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Association between the intensity of statin therapy and physical activity 1 year after acute coronary syndrome: a multicentre prospective cohort study in Switzerland

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ABSTRACT

Objectives To assess the association between the intensity of statin therapy and the level of physical activity in patients 1 year after an acute coronary syndrome (ACS).

Design Prospective cohort study from the Special Program University Medicine-Acute Coronary Syndromes.

Setting Four university hospital centres in Switzerland.

Participants 2274 patients with a main diagnosis of ACS between 2009 and 2017 who were available for a 1-year follow-up visit 1 year after hospital discharge.

Outcome measures Self-reported physical activity was assessed with the International Physical Activity Questionnaire. The level of physical activity in metabolic equivalent-minutes per week (MET-min/week) was first stratified into sedentary and physically active categories and then analysed continuously among physically active patients. Analyses were performed using a propensity score weighting approach.

Results One year after ACS, 1222 (53.7%) patients were on high-intensity statin therapy, 890 (39.1%) were on low/moderate-intensity statin therapy and 162 (7.1%) were not on statin therapy. Compared with non-statin users, low-/moderate-intensity statin users and high-intensity statin users were more likely to be physically active than sedentary, with a fully adjusted OR of 2.86 (95% CI 1.12 to 7.26) and 4.52 (95% CI 1.68 to 12.20), respectively. Among physically active patients, physical activity level was similar across all statin user categories, with median levels of 2792.5, 2712.0 and 2839.5 MET-min/week in non-statin, moderate/low-statin and high-statin users, respectively (p=0.307).

Conclusions One year after ACS, neither low-/moderate-intensity nor high-intensity statin uses were associated with reduced self-reported physical activity compared with non-statin use. The concern that statin therapy may impair physical activity among ACS patients was not confirmed in this study.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ We studied a large number of 'real-world' patients who were very well characterised by a clinical team from a multicentre observational study.
- ⇒ We used an adapted regression model that takes into account sedentary behaviour and fits the data well.
- ⇒ The International Physical Activity Questionnaire is a self-administered questionnaire that may be subject to measurement error or recall bias.
- ⇒ Information on statin-associated muscle symptoms was not available, whereas it may influence both statin use or intensity and physical activity.

INTRODUCTION

Physical activity and a healthy lifestyle combined with lipid-lowering drugs are cornerstones of secondary prevention of cardiovascular disease.[1] The WHO recommends more than 150 min per week of moderate-intensity to vigorous-intensity physical activity (MVPA) to maintain global health.[2] Higher levels of physical activity are also encouraged, and 3 hours per week of vigorous-intensity activity further decreases the risk of myocardial infarction and cardiovascular mortality.[3 4] Lipid-lowering drugs such as statin therapy have been studied over the past years in their potential at preventing recurrent cardiovascular events and are now systematically recommended after a first cardiovascular event. Regular physical activity and statin therapy are independently beneficial to reduce the risk of cardiovascular disease, and their combination seems to be more effective than either alone.[5 6] However, statin-associated muscle symptoms (SAMS) were reported by 10 to 15% of patients on statin therapy. When present, this frequent side effect may limit physical activity.[7 8] Although the mechanism of SAMS remains unclear,[5 9 10] an association with statin intensity

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or dose has been proposed.[7] Therefore, even if recommended by numerous prevention guidelines, physicians may be reluctant to prescribe or sustain high-intensity statin after an acute coronary syndrome (ACS) to avoid limitations in physical activity. To disentangle this issue, we aimed to study the association between the intensity of statin therapy and the level of physical activity in a large well-characterised prospective cohort of patients 1 year after their hospitalisation for ACS.

METHODS

Study population

The Special Program University Medicine-Acute Coronary Syndromes (SPUM-ACS) study is an observational prospective Swiss cohort of patients hospitalised for ACS in four university hospitals in Switzerland (Bern, Geneva, Lausanne and Zürich). Details concerning the SPUM-ACS study have been reported previously.[11] The recruitment was performed from 2009 to 2017. Patients were eligible if they were 18 years and older, both men and women, presenting with the main diagnosis of ACS. Patients were excluded if they had a severe psychic handicap, were not able to comprehend the study (dementia and language barrier), had an estimated life expectancy of less than 1 year due to a non-cardiac pathology or were not able to be present for follow-up (non-Swiss resident or planned departure). Patient's questionnaires, including physical activity, biological parameters, and medication use, were recorded at discharge and at the 1-year follow-up study visit by a trained study team. For this cross-sectional analysis, we assessed statin use and physical activity level 1 year after the index hospitalisation for ACS. In a supplementary analysis, the evolution of statin use from discharge to the 1-year visit was also reported with the aim of assessing its impact on the level of physical activity 1 year after the index ACS.

