Significant improvement in statin adherence and cholesterol levels after acute myocardial infarction

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ABSTRACT

INTRODUCTION: Not all patients recovering from acute myocardial infarction (AMI) are optimally treated with statin, and their adherence to statin treatment may be inadequate. We set out to describe changes in statin treatment adherence and cholesterol values over time.

MATERIAL AND METHODS: Data from two cohorts of AMI patients discharged from the Department of Cardiology, Odense University Hospital, in 2003 (n = 474, mean age 68 years, 66% males) and 2008 (n = 550, mean age 67 years, 69% males) were compared. Based on the number of tablets collected at the pharmacy, patients' adherence to statin treatment in a period of two years after discharge was analysed. Patients were considered adherent when in possession of medication ≥ 80% of the period. From the day of admission and at follow-up, cholesterol values and the relative number of patients with a total-cholesterol < 4.5 mmol/l were calculated.

RESULTS: A significant improvement in statin adherence was noted: 42% versus 75% ($p < 0.0001$). The most significant difference was observed in patients ≥ 80 years, who improved from 25% to 72% ($p < 0.0001$). Furthermore, an overall significant reduction in follow-up cholesterol levels was observed: from 4.4 to 4.2 mmol/l ($p = 0.003$). Moreover, an increase was observed in the proportion of patients with a follow-up cholesterol value < 4.5 mmol/l: from 57% to 67% ($p = 0.001$). The most significant changes were demonstrated in patients ≥ 70 years.

CONCLUSION: Over the five-year period from 2003 to 2008, statin adherence and cholesterol values significantly improved. However, room for improvement remains, particularly in younger patients.

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Cardiovascular disease (CVD) is a major cause of morbidity and premature death. A high cholesterol level is one of the most significant risk factors for CVD and was in a WHO report from 2002 estimated to cause 56% of cases of ischaemic heart disease [1]. Statin therapy can reduce the five-year incidence of major coronary events and stroke by about one fifth per mmol/l reduction in low-density lipoprotein (LDL)-cholesterol [2]. Such reduction is related to the patient's individual absolute risk of such events; still, no minimum cholesterol value at which statin treatment is ineffective has been identified [2, 3]. Previous studies have indicated that the risk reduction of coronary and all-cause mortality gained through statin treatment is similar for men, women, elderly and middle-aged persons [4]. Despite evidence in support of the beneficial effect of statin treatment, adherence to statin therapy after AMI is not optimal [5]. In 2005 the Cardiac Rehabilitation Clinic was established at Odense University Hospital (OUH) to address these problems and to optimize treatment of risk factors. The Cardiac Rehabilitation Clinic invites all AMI patients to attend an individually designed follow-up programme after discharge. The programme focuses on cessation of smoking, use of secondary prevention medication, blood pressure, cholesterol values, exercise, body mass index and waist measure. The programme takes the form of individual sessions, information meetings and group exercise. [6]. Patients are treated according to Danish guidelines for patients with established CVD, and the goal of treatment is a total-cholesterol < 4.5 mmol/l, and a LDL < 2.5 mmol/l [7].

The aim of this study was to investigate patients' adherence to statin treatment and the potential changes in cholesterol values over time. We also wanted to assess if a potential improvement in these parameters can be related to the introduction of the Cardiac Rehabilitation Clinic.

MATERIAL AND METHODS

This was a retrospective cohort study. We included all patients discharged with the diagnosis of AMI (ICD-10 code I21) from the Department of Cardiology, OUH, during the period from 2003 to 2008. General exclusion criteria were death within 90 days after discharge and abode outside of the Region of Fyn. In Demark all citizens have a unique civil registration number (CPR number), which is used at all contacts with public health care; e.g. during hospitalisation and when prescribing medication for dispensation at a pharmacy. All residents in Denmark are covered by a national health security system and the costs of drugs are partly reimbursed, independently of individual income or other factors. The Danish Data Protection Agency approved this study, and

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TABLE 1

Adherence to statin (medication possession ratio ≥ 80%).

