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Association of Dyslipidemia and Concomitant Risk Factors with In-Hospital Mortality in Acute Coronary Syndrome in Switzerland

The Acute Myocardial Infarction and Unstable Angina Registry in Switzerland (AMIS Plus)

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Key Words

Acute coronary syndrome · Dyslipidemia · Hypercholesterolemia · In-hospital mortality · Risk factors

Abstract

Background: Although dyslipidemia is one of the main risk factors for cardiovascular diseases, very few randomized trials have provided data on the association of dyslipidemia and in-hospital mortality in patients with acute coronary syndrome (ACS). ***Objective:*** The study assessed the association of dyslipidemia and concomitant risk factors, and early lipid-lowering therapy (LLD) on in-hospital mortality in patients admitted for ACS. ***Methods:*** Using AMIS Plus registry data, 13,482 patients admitted between January 1997 and October 2003 were analyzed, and logistic regression was used for predicting in-hospital mortality. ***Results:*** Baseline characteristics of patients with dyslipidemia (n = 6,079) significantly differed from those without, and in-hospital mortality was lower (5.5 vs. 9.4%; $p < 0.001$). Subgroup analyses of 9,383 patients with one or more of four preexisting main risk factors (hypertension, diabetes, coronary heart disease, CHD, or dyslipidemia) showed that whenever dyslipidemia was combined with another risk factor, the mortality rate clearly decreased. Patients with dyslipidemia were, in all subgroups, significantly younger ($p < 0.001$) and predominantly male, and they had more frequently primary percutaneous coronary intervention (PCI). However, this was only significant in patients with hypertension or hypertension and CHD. Independent in-hospital mortality predictors were age (odds ratio, OR: 1.08 per year, 95% confidence interval, CI, 1.07–1.09), diabetes (OR: 1.96, 95% CI: 1.56–2.46, $p < 0.0001$) and primary PCI (OR: 0.62, 95% CI: 0.44–0.86, $p < 0.0001$). In patients who received LLD, mortality was significantly lower regardless of the total cholesterol level measured within 24 h after symptom onset. ***Conclusion:*** Patients with dyslipidemia admitted for ACS had significantly lower in-hospital mortality than patients without dyslipidemia, mainly but not only due to the younger age of these patients. Early administration of LLD was associated with lower in-hospital mortality.

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Introduction

Coronary heart disease (CHD) is the leading cause of premature death and disability in developed countries [1]. Worldwide, cardiovascular diseases account for half of all deaths in middle age and one third of all deaths in old age [2]. Of the 62,545 deaths occurring in Switzerland in 2000, 24,893 (39.8%) were caused by cardiovascular disease [3].

Dyslipidemia is one of the main risk factors for cardiovascular diseases, in particular for acute myocardial infarction (AMI) [2, 4, 5]. The risk of death from coronary heart disease increases significantly in patients with a high cholesterol level [6, 7]. It is also known that serum cholesterol levels fall with increasing age [8] and that all-cause mortality is inversely related to cholesterol level [9, 10]. Among elderly hospitalized patients, low serum cholesterol levels appear to be an independent predictor of short-term mortality [11] and cardiothoracic surgery [12].

Many studies demonstrated the benefit of cholesterol-reducing therapy for patients with coronary artery disease, even for those with mildly increased levels of LDL cholesterol [13–17]. Starting lipid-lowering secondary prevention during hospitalization may have the potential to substantially reduce morbidity and mortality of stable and unstable coronary artery disease [18, 19].

To our knowledge, this is the first study investigating the association between dyslipidemia and in-hospital mortality in patients with the acute coronary syndrome (ACS) in one registry.

The aim of this study was to examine the relevance of dyslipidemia and concomitant risk factors on in-hospital mortality and to determine the influence of lipid-lowering therapy in primary and early secondary prevention on in-hospital mortality in patients admitted for ACS in Switzerland between January 1997 and October 2003.

