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Diabetes Mellitus and Cardiovascular Events in Older Patients With Myocardial Infarction Prescribed Intensive-Dose and Moderate-Dose Statins

Dennis T. Ko, MD, MSc; Harindra C. Wijeysundera, MD, PhD; Cynthia A. Jackevicius, PharmD, MSc; Altayyeb Yousef, MB, BSc; Julie Wang, MSc; Jack V. Tu, MD, PhD

Background—Practice guidelines recommend intensive-dose statins for patients with acute coronary syndrome, but recent data about the risk of new-onset diabetes mellitus have raised concerns about its use. Our main objective was to evaluate the association between intensive statin therapy and new-onset diabetes mellitus in patients with myocardial infarction and to evaluate the association of intensive statin therapy with long-term adverse clinical outcomes.

Methods and Results—A propensity score–matched cohort was created consisting of 17 080 patients with myocardial infarction aged >65 years old, hospitalized in Ontario, Canada, from 2004 to 2010. Clinical outcomes were compared in patients prescribed intensive-dose versus moderate-dose statins at hospital discharge. At 5 years, 13.6% of patients receiving intensive-dose statins and 13.0% of patients receiving moderate-dose statins had new-onset diabetes, which was not significantly different (P=0.19). By contrast, the 5-year rate of death or acute coronary syndrome was significantly lower at 44.8% in the intensive-dose statin group compared with 46.5% in the moderate-dose group (P=0.044). The reduction in combined clinical outcome was driven mainly by a significantly lower rate of acute coronary syndrome (P=0.039) associated with intensive-dose statins. No significant difference in mortality rates (34.8% in both groups) was observed between the treatment groups during the study period (P=0.89).

Conclusions—In older patients with myocardial infarction, we found intensive-dose statin therapy to be effective in reducing repeat hospitalization for acute coronary syndrome. The rate of new-onset diabetes mellitus at long term was not significantly different between intensive-dose and moderate-dose statins. **(*Circ Cardiovasc Qual Outcomes*. 2013;6:315-322.)**

Key Words: acute coronary syndrome ■ intensive-dose statins ■ new-onset diabetes mellitus

Lipid-lowering therapy with statin medications has been well established to improve cardiovascular outcomes in patients with acute coronary syndrome (ACS).[1] Data from randomized controlled trials have further supported that intensive lipid lowering with statins provides additional clinical benefits.[2,3] Accordingly, present practice guidelines strongly support early intensive-dose statin therapy in ACS.[1] Despite these recommendations, at least 1 report suggested that intensive statin therapy is underused and prescribed in ≈1 of 3 patients with ACS.[4] The same study also suggested that older patients are much less likely to be prescribed intensive-dose statins as compared with younger patients, likely relating in part to concerns about adverse effects.[4,5]

Several studies have recently shown a strong association between the use of statins and subsequent development of diabetes mellitus.[6–11] This finding has led to a labeling change by the Food and Drug Administration to include a warning regarding increased risk of diabetes mellitus with statins.[12] Although it has been suggested that the net cardiovascular benefit for secondary prevention generally favors treatment,[13,14] whether the incremental benefits of intensive-dose statins outweigh its potential risks in the elderly is less certain because prior ACS studies included only a small number of older patients.[6] For example, in landmark studies, such as the Pravastatin or Atorvastatin Evaluation and Infarction Therapy (PROVE-IT) and the Aggrastat to Zocor (A to Z) trials, the mean age of enrollment was only 58 years and 61 years, respectively.[2,3] Therefore, there remains a gap in knowledge regarding the association of intensive statin therapy with new-onset diabetes mellitus in older patients who survived an acute cardiac event. Similarly, there is also an opportunity to augment data on the potential clinical benefit of intensive statin therapy in this population because of the lack of efficacy suggested in earlier reports.[2,15,16]

Accordingly, the first objective was to evaluate the association between intensive statin therapy and new-onset diabetes

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From the Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada (D.T.K., H.C.W., C.A.J., A.Y., J.W., J.V.T.); Schulich Heart Centre, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada (D.T.K., H.C.W., J.V.T.); Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada (D.T.K., H.C.W., C.A.J., J.V.T.); College of Pharmacy, Western University of Health Sciences, Pomona, CA (C.A.J.); and VA Greater Los Angeles Healthcare System, Los Angeles, CA (C.A.J.).

