Use of β-blocker therapy in older patients after acute myocardial infarction in Ontario

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Abstract

Background: Despite its proven efficacy, β-blocker therapy remains underused in elderly patients after myocardial infarction (MI). The objectives of this study were to identify undertreated groups of seniors and to determine whether older and frailer patients are being selectively dispensed low-dose β-blocker therapy.

Methods: From a comprehensive hospital discharge database, all people aged 66 years or more in Ontario who survived an acute MI between April 1993 and March 1995 were identified and classified into those who did not receive β-blocker therapy and those dispensed low, standard or high doses of this agent. Logistic regression models were used to study the effect of age, sex, comorbidity, potential contraindications to β-blocker therapy and residence in a long-term-care facility on the odds of not being dispensed a β-blocker. Among β-blocker users, the odds of being dispensed low relative to standard or high doses of this agent were evaluated.

Results: Of the 15 542 patients, 7549 (48.6%) were not dispensed a β-blocker. Patients 85 years of age or more were at greater risk of not receiving β-blocker therapy (adjusted odds ratio [OR] 2.8, 95% confidence interval [CI] 2.5–3.2) than were those 66 to 74 years. Having a Charlson comorbidity index of 3 or greater was associated with an increased risk of not receiving β-blocker therapy (adjusted OR 1.5, 95% CI 1.3–1.8) compared with having lower comorbidity scores. Patients who resided in a long-term-care facility were at increased risk of not being prescribed β-blocker therapy (adjusted OR 2.6, 95% CI 2.0–3.4). Among the 5453 patients with no identifiable contraindication to β-blocker therapy, women were significantly less likely than men to receive this agent ($p = 0.005$). Of the 6074 patients who received β-blockers, 2248 (37.0%) were dispensed low-dose therapy. Patients aged 85 years or more had an increased risk of being dispensed low-dose therapy (adjusted OR 1.6, 95% CI 1.3–2.0) compared with those aged 66 to 74 years. Compared with those who had the lowest comorbidity scores, patients with the highest comorbidity scores were more likely to be dispensed low-dose β-blocker therapy (adjusted OR 1.3, 95% CI 1.0–1.8).

Interpretation: Almost half of Ontario patients aged 66 or more who survived an MI, particularly those who were older or frailer, did not receive β-blocker therapy. Among those dispensed β-blocker therapy, older and frailer patients were more frequently dispensed low-dose therapy.

Despite its proven efficacy, β-blocker therapy remains underused in elderly patients after myocardial infarction (MI). Neither Canadian[1] nor US[2] guidelines identify age as a contraindication to the use of β-blocker therapy for secondary prevention after MI. Only 21% of highly selected elderly Medicaid recipients in New Jersey,[3] 19% of seniors in a hospital-based geriatric practice and 8% of older people admitted to a nursing home[4] received the benefit of β-blocker therapy after MI. Seniors of advanced age and those who are frail may be a particularly undertreated group.

Evidence

Études

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Older patients, particularly women, are more susceptible to adverse drug effects (an estimated 76% of which are dose dependent)[5] than are other patients. Dosing is, therefore, a critical issue when prescribing drug therapy for seniors. The major randomized controlled trials documenting the benefit of atenolol,[6] metoprolol,[7] timolol[8] and propranolol[9] after MI used relatively high dosages of these agents. Only the Beta Blocker Heart Attack Trial[9] allowed for any dosage adjustment. Older people may be less tolerant than others to these high dosages because of their frailty, low weight and use of several medications.[10–12] We know little about the most appropriate β-blocker dosage for seniors.

For these reasons, we performed a study using a population-based sample of all elderly people surviving an acute MI in Ontario. Our objectives were to identify undertreated groups of seniors and to determine whether older and frailer patients are being selectively dispensed low-dose β-blocker therapy.

Methods

We used a comprehensive hospital discharge database containing information on demographic characteristics, concomitant conditions and drug use obtained from linked administrative databases in Ontario. The data came from the Canadian Institute for Health Information database, an administrative database based on hospital discharge abstracts linked by unique health card numbers to the Ontario Drug Benefit Plan (ODB) database. The ODB provides comprehensive drug coverage to people aged 65 years or more in the province.