Patients and Methods

The AMIS Plus Registry

In 1997, the Swiss Societies of Cardiology, Internal Medicine and Intensive Care initiated a nationwide prospective registry to assess the diagnostic and therapeutic measures in patients with AMI in Switzerland (AMIS). Academic and non-academic hospitals participate voluntarily and provide blinded data on these patients to the AMIS Data Center through an internet- or paper-based questionnaire of 140 questions. The Data Center controls and checks the data for plausibility and cross-checks in case of queries. In 2000, patients with unstable angina were added to the registry. AMIS Plus is an industry-sponsored project, but the supporting institutions do no play any role in the design of the registry, data collection, analysis or interpretation. The project is led by a Steering Committee comprised of members of the founding societies. The registry was approved by the Overregional Ethical Committee for Clinical Studies and the Swiss Board for Data Security.

Patients

The AMIS Plus Registry documented data from 13,482 patients admitted to hospital for ACS between January 1997 and October 2003. The AMIS Plus registry included all patients with ACS: AMI defined by characteristic symptoms and or ECG changes and enzymes (total creatine kinase or creatine kinase, MB fraction greater than twice the upper limit of normal), minimal necrosis (same, but the enzymes below twice the upper limits and troponin positive) and unstable angina (symptoms and/or ECG typical for ACS, normal enzymes). Dyslipidemia was defined when the patient was treated for dyslipidemia or when previously diagnosed as having dyslipidemia by the primary physician according to Swiss guidelines [20]. Other risk factors previously diagnosed, treated and/or documented in the patients' medical history were also identified.

Statistical Analyses

Data are presented as percentages for discrete variables for evaluable cases and as means ± SD and medians for continuous variables. Patients with unknown risk factors were excluded from the risk factor analysis. The non-parametric Mann-Whitney rank sum test was used for group comparisons. A p value <0.05 was considered significant.

Logistic regression models for predicting hospital mortality were conducted using the following variables: age, sex, history of CHD, hypertension, diabetes, dyslipidemia, overweight (body mass index >25 kg/m^2), currently smoking, thrombolysis and primary percutaneous coronary intervention (PCI). Separate univariate logistical models were first fitted for each variable, and then backward elimination with a significance level of 0.05 was performed. Odds ratios (OR) were simultaneously adjusted for all the other predictors included in the multivariate logistic regression model. The endpoint has been defined as major adverse cardiac events and included stroke, re-infarction and death as well as in-hospital mortality.

SPSS (Chicago, Ill., USA; version 11.5) was used for all statistical analyses.

Results

In this study population including 13,482 patients admitted for ACS, 72.2% were male and 27.8% female, 83.8% had a definitive diagnosis of AMI, 12% had minimal necrosis and 4.2% unstable angina. The mean age of the patients was 65.2 ± 12.9 years (median 66 years; in males 63.3 ± 12.8 years; median 64 years, and in females 70.4 ± 11.9 years; median 72 years; $p < 0.001$).

The most frequent risk factors were overweight (63.4%), dyslipidemia (56.7%) and hypertension (53.2%). Of the patients, 40.4% had a previous history of CHD, 39.7% were current smokers and 20.3% had diabetes.

Table 1. Characteristics of the patients (%) admitted for ACS with or without dyslipidemia (n = 12,299)