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Correspondence to Dennis T. Ko, MD, MSc, Institute for Clinical Evaluative Sciences G1-06, 2075 Bayview Ave, Toronto, Ontario, Canada M4N 3M5. E-mail dennis.ko@ices.on.ca

WHAT IS KNOWN

- Practice guidelines recommend intensive-dose statins for patients with acute coronary syndrome.
- Recent data about the risk of new-onset diabetes mellitus have raised concern about its use.

WHAT THE STUDY ADDS

- We evaluated the association between intensive-statin therapy and new-onset diabetes mellitus in myocardial infarction patients, and evaluated the association of intensive statin therapy with long-term adverse clinical outcomes.
- Intensive-dose statin therapy is effective in reducing repeat hospitalization for acute coronary syndrome and not associated with significantly increased risk of new-onset diabetes mellitus among older patients.

mellitus among a cohort of older patients hospitalized with myocardial infarction. The second objective was to evaluate the association of intensive statin therapy with long-term adverse clinical outcomes of death or recurrent ACS. We made use of the Ontario Myocardial Infarction Database (OMID), which is a longitudinal cohort that captures all patients admitted with an acute myocardial infarction in Ontario.

Methods

Data Sources

OMID was created by linking together several healthcare administrative databases in Ontario.[17,18] Residents with myocardial infarction admitted to any acute care hospitals in Ontario were identified using the *International Classification of Disease, 10th Revision code* (I21) in the Canadian Institute for Health Information discharge abstract database. OMID excluded patients aged <20 years or >105 years, those with an invalid health card, and those who had an infarction caused by a complication from other conditions. The first myocardial infarction during the study period was considered as the index event, and subsequent hospitalizations were considered as outcomes. The rationale for these inclusion and exclusion criteria is detailed elsewhere.[17,18] The diagnostic accuracy of myocardial infarction in OMID has been demonstrated to be >94%.[17,18] The OMID information was then linked to the following: (1) the Ontario Registered Persons Database, which contains information on the vital status of all Ontario residents; (2) the Canadian Institute for Health Information discharge abstract database, which contains information on all repeat hospitalizations; and (3) the Ontario Drug Benefit prescription claims database, which contains information on outpatient prescription drug use and costs for all residents aged ≥65 years. Linkages of these large databases were performed using unique encrypted patient identifiers to protect patient confidentiality. The study was approved by the Sunnybrook Health Sciences Center Research Ethics Board.

Study Cohort

The study cohort consisted of patients aged >65 years who survived to myocardial infarction after hospital discharge between April 1, 2004, and March 31, 2010. Only the initial hospitalization in the study period was included in the cohort. We excluded patients with diabetes mellitus and patients who were not prescribed statin medications because the main objective of the study was to compare the development of diabetes mellitus with intensive-dose versus moderate-dose statin therapy.

Definitions of Intensive-Dose and Moderate-Dose Statin Therapy

Atorvastatin ≥40 mg, rosuvastatin ≥20 mg, and simvastatin ≥60 mg were categorized as intensive-dose statin therapy because these formulations are anticipated to achieve ≈50% reduction in low-density lipoprotein.[4,19] This definition was also consistent with a prior study that examined the pattern of care of intensive lipid-lowering treatment in the United States.[4] Other statin formulations (atorvastatin <40 mg, rosuvastatin <20 mg, simvastatin <60 mg, and any dosage of Fluvastatin, Lovastatin, or Pravastatin) were considered to be moderate-dose statin therapy. Treatment groups were assigned on the basis of an intention to treat approach, where intensity of statins was determined by calculating the average daily dosage of statin medications prescribed within 100 days after hospital discharge. The Ontario Drug Benefit prescription database included information on daily dosage and number of days supplied for each prescribed prescription. A previous study has validated the accuracy of dose estimation in the Ontario Drug Benefit database, which found an accuracy rate of 89% in determining the daily dose of statins.[20] We also examined statin persistence at 1 year in patients prescribed intensive- and moderate-dose statins by determining whether patients continued to fill their statin prescription.[21,22]

Outcomes

The primary outcome of interest was the new development of diabetes mellitus after hospital discharge. This outcome was ascertained using the Ontario Diabetes Mellitus Database, which is an ongoing registry used to identify adults with diabetes mellitus, with validated high sensitivity (86%) and specificity (97%) for identifying patients with diabetes mellitus in the province.[23] Other outcomes that were assessed included all-cause mortality and repeat hospitalization for ACS. Mortality was determined from the Ontario Registered Persons Database. Repeat hospitalization for ACS (acute myocardial infarction or unstable angina) was determined using the Canadian Institute for Health Information discharge abstract database (*International Classification of Disease, 10th Revision code* I20, I21, I22, and I24).[24]