	2003		2008			
	n/all	%	n/all	%	OR (CI)	p value[a]
All	198/474	42	414/550	75	4.2 (3.2-5,6)	< 0.0001
Male	136/312	44	292/380	77	4.3 (3.1-6.0)	< 0.0001
Female	62/162	38	122/170	72	4.1 (2.5-6.7)	< 0.0001
Age < 60 years	56/126	44	108/145	74	3.6 (2.1-6.3)	< 0.0001
Age 60-69 years	56/122	46	131//159	82	5.5 (3.1-9.9)	< 0.0001
Age 70-79 years	64/137	47	98/139	71	2.7 (1.6-4.6)	< 0.0001
Age ≥ 80 years	22/89	25	77/107	72	7.8 (3.9-15.6)	< 0.0001

all = number of patients; CI = 95% confidence interval; n = number of adherent patients; OR = odds ratio. a) Fisher's exact test.

TABLE 2

Mean cholesterol values in 2003 and 2008.

	Admission cholesterol values						Follow-up cholesterol values					
	2003		2008				2003		2008			
	n	M	n	M	D	Pv[a]	n	M	n	M	D	Pv[a]
All	317	5.1	389	5.0	–0.09	0.33	434	4.4	518	4.2	–0.20	0.003
Men	223	5.0	270	4.9	–0.09	0.42	293	4.2	361	4.1	–0.18	0.02
Women	94	5.4	119	5.3	–0.11	0.53	141	4.7	157	4.5	–0.22	0.09
Age < 60 years	93	5.2	116	5.4	0.18	0.30	118	4.4	142	4.4	0.03	0.81
Age 60-69 years	94	5.0	120	5.2	0.12	0.44	119	4.3	158	4.2	–0.10	0.39
Age 70-79 years	83	5.1	94	4.7	–0.44	0.01	127	4.4	133	4.0	–0.34	0.005
Age ≥ 80 years	47	5.1	59	4.7	–0.48	0.04	70	4.6	85	4.1	–0.56	0.007

D = difference; M = mean cholesterol value in mmol/l; Pv = p value.
a) Unpaired T-test.

TABLE 3

Number of patients with cholesterol values below 4.5 mmol/l.

	Admission					Follow-up				
	2003		2008			2003		2008		
	n	%	n	%	p value[a]	n	%	n	%	p value[a]
All	94	30	135	35	0.17	247	57	349	67	0.001
Men	76	34	106	39	0.22	184	63	260	72	0.02
Women	19	20	29	24	0.51	63	45	89	57	0.05
Age < 60 years	24	26	29	25	1.00	70	59	83	58	0.90
Age 60-69 years	30	32	38	32	1.00	69	58	106	67	0.13
Age 70-79 years	24	29	41	44	0.06	69	54	98	74	0.001
Age ≥ 80 years	16	33	27	46	0.24	39	56	62	73	0.03

a) Fisher's exact test.

data were made available to the authors in a manner excluding the identification of individual patients.

Statin adherence

By use of the CPR number, patients were linked to a medical database (OPED) that registers all prescribed medication released at Danish pharmacies. All prescriptions of lipid-lowering drugs (ATC code C10) following hospital discharge and during the two-year follow-up period were used to measure statin adherence. Adherence was measured as a percentage: (number of tablets released from pharmacy)/(730 days), and if a patient died within the two years (number of tablets released from pharmacy)/(number of days from discharge until date of death). The adherence values were set to: 0%, > 0% to < 40%, ≥ 40% to < 80%, and ≥ 80%. This Medication Possession Ratio (MPR) is an internationally recognised metric for measurement of adherence, and most studies consider an adherence ≥ 80% to be equivalent to compliance to chronic medications [8].

Cholesterol values

Cholesterol values in the 2003 and 2008 cohorts were analysed and compared. The first cholesterol value was drawn at the time of the index AMI (admission ± 1 day), and the last cholesterol value was defined as the latest value obtained during the two years of follow-up. In addition, the proportion of patients reaching a total cholesterol value < 4.5 mmol/l within the follow-up period was registered.

