Pharmacotherapy in patients with chronic coronary syndromes

over a 20-year period (1997–2017)


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Authors:
Piotr Jankowski¹, Paweł Koziel¹, Piotr Bogacki², Piotr Gomuła³, Ewa Mirek-Bryniarska⁴, Jadwiga Nessler⁵, Piotr Podolec⁶, Dirk De Bacquer⁷, Guy De Backer⁷, Kornelia Kotseva⁸, David Wood⁹, Danuta Czarnecka¹, Kalina Kawecka-Jaszczyk¹, Andrzej Pająk⁹

¹ I Department of Cardiology, Interventional Electrocardiology and Hypertension, Institute of Cardiology, Jagiellonian University Medical College, Kraków, Poland
² Department of Cardiology, Ludwik Rydygier District Hospital, Kraków, Poland
³ Department of Cardiology, Gabriel Narutowicz Memorial General Hospital, Kraków, Poland
⁴ Department of Cardiology, Jozef Dietl Hospital, Kraków, Poland
⁵ Department of Coronary Heart Disease, Institute of Cardiology, Jagiellonian University, Medical College, Kraków, Poland
⁶ Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University Medical College, Kraków, Poland
⁷ Department of Public Health and Primary Care, Ghent University, Belgium
⁸ Imperial College Healthcare NHS Trust and National Institute of Preventive Cardiology, National University of Ireland-Galway, Galway, Ireland
⁹ Department of Clinical Epidemiology and Population Studies, Institute of Public Health, Jagiellonian University Medical College, Kraków, Poland
Short title:

Drug use trends in patients with chronic coronary syndromes

Corresponding author:

Piotr Jankowski, MD, PhD

I Department of Cardiology, Interventional Electrocardiology and Hypertension, Institute of Cardiology, Jagiellonian University Medical College, Jakubowskiego St. 2, 30-688 Kraków, Poland Tel: +48 12 400 21 50, Fax: +48 12 400 21 67, E-mail: piotrjankowski@interia.pl

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Introduction

Cardiovascular disease is a leading cause of death in developed countries [1]. Recent years have shown that mortality following a myocardial infarction is still high despite development of pharmacological and invasive methods of treatment of CAD (coronary artery disease), being about 10% within one year after myocardial infarction [2]. The main causes of high mortality following myocardial infarction, among others, are unsatisfactory control of risk factors, insufficient lifestyle changes and not adequate pharmacotherapy [3]. Secondary prevention of cardiovascular events relies on lifestyle changes, risk factor control and optimal pharmacotherapy [4-7]. The aim of present analysis was to assess the trends in the major drug groups use in patients with chronic coronary syndromes within two decades.

Methods

We analyzed data of participants of five surveys assessing secondary prevention following hospitalization due to CAD carried out in 1997-1998, 1999-2000, 2006-2007, 2011-2013, and 2016-2017 [8-12]. The same five hospitals serving the city and surrounding districts participated in each survey. Methods used in surveys were published previously and were similar each time [8-13]. Shortly, in each survey the study sample consisted of consecutive patients hospitalized for coronary artery bypass grafting or percutaneous coronary intervention or myocardial infarction or unstable angina. As the age limit in the first (1997-1998) and second (1999-2000) surveys was < 71 years at the time of hospitalization we excluded all older participants of the other three surveys from present analysis.

The examination took part 6-18 month after the index hospitalization. Data on medications used were obtained using a standard questionnaire and were based on the patients’ declarations. The surveys protocols were approved by the institutional Bioethics Committee. All patients signed the informed consent form.
Statistical analysis

Categorical variables were reported as percentages and continuous variables as means and standard deviation (SD). The Pearson $\chi^2$ test was applied to all categorical variables. Normally distributed continuous variables were compared using the analysis of variance. Variables without normal distributions were evaluated using the Kruskal–Wallis analysis of variance. Generalized linear model (logit model) as implemented in the Statistica 13 software (TIBCO Software, USA) were used to compare adjusted for sex, age, education, and index event proportions of patients using drugs from the specific group. A two-tailed $P$ value of less than 0.05 was regarded as indicating statistical significance.

Results and discussion

The numbers of participants in the surveys were as follows: 418 in 1997-1998, 427 in 1999-2000, 425 in 2006-2007, 469 in 2011-2013 and 274 in 2016-2017. The mean age (SD) of study participants was 57.8 (8.3) years in 1997-98, 58.6 (8.1) years in 1999-2000, 59.9 (7.6) years in 2006-07, 61.1 (6.9) years in 2011-13, and 62.6 (6.9) years in 2016-17, $P < 0.001$. There was no significant difference in the gender distribution between surveys (in total 70.9% men and 29.1% women), whereas the mean (SD) duration of education gradually increased: 11.4 (3.6) years in 1997-98, 11.6 (3.5) years in 1999-2000, 11.9 (3.4) years in 2006-07, 12.1 (3.1) years in 2011-13, and 13.0 (3.1) years in 2016-17, $P < 0.001$.

