Statin Use and Decline in Gait Speed in Community-Dwelling Older Adults

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OBJECTIVES: To examine the association between statin use and objectively assessed decline in gait speed in community-dwelling older adults.

DESIGN: Longitudinal cohort study.

SETTING: Health, Aging and Body Composition (Health ABC) Study.

PARTICIPANTS: Two thousand five participants aged 70–79 at baseline with medication and gait speed data at 1998–99, 1999–2000, 2001–02, and 2002–03.

MEASUREMENTS: The independent variables were any statin use and their standardized daily doses (low, moderate, high) and lipophilicity. The primary outcome measure was decline in gait speed of 0.1 m/s or more in the following year of statin use. Multivariable generalized estimating equations were used, adjusting for demographic characteristics, health-related behaviors, health status, and access to health care.

RESULTS: Statin use increased from 16.2% in 1998–99 to 25.6% in 2002–03. The overall proportions of those with decline in gait speed of 0.1 m/s or more increased from 22.2% in 1998 to 23.9% in 2003. Statin use was not associated with decline in gait speed of 0.1 m/s or more (adjusted odds ratio (AOR) = 0.90, 95% confidence interval (CI) = 0.77–1.06). Similar nonsignificant trends were also seen with the use of hydrophilic or lipophilic statins. Users of low-dose statins were found to have a 22% lower risk of decline in gait speed than nonusers (AOR = 0.78, 95% CI = 0.61–0.99), which was mainly driven by the results from 1999–2000 follow-up.

CONCLUSION: These results suggest that statin use did not increase decline in gait speed in community-dwelling older adults. **J Am Geriatr Soc 63:124–129, 2015.**

Key words: hydroxymethylglutaryl-CoA reductase inhibitors; statins; gait speed; physical function; aged

Gait speed is a simple but important indicator of functional status in older adults and a strong predictor of mortality and other health-related outcomes.[1,2] A growing body of evidence has identified a relationship between chronic inflammation, age-related functional decline, and risk of disability.[3] Several studies indicate that statins have anti-inflammatory effects beyond their cholesterol-lowering and antiatherosclerosis properties.[4] For these reasons, statins could have a protective effect on age-related functional decline.

Current evidence on the association between statin use and physical function decline in older adults is mixed.[5–13] Studies whose sample consisted primarily of individuals with peripheral arterial disease (PAD) have reported that statin users had less annual decline in walking speed or distance than nonusers,[5–8] although these effects were modest, and their clinical relevance is unclear. In addition,

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four of the studies that were not restricted to individuals with PAD did not find associations between statin use and self-reported or other physical function measures,[9–12] whereas one study found that fast walking speed of users of lipid-lowering medication declined 25% slower than that of nonusers.[13] Previous studies show that the criterion for substantial change in decline in gait speed for clinical and research use is approximately 0.10 m/s, which was strongly associated with morbidity and mortality in older adults.[2,14]

Given these conflicting findings and the importance of maintaining adequate physical function, the objective of the current study was to examine the association between statin use and risk of decline in gait speed of 0.1 m/s or more in community-dwelling older adults. The hypothesis was that statin use would be protective for the development of decline in gait speed of 0.1 m/s or more.

METHODS

Study Design, Sample, and Data Source

This longitudinal study used data from the Health, Aging and Body Composition (Health ABC) Study, which enrolled 3,075 white and black adults aged 70–79 without mobility problems.[15] Participants were recruited in 1997–98 from a random sample of Medicare beneficiaries residing in Pittsburgh, Pennsylvania, and Memphis, Tennessee. The sample for the current study included 2,405 participants from 1998–99 who had medication and 20-m gait speed data (obtained for the first time). The institutional review boards of the Universities of Pittsburgh, Tennessee, and California at San Francisco approved the study, and written informed consent was obtained from each participant.

Data Collection and Management

Data were collected during annual in-person visits from 1998 to 2003 from blood tests; physiological measurements using standardized methods; and responses to structured questionnaires regarding demographic characteristics, multiple aspects of health behavior, and health status.[15] The Health ABC morbidity and mortality committee centrally adjudicated incident comorbidities examined in the current study (coronary heart disease (CHD), congestive heart failure (CHF), stroke, PAD) based on conclusive evidence from hospitalization or death records.[15] Prevalent disease is based on self-report of or medication use for a certain disease.

