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A comparison of the management and five-year outcomes of patients treated for chronic coronary syndrome between 2006–2007 and 2015–2016 — insights from the PRESAGE registry

Authors: Izabela Kozłowska-Karaca, Piotr Desperak, Mariusz Gąsior, Przemysław Trzeciak

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ORIGINAL ARTICLE

A comparison of the management and five-year outcomes of patients treated for chronic coronary syndrome between 2006–2007 and 2015–2016 — insights from the PRESAGE registry

Running title: Management and outcomes of patients with CCS

Izabela Kozłowska-Karaca[1] https://orcid.org/0000-0002-1476-9158, Piotr Desperak[2], Mariusz Gąsior[3], Przemysław Trzeciak[3] https://orcid.org/0000-0003-4790-291X

[1]Department of Hematology and Cancer Prevention, Municipal Hospital in Chorzów, Poland

[2]Cardiology Department, Voivodeship Specialist Hospital in Rybnik, Poland

[3]3rd Department of Cardiology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia in Katowice, Silesian Center for Heart Diseases, Zabrze, Poland

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Address for correspondence: Izabela Kozłowska-Karaca, M.D., Department of Hematology and Cancer Prevention, Municipal Hospital in Chorzów, Strzelców Bytomskich 11 St., 41–500 Chorzów, Poland; tel: +48 32 3499265, e-mail: ikozlowska777@gmail.com

ABSTRACT

Background: Changes in the management of patients with chronic coronary syndromes (CCS) require continuous monitoring of results of treatment in daily clinical practice.

The present study contains a comparison of the clinical characteristics, management, and in-hospital and five-year outcomes of patients with CCS enrolled on the Prospective REgistry of Stable AnGina management and trEatment (PRESAGE).

Methods: A group of 3475 patients with CCS were selected who underwent coronary angiography and were divided into two groups who were treated in the years 2006–2007 (1300 [37.4%]) – group I, and during 2015–2016 (2175 [62.6%] – group II). The composite endpoints involved death, non-fatal myocardial infarction (MI), and acute coronary syndrome-driven revascularization.

Results: Comparing patients from group I to those from group II, group I were younger; 61.8 (54.9–68.5) vs. 66.1 (59.7–72.7) years respectively, with a higher incidence of previous MI and percutaneous intervention. Patients from the group II had a higher incidence of hypertension, diabetes, obesity, atrial fibrillation, New York Heart Association class III or more. The incidence of the composite endpoints did not vary significantly between the two groups during the entire period after the index hospitalization, but patients from the group I had a lower mortality rate both within three and five years after discharge (8.5% vs. 10.7, $p = 0.03$ and 13.2% vs. 17.9%, $p < 0.001$, respectively).

Conclusions: Patients treated during 2006–2007 and 2015–2016 differed in age, clinical characteristics, and comorbidities. The composite endpoint incidence was similar in both groups, but long-term mortality rates were higher in the 2015–2016 cohort.

Keywords: chronic coronary syndromes, comorbidity, mortality, prognosis

Introduction

Chronic coronary syndromes (CCS) [previously stable angina (SA)] are a prevalent manifestation of coronary artery disease (CAD) [1]. It is a consequence of prolonged life expectancy, the growing incidence of CAD risk factors, and the improved survival of patients with acute coronary syndrome (ACS) [2]. Due to significant advances in both the diagnosis and treatment of CAD, the guidelines for CCS management have been modified by the European Society of Cardiology (ESC) three times [3–5].

Changes in the recommendations for the management of patients with CCS require continuous monitoring of the results of treatment in daily clinical practice. Despite that, the number of studies regarding the early and long-term outcomes in this group of patients is limited [6–12]. Randomized trials and international registries often recruit carefully selected patients, which are often not representative of populations in daily practice in aspects of clinical characteristics, management, and treatment. [7–10, 13, 14].

Therefore, the aim herein was to compare the clinical characteristics, management, and in-hospital and five-year outcomes of patients with CCS enrolled in the Prospective REgistry of Stable AnGina management and treatment (PRESAGE; ClinicalTrials.gov identifier, NCT03781492), treated in the years 2006–2007 and 2015–2016.

Methods

Registry design

The study was based on the data from the PRESAGE Registry. In brief, the PRESAGE Registry is an ongoing, single-center, prospective observational study recruiting consecutive patients who underwent coronary angiography and were discharged from the 3rd Department of Cardiology, Silesian Center for Heart Diseases in Zabrze, Poland, with the diagnosis of

CCS [12]. The hospital is a tertiary referral cardiology center with advanced diagnostic and treatment facilities.

All admitted patients with suspected CCS were screened for eligibility to enter the registry, and they were not enrolled until CCS was confirmed. The diagnosis of CCS was based on clinical symptoms, electrocardiography, and coronary angiography, following contemporary guidelines of the European Society of Cardiology (ESC) [3–5, 15]. Patients with microvascular or vasospastic angina were also enrolled on the registry. Pharmacological treatment and interventional strategies were used following the current recommendations of the ESC [3–5, 15].