Statistical Analysis

Propensity score-matching analysis was used to minimize the influence of potential confounding and selection biases between patients prescribed intensive-dose and moderate-dose statins.[25,26] We calculated the predicted probability of receiving intensive-dose or moderate-dose statins by fitting a logistic regression model using all the clinically relevant variables that would predict the development of diabetes mellitus and adverse cardiovascular outcomes. Variables included in the propensity analysis included demographics (age, sex), factors used in the Ontario myocardial infarction mortality prediction rule,[27,28] the Charlson comorbidity index,[29,30] and the use of a cardiac invasive procedure. The Ontario myocardial infarction prediction rule was developed and validated using the OMID database and has been shown to have good prediction ability for mortality after myocardial infarction.[27,28] Variables in this prediction rule included shock, congestive heart failure, cancer, cerebrovascular disease, pulmonary edema, acute renal failure, and cardiac dysrhythmias.[27,28] The Charlson comorbidity index, a composite score based on 19 variables, is used widely to measure the burden of disease or to adjust case mix with administrative data.[29,30]

A greedy, nearest neighbor 1:1 matching algorithm was used to match patients, with matching occurring if the difference in the logits of the propensity scores was <0.2 times the SD of the scores (calliper width).[25,26] Patients were used only in 1 propensity score-matched pair, and those without a suitable match were excluded from the analysis. After constructing a propensity score-matched cohort, matched pairs were compared by calculating the standardized difference between the 2 groups, with differences of <0.1 used to indicate good balance in the matched cohort. Kaplan–Meier survival curves between the 2 groups were compared using stratified log rank test.[25,26]

SAS version 9.2 (SAS Institute, Cary, NC) was used for statistical analyses. A 2-sided P value of ≤0.05 was considered as statistically significant in the comparison of outcomes.

Results

Study Sample

There were 61 557 patients aged >65 years who were hospitalized with a myocardial infarction in Ontario from April 1, 2004, to March 31, 2010. We excluded 9619 patients who did not survive to hospital discharge, 2062 patients with multiple myocardial infarction hospitalizations during the study period, 20 323 patients who had diabetes mellitus, 5817 patients who were not prescribed statins, and 26 patients with incomplete data. Our study cohort before propensity score-matched analysis included 23 710 patients. Among them, slightly more than half (52.2%, 12 380 patients) were prescribed intensive-dose statin therapy. The baseline characteristics of patients prescribed intensive-dose statins and moderate-dose statins before propensity score matching are shown in Appendix Table I in the online-only Data Supplement. Significant differences between the treatment groups were observed in which patients prescribed intensive-dose statins were younger and had fewer comorbidities as compared with patients prescribed moderate-dose statins.

Characteristics of the Propensity-Matched Cohort

After propensity score matching, we identified 8540 matched pairs (17 080 patients) who had a similar likelihood of receiving intensive-dose or moderate-dose statins. The mean age of the propensity score-matched cohort was 78 years, 46% were women, and 17% had prior heart failure. The mean Charlson comorbidity score of this cohort was 0.63±1.04. All demographics, clinical, and procedural characteristics were well balanced between the matched pairs. None of the characteristics had a standardized difference of the means exceeding 0.1, indicating a balanced and comparable cohort (Table 1).

The specific statin therapy used in the intensive-dose group and the moderate-dose groups is shown in Table 2. Almost all (92%) of the patients in the intensive-dose group were prescribed atorvastatin, and the mean dosage was 53 mg per day. In the moderate-dose group, atorvastatin was prescribed in 61% of the patients, with a mean dosage of 17 mg per day. Among the 7546 patients in the intensive-dose statin group who survived until 1 year, 88.9% were still on statin therapy. Similarly, 89.2% of the 7504 survived patients in the moderate-dose group were maintained on statin at 1 year. No cases of rhabdomyolysis requiring hospitalization were identified in our cohort.

