Guideline-directed medical therapy for secondary prevention after coronary artery bypass grafting in patients with depression ☆

Malin Stenman [a,b], Martin J. Holzmann [c,d], Ulrik Sartipy [a,b],*

[a] Department of Cardiothoracic Surgery and Anesthesiology, Karolinska University Hospital, Sweden
[b] Department of Molecular Medicine and Surgery, Karolinska Institutet, Sweden
[c] Department of Emergency Medicine, Karolinska University Hospital, Sweden
[d] Department of Internal Medicine, Karolinska Institutet, Stockholm, Sweden

ABSTRACT

Background: We hypothesized that depressed patients would have lower use of guideline-directed medical therapy for secondary prevention of cardiovascular events following coronary artery bypass grafting (CABG).
Methods: We included all patients who underwent primary isolated CABG in Sweden between 2006 and 2008. We cross-linked individual level data from national Swedish registers. Preoperative depression was defined as at least one antidepressant prescription dispensed before surgery. We defined medication use as at least two dispensed prescriptions in each medication class (antiplatelet agents, beta-blockers, angiotensin-converting enzyme inhibitors (ACEI)/angiotensin II receptor blocker (ARB), and statins) within a rolling 12 month period. We calculated adjusted risk ratios (RR) for the use of each medication class, and for all four classes, after one and four years, respectively.
Results: During the first year after CABG, 93% of all patients (n = 10,586) had at least two dispensed prescriptions for an antiplatelet agent, 68% for an ACEI/ARB, 91% for a beta-blocker, and 92% for a statin. 57% had prescriptions for all four medication classes. After four years (n = 4034), 44% had filled prescriptions for all four medication classes. Preoperative depression was not significantly associated with a lower use of all four medication classes after one year (RR 0.98, 95% confidence interval (CI) 0.93–1.03) or after four years (RR 0.97, 95% CI 0.86–1.09).
Conclusions: Preoperative depression was not associated with lower use of guideline-directed medical therapy for secondary prevention after CABG. These findings suggest that the observed higher mortality following CABG among depressed patients is not explained by inadequate secondary prevention medication.

1. Introduction

Prior research has shown that depression is common in patients with coronary artery disease and that it is independently associated with increased cardiovascular morbidity and mortality [1,2]. Approximately 30 to 45% of all patients with coronary artery disease are suffering from clinically significant depression [3]. Optimal secondary prevention medications after coronary artery bypass grafting (CABG) include antiplatelet agents, statins, beta-blockers and angiotensin-converting inhibitors (ACEI) and are important to reduce the risk for recurrent cardiovascular events [4]. Clinical practice guidelines provide information and recommendations about patient lifestyle and medical therapy after CABG [5,6]. Because depression has been established as a strong and important independent risk factor for recurrent cardiovascular events and mortality in patients with coronary heart disease, the use of evidence-based secondary prevention is even more essential among these patients. However, the coexistence of depression and coronary heart disease may complicate several aspects of secondary prevention for coronary heart disease. Psychosocial risk factors such as smoking, unhealthy food choice, less physical exercise tend to accumulate in the same individuals and behavioral phenomena common in depressed patients, e.g. social isolation, a feeling of hopelessness and little belief in that anything is worthwhile, may act as barriers to secondary preventive efforts [7,8]. Based on these observations, it is not unlikely that depressed patients could face an increased risk of receiving less than optimal secondary prevention medications. Lower use of secondary prevention medications may partly explain the higher mortality observed in patients with depression and coronary heart disease. The hypothesis

was that depressed patients would have lower use of medications recommended for secondary prevention of cardiovascular events following CABG than patients without preoperative depression. The primary aim was to analyze the association between preoperative depression and guideline-directed medical therapy after CABG. A secondary aim was to investigate possible changes in medication use over time. We also investigated possible gender differences in secondary prevention medication use.

2. Methods

2.1. Study design

We performed a nationwide population-based cohort study. The study complied with the Declaration of Helsinki and was approved by the regional Human Research Ethics Committee in Stockholm, Sweden.

2.2. Study population

We identified all patients who underwent CABG in Sweden between 2006 and 2008 from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) registry [9]. We excluded patients who had undergone previous cardiac surgery, and patients who had concomitant procedures in addition to CABG. We also excluded patients who underwent surgery within 24 h from decision to operate. Finally, we excluded patients who died within one year of surgery, because the outcome of interest was dispensed prescriptions after a minimum of one year of follow-up. The final study population consisted of patients who underwent primary isolated non-emergent CABG in Sweden between 2006 and 2008.

