after an hour of renal ischemia and throughout 24 hours of reflow resulted in the maintenance of proximal tubule integrity and improved proximal reabsorption and nephron filtration rate (unpublished observations). These results were likely the consequence of reductions in proximal tubular metabolic demands or "tubular work," but they may have also derived from greater osmolar clearance and tubular flow rates resulting in lesser degrees of tubular obstruction. There is a cogent logic to the application of diuretic agents that inhibit proximal tubular reabsorption under clinical conditions in which renal ischemia is likely, since the proximal tubule is an early site of ischemic damage in vivo.

Reductions in tubular reabsorption and decreases in the metabolic demands of tubular epithelia may diminish the degree of tubular injury in experimental acute renal failure; what, then, should be the consequences of increasing the GFR early in the course of incipient acute tubular necrosis? This is not a straightforward question to answer. Because GFR is highly dependent on renal blood flow, its improvement by pharmacologic intervention should improve blood flow and oxygen and substrate delivery to renal cells, a potentially beneficial effect. In addition, a higher GFR early in this process should increase the tubular flow rate and could diminish the tendency for tubular obstruction. Although this scenario would imply that an improvement in the GFR soon after tubular injury should prevent or ameliorate acute tubular necrosis, some studies suggest that early improvements in the GFR after tubular injury might produce adverse effects. Continuing tubular structural damage may be a consequence of a balance between the magnitude of the tubular insult, either ischemic or toxic, and the concurrent metabolic demands. The use of oxygen and substrate by the kidney is strictly linked to sodium chloride and sodium bicarbonate reabsorption. Improvements in renal blood flow and GFR lead directly to enhanced tubular reabsorption through glomerulotubular balance. Therefore, higher renal blood flow rate and GFR obligate greater tubular work, increasing the risk of tubular injury.

Recent studies from our laboratory have provided evidence for this phenomenon. We observed that pretreatment with the antioxidant probucol in a model of one-hour renal ischemia led to an increase in the nephron filtration rate two hours after reflow.[7] At 24 hours after reflow, however, proximal tubular damage and the impairment of proximal reabsorption were greater in probucol-treated rats.[2] The best explanation for these findings was that increases in the single-nephron GFR after tubular injury placed greater reabsorption-linked metabolic demands on injured tubules, leading to greater tubular necrosis (and prolonged duration of acute renal failure). Acute tubular necrosis represents a complex balance of glomerular and tubular events that act in concert to produce the clinical syndrome of acute renal failure.

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Why Is Cardiac Rehabilitation Not Widely Used?

THE REVIEW OF cardiac rehabilitation elsewhere in this issue clearly outlines the development of cardiac rehabilitative services and their current and future applications.[1] Gattiker and co-workers rightly focus on the goals, indications, and rationale for cardiac rehabilitative services, with an emphasis on exercise training; modification of coronary risk factors, especially hypercholesterolemia and smoking; behavioral treatments; education and counseling; and vocational rehabilitation. The review reflects, however, a major disconnection between what *ought* to be done in cardiac rehabilitation in an ideal world and what *is* done or *could* be done in a world of limited resources.

Rehabilitative and preventive services are generally underprovided in a medical care system that is primarily oriented to providing care for acute illness. The primary focus of cardiac rehabilitation is exercise training, which is generally given in a group setting. Risk factor modification is often provided by cardiac rehabilitation programs as well, but generally in a less well-developed and integrated way. The nearly 2,000 American cardiac rehabilitation programs are prized by patients for the supportive environment, peer support, and access to medical information that they provide. These programs offer many unique services that are lacking in the increasingly time-pressured acute care setting. Risk factors for coronary heart disease may indeed be more effectively managed through cardiac rehabilitation programs than through the usual channels of care. The current model of cardiac rehabilitation suffers from the following shortcomings:

- *Difficulty in distinguishing the effects of cardiac rehabilitation from those of physicians' usual care.* Effective therapies, including the use of thrombolytic and adjunctive drugs (antiplatelet, anticoagulant, and β-blocking agents) at the onset of acute myocardial infarction and mechanical revascularization (balloon angioplasty and coronary artery surgery) provided days or weeks later have not only reduced mortality but have improved the prognosis, enhanced functional capacity, and maximized occupational work potential. The success of these therapies has, or should have, shifted the focus of cardiac rehabilitation from exercise training to coronary risk factor management. Whether participating in cardiac rehabilitation programs substantially enhances the overall level of function of patients compared with usual care is not clear.

