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Immune System Activation Follows Inflammation in Unstable Angina: Pathogenetic Implications

ABSTRACT & COMMENTARY

Synopsis: *This study supports the hypothesis that an inflammatory process is associated with unstable angina pectoris.*

Source: Caligiuri G, et al. *J Am Coll Cardiol* 1998;32:1295-1304.

A new study from caligiuri and colleagues is consistent with a putative role for inflammation and especially immune responses in unstable angina. Caligiuri et al carefully studied a cohort of patients with unstable angina as well as a control group with chronic stable angina; they measured a variety of immune markers at several time intervals. The study was stimulated by prior work from this group as well as others indicating that elevated systemic levels of inflammatory and immune markers were common in unstable angina, and indicated a poorer outcome in such individuals. Thirty-five patients with severe unstable angina underwent serial studies for six months. This cohort was subdivided into a group that quickly stabilized and another that had more than two unstable ischemic episodes after 48 hours on maximum medical therapy. Thirty-five individuals with stable effort angina, a positive stress test, and a documented coronary obstruction served as the controls. Analyses were carried out for C-reactive protein, immunoglobulins and complement fractions, IgG and IgM titers for *C. pneumoniae*, interleukin-2 levels, and a variety of lymphocyte subpopulations. The results indicated that unstable angina patients as a group had higher admission CRP levels and a higher percentage of circulating T-helper lymphocytes (CD4 +) than in chronic stable angina, as well as less circulating T-suppressor cells. CRP levels tended to fall in the unstable patients, although IgM levels increased at 7-15 days. Unstable angina patients who had persistent and severe ischemia had higher CRP levels than those who responded to therapy, and these patients also had higher IgM levels and activated T-cells at two weeks. Interleukin-2 levels were increased in unstable angina patients; activation of lymphocytes in general was greater in the unstable patients, but not in the chronic stable angina. Caligiuri et al conclude that the unstable angina cohort manifests a "transient specific

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immune response" within 1-2 weeks, and that increases in circulating activated T-cells and IgM levels were associated with a more favorable short-term clinical outcome. Caligiuri et al believe that the elevated CRP levels, declining rapidly but remaining high in the unfavorable unstable angina cohort, support the hypothesis that an inflammatory process is associated with unstable angina pectoris. This inflammation may come from the complex culprit plaque and/or systemic activation. Furthermore, their data are consistent with the view that the inflammatory process is not related to thrombosis or reperfusion injury. Caligiuri et al suggest that this inflammatory response may be antigen-stimulated, although the precise antigens that might be implicated are not identified in this study. These could be "self-modified proteins" or infectious agents, as has been suggested in previous studies. However, antibody levels in this study did not support a reaction to *C. pneumoniae*. In fact, Caligiuri et al conclude that an increase in total antibody titers as well as a presumed polyclonol origin of plaque T-cells suggest that different antigenic stimuli might play a role in different patients or even the same patient over time. In the chronic stable angina patients, T-cell activation was noted, particularly in the individuals that had severe effort angina, but none of the other immune parameters, such as CRP, IgM, or interleukin-2, appeared to be important in stable angina cohorts.

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COMMENT BY JONATHAN ABRAMS, MD

These data are fascinating and lend credence to the many reports suggesting that inflammatory and/or immune activation are present in unstable angina patients and even to some degree in chronic stable angina. The dynamic nature of the rise and fall of a number of parameters in the unstable angina cohort, particularly the differences between the stable vs. less stable subjects, further supports the possibility of a causal contribution of the immune system in unstable angina. Obviously, a great deal of additional research is necessary, and no immediate therapeutic implications can be identified. However, as Eugene Braunwald (*Circulation* 1998;98:2219-2222) points out in his editorial, it is time that physicians become more comfortable with these interesting pathogenetic phenomena. The evidence that coronary events may be in part related to immune phenomena appears to be solid. There is considerable evidence that elevated CRP levels are associated with adverse prognosis in ischemic heart disease cohorts; these data in unstable angina patients begin to explore the immune system in much greater detail than simply measuring common acute phase reactants.

