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POST-MI CARDIAC REMODELING: NEW PERSPECTIVES

The reshaping of the heart following myocardial infarction (MI) is a primary determinant of survival. Cardiac dilatation in the post-MI patient signals a very poor prognosis; it correlates with poor left ventricular function and therefore with the development of lethal ventricular arrhythmias and first-year mortality.

Cardiac remodeling after transmural MI is characterized by infarct expansion which in turn may lead to aneurysm formation and rupture, and hypertrophy of noninfarcted myocardium. Our challenge in the 1990s is to intervene in this sequence of events, thereby changing the quality of the infarct to preserve the structural integrity of the heart.

INFARCT EXPANSION

Regional dilatation occurs almost immediately post-MI. It can be detected at the bedside by echocardiography within hours, and it continues over the next 1 to 2 days. Whatever the final outcome, 90% of restructuring occurs in the first 3 days. This "paralysis" of the muscle leads to an aneurysmal ischemic bulge that is directly related to transmural ischemia. If the ischemia is reversed, or if the transmural ischemia is converted to a nontransmural insult, the myocardium will recover its shape. But if the transmural insult advances to irreversible transmural necrosis, reshaping of the heart with ballooning, dilatation, and thinning of the myocardium is likely to occur.

ANEURYSM AND RUPTURE

Infarct expansion with regional dilatation is the substrate of aneurysm formation and rupture. The classic teaching is that aneurysm is a late consequence of MI, occurring months, or even years, afterward; this is not the case. An aneurysm, if it is to occur, develops by the time the patient leaves the hospital.

When rupture occurs, it is almost always in the setting of a transmural MI, with a first MI, and in the first 3 to 5 days. This is when infarct expansion peaks, with maximal dilatation of a soft myocardium that is under tension because of a thin bulging wall with increased radius. Rupture virtually never occurs in a heart that has not undergone expansion.

HYPERTROPHY

The noninfarcted myocardium hypertrophies as a result of infarct expansion. This is not physiologic or normal hypertrophy, as occurs in an exercising individual. It is asymmetrical and creates both biochemical and regional blood flow disadvantages to the myocardium.

REDUCING INFARCT EXPANSION

Jugdutt and Basauldo have demonstrated that afterload reduction and reperfusion therapy can reduce infarct expansion. When intravenous nitroglycerin followed by buccal nitroglycerin was compared with placebo in patients with anterior wall transmural infarcts, increased segment length of the infarcted region was demonstrated in the placebo group, but there was no progression of expansion in the group given nitroglycerin.

The angiotensin-converting enzyme (ACE) inhibitor captopril positively affects cardiac remodeling—more than other vasodilators. For example, in animal studies, captopril prevents hypertrophy in hypertensive subjects. Other agents achieve normal blood pressures, but do not prevent myocardial hypertrophy. Pfeffer and associates have also shown that captopril decreases infarct expansion.

Captopril blocks the effects of angiotensin II in the periphery. This benefits the weak, dilated heart because of reduced afterload, systemic blood pressure, systemic vascular resistance, and preload. It also peripherally inhibits the sympathetic and neurohumoral effects of angiotensin II. It appears to achieve these effects without blocking the direct, beneficial effect that angiotensin II has on the heart—its inotropic effect, which increases contractility.

Researchers at the Cleveland Clinic Research Institute, led by Dr. Ahsan Husain, have in the last year

identified an enzyme, "convertase", in human myocardium that converts angiotensin I to angiotensin II and that enables local AII formation in the face of ACE inhibition by captopril. Thus, the heart benefits from the peripheral effects of captopril, but it does not lose the inotropic benefit of angiotensin II.

When heart failure patients are being treated with captopril, angiotensin I levels get very high. Because the heart is bathed in blood in which angiotensin I levels may be many times higher than normal, the substrate for myocardial conversion from angiotensin I to angiotensin II is correspondingly greater.

These effects, which require further study, have significant implications for the management of post-MI cardiac remodeling, as well as for the patient with congestive heart failure.

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FOOT CARE IN DIABETES: VIGILANT INSPECTION STILL BEST

It is up to the physician to identify signs of trouble that could lead to lower extremity amputation in diabetic patients, because patients themselves may not notice and report potentially serious problems. Diabetes mellitus is the leading cause of nontraumatic lower extremity amputation, and about half of these amputations are preventable. Yet only 10% of the 5 to 7.5 million diabetic persons in the United States seek help for neuropathic symptoms such as numbness. This loss of sensation due to neuropathy often allows treatable callus formations, fissures, ulcerations, and altered biomechanics to develop which are often unrecognized by the patient.

PROGRESSION OF DISEASE

Neuropathy, peripheral vascular disease, and infection are the major predisposing factors that lead to lower extremity amputation. In addition to loss of sensation, neuropathy alters sweating patterns and skin lubrication, increasing the susceptibility to drying, cracking, and bacterial invasion. Because of blunted sensation, problems such as cracked calluses, blisters, fungal infections, foreign bodies in the shoes, and burns can remain undetected for prolonged periods. Significant neuropathy can occur even in relatively "mild" diabetes; severity is thought to be related to duration of disease.

The diffuse peripheral vascular disease common to diabetic patients compromises healing capacity. Impaired blood flow to lower extremity ulcers reduces healing and defense against infection. However, foot problems can occur even in the absence of significant vascular disease, and patients with normal pulses still may be at risk of significant foot deformity and injury.

CLINICAL PRESENTATION

Since patients with numbness from neuropathy do not note any discomfort from pressure points on their feet, callus formation and ulceration may occur, especially over the metatarsal heads. Furthermore, because of weak intrinsic muscles of the foot, the toes may become clawed—pulled up by the stronger muscles of the calf. Claw-foot deformity alters the biomechanics of the foot so that more weight is placed on the metatarsal heads. Underneath the resulting callus, inflammatory autolysis occurs, then hemorrhaging and tissue necrosis—all painless to the patient and not immediately obvious to an untrained observer. Eventually a serous cavity forms and ruptures, with ulceration.

MANAGEMENT

Evidence is accumulating that rigorous control of blood glucose slows and may even reverse the progression of neuropathy, but more studies are needed before conclusions can be drawn about the relationship between blood glucose and neuropathy. In the meantime, patient education and active physician participation are essential to prevent and treat diabetic foot problems.