We identified all patients aged 66 years or more residing in Ontario who were admitted to an acute care hospital between Apr. 1, 1993, and Mar. 31, 1995, with a most responsible diagnosis (i.e., the diagnosis most responsible for the hospital stay) of acute MI (code 410, International Classification of Diseases, 9th revision, clinical modification [ICD-9-CM][13]). We excluded patients aged 65 years at the time of their MI because their drug therapy dispensed in the previous year (i.e., age 64) could not be evaluated.

There were 19 970 acute care hospital discharges of patients who had had an MI. To avoid misdiagnosing acute MI, we excluded 96 admissions where the patients had signed themselves out of hospital, 2113 admissions where the length of stay was less than 4 days, as these were unlikely to represent MI,[14–17] and 30 admissions where the patient was readmitted with MI within 8 weeks of the previous discharge. In addition, we excluded 88 admissions associated with a lengthy stay (60 days or more) because they were not typical of usual patients with MI. Admissions of non-Ontario residents and of people with invalid health card numbers (383 cases) were not included because accurate follow-up was unavailable. Finally, 190 patients discharged to chronic care facilities were excluded because they did not obtain their medications from the ODB. A total of 2900 admissions representing 1786 patients were removed, leaving a sample of 15 542 patients. The first admission with a most responsible diagnosis of MI during the study period was identified as the index admission.

Age was classified into 3 groups: 66 to 74 years, 75 to 84 years, and 85 years or more.[18] Comorbidity was measured with the use of the Charlson Index[19] adapted by Deyo, Cherkin and Ciol[20] for use in computerized databases and was calculated based on information available from the index admission. Charlson Index scores were divided into 3 groups: low (0 or 1), mid (2) and high (3 or greater).

For each patient, we determined whether any oral β-blocker therapy had been dispensed in the year following discharge. The β-blocker dosage was calculated for all seniors with at least 2 claims for the same β-blocker therapy. Prescription intervals of more than 100 days were excluded because the maximum prescription interval allowed by the ODB is 100 days. To avoid miscalculating drug dosage, we excluded drug claim information inconsistent with clinical practice, such as calculated dosages of more than 8 pills per day (30 cases) and time between index and next prescription of less than 7 days (84 cases).

For each course of β-blocker therapy, we estimated the daily dosage. The ODB provides information on the quantity of pills dispensed, not the daily dosage. We calculated the average dosage using the interval between the index and the next claim for the same drug therapy. For example, if the patient was dispensed metoprolol at a dosage of 50 mg for 30 days and was given 15 pills, the calculated drug dosage would be (15 tablets/30 days) × 50 mg/tablet, for an estimated daily dosage of 25 mg. We rounded the calculated average dosage to one that was clinically plausible.[21–23] This method of dosage calculation has been used in a previous study.[24]

The β-blocker dosage was classified into 4 mutually exclusive groups: not dispensed, low, standard or high. A low dosage was defined as a dosage lower than that achievable with the smallest tablet size available, a standard dosage as that achieved with available tablet sizes, and a high dosage as a dosage at least as high as those evaluated in clinical trials[6–9] (Table 1).

We identified patients with potential contraindications to β-blocker therapy using a definition similar to that used in the Canadian consensus guidelines for the management of patients after MI.[1] For the year before the index admission, we evaluated the Canadian Institute for Health Information discharge abstracts to identify hospital admissions with a primary diagnosis of asthma (ICD-9-CM code 493) or chronic obstructive pulmonary disease (COPD) (ICD-9-CM code 496), congestive heart failure (ICD-9-CM code 428), heart block (ICD-9-CM code 426), hypotension (ICD-9-CM code 458) or bradycardia (ICD-9-CM code 427.8). We used the ODB database to identify patients dispensed medications to treat these conditions. For example, patients with asthma or COPD were identified by their use of re-

Table 1: Classification of low-, standard- and high-dose therapy for all β-blocker therapy available from the Ontario Drug Benefit Plan database