Incidence of New-Onset Diabetes Mellitus

The incidence of new-onset diabetes mellitus in the intensive-dose statin group and the moderate-dose statin groups is

Table 1. Baseline Characteristics of the Study Cohort After Propensity Match*

	Total (n=17 080)	Moderate-Dose Statin Therapy (n=8540)	Intensive-Dose Statin Therapy (n=8540)
Characteristics			
Age, y	77.97±7.19	77.99±7.14	77.95±7.24
Female, n (%)	7912 (46.3)	3980 (46.6)	3932 (46.0)
Cardiovascular comorbidities			
Shock, n (%)	102 (0.6)	52 (0.6)	50 (0.6)
Pulmonary edema, n (%)	79 (0.5)	40 (0.5)	39 (0.5)
Prior myocardial infarction, n (%)	892 (5.2)	447 (5.2)	445 (5.2)
Heart failure, n (%)	2860 (16.7)	1415 (16.6)	1445 (16.9)
Cardiac dysrhythmias, n (%)	2586 (15.1)	1298 (15.2)	1288 (15.1)
Hypertension, n (%)	13 743 (80.5)	6866 (80.4)	6877 (80.5)
Cerebrovascular disease, n (%)	425 (2.5)	202 (2.4)	223 (2.6)
Peripheral vascular disease, n (%)	431 (2.5)	177 (2.1)	254 (3.0)
Medical comorbidities			
Chronic lung disorders, n (%)	1400 (8.2)	731 (8.6)	669 (7.8)
Acute renal failure, n (%)	611 (3.6)	285 (3.3)	326 (3.8)
Chronic renal failure, n (%)	990 (5.8)	494 (5.8)	496 (5.8)
Peptic ulcer disease, n (%)	98 (0.6)	41 (0.5)	57 (0.7)
Mild liver disorder, n (%)	28 (0.2)	19 (0.2)	9 (0.1)
Moderate to severe liver disease, n (%)	5 (0.0)	4 (0.0)	1 (0.0)
Dementia, n (%)	574 (3.4)	279 (3.3)	295 (3.5)
Rheumatologic disorders, n (%)	112 (0.7)	63 (0.7)	49 (0.6)
Hemiplegia or paraplegia, n (%)	54 (0.3)	26 (0.3)	28 (0.3)
Cancer, n (%)	485 (2.8)	233 (2.7)	252 (3.0)
Charlson comorbidity score	0.63±1.04	0.62±1.00	0.65±1.07
Cardiac invasive procedures			
Coronary catheterization, n (%)	10 043 (58.8)	5011 (58.7)	5032 (58.9)
Percutaneous coronary intervention, n (%)	4914 (28.8)	2443 (28.6)	2471 (28.9)

*All standardized differences of the mean between the intensive-dose and moderate-dose statin groups were <0.1, indicating the creation of a balanced propensity score-matched cohort.

Table 2. Dose and Formulation of Statin Medication Received in the Treatment Groups

	Number, n (%)	Mean Dose±SD
Moderate-dose statins (n=8540)		
Atorvastatin	5228 (61.2)	16.6±4.8
Fluvastatin	26 (0.3)	37.7±20.7
Lovastatin	93 (1.1)	28.1±13.0
Pravastatin	362 (4.2)	30.2±13.7
Rosuvastatin	1293 (15.1)	9.5±1.6
Simvastatin	1533 (18.0)	30.4±11.8
Intensive-dose statins (n=8540)*		
Atorvastatin	7858 (92.0)	52.8±19.1
Rosuvastatin	638 (7.5)	24.4±8.5
Simvastatin	80 (0.4)	80±0

*Intensive-dose statin was defined as atorvastatin ≥40 mg, rosuvastatin ≥20 mg, and simvastatin ≥60 mg. Moderate-dose statin was defined as atorvastatin <40 mg, rosuvastatin <20 mg, and simvastatin <60 mg, and all doses of fluvastatin, lovastatin, and pravastatin.

shown in Table 3 and Figure 1. At 5 years, after hospitalization with myocardial infarction, 13.6% of patients receiving intensive-dose statins and 13.0% of the patients receiving moderate-dose statins had a new diagnosis of diabetes mellitus. The increased incidence of diabetes mellitus associated with intensive-dose statins was 0.3% at 1 year (2.6% in the intensive-dose statin group versus 2.3% in the moderate-statin group) and largest at 4 years, at which time the absolute difference was 1.0% (11.7% in the intensive-dose group versus 10.7% in the moderate-dose group). However, these differences did not reach statistical significance (P=0.18).

