The Message is Clear:
Prevent as Well as Treat Acute Myocardial Infarction

Running title: Cohn; Prevention and Treatment

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The ultimate goal of all cardiovascular clinical research should be to reduce the morbidity and mortality from cardiovascular diseases at an acceptable cost. In no area of medicine has clinical research led to a greater change in medical care than in the management of acute myocardial infarction (AMI). We now try to accomplish early coronary reperfusion in all ST-elevation MIs and administer a combination of drugs in the post-infarction period to halt or slow the progressive remodeling process that leads to heart failure and shortened survival. Clinical trials have documented the dramatic efficacy of these therapeutic interventions on morbidity and mortality.

The old non-therapeutic approach was not so long ago. During my internship in Boston in 1956 my first admission was a middle-aged man with an acute transmural anterior wall MI. After ministering to him for his 4-week hospital stay, which was mandatory in those days, he went home stable, only to return in 6 months with fulminant heart failure which took his life. What had happened to him in that six months was mysterious to me as well as to my Harvard attending physicians, who viewed the patient’s course as a rather uninteresting response to heart damage. It was 30 years before the concept of structural remodeling became recognized and effectively treated.

Chin et al in this issue of Circulation explore changes in the course of patients like mine as a consequence of our new aggressive therapeutic approach. They have used a complete national sample of AMI hospitalizations in nearly 3 million Medicare fee-for-service beneficiaries. Their focus is on hospitalization for heart failure within a year after the index infarction, and the mortality in the year after this heart failure hospitalization. My patient had an adverse outcome on both end-points. Certainly with our new insights and tools for intervention we must have greatly reduced the morbidity and mortality following an AMI. Clinical trials have
documented the profound benefit not only of reperfusion\textsuperscript{2} but also of renin-angiotensin inhibitors\textsuperscript{3}, beta blockers\textsuperscript{4}, aldosterone inhibitors\textsuperscript{5} and statins\textsuperscript{8}, drugs which are growingly prescribed after an MI\textsuperscript{9}.

But clinical trials are not clinical practice. The patients may differ, the drugs may not be administered as they were in the trials, and the patients may stop the medication in the absence of the oversight of study personnel. The unanswered question is whether the benefits found in these trials are reflected in the real world of health care. If not, we should spend more time and effort resolving the paradox than in doing more clinical trials.

The good news is that Chin et al demonstrated a progressive decline in the re-admission rate for heart failure. The bad news is that the decline was preciously small, not nearly the magnitude that we might have expected from the clinical trial data, and the mortality within one year after re-hospitalization was not reduced over this time period. On first look these data would appear to suggest that the real world of clinical practice has not benefited from our mechanism-based interventions nearly to the extent that we would have expected.

But the design of the study and its metric for measuring efficacy may be partially at fault. The baseline for the study was 1998, more than a decade into the era of reperfusion therapy and anti-remodeling pharmacotherapy. These aggressive approaches to management certainly have become more widely employed in the past 15 years, but perhaps the 1998 data were already heavily influenced by efforts to salvage myocardium and inhibit structural remodeling.

There are, however, other problems with interpreting the data. The diagnosis of AMI in the Medicare database may not distinguish between ST-elevation, coronary occlusion MI’s (STEMIs) and non-occlusive non-STEMIs. Our therapeutic revolution has been in STEMIs, which respond to reperfusion and anti-remodeling therapy. Changes in the course of non-
STEMIs may be less dramatic and they may represent a substantial fraction of the population evaluated.

The metric used by the investigators was hospitalization for heart failure within a year after their hospitalization for AMI. Hospitalization is a growingly attractive end-point because it is not only costly to the health care system but it reduces quality of life and is associated with a higher subsequent mortality. It is becoming a metric of choice for hospitals and health care systems. However, hospitalizations compete with death as an end-point. Death in the first year after the infarct, which was not reported in this study, would preclude future hospitalization. Furthermore, enhanced survival likely preserves a population with more cardiac damage and more advanced atherosclerotic disease that places them at enhanced risk for subsequent heart failure. This latter likelihood is borne out by the Medicare data base, which reveals the increasing age and worsening renal function in the hospitalized cohort over time. Thus the heart failure hospitalization metric may not be a useful guide to the effectiveness of contemporary therapy, and the mortality after this hospitalization not an adequate test of our improved management of heart failure over the past 15 years.

What the data do demonstrate is that once a patient suffers from a myocardial infarction he or she is likely eventually to succumb to their cardiovascular disease. Under these conditions health care costs will continue to rise because prevention of early death will lead to enhanced downstream costs. The expensive interventional programs to deal with the acute phase of MI do not necessarily prevent subsequent progression of disease nor the population risk for heart failure (Figure 1).

The message from these data should be that prevention of myocardial infarction should receive at least as much attention as treatment for myocardial infarction. Hospitals and
interventional cardiologists generate robust revenue from efforts at early reperfusion. No one would advocate for a return to the days of passive management which characterized my training in Boston in 1956. But not enough attention has been devoted to prevention. Admittedly it does not generate much revenue, either for doctors or hospitals. But appropriately targeted pharmacopreventive therapy saves lives. By evaluating individuals for early functional and structural abnormalities of the cardiovascular system\textsuperscript{10,11}, it is possible to identify the phenotype of early disease likely to lead to morbid events such as AMI\textsuperscript{12}. Intervention with statins, inhibitors of the renin-angiotensin system, aspirin and other preventive therapies in such patients would prevent the AMIs that lead to such a dismal prognosis. It is sad that so few individuals who are at clear risk remain untreated with these effective agents\textsuperscript{13}.

Chin et al have made it clear that our contemporary management strategies for AMI have not solved the real-world problem of mounting morbidity, mortality and costs of cardiovascular disease. Prevention of AMI is possible. Whether by a polypill to be administered to every adult\textsuperscript{14} or an evaluation process to identify early disease in order to intervene with individualized management\textsuperscript{15}, the agenda should be clear to any thoughtful observer. We should continue to employ our best methods for treatment once people get sick, but we must mount a new and more effective effort at identifying risk and intervening to keep people free of progressive symptomatic disease.

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References:


**Figure Legend**

**Figure 1.** Natural history of atherothrombotic disease. Progression to acute myocardial infarction (AMI) may be followed by heart failure and death. Aggressive treatment after the event alters the slope of progression with delay but ultimate complications of heart failure and death. Early detection of the process can lead to preventive therapy that reduces the slope of progression and may eliminate the associated morbidity before the age of 100 years.
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