Exposure: statin therapy intensity

Statin therapy intensity use 1 year after the index ACS was categorised into three groups: a high-intensity regimen was defined as the dose of statin that reduces low-density lipoprotein cholesterol (LDL-cholesterol) by 50% or more and included atorvastatin 40 mg/day or more and rosuvastatin 20 mg/day or more; moderate-intensity and low-intensity therapies included the use of atorvastatin 20 mg/day or less, rosuvastatin 10 mg/day or less, simvastatin, pravastatin, lovastatin, fluvastatin or pitavastatin; and non-statin therapy included the use of other hypolipaemic therapies as fibrates or natural therapies, or patients with no lipid-lowering therapy.[12] In a supplementary analysis, we further defined three categories according to the evolution of the intensity of statin therapy from hospital discharge to the 1-year follow-up visit after the index ACS. These categories were non-modification of doses, increased intensity when doses changed from low/moderate intensity to high intensity or when statin therapy was introduced, and decreased intensity when doses changed from high intensity to low/moderate intensity or when statin therapy was withdrawn.

Outcome: physical activity

At the 1-year follow-up visit, patients were asked to complete the International Physical Activity Questionnaire (IPAQ).[13] IPAQ is a validated self-reported questionnaire to assess the level of physical activity in metabolic equivalent-minutes per week (MET-min/week). Patients evaluated their types of activity (walking, moderate-intensity activities and vigorous-intensity activities) in different domains including leisure time, domestic/gardening, work-related and transport-related activities. A metabolic equivalent, or MET, is a measure of the ratio of energy expense for physical activity compared with the basis metabolic rate which MET equals 1 (sitting quietly). This weighting factor is calculated in the IPAQ as follows: 3.3 for walking, 4.0 for moderate-intensity activities and 8.0 for vigorous-intensity activities, and is defined by the mean MET of the different activities in each category. A MET-minute is computed by multiplying the MET score of an activity by the minutes performed. Computation of the total score requires the summation of the duration (minutes) and frequency (days per week) of all the types of activities in all domains. Sedentary behaviour was defined as the absence of any physical activity, namely a physical activity level in MET-min/week equal to 0, for example, somebody reporting 0 min and/or days of physical activity in all types of activity. As recommended, patients with missing information on the IPAQ were excluded as follows: in at least one type of activity, there was missing information for both duration and frequency, or there was only missing duration information with a frequency superior to zero, or there was only information about duration without frequency. Outliers, defined as patients with unrealistic scores, namely reporting more than 16 hours per day or more than 7 days per week of physical activity, were also excluded.

Covariates

Education status was dichotomised as having graduated from high school or university or having a lower-level education. Smoking status was categorised into current, former and never-smokers. LDL-cholesterol level was processed locally using standardised dosage methods. Type of ACS was categorised as ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction and unstable angina. Congestive heart failure was defined as a Killip score of II or higher at admission for the index ACS. Premature coronary heart disease (CHD) was defined as a previous diagnosis of CHD before 55 years old in men and before 60 years old in women. Heterozygous familial hypercholesterolaemia was defined as possible or probable using Dutch Lipid Clinic Network diagnostic criteria, as a score greater than 2. Diabetes was either self-reported or diagnosed using antihyperglycaemic medication or a haemoglobin A1c of 6.5% or greater at admission. Body mass index

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(BMI) is calculated as weight in kilograms divided by height in metres squared. Elevated alcohol consumption was defined as more than 14 units per week based on patients' self-report. Depression was characterised as the use of antidepressant drugs or with a Center for Epidemiological Studies-Depression Scale score greater than 15.[14] Chronic disease was defined as the merging of chronic lung disease, malignancy history, chronic liver disease, chronic inflammatory disease, dialysis history, immunosuppressive therapy and hormonal therapy use. Antihypertensive drugs included ACE inhibitors, or angiotensin II receptor blockers, or beta-blockers, or calcium-channel blockers, or diuretics.