Repeat Hospitalization for Death or ACS

The rate of death or ACS was significantly lower among patients treated with intensive-dose statins compared with moderate-dose stains (Table 3 and Figure 2). At 5 years, the rate of ACS or death was significantly lower at 44.8% in the intensive-dose statin group compared with 46.5% in

Table 3. Outcomes of Moderate-Dose and Intensive-Dose Statins

Outcomes	Moderate-Dose Statin Therapy (n=8540)	Intensive-Dose Statin Therapy (n=8540)	*P* Value*
Incidence of new-onset diabetes mellitus, %			0.19
1 y	2.3	2.6	
2 y	5.5	6.1	
3 y	8.1	8.9	
4 y	10.7	11.7	
5 y	13.0	13.6	
Rate of death or acute coronary syndrome, %			0.044
1 y	21.4	20.1	
2 y	29.5	28.3	
3 y	35.7	34.4	
4 y	41.6	40.2	
5 y	46.5	44.8	
Rate of acute coronary syndrome, %			0.039
1 y	12.7	11.8	
2 y	16.6	15.4	
3 y	19.5	17.8	
4 y	21.5	20.2	
5 y	23.5	22.2	
Death rate, %			0.89
1 y	12.0	11.6	
2 y	18.7	18.7	
3 y	24.2	23.9	
4 y	30.1	30.1	
5 y	34.8	34.8	

**P* values compare characteristics between moderate-dose and intensive-dose statin therapy obtained by paired Kaplan–Meier curves.

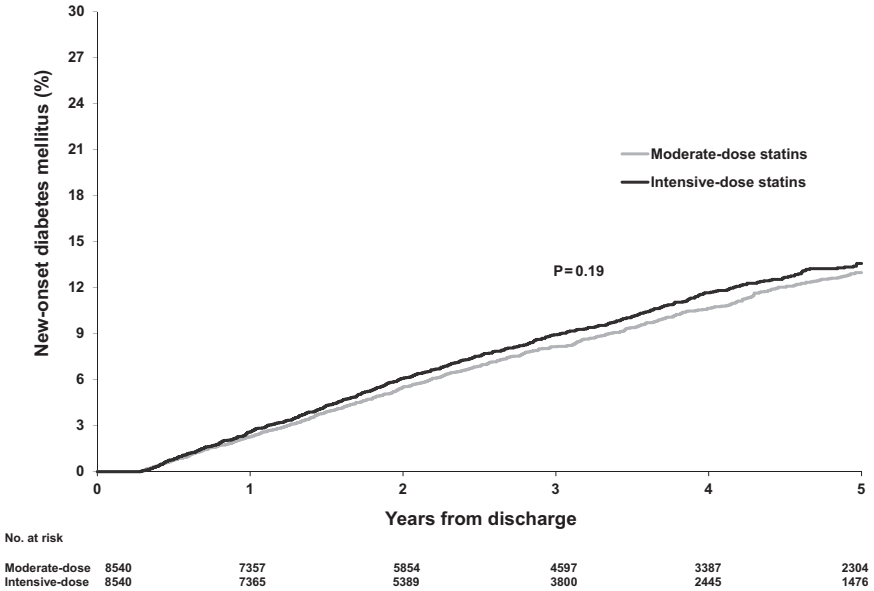

Figure 1. Incidence of new-onset diabetes mellitus in the propensity score–matched cohort comparing intensive-dose statins and moderate-dose statins.

the moderate-dose statin group (*P*=0.044). The reduction in death or ACS was observed at 1 year and remained consistent throughout the study period. The improvement in combined clinical outcome was almost driven entirely by a lower rate of repeat ACS associated with the intensive-dose statin group (Table 3 and Figure 3). At 5 years, the rate of ACS was significantly lower with intensive-dose statins at 22.2% versus 23.5% compared with moderate-dose statins (*P*=0.039). Rate of death was not significantly different in the treatment groups (34.8% in both groups) during the study period (*P*=0.89; Table 3 and Figure 4).

Discussion

Recent concerns about the development of diabetes mellitus associated with statin therapy have left many physicians uncertain about whether to prescribe intensive-dose or moderate-dose statins for older patients with acute cardiac events after hospital discharge. We found a slightly increased rate of new-onset diabetes mellitus in patients prescribed intensive-dose statins as compared with moderate-dose statins, but this difference did not reach statistical significance. By contrast, we observed a larger and significant reduction in recurrent ACS among patients prescribed intensive-dose statins compared with moderate-dose statins. This present study should be of assistance in determining the trade-off between risks and benefits of intensive-dose statin therapy in elderly patients.