Prescription medication information was collected annually from 1998 to 2003, except in 2000–01. Participants were asked to bring all prescription medications taken in the previous month, and trained research assistants transcribed the drug name, strength, and dosage from the medication bottle, and participants reported number of units taken in the previous day, week, or month and whether the medication was taken regularly or as needed. This medication information was coded using the Iowa Drug Information Service and entered into a computerized database.[16]

Primary Outcome Measures

Usual gait speed was measured over a 20-m course in an unobstructed corridor annually from 1998 to 2003. Timing started with the first step over the starting line and ended at the first footfall over the finishing line. The primary outcome variable was decline in gait speed of 0.1 m/s or more in the following year of statin use, based on previous studies.[2,14]

Primary and Secondary Independent Variables

Statin use was identified according to Iowa Drug Information Service codes 24060202 to 24060208. The primary independent variable was use versus no use of statins at baseline (1998–99) and annually (as a time-varying variable). Several secondary independent variables were created for lipophilicity and standardized daily dose (SDD). To create the SDD measure, the daily dose was first calculated by multiplying the number of dosage forms taken the previous day according to medication strength. Then the daily dose was divided by the equivalent dose of that statin that has been reported to decrease low-density lipoprotein cholesterol by 37%.[17] The following daily doses were considered to equal 1 U of equivalent dose: atorvastatin 10 mg, fluvastatin 80 mg, lovastatin 40 mg, pravastatin 40 mg, simvastatin 20 mg, rosuvastatin 5 mg.[17] SDD was categorized as low dose (<1 SDD), moderate dose (1 SDD), and high dose (>1 SDD), based on the distribution of the data and clinical relevance. Finally, a dichotomous measure was created in which statins were categorized as being lipophilic (lovastatin, simvastatin, atorvastatin, fluvastatin) or hydrophilic (pravastatin, rosuvastatin).[18]

Covariates

Several characteristics that could confound or modify the association between statin use and gait speed were adjusted for in the analyses and grouped into four domains: demographic characteristics, health-related behaviors, health status, and access to health care. Demographic variables included baseline age, sex, race (black or white), study site, education (postsecondary education, high school graduate, or <high school graduate), and living status (alone or not alone) as a time-varying variable.

Health-related behaviors included smoking status, alcohol use (current, past, never), and self-report of doing moderate- to high-intensity exercise in the previous week (yes vs no) as time-varying variables. Health status factors for which statins may be indicated were characterized as time-varying dichotomous measures (present vs absent) for adjudicated comorbidities including CHD, stroke, and PAD.[19] Time-varying dichotomous measures (present vs absent) were used for self-reported hypertension, diabetes mellitus, CHF, pulmonary disease (baseline), osteoarthritis, and Parkinson's disease (baseline). Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate of less than 60 mL/min.[20] A time-varying dichotomous variable was created for self-rated health (good to excellent vs fair to poor). A time-varying categorical variable for body mass index (BMI: underweight or normal (<25.0 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese

(≥30.0 kg/m^2)) and a continuous variable for average total body mass (kg) were created. In addition, voluntary isokinetic knee extensor strength (average maximum torque (Nm)) was considered as a time-varying continuous variable.[21] Time-varying dichotomous variables were created for cognitive impairment (Modified Mini-Mental State Examination score <80)[22] and high depressive symptoms (Center for Epidemiologic Studies Depression Scale score >15).[23] Several time-varying dichotomous covariates (yes vs no) of the use of medications related to falls and mobility problems (benzodiazepines, angiotensin-converting enzyme inhibitors (ACEIs), anticholinergic medications, nonsteroidal anti-inflammatory drugs (NSAIDs), and other medications with anti-inflammatory effects (systematic glucocorticoids; immunosuppressive medications; some medications for rheumatoid arthritis, asthma, inflammatory bowel disease, systemic lupus erythematous, other systemic inflammatory diseases)) were controlled for in the analyses.[24] A time-varying continuous variable of the number of overall prescription medications (excluding statins, benzodiazepine, ACEIs, and other medications with anti-inflammatory effects) was included.[25]

Two time-varying dichotomous access to healthcare factors (yes vs no) were created (having an influenza vaccination in the past year (as a proxy related to an individual's care-seeking behavior and access to health care to adjust for healthy user effect and a provider's availability)[26] and having prescription drug coverage), to account for individuals who had and did not have insurance coverage over time.