	Type of therapy; dosage, mg/d		
β-blocker	Low dose	Standard dose	High dose
Atenolol[6]	< 50	50 to < 100	≥ 100*
Metoprolol[7]	< 100	100 to < 200	≥ 200*
Propranolol[9]	< 30	30 to < 180	≥ 180*
Timolol[8]	< 10	10 to < 20	≥ 20*
Acebutolol	< 200	200 to < 600	≥ 200†
Labetalol	< 200	200 to < 800	≥ 800†
Nadolol	< 40	40 to < 240	≥ 240†
Pindolol	< 5	5 to < 40	≥ 40†
Sotalol	< 160	160 to < 320	≥ 320†

*Based on dosages equal to or greater than those evaluated in randomized controlled trials.
†Based on highest recommended dosage for angina.[23]

lated medications (e.g., salbutamol, ipratropium or beclomethasone dipropionate), patients with congestive heart failure through their receipt of furosemide and digoxin, or of furosemide and an angiotensin-converting enzyme (ACE) inhibitor, or of an ACE inhibitor and digoxin, and diabetic patients by their use of insulin therapy.

We used descriptive statistics to compare age, sex, comorbidity and presence of potential contraindications to β-blocker therapy between patients who were dispensed β-blocker therapy and those who were not. We estimated odds ratios (ORs) contrasting β-blocker therapy in one subgroup versus another (e.g., patients aged 66 to 74 v. those aged 75 to 84) and determined 95% confidence intervals (CIs) using logistic regression to adjust for other factors. For all analyses we included the patient's age, sex, Charlson comorbidity score and presence of potential contraindications to β-blocker therapy (i.e., congestive heart failure, asthma or COPD, diabetes mellitus, heart block, hypotension or bradycardia) and whether the patient was a resident of a long-term care facility.

For the 6074 β-blocker users for whom dosage could be calculated, we used these same factors to identify the characteristics of patients dispensed low-dose relative to standard-dose or high-dose therapy. We used logistic regression to adjust for other factors.

For each of the analyses, p values of less than 0.05 were considered significant.

Results

Of our sample of 15 542 patients, 6940 (44.6%) were women. The women were significantly older than the men (median age 76 v. 73 years, $p = 0.001$). Women were disproportionately represented among those aged 85 years or more (994 women [14.3%] v. 595 men [6.9%], $p = 0.001$). The patients were relatively frail: 3477 (22.4%) had a Charlson comorbidity score of 2 or more.

Of the 15 542 patients, 5453 (35.1%) had no identifiable contraindications to β-blocker therapy. Of the 5453, 1607 (29.5%) were not dispensed this agent despite being "ideal candidates" for β-blocker therapy. Women in this group were significantly more likely than men not to receive β-blocker therapy ($p = 0.005$).

Table 2 shows the characteristics of the study population and of the 7549 patients (48.6%) who were not dispensed β-blocker therapy. Compared with those 66 to 74 years of age, patients 85 years or older were at greater risk of not being dispensed β-blocker therapy (adjusted OR 2.8, 95% CI 2.5–3.2). After age and clinical factors were controlled for, women and men had a similar risk of not being

Table 2: Characteristics of Ontario patients aged 66 years or more who survived an acute myocardial infarction between Apr. 1, 1993, and Mar. 31, 1995, and their relation to not being dispensed β-blocker therapy

Characteristic	Group; % of patients: All *n = 15 542*	Not dispensed β–blocker therapy *n = 7549*	Unadjusted OR (and 95% CI)	Adjusted OR (and 95% CI)
Age, yr				
66–74*	50.0	40.6	1.0	1.0
75–84	39.8	53.3	1.3 (1.3–1.4)	1.5 (1.4–1.6)
≥ 85	10.2	69.2	1.7 (1.6–1.8)	2.8 (2.5–3.2)
Sex				
Male*	55.3	47.3	1.0	1.0
Female	44.7	50.1	1.1 (1.0–1.1)	0.9 (0.9–1.0)
Charlson comorbidity index score				
0–1*	77.6	43.0	1.0	1.0
2	14.7	66.7	1.6 (1.5–1.6)	1.5 (1.4–1.7)
≥ 3	7.7	70.6	1.6 (1.6–1.7)	1.5 (1.3–1.8)
Potential contraindications to β-blocker therapy†				
CHF	38.2	67.4	1.8 (1.8–1.9)	2.6 (2.4–2.8)
COPD/asthma	27.4	62.5	1.4 (1.4–1.5)	2.0 (1.9–2.2)
Diabetes mellitus	20.7	57.5	1.2 (1.2–1.3)	1.3 (1.2–1.4)
Heart block	7.3	59.7	1.3 (1.2–1.3)	1.5 (1.3–1.7)
Hypotension	2.3	55.7	1.2 (1.0–1.3)	1.1 (0.9–1.4)
Bradycardia	4.4	53.4	1.1 (1.0–1.2)	1.1 (1.0–1.3)
Residence in long-term care facility				
No*	97.1	47.6	1.0	1.0
Yes	2.9	80.8	1.7 (1.6–1.8)	2.6 (2.0–3.4)

