressure two approaches were adopted. First, we analyzed the proportions of patients achieving the goals recommended at the time of each survey [6,15]. Second, we also analyzed the proportions of patients with blood pressure ≥140/90 mmHg.

The prevention index was calculated in the following way: one point was given for each controlled risk factor (non-smoking, blood pressure at goal, LDL cholesterol at goal, glucose <7.0 mmol/l, BMI <25 kg/m²) during the follow-up examination. The target values for blood pressure and LDL cholesterol were based on the ESC guidelines, which were valid at the time each survey was carried out. Additionally, one point was awarded to a patient for taking an antiplatelet agent and an angiotensin converting inhibitor (ACEI) or an angiotensin II receptor blocker (ARB). Thus, a patient’s prevention index could vary from 0 to 7 [8,12].
Ethics

The survey protocol was approved by the bioethics committee of the Jagiellonian University. All participants provided signed the informed consent.

Statistical analysis

Categorical variables were reported as percentages and continuous variables as means ± standard deviation. The Pearson $\chi^2$ test was applied to all categorical variables. Normally distributed continuous variables were compared using the Student’s $t$ test. Variables without normal distributions were evaluated by means of the Mann-Whitney $U$ test [16,17]. Multivariable analyses were performed on the basis of the generalized linear model as implemented in the Statistica 13 software (TIBCO Software Inc., Palo Alto, CA, USA). A two-tailed $P$ value of less than 0.05 was regarded as statistically significant.

RESULTS

Overall, the present analysis covered the data of 1005 patients (616 examined in 2011–2013 and 389 in 2016–2017). Participants of the second survey were older and the proportion of men was higher among them (Table 1). More participants of the second survey underwent percutaneous coronary intervention. On the other hand, the proportion of those with a diagnosis of unstable angina was higher in the first survey.

The temporal changes in mean blood pressure, lipids and glucose level are presented in Table 2. We found significant differences in terms of the carbon monoxide present in exhaled air, systolic blood pressure, LDL cholesterol, triglycerides, and glucose levels. When we limited the analysis to smokers the difference in carbon monoxide in exhaled air was not significant [10.7 (5.0) ppm vs 9.9 (6.0) ppm; $p = 0.37$]. Table 3 presents proportions of patients with the main risk factors uncontrolled. The proportion of patients failing to achieve treatment targets for blood pressure and LDL cholesterol decreased significantly. We did not find any significant differences in the control of the other main risk factors. The proportions
of patients prescribed antiplatelets, β-blockers, ACEIs/ARBs, calcium antagonists and anticoagulants were higher in 2016–2017 compared to 2011–2013 (Table 4).

The mean number of well controlled main risk factors (smoking, blood pressure, LDL cholesterol, glucose, and body mass index) were 2.98 (0.99) in 2011–2013 and 3.07 (1.00) in 2016–2017 (p = 0.19). Multivariable adjustment did not change the result significantly (p = 0.14). In 2011–2013 0.4%, 5.7%, 20.8%, 39.1%, 27.6%, and 6.4% of the patients had zero, one, two, three, four, and five risk factors well controlled. The corresponding proportions in 2016/2017 were: 0.0%, 7.1%, 23.5%, 38.2%, 26.1%, and 5.1%, respectively. The mean value of the prevention index increased form 4.40 (1.18) to 4.62 (1.05), (p <0.004, Figure 1). However, the difference was not significant when adjusted for co-variates (p = 0.07).

DISCUSSION

The presented data allows for comparison of implementation of the ESC guidelines in everyday clinical practice. Although we found a significant increase in the proportions of patients who achieved their treatment targets for blood pressure and LDL cholesterol, the control of the other risk factors did not change significantly. In addition, although the value of the prevention index increased, the multivariable adjustment diminished the difference. Our results suggest that the potential for a further reduction in cardiovascular risk in CAD patients has not decreased significantly and that revision of state funded cardiac prevention programs is rational. Indeed, several initiatives aimed at improving cardiovascular risk in patients with CAD have been published recently [10,11,18,19]. Among them is the idea of managed care for myocardial infarction survivors, which was introduced in 2017 [11].

The increase in the uptake of blood-pressure lowering drugs might be related to a significantly higher proportion of patients with blood pressure at goal in 2016–2017. Nevertheless, a considerable proportion of CAD patients still have uncontrolled blood pressure. Furthermore, the high proportion of patients with elevated LDL cholesterol levels
despite wide use of lipid-lowering drugs, as well as the high proportion of overweight or obese patients suggests a considerable potential for lifestyle modification [6,10,20,21].