Primary and Secondary Statistical Analyses

Appropriate descriptive statistics were used to summarize participant characteristics and main analytical variables. Statin exposure was defined as use in the year preceding ascertainment of gait speed measures. Multivariable generalized estimating equation models were used to examine the association between statin use and decline in gait speed of 0.1 m/s or more.[27] An autoregressive working correlation structure was used to account for potential multiple years of data from the same participants and the resulting stochastic nonindependence of observations.[27] In the final multivariable models, adjusted odds ratios (AORs) and 95% confidence intervals (CIs) for statin use were computed, adjusting for demographic characteristics, potential confounders by indication, gait speed measures in previous years, a factor related to access to health care, and covariates with a $P < .15$ from a forward selection procedure. Secondary analyses used a similar approach that adjusted for the same covariates but included other operational definitions of statin use as main predictors to test dose-response and lipophilicity relationships. All analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC).

RESULTS

The mean age of the 2,405 sample participants was 74.6, 51% were female, 37% were black, 63% had prescription medication coverage, and 16.2% used statins (Table 1). Statin users were younger on average and more likely to be white, to be from the Pittsburgh site, to have prescription drug coverage, to have smoked previously, to drink alcohol currently, to perform high- or moderate-intensity exercise, and to have more chronic comorbidities (hypertension, diabetes mellitus, CHD, CHF, stroke, PAD, CKD) than nonusers. Statin users were also more likely to take benzodiazepines, ACEIs, and multiple prescription drugs.

At baseline, 48% of statin users used low doses, and 86% took lipophilic statins (Table 2). Any use of statin increased steadily, from 20.1% in 1999–2000 to 25.6% in 2001–02. Overall proportions of decline in gait speed of 0.1 m/s or more ranged from 22.2% to 23.9% between 1998 and 2003. Statin users were less likely to experience decline in gait speed (18.0% vs 23.3%, $P = .03$) than nonusers in 1999–2000, but not ($P > 0.05$) in 2000–01 (25.7% vs 22.0%) or 2002–03 (23.6% vs 24.0%).

Statin use was not associated with decline in gait speed of 0.1 m/s or more (AOR = 0.90, 95% CI = 0.77–1.06) (Table 3). Statistically nonsignificant differences were also seen in high- and moderate-dose and lipophilic and hydrophilic statin use, although only a 22% lower risk of decline in gait speed in low-dose users than in statin nonusers was found to be statistically significant (AOR = 0.78, 95% CI = 0.61–0.99), which was mainly determined by the results of the 1999–2000 follow-up.

DISCUSSION

The overall results of this study demonstrated no substantial associations between statin use and decline in gait speed of 0.1 m/s or more, which has been found to be related to self-reported morbidity and mortality, in a large elderly community dwelling sample. These overall results are consistent with studies conducted in individuals without PAD.[9–12] Large cohort studies have found that statin use is not associated with self-reported mobility limitations;[9] objective physical performance measures[10] and incidence of frailty in postmenopausal women;[11] and muscle strength, balance, mobility, and falls,[12] although two randomized trials[7,8] and three longitudinal studies[5,6,13] in individuals with PAD have reported that statin use is associated with lower risk of decline in gait speed than in nonusers. Possible explanations of these differences include use of different populations (e.g., women only, younger baseline age), less-precise self-reported outcomes, modest improvement in using continuous outcomes but possible lack of clinical relevance, and lack of attention to dose response.

What are the clinical implications of these study findings for older adults? Given that statin use may continue to increase because of the new 2013 American College of Cardiology/American Heart Association guideline on the Treatment of Blood Cholesterol,[28] the overall nonsignificant association between statin use and decline in gait speed is reassuring because it was possible that adverse statin-related muscular events in older adults could have resulted in slower gait speed. Generally, the muscle-related adverse effects of statin use are associated with higher doses and blood levels.[29] These adverse events may occur in up to 10% of adults receiving high-dose statins,[30] although the precise estimate is unknown for older frail adults. Low-dose statin use, as shown in the results of the

Table 1. Baseline Characteristics of the Study Sample Overall and According to Statin Use

