

In-hospital initiation of statins: Taking advantage of the ‘teachable moment’

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NEARLY EVERY PATIENT who has had an acute coronary event or who has undergone a coronary intervention should be started on a statin—and the sooner the better.

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Starting statins early is safe, improves compliance, and reduces events

In fact, the best time to start is while the patient is still in the hospital for the event or intervention. The hospital stay can serve as a “teachable moment” for patients and their physicians regarding the importance of lipid-lowering and other cardioprotective therapy to their long-term cardiovascular health.

■ TO START SOONER VS LATER

We have overwhelming evidence from clinical trials that lipid-lowering therapy with statins (properly called 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) significantly reduces clinical events and mortality in patients with atherosclerosis.^{1–5} But *when* to start this therapy and whether there is a threshold level of low-density lipoprotein (LDL) cholesterol below which patients do not benefit have been controversial.

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Adding to the controversy was a lack of data on therapeutic benefits, associated risks, and costs.⁶ In most trials of statins in patients with coronary heart disease, the drug was started no less than 3 months after an acute event or cardiovascular procedure.^{1,2,4}

This was standard practice. Past guidelines^{7,8} recommended delaying baseline lipid assessment and treatment until 6 weeks after the acute presentation or cardiovascular procedure. The reasons were that the acute-phase response triggered by an acute myocardial infarction or coronary artery bypass grafting can substantially lower total and LDL-cholesterol levels.

It was also commonly held that patients were too distracted and overwhelmed for secondary prevention measures to be started effectively in the hospital. A practical concern was that inpatient physicians might be reluctant to start patients on statin therapy in the hospital because they would not be following them in the long term.

Other arguments against starting statins early were that “unstable” patients would be more vulnerable to adverse events, and that these drugs might not be necessary if patients undertook lifestyle interventions.

■ PROBLEMS WITH WAITING

These views are changing. Numerous studies have documented that the conventional practice of delaying starting lipid-lowering medications is simply not very effective.^{9–11} Very few patients actually start lipid-lowering therapy on an outpatient basis after a cardiovascu-

lar event or procedure, and of those who do start, up to half stop within the first 12 months.¹²

Moreover, patients, their families, and primary care physicians perceive the inadequate advice and treatment they receive in the hospital for risk-factor management as a lack of endorsement for these strategies.

■ ADVANTAGES OF STARTING IN THE HOSPITAL

Recent evidence has demonstrated that starting lipid-lowering therapy in the hospital is safe^{13–17} and provides substantial benefits with respect to the patient's long-term compliance, the likelihood of achieving lipid treatment targets, and long-term survival.^{18,19}

This strategy has several intrinsic advantages¹⁹:

- It starts treatment when patients and their family are most focused on the patient's cardiovascular risk.
- It may help alleviate patient concerns about monitoring, medication tolerability, and side effects.
- It strengthens the patient's perception that the therapy is essential for preventing recurrent events or the need for repeat procedures and is an essential part of his or her long-term care.^{9,18}
- It can take advantage of the expertise of inpatient nurses and pharmacists, facilitating patient education.
- It may facilitate coordination of secondary preventive care between cardiologists and primary care physicians by its inclusion in the discharge summary.

■ CHAMP: A HOSPITAL-BASED PROGRAM

The Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP) was one of the first programs to demonstrate that in-hospital initiation of lipid-lowering medications and other secondary protective measures is feasible, safe, and more effective than conventional care.¹⁸

Launched at the University of California-Los Angeles in 1994, this program focuses on starting the following therapy in patients with coronary artery disease before they leave the

hospital:

- Aspirin
- Beta-blockers
- Angiotensin-converting enzyme inhibitors
- Statins (regardless of baseline LDL levels, titrated to achieve a LDL of < 100 mg/dL)
- Dietary and exercise counseling.

Results of the program

CHAMP demonstrated that in-hospital initiation of lipid-lowering and other cardioprotective therapies dramatically improves long-term patient compliance and clinical outcomes. For example:

- Use of lipid-lowering medication at the time of discharge increased from 6% before the program to 86% after CHAMP was implemented.¹⁸ These increases persisted at 12-month follow-up.
- The percentage of patients achieving a LDL level lower than 100 mg/dL at 1 year increased almost 10-fold.
- Most important: the rate of fatal and non-fatal clinical events during the 12 months after discharge decreased.¹⁸

■ RESULTS REPLICATED

These results have been replicated in other hospitals.

