Atherosclerosis 239 (2015) 118–124

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Expected impact of applying new 2013 AHA/ACC cholesterol guidelines criteria on the recommended lipid target achievement after acute coronary syndromes

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ARTICLE INFO

Article history:
Received 7 November 2014
Received in revised form
14 December 2014
Accepted 18 December 2014
Available online 6 January 2015

Keywords:
Acute coronary syndromes
Secondary prevention
Lipids
Guidelines adherence

ABSTRACT

Background: 2013 AHA/ACC guidelines on the treatment of cholesterol advised to tailor high-intensity statin after ACS, while previous ATP-III recommended titration of statin to reach low-density lipoprotein cholesterol (LDL-C) targets. We simulated the impact of this change of paradigm on the achievement of recommended targets.

Methods: Among a prospective cohort study of consecutive patients hospitalized for ACS from 2009 to 2012 at four Swiss university hospitals, we analyzed 1602 patients who survived one year after recruitment. Targets based on the previous guidelines approach was defined as (1) achievement of LDL-C target < 1.8 mmol/l, (2) reduction of LDL-C ≥ 50% or (3) intensification of statin in patients who did not reach LDL-C targets. Targets based on the 2013 AHA/ACC guidelines approach was defined as the maximization of statin therapy at high-intensity in patients aged ≤75 years and moderate- or high-intensity statin in patients >75 years.

Results: 1578 (99%) patients were prescribed statin at discharge, with 1120 (70%) at high-intensity. 1507 patients (94%) reported taking statin at one year, with 909 (57%) at high-intensity. Among 482 patients discharged with sub-maximal statin, intensification of statin was only observed in 109 patients (23%). 773 (47%) patients reached the previous LDL-C targets, while 1014 (63%) reached the 2013 AHA/ACC guidelines targetsone year after ACS (p value < 0.001).

Conclusion: The application of the new 2013 AHA/ACC guidelines criteria would substantially increase the proportion of patients achieving recommended lipid targets one year after ACS.
Clinical trial number, NCT01075868.

1. Introduction

Statin therapy is strongly recommended in the long-term management of patients with acute coronary syndromes (ACS) [1–5]. The Adult Treatment Panel (ATP III) recommended reaching a low-density lipoprotein cholesterol (LDL-C) target < 1.8 mmol/l (70 mg/dL) in very high-risk patients, such as patients with ACS [6,7]. The paradigm of targeting statin dose for a specific LDL-C goal means that an adequate dose of statin should be prescribed or adapted to reach recommended LDL-C [8]. Nevertheless, previous observational studies have shown that poorly controlled LDL-C levels after ACS are common and statin intensification sub-

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http://dx.doi.org/10.1016/j.atherosclerosis.2014.12.049
0021-9150/

optimal [9–11].

The 2013 AHA/ACC guidelines on the treatment of blood cholesterol abandoned the strategy of using LDL-C targets given the lack of evidence from randomized controlled trials [12]. Patients with ACS are classified as *very high-risk patients* and physicians have to initiate high-intensity statin in those age ≤ 75 years old and moderate- or high-intensity statin in those > 75 years old if no documented contraindications [12]. This new recommended approach represents a change in paradigm regarding statin therapy in secondary prevention, with unknown clinical consequences.

Therapy modification in response to poorly controlled dyslipidemia and achievement of recommended targets have been described as a measure of quality of care [13,14]. However, little is known regarding the simulated expected impact of applying new 2013 AHA/ACC guidelines criteria compared to previous ATP-III criteria on the achievement of recommended lipid targets. In this study, we described in the same cohort population the achievement of lipid targets according to both guidelines, as well as the associated clinical factors with both approach.

2. Methods

2.1. Study population

We analyzed data from September 2009 to December 2012 of patients included in the SPUM-ACS cohort (NCT01075868). Patients hospitalized with a main diagnosis of ACS at four Swiss academic centers (University of Bern, Geneva, Lausanne and Zürich) were screened and written consent obtained [15]. Inclusion criteria were age older than 18 years with clinical features of ischemia (e.g. chest pain, breathlessness) and at least one of following criteria: (a) persistent ST-segment elevation or depression, T inversion or dynamic ECG changes, new left bundle branch block, (b) evidence of positive troponin or creatine kinase (CK) and (c) evidence of a significant coronary artery disease at the angiography (≥50% stenosis) [16]. The participants were contacted for a clinical visit at the enrollment site 12 months after hospitalization for ACS. Of 2355 patients discharged from the index hospitalization, the one-year follow-up was performed in 2213 (94%) patients, 52 died, 60 refused follow-up and 30 were lost to follow-up, yielding a final sample of 1602 patients with available data on LDL-C and statin for the main analysis (Supplemental Fig. 1).

2.2. Statin therapy classification

Based on the 2013 AHA/ACC guidelines on the treatment of cholesterol, we classified statin intensity: (1) high-intensity (atorvastatin 40–80 mg, rosuvastatin 20–40 mg); (2) moderate-intensity (atorvastatin 10–20 mg, rosuvastatin 5–10 mg, simvastatin 20–40 mg, pravastatin 40–80 mg, fluvastatin 80 mg) and (3) low-intensity (simvastatin 10 mg, pravastatin 10–20 mg, fluvastatin 20–40 mg) [12]. We defined intensification of statin therapy as a switch to higher potency among patients discharged without high-intensity statin (no, low or moderate intensity statin) [11]. If the statin was not prescribed at discharge or discontinued during the year, we collected the documented reasons.

