Statin Therapy After Acute Myocardial Infarction: Are We Adequately Treating High-risk Patients?

Gregg C. Fonarow, MD

Address
Ahmanson-UCLA Cardiomyopathy Center, UCLA Division of Cardiology, 47-123 CHS, 10833 LeConte Avenue, Los Angeles, CA 90095-1679, USA.
E-mail: gfonarow@mednet.ucla.edu

Current Atherosclerosis Reports 2002, **4**:99–106
Current Science Inc. ISSN 1523-3804

After acute myocardial infarction, patients remain at high risk for recurrent cardiovascular events and mortality. Despite the compelling scientific and clinical trial evidence that lipid-lowering medications reduce mortality in patients after acute myocardial infarction, this life-saving therapy continues to be underutilized. A number of studies in a variety of clinical settings have documented that a significant proportion of patients after myocardial infarction are not receiving treatment with lipid-lowering medications when guided by conventional care. It has recently been demonstrated that implementation of a hospital-based system for initiation of statins prior to hospital discharge results in a marked increase in treatment rates, improved long-term patient compliance, more patients reaching low-density lipoprotein levels of less than 100 mg/dL, and improved clinical outcomes. Adopting in-hospital initiation of lipid-lowering medications as the standard of care for patients hospitalized with acute myocardial infarction could dramatically improve treatment rates and thus substantially reduce the risk of future coronary events and prolong life in the large number of patients hospitalized each year.

Introduction

There is compelling scientific evidence that lipid-lowering therapy reduces the risk of recurrent coronary events and improves survival in patients who have suffered a myocardial infarction (MI). Despite this evidence, as well as national and international clinical guidelines recommending lipid-lowering treatment in patients with clinically evident atherosclerotic vascular disease, including post-MI patients, a number of studies have documented low treatment rates in this patient population. The use of lipid-lowering medications in the post-MI setting represents a major clinical practice and public health issue. This article reviews the studies documenting the current under-use of lipid-lowering therapies and identifies successful strategies and programs that have been demonstrated to improve treatment rates and clinical outcomes in this high-risk patient population.

Cardiovascular Risk After Myocardial Infarction

This year, 1.1 million individuals in the United States will have a new or recurrent acute MI [1]. It is estimated that there are 7.3 million individuals (4.5 million men and 2.8 million women) who have a history of acute MI [1]. The cardiovascular risk after acute MI remains substantial. Within 1 year after an acute MI, 25% of men and 38% of women will die [1,2]. Within 6 years of a clinically evident event, 18% of men and 35% of women will have had a recurrent MI. During this time frame, approximately 22% of men and 46% of women will go on to develop congestive heart failure [1]. Patients with a prior history of MI are five to seven times more likely to sustain a cardiovascular event compared with individuals without clinically evident atherosclerotic vascular disease. These patients remain at risk for recurrent events even if they are entirely asymptomatic, have no demonstrated ischemia on stress testing, and even if they have undergone complete revascularization. Patients after acute MI thus constitute a very high-risk group for recurrent coronary events and cardiovascular mortality.

Benefits of Lipid-lowering Medications

There is overwhelming scientific evidence that lipid-lowering therapy reduces the risk of recurrent cardiovascular events and improves survival in patients after MI [3,4••,5,6,7••]. Prospective, randomized clinical trials, including the Scandinavian Simvastatin Survival Study (4S) [5] and the Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) [6] trials, demonstrate a significant reduction in mortality with 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors (statins) in post-MI patients, including those

patients with elevated, mildly elevated, or normal cholesterol levels [5,6]. The LIPID trial demonstrated that in patients after MI or with unstable angina with baseline cholesterol levels of 155 to 271 mg/dL, there is a substantial reduction in all-cause mortality when a lipid-lowering medication (statin) is added to modified diet alone [6]. The benefits of lipid-lowering medications apply to both men and women, patients older and younger than 65 years of age, and to both diabetic and nondiabetic patients [7••8–10]. Thus, the vast majority of the post-MI patients would be expected to be appropriate candidates for lipid-lowering medication. The magnitude of benefit with lipid-lowering medications matches or exceeds the benefits seen with other secondary prevention medications (*eg*, aspirin, β blockers, and angiotensin converting enzyme [ACE] inhibitors) in the post-MI patient [4••,11].