The syndrome of unstable angina pectoris is variably defined as heterogeneous with respect to pathogenesis as well as clinical manifestations. Braunwald suggests that more effort be made to identify the various etiologies of unstable angina, and that specific therapies should be appropriately chosen depending on causation. He defines five different causes—not necessarily mutually exclusive. These include the most common etiology, nonocclusive thrombus on a pre-existing coronary lesion; dynamic obstruction of a normal or abnormal coronary artery, with focal or diffuse vasoconstriction/spasm resulting in myocardial ischemia; progressive atherosclerosis with luminal narrowing, such as has been documented to occur at the site of the "culprit lesion" or in restenosis following PTCA; inflammation and possible systemic infection; and, finally, "secondary unstable angina" (i.e., myocardial ischemia rated to exogenous factors, such as tachycardia, hypertension, thyrotoxicosis, etc.). Clearly, identification of the etiology of unstable angina in a specific patient might influence therapy. For instance, the thrombotic cause would benefit from antiplatelet and antithrombotic agents; the severe obstruction requires revascularization; a variety of potential therapies might be appropriate for an inflammatory-infectious causation, etc. It is conceivable that short- and long-term prognosis might be different among the various causes of unstable angina. Braunwald's construct, while not new, should assist clinicians as well as investigators regarding their thoughts about unstable angina and its therapy. ❖

Mechanisms of unstable angina include:

a. inflammation/infection.
b. nonocclusive thrombus.
c. progressive atherosclerosis.
d. All of the above

Health Outcomes Associated with Beta-Blocker and Diltiazem Treatment of Unstable Angina

ABSTRACT & COMMENTARY

Synopsis: *Diltiazem demonstrated no survival benefit compared to beta-blockers in unstable angina.*

Source: Smith NL, et al. *J Am Coll Cardiol* 1998; 32:1305-1311.

Therapy for unstable angina was explored in a retrospective outcome study from the Seattle VA hospital. This analysis sought to assess outcomes in unstable angina in men discharged with this diagnosis who were treated with a beta-blocker or diltiazem. Eligible veterans discharged from the Seattle VA Healthcare System between 1989 and 1995 were identified by chart review. Discharge medications and clinical outcomes were documented, including rehospitalization and revascularization. Complex statistical analyses were used, including a multivariate model that "adjusted for potential confounders using propensities score matching." From an initial cohort of almost 1500 individuals, 247 were identified who had accurate pharmacy records concerning drug use within 30 days of discharge, identifying those on a beta-blocker or diltiazem monotherapy. The characteristics and demographics of these individuals were typical for a VA population with unstable angina. Two-thirds were on either a beta-blocker or a calcium blocker on admission, and most were discharged on similar medications. Diltiazem use was threefold more common; those on this drug were more likely to have had prior heart failure, COPD, and higher blood pressures. In outcomes analysis, an unadjusted proportionate hazards regression model, diltiazem was associated with a 60% increase in all-cause mortality but, after adjustment for potential confounders, there was no longer any difference in risk for subsequent death between patients taking diltiazem or a beta-blocker. The risk ratio was also similar when the analysis was restricted to men without lung disease or heart failure. An analysis of veterans who were Washington residents was comparable, showing a nonstatistical increased risk ratio for diltiazem, even after adjustments. Smith and colleagues conclude that "Veterans treated with diltiazem for unstable angina … had no overall survival advantage compared with … beta blockers." The composite end point of rehospitalization or death was associated with a nonsignificantly elevated risk with diltiazem; however, confidence intervals were wide. The data related to these drugs in unstable angina were inconclusive with respect to the question of calcium blockers vs. beta-blockers. Multiple study limitations are discussed, most important, that this was not a prospective randomized trial. Diltiazem users at baseline were less healthy. Patients who were on polypharmacy for myocardial ischemia were not included in the analysis. Finally, the use of beta-blocker monotherapy was low and substantially less than diltiazem. Smith et al conclude that beta-blockers were chronically underused and that diltiazem demonstrated no clinical benefits following hospitalization in unstable angina.