• *Lack of support by physicians.* Physicians may perceive that advice provided by cardiac rehabilitation programs regarding smoking cessation and hypercholesterolemia is duplicative or conflicts with their own. They are also often unfamiliar with methods for exercise training and skeptical that exercise improves the prognosis. Both of these factors have tended to limit physicians' willingness to refer their patients to cardiac rehabilitation programs.

• *Inconvenience of the group format.* Given a choice, many, if not most, patients prefer home-based to group-based exercise training because of the greater convenience of the former. Indeed, dropout rates from group programs at six months approach 50%. The proportion of patients classified as low risk and possibly eligible for home-based exercise training after an acute myocardial infarction has been substantially increased by the provision of effective therapy at the very start of an acute myocardial infarction.

• *Relatively low participation rates among eligible patients.* Fewer than 15% of patients undergo cardiac rehabilitation for a number of reasons. There may be logistical obstacles, especially the inconvenience of attending several class sessions for activities such as exercise training, which can be safely carried out by most patients at home. In one study, patients undergoing group-based training spent more time in their cars going to and from the program than patients in the home training program spent on their exercise cycles.[2] Moreover, many patients live a considerable distance from cardiac rehabilitation programs. Patients may not perceive any medical benefit of cardiac rehabilitation, especially those who are in a low-risk category. This diminishes their willingness to devote time and money to it. Insurance may not cover cardiac rehabilitation programs. Even if insurance reimbursement were not an issue, however, it seems unlikely that the proportion of patients participating in cardiac rehabilitation programs would more than double—that is, from 15% to 30%.

In fact, in recent years there has been a relative decline in the need for exercise rehabilitation after a myocardial infarction. There are several reasons for this that will be commented on briefly.

In the contemporary era of thrombolysis, exercise training does not measurably enhance the prognosis of patients after a myocardial infarction. Equally effective therapy, such as the use of β-blocking drugs, is much more convenient than exercise training and, unlike exercise training, is covered in the cost of usual care. More effective therapies, such as thrombolytic agents and adjunctive medical therapy provided at the start of an infarction, have dramatically decreased not only in-hospital but after-hospital mortality, which diminishes the potential of exercise training to lower mortality still further.

In the randomized Thrombolysis in Myocardial Infarction trial, phase IIB, in which patients receiving thrombolysis for myocardial infarction were randomly assigned to routine or elective balloon angioplasty, the total first-year mortality in both groups at one year was 7%: 5% through the 6th week and 2% through the 52nd week.[3] In contrast, in a study of cardiac rehabilitation conducted in the mid-1970s, the first-year after-hospital mortality alone was 15% among patients receiving usual care and significantly less—10%—among those undergoing exercise training.[4] In-hospital mortality in that era approximated 10% to 15%. It is clear that dramatic progress has recently been made in reducing the mortality of patients with acute myocardial infarction.

Of the studies of cardiac rehabilitation carried out in the 1970s, only that cited provides an accurate picture of prognosis after myocardial infarction because only this study randomly selected a consecutive series of patients soon—that is, 14 days—after the event.[4] This is in marked contrast to other exercise rehabilitation studies of that era in which the mortality in the year after enrollment was generally 3% to 5%. Indeed, many patients were enrolled as long as three years after a myocardial infarction. Because the death rate is highest during the first six months after such an event, late enrollment equates with low risk. Demonstrating the efficacy of *any* intervention is difficult in low-risk patients.

Today, with optimal thrombolytic and adjunctive medical therapy and mechanical revascularization starting at the onset of myocardial infarction, the first-year mortality is so low that many thousands of patients would be required to demonstrate the prognostic value of exercise training. The same is true of any therapy provided days or weeks rather than hours after myocardial infarction. Moreover, patients receive "bundled" medical therapy, including β-blocking, antiplatelet, and anticoagulant agents, that also contributes to a reduction in mortality.