National and international clinical practice guidelines call for the use of lipid-lowering medications in patients after MI. The National Cholesterol Education Program (NCEP)-Adult Treatment Panel II [12] and III [13••] Guidelines and the American Heart Association/American College of Cardiology (AHA/ACC) Secondary Prevention Clinical Guidelines recommend that patients with documented coronary artery disease, including those who are post-MI, be treated to achieve a low-density lipoprotein (LDL) cholesterol level of less than 100 mg/dL [4••]. It has been documented that only 3% to 7% of patients with acute MI have baseline steady-state LDL cholesterol levels that are below 100 mg/dL or achieve this target with diet and exercise alone [14–16]. Thus, the vast majority of patients after MI will be candidates for lipid-lowering medications in addition to lifestyle modification [17]. Measurement of treatment rates with lipid-lowering therapy in patients after MI is increasingly being viewed as an appropriate quality-of-care performance indicator. The frequency of lipid measurement and treatment to goal in patients hospitalized with coronary artery disease were recently added to the Health Plan Employer and Data Information Set (HEDIS) 2000 quality-of-care measures [18•].

Treatment Gap in Patients After Myocardial Infarction

Despite the effectiveness of lipid-lowering therapy in altering subsequent cardiovascular mortality and widespread dissemination of national treatment guidelines, studies continue to document low treatment rates in patients with established coronary artery disease, including high-risk, post-MI patients (Table 1) [19•,20•,21,22,23•,24–26].

Recent physician practice in the United States regarding prescribing lipid-lowering medication to patients hospitalized for acute MI was assessed in an analysis of 138,001 patients from 1470 hospitals in the National Registry of Myocardial Infarction 3 from July, 1998 to June, 1999 [19•]. This study revealed that only 31.7% of patients hospitalized with acute MI were discharged on a lipid-lowering medication. Among patients with prior history of coronary artery disease, revascularization procedure, or diabetes, less than half the patients were discharged on treatment. Elderly patients, independent of associated co-morbidities, were at increased risk for being discharged without lipid-lowering therapy. Women were also less likely to be treated with lipid-lowering medications, with 34.8% of men discharged on lipid-lowering therapy as compared with 26.8% of the women ($P<0.0001$). This difference was not entirely due to differences in age of presentation with MI (Fig. 1). A variety of other clinical, demographic, treatment, and process of care factors that significantly influenced treatment utilization of lipid-lowering medications were also identified.

Other studies have shown similar under-use of lipid-lowering therapy in high-risk hospitalized patients. Among the 20,809 patients hospitalized with an acute coronary syndrome and enrolled in the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial or Global Use of Streptokinase or t-PA for Occluded Coronary Arteries (GUSTO) IIb trial, only 3653 patients (17.6%) were discharged on lipid-lowering therapy [20•]. This low use of lipid-lowering therapy was seen despite the fact that 68% of the patients in these two studies had a history of MI or a MI at the time of enrollment. In a study of 19,599 acute MI patients hospitalized at 58 Swedish Hospitals, only 28.2% of patients younger than 80 years of age were discharged on statins [21]. An analysis of elderly patients hospitalized for acute MI in 37 community hospitals in Minnesota from 1995 to 1996 showed a treatment rate of 37% at time of discharge in patients with cholesterol levels greater than 200 mg/dL [22].

In the outpatient setting, this treatment gap for lipid-lowering therapy in post-MI patients persists. The Quality Assurance Project (QAP) analyzed treatment rates in 48,586 outpatients with documented coronary heart disease (29% with prior history of MI) from 140 medical practices (80% cardiology) [23•]. Only 39% of these patients were treated with lipid-lowering medications, and only 11% were documented to have a LDL cholesterol level less than 100 mg/dL. In the Third National Health and Nutrition Examination Survey (NHANES III), lipid-lowering medication was used in only an estimated 11% of participants with a history of MI [24]. In the Lipid Treatment Assessment in Practice (L-TAP) study [25], only 18% of outpatients with coronary heart disease treated for hyperlipidemia had LDL cholesterol less than 100 mg/dL. This was not due to a lack of provider knowledge, because 95% of the surveyed physicians reported that they were knowledgeable on the National Cholesterol Education Program guidelines, and 65% reported they follow the guidelines on most patients (Fig. 2). A significant treatment gap for secondary prevention has also been documented in 47 centers in 15 European countries that participated in the EURO-ASPIRE II study [26].