COMMENT BY JONATHAN ABRAMS, MD

This report is of interest but is not terribly useful to clinicians. Underuse of beta-blockers is not a new subject, particularly in a cohort that has significant co-morbidity of asthma and COPD. In that there was no placebo group, it is impossible to know whether diltiazem or a beta-blocker was beneficial during the average follow-up (51 months). While Smith et al conclude that diltiazem imparted no survival benefit, another interpretation would be that diltiazem was as good as beta-blocker treatment, which is the case after the propensity score adjustment. The statistical methods used are complex and it is unclear whether the propensity score analysis solved the problem of nonequality between the cohorts in this retrospective analysis. Clearly, data from a variety of sources indicate that for individuals with preserved left ventricular function, diltiazem is safe and, at least in the post-non-Q myocardial infarction population, is beneficial when compared to placebo. These data indicate that diltiazem is safe in unstable angina. Prior experience confirms that this drug should not be used in individuals with overt heart failure when associated with a depressed LV ejection fraction (< 40%). The current interest in beta-blockers for heart failure may lower the threshold to use these drugs in patients with depressed LV function and unstable angina; overall, beta-blocker use remains inadequate for coronary dis-

ease, as seen in this database as well as recent major Medicare cohort analyses. I would conclude that either drug, if appropriately selected, can be used safely for unstable angina patients. Physicians should pay attention to the status of LV function as well as other co-morbidity in making a choice of therapy. ❖

Diltiazem treatment of unstable angina:

a. is rare in a VA hospital population.
b. increases adjusted mortality.
c. results in similar outcomes as beta-blockers.
d. results in an excess incidence of heart failure.

Bundle Branch Block Revisited

ABSTRACT & COMMENTARY

Synopsis: *Bundle branch block is a marker of a slowly progressive degenerative disease that affects the myocardium.*

Source: Eriksson P, et al. *Circulation* 1998; 98:2494-2500.

Conflicting data exist concerning the etiology and significance of bundle branch block (BBB) on the electrocardiogram (ECG). Thus, Eriksson and colleagues recorded 12-lead ECGs in a random sample of 855 men who were 50 years old in 1963 when they were recruited in the city of Goteborg, Sweden, and followed them for 30 years with periodic examinations. During the 30 years, 82 subjects with BBB were found (10%). Most acquired BBB after entry; only 1% had BBB at entry. BBB became more prevalent with aging. At age 75 years, right BBB was four times more prevalent than left BBB (39 vs 9%). ECG evidence of left ventricular hypotrophy preceded left BBB in one-quarter of the subjects vs. 6% for right BBB. Risk factors for atherosclerosis, myocardial infarction (MI), and a diagnosis of ischemic heart disease were no different between those who developed BBB and those who did not. However, cardiomegally on chest x-ray ($P < 0.05$) and congestive heart failure (36% BBB vs 14% of controls; $P < 0.01$) were more common with BBB. Also, among those who died of cardiovascular causes, more subjects had a history of chronic heart failure with BBB (61%) vs. no BBB (28%; $P < 0.01$). Eriksson et al conclude that BBB is a marker of a slowly progressive degenerative disease that affects the myocardium.

COMMENT BY MICHAEL H. CRAWFORD, MD

This study is consistent with the old adage that BBB is more commonly associated with cardiomyopathy rather than coronary artery diseases (CAD). In fact, no relation could be established between BBB and risk factors for atherosclerosis or overt CAD. This is consistent with other studies and the observation that BBB is not usually caused by acute MI. Also, the prevalence of BBB is highly correlated with advancing age, being 1% at age 50 and 17% at age 80 in men. Thus, CAD and BBB often coexist and this combination is known to increase mortality in acute MI and chronic CAD patients. Other studies suggest this may be due to a greater propensity to ventricular arrhythmias and sudden death, possibly due to prolonged repolarization. However, acute MI superimposed on a chronic progressive cardiomyopathy may result in a higher than expected mortality due to pump failure.

The major limitation of this study was that the small number of patients with BBB reduced the power for comparing left to right BBB, which many believe are of different significance. Also, ECGs were only recorded every 5-17 years, so details about the onset and potential causes of BBB are hard to decipher. In addition, there are few objective data about other cardiac diseases in this study. Nor are there electrophysiologic data about the site of block or the need for pacing. The implications of this study are that patients who develop or present with BBB should have an echocardiogram done to assess left ventricular function. The need for stress tests or coronary angiography is less clear in the absence of other indications for these procedures. ❖

New bundle branch block on ECG suggests:

a. ischemic heart disease.
b. cardiomyopathy.
c. valvular heart disease.
d. hypertrophic cardiomyopathy.