Characteristics	With dyslipidemia	Without dyslipidemia	Significance
Cases	6,979	5,320	
Sex, %			
Male	74.1	71.5	$p < 0.001$
Female	25.9	28.5	
Age, years (mean ± SD)	63.3 ± 12.1 years	66.9 ± 13.4 years	$p < 0.001$
Killip class, %			$p < 0.001$
Class I	76.7	71.0	
Class II	16.4	20.8	
Class III	4.7	6.2	
Class IV	2.1	1.9	
Past medical history, %			
CHD	46.6	31.6	$p < 0.001$
Hypertension	57.4	46.7	$p < 0.001$
Diabetes	22.0	17.1	$p < 0.001$
Smoking (current)	40.8	38.3	$p < 0.004$
Overweight	67.0	58.5	$p < 0.001$
Immediate therapy, %			
Aspirin	93.3	93.3	$p = 0.987$
Ticlopidine, clopidogrel	33.2	21.1	$p < 0.001$
Standard heparin	79.2	81.3	$p < 0.05$
LMWH	26.3	29.2	$p < 0.007$
β-Blocker	75.5	67.1	$p < 0.001$
ACE inhibitor	38.7	37.0	$p = 0.065$
Angiotensin II antagonist	4.1	3.5	$p = 0.299$
Nitrate	71.6	74.2	$p < 0.002$
LLD	73.9	51.0	$p < 0.001$
Thrombolysis, %	24.0	25.4	$p = 0.185$
Primary PCI, %	24.9	17.8	$p < 0.001$
GPIIb/IIIa antagonist, %	38.7	29.5	$p < 0.001$
Major adverse cardiac events, %	8.6	12.5	$p < 0.001$
In-hospital mortality, %	5.5	9.4	$p < 0.001$

Overweight: body mass index >25 kg/m^2. LMWH = Low-molecular-weight heparin; ACE inhibitor = angiotensin-converting enzyme inhibitor.

Patients were treated in accordance with international guidelines [21, 22]. Use of medication has been described and published elsewhere [23]. Thrombolysis was performed in 24.4% and primary PCI in 20.9% of the patients. Overall in-hospital mortality was 8.3%. Major adverse cardiac events occurred in 11.5% of patients.

Table 1 shows the characteristics of 12,299 patients admitted for acute coronary syndrome with or without dyslipidemia. For 1,183 patients (8.8%), the dyslipidemia data were unknown and they were therefore excluded. The 6,979 patients with dyslipidemia were compared with the 5,320 without. Patients with dyslipidemia were younger, had a higher percentage of males, a better Killip classification, more concomitant risk factors, received less frequently heparin (standard and low molecular weight) and nitrate, and received more frequently ticlopidine/clopidogrel, β-blockers and lipid-lowering drugs (LLD) as immediate therapy within 48 h after symptom onset. No difference was found between the two groups for thrombolysis, aspirin, ACE inhibitors and angiotensin II antagonists. Primary PCI was more often performed in patients with dyslipidemia and in patients who received GPIIb/IIIa antagonists. Major adverse cardiac events and in-hospital mortality were significantly lower in these patients.

In 9,383 patients (70%), four main cardiovascular risk factors were known (fig. 1). In 4,099 patients, one or more of the risk factors were unknown. An analysis of dyslip-