Whether statin therapy is associated with increased risk of incident diabetes mellitus has recently been a subject of intense research. Sattar et al[8] performed a meta-analysis by pooling data from 12 randomized studies comparing statins and placebo, enrolling a total of 91 140 individuals. They found that, during a follow-up period of 4 years, the incidence of new-onset diabetes mellitus was 4.9% among patients assigned statins as compared with 4.5% among patients assigned placebo (odds ratio, 1.09; 95% confidence interval, 1.02–1.17).[8] The authors also suggested that older individuals may be at higher risk of developing new-onset diabetes mellitus from statins.[8] Preiss et al[6] extended the analysis and pooled trials comparing intensive-dose and moderate-dose

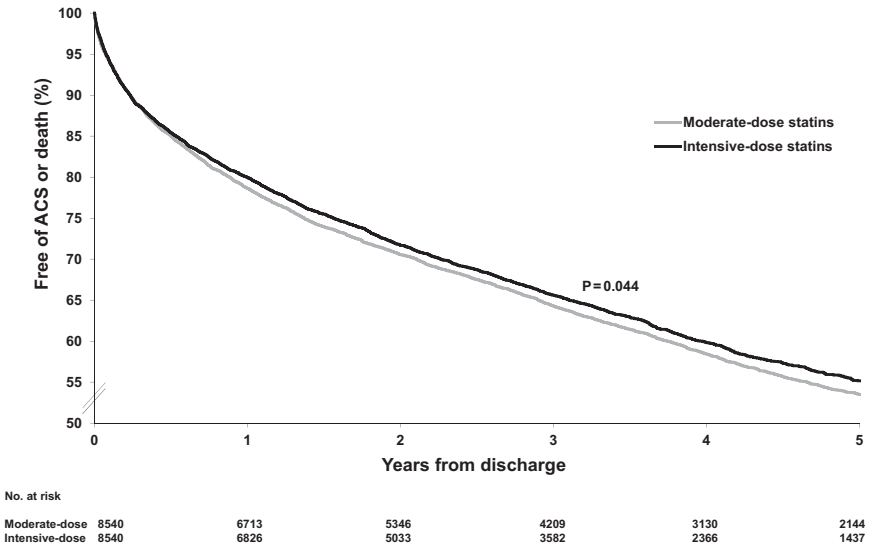

Figure 2. Rate of death or acute coronary syndrome (ACS) in the propensity score–matched cohort comparing intensive-dose statins and moderate-dose statins.

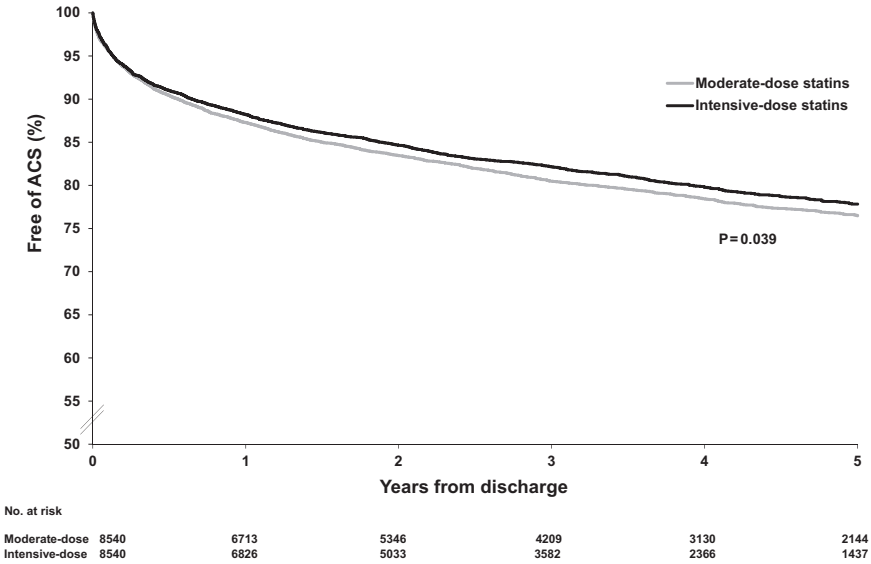

Figure 3. Rate of acute coronary syndrome (ACS) in the propensity score–matched cohort comparing intensive-dose statins and moderate-dose statins.