2.3. Blood lipid measurements

Baseline LDL-C corresponded to the first available fasting values within the first 24 h of the hospital admission [17–19]. LDL-C was calculated using the Friedewald equation [(total cholesterol-high-density cholesterol-triglycerides)/2.2], unless trigylcerides were elevated (>4.5 mmol/L) [20]. The one-year lipid profile was collected from venous blood samples after twelve-hour fasting.

2.4. Recommended target achievement

At one-year, we defined recommended targets based on new 2013 AHA/ACC guidelines criteria and based on previous ATP-III guidelines criteria [4,12,21]. Recommended targets based on previous -ATP-III criteria was defined as the (1) achievement of LDL-C target < 1.8 mmol/l. In patients who did not reach LDL-C targets, (2) we additionally defined as achieved targets the reduction of LDL-C ≥ 50% or (3) the intensification of statin therapy (Supplemental Table 1) We defined achievement of recommended targets based on the new 2013 AHA/ACC guidelines criteria as the use of high-intensity statin therapy in patients aged ≤ 75 years and moderate- or high-intensity statin therapy in patients aged > 75 years.

We performed sensitivity analyses to address potential limitations: (1) To take into account the potential modifications of lipid baseline profile after the onset of ACS symptoms, we excluded participants with chest pain duration greater than 24 h at admission [18,19]. (2) To validate the reported use of statin at one year, we asked in 1472 patients the published self-reported adherence question: « In the past month, how often did you take your medications as the doctor prescribed? ». Possible answers were: « all the time (100%) », « nearly all of the time (75%) », « about half of time (50%) », «less than half the time (<50%) » [22]. In sensitivity

Table 1
Baseline clinical characteristics of patient population (N = 1602).

Variables	
Socio-demographics	
Age (years), (mean ± SD)	61.8 ± 11.9
Elderly (>75 years old), n (%)	256 (16)
Women, n (%)	310 (19)
Married, n (%)	1056 (66)
Living alone, n (%)	1231 (77)
Active working, (%)	829 (52)
High educational level, n (%)[a]	245 (16)
Co-morbidities, n (%)	
History of hypertension	851 (53)
History of hypercholesterolemia[b]	977 (61)
History of diabetes	262 (16)
History of MI	225 (14)
Current smoker[c]	641 (40)
Obesity (BMI ≥ 30 kg/m^2)	339 (21)
Prior statin use	445 (28)
ACS diagnosis, n (%)	
STEMI	897 (56)
NSTEMI/UA	701 (44)
Index procedure, n (%)	
PCI	1477 (92)
CABG	5 (0)
Conservative	120 (7)
Onset of chest pain before admission, n (%)	
< 24 h	1056 (67)
≥ 24 h	531 (33)
Baseline LDL-C, (mean ± SD)	3.2 ± 1.1
Length of stay, (median ± IQR)	3 ± 5
Attendance to CR, n (%)	1121 (71)

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; CABG, coronary artery by-pass graft; CR, cardiac rehabilitation; CV, cardiovascular; IQR, interquartile range; LDL-C, low density lipoprotein-cholesterol; MI, myocardial infarction; NSTEMI, Non ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction; UA, unstable angina.
Missing values: 4 for ACS diagnosis, 21 for BMI, 4 for marital status, 10 for living status, 15 for working status, 42 for education status, 1 for MI history, 1 for smoking status, 2 for baseline statin, 190 for LVEF, 15 for onset of chest pain and 25 for attendance to CR.
[a] High educational was defined by university graduation.
[b] History of hypercholesterolemia was defined as the documentation of a baseline total cholesterol >5.0 mmol/l or any use of lipid-lowering treatment (statin, fibrates, niacin, ezetimibe, resins).
[c] Smoking variable was coded (current smoking vs. no/former smoker).

analyses, we assessed the achievement of recommended LDL-C targets in patients with complete self-reported adherence to statin (100%) (Supplemental Fig. 1) (3) To address potential selection bias related to the missing LDL-C data at the one-year follow-up, we evaluated the statin intensity in an extended sample of the cohort using data from 2154 patients with available statin intensity (e.g. data collected with phone call) (Supplemental Fig. 1).

2.5. Statistical analyses

The percentage of patients in various statin intensity categories was summarized at the time of hospital discharge and at one-year follow-up. The percentage of patients reaching the recommended targets at one-year was presented according both guidelines. We used the chi-square test to assess whether proportions were statistically significant. Using logistic regression model adjusted by site, we evaluated the odds ratios (OR) and the 95% confidence intervals (95% CI) of the association between patient factors and the appropriate care targets according to both guidelines. Covariates were selected a priori based on clinical signification: age, gender, working, living, smoking and educational status, history of hypercholesterolemia, of diabetes, of hypertension, of myocardial infarction (MI), prior use of statin, body mass index (BMI), baseline LDL-C levels, final diagnosis of ACS (STEMI vs. NSTEMI/UA) and attendance to cardiac rehabilitation (CR) [11]. As missing LDL-C values at one year could be a source of selection bias, we tested the sensitivity of the reported OR by using inverse probability of censoring weights (IPCW) [23]. The level of significance was established a priori at 2-sided $P < 0.05$. All patients provided informed consent and each enrolling center obtained institutional review board approval. All analyses were performed using Stata version 12.1 (Stata Corporation, College Station, Texas).