Data collection

Complete patient baseline characteristics, treatments, and in-hospital data were obtained by reviewing the hospital records. A subsequent analysis included only data from the first hospitalization due to CCS. Five-year follow-up data after index hospitalization were acquired from the National Health Fund, including diagnosis (ICD-10 codes) and procedures (ICD-9 codes) of the following hospitalization. To obtain complete follow-up data, only inhabitants of the Silesia Province, inhabited by 4.5 million residents, were selected for analysis.

Endpoints and definitions

The composite endpoints involved death, non-fatal myocardial infarction (MI), and acute coronary syndrome (ACS)-driven unplanned revascularization within a five-year observation period. Death was considered as an all-cause death. Non-fatal MI was defined as an ischemic event that met the ESC/American College of Cardiology criteria for MI [16]. ACS-driven repeated revascularization was defined as additional, unplanned percutaneous coronary angioplasty (PCI) or coronary artery bypass grafting (CABG), performed as an urgent procedure because of acute ischemic symptoms [17].

Major bleeding was defined as clinically overt bleeding: i) with an ensuing decrease in hemoglobin to below 5 g/dL (3.1 mmol/L) or an absolute decrease of hematocrit by more than 15%; or ii) resulting in hemodynamic disorders; or iii) requiring blood transfusion. Hypertension was defined as repeated systemic blood pressure measurements exceeding 140/90 mm Hg or treatment with antihypertensive drugs for a known diagnosis of hypertension. Diabetes mellitus was diagnosed by the fasting plasma glucose level > 125 mg/dL (7.0 mmol/L), a random plasma glucose level > 200 mg/dL (11.1 mmol/L), or a history of diabetes mellitus, including patients treated with diet, oral medications, or insulin. Hypercholesterolemia was defined as a baseline cholesterol level greater than 200 mg/dL (5.2 mmol/L) and/or a low-density lipoprotein level greater than 130 mg/dL (3.4 mmol/L), or previously diagnosed and treated hypercholesterolemia. Obesity was diagnosed as a body mass index ≥ 30 kg/m2. Positive family history (PFH) of premature CAD was recognized if CAD was revealed in a first-degree relative < 50 years of age in men and < 60 years in women. Contrast-induced nephropathy (CIN) was defined as impaired renal function based on relative (≥ 25%) or absolute (≥ 44 umol/L) increase of creatinine concentration in the blood serum up to 3 days after the first or subsequent coronary angiography and the absence of an alternative explanation of renal dysfunction [18]. Significant CAD was defined as hemodynamically significant stenosis in coronary arteries with a diameter ≥ 2.0 mm as determined by visual assessment. A ≥ 50% stenosis of the left main (LM) artery or the proximal segment of the left anterior descending (LAD) artery and a ≥ 70% stenosis in other segments were considered hemodynamically significant.

Non-significant CAD was defined as < 50% lesions in LM or proximal LAD and < 70% lesions in other segments of coronary arteries with a diameter ≥ 2.0 mm as determined by visual assessment. Smooth coronary arteries were defined as the lack of any atherosclerotic lesions in the coronary arteries.

Patients enrolled on the PRESAGE Registry were divided into two groups: those treated in the years 2006–2007 and those treated in the years 2015–2016. Differences were assessed in clinical presentation and treatment, and both in-hospital and five-year outcomes, including the occurrence of the composite endpoint.

Statistical analysis

Continuous variables were expressed as median with 1st and 3rd quartile (Q1-Q3) due to non-normal distribution. The normality assumption was checked with the use of the Kolmogorov-Smirnov test. Differences between the groups were calculated with the use of the Student t-test or Mann-Whitney U test for normally or non-normally distributed data, respectively. Categorical variables were summarized using frequency tables and compared with the chi-square test or the Fisher exact test.

To evaluate the independent predictors of composite endpoints and all-cause mortality, Cox proportional hazard regression analysis was used. Variables with P values less than 0.20 in the univariable Cox regression analysis were entered into the multivariable Cox regression model with backward elimination. Schoenfeld residuals were used to check the proportional hazards assumption. Results from the Cox regression analysis were presented as hazard ratios (HRs) with 95% confidence intervals (CIs). For all analyses, a 2-tailed P-value < 0.05 was considered as significant. Between groups differences in survival time were assessed by means of the Kaplan-Meier method and compared using log-rank test. Moreover confounder-adjusted survival curves were also plotted using a direct standardization method.

The SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.4 (R Foundation for Statistical Computing, Vienna, Austria.) were used for all calculations [19].

Results

From January 2006 to December 2016, a total of 11,000 consecutive patients were enrolled in the PRESAGE Registry. Patients who died during hospitalization, numbered 59 (0.54%), and those treated between 2008-2014, totaling 7466 (67.9%), were excluded from the analysis. Consequently, the analysis ultimately included a total of 3475 patients. The entire cohort consisted of Caucasian patients.

