

Suboptimal Use of Cardioprotective Drugs in Newly Treated Elderly Individuals With Type 2 Diabetes

CAROLINE SIROIS, BPHARM, MSC^{1,2,3}
JOCELYNE MOISAN, PHD^{1,2}

PAUL POIRIER, MD, PHD^{1,4}
JEAN-PIERRE GRÉGOIRE, MPH, PHD^{1,2}

Cardiovascular disease is the main complication experienced by elderly individuals with diabetes (1). Despite randomized trials showing the benefits of individual (2–4) or combined (5) pharmacological treatments of cardiovascular risk factors in diabetes, observational studies have shown suboptimal use of medications (6–8). However, little is known about the use of cardioprotective medication among elderly individuals who were not already taking it before diabetes treatment was undertaken. We therefore studied a population of elderly individuals with type 2 diabetes in the province of Quebec, Canada, who had not been treated with any antihypertensive, lipid-lowering, or antiplatelet drugs in the year before oral antidiabetes drug initiation. We assessed whether they used a comprehensive cardioprotective regimen (CCR) of those three medications in the year following oral antidiabetic initiation. We also identified the determinants of a CCR use.

RESEARCH DESIGN AND METHODS

— We carried out a population-based inception cohort study using the Quebec Diabetes Surveillance System, which is the product of linking public health administrative databases managed by the Quebec Health Insurance Board. It includes information on patient demographics, physician and hospital services, and data from the public drug plan for

individuals who had been diagnosed with diabetes.

We selected individuals aged ≥ 66 years who had initiated an oral antidiabetes medication treatment between 1 January 1998 and 31 December 2002. The date of the first claim was the index date. We excluded individuals who had received any insulin or oral antidiabetes, antiplatelet, antihypertensive, or lipid-lowering drugs during the 365 days before the index date. We also excluded those who had not been beneficiaries of the drug plan for the entire 365-day period before the index date and individuals who had not for at least 1 year of follow-up.

A person was deemed to have a CCR if there was at least one claim for each of the following: an antihypertensive, lipid-lowering, and antiplatelet drug in the year following the index date. Each of the three drugs could be used at different times during follow-up.

Potential determinants of CCR use included sex, age, and residential area of the individuals; year of oral antidiabetes agent initiation; and whether the oral antidiabetes therapy was initiated in the 14 days posthospitalization. Other potential determinants measured in the year before the index date were included: 1) number of outpatient medical visits, 2) hospitalization, and 3) cardiovascular disease.

The proportion of individuals using a CCR was calculated. Determinants of CCR use were identified using multivariate

logistic regression. Odds ratios and their 99% CIs were calculated. Analyses were carried out using SAS, version 9.1.

This research was approved by the Commission d'accès à l'information du Québec and the Comité d'éthique à la Recherche du Centre Hospitalier Affilié Universitaire de Québec.

RESULTS — Among the 12,150 individuals included in the cohort, 2,649 (21.8%) received an antiplatelet drug, 4,813 (39.6%) received an antihypertensive drug, and 2,562 (21.1%) received a lipid-lowering drug in the year following the oral antidiabetes medication initiation. Only 882 (7.6%) individuals received a CCR.

In the multivariate analysis, three out of eight potential determinants of CCR use remained statistically significant at the α level of 0.01 (Table 1). An older age at oral antidiabetes medication therapy initiation was inversely associated with CCR use, whereas suffering from cardiovascular disease was positively associated with the use of a CCR. The odds of being exposed to a CCR also increased over the time period (3.5% in 1998, 3.8% in 1999, 7.3% in 2000, 10.4% in 2001, and 12.9% in 2002).

CONCLUSIONS — Among elderly individuals not exposed to cardiovascular drugs in the year before the initiation of oral antidiabetes medication therapy, the proportion of CCR users is low (7.6%). If diabetes is to be considered a cardiovascular equivalent (9), these results suggest that the management of cardiovascular risk for those patients is less than appropriate.

Other studies have demonstrated gaps in the use of cardiovascular risk-modifying drugs among elderly individuals with diabetes (10–11). Of 105,715 elderly individuals in Ontario, Canada, around two-thirds used antihypertensive agents and about one-quarter received a lipid-lowering drug in a period of 6 months following the 1st year of diabetes diagnosis (11).

A low proportion of the combined use

From the ¹Faculty of Pharmacy, Laval University, Quebec, Canada; the ²Population Health Research Unit, Centre Hospitalier Affilié Universitaire de Québec, Quebec, Canada; the ³Institut National de Santé Publique du Québec, Quebec, Canada; and the ⁴Quebec Heart Institute, Laval Hospital, Quebec, Canada.

Address correspondence and reprint requests to Jean-Pierre Grégoire, Population Health Research Unit, Centre Hospitalier Affilié Universitaire de Québec, 1050, Chemin Sainte-Foy, Québec, Quebec City, Canada, G1S 4L8. E-mail: jean-pierre.gregoire@pha.ulaval.ca.