Post-Resuscitation Ventricular Tachycardia

ABSTRACT & COMMENTARY

Synopsis: *Regular, rapid ventricular tachycardia is the most common recurrent arrhythmia noted in patients resuscitated from an initial episode of ventricular fibrillation.*

Source: Ruppel R, et al. *J Am Coll Cardiol* 1998; 32:1724-1730.

Little is known about recurrent arrhythmia events in resuscitated patients. Thus, Ruppel and associates describe their experience in a group of

patients who were resuscitated from ventricular fibrillation (VF) unassociated with myocardial infarction and then received implantable cardioverter defibrillators (ICDs) that were capable of storing intracardiac electrograms. Forty patients entered the study between November 1991 and January 1995. Twenty-eight of the patients had coronary artery disease with a mean left ventricular ejection fraction of 38%. Twenty-four of these 28 patients (86%) had a prior myocardial infarction. Four patients had idiopathic VF. Five patients had dilated cardiomyopathy and three patients had other types of cardiac disease with an overall ejection fraction in this group of 42 ± 17%. Patients were eligible for inclusion if they were resuscitated from documented VF that was not related to an associated myocardial infarction, if VF was the only arrhythmia documented, and if they went on to have an ICD capable of intracardiac electrogram recording and storage implanted. Prior to ICD implantation, all patients underwent a baseline electrophysiologic study that used up to three extrastimuli during ventricular pacing at three basic cycle lengths from two right ventricular sites. Patients received a transvenous ICD system using either a Guidant/CPI Ventak P2 or PRX-II/III device. These systems store intracardiac electrograms recorded between the two shock coils on the ICD connected in a bipolar configuration. Patients were discharged from the hospital off all antiarrhythmic drugs. When supraventricular arrhythmias with high ventricular rates occurred, either AV nodal blocking agents were added or AV nodal catheter ablation was performed. Patients were followed up at intervals of every 2-3 months. The ICDs were interrogated and intracardiac electrograms from any therapies delivered were recorded and analyzed. Arrhythmias at the time of therapy were classified as VF, ventricular tachycardia, atrial flutter, atrial fibrillation, or sinus tachycardia.

During a mean follow-up of 23 ± 11 months, seven patients died, with six of the deaths being attributed to congestive heart failure and one death due to carcinoma of the lung. Thirteen of the initial 40 patients (33%) developed recurrent ventricular arrhythmias that were appropriately treated by their ICD. Thirteen patients (33%) also received inappropriate therapies because of either supraventricular arrhythmias or system failures. Three of these latter patients also received inappropriate therapies for ventricular arrhythmias. A repeat episode of VF was uncommon in the series. There were only five episodes of VF observed in two patients. One of these patients had no structural heart disease and the other had a surgically corrected atrial septal defect. In both of these patients, VF was the only arrhythmia documented during follow-up. Eleven patients experienced a total of 36 episodes of monomorphic ventricular tachycardia. In only two of these patients was degeneration of ventricular tachycardia to VF documented. Of these 11 patients, seven had coronary artery disease, three had dilated cardiomyopathy, and one had no structural heart disease. Atrial fibrillation and atrial flutter were the most common reasons for inappropriate therapy. Four of the 40 patients (10%) received inappropriate therapy due to device malfunction or lead displacement.

Age, gender, cardiac diagnosis, and left ventricular ejection fractions failed to distinguish between those with clinical recurrence of ventricular arrhythmias and those without. The data from the baseline electrophysiologic study were also not helpful. At baseline electrophysiologic study, monomorphic ventricular tachycardia was induced in 14 patients and VF in seven patients. No ventricular arrhythmias were inducible in the remaining 19 patients. Five of the 14 patients with ventricular tachycardia induced had spontaneous ventricular tachycardia during follow-up and none had VF. One of the seven patients who had VF at the initial study had VF during follow-up. Six of the 19 patients who had no ventricular arrhythmias induced at the initial study had ventricular tachycardia and one had VF during follow-up. Ruppel et al conclude that regular, rapid ventricular tachycardia is the most common recurrent arrhythmia noted in patients resuscitated from an initial episode of VF and that the ability to predict recurrence of either ventricular tachycardia or VF is limited.