Statistical analyses

We categorised patients according to statin intensity 1 year after the index ACS and compared clinical characteristics across categories. For group comparisons, different statistical tests were used according to the variable to analyse: Analysis of variance (ANOVA test) for means, χ^2 test for categorical variables, Fisher's exact test for variables with unbalanced distribution or Kruskal-Wallis test for medians. Confounders were determined by biological plausibility, as well as their potential clinical association with SAMS. We assessed the associations between statin intensity, evolution in statin intensity over 1 year and patient-reported physical activity level using propensity score (PS) weighting.[15] Pairwise contrasts were defined for low-/moderate-intensity statin use versus non-statin use, high-intensity statin use versus non-statin use, decreased-intensity versus non-modification, and increased-intensity versus non-modification. Due to the significant presence of zeros in the distribution of physical activity score (sedentary patients), strongly impacting the mean MET-min/week, contrast effects on being non-sedentary were estimated separately using PS-weighted odds ratios, while we described contrast effects on the positive score using PS-weighted mean differences. The last is expressed on a logarithmic scale because of the strong right asymmetry of the physical activity score distribution. Three incremental adjustments were made in the PS estimation: in a first model, we adjusted for age and gender. In a second model, we further adjusted for formal education, BMI, depression, type of ACS and chronic disease. In the final model, we further adjusted for premature CHD, congestive heart failure at admission, LDL cholesterol, antihypertensive treatment, attendance to cardiac rehabilitation after hospital stay and follow-up medical visits after ACS.

All hypothesis tests were two-sided and the significance level was set at 5%. Statistical analyses were performed using STATA 16 (STATA Corp, College Station, Texas, USA) and R software. For PS analysis, we used the R package *PSweight*, including a general class of balancing weights as the 'overlap weights', that proved to lead to optimal covariate balance and estimation efficiency diagnostic graphs for covariate balance assessment, and handling multiple treatments.[16 17]

Patient and public involvement

None.

RESULTS

Among the 6359 patients of the SPUM-ACS observational cohort included, 6099 (96%) were alive at the 1-year follow-up visit. Of these, 3814 (63%) were excluded because of missing or invalid IPAQ. An additional 11 patients were excluded because of missing data on statin use at the 1-year follow-up visit, leaving 2274 patients for this analysis (online supplemental figure 1 in the Supplementary Material).

Characteristics of the 2274 patients according to statin intensity at the 1-year follow-up visit after the index ACS are reported in table 1. Most patients (53.7%) were using high-intensity statin, 39.1% had a low-intensity or moderate-intensity statin and 7.1% were not using statin. High-intensity statin users were younger with a greater BMI, were more likely to have an ST-elevation myocardial infarction and were less likely to suffer from a chronic disease or from depression than other statin categories. Non-statin users had higher LDL-cholesterol levels and were less likely to have other preventive treatments such as aggregation inhibitors or hypotensive drugs compared with other statin intensity categories. Non-statin users also participated less frequently in cardiac rehabilitation after hospital discharge and were less likely to have both primary care and cardiologist medical follow-up than other statin intensity categories.

The distribution of physical activity levels within the 2274 patients is reported in figure 1 and table 2. 92 patients (4%) reported being sedentary with an IPAQ score of 0. Non-statin users had a higher probability of being sedentary compared with other statin intensity categories (p=0.007). Characteristics of patients according to sedentary behaviour are reported in online supplemental table 1 in the Supplementary Material. Compared with physically active patients, sedentary patients were on the one hand less likely to have a higher education, to live with someone, to participate in rehabilitation after hospital stay or to have a cardiologist follow-up, and on the other hand, they were more likely to suffer from cardiovascular event recurrence, diabetes, chronic disease or depression, or to have a greater body mass index or an antiarrhythmic treatment.

In the 2274 patients, we found that statin use increases the odds of not being sedentary, with a multivariate-adjusted OR of 2.86 (95% CI 1.12, 7.26, p=0.027) and 4.52 (95% CI 1.68, 12.20, p=0.003), respectively, for low-/moderate-intensity statin use and high-intensity statin use, compared with non-statin use (table 3, fully adjusted). However, in the 2182 non-sedentary patients (96%), we found no significant effect of statin use on physical activity level, with a multivariate-adjusted mean difference of 0.16 (95% CI −0.36, 0.68, p=0.550) and 0.19 (95% CI −0.33, 0.71, p=0.478) on the logarithmic scale, respectively, for low/moderate-intensity statin use and

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Table 1 Characteristics of patients according to statin intensity 1 year after acute coronary syndromes (n=2274)