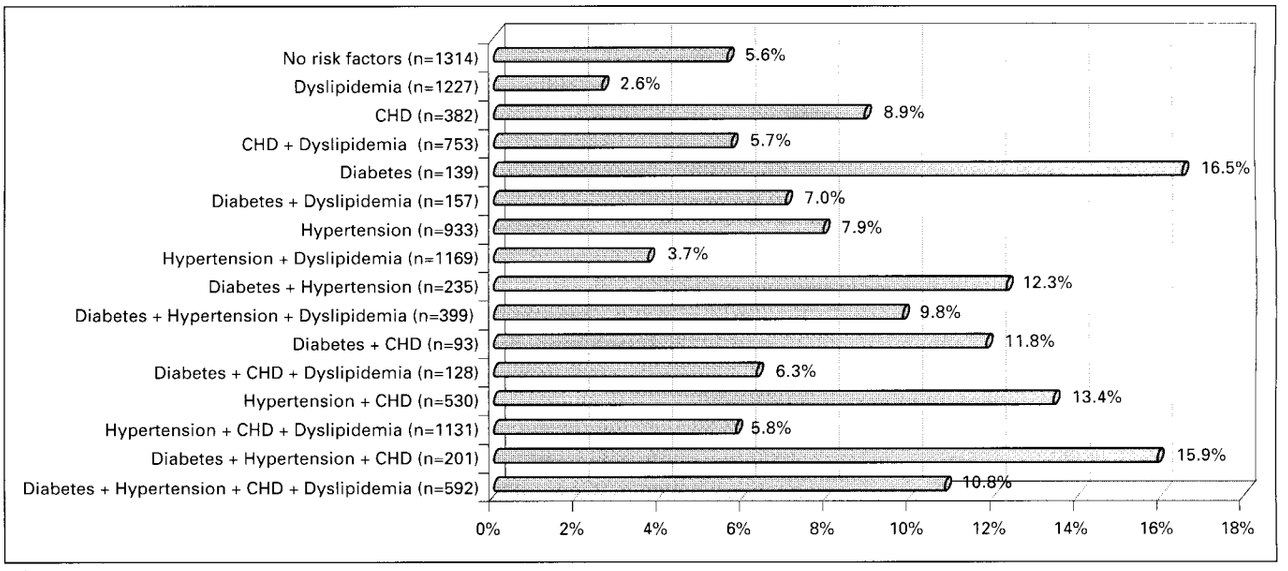

Fig. 1. In-hospital mortality and risk factors of patients admitted for ACS in Switzerland between January 1997 and October 2003.

Table 2. In-hospital mortality, dyslipidemia, concomitant risk factors and characteristics of the patients admitted for ACS

Risk factors known in 9,383 patients with ACS	Death %	p value	Median age, years	p value	Male %	p value	Primary PCI, %	p value
No risk factors (n = 1,314)	5.6		61.5		77.1		25.5	
Dyslipidemia (n = 1,227)	2.6	0.0001	57.0	0.001	78.5	0.431	34.8	0.001
CHD (n = 382)	8.9		72.0		75.3		19.6	
Dyslipidemia + CHD (n = 753)	5.7	0.045	63.0	0.0001	82.9	0.003	24.7	0.062
Diabetes (n = 139)	16.5		68.0		69.5		23.6	
Dyslipidemia + diabetes (n = 157)	7.0	0.011	62.0	0.001	77.5	0.144	31.2	0.154
Hypertension (n = 933)	7.9		69.0		65.7		23.6	
Dyslipidemia + hypertension (n = 1,169)	3.7	0.001	65.0	0.001	67.4	0.424	29.5	0.003
Diabetes + hypertension (n = 235)	12.3		74.0		67.8		16.9	
Dyslipidemia + diabetes + hypertension (n = 399)	9.8	0.353	68.0	0.001	58.4	0.02	23.6	0.056
Diabetes + CHD (n = 93)	11.8		74.0		73.1		17.2	
Dyslipidemia + diabetes + CHD (n = 128)	6.3	0.154	65.0	0.001	78.7	0.340	18.8	0.860
Hypertension + CHD (n = 530)	13.4		75.0		68.1		15.4	
Dyslipidemia + hypertension + CHD (n = 1,131)	5.8	0.001	69.0	0.001	73.3	0.035	25.0	0.0001
Diabetes + hypertension + CHD (n = 201)	15.9		76.0		60.2		15.3	
Dyslipidemia + diabetes + hypertension + CHD (n = 592)	10.8	0.061	70.0	0.001	70.9	0.006	21.8	0.054

idemia in combination with other risk factors is shown in figure 1. For patients with diabetes combined with CHD and/or hypertension, there was no significant decrease in in-hospital mortality associated with dyslipidemia. In all other subgroups of patients with dyslipidemia, mortality was significantly lower (table 2).

This paradox is partly explained by the fact that these patients were significantly younger. In other words, patients with a medical history of dyslipidemia developed ACS requiring hospitalization at an earlier age than patients without dyslipidemia. In the dyslipidemia group, there were significantly more men, and in the hyperten-