In the contemporary era of thrombolysis, exercise training also exerts less effect on functional capacity. Thrombolysis, adjunctive medical therapies, and revascularization, which decrease early and late mortality, also preserve functional capacity. This reflects the extent of underlying left ventricular dysfunction and myocardial ischemia. A good prognosis, therefore, is tantamount to a well-preserved functional capacity, especially when the brief duration of contemporary hospital admissions for myocardial infarction minimizes physical deconditioning. Even before the thrombolytic era, the 50% of patients who were at low risk for subsequent cardiac events had a substantial spontaneous increase in functional capacity during the first three months after myocardial infarction.[5]

Exercise training designed to facilitate weight management and enhance psychological status and physical endurance can be provided in a home setting to a number of patients recovering from myocardial infarction. For example, exercise training can be safely carried out at home for most of the 50% of patients without significant left ventricular dysfunction or exercise-induced myocardial ischemia, whose risk is low. For the 30% of patients with exercise-induced myocardial ischemia whose risk for subsequent cardiac events has been diminished by revascularization, home exercise training can be safely carried out beginning four to five weeks after coronary artery operation or within two weeks after balloon angioplasty. For the 20% of patients with isolated left ventricular dysfunction, low-level home-based exercise training at an intensity approximating brisk walking can usually be carried out safely. Even relatively low-intensity exercise training continued over a six-month period enhances functional capacity. The risk of training-induced cardiac arrest is closely related to the intensity of exercise training. Reducing the intensity of exercise training is an important safeguard, therefore, especially when exercise training is home-based.

In the contemporary era of thrombolysis, exercise training does not significantly enhance the occupational work potential (as opposed to the functional capacity) of patients who have had a myocardial infarction, for the following rea-

sons. In the contemporary job market, the prognosis is much more important than functional capacity in determining occupational work potential. If the prognosis is good, functional capacity is generally well preserved.[6] In any event, there is little evidence that "work hardening"—exercise conditioning—is a prerequisite for return to work after a myocardial infarction, even for "blue collar" workers. Furthermore, functional capacity has declined markedly as a determinant of employability after such an event. Automation and mechanization have eliminated many jobs requiring heavy physical effort. Demographic shifts have further reduced the number of patients with ischemic heart disease whose jobs involve heavy physical work. The rate of retirement from the work force at age 62 is high even among patients without ischemic heart disease; young workers have supplanted older ones in performing the few remaining jobs that are physically taxing. Older workers whose prognosis is good—that is, those who do not manifest exercise-induced myocardial ischemia or left ventricular dysfunction—can continue to do heavy work. There is little evidence that subsequent cardiac events are more frequent among patients performing heavy work than among those doing little or no physical work.

Occupational work evaluation hastens patients' return to work because it reassures them and their primary care physicians about the safety of an earlier than customary return to work.[7] Cardiac rehabilitation programs lack control over the medical decision to advise patients to return to work after a myocardial infarction. This decision, which is fraught with perceived medicolegal liability, is generally considered to lie within the province of the physician-patient relationship.

The perceived need for coronary risk factor management has increased with the use of thrombolysis. For example, coronary arteriosclerosis may partially regress with lipid-lowering drugs.[8,9] This demonstration will doubtless stimulate the use of these agents. Smoking cessation and diet-drug management of hypercholesterolemia are important objectives in cardiac rehabilitation. These are relatively time-intensive interventions. Because Medicare provides reimbursement only for exercise training (and only three months of it), it is not surprising that these interventions are not better integrated into cardiac rehabilitation programs.

Incorporating more effective and efficient techniques for smoking cessation and diet-drug management for hypercholesterolemia might enhance the attractiveness of rehabilitation programs for physicians and patients alike. Physicians' unwillingness to relinquish responsibility for risk factor management, however, may continue to frustrate the delivery of these preventive services by cardiac rehabilitation programs. Physicians may relinquish certain aspects of management such as exercise training with which they are generally unfamiliar, or smoking cessation or the dietary management of hypercholesterolemia, for which they often manifest little enthusiasm. In contrast, drug management of hypercholesterolemia is an element of health care over which they generally prefer to maintain control, if only because of the medicolegal considerations.

In summary, the success of contemporary medical and surgical therapy for acute ischemic chest pain syndromes and a dramatic shortening of hospital stays have changed the focus of cardiac rehabilitation. Cardiac rehabilitation programs can now best serve the needs of patients with ischemic heart disease by facilitating smoking cessation and diet-drug management of hypercholesterolemia. Whether such a shift in emphasis away from exercise conditioning will attract a large number of the patients who do not presently undergo cardiac rehabilitation depends on the efficacy, convenience, and cost of risk factor modification offered by these programs. In today's increasingly competitive environment, cardiac rehabilitation programs must demonstrate to patients and physicians alike that they provide benefits not available in usual care.

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