Table 1. Lipid-lowering treatment use in patients after myocardial infarction

Study	No. of patients	% post-MI	% Rx LLA	% LDL <100 mg/dL	Setting
Fonarow *et al.* [19•]	138,001	100%	32%	-	Hospital discharge
Aronow *et al.* [20•]	20,809	68%	18%	-	Hospital discharge
Stenestrand and Wallentin [21]	19,599	100%	28%	-	Hospital discharge
Sueta *et al.* [23•]	48,586	29%	39%	11%	Outpatient
Schrott *et al.* [28]	2763	39%	47%	9%	Outpatient
Pearson *et al.* [25]	4888	25%	NA	18%	Outpatient
Pearson *et al.* [29]	6555	52%	66%	28%	Outpatient

LDL—low-density lipoprotein; LLA—lipid-lowering agent; MI—myocardial infarction.

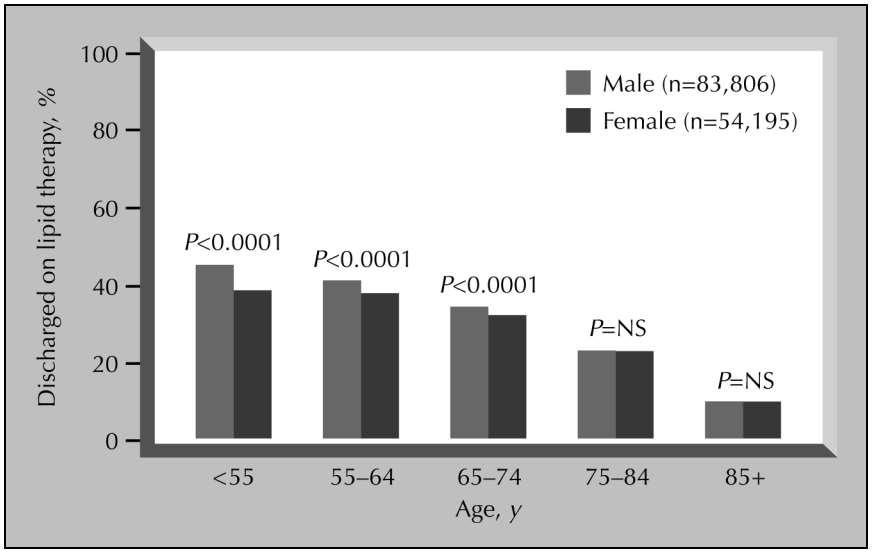

Figure 1. The association of patient age and sex with the prescription of lipid-lowering medications at hospital discharge for acute myocardial infarction in 138,001 patients in the National Registry of Myocardial Infarction 3. (*Data from* Fonarow *et al.* [19•].)

Low lipid-lowering treatment rates for patients after MI in the outpatient setting extend to leading academic medical centers, centers participating in secondary prevention trials, and prominent community cardiovascular care centers. Miller *et al.* [27] evaluated the use of lipid-lowering therapy for patients with coronary artery disease in 825 men and women who were recruited from 16 academic medical centers for the Prospective Evaluation of the Vascular Events of Norvasc Trial, 45% of whom had a prior history of acute MI. At study completion in 1997, only 31% of men and 12% of women were treated to a LDL cholesterol level of less than 100 mg/dL. In the Heart and Estrogen/Progesterone Replacement Study (HERS) among 2763 postmenopausal women with documented coronary heart disease, only 9% had been treated to a LDL cholesterol level of less than 100 mg/dL [28]. The American College of Cardiology Evaluation of Preventive Therapeutics (ACCEPT) study [29], which evaluated 6875 patients from 55 centers in the United States, showed that at 6 months after cardiac hospitalization, despite prospective monitoring, only 28% of patients were at goal for LDL cholesterol.

Together, these studies demonstrate that under conventionally guided management, regardless of the healthcare delivery system, an unacceptably large number of MI patients are left untreated or undertreated with lipid-lowering therapy. Given the substantial number of patients at risk and the benefits of therapy, there is an urgent need to adopt effective strategies that will improve the number of post-MI patients who are being effectively treated with lipid-lowering therapy.

Barriers to Treatment and Contributing Factors

A number of barriers to implementing risk factor modification, including lipid-lowering therapy, in patients with coronary heart disease were highlighted at the 27th American College of Cardiology Bethesda Conference [30]. These included physicians being focused on acute problems, time constraints and lack of incentives, lack of training, and limited resources and outpatient facilities. It has more recently been recognized that the setting in which treatment is initiated may be a very import factor influencing treatment rates [31]. Early treatment guidelines and algorithms, such as the NCEP I and II, had recommended delaying baseline lipid assessment and treatment until 6 weeks after acute presentation in recognition that the