Statistics

The data were tested for normality, and further analysed considering sex and age groups. An unpaired t-test was used to compare mean statin adherence (number of tablets/days) together with mean cholesterol values in the 2003 and 2008 cohorts. Fisher's exact test was applied to evaluate changes in statin MPR ≥ 80% and the proportion of individuals with cholesterol < 4.5 mmol/l. STATA statistical software, version 11.0 was used for statistical analysis.

Trial registration: not relevant.

RESULTS

In 2003, 681 patients were discharged with the diagnosis of AMI. After excluding patients not living in the Region of Fyn, the cohort consisted of 524 patients. A total of 50 patients died within 90 days after discharge leaving 474 patients in the 2003 cohort; 162 women (34%) and 312 men (66%). The median age was 68 years (± 12.5 years). In 2008 the cohort consisted of 1,119 patients, and after applying the above-mentioned exclusion criteria, 550 patients were included; 170 women (31%) and 380 men (69%), median age 67 years (± 12.7).

Statin adherence

Independently of age and gender, statin adherence significantly improved from 2003 to 2008. Patients aged 60-69 years had the highest adherence, while the group with the largest improvement in adherence was patients > 80 years, **Table 1**. No significant difference in adher-

ence was found between males and females (p = 0.33). Considering the results for patients ≥ 90% adherence, a similar range was observed, with a significant increase in all groups from 2003 to 2008 (data not shown).

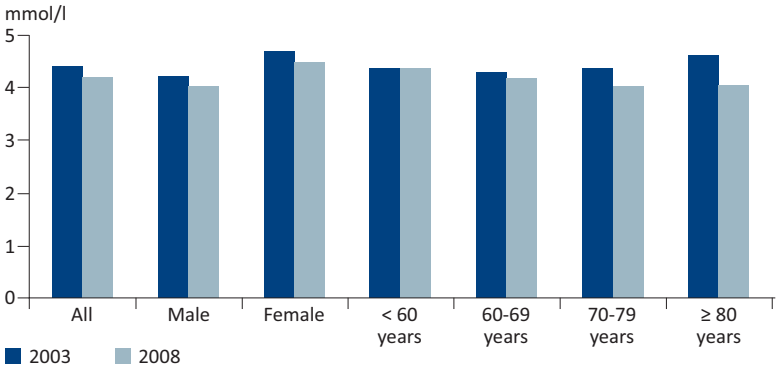
Cholesterol values

In the 2003 cohort, admission cholesterol values were available in 317 patients (67%), while follow-up cholesterol values could be identified in 434 (92%). In the 2008 cohort, admission cholesterol values were available in 389 patients (71%), and 518 patients (94%) had follow-up values. A non-significant reduction was observed when 2003 and 2008 admission cholesterol values were compared. In the age groups 70-79 years and ≥ 80 years, however, a significant decrease in admission cholesterol values was observed, **Table 2**. Concerning the follow-up cholesterol values, a significant improvement was observed in the 2008 as compared with the 2003 findings (p = 0.003), **Figure 1** and Table 2. This result was mainly owed to a reduction in cholesterol values in the elderly (age group 70-79 years and > 80 years).

Generally, no significant difference in the overall frequency of patients with an admission cholesterol < 4.5 mmol/l was noted. However, in the age group 70-79 years, the level of significance was reached. At follow-up, significantly more patients in the 2008 cohort demonstrated cholesterol levels < 4.5 mmol/l. The difference was significant for both men and women and in the age groups 70-79 years and ≥ 80 years, **Table 3**.

FIGURE 1

Mean follow-up cholesterol values.