Received for publication 3 November 2006 and accepted in revised form 14 March 2007.

Published ahead of print at <http://care.diabetesjournals.org> on 20 March 2007. DOI: 10.2337/dc06-2257.

Abbreviations: CCR, comprehensive cardioprotective regimen.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

© 2007 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Table 1—Determinants of CCR* use among individuals who did not receive any cardioprotective drug in the year prior to antidiabetes treatment initiation (n = 12,150)

Characteristics	n (%)	Unadjusted OR (99% CI)	P	Adjusted OR (99% CI)	P
Age (years)	72.4 ± 5.8	0.92 (0.90–0.94)	<0.0001	0.90 (0.89–0.92)	<0.0001
Sex					
Male	6,996 (57.6)	1.36 (1.12–1.63)	<0.0001	1.08 (0.89–1.32)	0.2971
Female	5,154 (42.4)	1.00	—	1.00	—
Residency area†					
Rural	3,163 (26.0)	1.24 (1.01–1.52)	0.0076	1.21 (0.98–1.51)	0.0225
Agglomeration	1,379 (11.4)	1.21 (0.92–1.61)	0.0763	1.18 (0.88–1.59)	0.1536
Metropolitan	7,477 (61.5)	1.00	—	1.00	—
Unknown	131 (1.01)	—	—	—	—
Reference year					
1998	2,815 (23.2)	1.00	—	1.00	—
1999	2,563 (21.1)	1.08 (0.74–1.57)	0.6012	1.06 (0.72–1.56)	0.6849
2000	2,287 (18.8)	2.15 (1.54–3.00)	<0.0001	2.17 (1.53–3.06)	<0.0001
2001	2,315 (19.1)	3.19 (2.32–4.37)	<0.0001	3.35 (2.41–4.65)	<0.0001
2002	2,170 (17.9)	4.05 (2.97–5.52)	<0.0001	4.44 (3.21–6.13)	<0.0001
Antidiabetes agent initiated posthospitalization					
Yes	428 (3.5)	2.53 (1.78–3.61)	<0.0001	1.48 (0.97–2.25)	0.0171
No	11,722 (96.5)	1.00	—	1.00	—
Cardiovascular disease in the year prior to antidiabetes treatment initiation‡					
Yes	1,467 (12.1)	5.65 (4.64–6.87)	<0.0001	5.85 (4.65–7.37)	<0.0001
No	10,683 (87.9)	1.00	—	1.00	—
Medical visits in the year prior to antidiabetes treatment initiation	4.5 ± 4.7	0.99 (0.96–1.01)	0.0787	0.99 (0.96–1.01)	0.0920
Hospitalization in the year prior to antidiabetes treatment initiation					
Yes	2,851 (23.5)	2.063 (1.71–2.49)	<0.0001	1.20 (0.94–1.52)	0.0530
No	9,299 (76.5)	1.00	—	1.00	—

Data are means ± SD or n (%) unless otherwise indicated. *A person was deemed to have a CCR if there was at least one claim for each of the following in the year following the index date: an antihypertensive, lipid-lowering, and antiplatelet drug. Each of drug could be used at different times during follow-up. †Metropolitan: urban core of at least 100,000 people and its adjacent municipalities; agglomeration: urban core of at least 10,000 people and its adjacent municipalities; rural: municipalities not included in the two former categories. ‡A person was deemed to have a cardiovascular disease if there were any outpatient or hospital ICD (International Classification of Diseases)-9 code for ischemic cardiac disease, heart failure, or cerebrovascular disease or a procedural code of revascularization, coronary bypass, or peripheral limb revascularization recorded. A person with a prescription claim for a nitrate was also considered to have cardiovascular disease.

of antiplatelet drugs, statins, and ACE inhibitors was also found in a cohort of individuals with various length and duration of diabetes in Saskatchewan, Canada (12). In that study, of 12,106 patients aged 30–105 years, 596 (5%) used the combined treatment (12).

Some of the factors associated with CCR use in our study have been observed by others. Younger type 2 diabetic patients (13) and those suffering from cardiovascular disease (14) were found to be more likely to obtain aggressive cardiovascular treatments. Improvement in use of cardiovascular drugs through recent years has been reported (8,15). On the other hand, it has been reported that women with diabetes were less likely than men to receive acetylsalicylic acid (14,16) or lipid-lowering drugs (17) or to have

blood pressure and cholesterol levels below current targets (18). In our population of newly treated individuals, sex did not appear to influence the use of a CCR.

The unavailability of clinical data in the administrative data used represents a limitation of the study, making it difficult to evaluate individual appropriateness of CCR use. However, according to clinical guidelines, the majority of individuals would qualify for CCR use. Most elderly individuals require pharmaceutical agents to reach aggressive blood pressure (130/80 mmHg) and LDL cholesterol (2.6 mmol/l) targets (19,20). The vast majority of elderly individuals with diabetes should also be using ACE inhibitors or angiotensin receptor antagonists for vascular protection (21). Moreover, all individuals included in our study should have

received an antiplatelet drug unless contraindicated (19,20).