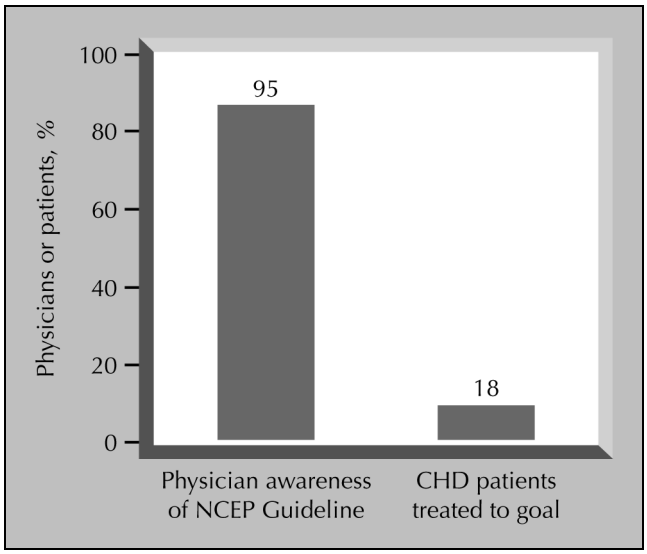

Figure 2. Results of a multicenter survey to evaluate the percentage of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. Although 95% of physicians surveyed responded that they were aware of the National Cholesterol Education Program (NCEP) treatment goals, only 18% of these physician's coronary heart disease (CHD) patients had been treated to goal. Provider awareness alone is not sufficient to ensure adequate lipid-lowering treatment in the out-patient setting. (*Data from* Pearson *et al*. [25].)

acute phase response triggered by acute MI and coronary artery bypass grafting can substantially lower total and LDL cholesterol [12]. As a result, the first opportunity for beginning treatment was delayed to a time when the patient may no longer feel they are at risk for recurrent events. There are frequently fewer resources available in the out-patient, as opposed to the in-patient, setting and coordination of care between cardiologists and generalists may be more difficult. When treatment is initiated in the out-patient setting, a number of studies have shown low patient-compliance rates with lipid-lowering medications [32,33]. By recommending a delay in the assessment of lipid levels and the initiation of lipid-lowering treatment in hospitalized coronary heart disease patients, an important treatment opportunity was missed inadvertently.

The studies assessing utilization of lipid-lowering therapy in patients after MI have consistently identified a variety of clinical, demographic, treatment, and process-of-care factors that significantly influenced treatment use of lipid-lowering medications [19•,20•,21,22,23•]. This would seem to indicate that lipid-lowering medication use is impacted by physician education and the process of care in place within the healthcare delivery system, and thus could be favorably impacted by educational initiatives, quality improvement programs, and treatment systems.

Effective Strategies to Improve Treatment

Institution of lipid-lowering therapy in the in-patient setting for patients hospitalized with acute MI has a number of advantages. Measurement of lipid levels can be systematically integrated into the diagnostic testing performed during cardiac hospitalization through the use of preprinted orders and care maps. The fact that lipid panels obtained in the first 12 to 24 hours of hospital admission have been shown to reasonably reflect steady-state lipid levels at 6 weeks removes a perceived barrier to initiating lipid-lowering therapy in the hospital setting [34,35]. The structured setting within the hospital can facilitate the initiation of lipid-lowering treatment through the use of physician prompts and reminders such as preprinted order sets, discharge forms, and involvement of other healthcare professionals. Hospital-based initiation of therapy may help to alleviate patient concerns regarding medication tolerability and side effects. Linking the initiation of lipid-lowering medication and other secondary prevention measures to the patient's cardiac hospitalization conveys the message that this therapy is essential for the prevention of recurrent events and is an essential part of the patient's long-term treatment.

Other evidence provides support for the concept that in-hospital initiation of lipid-lowering medications could be a more effective way to ensure treatment is started and continued. Studies in other patient populations, such as those with heart failure, have demonstrated that ACE inhibitors initiated at the time of hospitalization as part of a disease-management program result in higher utilization rates at 6 months as compared with treatment-utilization rates in conventionally managed out-patients [36]. Initiation of interventions for smoking cessation while patients are hospitalized with acute MI have been shown to result in higher cessation rates than interventions initiated in the out-patient setting [37]. There have been substantially higher utilization rates 1 year after hospital discharge for therapies such as aspirin and β blockers, which are initiated prior to hospital discharge, as compared with therapies such as lipid-lowering medications, which are conventionally initiated on an outpatient basis [26,29]. Studies have also demonstrated that treatment rates for aspirin and β blockers in acute MI patients can be significantly improved though the use of hospital-based programs, and these type of programs would be expected to be similarly effective in improving utilization of lipid-lowering medications [38].

