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CARDIOVASCULAR SECONDARY PREVENTION BY STATIN IN SOUTHERN FRENCH NURSING HOME

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Abstract: *Objectives:* To examine the prevalence of blood lipid monitoring and statin use in secondary prevention of residents in southern French nursing homes for dependent elderly people. *Design, Setting and Participants:* Observational study in 12 southern French nursing homes for dependent old persons with coronary heart disease, ischemic stroke, peripheral artery disease or diabetes. *Measurements:* Collection from medical charts of blood lipid monitoring, LDL-C levels, statin use and geriatric assessment among 965 residents. *Results:* 410/965 residents were eligible for secondary prevention of atherosclerotic complications. Blood lipid was measured in 195 residents and lipid-lowering drugs were given to 106 (statin in 101). The rate of statin use was significantly reduced with increasing age and dependence severity. One third of residents under statin were not monitored for blood lipid. *Conclusion:* Blood lipid monitoring and statin use were subnormal in nursing home residents under secondary prevention. There is a need for prospective studies in this population and precise recommendations taking into account geriatric assessment criteria.

Key words: Atherosclerotic pathologies, secondary prevention, statin, nursing home.

Introduction

Atherosclerotic cardiovascular diseases are the major (63 %) cause of death in nursing home residents (1). Thus, efforts to reduce their incidence, recurrence and complications are important in such patients. There has been some controversy on the influence of cholesterol on atherosclerotic complications in very old persons, but it is now recognized that the absolute effects of cholesterol on annual ischemic heart mortality rates are much greater in older than in younger although its relative role in atherosclerotic diseases decreases with age (2, 3).

Statins are highly effective for reducing cardiovascular morbi-mortality as well as all-cause mortality in secondary prevention and in primary prevention of high risk adults (4). However, patients older than 75 years have been excluded from large randomized clinical trials (5). Lack of evidence, doubts about their benefits and concerns about their side effects have led to an underutilization of statin in this population. Actually, statin indication in older (6,7) and in nursing home is a matter of debate (8).

Residents in nursing home are a special subset of older people with high incidence of dependency, co-morbidities, poly-medications and limited life expectancy. It has been recommended that in secondary prevention statin prescription in older than 75 should be personalized and should take into account indices of geriatric assessment (9-11). The objectives of our observational study was (1) to evaluate the prevalence of statin treatment and lipid monitoring in secondary prevention (coronary heart disease [CHD]; ischemic stroke; peripheral artery disease [PAD] and diabetes) in southern French nursing home, (2) to study their association with geriatric assessment and physicians attitude.

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Patients and methods

Study population

The study was approved by the Ethical Committee of the Departmental Geriatrics Center. The study population consisted of 965 residents living in 04 public and 08 private nursing homes in Marseille and its surroundings.

Data collection

Age, gender, geriatric assessment (GA), atherosclerotic vascular diseases (CHD, ischemic stroke, PAD), congestive heart failure (CHF), atrial fibrillation and diabetes data were collected from computerizedmedical charts. GA includes functional and cognitive status, mobility and polymedication. Functional status was assessed by the 1-6 «Autonomie Gerontologie Groupe Iso Ressources» (AGGIR) composite scale (12). This scale used in French geriatric setting as a proxy for dependency estimates the ability of old persons to perform cognitive and daily-life activities without the help of someone else. The residents were ranked in heavily (scores 1-2) or mildly (scores 3-4) functional dependent and independent (scores 5-6). Mini Mental State Examination (MMSE) was used to identify mild and severe cognitive impairment. Resident's mobility was separated into normal (walking one block without help), limited (walking with stick or walker aid) and very limited (chair ridden). Polypharmacy (defined as four or more medications per day) was further separated into three classes: 4-6, 7-8 and ≥ 9. Glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease equation. Moderate or severe renal insufficiency was diagnosed if the GFR was less than 60 or 30 ml/min/1.73 m^2 respectively. Nutritional status has been evaluated with body

mass index (BMI), weight change over the last 1-6 month and serum albumin. Moderate undernutrition was defined by one of these indices: BMI ≤ 21, weight loss ≥ 5 % or 10 % during the last 1 or 6 months respectively or serum albumin ≤ 35 gram/liter. Severe undernutrition was defined by one of these criteria: BMI ≤ 18, weight loss ≥ 10 % or 15 % during the last 1 or 6 months respectively or serum albumin ≤ 30 gram/liter. Specific treatment for cardiovascular diseases including lipid lowering drugs, anti-platelets, anticoagulant and antihypertensive drugs were collected.