Patients were divided into two groups: those treated in the years 2006-2007 [1300 (37.4%)] and those treated in the years 2015-2016 [2175 (62.6%)]. Patients treated in the years 2006–2007, compared to those treated in 2015–2016, were younger, with a greater prevalence of previous CAD, MI, and PCI, but with a lower incidence of comorbidities (TABLE 1). Patients treated in the years 2015-2016 had angiographically less extensive CAD with a lower frequency of surgical revascularization procedures (TABLE 2).

The in-hospital, six-month, one-, three- and five-year outcomes are presented in TABLE 3 and FIGURE 1. Patients treated in the years 2006-2007 had a lower frequency of non-fatal MI and major bleeding during the index hospitalization. The incidence of composite endpoints did not vary significantly between the two groups during the entire period after the index hospitalization. Patients treated in the years 2006–2007 had a lower mortality rate both within three and five years after discharge.

In the multivariable analysis of the entire study population, left main disease was the strongest factor associated with both mortality and the composite endpoint incidence during the five-year follow-up period (adjusted hazard ratio [HR] 2.32, 95% confidence interval [CI] 1.36 to 3.96, $p = 0.002$, HR, 2.18, 95% CI, 1.42 to 3.34, $p < 0.001$, respectively, FIGURES 2 and 3). Results of the univariable Cox regression analysis for the mortality (Table 4) and for the composite endpoint as well as its components (Table 5) are also provided. The time of

treatment was taken into account in the multivariable analysis, but was not an independent predictor of five-year outcomes (FIGURES 2 and 3).

Discussion

Despite the changes in the ESC guidelines [3, 4], an improvement in the long-term outcomes measured by the occurrence of death, non-fatal MI, and the ACS-driven revascularization were not observed. Moreover, patients treated in the years 2006–2007 had a lower mortality rate both at three and five years after discharge**.** Although this earlier group had more extensive CAD as evidenced by angiography, they were younger and had a lower incidence of comorbidities compared to patients treated in 2015–16. The distant results of treatment appear to depend not only on the therapeutic tools utilized but also on factors like age and the presence of coexisting comorbidities.

The current data about treatment and outcomes of patients with stable angina derive mainly from randomized studies [20–24] with specific inclusion or exclusion criteria. By contrast, there are only a few registries assessing characteristics and long-term outcomes of patients with CCS over a timespan similar to the present analysis [7–9, 25]. They differ in enrollment criteria. In the Euro Heart Survey (EHS) Registry, consecutive outpatients with de novo CCS were enrolled in 2002 [9]. In the CLARIFY (Prospective Observational Longitudinal Registry of Patients with Stable Coronary Artery Disease), patients with previous MI, evidence of coronary stenosis > 50%, confirmed symptomatic myocardial ischemia, or a prior revascularization procedure were recruited in the years 2009 and 2010 [7, 8]. In the START (STable coronary Artery diseases RegisTry), patients with stable CAD discharged from cardiology wards were enrolled into the registry in the years 2016–2017 if they had at least one of the following clinical conditions: typical or atypical stable angina, documented ischemia at stress test, previous coronary revascularization, or prior episode of

ACS [25].

Similar to our analysis, both demographic and clinical characteristics of patients enrolled on the mentioned registries have changed over the years. The mean age of the study population increased from 61 years in the EHS study to 64.2 years in the CLARIFY registry and to 67.6 years in the START registry [7, 8, 25].

The available registries of patients with stable CAD, similar to the current analysis, demonstrate that women constitute a minority. Women included in these reports were older and had a higher incidence of arterial hypertension, type 2 diabetes. Despite that, they had less extensive CAD and were less frequently qualified for revascularization treatment [26–28]. In another paper based on the PRESAGE registry, it was demonstrated that women had a lower incidence of death and the composite endpoint during 12-month follow-up [28].

The incidence of some CAD risk factors and comorbidities increased during this time. Hypertension was noted in 62% of patients in the EHS [9], 71% in the CLARIFY [7, 8], and 79.4% in the START registry [25]. The incidence of diabetes mellitus increased from 18% in the EHS [9], to 29%, and in the CLARIFY [7, 8], to 35.3% amongst patients treated in the years 2015-16 in the PRESAGE registry.

Despite the greater prevalence of previous MI, PCI, and significant CAD in angiography, patients included in the present analysis, who were treated in the years 2006–2007, surprisingly, had a lower mortality rate both three and five years after index hospitalization compared to those treated in 2015–2016. It is worth mentioning that patients treated in the years 2015–2016 were nearly five years older. Unfortunately, it was not possible to indicate the causes of their deaths, but it should be assumed that many of them were of non-cardiac origin.

Spoon et al. noted a marked modification in causes of death after PCI from predominantly cardiac in 1991 to non-cardiac in 2008 [29]. The predominance of non-cardiac deaths was

reported by Wang et al. in patients with stable CAD included in the Heart and Soul study [30]. The COROnariens stables en régionNORd-pas-de-Calais (CORONOR) registry included patients with an average age of 67 ± 12 years with stable CAD and a history of MI or coronary revascularization, or at least 50% obstruction in at least one coronary vessel [31]. During a five-year follow-up period, most deaths were non-cardiovascular (52%) and one of the strongest factors associated with cardiovascular death was age.