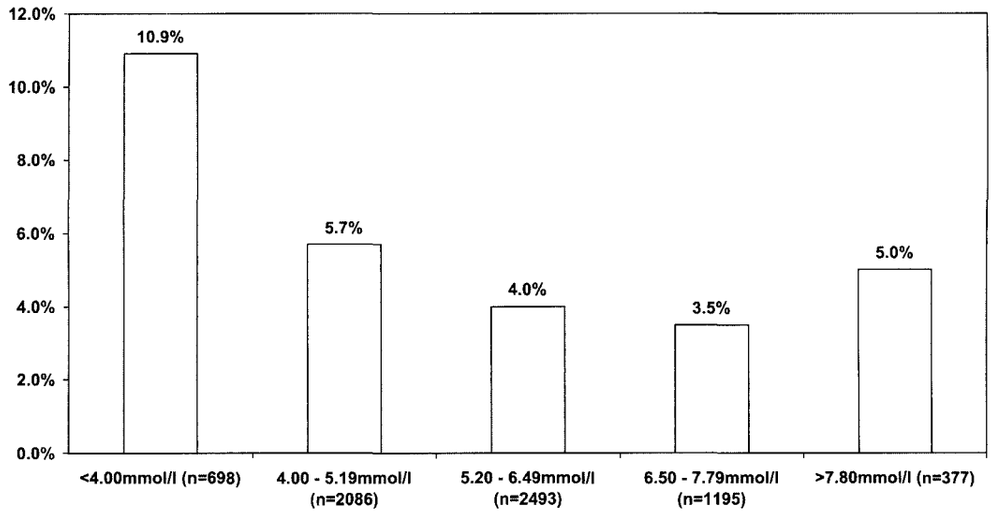

Fig. 2. In-hospital mortality according to the serum total cholesterol level measured within 24 h after symptom onset in patients admitted for ACS.

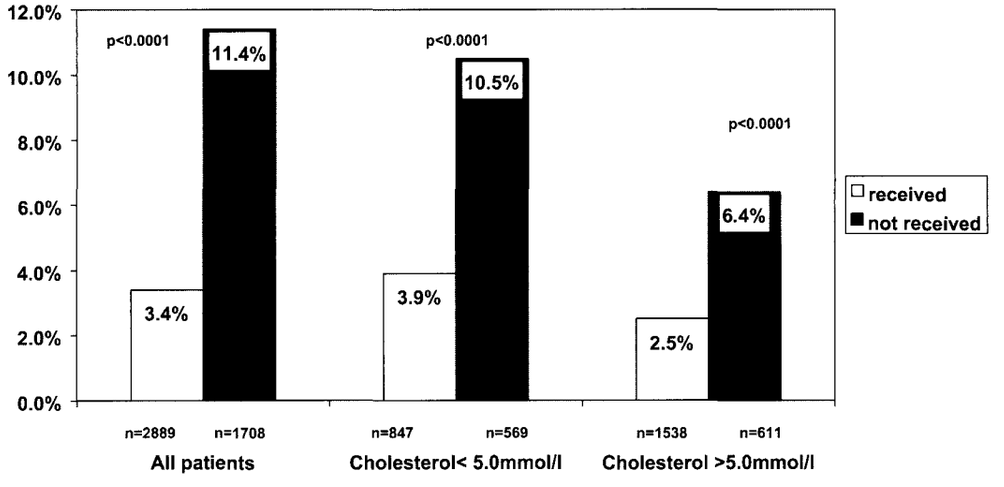

Fig. 3. LLD received within 48 h of symptom onset, in-hospital mortality and the serum TC level measured within 24 h after symptom onset in patients admitted for ACS.

sive patients significantly more received primary PCI. However, these differences were not constant for all subgroups (table 2).

The multivariate logistic regression model was based on nine variables and 6,859 patients (6,494 survivors and 365 deceased). The independent in-hospital mortality predictors were age (odds ratio, OR: 1.08/year, 95% confidence interval, CI: 1.07–1.09) and diabetes (OR: 1.96, 95% CI: 1.56–2.46; $p < 0.0001$). Primary PCI was associated with a decreased risk of mortality (OR: 0.62, 95% CI: 0.44–0.86; $p < 0.0001$). OR for dyslipidemia was 0.80 (95% CI: 0.64–1.00; $p = 0.052$).