Note: OD = odds ratio, CI = confidence interval, CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease.
*Reference group.
†Categories are not mutually exclusive.

dispensed β-blocker therapy (adjusted OR 0.9, 95% CI 0.9–1.0). Patients with a Charlson comorbidity index score of 3 or greater had a higher risk of not being dispensed β-blocker therapy than patients with lower comorbidity scores (adjusted OR 1.5, 95% CI 1.3–1.8). Being a resident of a long-term care facility was associated with a higher risk of not being dispensed β-blocker therapy (adjusted OR 2.6, 95% CI 2.0–3.4).

Among the 6074 patients who received β-blockers, the agents dispensed most frequently were metoprolol (3105 patients [51.1%]), atenolol (1603 [26.4%]) and acebutolol (710 [11.7%]). Of the 6074, 2248 (37.0%) received low-dose β-blocker therapy, 3068 (50.5%) received standard-dose therapy, and 758 (12.5%) received high-dose therapy.

The characteristics of patients who received low-dose therapy relative to those who received standard-dose or high-dose therapy are given in Table 3. The mean age (and standard deviation) of the patients in the 2 groups was 74.8 (6.2) and 73.5 (5.7) years respectively, and the mean Charlson comorbidity scores (and standard deviation) were 0.68 (1.0) and 0.58 (0.9) respectively. Patients 85 years of age or older had a higher risk of receiving low-dose therapy than patients aged 66 to 74 (adjusted OR 1.6, 95% CI 1.3–2.0). No significant sex difference was found in the use of low-dose therapy versus standard- or high-dose therapy. Patients with the highest Charlson comorbidity index scores had a higher risk of receiving low-dose therapy than patients with the lowest comorbidity scores (adjusted OR 1.3, 95% CI 1.0–1.8). Patients who received low-dose therapy were more likely than those who received higher dosages to have a previous history of CHF (adjusted OR 1.3, 95% CI 1.2–1.5). No differences were found in the dispensing of low-dose therapy on the basis of residence in a long-term care facility.

Interpretation

We found that almost half of patients in Ontario aged 66 or more who survived an MI and who had no identifiable contraindications did not receive β-blocker therapy despite its proven secondary prevention benefit. This result is more encouraging than those published in the United States. Soumerai and colleagues[3] evaluated a group of low-income seniors in New Jersey who had had an MI. After excluding patients with potential contraindications to β-blocker therapy, they found that only 21% of the 3737

Table 3: Characteristics of patients dispensed low-dose β-blocker therapy relative to standard- or high-dose therapy