3. Results

3.1. Population characteristics

In our sample of 1602 patients, the mean age of participants was 61.8 ± 12 years, 310 (19%) were female, 225 (14%) had previous history of MI, 977 (61%) had hypercholesterolemia, 897 (56%) presented STEMI (Table 1). 1121 patients (71%) attended to a CR program after discharge. 1565 (99%) patients had a medical follow-up by physician.

3.2. Statin prescription and reasons for non-prescription

1578 (99%) of patients were discharged with statin therapy. Among 24 patients without statin prescription, 7 (29%) patients had documented reasons for non-prescription in the medical records: 3 had statin tolerance or side effects, 2 had another lipid-lowering therapy, 1 had to start in the outpatient, 1 had hepatic enzyme disturbances) and 3 had baseline LDL-C values < 1.8 mmol/l. At one year, 1507 (94%) were treated with statin and 88 (6%) had discontinued statin therapy after discharge. The reasons for discontinuation according to the patients were as follows: the physician stopped the treatment in 37 (42%) patients, 28 (32%) patients stopped due to side effects, 3 (3%) patients could not afford the statin therapy, 10 (11%) patients felt it was unnecessary to continue and in 10 (11%) of cases the reasons were unknown.

3.3. Statin therapy intensification

Of the 1602 patients, 1120 were discharged with high-intensity (70%), 444 on moderate-intensity (28%) and 14 (1%) were on low-intensity statin therapy. At one year, the use of high-intensity statin decreased to 57% (909 patients), while the proportion of moderate-intensity statin increased to 35% (560 patients), as well as low-intensity statin to 2% (38 participants) (Fig. 1). Patients using high-intensity statin at one year were more likely to have well-controlled LDL-C targets (64%) compared to those with lower-intensity statin (53%). Of the 472 patients on sub-maximal statin therapy at discharge (no, low or moderate intensity statin), only 109 (23%) had the statin therapy intensified during the year (Table 2). Most commonly used high-intensity statin at one year were atorvastatin 40 mg (29%) or rosuvastatin 20 mg (23%). (Supplemental Table 2) In sensitivity analyses among 2154 participants with complete data on statin use, results were similar: 1487 (69%) patients had maximal statin at discharge and 1205 (56%) at one year.

3.4. Recommended targets achievement based on previous and new guidelines

Of the 1602 patients, 552 patients (35%) reached the recommended LDL-C target < 1.8 mmol/l at one year, while 117 patients (7%) reduced LDL-C of ≥50% and 76 (5%) had an intensification of treatment for those with LDL-C ≥ 1.8 mmol/l, yielding to 745 (47%) patients reaching targets of ATP-III guidelines. In secondary analysis using a target LDL-C < 2.6 mmol/l, 1156 patients reached this less stringent target (72%), in addition 13 (1%) had a decrease in LDL-C ≥ 50% and 31 (2) had an intensification of statin therapy, yielding to 1200 (75%) patients reaching tailored LDL-C target. At one year, 909 (57%) patients were treated with high-intensity statin and in addition 105 elderly had moderate-intensity, yielding to 1014 (63%) patients reaching targets of 2013 AHA/ACC guidelines » (Fig. 2). The proportions were highly statistically significant (P value < 0.001). When comparing targets according to both strategies, we observed that 536 (33%) patients had achieved both targets, while 379 (24%) did not achieve any of them, 478 (30%) patients achieved only targets of tailored-statin intensity strategy and 209 (13%) patients achieved only targets of LDL-C targets strategy (Table 3). Among 1432 patients with data on self-reported adherence, 1223 (85%) patients reported always to take medication as prescribed by the physician. In sensitivity analyses, we found similar results after excluding those without complete self-reported adherence and those with onset of symptoms greater than 24 h. We also performed sensitivity analyses to assess whether LDL-C missing values could be a concern in term of selection bias and found similar rate of patients reaching the 2013 AHA/ACC guidelines (63%).

3.5. Factors associated with recommended targets

Using multivariate models, we examined associated factors with achievement of recommended targets based on both guidelines. (Table 4) Patients who attended a CR program were more likely to achieve ATP-III criteria (p value 0.01), while those with elevated LDL-C at hospital admission (p value 0.01) and those taking statin prior to ACS (p value 0.001) were less likely. Regarding the new 2013 AHA/AHA guidelines criteria, patients were more likely to reach if they were older (p value < 0.001), obese (p value 0.003), had STEMI (p value 0.006) and had elevated LDL-C at hospital admissions (p value 0.001). In sensitivity analyses, the ORs were unchanged after IPCW (Supplemental Table 3).