Table 1 presents crude proportions of patients taking antiplatelet agents, beta-blockers, angiotensin converting enzyme inhibitors/sartans, calcium antagonists, diuretics, anticoagulants, lipid-lowering drugs and antidiabetic agents. We observed significant differences in the use of all analyzed groups in univariate analysis. The multivariate adjustments did not change the results significantly (Table 1).
The scientific evidence suggests the survival of coronary patients may be improved through providing optimal secondary prevention, which includes control of main risk factors and optimal pharmacotherapy [4, 6, 7]. Our analysis provides evidence for a substantial improvement in respect of all drug classes, which improve prognosis in patients with CAD, including postinfarction patients and those with heart failure. The found differences in the drug use could not be explained by differences in mean age and education only. It seems that the increasing drug uptake reflects both increasing prevalence of hypertension, heart failure, diabetes and other diseases as well as the improvement in the quality of treatment of these conditions. Interestingly, bigger differences could be seen in decade 1997/1998 – 2006/2007 than 2006/2007 – 2016/2017. This could be related to the disseminating awareness of guidelines implementation importance in the beginning of the current century. It should be, however, underlined that despite a considerable increase in the cardiovascular drugs use over the 20-year period, the wider use of „newly” developed drugs, including protein convertase subtilisin/kexin type 9 inhibitors, inhibitors of type 2 renal sodium-glucose co-transporter, ticagrelor, new antithrombotic agents, and angiotensin receptor neprilysin inhibitor could further decrease cardiovascular risk. In addition, the present results should be seen in the light of studies showing high rate of CAD patients with uncontrolled risk factors [13-15].

A lot of studies have been published assessing the quality of medical care in the field of secondary prevention of CAD, including the prescription rates of cardiovascular drugs [13,14]. To our best knowledge the present study analyzes the only data available allowing for estimating the operational efficiency in the area of secondary prevention of CAD of the same hospitals over 20 years of observation. This provides a unique possibility of tracking long-term changes in prescription rates in patients with CAD living in a defined area and being hospitalized in the same hospitals.
Our analysis has several limitations. Although our results were obtained by consecutive surveys of samples of patients with established CAD who were inhabitants of the same residential area, the observation was restricted to those who experienced an acute CAD event or underwent a revascularization procedure. Therefore, participants were not representative of all CAD patients and the applicability of the results to other regions is uncertain. On the other hand, the showed trends agree with short-time changes in patients with CAD in other European countries [15]. The study groups could differ in respect of a number of unidentified factors which could explain the found differences. It should be also underlined that most analyzed drug classes should be prescribed in particular conditions dependent on left ventricular function, blood pressure, glucose metabolism, heart rate, presence of angina or arrhythmia, etc. Therefore, one should not expect that 100% of analyzed patients are prescribed agents from a particular drug class.

In conclusion, the analysis of five multicenter surveys provides evidence for graduate increase in the uptake of major groups of cardiovascular drugs in patients with chronic coronary syndromes over a 20-year period.
References:


**Table 1.** Prescription rates of drug classes 6-18 months after hospitalization due to index event.

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<tr>
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<tbody>
<tr>
<td>Antiplatelets (at least one agent), %</td>
<td>76.1</td>
<td>86.9</td>
<td>90.1</td>
<td>90.0</td>
<td>96.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>β-blockers, %</td>
<td>59.1</td>
<td>63.9</td>
<td>87.5</td>
<td>80.8</td>
<td>92.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ACE inhibitors / sartans, %</td>
<td>45.9</td>
<td>47.5</td>
<td>79.0</td>
<td>76.8</td>
<td>89.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ACE inhibitors, %</td>
<td>45.9</td>
<td>47.5</td>
<td>74.6</td>
<td>66.1</td>
<td>74.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sartans, %</td>
<td>0.0</td>
<td>0.0</td>
<td>5.4</td>
<td>12.6</td>
<td>14.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Calcium antagonists, %</td>
<td>28.7</td>
<td>33.3</td>
<td>20.9</td>
<td>21.1</td>
<td>27.7</td>
<td>&lt; 0.001</td>
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<tr>
<td>Diuretics, %</td>
<td>17.0</td>
<td>21.0</td>
<td>31.8</td>
<td>36.3</td>
<td>41.2</td>
<td>&lt; 0.001</td>
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<tr>
<td>Lipid lowering drugs, %</td>
<td>33.7</td>
<td>41.9</td>
<td>86.8</td>
<td>83.4</td>
<td>90.8</td>
<td>&lt; 0.001</td>
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<tr>
<td>Statins, %</td>
<td>19.4</td>
<td>34.2</td>
<td>85.4</td>
<td>83.2</td>
<td>90.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fibrates, %</td>
<td>14.1</td>
<td>7.7</td>
<td>3.5</td>
<td>2.6</td>
<td>1.1</td>
<td>&lt; 0.001</td>
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<tr>
<td>Ezetimibe, %</td>
<td>0.0</td>
<td>0.0</td>
<td>0.2</td>
<td>0.6</td>
<td>3.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Antidiabetic agents, %</td>
<td>10.3</td>
<td>13.4</td>
<td>19.6</td>
<td>25.6</td>
<td>34.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anticoagulants, %</td>
<td>12.4</td>
<td>5.6</td>
<td>6.4</td>
<td>5.4</td>
<td>13.1</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin converting enzyme

* - adjusted for sex, age, education, and index event