Proof of concept that in-hospital initiation of lipid-lowering medications and other secondary prevention measures improves treatment rates and long-term patient compliance was provided by the University of California, Los Angeles Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP) [39••]. This program, initiated in a university hospital setting in 1994, focused on initiation of aspirin, statin (titrated to achieve LDL cholesterol levels <100 mg/dL), β blocker, and ACE inhibitor therapy in conjunction with dietary and exercise counseling in patients with established coronary heart disease prior to hospital discharge. Preprinted orders, care

maps, discharge forms, physician/nursing education, and treatment utilization reports were employed to facilitate program implementation. Lipid-lowering medication use at the time of discharge increased from 6% before initiation of the program to 86% after CHAMP was implemented ($P<0.001$). Improved utilization of aspirin, β blockers, and ACE inhibitors was also observed (Table 2). Importantly, the in-hospital initiation of lipid-lowering had a dramatic effect on long-term treatment rates and patient compliance. With CHAMP, 1 year after hospital discharge 91% of coronary heart disease patients were treated with statins and 58% were documented to have LDL cholesterol of less than 100 mg/dL, compared with 10% and 6%, respectively, with conventional management before CHAMP was implemented ($P<0.01$). This improved use of lipid-lowering medications, along with other cardioprotective therapies, was associated with a significant reduction in clinical events the first year after discharge: the death and nonfatal MI rate decreased from 14.8% to 7.3% (odds ratio of 0.43; $P<0.01$) [39••]. These improved treatment rates have been sustained over an 8-year period.

More recently, other studies have demonstrated that high rates of lipid-lowering treatment initiation can be achieved with a hospital-based system. A pharmacy-based program that included placing lipid-treatment reminders on charts of patients hospitalized with coronary heart disease demonstrated an increase in treatment rates to 77% at time of discharge [40]. In an analysis of the 10,288 patients in the OPUS-TIMI 16 study of patients hospitalized with an acute coronary syndrome, 90% of patients who were started on statin treatment in the hospital remained on therapy at 10 months [41]. These and other studies demonstrate that hospital-based programs can substantially improve the lipid-lowering medication treatment rates in patients after acute MI.

Potential Early Benefits of Statin Treatment

Beyond the long-term benefits of improved treatment with lipid-lowering medications, in-hospital initiation of statin treatment may also be associated with an early benefit in reducing cardiovascular events, one that could be missed if therapy is delayed. In the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) study [42], 3086 patients hospitalized for unstable angina or non–Q-wave MI were randomized within 24 to 96 hours of admission to receive 80 mg/d of atorvastatin or placebo. Although patients with total cholesterol greater than 270 mg/dL were excluded, there was no lower limit for total cholesterol or LDL cholesterol, and mean LDL cholesterol was only 124 mg/dL. In the brief follow-up of only 4 months, there was a 16% relative risk reduction in cumulative ischemic events (14.8% vs 17.4%; $P=0.048$), with the majority of benefit due to a reduction in worsening angina with new objective evidence of ischemia requiring urgent rehospitalization (6.2% vs 8.4%; $P=0.02$). In-hospital initiation of statin therapy was also safe and well tolerated, with no difference in the withdrawal rate between statin and placebo treatment [42]. A number of cohort studies comparing patients who received statin therapy in-hospital with those discharged without statin therapy have shown that being discharged home on statin therapy after an acute coronary syndrome is associated with an early and striking reduction in mortality [20•,21,41].

In-hospital initiation of therapy can also work in a complimentary fashion with out-patient disease management and preventive cardiology programs. Prior studies have demonstrated the value of these out-patient programs to improve risk factor modification in patients after MI. A physician-directed, nurse-managed, home-based case-management system was compared with usual medical care in 585 men and women discharged after MI in a health maintenance organization [16]. Specialty trained nurses initiated interventions for smoking cessation, exercise training, and diet counseling prior to hospital discharge, followed by monitoring and drug therapy for hyperlipidemia on an out-patient basis. In this study, 93% of the special-intervention patients required lipid-lowering medications, as their LDL cholesterol level remained above 100 mg/dL 90 days after discharge, despite intensive diet and exercise counseling and monitoring. The special-intervention patients had greater rates of smoking cessation, improved functional capacity, and lower LDL cholesterol (107 ± 30 mg/dL vs 132 ± 30 mg/dL) as compared with usual care. The need to hire additional medical personnel (*ie*, specialty trained nurses) may limit the application of this type of system outside of health maintenance organizations. Other studies have demonstrated improved treatment rates in specialty lipid clinics and cardiac rehabilitation programs, but these systems were applied to a selected patient population representing only a small proportion of the patients with coronary artery disease being cared for in the healthcare delivery system from which the patients were drawn [43,44]. In-hospital initiation of therapy can help to ensure lipid-lowering treatment in patients who will not have access to outpatient disease management and preventive cardiovascular care programs.