Our data allows for a comparison of risk factors control in Krakow and other European centers participating in the EUROASPIRE survey [22]. The proportion of smokers in Krakow was 16% whereas the corresponding figure in EUROASPIRE centers was 19% [22]. Similarly, the proportion of patients with high blood pressure was 41% and 42%, while the proportion of patients with high LDL cholesterol was 60% and 71%, and proportion of obese patients was 38% and 38%, respectively. The proportion of patients prescribed cardioprotective drugs in Polish centers was generally higher compared to EUROASPIRE centers (antiplatelets 96% vs. 93%, β-blockers 91% vs. 81%, ACEIs/ARBs 88% vs. 75%, lipid-lowering drugs 91% vs. 84%). Similar conclusions could be drawn when Polish patients with stable coronary artery disease were juxtaposed alongside patients from other European countries participating in the CLARIFY registry [23].

The present analysis has several limitations, which are similar to previously published analyses in the field [8,14,24]. Firstly, we were unable to assess what impact the implementation of cardiovascular prevention guidelines had on the risk of cardiovascular complications [8,14,24]. Secondly, participants in the present study were not representative of all patients with CAD. Participants were limited to those who had experienced an acute CAD event or had undergone a revascularization procedure. As a consequence, the present results should not be directly addressed to other groups of patients with CAD. Thirdly, we only studied patients aged ≤80 years, and hence our results should not be applied directly to older patients. Fourth, examined factors could be not stable over one year period in some patients. Finally, we did not analyze the doses of cardioprotective drugs taken by patients. It is possible that blood pressure, lipids, and glucose were not controlled in some cases due to insufficient doses of the prescribed drugs. It should also be noted that we had no information on the
patients’ compliance with instructions regarding prescriptions. It is reasonable to suspect that some patients had taken their medications irregularly [25-27]. According to a previously published study patients’ self-reported drug intake is often misleading [26]. However, an important advantage of our analysis is that our results are not based on abstracted medical record data but on face-to-face interviews and examinations using the same protocol and standardized methods and instruments [8,14,24]. Therefore, the present analysis provides reliable information on lifestyle, risk factors, and therapeutic management for prevention of recurrent CAD.

**Conclusions**

We found increased proportion of patients who were prescribed several classes of cardiovascular drugs and consequently a slight improvement in control of blood pressure and LDL cholesterol in years 2016-2017. However, no major changes occurred in other main cardiovascular risk factors prevalence.

**Contribution statement:** PJ, PK, PB, PG, EM-B, JN, PP, AW, DC, AP were involved in organizing of the study and managing data collection. PJ designed the analysis and performed the statistical analyses. JWP and PJ drafted the manuscript and contributed to analyses and interpretation. All authors revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

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| Variable                          | 2011–2013 (n = 616) | 2016–2017 (n = 389) | P value |
|----------------------------------|---------------------|---------------------|---------|
| Mean age, y (SD)                 | 64.7 (8.8)          | 66.4 (8.4)          | 0.003   |
| Sex                              |                     |                     |         |
| Men, n (%)                       | 399 (64.7)          | 277 (71.2)          | 0.03    |
| Women, n (%)                     | 217 (35.2)          | 112 (28.8)          |         |
| Mean duration of education, y (SD)| 11.9 (3.2)         | 12.6 (3.2)          | <0.001  |
| Professionally active, n (%)     | 131 (21.3)          | 123 (31.7)          | <0.001  |
| Index diagnosis                  |                     |                     |         |
| Myocardial infarction, n (%)     | 213 (34.6)          | 133 (34.2)          | 0.90    |
| Unstable angina, n (%)           | 203 (33.0)          | 66 (17.0)           | <0.001  |
| PCI, n (%)                       | 141 (22.9)          | 171 (44.0)          | <0.001  |
| CABG, n (%)                      | 59 (9.6)            | 19 (4.9)            | 0.007   |

Abbreviations: CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; y, years
Table 2. Temporal changes in risk factors 6-18 months after discharge

| Survey       | CO in exhaled air, ppm (first – third quartile) | SBP, mmHg (SD) | DBP, mmHg (SD) | Total cholesterol, mmol/l (SD) | HDL cholesterol, mmol/l (SD) | LDL cholesterol, mmol/l (SD) | Triglycerides, mmol/l (first – third quartile) | Fasting glucose, mmol/l (SD) | HbA1c, % (SD) | BMI, kg/m² (SD) |
|--------------|------------------------------------------------|----------------|----------------|-------------------------------|----------------------------|----------------------------|--------------------------------|------------------|----------------|------------------|
| 2011–2013    | 3.0 (2.0 - 4.0)                                | 135.3 (22.1)   | 81.0 (12.5)    | 4.55 (1.27)                   | 1.35 (0.42)                | 2.49 (1.07)                | 1.30 (1.00 - 1.80)               | 6.10 (2.03)                | 6.22 (0.97)   | 28.7 (4.4)       |
| 2016–2017    | 2.0 (1.0 - 3.0)                                | 134.1 (18.4)   | 79.7 (10.6)    | 4.09 (1.09)                   | 1.30 (0.37)                | 2.12 (0.92)                | 1.25 (0.96 - 1.73)               | 6.41 (2.07)                | 6.18 (0.95)   | 29.0 (4.4)       |
| P value      | 0.001                                          | 0.36           | 0.55           | <0.001                        | 0.05                       | <0.001                     | 0.04                           | 0.02             | 0.59           | 0.33             |