Characteristic	Full Sample, N = 2,405	Statin Users, n = 390	Statin Nonusers, n = 2,015
Demographic			
Age, mean ± SD	74.6 ± 2.8	74.3 ± 2.7[a]	74.7 ± 2.9
Female, n (%)	1,235 (51.4)	195 (50.0)	1,040 (51.6)
Black, n (%)	894 (37.2)	114 (29.2)[c]	780 (38.7)
Pittsburgh site, n (%)	1,257 (52.3)	239 (61.3)[c]	1,018 (50.5)
Education, n (%)			
Postsecondary	1,084 (45.2)	192 (49.4)	892 (44.4)
High school	793 (33.1)	129 (33.1)	664 (33.0)
<High school graduate	522 (21.8)	68 (17.5)	454 (22.6)
Living alone, n (%)	697 (29.0)	105 (26.9)	592 (29.4)
Health-related behaviors, n (%)			
Smoking status			
Current	206 (8.6)	22 (5.6)[c]	184 (9.2)
Past	1,119 (46.6)	219 (56.2)	900 (44.7)
Never	1,077 (44.8)	149 (38.2)	928 (46.1)
Alcohol use			
Current	1,226 (51.2)	223 (57.2)[a]	1,003 (50.0)
Past	507 (21.2)	79 (20.3)	428 (21.3)
Never	663 (27.7)	88 (22.5)	575 (28.7)
Performed moderate- to high-intensity exercise in the past week	690 (28.7)	141 (36.2)[c]	549 (27.3)
Health status factors			
Hypertension, n (%)	1,104 (45.9)	220 (56.4)[c]	884 (43.9)
Diabetes mellitus, n (%)	363 (15.1)	75 (19.2)[a]	288 (14.3)
Coronary heart disease, n (%)	450 (18.7)	165 (42.3)[c]	285 (14.1)
Stroke, n (%)	133 (5.5)	33 (8.5)[b]	100 (5.0)
Peripheral artery disease, n (%)	151 (6.3)	48 (12.3)[c]	103 (5.1)
Congestive heart failure, n (%)	103 (4.3)	28 (7.2)[b]	75 (3.7)
Chronic kidney disease, n (%)	484 (20.3)	108 (27.8)[c]	376 (18.8)
Pulmonary disease, n (%)	99 (4.1)	10 (2.6)	89 (4.4)
Osteoarthritis, n (%)	1,345 (55.9)	219 (56.2)	1,126 (55.9)
Parkinson's disease, n (%)	15 (0.6)	0 (0)	15 (0.7)
Good to excellent self-rated health, n (%)	2,057 (85.5)	327 (83.9)	1,730 (85.9)
Body mass index, n (%)			
Under- or normal weight	798 (33.2)	110 (28.2)[a]	688 (34.1)
Overweight	1,030 (42.8)	187 (48.0)	843 (41.8)
Obese	577 (24.0)	93 (23.8)	484 (24.0)
Total-body lean mass (kg) mean ± SD	48.8 ± 10.3	48.6 ± 9.7	48.8 ± 10.4
Voluntary isokinetic knee extensor strength, average maximum torque (Nm) mean ± SD	104.6 ± 37.3	106.1 ± 38.5	104.4 ± 37.1
Cognitively impaired (Modified Mini-Mental State Examination score <80)	187 (7.8)	22 (5.6)	165 (8.2)
Severe depression (Center for Epidemiologic Studies Depression Scale score >15), n (%)	102 (4.3)	16 (4.1)	86 (4.3)
Medication use, n (%)			
Anticholinergic	345 (14.4)	52 (13.3)	293 (14.5)
Benzodiazepine	146 (6.1)	33 (8.5)[a]	113 (5.6)
Angiotensin-converting enzyme inhibitor	402 (16.7)	90 (23.1)[c]	312 (15.5)
Nonsteroidal anti-inflammatory drug	513 (21.3)	71 (18.2)	442 (21.9)
Other anti-inflammatory drug	96 (4.0)	17 (4.4)	79 (3.9)
Number of prescription drugs, mean ± SD	2.7 ± 2.4	3.4 ± 2.5[c]	2.6 ± 2.3
Healthcare access			
Prescription drug coverage	1,521 (63.3)	282 (72.3)[c]	1,239 (61.6)
Having an influenza vaccination in past year	1,798 (74.8)	317 (81.3)	1,481 (73.5)

SD = standard deviation.

