Advances in Clinical Management of Acute Myocardial Infarction in the Past 25 Years

ELIOT CORDAY, MD, FACC, STEPHEN R. CORDAY, MD, FACC

Los Angeles, California

The management of acute myocardial infarction in the past 25 years has emerged from a state of masterful inactivity to one of intensive care based on a new discipline of aggressive management. This has increased the chances of survival of the victim of infarction and could well be one of the major reasons for the decline in mortality due to coronary heart disease in the United States since 1968. Because resuscitative techniques must be instituted within 4 minutes after the onset of cardiac arrest, the attendant nurse had to learn the new emergency lifesaving techniques and assume a crucial role as a physician's assistant. The various stages in the evolution of coronary care discipline began with cardiopulmonary resuscitation and were followed by pacemaker application, arrhythmia prophylaxis and insertion of pulmonary venous flow-directed catheters and arterial lines that permit monitoring and control of ventricular filling pressures. Other developments in better management of the failing heart have included methods to salvage jeopardized myocardium, strategies for the prevention of sudden death, the application of revascularization techniques after acute coronary occlusion and new noninvasive computerized technology to provide enhanced contrast images of cardiac perfusion that can be directly integrated with measurement of function.

Myocardial infarction, the nation's biggest killer 25 years ago, retains that position despite the revolutionary innovations established in 1965 for its more aggressive management (1). Before that historic date, this treacherous condition was considered the natural end result of coronary heart disease, which terminated life as though it were an unavoidable act of fate. In fact, the medical profession of 1965 could provide little in the way of specific treatment to influence the course of this disease. The standard treatment of acute myocardial infarction was bed rest, the oxygen mask and the judicious use of opiates to relieve pain. Anticoagulant therapy was adopted as standard practice to prevent mural thrombus from embolizing, but there was considerable debate about the actual benefit of this treatment because clinical study had shown that it could have harmful effects. The customary regimen of 4 to 6 weeks' bed rest was also being challenged because of an increasing belief that such inactivity caused phlebothrombosis of the peripheral circulation that could result in death from pulmonary embolization.

Comprehensive investigations in the late 1950s and early 1960s demonstrated the ominous hemodynamic consequences of arrhythmias and their ability to cause significant ischemia of the target organs, particularly of the myocardium, when they were associated with a reduction in systemic blood pressure (2–4). Therefore, administration of vasopressors was advised for supportive treatment of arrhythmias associated with hypotension and this often aborted tachyarrhythmias (5).

Cardiogenic shock, which often supervenes after coronary occlusion, was considered a serious emergency because it was accompanied by an 80 to 90% mortality rate. It was advocated that shock be treated by restoring diastolic coronary filling pressures with blood transfusions or peripheral vasoconstrictors, such as norepinephrine or metaraminol (6–8). However, some authorities feared that these agents might cause a further increase in the work load for the already failing heart (9). If ventricular fibrillation or cardiac standstill occurred during acute myocardial infarction, it was considered an untreatable terminal condition.

A New Era Emerges

Closed chest cardiac resuscitation. When electrical defibrillation proved effective for cardiac resuscitation in the operating room (10–15), this maneuver was also recommended for resuscitation of the victim of myocardial infarction. But at that time, successful defibrillation necessitated open chest massage and direct contact of the electrodes

From the Cedars-Sinai Medical Center, Los Angeles, California.
Address for reprints: Eliot Corday, MD, Halper Research Building, Cedars-Sinai Medical Center, 8700 Beverly Boulevard, Los Angeles, California 90048.

0735-1097/83/010126-07$03.00

with the heart. By 1960 it was advocated that open chest resuscitative techniques be replaced by the simple and more practical closed chest resuscitation methods developed by Kouwenhoven et al. (12–14). "Space age" bedside electrocardiographic cathode ray monitor scopes with alarms for high and low heart rates were developed to warn the nursing staff of arrhythmias and of the onset of a cardiac arrest (11–13). Investigations on the fate of patients who had cardiac arrest in the operating rooms of Los Angeles hospitals established that if resuscitative measures were not instituted within a 4 minute time limit (15), the heart might be resuscitated, but the brain, which could not withstand such prolonged anoxia, was likely to become so severely damaged that the victim would survive only as a helpless decerebrate. It was repeatedly shown that in 60% of animals and human beings who developed cardiac arrest, the arrest occurred within the first hour after the acute myocardial infarction. Therefore, it was urged that all patients suspected of having an infarction be rushed to a facility where emergency resuscitative measures were possible (16).