The NCEP and AHA/ACC national guidelines have very recently been revised and now recommend the assessment of lipid levels within 24 hours of admission and in-hospital initiation of lipid-lowering medications in appropriately selected patients hospitalized with cardiovascular disease [4••,13••]. An essential element of the new AHA program, "Get With The Guidelines", is the use of protocols and an Internet-based discharge tool to encourage in-hospital initiation of lipid-lowering medications and other secondary-prevention measures proven to save lives in patients hospitalized with coronary heart disease. The marked improvement in achievement and maintenance of LDL cholesterol targets for the long term, coupled with potential early benefits and low risks of therapy, are

Table 2. Treatment rates at hospital discharge and at 1-year follow-up with the Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP)

	Pre-CHAMP (n=256)		Post-CHAMP (n=302)	
Therapy	**Discharge**	**1 year**	**Discharge**	**1 year**
Aspirin	78%	68%	92%	94%
Beta blocker	12%	18%	61%	57%
ACE inhibitor	4%	16%	56%	48%
Statin	6%	10%	86%	91%
LDL <100 mg/dL	-	6%	-	58%

ACE—angiotension-converting enzyme; LDL—low-density lipoprotein.

compelling enough to make in-hospital initiation of lipid-lowering medications the standard of care [45].

As reviewed in this article, it has been clearly documented that not enough has been done to ensure the use of lipid-lowering therapy in high-risk patients after MI. Projecting available data nationwide, in the year 2000 there were over 750,000 potentially eligible patients discharged home without lipid-lowering medications after being hospitalized with an acute MI [19•]. A review of the evidence from recent trials and clinical studies provides a compelling argument for implementing lipid-lowering medications in-hospital as part of a systematic approach to address the patient's underlying atherosclerotic disease process. With optimal use of lipid-lowering medications in the high-risk patient with coronary heart disease, as many as 83,000 additional lives could be saved each and every year.

Conclusions

Despite compelling scientific evidence of the benefits of lipid-lowering medications in patients with clinically evident coronary artery disease, a substantial proportion of patients after acute MI are not on treatment. Applying hospital-based systems to ensure initiation of lipid-lowering medications and other cardioprotective therapies has been demonstrated to improve treatment rates, long-term patient compliance, and clinical outcomes. The national guidelines have been revised to recommend that, in addition to diet and exercise counseling, lipid-lowering medications be initiated prior to hospital discharge in patients hospitalized with a cardiovascular event. Widespread application of hospital-based treatment programs could dramatically increase lipid-lowering treatment rates with this proven, cost-effective therapy, and thus substantially reduce the risk of recurrent events and death in the large number of high-risk patients hospitalized each and every year.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. American Heart Association: *2001 Heart and Stroke Statistical Update.* Dallas, TX: American Heart Association 2000.
2. Rosamond WD, Chambless LE, Folsom AR, *et al.*: **Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994.** *N Engl J Med* 1998, **339:**861–867.
3. Rossouw JE, Lewis B, Rifkind BM: **The value of lowering cholesterol after myocardial infarction.** *N Engl J Med* 1990, **323:**1112–1119.
4. •• Smith SC, Blair SN, Bono RO, *et al.*: **AHA/ACC Guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update.** *Circulation* 2001, **104:**1577–1579.

Important new guidelines from the American Heart Association and the American College of Cardiology on the recommended clinical trial evidence-based therapies for preventing cardiovascular events and death in patients with established coronary heart disease

5. The 4S Investigators: **Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S).** *Lancet* 1994, **344:**1383–1389.
6. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group: **Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels.** *N Engl J Med* 1998, **339:**1349–1357.
7. •• LaRosa JC, He J, Vupputuri S: **Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials.** *JAMA* 1999, **282:**2340–2346.

This important study performs a meta-analysis of available clinical trials of the effects of statins in patients with documented coronary artery disease. A clear reduction in all-cause mortality is demonstrated, with benefits seen across a variety of subgroups of patients. No increase in noncardiac mortality was seen in the pooled analysis.