Characteristic	Group; % of patients: All *n = 6074*	Low-dose *n = 2248*	Unadjusted OR (and 95% CI)	Adjusted OR (and 95% CI)
Age, yr				
66–74*	58.7	33.4	1.0	1.0
75–84	35.3	41.4	1.2 (1.2–1.3)	1.4 (1.2–1.5)
≥ 85	6.0	46.3	1.4 (1.2–1.6)	1.6 (1.3–2.0)
Sex				
Male*	56.4	36.4	1.0	1.0
Female	43.6	37.8	1.0 (1.0–1.1)	1.0 (0.9–1.1)
Charlson comorbidity index score				
0–1*	86.8	36.3	1.0	1.0
2	9.2	39.9	1.1 (1.0–1.2)	1.1 (0.9–1.3)
≥ 3	4.0	46.1	1.3 (1.1–1.5)	1.3 (1.0–1.8)
Potential contraindications to β-blocker therapy†				
CHF	23.0	44.0	1.3 (1.2–1.4)	1.3 (1.2–1.5)
COPD/asthma	19.3	38.1	1.0 (1.0–1.1)	1.0 (0.9–1.1)
Diabetes	16.7	34.4	0.9 (0.8–1.0)	0.8 (0.7–0.9)
Heart block	5.6	44.1	1.2 (1.1–1.4)	1.3 (1.0–1.6)
Hypotension	2.0	47.9	1.3 (1.1–1.6)	1.4 (1.0–2.1)
Bradycardia	4.0	42.3	1.1 (1.0–1.3)	1.1 (0.9–1.5)
Residence in long-term care facility				
No*	99.0	36.9	1.0	1.0
Yes	1.0	45.0	1.2 (0.9–1.6)	1.1 (0.6–1.8)

*Reference group.
†Categories are not mutually exclusive.

patients evaluated received β-blocker therapy. Only 34% of the patients in the Cooperative Cardiovascular Project database, containing information for 201 752 Medicare recipients surviving an MI, received β-blocker therapy.[25] Of the subset of 45 308 patients considered "ideal candidates" for β-blocker therapy, 50% were prescribed it at discharge. Our sample of over 15 000 MI survivors reflects all seniors in Ontario, independent of socioeconomic status, and our analyses adjusted for potential contraindications to β-blocker therapy. Thus, our sample may more adequately reflect β-blocker use in elderly people.

As might be expected, we found that the oldest patients, those with higher comorbidity scores and those who resided in long-term-care facilities were undertreated with β-blocker therapy. Furthermore, our findings suggest that many seniors who receive β-blocker therapy have an identifiable potential contraindication to this agent. Our results are consistent with those of Gottlieb, McCarter and Vogel,[26] who documented that MI survivors with CHF, COPD or diabetes are frequently prescribed β-blockers. Because treatment with β-blockers in these high-risk groups is associated with lower death rates,[26] our findings highlight the need to prescribe a β-blocker if it can be tolerated by the patient.

Our results suggest that women may be undertreated with β-blocker therapy. Almost 30% of the women in our study with no identifiable contraindication to β-blocker therapy were not dispensed this therapy. Undertreatment of women may be due in part to the difference in age, women being on average 10 years older than men when coronary symptoms first develop.[27] Nonetheless, underprescribing of β-blocker therapy for women is particularly troubling given that short-term prognoses after MI may be worse for women than for men.[10] These findings indicate an opportunity to target women for secondary prevention therapy.

Our results suggest that low-dose therapy is being preferentially dispensed in clinical practice to more vulnerable groups of older and frail seniors. We found that older patients, those with greater comorbidity and those with CHF as a potential contraindication to therapy were more likely to be dispensed low-dose β-blocker therapy. We do not know the optimal β-blocker dosage for these groups, as generally they were excluded from participation in the major trials.[6–9] Given that only 4.9% of the patients in our entire sample were prescribed β-blocker therapy at the high dosages evaluated in these trials, we need to determine the minimum effective β-blocker dosage for seniors.

Our study has several important limitations. First, our database cannot control for all the factors that may influence a physician's decision to prescribe β-blocker therapy. We are confident, however, in our ability to control for key variables, such as age, sex and concomitant conditions. Second, no single set of criteria are available that define contraindications to β-blocker therapy. We chose to model our list of contraindications to β-blocker therapy after those outlined in the Canadian guidelines[1] as these may be followed most closely by Canadian physicians and are similar to US guidelines.[2] The proportion of patients we identified as ideal candidates for β-blocker therapy is consistent with the proportions reported in the Cooperative Cardiovascular Project using the American College of Cardiology/American Heart Association criteria. Third, our data may overestimate some contraindications to β-blocker therapy. For example, although CHF can be a complication of β-blocker therapy, this same therapy can be used as CHF treatment. Finally, our data are from Ontario and may not reflect prescribing practices in other jurisdictions. However, Ontario is the largest Canadian province and contains over one-third of the Canadian population.

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