4. Discussion

4.1. Main findings

In this prospective cohort of patients with ACS, we found that

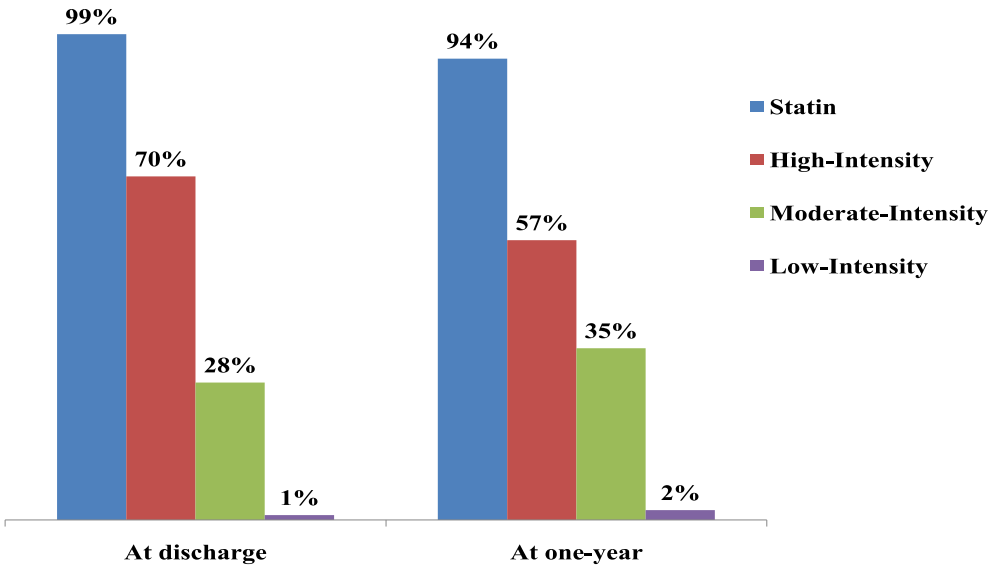

Fig. 1. Prescribed rate of statin therapy at discharge and self-reported use at one year (N = 1602).

Table 2
Statin therapy intensification during the year.

Statin-intensity at discharge	Statin-intensity at one year					Intensification
	No	Low	Moderate	High	Total	N (%)
No	7	3	12	2	24	17 (71)
Low	2	4	6	2	14	8 (57)
Moderate	29	11	320	84	444	84 (19)
Total	38	18	338	88	482	109 (23)
In Those With Baseline LDL-C < 1.80 mmol/L						
No	2	0	0	1	3	1 (33)
Low	0	1	0	0	1	0 (0)
Moderate	1	0	33	6	40	6 (15)
Total	3	1	33	7	44	7 (16)
In Those With Baseline LDL-C ≥ 1.80 mmol/L						
No	5	3	12	1	21	16 (76)
Low	2	3	6	2	13	8 (62)
Moderate	28	11	287	78	404	78 (19)
Total	35	17	305	81	438	101 (24)

Abbreviations: LDL-C, low-density lipoprotein cholesterol.
Intensification of statin therapy was defined as a switch of a statin from a lower to a higher potency statin among patients discharged without high-intensity statin (no, low or moderate intensity statin).

targets according to the previous 2004 ATP-III guidelines were reached in 47% of all patients, while this rate was 63% for targets of the new 2013 AHA/ACC guidelines. Our study suggests that new 2013 AHA/ACC guidelines criteria are less stringent to reach than previous 2004 ATP-II criteria. The associated clinical factors with the achievement of 2013 AHA/ACC guidelines were age, STEMI, higher baseline LDL-C and increased BMI.

4.2. Added value of our findings

Few prospective studies assessed statin therapy intensity and modification in patients hospitalized with ACS. The TRIUMPH registry among 4340 patients hospitalized with myocardial infarction (MI) reported a high prescription (90%) of statin at hospitalization, but uncommon (23–26%) intensification and maximization of statin after hospitalization [11]. In the same registry, only one-third of patients met the recommended LDL-C target < 100 mg/dL [9]. The sub-optimal dosage of statin prescription in secondary prevention, as well as the poor achievement of LDL-C targets (less than 40%) was also reported in two other US registries of patients with ACS [1014]. We found also a sub-optimal achievement of LDL-C in secondary prevention and poor intensification of statin therapy in the outpatient setting [24].

4.3. Perspectives

Assessing therapy modifications to poorly controlled targets has been shown to be an additional measure of quality performance [13]. The 2013 AHA/ACC guidelines imply to treat all patients with ACS with an intensive statin regimen rather than targeting a specific goal of LDL-C [12]. Regarding the elderly (>75 years), moderate-intensity statin treatment is *at minima* recommended, as the benefit of high-intensity was not shown in this specific condition. However, the question of the best approach in terms of prevention of cardiovascular events remains open in this high risk group of patients with ACS. The point that adherence to guidelines that more easy to follow needs further explorations.

4.4. Limitations

The use of statin therapies was self-reported and not validated with a direct measure (e.g. pharmacy data), as such data are not available in Switzerland. We asked patients to bring the list of medications, as well as the pill boxes to confirm their statement and collected data on self-reported adherence by a validated questionnaire. Self-reported measure of medication adherence has been used in several publications and has been associated with clinical outcomes [22,25–28]. However, the achievement rate of LDL-C targets was similar after excluding those who did not report complete adherence. To check a potential selection bias due to missing LDL-C, we performed sensitivity analyses for statin prescription in those patients with missing LDL-C and found similar results, suggesting that participants with missing LDL-C were similarly treated. Furthermore, the ORs of associated factors were similar after adjusting for IPCW, suggesting that selection bias due to non-random drop-out was unlikely.