stains. In their meta-analysis that included 32 752 individuals with a mean age of 58 to 64 years, the incidence of new-onset diabetes mellitus at 4.9 years was 8.8% in the intensive-dose group versus 8.0% in the moderate-dose group (odds ratio, 1.12; 95% confidence interval, 1.02–1.22).[6] Although the mean age of our cohort was ≥15 years older and the incidence of new-onset diabetes mellitus was substantially higher than in prior studies, the increased rate of new-onset diabetes mellitus of 0.6% at 5 years between the treatment groups was almost identical to previous findings.[6,8] As such, despite having >17 000 older patients with myocardial infarction, it is possible that our study was still underpowered to detect a significant difference. Nonetheless, even if this difference were statistically significant, the number needed to harm for intensive-dose statin therapy was 167 over 5 years.

Although we did not detect a difference in mortality rate between those prescribed intensive-dose versus moderate-dose statins in the propensity-matched cohort, we did observe an absolute reduction in recurrent ACS that ranged from 0.9% to 1.7% during the study period. The number needed to treat was 77 for intensive-dose statin therapy in preventing a recurrent ACS at 5 years. Although our findings may seem at odds with the results of the PROVE-IT trial, which demonstrated a larger reduction (26.3% in the intensive group versus 22.4% in the moderate group), the absolute benefit among patients aged ≥65 years in the trial was only 1.4% (28.1% in the intensive group versus 29.5% in the moderate group, not statistically significant),[2] which is similar to our finding.

Prior epidemiological studies have shown that the association between cholesterol levels and coronary risk diminishes with age.[31,32] A study conducted in Medicare patients with myocardial infarction suggested an age and statin interaction and questioned the efficacy of statin therapy in older patients.[16] At least 1 observational study has found no added benefit of intensive-dose versus moderate-dose statin therapy.[15] On the basis of these observations, it is not surprising that many studies have demonstrated that statin therapy, specifically intensive-dose statins, are substantially underused among older patients

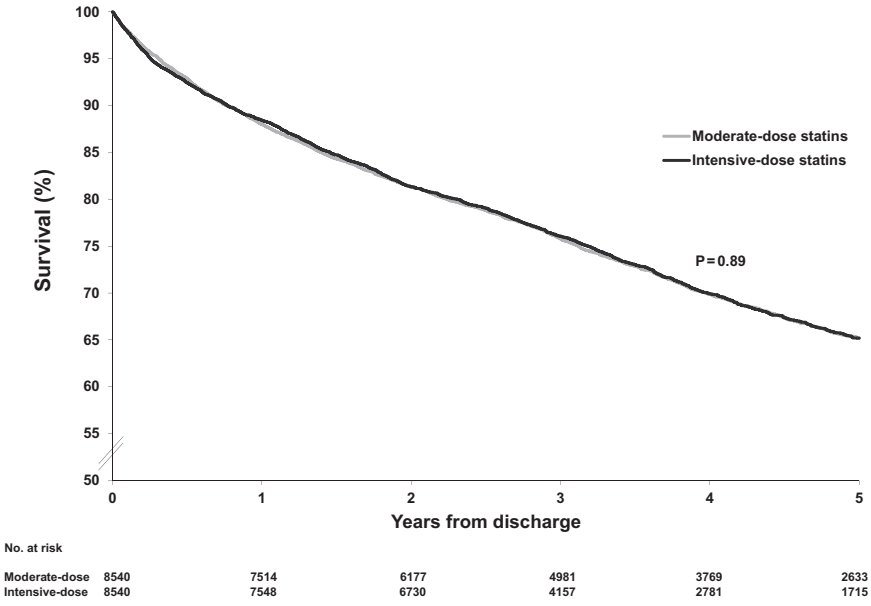

Figure 4. Rate of death in the propensity score-matched cohort comparing intensive-and moderate-dose statins.

with coronary artery disease.[4,5] Our present study extends prior knowledge and provides clarification on the existing clinical uncertainties surrounding the management of hyperlipidemia among older patients with coronary artery disease.

