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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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.

**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-
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.

LITERATURE