Characteristic	N	Non-statin (n=162)	Moderate/low-intensity statin (n=890)	High-intensity statin (n=1222)	P value
Age, year, mean (SD)	2274	62.9 (12.2)	63.0 (11.9)	61.0 (11.6)	0.000[a]
Women, N (%)	2274	37 (22.8)	169 (19.0)	212 (17.3)	0.199[b]
Ethnic background*, N (%)	2274	157 (96.9)	846 (95.1)	1176 (96.2)	0.315[b]
Higher education†, N (%)	2221	62 (38.8)	295 (34.1)	394 (33.0)	0.342[b]
Living status‡, N (%)	2266	114 (70.4)	673 (76.0)	950 (77.9)	0.088[b]
Smoking status, N (%)	2273				
Never	675	56 (34.6)	259 (29.1)	360 (29.5)	0.388[b]
Former	1113	70 (43.2)	451 (50.7)	592 (48.4)	
Current	485	36 (22.2)	179 (20.1)	270 (22.1)	
LDL-cholesterol, mmol/L, median (IQR)	2042	2.8 (3.4–4.1)	1.6 (2.1–2.7)	1.6 (2.0–2.4)	0.000[d]
Type of ACS, N (%)	2270				
STEMI	1242	74 (46.0)	426 (48.0)	742 (60.7)	0.000[b]
NSTEMI	922	75 (46.6)	407 (45.9)	440 (36.0)	
Unstable angina	106	12 (7.5)	54 (6.1)	40 (3.3)	
Congestive heart failure§, N (%)	2248	18 (11.1)	83 (9.4)	116 (9.6)	0.797[c]
Two or more CV events, N (%)	2274	49 (30.2)	259 (29.1)	309 (25.3)	0.098[b]
Premature CHD¶, N (%)	2274	55 (34.0)	264 (29.7)	425 (34.8)	0.044[b]
Heterozygous familial HCL**, N (%)	2274	39 (24.1)	148 (16.6)	276 (22.6)	0.002[c]
Diabetes mellitus††, N (%)	2274	28 (17.3)	169 (19)	218 (17.8)	0.754[b]
Body mass index, kg/m^2, mean (SD)	2138	26.4 (4.2)	26.8 (4.2)	27.5 (4.4)	0.000[a]
Elevated alcohol use‡‡, N (%)	1871	21 (16.5)	108 (14.8)	278 (22.8)	0.713[b]
Depression§§, N (%)	2274	49 (30.2)	201 (22.6)	278 (22.8)	0.089[b]
Chronic disease¶¶, N (%)	2266	24 (15.0)	155 (17.5)	150 (12.3)	0.004[b]
Aggregation inhibitors or anticoagulant, N (%)	2270	157 (98.1)	888 (100)	1222 (100)	0.000[c]
Antiarrhythmics, N (%)	2273	10 (6.2)	32 (3.6)	37 (3.0)	0.118[b]
Antihypertensive treatment***, N (%)	2274	130 (80.2)	833 (93.6)	1168 (95.6)	0.000[b]
NSAIDs, N (%)	2269	1 (0.6)	17 (1.9)	26 (2.1)	0.530[c]
Antiretroviral, N (%)	2269	2 (1.3)	11 (1.2)	6 (0.5)	0.116[c]
Rehabilitation after ACS, N (%)	2274	53 (32.7)	411 (46.2)	601 (49.2)	0.000[b]
Duration, days, median (IQR)	1284	23 (32.0–44.0)	28 (38.0–56.0)	27 (39.0–62)	0.003[d]
Medical follow-up after ACS, N (%)	2156	102 (68.0)	636 (75.1)	882 (76.1)	0.097[b]
No medical follow-up	2	0 (0.0)	1 (0.1)	1 (0.1)	0.033[b]
Cardiologist only	160	14 (9.3)	78 (9.2)	68 (5.9)	
Primary care only	374	34 (22.7)	132 (15.6)	208 (17.9)	
Both primary care and cardiologist	1620	102 (68.0)	636 (75.1)	882 (76.1)	