The SPUM-ACS cohort might not represent all patients with ACS, as only patients who gave consent were included. The recruitment period of the cohort preceded the publication of the 2013 AHA/ACC guidelines; for this reason, the findings of our study cannot be used

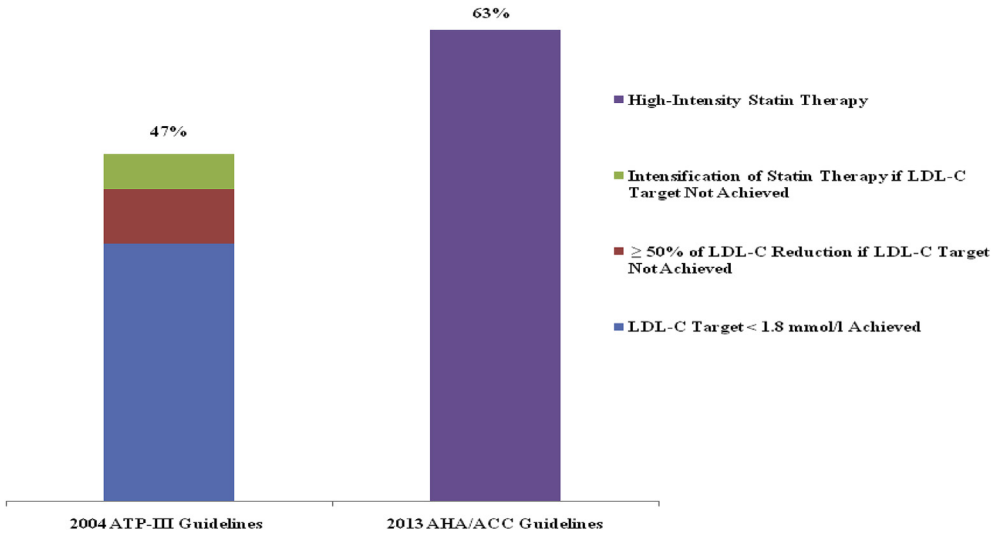

Fig. 2. Achievement of recommended targets after ACS according to 2004 ATP-II and new 2013 AHA/ACC guidelines. High-intensity statin is defined as rosuvastatin 20 or 40 mg or atorvastatin 40 or 80 mg. Intensification is defined by a switch to a higher potency statin if statin prescription was not high-intensity. The chi-square test was significant (P value < 0.001).

Table 3
Achievement of recommended targets according to both guidelines criteria.

		2013 AHA/ACC guidelines not achieved N (%)	2013 AHA/ACC guidelines achieved N (%)	Total
2004 ATP-III guidelines not achieved	N(%)	379 (24)	478 (30)	857 (53)
2004 ATP-III guidelines achieved	N(%)	209 (13)	536 (33)	745 (47)
Total	N(%)	588 (37)	1014 (63)	1602

Abbreviations: LDL-C, low-density lipoprotein cholesterol.

for assessing physicians' behavior about the new guidelines.

Finally, by nature of the inclusion criteria ACS, the baseline lipid levels were measured within the first 24 h of admission, but not necessarily in the fasting state. However, to take into account the potential modifications of lipid baseline profile after the onset of ACS symptoms, we excluded participants with chest pain duration greater than 24 h at admission, as their baseline lipid values may be lower than the stable values before the occurrence the ACS event.

Table 4
Patient factors associated with target achievement according to previous 2004 ATP-III and new 2013 AHA/ACC guidelines.

	2004 ATP-III Guidelines[a] OR (95% CI)[b]	p-value	2013 AHA/ACC Guidelines[a] OR (95% CI)[b]	p-value
Socio-demographics				
Women	0.97 (0.73–1.29)	*0.85*	0.98 (0.73–1.32)	*0.89*
Age (per unit of 10 years)‡	1.15 (0.98–1.34)	*0.09*	2.08 (1.73–2.51)	*< 0.001*
Living with someone	1.24 (0.96–1.59)	*0.10*	1.04 (0.80–1.36)	*0.77*
Full/part working	0.93 (0.71–1.23)	*0.63*	1.26 (0.95–1.68)	*0.12*
High education level[c]	1.08 (0.80–1.46)	*0.60*	1.13 (0.83–1.54)	*0.44*
Co-morbidities				
Current smoker[d]	1.05 (0.83–1.32)	*0.71*	1.25 (0.98–1.59)	*0.07*
History of hypercholesterolemia[e]	1.06 (0.82–1.37)	*0.66*	1.08 (0.83–1.41)	*0.58*
History of diabetes	1.29 (0.96–1.75)	*0.09*	0.81 (0.59–1.10)	*0.18*
History of hypertension	1.03 (0.82–1.30)	*0.80*	0.97 (0.76–1.24)	*0.80*
History of MI	0.71 (0.50–1.01)	*0.06*	0.83 (0.58–1.20)	*0.33*
BMI (per unit of 5 kg/m^2)‡	1.14 (0.97–1.33)	*0.11*	1.31 (1.10–1.57)	*0.003*
On statin use	0.58 (0.42–0.80)	*0.001*	1.32 (0.95–1.85)	*0.10*
Hospital admission				
ST-elevation ACS	0.96 (0.77–1.20)	*0.71*	1.38 (1.10–1.75)	*0.006*
Baseline LDL-C (per unit mmol/)	0.86 (0.77–0.97)	*0.01*	1.23 (1.09–1.39)	*0.001*
Attendance to CR	1.43 (1.10–1.85)	*0.007*	1.24 (0.95–1.63)	*0.12*