Moreover, at discharge, patients from the current registry treated in the years 2015–2016 were prescribed an angiotensin-converting enzyme inhibitor (ACEI), an angiotensin receptor blocker (ARB), statins, and — less frequently — beta blockers. It was probably related to the lower percentage of significant CAD, previous MI, and revascularization procedures. The outcomes only confirm the role of optimal medical therapy (OMT) in patients with less evident atherosclerosis, especially with coexisting risk factors and comorbidities. They correspond to the outcomes of COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) and ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches), both of which confirmed the role of the aggressive use of OMT [23, 24].

Long-term mortality rates in patients with CCS vary in several studies, depending on clinical characteristics and enrolment criteria. In the REACH registry, in the subgroup of patients with established cerebrovascular disease, the mortality rate was 2.8% per year [32]. The five-year all-cause death rate in the CLARIFY and CORONOR registries was 8.5% and 16.5%, respectively [8, 31].

Some factors related to poor prognosis in the CORONOR and PRESAGE registries were similar. The strongest factor related to both mortality and composite endpoint incidence in the present analysis was the left main disease. Its role in prognosis in patients with CCS is well documented [33, 34]. Variables associated with cardiovascular death in the CORONOR

registry during a five-year follow-up included age, prior aortic or peripheral intervention, low left ventricular ejection fraction, and low estimated glomerular filtration rate. In the CICD (Chronic Ischemic Cardiovascular Disease) Pilot registry, independent predictors of all-cause mortality/hospitalization included age, history of previous peripheral revascularization, chronic kidney disease, or chronic obstructive pulmonary disease (COPD) during a six-month follow-up [10]. Both the current study and other ones confirmed the role of non-cardiological factors. The analysis involved consecutive patients treated in a highly specialized cardiovascular center featuring complete diagnostic workup and therapeutic management. Despite a relatively high rate of ACE-I/ARBs, statins, and beta blockers prescribed at discharge, the five-year mortality in the two following periods was 13.2% and 17.9%. It only confirms the role of proper treatment of comorbidities like PAD, diabetes mellitus, renal failure, or COPD, which might increase both cardiovascular and non-cardiovascular risk of death. Finally, insufficient specialized outpatient care might play a role in a relatively higher distant mortality rate.

Identifying patients with a high risk of not only cardiovascular but also non-cardiovascular death should be an integral part of medical management. It has special importance due to the ageing CCS population and the increasing problem of coexisting diseases in recent years.

Conclusions

Patients with CCS treated in the years 2006-07 compared to those treated in 2015–16 were younger, with a greater prevalence of previous MI, PCI, and more extensive CAD in angiography, but with lower incidence of comorbidities and death three and five years after index hospitalization. The strongest factor related to the risk of death and composite endpoint during

the five-year follow-up was left main disease. The time of treatment was not an independent predictor of five-year outcomes.

Limitations

In addition to the typical limitations associated with the retrospective design, several other limitations need to be considered in the present study. First, the present analysis was based on the data of patients treated in a single, high-volume, tertiary referral hospital with advanced diagnostic and treatment facilities. Second, fractional flow reserve measurement, Syntax score values, and the completeness of revascularization were available only for a very limited number of patients and therefore were not included in the analysis. Third, there was no data regarding the Canadian Cardiovascular Society Angina score at admission and causes of death during the follow-up period.

Statement of competing interests: The authors report no competing interests.

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Figure 1. Kaplan-Meyer curves for mortality (A) and the composite endpoint (B) at 60 months. Grey lines represent adjusted survival curves for parameters selected in multivariable cox model. The log-rank p value is presented for unadjusted curves