The coronary care unit. By 1965, effective closed chest resuscitation and safe electrical countershock and defibrillation techniques began to be accepted by cardiologists (11–17). Although approximately 14 coronary care units had been established across the continent, most cardiologists questioned the clinical benefits of such units. Many believed that the aggressive management of coronary occlusion was an expensive exercise in futility, but a few investigators reported dramatic lifesaving results. A Bethesda Conference of coronary care unit directors convened at the American College of Cardiology headquarters in December 1965 to determine if the newly proposed aggressive management in an intensive coronary care unit could ever be of practical benefit (1). During the deliberations, participants soon realized that the coronary care directors at three centers—Hughes Day in Kansas City, Lawrence Meltzer in Philadelphia and Paul Unger in Miami—were reporting salvage of a significant number of victims of cardiac arrest. They were able to accomplish this feat because their nurses were in constant attendance in the coronary care unit and had been trained to read the abnormal heart rhythms that could document onset of cardiac arrest on the fast-moving cathode ray electrocardiographic monitor. These nurses had also been trained to perform immediate cardiac resuscitation using closed chest ventilation and electrical defibrillation (1). By allowing the attending nurses to defibrillate the patient's heart even in the absence of a physician, many patients could be saved. The Conference concluded that because of the narrow 4 minute time limit, the nursing staff must be trained to perform cardiopulmonary resuscitation and to administer appropriate prophylactic pharmacologic interventions, such as antiarrhythmic drugs, to prevent cardiac arrest. The Conference report (1) recommended that the U.S. Congress appropriate funds for training the coronary care nursing staff in their new responsibilities. By March 1966, the president of the American College of Cardiology, accompanied by the executive director, presented Senator Lister Hill with the Bethesda Conference Committee's recommendation for 3 years' funding of a nationwide training program for nurses. The senator agreed with the report and within 5 days arranged to have the necessary appropriation of $27 million attached to a railroad bill that was subsequently signed by President Lyndon Johnson. This is really a most appropriate use of the term "railroading."

Under the strong leadership of Samuel Fox III, head of the Heart Disease Control Section of the U. S. Public Health Service, training programs based on new aggressive principles for treating the victim of myocardial infarction were rapidly instituted across the nation and by 1968, some 6,000 of the larger hospitals in the country were prepared to administer immediate resuscitation and defibrillation in the newly established coronary care units. New state laws had to be instituted to permit nursing staffs to assume duties that were previously performed only by physicians. Soon other aggressive programs, including the judicious use of pacemakers and antiarrhythmic drugs, were adopted to prevent further complications from arrhythmias that might otherwise herald the onset of cardiac arrest (18).

Benefits derived from coronary care units. The coronary care programs of the American College of Cardiology and the American Heart Association were accepted with unanticipated vigor because of widespread publicity that the lives of thousands of people with a heart "too good to die" were being saved. Within a few years, most states had passed laws requiring practitioners to pass a cardiopulmonary resuscitation examination before they could renew their annual staff privileges. The conferees of the Bethesda Conference estimated that 45,000 lives per year would be saved with the adoption of the new aggressive methods in the coronary care unit (1). However, the health planners did not set up randomized studies to learn exactly how many lives could be saved by the coronary care units. In recent years, some attempts to determine the survival rates have yielded statistics that seem to refute any possible benefits derived from the coronary care unit concept. However, these efforts have been discounted by some because the numbers were too small and the subgroups were not appropriately organized to provide statistically meaningful results. The cardiac care units in the studies were considered substandard in organization and quality, and many patients were transferred in and out of the coronary care unit because their risk of death changed after initial randomization. It now seems to be too late to perform an appropriate randomized study because there is such great faith in the coronary care unit and the aggressive management entailed has become standard practice. To those who doubt the efficacy of the coronary care unit, we suggest they review the survival statistics of the thousands who were resuscitated in their local facil-

ities to see that without such resuscitative maneuvers, survival of victims of cardiac arrest would be rare.