8. Grundy SM, Cleeman JI, Rifkind BM, *et al.*: **Cholesterol lowering in the elderly population.** *Arch Intern Med* 1999, **159:**1670–1678.
9. Mosca L, Grundy SM, Judelson D, *et al.*: **Guide to Preventive Cardiology for Women. AHA/ACC Scientific Statement Consensus panel statement.** *Circulation* 1999, **99:**2480–2484.
10. Grundy SM, Benjamin IJ, Burke GL, *et al.*: **Diabetes and cardiovascular disease. a statement for healthcare professionals from the American Heart Association.** *Circulation* 1999, **100:**1134–1146.

11. 27th Bethesda Conference: **Matching the Intensity of Risk Factor Management with the Hazard for Coronary Disease Events.** *J Am Coll Cardiol* 1996, **27:**957–1047.
12. Adult Treatment Panel II: **Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.** *JAMA* 1993, **269:**3015–3023.
13.•• Adult Treatment Panel III: **Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.** *JAMA* 2001, **285:**2486–2497.

Important new guidelines from the National Cholesterol Education Program on the recommended treatments and approaches to reduce cardiovascular risk through lipid-lowering treatment in patients with and without cardiovascular disease.

14. Hunninghake DB, Stein EA, Dujovne CA, *et al.*: **The efficacy of intensive dietary therapy alone or combined with lovastatin in outpatients with hypercholesterolemia.** *N Engl J Med* 1993, **328:**1213–1219.
15. Ramsay LE, Yeo WW, Jackson PR: **Dietary reduction of serum cholesterol concentration: time to think again.** *BMJ* 1991, **303:**953–957.
16. Debusk RF, Miller NH, Superko HR, *et al.*: **A case-management system for coronary risk factor modification after acute myocardial infarction.** *Ann Intern Med* 1994, **120:**721–729.
17. Grundy SM, Balady GJ, Criqui MH, *et al.*: **When to start cholesterol-lowering therapy in patients with coronary heart disease. A statement for healthcare professionals from the American Heart Association Task Force on Risk Reduction.** *Circulation* 1997, **95:**1683–1685.
18.• Lee TH, Cleeman JI, Grundy SM, *et al.*: **Clinical goals and performance measures for cholesterol management in secondary prevention of coronary heart disease.** *JAMA* 2000, **283:**94–98.

This article describes the rationale and process for developing performance measures for lipid management in patients hospitalized with coronary artery disease.

19.• Fonarow GC, French WJ, Parsons LS, *et al.*, for the National Registry of Myocardial Infarction 3 Participants: **Use of lipid-lowering medications at discharge in patients with acute myocardial infarction: data from the National Registry of Myocardial Infarction 3.** *Circulation* 2001, **103:**38–44.

This study documents recent use of lipid-lowering medications in a large national cohort of patients hospitalized for acute myocardial infarction. Only 31.7% of high-risk post-myocardial infarction patients were discharged on lipid-lowering medications.

20.• Aronow HD, Topol EJ, Roe MT, *et al.*: **Effect of lipid-lowering therapy on early mortality after acute coronary syndromes: an observational study.** *Lancet* 2001, **357:**1063–1068.

This observational study showed that only 17.8% of patients enrolled in two large, acute coronary syndrome trials received lipid-lowering therapy at the time of hospital discharge. Those patients that were treated in-hospital with lipid-lowering medications had an early and marked reduction in mortality.

21. Stenestrand U, Wallentin L, for the Swedish Register of Cardiac Intensive Care (RIKS-HIA): **Early statin treatment following acute myocardial infarction and 1-year survival.** *JAMA* 2001, **285:**430–436.
22. Majumdar SR, Gurwitz JH, Soumerai SB: **Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease.** *J Gen Intern Med* 1999, **14:**711–717.
23.• Sueta CA, Chowdhury M, Boccuzzi SJ, *et al.*: **Analysis of the degree of undertreatment of hyperlipidemia and congestive heart failure secondary to coronary artery disease.** *Am J Cardiol* 1999, **83:**1303–1307.

This study analyzes the degree of lipid-lowering therapy use in 48,586 outpatients with documented coronary artery disease. A variety of clinical and physician-related variables impacted lipid-lowering treatment use.