Statistic tests were performed as follows: [a]Analysis of variance (ANOVA test); [b]χ^2 test; [c]Fisher's exact test; [d]Kruskal-Wallis.
*Defined as Caucasian.
†Defined as a high school or university graduation or higher.
‡Defined as living with someone.
§Defined as Killip score of II or higher at admission for the index ACS.
¶Defined as CHD event <55 years for men and <60 years for women.
**Defined as possible or probable using Dutch Lipid Clinic Network diagnostic criteria.
††Based on patients' self-report, use of antihyperglycaemic medication/insulin or haemoglobin A1c of ≥6.5%.
‡‡Defined as more than 14 units alcohol/week.
§§Defined as use of antidepressant drugs or with a Center for Epidemiological Studies-Depression Scale score >15.
¶¶Defined as chronic lung disease, malignancy history, chronic liver disease, chronic inflammatory disease, dialysis history, immunosuppressive therapy use or hormonotherapy use.
***Include ACE inhibitors, or angiotensin II receptor blockers, or beta-blockers, or calcium-channel blockers, or diuretics.
ACS, acute coronary syndrome; CHD, coronary heart disease; CV, cardiovascular; HCL, hypercholesterolaemia; LDL-cholesterol, low-density lipoprotein cholesterol; NSAIDs, non-steroidal anti-inflammatory drugs; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.;

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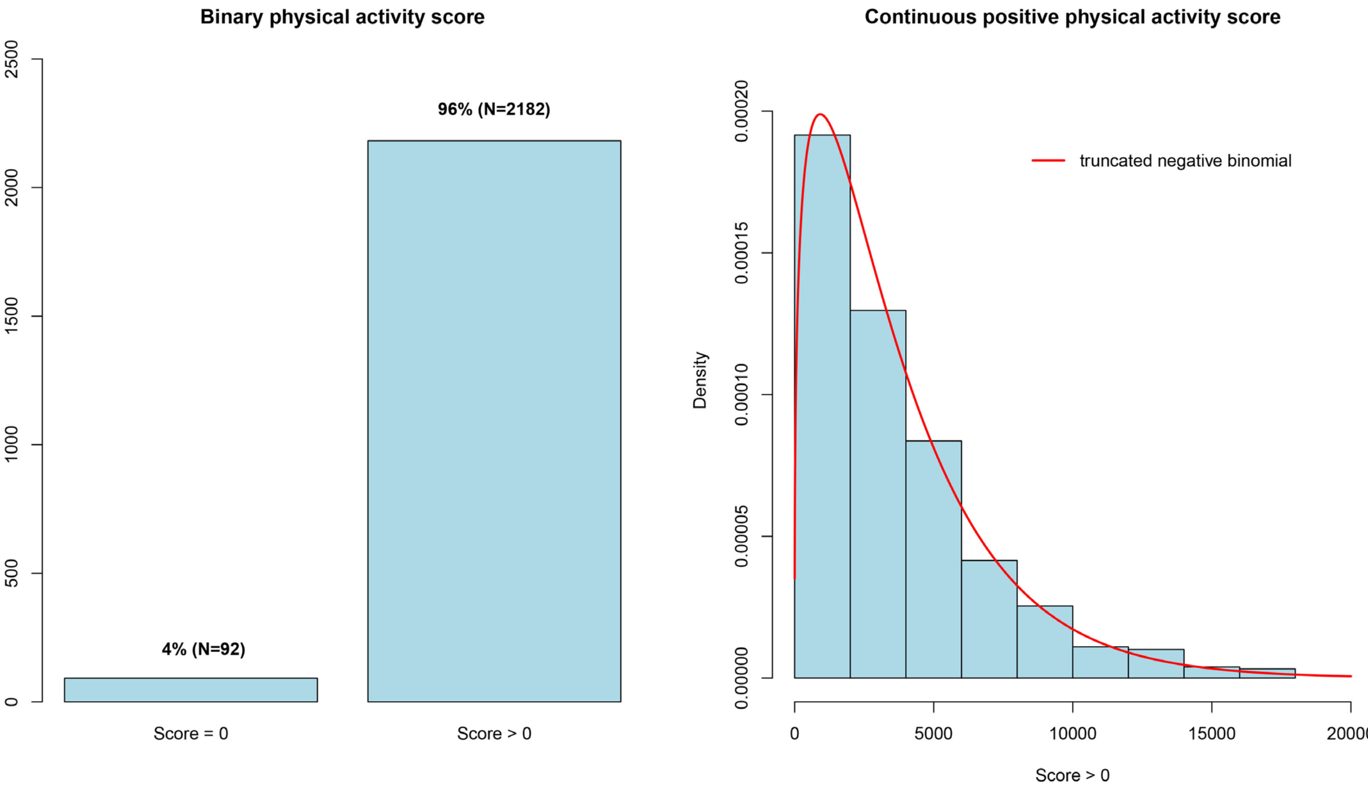

Figure 1 Physical activity distribution at 1-year follow-up (n=2274).

high-intensity statin use compared with non-statin use (table 3, fully adjusted). The distribution of the positive physical activity score (MET-min/week >0) reported in online supplemental figure 2 in the Supplementary Material showed no differences between the three categories of statin use.