Several limitations of our study merit consideration. First, we did not have access to cholesterol results on an individual level and therefore categorized intensity of statin treatment based on the prescribed dosage rather than the actual reduction in cholesterol levels. However, this method of assigning statin intensity groups is analogous to prior randomized studies.[2,3] In addition, some authorities have recently suggested that treatment intensity should be based on the risk profile of patients rather than cholesterol targets.[33] Second, observational studies are subject to the influence of confounding. Although we adjusted for several known factors for diabetes mellitus development, such as age, hypertension, and hyperlipidemia, we were unable to adjust for several risk factors in the propensity model, such as smoking, obesity, diet, and physician activity levels, because these variables were not available in our data set. To our knowledge, these factors are not known to be associated with the intensity of medication prescribing. Therefore, it is difficult to know their potential impact on our results. Finally, our study was limited to an older cohort, and therefore findings from our study may not be applicable to a younger cohort. However, older patients had the most clinical uncertainty regarding the potential risks and benefits of intensive-dose statin therapy because they have been shown to have the greatest risk of developing diabetes mellitus from statins and also the least conclusive data to support the use of intensive-dose statins.[2,8,15]

In conclusion, this large population-based study of older patients with myocardial infarction provides evidence that intensive-dose statin therapy is associated with, at most, a small absolute increased risk of incident diabetes mellitus. At the same time, intensive-dose statin therapy is associated with a larger and significant reduction of recurrent ACS.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

CIRCCQO/2012/000015R1

Diabetes and Cardiovascular Events in Older Myocardial Infarction Patients Prescribed Intensive-Dose and Moderate-Dose Statins

Appendix Table 1. Baseline characteristics of the study cohort before propensity match

	Total	Moderate-dose statin therapy	Intensive-dose statin therapy	P Value*
	N=23,710	N=11,330	N=12,380	
Characteristics				
Age	77.96 ± 7.34	79.26 ± 7.38	76.77 ± 7.11	< 0.001
Female	10,799 (45.5%)	5,685 (50.2%)	5,114 (41.3%)	< 0.001
Cardiovascular comorbidities				
Shock	153 (0.6%)	65 (0.6%)	88 (0.7%)	0.188
Pulmonary edema	120 (0.5%)	74 (0.7%)	46 (0.4%)	0.002
Prior myocardial infarction	1,191 (5.0%)	617 (5.4%)	574 (4.6%)	0.004
Heart failure	3,941 (16.6%)	2,215 (19.5%)	1,726 (13.9%)	< 0.001
Cardiac dysrhythmias	3,615 (15.2%)	1,941 (17.1%)	1,674 (13.5%)	< 0.001
Hypertension	18,817 (79.4%)	9,293 (82.0%)	9,524 (76.9%)	< 0.001
Cerebrovascular disease	591 (2.5%)	312 (2.8%)	279 (2.3%)	0.014
Peripheral vascular disease	607 (2.6%)	281 (2.5%)	326 (2.6%)	0.456
Medical comorbidities				
Chronic lung disorders	1,893 (8.0%)	1,056 (9.3%)	837 (6.8%)	< 0.001
Acute renal failure	888 (3.7%)	499 (4.4%)	389 (3.1%)	< 0.001
Chronic renal failure	1,416 (6.0%)	829 (7.3%)	587 (4.7%)	< 0.001
Peptic ulcer disease	133 (0.6%)	60 (0.5%)	73 (0.6%)	0.536
Mild liver disorder	40 (0.2%)	27 (0.2%)	13 (0.1%)	0.012
Moderate to severe liver disease	7 (0.1%)	1 (0.0%)	8 (0.0%)	0.025
Dementia	836 (3.5%)	517 (4.6%)	319 (2.6%)	< 0.001
Rheumatologic disorders	84 (0.7%)	78 (0.6%)	162 (0.7%)	0.299
Hemiplegia or paraplegia	92 (0.4%)	57 (0.5%)	35 (0.3%)	0.006
Cancer	653 (2.8%)	357 (3.2%)	296 (2.4%)	< 0.001
Charlson comorbidity score†	0.64 ± 1.05	0.74 ± 1.12	0.54 ± 0.97	< 0.001
Cardiac invasive procedures				
Cardiac catheterization	13,916 (58.7%)	5,048 (44.6%)	8,868 (71.6%)	< 0.001
Percutaneous coronary intervention	8,105 (34.2%)	2,443 (21.6%)	5,662 (45.7%)	< 0.001

* P value compares characteristics between moderate-dose and intensive-dose statin therapy

† The Charlson comorbidity score is comprised of diabetes, prior myocardial infarction, heart failure, cerebrovascular disease, peripheral vascular disease, chronic lung disorders, chronic renal failure, peptic ulcer disease, chronic liver disease, dementia, hemiplegia or paraplegia, and cancer. The calculated score did not include current hospitalization for myocardial infarction.