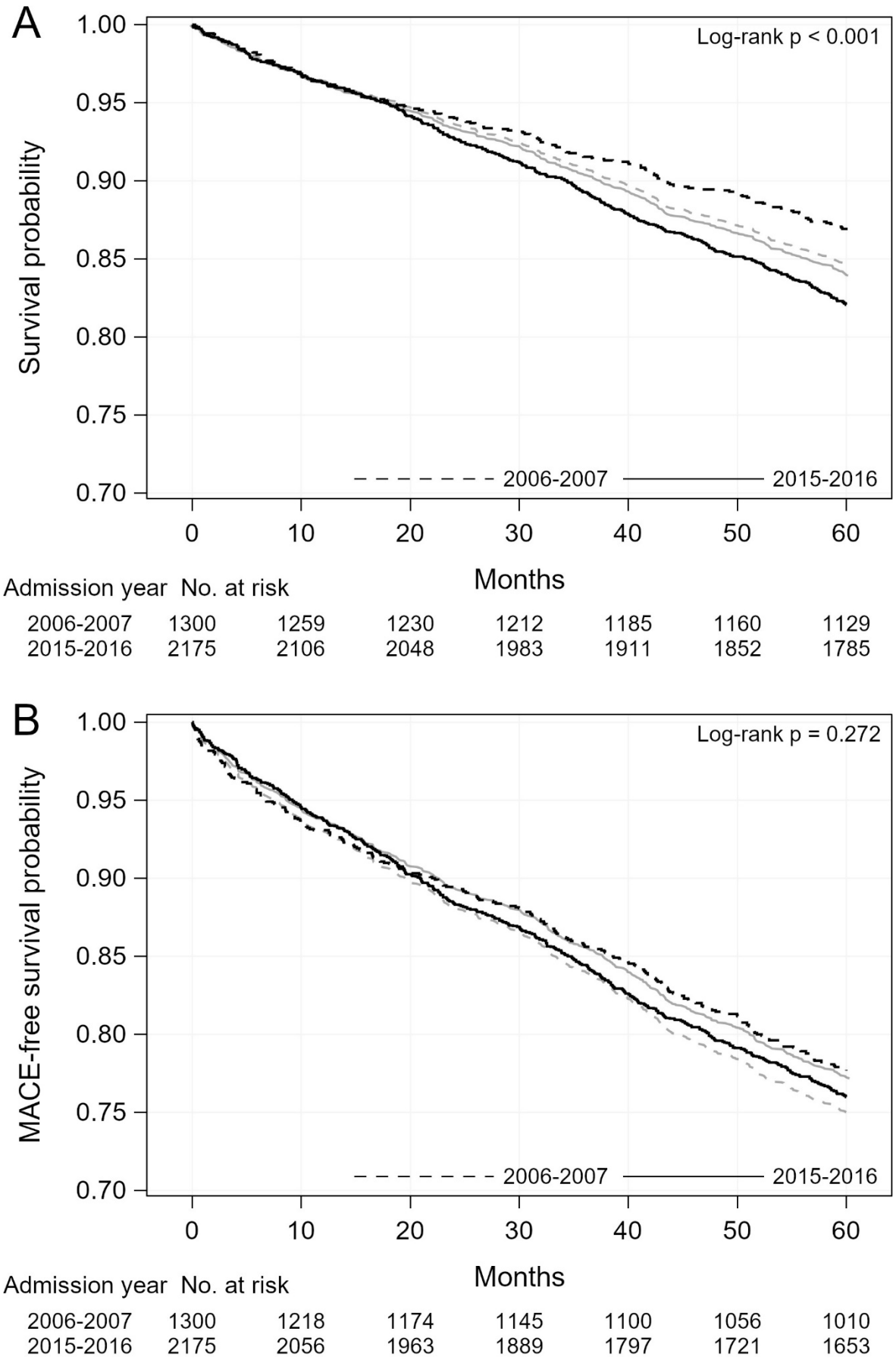
A
Survival probability
1.00
0.95
0.90
0.85
0.80
0.75
0.70
Log-rank p < 0.001
2006-2007
2015-2016
0
10
20
30
40
50
60
Months
Admission year No. at risk
2006-2007 1300 1259 1230 1212 1185 1160 1129
2015-2016 2175 2106 2048 1983 1911 1852 1785
B
MACE-free survival probability
1.00
0.95
0.90
0.85
0.80
0.75
0.70
Log-rank p = 0.272
2006-2007
2015-2016
0
10
20
30
40
50
60
Months
Admission year No. at risk
2006-2007 1300 1218 1174 1145 1100 1056 1010
2015-2016 2175 2056 1963 1889 1797 1721 1653

Figure 2. A multivariable analysis of independent risk factors for mortality at 5 years. HR — hazard ratio; CABG — coronary artery bypass grafting; CAD — coronary artery disease; COPD — chronic obstructive pulmonary; GFR — glomerular filtration rate; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NYHA — New York Heart association; PCI — percutaneous coronary intervention