All in all, this study indicates that initiating a new antidiabetes agent does not much influence the use of a CCR. Future studies should evaluate the underlying risk of patients with clinical information and assess whether a CCR is beneficial in terms of outcomes.

Acknowledgments

C.S. was a recipient of Canada's Research-Based Pharmaceutical Companies (Rx&D) Health Research Foundation/Canadian Institute of Health Research graduate research scholarship and is a recipient of a scholarship from the Fonds de la Recherche en Santé du Québec (FRSQ). P.P. is a research scientist with the FRSQ.

The authors thank Danielle St-

Laurent, Valérie Émond, and Louis Rochette from the Institut National de Santé Publique du Québec and Joanne Vidal for editing the manuscript.

References

1. Bertoni AG, Krop JS, Anderson GF, Brancati FL: Diabetes-related morbidity and mortality in a national sample of U.S. elders. *Diabetes Care* 25:471–475, 2002
2. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G, The Heart Outcomes Prevention Evaluation Study Investigators: Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 342:145–153, 2000
3. Collins R, Armitage J, Parish S, Sleight P, Peto R: MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 361: 2005–2016, 2003
4. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, Menard J, Rahn KH, Wedel H, Westerling S: Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. *Lancet* 351:1755–1762, 1998
5. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O: Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 348:383–393, 2003
6. Klinkle JA, Johnson JA, Guirguis LM, Toth EL, Lee TK, Lewanczuk RZ, Majumdar SR: Underuse of aspirin in type 2 diabetes mellitus: prevalence and correlates of therapy in rural Canada. *Clin Ther* 26:439–446, 2004
7. Toth EL, Majumdar SR, Guirguis LM, Lewanczuk RZ, Lee TK, Johnson JA: Compliance with clinical practice guidelines for type 2 diabetes in rural patients: treatment gaps and opportunities for improvement. *Pharmacotherapy* 23:659–665, 2003
8. Saaddine JB, Cadwell B, Gregg EW, Engelgau MM, Vinicor F, Imperatore G, Narayan KM: Improvements in diabetes processes of care and intermediate outcomes: United States, 1988–2002. *Ann Intern Med* 144:465–474, 2006
9. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M: Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med* 339:229–234, 1998
10. Emberson JR, Whincup PH, Lawlor DA, Montaner D, Ebrahim S: Coronary heart disease prevention in clinical practice: are patients with diabetes special? Evidence from two studies of older men and women. *Heart* 91:451–455, 2005
11. Shah BR, Huz JE, Laupacis A, Zinman B, Booth GL: Use of vascular risk-modifying medications for diabetic patients differs between physician specialties. *Diabet Med* 23:1117–1123, 2006
12. Brown CL, Johnson JA, Majumdar SR, Tsuyiki RT, McAlister AF: Evidence of suboptimal management of cardiovascular risk in patients with type 2 diabetes mellitus and symptomatic atherosclerosis. *CMAJ* 171:1189–1192, 2004
13. Safford M, Eaton L, Hawley G, Brimacombe M, Rajan M, Li H, Pogach L: Disparities in use of lipid-lowering medications among people with type 2 diabetes mellitus. *Arch Intern Med* 163: 922–938, 2003
14. Ferrara A, Williamson DF, Karter AJ, Thompson TJ, Kim C: Sex differences in quality of health care related to ischemic heart disease prevention in patients with diabetes: the translating research into action for Diabetes (TRIAD) study, 2000–2001. *Diabetes Care* 27:2974–2976, 2004
15. Kopp A, Mamdani M, Shah BR: Drug use in older people with diabetes. In *Diabetes in Ontario: An ICES Practice Atlas* Booth GL, Hux JE, Laupacis A, Slaughter PM, Eds. Toronto, Institute for Clinical Evaluative Sciences, 2003, p. 3.51–53.75
16. Wexler DJ, Grant RW, Meigs JB, Nathan DM, Cagliero E: Sex disparities in treatment of cardiac risk factors in patients with type 2 diabetes. *Diabetes Care* 28: 514–520, 2005
17. Nau DP, Mallya U: Sex disparity in the management of dyslipidemia among patients with type 2 diabetes mellitus in a managed care organization. *Am J Manag Care* 11:69–73, 2005
18. Petri A, de Lusignan S, Williams J, Chan T, Majeed A: Management of cardiovascular risk factors in people with diabetes in primary care: cross-sectional study. *Public Health* 120:654–663, 2006
19. Canadian Diabetes Association: Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 27 (Suppl. 2):S1–S152, 2003
20. American Diabetes Association: Standards of medical care in diabetes—2007 (Position Statement). *Diabetes Care* 30 (Suppl. 1):S4–S41, 2007
21. Rosen AB: Indications for and utilization of ACE inhibitors in older individuals with diabetes: findings from the National Health and Nutrition Examination Survey 1999–2002. *J Gen Intern Med* 4:315–319, 2006