$P <$ [a].05, [b].01, [c].001 from chi-square or *t*-test between statin users and nonusers.

current study, may minimize muscle-related adverse effects in older adults and therefore may be less likely to counteract beneficial effects of statins.

Strengths of this study include the prospective design in a large community-dwelling older-adult sample; medication information collected using a state-of-the-art approach; availability of serially obtained, standardized gait speed measures; and adjustment for numerous potential confounders, although inherent to longitudinal studies examining older adults, potential survivor bias should be considered. The results from a sensitivity analysis, restricted to participants alive during all study years

Table 2. Prevalence of Statin Use over Time

Statin Use	1998–99, n = 2,405	1999–2000, n = 2,206 n (%)	2001–02, n = 1,968
Any	390 (16.2)	444 (20.1)	504 (25.6)
High dose (>1 SDD)	59 (2.5)	76 (3.5)	137 (7.0)
Moderate dose (1 SDD)	143 (6.0)	195 (8.8)	235 (11.9)
Low dose (<1 SDD)	188 (7.8)	173 (7.8)	132 (7.0)
Lipophilic[a]	334 (13.9)	398 (18.0)	461 (23.4)
Hydrophilic[b]	56 (2.3)	46 (2.1)	43 (2.2)

SDD = standardized daily dose.
[a]Atorvastatin, lovastatin, fluvastatin, simvastatin.
[b]Pravastatin, rosuvastatin.

Table 3. Multivariable Generalized Estimating Equation Models of Statin Use and Decline in Gait Speed

Statin Use	Decline in Gait Speed ≥ 0.1 m/s, Adjusted Odds Ratio (95% Confidence Interval) *P*-Value
Any use	0.90 (0.77–1.06) .21
High dose (>1 SDD)	0.90 (0.67–1.22) .50
Moderate dose (1 SDD)	1.02 (0.82–1.27) .86
Low dose (<1 SDD)	0.78 (0.61–0.99) .04
Lipophilic[a]	0.93 (0.79–1.09) .37
Hydrophilic[b]	0.72 (0.47–1.12) .15

Separate multivariable generalized estimating equation analyses were used to adjust for baseline demographic characteristics (race, sex, site). Final models also included time-varying statin use, age, coronary heart disease, diabetes mellitus, stroke, peripheral arterial disease, self-rated health, gait speed at previous year, anticholinergics, benzodiazepines, angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, other anti-inflammatory drugs, number of prescription drugs, and having an influenza vaccination in the past 12 months.
SDD = standardized daily dose.
[a]Atorvastatin, lovastatin, fluvastatin, simvastatin.
[b]Pravastatin, rosuvastatin.

(1998–2003), yielded similar results (data not shown). Second, medication data were collected at fixed nearly yearly points in time, preventing documentation of the exact date on which statins were initiated, dosage was changed or discontinued, or adverse events that could affect gait speed occurred. Moreover, unmeasured confounders such as adherence to medications cannot be excluded. Last, this sample was drawn from two U.S. cities and may not be generalizable to other populations.

CONCLUSION

These results suggest no greater decline in gait speed with statin use than with nonuse in community-dwelling older adults. Future studies are needed to confirm the inconclusive, observed lower risk of decline in gait speed with low-dose statin use than with nonuse in varied older adult populations.

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Author Contributions: Drs. Lo-Ciganic and Hanlon had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Hanlon. Acquisition of data: Newman. Analysis and interpretation of data: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Hanlon. Drafting of the manuscript: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Hanlon. Critical revision of the manuscript for important intellectual content: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Newman, Simonsick, Bauer, Satterfield, Caserotti, Harris, Shorr, Hanlon. Statistical analysis: Lo-Ciganic. Administrative, technical, or material support: Lo-Ciganic. Study supervision: Hanlon.