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; ACS, acute coronary syndromes; ATP-III, Adult Treatment Panel-III; BMI, body mass index; CI, confidence intervals; CR, cardiac rehabilitation; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; OR, odds ratios.
‡ P value < 0.05 was considered significant.
[a] The analysis was done using the LDL-C target <1.8 mmol/l based on the 2004 ATP-III guidelines. Statin-intensity was defined according to the 2013 AHA/AHA guidelines on the cholesterol treatment.
[b] OR were adjusted for variables listed in the table and the site.
[c] High education was defined by university graduation.
[d] Smoking variable was coded (current smoking vs. no/former smoker).
[e] History of hypercholesterolemia was defined as documentation of a baseline total cholesterol >5.0 mmol/l or any use of lipid-lowering treatment (statin, fibrates, niacin, ezetimibe, resins).

For the assessment of targets at 1 year, the lipid panels have always been performed in a stable condition.

5. Conclusions

In patients with ACS, we found that applying criteria of the new 2013 AHA/ACC guidelines increased the proportion of patients on target compared to the previous 2004 ATP-III guidelines criteria. Our observations suggest that new 2013 AHA/ACC guidelines may be easier to follow for clinicians, but the impact of this change of paradigm on clinical cardiovascular outcomes needs to be described in further studies.

Disclosures (to complete by co-authors)

RK received lecture fees from EliLilly, Servier and Bayer. FM has received research grants to the institution from Amgen, AstraZeneca, Boston Scientific, Biotronik, Medtronic, MSD, EliLilly and St. Jude Medical including speaker or consultant fees. SW has received research grants to the institution from Abbott, AstraZeneca, Boston Scientific, Biosensors, Biotronik, Cordis, EliLilly, Medtronic and St. Jude Medical. TFL received research grants to the institution from Bayer, Biosensors, Biotronik, Boston Scientific, Medtronic, MSD, Roche and Servier, including lecture fees. CMM received research grants to the institution from EliLilly, AstraZeneca, Roche and MSD including speaker or consultant fees. All other authors have no conflict of interest to declare.

Acknowledgments

The SPUM-ACS cohort is supported by the Swiss National Science Foundation (SNSF 33CM30-124112 and SPUM33C30-140336, Inflammation and acute coronary syndromes (ACS) – Novel strategies for prevention and clinical management), the Swiss Heart Foundation (to Prof Rodondi). Special gratitude is expressed to the excellent support provided by the local catheter and study nurse teams. Acknowledgements: with contributions of the Clinical Research Center, University Hospital and Faculty of Medicine, Geneva.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.atherosclerosis.2014.12.049.

References

[1] P.T. O'Gara, F.G. Kushner, D.D. Ascheim, D.E. Casey Jr., M.K. Chung, J.A. de Lemos, S.M. Ettinger, J.C. Fang, F.M. Fesmire, B.A. Franklin, C.B. Granger, H.M. Krumholz, J.A. Linderbaum, D.A. Morrow, L.K. Newby, J.P. Ornato, N. Ou, M.J. Radford, J.E. Tamis-Holland, C.L. Tommaso, C.M. Tracy, Y.J. Woo, D.X. Zhao, J.L. Anderson, A.K. Jacobs, J.L. Halperin, N.M. Albert, R.G. Brindis, M.A. Creager, D. DeMets, R.A. Guyton, J.S. Hochman, R.J. Kovacs, E.M. Ohman, W.G. Stevenson, C.W. Yancy, 2013 accf/aha guideline for the management of st-elevation myocardial infarction: a report of the American college of cardiology foundation/American heart association task force on practice guidelines, Circulation 127 (2013) e362–425.

[2] P.G. Steg, S.K. James, D. Atar, L.P. Badano, C. Blomstrom-Lundqvist, M.A. Borger, C. Di Mario, K. Dickstein, G. Ducrocq, F. Fernandez-Aviles, A.H. Gershlick, P. Giannuzzi, S. Halvorsen, K. Huber, P. Juni, A. Kastrati, J. Knuuti, M.J. Lenzen, K.W. Mahaffey, M. Valgimigli, A. van 't Hof, P. Widimsky, D. Zahger, Esc guidelines for the management of acute myocardial infarction in patients presenting with st-segment elevation, Eur. Heart J. 33 (2012) 2569–2619.