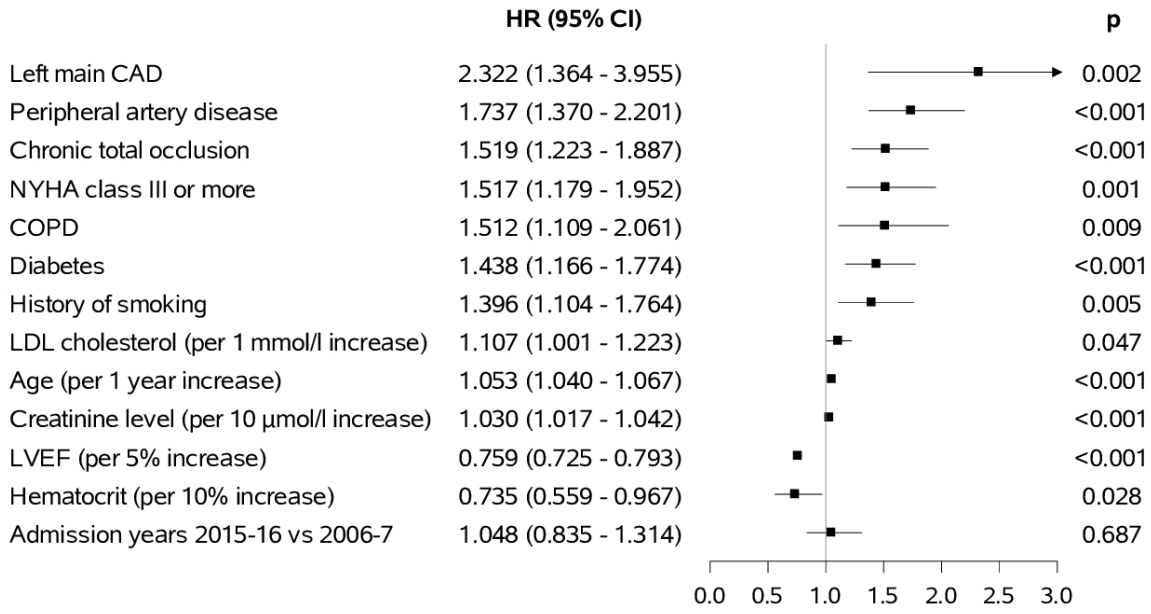

Figure 3. A multivariable analysis of independent risk factors for the composite endpoint at 5 years. CABG — coronary artery bypass grafting; CAD — coronary artery disease; COPD — chronic obstructive pulmonary; GFR — glomerular filtration rate; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NYHA — New York Heart association; PCI — percutaneous coronary intervention

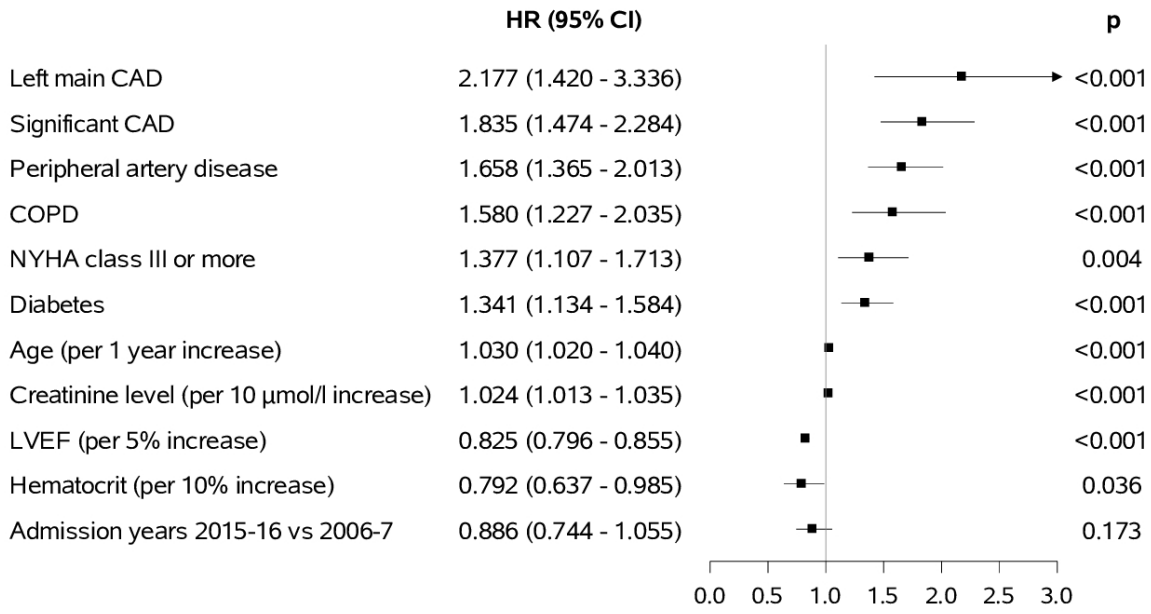
HR (95% CI)
p
Left main CAD
2.177 (1.420 - 3.336)
<0.001
Significant CAD
1.835 (1.474 - 2.284)
<0.001
Peripheral artery disease
1.658 (1.365 - 2.013)
<0.001
COPD
1.580 (1.227 - 2.035)
<0.001
NYHA class III or more
1.377 (1.107 - 1.713)
0.004
Diabetes
1.341 (1.134 - 1.584)
<0.001
Age (per 1 year increase)
1.030 (1.020 - 1.040)
<0.001
Creatinine level (per 10 µmol/l increase)
1.024 (1.013 - 1.035)
<0.001
LVEF (per 5% increase)
0.825 (0.796 - 0.855)
<0.001
Hematocrit (per 10% increase)
0.792 (0.637 - 0.985)
0.036
Admission years 2015-16 vs 2006-7
0.886 (0.744 - 1.055)
0.173
0.0 0.5 1.0 1.5 2.0 2.5 3.0