Data on the total cholesterol level (TC) within 24 h after chest pain started was only available for 6,849 of the 13,482 patients (50.8%). The mean TC value was 5.16 mmol/l (SD: 1.24 mmol/l; median: 5.00 mmol/l) in patients without a medical history of dyslipidemia (n = 2,515). In patients with dyslipidemia (n = 3,894) the mean TC value was 5.83 mmol/l (SD: 1.37 mmol/l; median: 5.80 mmol/l; $p < 0.001$). HDL cholesterol was known for 5,857 patients. There was no significant difference between these two groups. Patients with dyslipidemia had a mean HDL cholesterol of 1.28 mmol/l (median 1.14 mmol/l), and patients without dyslipidemia had a mean of 1.22 mmol/l (median 1.12 mmol/l).

The mortality rate for patients according to TC concentrations is shown in figure 2. From all patients with a medical history of dyslipidemia, 31.3% (of 6,854 evaluable cases) were on LLD regularly before admission. Early secondary prevention with LLD was added to the questionnaire in the year 2000 and since this time administered to 73.9% of patients with dyslipidemia and to 51.0% of patients without dyslipidemia (4,212 evaluable cases). LLD were prescribed at discharge to 83.3% of 6,533 patients with dyslipidemia and to 45.7% of 4,786 patients without dyslipidemia.

Associations between LLD received within 48 h after the onset of chest pain and in-hospital mortality in patients admitted with ACS are shown in figure 3. In patients given LLD as immediate treatment, the mortality rate was significantly lower compared with patients without LLD therapy regardless of the TC measured within 24 h after symptom onset.

Discussion

In this study, we show that patients with dyslipidemia admitted for ACS were significantly younger and had a lower in-hospital mortality than those with normal serum lipids.

Diagnostic criteria for myocardial infarction have been changed recently and have an important impact among patients admitted with suspected cardiac chest pain [24]. As ACS refers to the whole spectrum of cardiac disease, from unstable angina to ST-segment elevation MI, we evaluated all patients with ACS and not only patients with a defined ST-segment elevation MI.

In this study, dyslipidemia, being one of the main cardiovascular risk factors, seems to be a cause of unstable angina or AMI in younger patients regardless of the existence of other co-factors.

Apart from age, the most significant, independent risk factor of in-hospital mortality proved to be diabetes. Although main risk factors for cardiovascular disease varied between different populations [25–28], the results of risk factor assessment in our study population corresponded with data from the Euro Heart Survey [29].

In 50% of cardiac events, risk factors are responsible for cardiovascular disease and/or mortality [30]. Despite this evidence, the importance of risk factors seems to be systematically underestimated [2, 31].

Epidemiological studies carried out over the last few decades have shown that hypertension, dyslipidemia and smoking increase the risk of cardiovascular diseases, and randomized trials have shown that lowering blood pressure and cholesterol prevents cardiovascular disease [19, 32]. The relationship between serum cholesterol and CHD death rates in middle-aged American men was continuous, graded and strong [33].

It was found that many young adults with MI do not have multiple risk factors and 16% have moderately high LDL cholesterol levels [5]. In our study of 9,383 patients with cardiovascular risk factors being monitored, 14% had none, and 13% had only dyslipidemia. Thus more studies are needed to validate the new guidelines for young adults and to determine the statistical adjustments necessary to improve performance in young adults at risk of MI.

Risk factor counselling, education and treatment are crucial to prevent people from developing cardiovascular disease or dying prematurely [34]. Our study stresses the importance of the prevention of obesity and dyslipidemia especially in young males to prevent premature ACS.

TC and triglyceride concentrations predicted MI and death in women at different ages, and an age-specific association between serum lipids and endpoints in women were found [35]. In some studies, it has been shown that men frequently had increased cholesterol levels [34, 36].

It is known that a low cholesterol level is associated with an increase in all-cause mortality [11, 37], and an increased mortality in patients with cancer [10], in the elderly [9], in patients after cardiothoracic surgery [12] and in those with advanced heart failure [38]. An J- or U-shaped association between serum TC and all-cause mortality in the general population has been described, suggesting that subjects with very low or very high concentrations of cholesterol have an increased risk of death compared with patients with moderate concentrations [6, 39–41].