[3] C.W. Hamm, J.P. Bassand, S. Agewall, J. Bax, E. Boersma, H. Bueno, P. Caso, D. Dudek, S. Gielen, K. Huber, M. Ohman, M.C. Petrie, F. Sonntag, M.S. Uva, R.F. Storey, W. Wijns, D. Zahger, J.J. Bax, A. Auricchio, H. Baumgartner, C. Ceconi, V. Dean, C. Deaton, R. Fagard, C. Funck-Brentano, D. Hasdai, A. Hoes, J. Knuuti, P. Kolh, T. McDonagh, C. Moulin, D. Poldermans, B.A. Popescu, Z. Reiner, U. Sechtem, P.A. Sirnes, A. Torbicki, A. Vahanian, S. Windecker, S. Achenbach, L. Badimon, M. Bertrand, H.E. Botker, J.P. Collet, F. Crea, N. Danchin, E. Falk, J. Goudevenos, D. Gulba, R. Hambrecht, J. Herrmann, A. Kastrati, K. Kjeldsen, S.D. Kristensen, P. Lancellotti, J. Mehilli, B. Merkely, G. Montalescot, F.J. Neumann, L. Neyses, J. Perk, M. Roffi, F. Romeo, M. Ruda, E. Swahn, M. Valgimigli, C.J. Vrints, P. Widimsky, Esc guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation: the task force for the management of acute coronary syndromes (acs) in patients presenting without persistent st-segment elevation of the european society of cardiology (esc), Eur. Heart J. 32 (2011) 2999–3054.

[4] S.C. Smith Jr., E.J. Benjamin, R.O. Bonow, L.T. Braun, M.A. Creager, B.A. Franklin, R.J. Gibbons, S.M. Grundy, L.F. Hiratzka, D.W. Jones, D.M. Lloyd-Jones, M. Minissian, L. Mosca, E.D. Peterson, R.L. Sacco, J. Spertus, J.H. Stein, K.A. Taubert, Aha/accf secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American heart association and American college of cardiology foundation, Circulation 124 (2011) 2458–2473.

[5] J. Perk, G. De Backer, H. Gohlke, I. Graham, Z. Reiner, M. Verschuren, C. Albus, P. Benlian, G. Boysen, R. Cifkova, C. Deaton, S. Ebrahim, M. Fisher, G. Germano, R. Hobbs, A. Hoes, S. Karadeniz, A. Mezzani, E. Prescott, L. Ryden, M. Scherer, M. Syvanne, W.J. Scholte op Reimer, C. Vrints, D. Wood, J.L. Zamorano, F. Zannad, European guidelines on cardiovascular disease prevention in clinical practice (version 2012). The fifth joint task force of the European society of cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts), Eur. Heart J. 33 (2012) 1635–1701.

[6] 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 106 (2002), 3143–3421.

[7] S.M. Grundy, J.I. Cleeman, C.N. Merz, H.B. Brewer Jr., L.T. Clark, D.B. Hunninghake, R.C. Pasternak, S.C. Smith Jr., N.J. Stone, Implications of recent clinical trials for the national cholesterol education program adult treatment panel iii guidelines, Arterioscler. Thromb. Vasc. Biol. 24 (2004) e149–161.

[8] B.W. Karlson, P.J. Barter, M.K. Palmer, P. Lundman, S.J. Nicholls, Comparison of the effects of different statins and doses on lipid levels in patients with diabetes: results from voyager, Nutr. Metabolism, Cardiovasc. Dis.: NMCD 22 (2012) 697–703.

[9] S.S. Martin, K. Gosch, K.R. Kulkarni, J.A. Spertus, R. Mathews, P.M. Ho, T.M. Maddox, L.K. Newby, K.P. Alexander, T.Y. Wang, Modifiable factors associated with failure to attain low-density lipoprotein cholesterol goal at 6 months after acute myocardial infarction, Am. Heart J. 165 (2013) 26–33 e23.

[10] C. Melloni, B.R. Shah, F.S. Ou, M.T. Roe, S.C. Smith Jr., C.V. Pollack Jr., M. Ohman, W.B. Gibler, E.D. Peterson, K.P. Alexander, Lipid-lowering intensification and low-density lipoprotein cholesterol achievement from hospital admission to 1-year follow-up after an acute coronary syndrome event: results from the medications applied and sustained over time (maintain) registry, Am. Heart J. 160 (2010) 1121–1129, 1129 e1121.

[11] S.V. Arnold, M. Kosiborod, F. Tang, Z. Zhao, T.M. Maddox, P.L. McCollam, J. Birt, J.A. Spertus, Patterns of statin initiation, intensification, and maximization among patients hospitalized with an acute myocardial infarction, Circulation 129 (12) (2014) 1303–1309.

[12] N.J. Stone, J. Robinson, A.H. Lichtenstein, C.N. Merz, C.B. Blum, R.H. Eckel, A.C. Goldberg, D. Gordon, D. Levy, D.M. Lloyd-Jones, P. McBride, J.S. Schwartz, S.T. Shero, S.C. Smith Jr., K. Watson, P.W. Wilson, 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, Circulation 129 (25 Suppl. 2) (2013) S49–S73.

[13] N. Rodondi, T. Peng, A.J. Karter, D.C. Bauer, E. Vittinghoff, S. Tang, D. Pettitt, E.A. Kerr, J.V. Selby, Therapy modifications in response to poorly controlled hypertension, dyslipidemia, and diabetes mellitus, Ann. Intern Med. 144 (2006) 475–484.

