Post-Myocardial Infarction Survival: Plus Ça Change . . .

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The treatment of acute myocardial infarction today is aggressive and interventional, marked by early angioplasty, thrombolytic agents, and cardiac care unit monitoring. While large and expensive studies have shown small but statistically significant survival advantages for each of these technologies, an overview of the past 30 years shows that the more things change, the more they remain the same.

Marking the 40th anniversary of the American College of Cardiology in 1991, Braunwald[1] speaks of a "golden age" and of how current treatment has reduced mortality to one fifth of what it was in 1950. In a recent editorial, Hugenholtz[2] writes: ". . . the profession and the system together have brought mortality in acute myocardial infarction from >20% to <5% in just ten years. . . ." Looking back from the vantage point of 1974 over 11 years of increasing sophistication in intensive coronary care, Koch-Weser[3] states his belief that the case fatality rate, thanks to the new units and their control of arrhythmias, has been reduced by one third.

Other voices, however, have proposed restraint in crediting medicine with declining death rates. In 1979, Fabricius-Bjerre et al[4] wrote, "The immediate prognosis following acute myocardial infarction has been extensively studied. The results of treatment in nonspecialized hospital departments and even of home treatment now seem to equal those attained by close observation in coronary care units." One year later, Kuller[5] points out that death rates from arteriosclerotic heart disease have been declining for more than a decade, something that might be attributed to an understanding of the roles played by cholesterol, hypertension, and smoking in atherogenesis. "But there remains a small cloud in this beautiful picture," he continues. "We lack the experimental evidence that modification of risk factors, except perhaps at the extreme ranges, reduces the risk of a heart attack."

The 1950 edition of Friedberg's *Diseases of the Heart* recounts that "Master, Jaffe, and Dack[6] reported a mortality rate of 16.5% in 267 attacks. Among patients apparently suffering their first attack of coronary thrombosis, the observers noted a mortality rate of only 8%." Friedberg goes on to suggest that milder cases will be increasingly identified (he was writing 4 years before the connection between elevated AST (formerly SGOT) levels and myocardial infarction was recognized[7]) and to predict ". . . the mortality rate from first attacks . . . excluding those in which death struck before a physician was consulted, will not greatly exceed 10%." This estimate was made at a time when there was nothing to offer the patient beyond analgesia and bed rest!

There are many difficulties with studies of survival after coronary thrombosis. In particular, those that follow a cohort prospectively must report widely differing periods of observation leading up to a cardinal event.[8,9] Thus, if mortality is summarized after 5 years, survival may vary by almost that much between patients. Furthermore, as interventions proliferate, the controls in any given trial may receive several interventions comprising "usual treatment." Under a torrent of thrombolysis, aspirin, nitrates, anticoagulants, beta-blockers and calcium-channel blockers, intravenous magnesium, angiotensin enzyme inhibitors, and immediate revascularization, all vestiges of a natural history of myocardial infarction have been swept away, and standards of care are constantly being revised.

Once a treatment has been shown to reduce mortality, there is no turning back. In 1971, when surgeons were pushing ahead with coronary bypass without evaluating it through prospective, randomized trials, Braunwald[10] asks, "Will the physician who does not urge coronary arteriography in every person who might have coronary sclerosis be subject to criticism, even though the long-term effectiveness of direct revascularization has not yet been demonstrated?"

"To let the genie escape from the bottle" is a phrase

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that has been used[2,10,11] to mean the employment of a new therapy on the basis of anecdotal reports of success. A prominent example of this occurred in the 1930s when Prontosil was administered before the practice of randomized, controlled trials was instituted. At that time, decisions were made on the basis of individual cases, and the good of science—and possibly, future patients—was sacrificed for the benefit of the subject at hand.[12] It is said that Domagk, who was to win the Nobel Prize for his discovery of the red dye's bacteriostatic attributes, tried it on his own daughter for a streptococcal infection.[13]

Unfortunately, even a randomized controlled trial does not eliminate the possibility of patients being preselected by exclusion criteria. This accusation has been leveled against some recent experimental protocols for thrombolytic therapy[14,15] in which patients given a placebo fared better from the standpoint of short-term survival than did those who were excluded from the trials. In other words, some of the benefits of treatment could have stemmed from its being administered to subjects with the best prognosis.

One must inquire whether survival should be the criterion for success in a therapeutic trial and whether we would not be better off using indicators of functional status and quality of life. In an article aptly entitled "Death Is Not the Enemy," Landau and Gustafson[16] decry the "physical fundamentalism" of the dogma that demands of us ". . . to preserve life as long as medically and technically possible." They go on to say, "The emphasis on mortality statistics as a measure of medical care effectiveness has tended to obscure the fact that most of the time and effort of practicing physicians is devoted to improving the life of their patients. The real enemies are disease, discomfort, fear and anxiety."

There are explanations for an apparently improved survival rate in acute myocardial infarction that have little to do with the clinical activism so characteristic of recent years. The first emanates from progress in diagnosis that often accompanies but, unfortunately, does not always precede new therapies. If more sophisticated diagnostic tests enable us to identify milder instances of disease, the new therapies, in turn, will "dilute" mortality and "improve" prognosis.

A second possibility arises from the disease itself, which can have its own natural history independent of any individual suffering from it. For instance, the incidence of carcinoma of the stomach has been waning for some years in the United States without evident reason,[17] and a steady decline in stroke rates has been observed in Rochester County, Minnesota, since 1945, long before antihypertensive drugs were introduced.[18] It is not unreasonable to assume that myocardial infarction, too, may have "changed its spots."

It is virtually certain that treatments such as coronary artery bypass grafting and thrombolysis have saved lives, but making this statement is not equivalent to saying they do more good than harm. An 8% early mortality for a first acute myocardial infarction[6] reported nearly half a century ago when the disorder still possessed a natural history suggests that claims of a 75% to 80% reduction over the ensuing years may be extravagant. The real "genie" is our proclivity to attribute all favorable changes in morbidity and mortality to medical progress. If granted two wishes, ours should be for clear vision and a modicum of humility.

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