Differences adjusted for age, sex, index diagnosis, duration of education, professional activity (95% confidence intervals)

| 2016–2017 vs 2011–2013 | -0.68 (-1.26; -0.09) | -3.4 (-6.4; -0.3) | 0.1 (-1.6; 1.8) | -0.31 (-0.49; -0.12) | 0.00 (-0.05; 0.06) | -0.29 (-0.44; -0.13) | -0.09 (-0.25; -0.07) | 0.34 (0.01; 0.67) | 0.38 (-14.19; 14.95) | 0.28 (-0.41; 0.96) |
Abbreviations: BMI, body mass index; CO, carbon monoxide; DBP, diastolic blood pressure; HBA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ppm, parts per million; SBP, systolic blood pressure

*available for 362 patients in 2011–2013 and 383 patients in 2016–2017*
**Table 3. Temporal changes in proportions of patients who do not reach treatment goals 6-18 months after discharge**

| Survey        | Smoking, n (%) | BP not at goal<sup>a</sup>, n (%) | BP ≥140/90 mmHg, n (%) | LDL cholesterol ≥1.8 mmol/l, n (%) | HbA1c ≥7.0%<sup>b</sup>, n (%) | Fasting glucose ≥7.0 mmol/l, n (%) | BMI ≥25 kg/m<sup>2</sup>, n (%) | BMI ≥30 kg/m<sup>2</sup>, n (%) |
|---------------|----------------|----------------------------------|------------------------|----------------------------------|---------------------------------|----------------------------------|---------------------------------|---------------------------------|
| 2011–2013     | 117 (19.0)     | 310 (50.3)                       | 265 (43.0)             | 443 (71.9)                       | 87 (14.1)                       | 98 (15.9)                        | 500 (81.2)                      | 208 (33.8)                      |
| 2016–2017     | 63 (16.2)      | 158 (40.6)                       | 152 (39.1)             | 235 (60.4)                       | 58 (14.9)                       | 79 (20.3)                        | 324 (83.3)                      | 149 (38.3)                      |
| *P value*     | 0.26           | 0.003                            | 0.24                   | <0.001                           | 0.76                            | 0.09                             | 0.37                            | 0.14                            |

Differences adjusted for age, sex, index diagnosis, duration of education, professional activity (95% confidence intervals)

| 2016–2017 vs 2011–2013 | -0.2 (-6.0; 5.5) | -8.9 (-15.6; -2.1) | -6.7 (-14.3; 1.0) | -9.5 (-16.7; -2.2) | 2.0 (-3.4; 7.4) | 3.9 (-2.2; 10.0) | 3.8 (-3.9; 11.6) | 1.6 (-5.8; 9.0) |

Abbreviations: BMI, body mass index; BP, blood pressure; LDL, low-density lipoprotein

<sup>a</sup> BP goal of <140/90 mmHg (<130/80 mmHg in diabetics) in 2011–2013 and <140/90 mmHg (<140/85 mmHg in diabetics) in 2016–2017

<sup>b</sup> available for 362 patients in 2011–2013 and 383 patients in 2016–2017
Table 4. Temporal changes in proportion of patients taking cardioprotective drugs 6-18 months after discharge from the hospital.

| Survey       | Antiplatelets, n (%) | β-blockers, n (%) | ACEIs / ARBs, n (%) | Calcium antagonists, n (%) | Diuretics, n (%) | Lipid lowering drugs, n (%) | Antidiabetic agents, n (%) | Anticoagulants, n (%) |
|--------------|-----------------------|-------------------|---------------------|---------------------------|-----------------|-----------------------------|--------------------------|----------------------|
| 2011–2013    | 556 (90.3)            | 498 (80.8)        | 473 (76.8)          | 147 (23.9)                | 262 (42.5)      | 518 (84.1)                  | 164 (26.6)               | 42 (6.8)             |
| 2016–2017    | 374 (96.1)            | 352 (90.5)        | 343 (88.2)          | 125 (32.1)                | 186 (47.8)      | 353 (90.7)                  | 147 (37.8)               | 57 (14.7)            |
| *P* value    | <0.001                | <0.001            | <0.001              | 0.004                     | 0.10            | 0.002                       | <0.001                   | <0.001               |

Differences adjusted for age, sex, index diagnosis, duration of education, professional activity (95% confidence intervals)

|        | 2016–2017 vs 2011–2013 |  |  |  |  |  |  |  |
|--------|------------------------|  |  |  |  |  |  |  |
|        | 6.5 (2.6; 10.3)        | 7.4 (2.2; 12.6) | 8.6 (2.9; 14.3) | 8.1 (1.3; 15.0) | 6.2 (-1.2; 13.6) | 3.9 (-1.2; 9.1) | 6.3 (-0.9; 13.6) | 5.5 (0.7; 10.2) |

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers
Figure 1. Distribution of the prevention index values by survey ($P = 0.007$).