Another study reported that patients aged 65–84 years with moderate/high TC levels had an approximately 45%

lower risk of mortality [37]. Although elevated TC increases the incidence of CHD, morbidity and mortality, it did not affect in-hospital outcomes among patients with AMI in previous studies [11, 42], which corresponds with the in-hospital mortality of patients with ACS in our study. TC is measured within 24 h after the onset of chest pain because it has been shown that the lipid levels obtained early on admission for AMI are representative of a patient's baseline levels, being in contrast to those registered later during hospitalization [43]. In our study, patients with a very low TC concentration (<4 mmol/l) had the highest mortality rate.

Many studies have confirmed that treatment with LLD decreased cardiovascular morbidity and mortality in primary as well as secondary prevention of cardiovascular diseases. Swiss recommendations are in alignment with European and US guidelines [20].

The overall prescription rate of LLD at discharge in this study was 65.9%, in 1997 it was 40.3%, increasing to 83.6% in 2002. In the GRACE study, the overall rate of statin use at discharge was 47%, with geographical variations from 26 to 57% [44]. This result is slightly higher than that reported in the EUROASPIRE II study (43%) [45]. On one hand, this variation may be related to the current uncertainty about the early use of statins following a cardiac event (although their use in long-term secondary prevention is well established) and, on the other hand, to other factors including costs [44]. There are reports suggesting that LLD therapy in the secondary prevention of coronary artery disease may be underused [18], although it has been shown that prescribing LLD at hospital discharge was independently associated with reduced short-term mortality among patients after an ACS [46].

The importance of the lipid-lowering strategy rises after coronary revascularization [16]. LLD, although proven effective in the secondary prevention of coronary artery disease, were used in only one third of eligible patients. Among the patients receiving these drugs, only a few achieved the recommended lipid goals [18].

The results of the MIRACL study indicated that treatment with atorvastatin, initiated during the acute phase of unstable angina or non-Q-wave AMI reduces the risk of ischemic events requiring hospitalization [19]. In our study, there was a significant decrease in in-hospital mortality in patients who received LLD as early secondary prevention 48 h after symptom onset regardless of the TC level on admission. The studies examining the effects of statins on human coronary artery plaques indicated that statins could stabilize unstable plaques, regardless of a patient's baseline cholesterol level [47] and/or enhanced collateralization of severely diseased coronary arteries [48].

The results from one or several major clinical trials can change the attitudes of physicians regarding the prescription of medication [49].

Limitations of the Study

On-site validation of data collection was periodic and there were no audits for consistency between data base entries and medical chart notes. There were no assessments of clinical eligibility for each medication, and thus failure in the use of certain medications may reflect contraindication to their use. The number of participating hospitals during the time of this data collection varied, ranging from 18 to 54 of the 106 hospitals treating AMI in Switzerland. Therefore, the participating hospitals may not be representative of all Swiss hospitals.

Conclusions

Patients with a medical history of dyslipidemia admitted for ACS between 1997 and 2003 in Switzerland and included in the AMIS Plus National Registry had significantly lower in-hospital mortality compared with patients without dyslipidemia. The main, but not the single reason was the younger age of these patients. Patients with dyslipidemia had a higher incidence of other cardiovascular risk factors. In patients with mildly elevated cholesterol levels on admission, in-hospital mortality and major adverse cardiac events were lower compared to patients without elevated cholesterol levels.

Multivariate logistic regression analysis revealed that the strongest predictors for in-hospital mortality were age, the presence of diabetes and the use of PCI as a primary revascularization strategy. The administration of statins within 48 h was associated with lower in-hospital mortality irrespective of the cholesterol level on admission.