Table 1. Baseline demographic and clinical characteristics of the study patients

	Years 2006–2007 n = 1300	Years 2015–2016 n = 2175	P- value
Age, years, median IQR	61.8 (54.9–68.5)	66.1 (59.7–72.7)	< 0.001
Female sex, % (n/n)	27.3 (355/1300)	37.9 (824/2175)	< 0.001
Previous CAD, % (n/n)	62.2 (809/1300)	41.2 (876/2128)	< 0.001
Previous MI, % (n/n)	49.6 (645/1300)	28.1 (597/2128)	< 0.001
Previous PCI, % (n/n)	39 (507/1300)	28.9 (614/2128)	< 0.001
Previous CABG, % (n/n)	9.6 (125/1300)	10.1 (215/2133)	0.68
Previous stroke, % (n/n)	5.2 (67/1300)	6.3 (134/2143)	0.2
Arterial hypertension, % (n/n)	73.8 (960/1300)	83.5 (1801/2157)	< 0.001
Diabetes, % (n/n)	30.3 (392/1294)	35.3 (756/2140)	0.002
Hypercholesterolemia, % (n/n)	75.9 (985/1297)	71.4 (1526/2136)	0.004
Obesity, % (n/n)	28.2 (366/1300)	36.1 (746/2065)	< 0.001
History of smoking, % (n/n)	62.7 (815/1300)	46.2 (987/2136)	< 0.001
Active smoking, % (n/n)	23 (299/1300)	25.2 (538/2136)	0.15
COPD, % (n/n)	5.9 (76/1292)	6.6 (142/2136)	0.37
Atrial fibrillation, % (n/n)	8.7 (113/1292)	20.3 (434/2142)	< 0.001
Peripheral arterial disease, % (n/n)	11.6 (151/1300)	16.5 (353/2136)	< 0.001
LVEF < 35%, % (n/n)	15.1 (165/1091)	14.5 (216/1493)	0.64
GFR < 60 ml/min/1.73 m^2, % (n/n)	12.4 (161/1296)	19.4 (421/2168)	< 0.001
Family history of premature MI, % (n/n)	29.1 (378/1300)	26.1 (533/2044)	0.06
NYHA class III or more, % (n/n)	9.1 (118/1300)	11.7 (241/2065)	0.018

Data are presented as percentages (number of patients affected / number of patients for whom data were available). CABG — coronary artery bypass grafting; CAD — coronary artery disease; COPD — chronic obstructive pulmonary; GFR — glomerular filtration rate; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NYHA — New York Heart association; PCI — percutaneous coronary intervention

Table 2. Angiographic characteristics and interventional treatment of the study population

Variable	Years 2006–2007 n = 1300	Years 2015–2016 n = 2175	P-value
CAD			
Smooth arteries, n (%)	2 (0.2)	95 (4.4)	< 0.001
Significant CAD, n (%)	1061 (81.6)	1317 (60.6)	< 0.001
Single-vessel CAD, n (%)	462 (35.5)	594 (27.3)	< 0.001
Multivessel CAD, n (%)	599 (46.1)	723 (33.2)	< 0.001
Chronic total occlusion, n (%)	527 (40.5)	492 (22.6)	< 0.001
Interventional treatment			
PCI, n (%)	543 (41.8)	871 (40)	0.32
Bare-metal stent, n (%)	347 (26.7)	32 (1.5)	< 0.001
Drug-eluting stent, n (%)	99 (7.6)	772 (35.5)	< 0.001
Drug-eluting balloon, n (%)	0 (0)	49 (2.3)	< 0.001
CABG, n (%)	201 (15.5)	205 (9.4)	< 0.001

Data are presented as numbers (percentages) of patients. CABG — coronary artery bypass grafting; CAD — coronary artery disease; COPD — chronic obstructive pulmonary; GFR — glomerular filtration rate; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NYHA — New York Heart association; PCI — percutaneous coronary intervention

Table 3. In-hospital as well as mid- and long-term outcomes of the study population

	Years 2006–2007 n = 1300	Years 2015–2016 n = 2175	P-value
In-hospital complications			
Non-fatal MI, n (%)	0 (0)	12 (0.6)	0.005[a]
Target vessel revascularization, n (%)	0 (0)	6 (0.3)	0.09[a]
Stroke, n (%)	1 (0.1)	1 (0.05)	1.00[a]
Major bleeding, n (%)	17 (1.3)	8 (0.4)	0.003[a]
6-month composite endpoint			
Death, n (%)	25 (1.9)	50 (2.3)	0.46
Non-fatal MI, n (%)	26 (2)	17 (0.8)	0.002
ACS driven revascularization, n (%)	22 (1.7)	32 (1.5)	0.61
Any, n (%)	59 (4.5)	80 (3.7)	0.21
12-month composite endpoint			
Death, n (%)	47 (3.6)	80 (3.7)	0.92
Non-fatal MI, n (%)	31 (2.4)	28 (1.3)	0.015
ACS driven revascularization, n (%)	29 (2.2)	52 (2.4)	0.76
Any, n (%)	90 (6.9)	135 (6.2)	0.41
36-month composite endpoint			
Death, n (%)	110 (8.5)	233 (10.7)	0.03
Non-fatal MI, n (%)	53 (4.1)	76 (3.5)	0.38
ACS driven revascularization, n (%)	63 (4.8)	108 (5)	0.87
Any, n (%)	186 (14.3)	338 (15.5)	0.33
60-month composite endpoint			
Death, n (%)	171 (13.2)	390 (17.9)	< 0.001
Non-fatal MI, n (%)	87 (6.7)	116 (5.3)	0.1
ACS driven revascularization, n (%)	106 (8.2)	146 (6.7)	0.11
Any, n (%)	290 (22.3)	522 (24)	0.25