In an integrated health system of 10 hospitals, this model of care increased the statin treatment rate at discharge after a coronary-related hospitalization from 18% at baseline (1994–1997) to 88% after a program was put in place (1999–2000).²⁰ One-year readmission rates and 1-year mortality rates were also significantly reduced.

The American Heart Association has launched a national program called “Get With the Guidelines,” based in part on CHAMP. In a pilot phase in 24 New England hospitals in 2000, the use of lipid-lowering therapy increased from 54% before the program to 78% with the program.²¹

■ EVIDENCE FROM RANDOMIZED STUDIES

The Lescol Intervention Prevention Study (LIPS) provides further support for routinely starting statins in the hospital.¹³ This clinical

The American Heart Association has launched a program called “Get With the Guidelines”



trial, reviewed in this issue of the *Journal*,²² randomized patients an average of 2 days after successful percutaneous coronary intervention (PCI) to receive either fluvastatin 40 mg twice a day or placebo.

Statin therapy was safe and well tolerated and reduced long-term clinical events by 22%. This trial establishes the safety and long-term benefit of starting a statin shortly after PCI.

The safety of in-hospital initiation of statin therapy after an acute coronary syndrome, whether managed invasively or conservatively, has been demonstrated in other prospective randomized clinical trials, including the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial¹⁴ and the Pravastatin Acute Coronary Treatment (PACT).¹⁵

Together these trials have included 8,171 patients and have shown no significant adverse effects of in-hospital initiation of statin therapy overall or in the subgroup of patients with low levels of total cholesterol at initiation.

■ NO THRESHOLD LDL LEVEL FOR STARTING STATINS

This LIPS trial also calls into question whether there is a threshold LDL level below which patients do not benefit from statin therapy. In LIPS, fluvastatin was beneficial no matter whether the baseline LDL level was above or below the mean of 132 mg/dL.¹³

The most convincing evidence that statin therapy is beneficial irrespective of the patient's baseline LDL concentration comes from the Heart Protection Study,⁴ which included 3,421 patients at high risk but with baseline LDL cholesterol levels below 100 mg/dL. Not only did these patients derive major clinical benefits from simvastatin 40 mg/day vs placebo, but the relative risk reduction with simvastatin was similar to that in patients with much higher baseline LDL levels.

On the basis of these trials, statin therapy can be recommended for all patients after coronary events or coronary procedures, irrespective of the level of total or

LDL cholesterol, in the absence of contraindications.

■ IS BENEFIT SEEN EARLY?

Whether statins reduce myocardial infarction and cardiovascular mortality in the short term as well as in the long term is still debatable, since the composite end point in the MIRACL trial was driven mainly by a reduction in rehospitalizations for ischemia.¹⁴ Likewise, in post-PCI patients, the benefits of immediate statin therapy in the LIPS trial were seen only after 6 months of therapy.¹³

Ongoing trials of acute statin treatment in patients with acute coronary syndromes, such as the Aggrastat to Zocor (A to Z) trial²³ and the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT) trial,²⁴ may help to further define whether there are early benefits of in-hospital initiation of statins in addition to the clearly established long-term benefits.

■ NEW GUIDELINES

The evidence from recent trials, including LIPS, provides a compelling argument for starting lipid-lowering drugs in the hospital. The safety and the benefits associated with in-hospital initiation of statin therapy, such as improved compliance and long-term clinical benefit, are compelling enough to establish this as the standard of care.¹⁹

In this regard, the new guidelines from the National Cholesterol Education Program²⁵ and from the American Heart Association and American College of Cardiology^{5,26} recommend starting lipid-lowering medications before discharge in patients hospitalized with atherosclerotic vascular disease.

By starting statin therapy early, as part of an effective management plan, inpatient physicians and nurses can take advantage of the teachable moment, make a vital contribution to eliminating the gap between recommendations and actual treatment, and dramatically reduce the death and disability caused by atherosclerotic vascular disease. ■

After a coronary event, statins are beneficial no matter what the LDL level

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