Questionnaire-based survey of physicians

Physicians in charge of nursing home residents completed a questionnaire on their attitude about statin prescription in secondary prevention including initiating or not and discontinuing this treatment. They were asked to give the reasons why they do not initiate or discontinue statin treatment: doubts on its benefits, on statin tolerance or other priorities, polypathology, polypharmacy.

Statistical analysis

Results are given as mean ± standard deviation (SD). Between groups comparisons were tested for statistical significance with the $\chi 2$ test for categorical variables and with the Mann-Whitney U test for continuous variables as appropriate. Statistical significance was determined at $p < 0.05$. Statistical analysis was performed with the Graph Pad Prism 5 software (La Jolla, CA).

Results

Characteristics of patients

410 residents with atherosclerotic vascular diseases or diabetes were identified among the population of 965 residents (272 men and 693 women) from 04 public and 08 private nursing homes for dependent aged persons. They were separated into 138 men (mean age: 82.8 ± 9.7 years) and 272 women (mean age: 87.7 ± 6.9 years).

Atherosclerotic cardiovascular diseases and diabetes (table 1)

The prevalence of atherosclerotic cardiovascular diseases was 30.98 % (299/965 residents: 103 men and 196 women), separated into CHD (n=104), ischemic stroke (n=135), PAD (n= 50) and associated CHD -ischemic stroke (n=10). Residents with chronic atrial fibrillation (n= 86) and congestive heart failure (n=44) were not included in this group.

The prevalence of diabetes in the population of nursing homes participating in the study was 19.7 % (190/965 residents). The patients with diabetes were either insulin-treated (n=84), treated with oral antidiabetic agents (OAA, n=72) or without any antidiabetic medication (n= 34). Seventy-nine of these residents (39 insulin-treated, 26 OAA-treated and 14 without antidiabetic treatment) had an atherosclerotic pathology.

Geriatric assessment (table 1)

The majority of residents included in the survey showed a high degree of dependency as evidenced by the high percentage of residents with an 1-2 AGGIR score (54.6%), with a very limited mobility (40.2%) and with a severe cognitive impairment (39.3%). Residents displayed moderate renal insufficiency in 25.9 % of cases and severe renal insufficiency in 4.1 %. Moderate undernutrition was observed in 26.1 % and severe undernutrition in 12.5 %. Polymedication with 4 or more medications/day) was noticed in 92.7 % of residents; 28.1 % of them received 7-8 medications/day and 28.3 % received 9 or more medications/day.

Statin treatment

Lipid-lowering drugs including statin in 101 cases, fibrate in 3 cases, ezetimibe in 1 case and cholestyramine in 1 case were used in 106 residents. Atorvastatin and rosuvastatin were the most used statins. In the majority of residents, the intensity of statin was moderate: 5-10 mg for rosuvastatin, 10 mg for atorvastatin, 10-20 mg for simvastatin and 20-40 mg for pravastatin. Clinical and biological tolerance of statin was good in all cases: no increase in liver enzymes and creatine kinase (CK) levels were observed and no muscle complaints were recorded.

No significant difference was observed in statin prescription between CHD, ischemic stroke, PAD and the association CHD-ischemic stroke. Antiplatelets and antihypertensive drugs were significantly more used than statin (table 2). The majority of statin-treated residents (n= 101) were given antiplatelets (69/101; 68.3 %) or antihypertensive drugs (80/101; 79.2 %). The rate of statin use was similar in residents with diabetes than in residents with atherosclerotic diseases. Statin use was more frequent in insulin-treated (19/81; 23.5 %) than in OAA-treated (9/72; 12.5 %) and in non-treated residents (2/33; 6.1 %).