From hospital discharge to the 1-year follow-up visit after ACS, 1659 (73.0%) patients did not change their statin therapy intensity, 435 (19.1%) decreased statin intensity or ceased statin therapy and 180 (7.9%) initiated a statin therapy or increased statin intensity (figure 2). Characteristics and physical activity levels of the 2274 patients according to statin intensity evolution over the year after ACS are reported in online supplemental tables 2 and 3 in the Supplementary Material. Compared with non-modification or increased-intensity statin categories, patients in the decreased-intensity statin category had higher LDL-cholesterol levels, used less frequently preventive drugs such as aggregation inhibitors or antihypertensive treatments and had lower attendance at cardiac rehabilitation after ACS. There was no significant difference between statin categories regarding age, gender, education, type of ACS or pre-existing chronic disease. In all adjusted models, we found that neither the odds of being non-sedentary nor the level of physical activity among non-sedentary patients was influenced by changes in statin intensity over time (table 4).

DISCUSSION

In this large study of patients whose medication and physical activity level were assessed 1 year after their ACS, we first found that statin users were more likely to be physically active than sedentary, but with a large CI which can be explained by the unbalance of the two groups of sedentary (4%) and non-sedentary (96%) patients, and should be interpretated cautiously. Second, among physically active patients, neither statin use nor intensity

Table 2 Sedentary behaviour and level of physical activity 1 year after acute coronary syndrome according to the intensity of statin therapy (n=2274)

	Statin therapy			
	Non-statin (n=162)	Low/moderate-intensity (n=890)	High-intensity (n=1222)	P value
Sedentary behaviour*, N (%)	14 (8.6)	36 (4.0)	42 (3.4)	0.007
Level of physical activity, MET-min/week, median (IQR)	2792 (1246–5349)	2712 (1318–4836)	2839 (1385–5215)	0.307

*Defined as absence of any physical activity: score=0.
MET-min/week, metabolic equivalent-minutes per week.

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Table 3 Associations between the intensity of statin therapy and physical activity 1 year after acute coronary syndromes (n=2274)

Statin therapy intensity categories	Physical activity compared with sedentary behaviour PS-weighted OR (95% CI), p-value	Level of physical activity in physically active patients PS-weighted MD* (95% CI), p value
	Age-adjusted and gender-adjusted	
Non-statin	1.00 (reference)	0.00 (reference)
Low/moderate intensity	2.23 (1.18 to 4.22), *0.014*	0.03 (−0.16 to 0.23), *0.730*
High-intensity	2.51 (1.11 to 5.65), *0.002*	0.08 (−0.11 to 0.27), *0.427*
	Partially adjusted† (n=2080)	
Non-statin	1.00 (reference)	0.00 (reference)
Low/moderate intensity	2.53 (1.28 to 4.99), *0.007*	0.12 (−0.10 to 0.34), *0.278*
High intensity	3.62 (1.81 to 7.25), *<0.001*	0.14 (−0.08 to 0.35), *0.215*
	Fully adjusted‡ (n=1905)	
Non-statin	1.00 (reference)	0.00 (reference)
Low/moderate intensity	2.86 (1.12 to 7.26), *0.027*	0.16 (−0.36 to 0.68), *0.550*
High intensity	4.52 (1.6812.20), *0.003*	0.19 (−0.33 to 0.71), *0.478*

*Logarithm of MET-min/week.
†Model controlled for the following variables: age, gender, formal education, BMI, depression, type of ACS and chronic disease.
‡Model controlled for the following variables: age, gender, formal education, BMI, depression, type of ACS, chronic disease, premature CHD, CHF, LDL-cholesterol, antihypertensive treatment, rehabilitation after index ACS and both primary care and cardiologist visits after index ACS.
ACS, acute coronary syndrome; BMI, body mass index (calculated as weight in kilograms divided by height in metres squared); CHD, coronary heart disease; CHF, congestive heart failure; LDL-cholesterol, low-density lipoprotein cholesterol; MD, mean difference; MET-min/week, metabolic equivalent-minutes per week; PS, propensity score.

was associated with the level of MET-min performed each week. Third, we also found no association between changes in the intensity of statin therapy during the year after ACS and the level of physical activity. Taken together, these findings add to the evidence that neither the use nor the intensity of statin therapy limits physical activity in ACS patients.