24. Jacobson TA, Griffiths GG, Varas C, *et al.*: **Impact of evidence-based "clinical judgment" on the number of American adults requiring lipid-lowering drug therapy based on updated NHANES III data.** *Arch Intern Med* 2000, **160:**1361–1369.
25. Pearson TA, Laurora I, Chu H, *et al.*: **The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals.** *Arch Intern Med* 2000, **160:**459–467.
26. EUROASPIRE II Study Group: **Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries; principal results from EUROASPIRE II Euro Heart Survey Program.** *Eur Heart J* 2001, **22:**554–572.
27. Miller M, Byington R, Hunninghake D, *et al.*: **Sex bias and underutilization of lipid-lowering therapy in patients with coronary artery disease at academic medical centers in the United States and Canada.** *Arch Intern Med* 2000, **160:**343–347.
28. Schrott HG, Bittner V, Vittinghoff E, *et al.*: **Adherence to National Cholesterol Education Program Treatment goals in postmenopausal women with heart disease.** *JAMA* 1997, **277:**1281–1286.
29. Pearson TA, Peters TD, Feury D, *et al.*: **The American College of Cardiology Evaluation of Preventative Therapeutics (ACCEPT) study: attainment of goals for comprehensive risk reduction in patients with coronary disease in the US.** *J Am Coll Cardiol* 1998, **31:**186A.
30. Pearson TA, McBride PE, Miller NH, *et al.*: **27th Bethesda Conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 8. Organization of preventive cardiology service.** *J Am Coll Cardiol* 1996, **27:**1039–1047.
31. Fonarow GC, Gawlinski A: **Rationale and design of the Cardiac Hospitalization Atherosclerosis Management Program at the University of California Los Angeles.** *Am J Cardiol* 2000, **85:**10A–17A.
32. Andrade SE, Walker AM, Gottlieb LK, *et al.*: **Discontinuation of antihyperlipidemic drugs—do rates reported in clinical trials reflect rates in primary care settings?** *N Engl J Med* 1995, **332:**1125–1131.
33. Muhlestein JB, Horne BD, Bair TL, *et al.*: **Usefulness of in-hospital prescription of statin agents after angiographic diagnosis of coronary artery disease in improving continued compliance and reduced mortality.** *Am J Cardiol* 2001, **87:**257–261.
34. Gore JM, Goldberg RJ, Matsumoto AS, *et al.*: **Validity of serum total cholesterol level obtained within 24 hours of acute myocardial infarction.** *Am J Cardiol* 1984, **54:**722–725.
35. Rosenson RS: **Myocardial injury: the acute phase response and lipoprotein metabolism.** *J Am Coll Cardiol* 1993, **22:**933–940.
36. Fonarow GC, Stevenson LW, Walden JA, *et al.*: **Impact of a comprehensive heart failure management program on hospital readmission and functional status of patients with advanced heart failure.** *J Am Coll Cardiol* 1997, **30:**725–732.
37. Taylor CB, Houston-Miller N, Killen JD, *et al.*: **Smoking cessation after acute myocardial infarction: effects of a nurse-managed intervention.** *Ann Intern Med* 1990, **113:**118–123.
38. Marciniak TA, Ellerbeck EF, Radford MJ, *et al.*: **Improving the quality of care for Medicare patients with acute myocardial infarction: results from the Cooperative Cardiovascular Project.** *JAMA* 1998, **279:**1351–1357.
39.•• Fonarow GC, Gawlinski A, Moughrabi S, *et al.*: **Improved treatment of cardiovascular disease by implementation of a cardiac hospitalization atherosclerosis management program: CHAMP.** *Am J Cardiol* 2001, **87:**819–822.

This study provides proof of concept that in-hospital initiation of lipid-lowering and other cardioprotective therapy dramatically improves treatment rates, long-term patient compliance, achieving a low-density lipoprotein cholesterol level less than 100 mg/dL, and most importantly, clinical outcomes.

40. Birtcher KK, Bowden C, Ballantyne CM, *et al.*: **Strategies for implementing lipid-lowering therapy: pharmacy-based approach.** *Am J Cardiol* 2000, **85:**30A–35A.
41. Cannon CP, McCabe CH, Bentley J, *et al.*: **Early statin therapy is associated with markedly lower mortality in patients with acute coronary syndromes: observations from OPUS-TIMI-16.** *J Am Coll Cardiol* 2001, **35:**334A.
42. Schwartz GG, Olsson AG, Ezekowitz MD, *et al.*: **Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial.** *JAMA* 2001, **285:**1711–1718.
43. Harris DE, Record NB, Gipson GW, *et al.*: **Lipid lowering in a multidisciplinary clinic compared with primary physician management.** *Am J Cardiol* 1998, **81:**929–933.
44. Blair TP, Bryant FJ, Bocuzzi S: **Treatment of hypercholesterolemia by a clinical nurse using a stepped-care protocol in a nonvolunteer population.** *Arch Intern Med* 1988, **148:**1046–1048.
45. Fonarow GC, Ballantyne CM: **In-hospital initiation of lipid lowering therapy for patients with coronary heart disease: the time is now.** *Circulation* 2001, **103:**2768–2770.