A More Appropriate Research Program Initiated to Improve Basic Knowledge About Acute Myocardial Infarction

Stimulated by these dramatic breakthroughs, Robert Grant, Director of the National Heart Institute, noted that the research budget for myocardial infarction, the nation's leading cause of death, received only a meager 1% of the total research allotment made by the National Institutes of Health. After raising a congressional appropriation of about $15 million a year, with the help of Michael DeBakey, to support more intensive studies in basic research and clinical applications for the management of acute myocardial infarction, Grant died suddenly, the victim of a fatal heart attack. But the momentum created by his endeavor has continued to this day and made many other dramatic breakthroughs possible.

Myocardial infarction research units. The program eventually blossomed into nine productive myocardial infarction research units across the nation, under the direction of Peter Frommer, MD, of the National Heart Institute. Many new clinical concepts emanated from these myocardial infarction research units. One of the most important advances attributed to the program was the development of the Swan-Ganz pulmonary artery flotation catheter, which enables continuous hemodynamic monitoring of cardiac output and regulation of fluids and drugs to provide most appropriate left ventricular filling pressures (18). Intraarterial pressure lines were adapted to monitor systemic vascular resistance for better regulation of coronary filling pressures and the afterload of the failing heart by application of vasodilators, vasopressors or alpha- or beta-receptor blocking agents, or both. This ingenious online monitoring of hemodynamic function has saved many patients with complications of pump failure (18,19). The hemodynamic monitoring, now a standard form of therapy, was an effective aid in the management of interventions such as volume loading, intraaortic balloon assistance, afterload and preload reductions or administration of selective vasopressors. Thus, the occurrence of, and mortality from, cardiogenic shock is now markedly diminished (19).

Preservation of Jeopardized Ischemic Myocardium

Pharmacologic interventions. Starting in 1968, interest was renewed in methods that might preserve jeopardized ischemic myocardium (6,20,21). It was thought that such preservation would reduce infarct size and prevent subsequent chronic cardiac decompensation, troublesome arrhythmias and sudden death. Some pharmaceutical agents proposed for salvaging jeopardized myocardium were nitroglycerin, nitroprusside, hypertonic mannitol, propranolol hydrochloride, hyaluronidase, prednisolone, allopurinal and heparin. Although these investigations stimulated great interest, by 1976 the published data consisted of many conflicting claims and the status of the concept of myocardial salvage had to be reevaluated (21–24). Actually, each of the opinions seemed to be correct for the investigator's particular protocol design, but the contradictory results seemed to emanate from the differences in study models (dogs versus human beings) and in the mode and schedules of administration of the pharmaceutical agent or physical interventions. It appeared that the mode of administration and timing of an intervention must be uniform. In retrospect it appears that if more than 3 hours elapsed between the onset of the coronary occlusion and the intervention, the ischemic myocardium would have been so irreversibly damaged that any treatment stood little chance of salvaging significant amounts of myocardium (22–24).

Reperfusion phenomenon. In addition, some investigators revealed an unusual phenomenon that occurred in about 16% of animals undergoing reperfusion within 4 hours of occlusion (24). This phenomenon was associated with serious arrhythmias and a metabolic disturbance of the myocardium that included loss of potassium and anaerobic lactic acid production. At necropsy, the myocardium was characterized by hemorrhage, interstitial and intracellular edema of the ischemic area and fragmentation of the myofibrils. It was believed that such swelling in the ischemic area prevented blood from reentering the region, causing a "no reflow" phenomenon (24). It is evident that the earlier the reperfusion is started—by coronary bypass surgery, thrombolysis, synchronized retroperfusion or other general supportive hemodynamic measures (such as reduction in afterload or improved preload)—the better the possibility of preventing the reperfusion phenomenon (19).

Sudden Cardiac Death

New concepts have emerged since 1966 concerning sudden cardiac death, a syndrome that claims between 300,000 to 400,000 lives each year in the United States (25–29). Abnormal rhythms and atrioventricular conduction defects that might warn patients that they are in danger include high grade premature ventricular beats, ventricular tachyarrhythmias or bradycardias due to ischemic heart disease. Unfortunately, because of their ischemic origin, these arrhythmias are resistant to prophylactic therapy. The risk factors associated with sudden cardiac death appear to be those that indicate already well established coronary disease and include previous myocardial infarction, abnormal electrocardiograms or ventricular arrhythmias, but not the usual risk factors of arteriosclerosis as we now understand them (18,

19,25–29). There is a high risk of sudden cardiac death in patients who have sustained a myocardial infarction during the previous year, and particularly in those who have evidence of significant ectopic arrhythmias in the 2nd and 3rd weeks after acute myocardial infarction. Our main thrust must be to provide practical techniques to identify the candidate for sudden cardiac death and to provide more effective prophylactic agents that might prevent the catastrophe (19).