2.3. Data sources

The Swedish personal identity number [10] was used by The National Board of Health and Welfare to cross-link individual level data from national Swedish registers to assemble the study database. Baseline patient characteristics were obtained from SWEDEHEART [9], The National Patient Register, The Prescribed Drug Register and The Total Population Register (Statistics Sweden). The National Patient Register covers all diagnoses for all patients hospitalized in Sweden from 1987 [11,12]. The Prescribed Drug Register [13] was used to identify patients using antidepressants (Anatomical Therapeutic Chemical [ATC] code N06A) and who had at least one dispensed prescription with ATC-code N06A before the date of surgery. Patients were divided into an exposed group (preoperative antidepressant use) and an unexposed group (no preoperative antidepressant use).

2.4. Outcome measures

We identified patients using the personal identity number who had at least two dispensed prescriptions with the following ATC-codes: B01AC (antiplatelet agents), C09 (ACEI/angiotensin receptor blockers (ARB)), C07 (beta-blockers), and C10AA (statins) from the national Prescribed Drug Register [13]. The Prescribed Drug Register contains information about the ATC-code and the date of dispensing covering the whole population of Sweden since July 2005. The primary outcome measure was medication use defined as at least two dispensed prescriptions in each ATC group (medication class) after at least one year of follow-up, and at least four years of follow-up, respectively.

2.5. Statistical analyses

To describe baseline characteristics means and standard deviations were used for continuous variables and frequencies and percentages for categorical variables. We used modified Poisson regression [14] with a robust estimator of variance to calculate risk ratios (RR) for the use of each medication class for depressed patients with non-depressed patients as reference category. We reported unadjusted and multivariable adjusted RR with 95% confidence intervals (CI). The following variables were included in the full multivariable model: age (continuous variable), sex, current smoking (no/yes), atrial fibrillation (no/yes), diabetes mellitus (no/yes), hyperlipidemia (no/yes), hypertension (no/yes), chronic obstructive pulmonary disease (no/yes), peripheral vascular disease (no/yes), prior myocardial infarction (no/yes), prior stroke (no/yes), left ventricular ejection fraction (normal, moderate, or poor), and preoperative heart failure (no/yes). We also analyzed the distribution of medication class and medication use in men and women separately. Finally, we investigated the time trend in secondary prevention medication by comparing the distribution of medication class for patients who underwent surgery in 2006 to that of patients who underwent surgery during 2008.

2.6. Missing data

Data were missing for some variables: diabetes mellitus (2.8%), current smoking (13%), hyperlipidemia (10%), hypertension (10%), peripheral vascular disease (0.9%), and preoperative left ventricular function (0.9%). We used multiple imputation [15] to handle missing data and imputed 50 datasets. All multivariable analyses were performed on the imputed data.

Stata version 13.0 (StataCorp LP, College Station, TX) was used for all data management and statistical analysis.

3. Results

From the SWEDEHEART registry 14,032 patients who underwent CABG between January 2006 and December 2008 were identified. We excluded 227 patients who had previous heart surgery, 2261 patients who had another cardiac procedure than isolated CABG, 660 patients who were operated within 24 h from decision, and 298 patients who had a shorter follow-up time than one year. The final study population included 10,586 patients (1132 depressed and 9454 non-depressed) who underwent primary isolated non-emergent CABG. The baseline characteristics are presented in Table 1. Female sex, current smoking,

Table 1
Characteristics of the study population.

	All patients	Antidepressant use	
		No	Yes
Number of patients	10,586	9454	1132
Percent of study population	100	89	11
Age (years)	67.1 (9.2)	67.3 (9.1)	65.2 (9.4)
Female sex (%)	20	19	34
Estimated GFR (mL/min/1.73 m²)	82 (25)	82 (25)	83 (24)
Diabetes mellitus (%)	24	23	33
Atrial fibrillation (%)	3	3	2
Hypertension (%)	59	58	62
Hyperlipidemia (%)	60	59	64
Peripheral vascular disease (%)	8	8	10
Current smoking (%)	18	17	28
COPD (%)	6	6	10
Prior myocardial infarction (%)	46	45	47
Prior heart failure (%)	3	3	4
Prior stroke (%)	5	5	10
Left ventricular function			
Ejection fraction >50% (%)	71	71	70
Ejection fraction 30–50% (%)	25	25	26
Ejection fraction <30% (%)	4	4	4

GFR = glomerular filtration rate, CABG = coronary artery bypass grafting, COPD = chronic obstructive pulmonary disease. Age and GFR are given as means with standard deviations. All other values are percentages.