The effects of statin therapy on physical activity have been previously studied. Yet, this evidence suffers from a large heterogeneity in populations and outcome measures.[9 10 18] Many studies examined the effect of statin therapy on physical activity at a metabolic or physiological level. According to a recent review of randomised controlled trials on the effects of statin therapy on physical

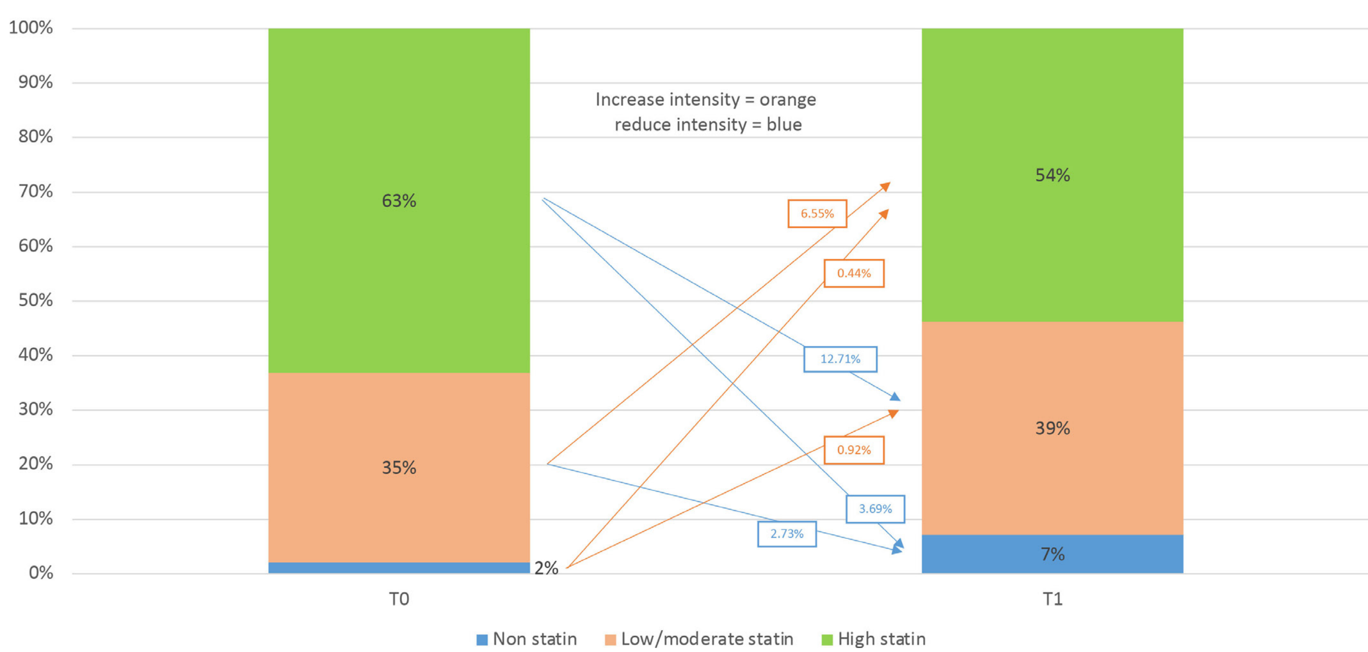

Figure 2 Statin intensity evolution over 1 year after acute coronary syndromes (n=2274).

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Table 4 Associations between statin intensity evolution over the year post-acute coronary syndromes and physical activity (n=2274)

Statin therapy evolution categories	Physical activity compared with sedentary behaviour PS-weighted OR (95% CI), p value	Level of physical activity in physically active patients PS-weighted MD* (95% CI), p value
	Age-adjusted and gender-adjusted	
Decreased intensity	1.16 (0.69 to 1.94), *0.569*	−0.06 (−0.16 to 0.05), *0.313*
Non-modification	1.00 (reference)	0.00 (reference)
Increased-intensity	1.72 (0.64 to 4.64), *0.286*	−0.08 (−0.26 to 0.09), *0.334*
	Partially adjusted† (n=2080)	
Decreased intensity	1.37 (0.80 to 2.37), *0.253*	−0.02 (−0.14 to 0.09), *0.691*
Non-modification	1.00 (reference)	0.00 (reference)
Increased intensity	2.70 (0.79 to 9.21), *0.113*	−0.03 (−0.21 to 0.14), *0.701*
	Fully adjusted‡ (n=1905)	
Decreased-intensity	0.98 (0.49 to 1.94), *0.953*	−0.01 (−0.13 to 0.11), *0.875*
Non-modification	1.00 (reference)	0.00 (reference)
Increased intensity	3.00 (0.62 to 14.4), *0.170*	0.02 (−0.17 to 0.20), *0.861*