New Diagnostic Technology of Acute and Chronic Ischemic Process

In the past decade, the limits of accuracy of both new and established techniques to diagnose the acute and chronic ischemic process, including electrocardiographic stress tests, angiography and enzymology, have been placed in their proper perspective (19). For instance, selective coronary angiography and ventriculography have been improved in the past 25 years to localize and measure the degree of obstruction within the native coronary circulation as well as abnormal ventricular wall motion, chamber volume and ejection fraction associated with myocardial ischemia (19). But diagnostic decisions must be based on the assessed degree of coronary artery narrowing, and these assessments are not clear cut and are often subject to large margins of error in quantitation (19). Cost-effective technology must be developed to improve the angiographic technique to provide even better images for quantitative measurements with less radiation and less financial expense to permit safer, more economic and more certain selection of the candidate for coronary bypass surgery, percutaneous coronary angioplasty or thrombolysis. Many clinicians recommend early coronary angiography for patients surviving myocardial infarction, but most believe that this expensive process should be reserved for patients with continuing symptoms.

New Image Technology

Recent advances have been made in imaging pathophysiologic phenomena of the beating heart with nuclear scintigraphy, two-dimensional echocardiography and digital subtraction angiography. Each of these techniques can portray normal or abnormal cardiac function, such as wall motion abnormalities that change from a normal inward contractile motion toward the center of the left ventricle to a loss of such contractility (akinesia) or ballooning outward (dyskinesia). They also can portray ventricular wall thickening during systole and reveal thinning of the wall in ischemic situations. Chamber volumes in diastole can be seen to increase within a few heartbeats after coronary occlusion, and ejection fraction diminishes. In addition, the nuclear tracer thallium will accumulate in normally perfused regions and its absence can be utilized to portray a region of ischemia or infarction.

Radionuclide technology. Although attempts had been made to apply radioisotopic methods to cardiology since 1947 (6,30–36), advances in this technology were not possible until improved scintigraphic techniques were developed to image the low concentration of nuclear material passing through the cardiac chambers or deposited in the myocardium. Computer applications and background subtraction in the last decade made significant image enhancement possible (36). Nuclear methods can now be applied for the management of patients with myocardial infarction to image the extent of an acute or chronic ischemic process, detect transient ischemic events after stress and correlate these findings with measurements of regional wall motion abnormalities, cardiac volume and ejection fraction.

Two-dimensional echocardiography. In the past 6 years, two-dimensional echocardiographic techniques were developed to quantitate alterations in cardiac function (37–40). Alterations of cardiac function ascribed to ischemia include regional and global alterations in chamber volume, wall motion and wall thickening. Most often these changes occur within the first few heartbeats after coronary occlusion. On early reperfusion all functional changes may be reversed. As the ischemic areas extend, further impairment of function occurs. Measurements of function with two-dimensional echocardiography that portray ischemia include those of regional wall kinetics (akinesia to dyskinesia), reduced fractional area of change, increase in right and left ventricular and atrial chamber areas and volumes, normal wall thickening that occurs during systole and changes toward thinning, ventricular aneurysm formation and papillary muscle dysfunction with prolapse of the mitral or tricuspid valve. Excellent images can now provide complete delineation of endocardial and epicardial borders for quantitating ejection fraction indexes, regional areas of change and chamber volumes. Computerization of cardiac endocardial and epicardial outlines and applied two-dimensional echocardiographic studies now provide data for evaluating changing quantitative measurements of ischemic dysfunction and physical and pharmaceutical interventions (38,39). Selected portions of the fast-moving phasic echocardiographic images processed by the computer can now be displayed side by side for serial comparison and quantitated automatically by the computer to depict the degree of progressive ischemic dysfunction or the benefits of interventions during the management of the patient in the coronary care unit (37). Contrast injection techniques developed by our group (41) permit identification of regions of ischemia for more accurate diagnosis of developing anatomic lesions or reperfusion phenomena. Further, two-dimensional echocardiographic bicycle stress tests have been perfected to provide diagnostic images of abnormal ischemic wall motion and changes in chamber volume while the patient is exercising (40).