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REFERENCES

1. Abellan van Kan G, Rolland Y, Andrieu S et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. J Nutr Health Aging 2009;13:881–889.
2. Studenski S, Perera S, Patel K et al. Gait speed and survival in older adults. JAMA 2011;305:50–58.
3. Corsonello A, Garasto S, Abbatecola AM et al. Targeting inflammation to slow or delay functional decline: Where are we? Biogerontology 2010;11:603–614.
4. Bu DX, Griffin G, Lichtman AH. Mechanisms for the anti-inflammatory effects of statins. Curr Opin Lipidol 2011;22:165–170.
5. Giri J, McDermott MM, Greenland P et al. Statin use and functional decline in patients with and without peripheral arterial disease. J Am Coll Cardiol 2006;47:998–1004.
6. McDermott MM, Guralnik JM, Greenland P et al. Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. Circulation 2003;107:757–761.
7. Mondillo S, Ballo P, Barbati R et al. Effects of simvastatin on walking performance and symptoms of intermittent claudication in hypercholesterolemic patients with peripheral vascular disease. Am J Med 2003;114: 359–364.
8. Mohler ER III, Hiatt WR, Creager MA. Cholesterol reduction with atorvastatin improves walking distance in patients with peripheral arterial disease. Circulation 2003;108:1481–1486.
9. Gray SL, Boudreau RM, Newman AB et al. Angiotensin-converting enzyme inhibitor and statin use and incident mobility limitation in community-dwelling older adults: The Health, Aging and Body Composition study. J Am Geriatr Soc 2011;59:2226–2232.
10. Gray SL, Aragaki AK, LaMonte MJ et al. Statins, angiotensin-converting enzyme inhibitors, and physical performance in older women. J Am Geriatr Soc 2012;60:2206–2214.
11. LaCroix AZ, Gray SL, Aragaki A et al. Statin use and incident frailty in women aged 65 years or older: Prospective findings from the Women's Health Initiative Observational Study. J Gerontol A Biol Sci Med Sci 2008;63A:369–375.

12. Haerer W, Delbaere K, Bartlett H et al. Relationships between HMG-CoA reductase inhibitors (statin) use and strength, balance and falls in older people. Intern Med J 2012;42:1329–1334.
13. Dumurgier J, Singh-Manoux A, Tavernier B et al. Lipid-lowering drugs associated with slower motor decline in the elderly adults. J Gerontol A Biol Sci Med Sci 2014;69A:199–206.
14. Perera S, Mody SH, Woodman RC et al. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc 2006;54:743–749.
15. Simonsick EM, Newman AB, Nevitt MC et al. Measuring higher level physical function in well-functioning older adults: Expanding familiar approaches in the Health ABC study. J Gerontol A Biol Sci Med Sci 2001;56A:M644–M649.
16. Pahor M, Chrischilles EA, Guralnik JM et al. Drug data coding and analysis in epidemiologic studies. Eur J Epidemiol 1994;10:405–411.
17. Jones PH, Davidson MH, Stein EA et al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR* Trial). Am J Cardiol 2003;92:152–160.
18. Hamelin BA, Turgeon J. Hydrophilicity/lipophilicity: Relevance for the pharmacology and clinical effects of HMG-CoA reductase inhibitors. Trends Pharmacol Sci 1998;19:26–37.
19. National Institutes of Health. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143–3421.
20. Fried LF, Boudreau R, Lee JS et al. Kidney function as a predictor of loss of lean mass in older adults: Health, Aging and Body Composition Study. J Am Geriatr Soc 2007;55:1578–1584.
21. Scott D, Blizzard L, Fell J et al. Statin therapy, muscle function and falls risk in community-dwelling older adults. QJM 2009;102:625–633.
22. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. J Clin Psychiatry 1987;48:314–318.
23. Radloff LS. The CES-D Scale: A self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
24. Peron EP, Gray SL, Hanlon JT. Medication use and functional status decline in older adults: A narrative review. Am J Geriatr Pharmacother 2011;9:378–391.
25. Schneeweiss S, Wang PS, Avorn J et al. Improved comorbidity adjustment for predicting mortality in Medicare populations. Health Serv Res 2003;38:1103–1120.
26. Shrank WH, Patrick AR, Brookhart MA. Healthy user and related biases in observational studies of preventive interventions: A primer for physicians. J Gen Intern Med 2011;26:546–550.
27. Diggle PJ, Heagerty P, Liang K-Y et al. Analysis of Longitudinal Data, 2nd Ed. New York: Oxford University Press Inc., 2002.
28. Stone NJ, Robinson J, Lichtenstein AH et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2889–2934.
29. Thompson PD, Clarkson PM, Rosenson RS. An assessment of statin safety by muscle experts. Am J Cardiol 2006;97:69C–76C.
30. Bruckert E, Hayem G, Dejager S et al. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients—the PRIMO study. Cardiovasc Drugs Ther 2005;19:403–414.