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Participants

The following hospitals participated in the AMIS Registry on which this report from 1997 to 2003 is based (places in alphabetical order): Kantonsspital, Altdorf (Dr. R. Simon), Kantonales Spital Altstätten, Altstätten (Dr. P.-J. Hangartner), Kantonsspital, Basel (PD Dr. P. Hunziker), St. Claraspital, Basel (Dr. C. Grädel), Inselspital, Bern (Prof. B. Meier), Spitalzentrum Biel, Biel (Dr. H. Schläpfer), Oberwalliser Kreisspital, Brig-Glis (Dr. D. Evéquoz), Spital Bülach, Bülach (Dr. R. Pampaluchi/Dr. A. Ciurea), Rätisches Kantons- und Regionalspital Chur, Chur (Dr. P. Müller), Kreuzspital, Chur (Dr. V. Wüscher), Spital Davos, Davos Platz (Dr. G. Niedermaier), Hôpital cantonal Fribourg, Fribourg (Dr. B. Quartenoud), Spital Frutigen, Frutigen (Dr. S. Moser), HUG, Genève (Dr. J.-M. Gaspoz), Kantonsspital, Glarus (Dr. W. Wojtyna), Spital Grenchen, Grenchen (Dr. P. Schlup/Dr. A. Oestmann), Bezirksspital Grosshöchstetten, Grosshöchstetten (Dr. C. Simonin), Kantonales Spital, Heiden (Dr. R. Waldburger), Kantonales Spital, Herisau (Dr. P. Staub), Spital Interlaken, Interlaken (Dr. P. Sula), Spital, Jegenstorf (Dr. H. Marty), Hôpital La Chaux-de-Fonds, La Chaux-de-Fonds (Dr. H. Zender), Spital Lachen, Lachen (Dr. I. Poepping), Kantonsspital, Luzern (Prof. P. Erne), Hôpital régional, Martigny (Dr. B. Jordan), Hôpital de la Tour, Meyrin (PD Dr. P. Urban), Hôpital du Chablis, Monthey (Dr. P. Feraud), Hôpital de Zone, Montreux (Dr. E. Beretta), Hôpital du Jura bernois, Moutier (Dr. Ch. Stettler), Regionales Spital Zentrum, Münsingen (Dr. F. Repond), Kreisspital für das Freiamt, Muri (Dr. A. Spillmann), Groupement hospitalier de l'Ouest Lémanique, Nyon (Dr. R. Polikar), Gesundheitszentrum Fricktal, Regionalspital Rheinfelden, Rheinfelden (Dr. H.-U. Iselin), Kantonales Spital, Rorschach (Dr. M. Pfister), Kantonsspital Obwalden, Sarnen (Dr. T. Kaeslin), Kantonsspital Schaffhausen, Schaffhausen (Dr. R. Frey), Spital Limmattal, Schlieren (Dr. B. Risti), Spital Schwyz, Schwyz (Dr. P. Eichhorn), Ospidal d'Engiadina Bassa, Scuol (Dr. G. Flury/Dr. C. Neumeier), Bürgerspital, Solothurn (Dr. P. Hilti), Kantonsspital, St. Gallen (Dr. W. Angehrn), Thusis Krankenhaus, Thusis (Dr. U.-P. Veragut), Spital Uster, Uster (Dr. D. Maurer/Dr. S. Heinbuch), Kantonales Spital Uznach, Uznach (Dr. A. Weber), Spital Zimmerberg, Wädenswil (Dr. G. Garzoli), Spital Wald, Wald (Dr. M. Schneider), GZO Spital Wetzikon, Wetzikon (Dr. M. Graber), Kantonsspital, Winterthur (Dr. A. Haller), Kantonales Spital Sursee-Wolhusen, Wolhusen (Dr. M. Peter), Spital Zofingen, Zofingen (Dr. H.J. Vonesch), Spital Zollikerberg, Zollikerberg (Dr. P. Siegrist), Zuger Kantonsspital, Zug (Prof. M. Vogt), Universitätsspital, Zürich (PD Dr. F. Eberli/PD Dr. M. Maggiorini), Stadtspital Triemli, Zürich (Prof. O. Bertel) and Stadtspital Waid/Medizinische Klinik, Zürich (Dr. M. Brabetz/Dr. S. Christen).

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