It is now evident that the clinician can confidently choose from a battery of electrocardiographic, ultrasonic and nu-

clear methods that complement and supplement the knowledge of a single test to detect the earliest abnormalities of ischemic dysfunction when a myocardial infarction occurs (32–42).

Unsolved Problems of Acute Myocardial Infarction

Existing controversies continue regarding fundamental concepts in causation of acute ischemia leading to infarction (19). Some workers believe that most cases of infarction result from coronary angiospasm, but others observe that this is a rare occurrence (43). Dynamic pathophysiologic concepts must explain when the irreversible ischemic changes occur. Are clinical infarct size measurements accurate? Is there an ischemic "twilight zone" around a central area of necrosis that can be reversed by delayed interventions? What is the significance of the collateral circulation in control of infarct size and how can it be implemented? Emerging concepts that are associated with ischemic syndromes must receive more attention, such as the excessive metabolic demands in hypertrophic cardiomyopathies and the relation of acute myocardial ischemia to the prolapsing mitral valve syndrome. The attending cardiologist needs to know if it is possible to reduce the obstructive arteriosclerotic lesion by control of risk factors after myocardial infarction occurs (19). However, there is considerable disagreement regarding the possible benefits of risk factor interventions to prevent atherosclerosis (44,45).

Revascularization of the Acute Ischemic Myocardium

New developments in the attempt to revascularize ischemic myocardium immediately after coronary occlusion are of great interest to the cardiologist (46,47). These interventions include: 1) immediate coronary bypass; 2) systemic intravenous administration, intravenous coronary sinus retroperfusion and antegrade coronary artery flushing of streptokinase to dissolve an occlusive thrombus (44,45); 3) percutaneous transluminal coronary angioplasty (PTCA) of a narrowed coronary artery (48); and 4) the use of synchronized retroperfusion of arterial blood that is cooled below body temperature and pumped into the heart by way of the coronary sinus (47). The latter two interventions are of great interest but must still be considered to be of an experimental nature. It is obvious from previous studies that these interventions must be applied as early as possible, at least within 3 to 4 hours after occlusion, before the heart damage becomes irreversible. These experimental methods will be discussed in more detail in early issues of this Journal (49).

Conclusions

Stages of New Aggressive Interventions for the Management of Acute Myocardial Infarction

The stages of the rapid developments in the modern management of myocardial infarction can be summarized chronologically:

Stage 1. Continuous electrocardiographic monitoring of the acute coronary patient

Stage 2. Authorization and training of attending nurses to defibrillate the heart of patients

Stage 3. Prophylactic and continuous intravenous drip treatment of the irritable heart

Stage 4. Electrical pacemakers for treatment of acute heart block and extreme bradycardia

Stage 5. Pulmonary artery flow-directed catheters for estimating left ventricular filling pressure

Stage 6. Treatment of the failing heart by control measures affecting afterload and preload

Stage 7. Interventions to salvage jeopardized ischemic myocardium, including revascularization with thrombolytic agents and coronary sinus retroperfusion

Stage 8. Coronary bypass surgery for: a) acute coronary occlusion, b) impending infarction, c) high risk lesions, d) extending infarction

Stage 9. New noninvasive imaging technology

Why the Reduction in Coronary Disease Mortality?

Many wonder about the probable reasons for the decreased mortality of coronary heart disease since 1966 despite an unchanged incidence of acute myocardial infarction (50). Many factors appear to be responsible: 1) public awareness of the acute coronary symptoms and the need to seek emergency skilled treatment; 2) practical resuscitation within the 4 minute limit for emergency treatment of cardiac arrest; 3) aggressive management of the acute coronary victim in the coronary care unit; 4) prophylactic treatment of ominous arrhythmias; 5) aggressive management of pacemaker problems; 6) acceptance of beta-receptor blocking agents and nitrates for treatment of angina pectoris; 7) coronary bypass surgery for up to 150,000 potential victims of coronary disease in the United States each year; 8) freedom from catastrophic epidemics of influenza in recent years which has improved longevity of all patients; 9) alterations in the International Classification of Diseases, which changed statistical methods for providing death classification each year; and 10) control of risk factors such as hypertension, tobacco smoking (43) and perhaps even serum lipids.

At present each cardiologist has his or her own private beliefs on how the battle is being won, and we must await

the renewed scientific analysis to determine which of the advances has contributed most to the reduced mortality.