A significant reduction in statin prescription was observed with increasing age (from 75 % in residents younger than 65 years old to 2Z % at 85-90 years and 16 % in older than 90. Similarly, statin was less used with increasing dependence as shown by the AGGIR score, very limited mobility and undernutrition. Statin prescription increases significantly and proportionally with polymedication rates. A moderate, but no significant reduction in statin use was observed in severe cognitive impairment and renal insufficiency (Table 3).

Blood lipid levels (table 4)

Blood lipid was measured in 195/410 residents (72/101 statin users). No lipid assay was available in 29/101 residents treated with statin. LDL-C levels lower than 1g/l were observed in 101 residents (50 statin users); LDL-C ranged between 1 and 1,3 g/l in 57 residents (13 statin users) while it was above 1.3g/l in 37 (7 statin users). LDL-C could not be calculated in 2 residents due to hypertriglyceridemia. LDL-C less than 1 g/l was significantly higher in residents treated with statin compared with those without statin (71.4 % vs 40.8 % in

secondary prevention; 71.7 % vs 40 % in atherosclerotic cardiovascular diseases; 69.2 % vs 41.5 % in diabetes; 62.2 % vs 40 % in diabetes + atherosclerosis).

Table 1
Characteristics of 410 residents with cardiovascular diseases and diabetes in nursing homes

	n (%)[a]
Age at survey, mean ± SD	86.1 ± 8.2
Female	272 (66.3)
Age classes (years)	
< 65	8 (2.0)
65-74	33 (8.0)
75-84	94 (22.9)
85-89	118 (28.8)
≥ 90	157 (38.3)
Geriatric assessment	
AGGIR score	
Heavy dependence (GIR 1-2)	224 (54.6)
Mild dependence (GIR 3-4)	154 (37.6)
Low or no dependence (GIR 5-6)	32 (7.8)
Mobility	
Normal	135 (33.0)
Limited	110 (26.8)
Very limited	165 (40.2)
Cognitive impairment	
None	99 (24.1)
Mild	150 (36.6)
Severe	161 (39.3)
Renal function	
Normal	279 (68.0)
Moderate renal insufficiency[b]	106 (25.9)
Severe renal insufficiency[b]	17 (4.1)
Nutritional status	
Normal	251 (61.2)
Moderate undernutritionb	107 (26.1)
Severe undernutritionb	51 (12.5)
Polypharmacy (medications/day)	
< 4	30 (7.3)
4-6	149 (36.3)
7-8	115 (28.1)
> 9	116 (28.3)
Cardiovascular diseases	299 (31.4)
Coronary heart disease	104 (34.8)
Ischemic stroke	135 (45.2)
Peripheral vascular disease	50 (16.7)
Coronary heart disease + stroke	10 (3.3)
Diabetes	190 (20.0)
Insulin	84 (44.2)
Oral antidiabetic agents	72 (37.9)
Nonpharmacological controlled	34 (17.9)

a. All data are presented as numbers (%) except when indicated otherwise; b. Some data were not available: 13 related to renal function and 2 related to nutrition status.

Table 2
Therapeutic prevention of cardiovascular diseases in various pathologies

	n (%)				
	CHD n = 104	**Ischemic stroke n = 135**	**PAD n = 50**	**CHD + stroke n = 10**	**P [b]**
Statin	31 (29.8)	31 (23.0)	13 (26.0)	6 (60.0)	0.0698
Antiplatelets	59 (56.7)	72 (53.3)	36 (72.0)	3 (30.0)	0.0402
Anticoagulants	30 (28.8)	30 (22.2)	8 (16.0)	4 (40.0)	0.1936
Antihypertensive	79 (76.0)	85 (63.0)	34 (68.0)	9 (90.0)	0.0799

a. All data are presented as numbers (%). CHD: coronary heart disease; PAD: peripheral artery disease; b. P values for differences between pathologies were calculated using the $\chi 2$ test.

Factors affecting physician's' decision

Thirty-three physicians (in charge of 188/410 residents; 45.9 %) completed the questionnaire. 14/33 physicians did not initiate statin treatment for several reasons: polypathology (100 %), polypharmacy (92.9 %), doubt on its benefits (71.4 %) and tolerance (28.6 %). The underlying factors to the discontinuation of statin were: polypharmacy (78.8 %), polypathology (75.8 %), doubt on statin benefit (51.7 %) or tolerance (37.9 %).