[14] S.V. Arnold, J.A. Spertus, F.A. Masoudi, S.L. Daugherty, T.M. Maddox, Y. Li, J.A. Dodson, P.S. Chan, Beyond medication prescription as performance measures: optimal secondary prevention medication dosing after acute myocardial infarction, J. Am. Coll. Cardiol. 62 (2013) 1791–1801.

[15] R. Auer, B. Gencer, L. Raber, R. Klingenberg, S. Carballo, D. Carballo, D. Nanchen, J. Cornuz, J.P. Vader, P. Vogt, P. Juni, C.M. Matter, S. Windecker, T.F. Luscher, F. Mach, N. Rodondi, Quality of care after acute coronary syndromes in a prospective cohort with reasons for non-prescription of recommended medications, PloS One 9 (2014) e93147.

[16] K. Thygesen, J.S. Alpert, A.S. Jaffe, M.L. Simoons, B.R. Chaitman, H.D. White, H.A. Katus, B. Lindahl, D.A. Morrow, P.M. Clemmensen, P. Johanson, H. Hod, R. Underwood, J.J. Bax, R.O. Bonow, F. Pinto, R.J. Gibbons, K.A. Fox, D. Atar, L.K. Newby, M. Galvani, C.W. Hamm, B.F. Uretsky, P.G. Steg, W. Wijns, J.P. Bassand, P. Menasche, J. Ravkilde, E.M. Ohman, E.M. Antman, L.C. Wallentin, P.W. Armstrong, J.L. Januzzi, M.S. Nieminen, M. Gheorghiade, G. Filippatos, R.V. Luepker, S.P. Fortmann, W.D. Rosamond, D. Levy, D. Wood, S.C. Smith, D. Hu, J.L. Lopez-Sendon, R.M. Robertson, D. Weaver, M. Tendera, A.A. Bove, A.N. Parkhomenko, E.J. Vasilieva, S. Mendis, Third universal definition of myocardial infarction, Circulation 126 (2012) 2020–2035.

[17] C.P. Cannon, R.G. Brindis, B.R. Chaitman, D.J. Cohen, J.T. Cross Jr., J.P. Drozda Jr., F.M. Fesmire, D.J. Fintel, G.C. Fonarow, K.A. Fox, D.T. Gray, R.A. Harrington,

K.A. Hicks, J.E. Hollander, H. Krumholz, D.R. Labarthe, J.B. Long, A.M. Mascette, C. Meyer, E.D. Peterson, M.J. Radford, M.T. Roe, J.B. Richmann, H.P. Selker, D.M. Shahian, R.E. Shaw, S. Sprenger, R. Swor, J.A. Underberg, F. Van de Werf, B.H. Weiner, W.S. Weintraub, 2013 accf/aha key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes and coronary artery disease: a report of the american college of cardiology foundation/American heart association task force on clinical data standards (writing committee to develop acute coronary syndromes and coronary artery disease clinical data standards), Circulation 127 (2013) 1052–1089.

[18] T. Fyfe, R.H. Baxter, K.M. Cochran, E.M. Booth, Plasma-lipid changes after myocardial infarction, Lancet 2 (1971) 997–1001.

[19] R.E. Ryder, T.M. Hayes, I.P. Mulligan, J.C. Kingswood, S. Williams, D.R. Owens, How soon after myocardial infarction should plasma lipid values be assessed? Br. Med. J. Clin. Res. Ed. 289 (1984) 1651–1653.

[20] W.T. Friedewald, R.I. Levy, D.S. Fredrickson, Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge, Clin. Chem. 18 (1972) 499–502.

[21] R.A. Hayward, H.M. Krumholz, Three reasons to abandon low-density lipoprotein targets: an open letter to the adult treatment panel iv of the national institutes of health, Circulation Cardiovasc. Qual. Outcomes 5 (2012) 2–5.

[22] A.K. Gehi, S. Ali, B. Na, M.A. Whooley, Self-reported medication adherence and cardiovascular events in patients with stable coronary heart disease: the heart and soul study, Arch. Intern Med. 167 (2007) 1798–1803.

[23] J.M. Robins, D.M. Finkelstein, Correcting for noncompliance and dependent censoring in an aids clinical trial with inverse probability of censoring weighted (ipcw) log-rank tests, Biometrics 56 (2000) 779–788.

[24] A.R. Jadad, M.J. To, M. Emara, J. Jones, Consideration of multiple chronic diseases in randomized controlled trials, JAMA: J. Am. Med. Assoc. 306 (2011) 2670–2672.

[25] P.M. Ho, D.J. Magid, S.M. Shetterly, K.L. Olson, T.M. Maddox, P.N. Peterson, F.A. Masoudi, J.S. Rumsfeld, Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease, Am. Heart J. 155 (2008) 772–779.

[26] P.M. Ho, C.L. Bryson, J.S. Rumsfeld, Medication adherence: its importance in cardiovascular outcomes, Circulation 119 (2009) 3028–3035.

[27] S.H. Naderi, J.P. Bestwick, D.S. Wald, Adherence to drugs that prevent cardiovascular disease: meta-analysis on 376,162 patients, Am. J. Med. 125 (2012) 882–887 e881.

[28] M. Lemstra, D. Blackburn, A. Crawley, R. Fung, Proportion and risk indicators of nonadherence to statin therapy: a meta-analysis, Can. J. Cardiol. 28 (2012) 574–580.