References

1. Training technics for the coronary care unit. Second Bethesda Conference of the American College of Cardiology, December 11 and 12, 1965, Washington DC. Am J Cardiol 1966;17:736–47.
2. Corday E, Williams JH, De Vera LB, Gold H. Hemodynamics of the coronary circulation during cardiac arrhythmias. Mod Concepts Cardiovasc Dis 1958;27:493–8.
3. Corday E, Irving DW. Effect of cardiac arrhythmias on the cerebral circulation. Am J Cardiol 1960;6:803–8.
4. Irving DW, Corday E. Effect of the cardiac arrhythmias on the renal and mesenteric circulation. Am J Cardiol 1961;8:32–40.
5. Gold H, Corday E. Vasopressor therapy in the cardiac arrhythmias. N Engl J Med 1959;260:1151–6.
6. Corday E, Bergman HC, Schwartz LL, Spritzler RJ, Prinzmetal M. Studies on the coronary circulation: the effect of shock on the heart and its treatment. Am Heart J 1949;37:560–81.
7. Kurland GS, Malach M. The clinical use of norepinephrine in the treatment of shock accompanying myocardial infarction and other conditions. N Engl J Med 1952;247:383–9.
8. Gold H, Corday E. The augmentation of coronary flow in experimental cardiogenic shock with combined drug therapy. Bull NJ Acad Med 1966;12:180–4.
9. Corday E, Lillehei RC. Pressor agents in cardiogenic shock. Am J Cardiol 1969;23:900–10.
10. Zoll PM. Resuscitation of the heart in ventricular standstill by external electrical stimulation. N Engl J Med 1952;247:768–71.
11. Day HW. An intensive coronary care area. Chest 1963;44:423–6.
12. Kouwenhoven WB, Jude JR, Knickerbocker GG. Closed chest cardiac massage. JAMA 1960;173:1064–7.
13. Meltzer LE. Concepts and system for intensive coronary care. Bull NJ Acad Med 1964;10:304.
14. Corday E, Pappelbaum S, Gold H, Bazika V. Closed chest massage: an effective resuscitative procedure for the maintenance of the circulation during cardiac arrest. Can Med Assoc J 1965;93:949–53.
15. Cole SL, Corday E. Four-minute time limit for cardiac resuscitation. JAMA 1956;161:1454–8.
16. Corday E, Heng MK, Meerbaum S, et al. Derangements of myocardial metabolism preceding onset of ventricular fibrillation after coronary occlusion. Am J Cardiol 1977;39:880–9.
17. Lown B, Amarasingham R, Newman J. New method for terminating cardiac arrhythmias: use of synchronized capacitance discharge. JAMA 1962;182:548–55.
18. Corday E, Swan HJC, ed. Myocardial Infarction. Baltimore: Williams & Wilkins, 1972.
19. Corday E, Swan HJC, ed. Clinical Strategies in Ischemic Heart Disease. Baltimore: William & Wilkins, 1978.
20. Maroko PR, Kjekshus JK, Sobel BE. Factors affecting infarct size. Circulation 1971;43:67–82.
21. Maroko PR, Braunwald E. Modification of myocardial infarction size after coronary occlusion. Ann Intern Med 1973;79:720–33.
22. Corday E. Interventions that might influence viability of ischemic jeopardized myocardium: introduction to symposium on the management of jeopardized ischemic myocardium. Am J Cardiol 1976;37:461–6.
23. Heng M, Corday E, Meerbaum S, Wyatt HL. Salvaging the ischemic myocardium: promises and limitations. Cardiovasc Med 1978;3:1017–24.
24. Corday E, ed. Symposium on reperfusion during acute myocardial infarction. Am J Cardiol 1974;33:49–81.
25. Hamer A, Vohra J, Hunt D, Sloman G. Prediction of sudden death by electrophysiologic studies in high risk patients surviving acute myocardial infarction. Am J Cardiol 1982;50:223–9.
26. Coronary Drug Project Research Group. Prognostic importance of premature beats following myocardial infarction. Experience in the coronary drug project. JAMA 1973;223:116–24.
27. Schultze RA, Strauss HW, Pitt B. Sudden death in the year following myocardial infarction. Relation to ventricular premature contractions in the late hospital phase and left ventricular ejection fraction. Am J Med 1977;62:192–9.
28. Moss AJ. Profile of high risk in people known to have coronary heart disease. A review. Circulation 1975;52(suppl III):III–147.