Discussion

Our results show that the prevalence of cardiovascular diseases and diabetes are high as already reported in the literature. In the present study, only one-fourth of the residents in secondary prevention were treated with statin, the rate of statin prescription decreasing with aging and dependence severity. Statin was also less used in residents with fewer daily medications. Blood lipid was measured in 47.6 % residents in secondary prevention and in 71.3 % residents treated with statin. Physicians in charge of these residents described other priorities due to polypathology and polymedication.

Our data confirm the cholesterol paradox previously reported in older people (13). Indeed, statin use is subnormal although cardiovascular diseases are the most frequent cause of death in persons 75 years and more (14, 15). In older people, statin is still underutilized as reported in several studies (13, 16-21). The prevalence of statin utilization in nursing home residents varies from 30 % in Spain (22) to 31,8 % after hospitalization in cardiology (23). Underutilization of lipid-lowering therapy in the elderly could have many explanations (24).

Firstly, physician could be inattentive to cardiovascular prevention because of multiple other diseases. Priority is then given to manage other chronic conditions due to constraints in time, expertise and preferences (25). Indeed, polypathology and polymedication are the main reasons for not initiating or discontinuing statin treatment in nursing home residents. The

lack of blood lipid assessment in one-third of patients under statin use supports this explanation.

Table 3
Characteristics of residents under secondary prevention treated or not with statin

	n (%)[a]		P[b]
	Statin	**No statin**	
Sex			0.0893
Male	41 (29.7)	97 (70.3)	
Female	60 (22.1)	212 (77.9)	
Age classes (years)			< 0.0001
< 65	6 (75.0)	2 (25.0)	
65-74	15 (45.5)	18 (54.5)	
75-84	28 (29.8)	66 (70.2)	
85-90	26 (22.0)	92 (78.0)	
> 90	26 (16.6)	131 (83.4)	
Geriatric assessment			
AGGIR score			0.0022
Heavy dependence (GIR 1-2)	42 (18.7)	182 (81.3)	
Mild dependence (GIR 3-4)	45 (29.2)	109 (70.8)	
Low or no dependence (GIR 5-6)	14 (43.7)	18 (56.3)	
Mobility			0.015
Normal	43 (31.9)	92 (68.1)	
Limited	29 (26.4)	81 (73.6)	
Very limited	29 (17.6)	136 (82.4)	
Cognitive impairment			
None	28 (28.3)	71 (71.7)	0.2825
Mild	40 (26.7)	110 (73.3)	
Severe	33 (20.5)	128 (79.5)	
Renal function			0.6446
Normal	74 (25.8)	213 (74.2)	
Moderate renal insufficiency[c]	24 (22.6)	82 (77.4)	
Severe renal insufficiency[c]	3 (17.6)	14 (82.4)	
Nutritional status			0.0154
Normal	74 (29.4)	178 (70.6)	
Moderate undernutritionc	20 (18.7)	87 (81.3)	
Severe undernutritionc	7 (13.7)	44 (86.3)	
Polypharmacy (medications/day)			< 0.0001
< 4	0	30	
4-6	18 (12.1)	131 (87.9)	
7-9	39 (33.9)	76 (66.1)	
> 9	44 (37.9)	72 (62.1)	

a. All data are presented as numbers (%); b. P values for differences between statin use or not were calculated using the $\chi 2$ test; c. Some data were not available: 13 related to renal function and 2 related to nutrition status.