Data are presented as numbers (percentages) of patients. [a] – Fisher's exact test, otherwise χ^2

Table 4. Results of the univariable Cox regression analysis for mortality at 5 years

Variable	HR (95% CI)	P-value
Left main CAD	3.319 (2.255–4.886)	< 0.001
Peripheral artery disease	2.738 (2.279–3.289)	< 0.001
Chronic total occlusion	2.057 (1.741–2.430)	< 0.001
NYHA class III or more	2.810 (2.295–3.441)	< 0.001
COPD	2.717 (2.135–3.457)	< 0.001
Diabetes	1.876 (1.587–2.217)	< 0.001
History of smoking	1.356 (1.144–1.607)	< 0.001
LDL cholesterol (per 1 mmol/l increase)	0.925 (0.850–1.007)	0.073
Age (per 1 year increase)	1.043 (1.034–1.053)	< 0.001
Creatinine level (per 10 μmol/l increase)	1.004 (1.003–1.005)	< 0.001
LVEF (per 5% increase)	0.735 (0.709–0.763)	< 0.001
Hematocrit (per 10% increase)	0.559 (0.451–0.692)	< 0.001
Admission years 2015-16 vs 2006-7	1.393 (1.163–1.667)	< 0.001

CAD — coronary artery disease; COPD — chronic obstructive pulmonary; LDL — low-density lipoprotein; LVEF — left ventricular ejection fraction; NYHA — New York Heart Association

Table 5. Results of the univariable Cox regression analysis for the composite endpoint and its components at 5 years

	Composite endpoint		Myocardial infarction	
Variable	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Left main CAD	2.752 (1.932–3.919)	< 0.001	1.309 (0.487–3.522)	0.5934
Significant CAD	2.379 (1.986–2.849)	< 0.001	3.096 (2.077–4.613)	< 0.001
Peripheral artery disease	2.277 (1.942–2.671)	< 0.001	1.614 (1.142–2.282)	0.0067
COPD	2.284 (1.844–2.830)	< 0.001	1.932 (1.230–3.036)	0.0043
NYHA class III or more	2.145 (1.788–2.572)	< 0.001	1.047 (0.660–1.661)	0.8452
Diabetes	1.701 (1.479–1.955)	< 0.001	1.332 (1.004–1.766)	0.0466
Age (per 1 year increase)	1.030 (1.023–1.038)	< 0.001	1.015 (1.000–1.030)	0.0505
Creatinine level (per 10 μmol/l increase)	1.003 (1.003–1.004)	< 0.001	1.003 (1.002–1.005)	< 0.001
LVEF (per 5% increase)	0.805 (0.780–0.831)	< 0.001	0.929 (0.865–0.998)	0.0443
Hematocrit (per 10% increase)	0.679 (0.566–0.814)	< 0.001	0.892 (0.615–1.294)	0.5465
Admission years 2015-16 vs 2006-7	1.084 (0.939–1.251)	0.2725	0.804 (0.609–1.061)	0.1237
	PCI		**CABG**	
Variable	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P -value**
Left main CAD	2.023 (0.954–4.290)	0.0663	–	0.9910
Significant CAD	3.603 (2.443–5.312)	< 0.001	4.590 (1.069–19.706)	0.0404
Peripheral artery disease	1.355 (0.964–1.905)	0.0803	3.984 (1.650–9.619)	0.0021
COPD	1.470 (0.920–2.351)	0.1075	–	0.9889
NYHA class III or more	1.223 (0.813–1.840)	0.3332	1.580 (0.465–5.367)	0.4636
Diabetes	1.410 (1.087–1.830)	0.0097	2.286 (0.971–5.384)	0.0585
Age (per 1 year increase)	1.012 (0.998–1.025)	0.0968	0.984 (0.941–1.028)	0.4688
Creatinine level (per 10 μmol/l increase)	1.001 (0.999–1.004)	0.3094	1.000 (0.988–1.011)	0.9582
LVEF (per 5% increase)	0.976 (0.912–1.046)	0.4968	1.212 (0.894–1.643)	0.2149
Hematocrit (per 10% increase)	1.073 (0.761–1.513)	0.6887	2.735 (0.841–8.895)	0.0946
Admission years 2015-16 vs 2006-7	0.853 (0.659–1.103)	0.2255	0.987 (0.409–2.382)	0.9769

CAD — coronary artery disease; COPD — chronic obstructive pulmonary; LVEF — left ventricular ejection fraction; NYHA — New York Heart Association