29. Corday E, ed. Symposium on identification and management of the candidate for sudden cardiac death. Am J Cardiol 1977;39:813–93.
30. Blum R, Alpern H, Lang TW, Corday E. Determination of intra-arterial coronary anastamosis by radioactive spherules. Am Heart J 1970;79:244–9.
31. Prinzmetal M, Corday E, Spritzler R, Flieg W. Radiocardiography: clinical application. JAMA 1949;139:617–22.
32. Berman DS, Garcia EV, Maddahi J. Thallium-201 myocardial scintigraphy in the detection and evaluation of coronary artery disease. In: Berman DS, Mason DT, eds. Clinical Nuclear Cardiology. New York: Grune & Stratton, 1981:49–106.
33. Maddahi J, Garcia EV, Berman DS, et al. Improved noninvasive assessment of coronary artery disease by quantitative analysis of regional stress myocardial distribution and washout of thallium 201. Circulation 1981;64:924–35.
34. Tanesescu D, Berman D, Staniloff H, et al. Apparent worsening of thallium-201 myocardial defects during redistribution: what does it mean (abstr)? J Nucl Med 1979;20:688.
35. Ritchie JL, Trobaugh GB, Hamilton GW, et al. Myocardial imaging with thallium-201 at rest and during exercise: comparison with coronary arteriography and stress electrocardiography. Circulation 1977;56:66–71.
36. Botvinick EH, Taradash MR, Shames DM, Parmley WW. Thallium-201 myocardial perfusion scintigraphy for the clinical clarification of normal, abnormal and equivocal electrocardiographic stress tests. Am J Cardiol 1978;41:43–51.
37. Garcia E, Gueret P, Bennett M, et al: Real time computerization of two-dimensional echocardiography. Am Heart J 1981;101:783–92.
38. Wyatt HL, Meerbaum S, Heng MK, Rit J, Gueret P, Corday E. Experimental evaluation of the extent of myocardial dyssynergy and infarct size by two-dimensional echocardiography. Circulation 1981;63:607–14.
39. Gueret P, Meerbaum S, Broffman J, Uchiyama T, Corday E. Differential effects of nitroprusside on ischemic and nonischemic myocardium demonstrated by two-dimensional echocardiography. Am J Cardiol 1981;48:59–68.
40. Zwehl W, Gueret P, Meerbaum S, Holt D, Corday E. Quantitative two-dimensional echocardiography during bicycle exercise in normal subjects. Am J Cardiol 1981;47:866–73.
41. Tei C, Sakamaki T, Corday E, et al. Intracoronary contrast echo in the assessment of regional myocardial asynergy and perfusion (abstr). Circulation 1982;65(suppl II):II–27.
42. Vas R, Diamond GA, Whiting JS, Forrester JS, Swan HJC. Computer enhancement of direct and venous injected left ventricular contrast angiography. Am Heart J 1981;102:719–8.
43. Johnson SM, Mauritson DR, Willerson JT, Hillis LD. A controlled trial of verapamil for Prinzmetal's variable angina. N Engl J Med 1981;304:862–6.
44. Corday E, Corday SR. Prevention of heart disease by control of risk factors: the time has come to face the facts. Am J Cardiol 1975;35:330–3.

45. Multiple risk factor intervention trial: risk factor changes and mortality results. Report of Multiple Risk Factor Intervention Trial Research Group (MR FIT), National Heart, Lung, and Blood Institute, National Institutes of Health. JAMA 1982;248:1465–77.

46. Meerbaum S, Lang T-W, Povzhitkov M, et al. Retrograde lysis of coronary artery thrombus by coronary venous streptokinase administration. J Am Coll Cardiol (in press).

47. Meerbaum S, Haendchen RV, Corday E, et al. Hypothermic coronary venous phased retroperfusion: a closed chest treatment of acute regional myocardial ischemia. Circulation 1982;65:1435–45.

48. Gruntzig AR, Senning A, Siegenthaler WE. Nonoperative dilatation of coronary artery stenosis. N Engl J Med 1979;301:61–8.

49. Corday E, Meerbaum S, eds. Symposium on advances in coronary reperfusion. J Am Coll Cardiol (in press).

50. Proceedings of the Conference on the Decline in Coronary Heart Disease Mortality. Bethesda, Maryland: National Heart, Lung, and Blood Institute, 1979: NIH publication no. 79–1610.