*Logarithm of MET-min/week.
†Model controlled for the following variables: Age, gender, formal education, BMI, depression, type of ACS and chronic disease.
‡Model controlled for the following variables: age, gender, formal education, BMI, depression, type of ACS, chronic disease, premature CHD, CHF, LDL-cholesterol, antihypertensive treatment, rehabilitation after ACS, and primary care and cardiologist visits after ACS.
ACS, acute coronary syndrome; BMI, body mass index (calculated as weight in kilograms divided by height in metres squared); CHD, coronary heart disease; CHF, congestive heart failure at admission; LDL-cholesterol, low-density lipoprotein cholesterol; MD, mean difference; MET-min/week, metabolic equivalent-minutes per week; PS, propensity score.

activity or physical fitness, eight trials reported no association with each other, two trials reported a decrease in physical fitness among statin users and six trials reported that statin therapy improved the level of physical activity,[9] possibly explained by a protective effect of moderate exercise training on SAMS.[19] In our study, we measured the level of physical activity with the IPAQ to compute MET-min/week on a daily life basis for each type of physical activity, and we analysed the data to identify sedentary behaviour as an independent cardiovascular risk factor.[20–22] Indeed, sedentary behaviour, defined by METs of 1.5 or less, is now thought to be different from physical inactivity, which is defined by not meeting physical activity guidelines, with distinct physiological effects and health hazards.[23 24] Finally, our population falls within the scope of secondary prevention, with a clear indication for statin therapy. Many previous studies assessed the association between statin therapy and physical activity in a healthy population. Our results are consistent with previous studies performed on this specific population of patients with CHD. Although physical activity assessment was different, Rengo *et al* demonstrated that long-term statin use does not attenuate aerobic training effects in cardiac rehabilitation patients.[25] Similarly, Toyama *et al*, who studied a 5-week combination of statin and exercise therapy in patients with CHD, demonstrated a significantly cardiopulmonary function increase after statin treatment, as measured by the maximum workload capacity.[26]

Many demographic or clinical conditions, such as older age, female sex, chronic diseases, obesity or high-statin dose, are associated with increased risk of SAMS, as recently reported by Bytyçi *et al*.[27] In our population, sedentary patients were more likely to have health conditions that could limit physical activity compared with physically active patients. We included those potential confounders in adjusted models and none of them strongly influenced the association between statin therapy intensity and physical activity. Similarly, physically active patients were more likely to have a higher education, to live with someone and to attend cardiac rehabilitation after hospital discharge than sedentary patients. These factors could be a reflection of patients' motivation to enhance their health condition but were not found to have a significant influence on the association between the intensity of statin therapy and the level of physical activity. These results also come up against the thought that fully sedentary patients could have been bedridden patients. We were also able to assess the type of medical follow-up after hospital discharge, which can be different between primary care physicians and cardiologists. Although sedentary patients were more likely to have a primary care follow-up only, and physically active patients were more likely to have a cardiologist follow-up only, this difference was not found to affect the association between statin intensity and level of physical activity. Finally, in our study, 73% did not change their statin therapy intensity, and 7% were not using statins 1 year after the index ACS.

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Reasons for discontinuation or change of statin intensity have been previously reported elsewhere in this cohort study.[28]

Our study presents some limitations. First, the IPAQ is a self-administered questionnaire and could be subject to measurement error or recall bias.[29] Future research should include objective measures of physical activity with multiple monitoring periods. Second, information about SAMS was not collected in our population. SAMS can influence both statin use and physical activity. We addressed this issue by including known risk factors of SAMS in our adjusted models. However, not all SAMS are necessarily related to statin use, and the nocebo effect may also play a role.[30 31] Another limitation is the absence of unmeasured factors that can impair physical activity. For example, as recently reported by Gonzalez-Jaramillo *et al*, peripheral artery disease is associated with an increased risk of sedentarity.[32]

Conclusions

In this large observational study of ACS patients, we found no effect of statin use or statin intensity on patients' self-reported physical activity level 1 year after ACS. These observational findings may reassure patients and health professionals that statin therapy does not affect physical activity after ACS. Patients should be encouraged to engage in physical activity after ACS, regardless of statin prescription.

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