DISCUSSION

This study presents original data addressing the adherence of patients to statin treatment and the association between statin treatment and cholesterol values in AMI survivors. The main observation from our study – when comparing the cohorts from 2003 and 2008 – is the demonstration of a trend in all study groups towards an improved statin adherence over time. However, the results are not ideal since 25% of the 2008 cohort shows unsatisfactory adherence. Despite this limitation we found an overall reduction in cholesterol values at follow-up with significantly more patients reaching a total-cholesterol < 4.5 mmol/l in the 2008 than in the 2003 cohort. This result is most likely driven by the improvement in adherence to statin observed in the elderly patients, who in 2008 received significantly more statin than those of the 2003 cohort. On the other hand, it is a matter of concern that the adherence in younger patients did not improve along with that of their elderly counterparts.

When comparing our results with other Danish studies, we can see similar trends of a general increase in the prescription rate of statin over the years, although levels remain less than optimal [9-11]. Our study shows that the adherence to statin of the Danish AMI patients is in the same range as in other developed countries [12-14].

Several studies have addressed patients' adherence to statin treatment after AMI. A meta-analysis of 22 studies showed that age had a U-shaped curve in relation to statin adherence, and that patients < 50 years and > 70 years had lower adherence than middle-aged patients [8]. In our 2008 cohort, patients aged 60-69 years had the highest adherence to statin. In both the meta-analysis and other studies, women are more likely to be non-adherent than men [5, 15]. In the present study, however, we found no significant difference between the sexes. Other factors reportedly associated with statin treatment adherence are stent implantation, adherence to other recommended preventive drugs after AMI and prior use of statin treatment before hospital admission [5, 11, 15]. In some studies, co-morbidities such as hypertension and diabetes were associated with increased adherence, [5, 15] but in other studies diabetes was associated with lower adherence [11, 12] as were other comorbidities including Alzheimer´s disease and depression [11]. Low income and lack of medical insurance are also associated with low adherence [5, 11, 15, 16].

A recent Cochrane review investigated different ways to improve adherence to lipid-lowering medication. Overall information, regular contact and reminders were associated with improved adherence to medical treatment. Six months after discharge seems to be the critical point in time to maintain the intervention [8].

The Cardiac Rehabilitation Clinic at the OUH was established to improve patient follow-up, making sure that patients have medication available and reach the target values of cholesterol levels. The rehabilitation programme is an offer to the individual patient, and it may be speculated whether those patients who are non-ad-

Adherence to statin in survivors of acute myocardial infarction remains suboptimal.

herent to medication also are the ones who reject participation in the rehabilitation programme. The rehabilitation programme is individual and typically lasts 6-12 months after hospital discharge.

Limitations of the study

The results presented cannot be evaluated without considering a number of flaws. In 2003 the recommended total-cholesterol value was < 5.0 mmol/l. Since the establishment of the Cardiac Rehabilitation Clinic in 2005, the recommended goal has been lowered to a total-cholesterol value of < 4.5 mmol/l. Also, in 2003 it was not a part of the routine regimen to treat elderly patients with statin after AMI. More recent studies have documented the beneficial effect of statin treatment regardless of age, and statin treatment has thus become a part of the routine treatment in patients ≥ 80 years [4].

The present study is based on retrospectively analysed data. The follow-up cholesterol values have not been taken at specific times following AMI. Further, only total-cholesterol values have been evaluated in this study, and it would, indeed, have been preferable if also LDL-cholesterol measurements had been included in the analysis. However, due to changes in the methods by which LDL has been calculated over time, it has not been possible to analyse and compare LDL data in this study.

Our study does not consider comorbidity, other medication or social, economic or psychological factors that might influence the patient's adherence to statin treatment. Furthermore, we have no data addressing the proportion of patients who have not been prescribed statins, or those who have had statin treatment withdrawn due to side effects. Finally, we are unable to precisely relate the importance of the Cardiac Rehabilitation Clinic to the results because of the lack of data revealing the number of AMI patients who accepted follow-up in the Cardiac Rehabilitation Clinic following hospital discharge.

CONCLUSION

We found a significantly improved statin adherence over the five-year study period with a concomitant reduction in cholesterol values. The results are mainly owed to significant improvements in elderly patients. However, there is a need for optimized statin adherence in patients < 70 years of age.

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