Table 4
Lipid management in secondary prevention. Data includes only residents with valid LDL assay

		n (%)[a]		P[b]
Pathology	**LDL-C (g/l)**	**Statin**	**No statin**	
Secondary prevention				0.0002
	< 1.0	50 (49.5)	51 (50.5)	
	1.0-1.3	13 (22.8)	44 (77.2)	
	> 1.3	7 (18.9)	30 (81.1)	
Atherosclerosis				0.0011
	< 1.0	38 (52.8)	34 (47.2)	
	1.0-1.3	10 (26.3)	28 (73.7)	
	> 1.3	5 (17.9)	23 (82.1)	
Diabetes				0.0163
	< 1.0	27 (50.0)	27 (50.0)	
	1.0-1.3	6 (19.4)	25 (80.6)	
	> 1.3	6 (31.6)	13 (68.4)	
Diabetes + atherosclerosis				0.1209
	< 1.0	15 (60.0)	10 (40.0)	
	1.0-1.3	3 (25.0)	9 (75.0)	
	> 1.3	4 (40.0)	6 (60.0)	

a. All data are presented as numbers (%); b. P values for differences between statin use or not were calculated using the $\chi 2$ test.

Secondly, the cholesterol paradox is likely due to misconception in benefit-harm tradeoff since there is a lack of perception of real risk by physicians in this age category (26, 27) although the excessive cardiovascular mortality attributable to elevated serum cholesterol levels increase with age (28).

Thirdly, there is a belief that treatment is less effective in older people despite counter evidence. Indeed, beneficial effects of statin have been reported in several studies on secondary prevention of cardiovascular diseases in very old persons. In an observational prospective study of 1410 older patients, mean age 81 years, with prior myocardial infarction and a serum LDL- C of 1.25 g/l or higher, use of statin for a 3-year period significantly reduced CHD related death or nonfatal myocardial infarction by 50%, stroke by 60% and heart failure by 48%. New coronary events were also significantly reduced in patients older than 90 years. (29). Beneficial effects of statin in secondary prevention have also been reported in elderly people with polypathology (30) and in nursing home residents (31). In older patients with diabetes, statin reduces cardiovascular morbidity (32) and all- cause of mortality (33).

Fourthly, there are also concerns about statin safety due to the higher comorbidities and polypharmacy. However, tolerance and safety of statin do not change in older people, especially with low or moderate doses (24). Intensive statin therapy is associated with a moderate, but significant increase

in muscular intolerance in older patients (34).

Physicians and geriatricians should be aware of the real-benefit risk of statin in older people. Interestingly, statin use in patients with coronary heart disease living in an academic nursing home increased from 21 % in 2002 to 70 % and to 87 % in 2003 and 2008, respectively, following an educational program (35).

According to the guidelines recently published, statin should be used in secondary prevention, although after 75, it should be limited to moderate doses (9, 36, 37). Statin treatment should be continued unless concerns about tolerance or safety emerge. The introduction of statin in so far untreated patient may be discussed: in the STOPP-START screening tool, statin use was advised in persons with CHD, ischemic stroke or PAD if the life expectancy is higher than 5 years and if they have a good activity daily life score; in persons with diabetes, statin should be given if one major cardiovascular risk factor present (38). Residents in nursing home are a specific subgroup of older persons with high incidence of comorbidities and limited life expectancy. Therefore, decisions about statin prescription or discontinuation should take into account their life expectancy (39). The minimal exposure to statin that could be beneficial ranges from 3.2 years (40) to 5.3 years (41). Law et al have reported that after lowering blood cholesterol by 10 % in the 55-64 years, CHD incidence is reduced by 7 % during the first two years, 22 % and 25 % after 2.1-5, and more than 5 years, respectively (3). When life expectancy is limited and especially in the palliative care setting, statin should be discontinued since no difference in life duration and even improved quality of life have been reported (42).

The strength of our study is based on the analysis of a large number of medical charts of residents living in several nursing homes under the medicare of numerous physicians. One limitation of our study is the lack of knowledge on blood lipid level and statin utilization on hospital discharge after cardiovascular events. Indeed, statin may have been prescribed to a larger number of residents prior to discontinuing its use for undetermined reasons. Besides, the putative beneficial effect of statin could not be investigated in our study.

In conclusion, secondary prevention of cardiovascular diseases by intervention on blood lipid levels remains underemployed in nursing home in the absence of guidelines for this population. Further extensive cohort studies on statin tolerance, safety and reduction of mortality or new cardiovascular events are needed to delineate the profiles of residents in nursing homes leading to the prescription or discontinuation of this treatment.

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