COMMENT BY JOHN P. DiMARCO, MD, PhD

This interesting paper is one of the first papers to report on patients resuscitated from cardiac arrest who received ICDs that can store electrograms. The size of this group is relatively small and we will no doubt see more conclusive data from some of the large cardiac arrest trials, such as the antiarrhythmic vs. implantable defibrillators (AVID) or the Canadian Implantable Defibrillator Study (CIDS) that have recently been completed. However, Ruppel et al make several interesting observations. The primary message from this study is the limited role of electrophysiologic studies in the evaluation of out-of-hospital cardiac arrest survivors. Electrophysiologic studies have their greatest sensitivity in patients with fixed arrhythmia substrates, such as prior myocardial infarction and monomorphic tachycardias. In patients who present with VF, the substrate is either less stable or the arrhythmia may be reproducible only under certain physiologic conditions. There are significant implications in this observation in terms of the use of electrophysiologic studies to predict future

events. In the Multicenter Automatic Defibrillator Implantation Trial, an inducible ventricular tachycardia at electrophysiologic study was used to identify the high-risk population that subsequently benefited with ICD implantation. We will soon have data from the Multicenter Unsustained Tachycardia Trial to confirm or refute this hypothesis. The latter trial, unlike the former, included three groups: an untreated group of patients who had no inducible arrhythmia, a group of patients who had inducible arrhythmia but were not treated, and a group of treated patients with inducible arrhythmia. If, as seen in this study, results during electrophysiologic study are not good predictors of cardiac arrest, our ability to intervene specifically in high-risk populations with expensive devices such as ICDs will be markedly limited.

It is interesting that only about 33% of the patients in this trial experienced recurrent arrhythmias during follow-up of all antiarrhythmic therapy. In the AVID and CIDS trials, mortality in drug-treated patients was almost as high as the frequency of appropriate shocks reported here. Therefore, one must suspect that either the patient population in this study was somewhat different than the one recruited for those large prospective trials or that drug therapy provides little benefit.

The other interesting finding in this paper is the relatively high frequency of inappropriate therapies. Atrial fibrillation and atrial flutter are common problems in patients with ICDs. The introduction of dual-chamber devices allows better identification of these arrhythmias when they occur and may allow programming that will decrease the frequency of inappropriate shocks. It is also striking that 10% of the patients had shocks related to system failures despite the fact that the median follow-up was only 22 months. Deterioration of the systems, which leads to inappropriate shocks or repeat operations, is likely to be a major factor complicating ICD therapy as patients live longer after implant and as the prophylactic use of ICDs becomes more common. ❖

Follow-up of resuscitated ventricular fibrillation patients often shows:

a. ischemic heart disease.
b. monomorphic ventricular tachycardia episodes.
c. reduced ejection fraction.
d. All of the above

Open Artery Hypothesis Revisited

ABSTRACT & COMMENTARY

Synopsis: *Late angioplasty post initial anteroseptal Q-wave MI reduces left ventricular volumes and decreases subsequent cardiac events.*

Source: Horie H, et al. *Circulation* 1998;98:2377-2382.

Late reperfusion after myocardial infarction (MI) has been associated with improved survival in observational studies, but many believe a randomized trial is necessary to prove the open artery hypothesis. Thus, Horie and associates from Japan conducted a randomized trial to assess the effects of late reperfusion post-MI by angioplasty on long-term clinical outcomes. Patients with first acute Q-wave anteroseptal MI more than 24 hours from symptom onset and total occlusion of the culprit artery were recruited if they were younger than 80 and had no confounding co-morbidities. Of the 101 consecutive patients admitted, 83 met these criteria and formed the study group. They were randomized in the catheterization laboratory to angioplasty or medical therapy (no thrombolysis). Mean time to reperfusion after symptom onset was eight days in the angioplasty group, and all but three patients were successfully reperfused (93%). At six months, all underwent repeat catheterization. Among the angioplasty patients, two had reoccluded and 12 restenosed, but all 14 had successful reperfusion procedures. Among the medical patients, five had spontaneously reperfused. Left ventricular angiography showed no difference in the two treatment groups at six months in ejection fraction, but left ventricular volumes were significantly smaller in the angioplasty group. Cardiac death occurred in one patient in the angioplasty group and four patients in the medical group ($P = 0.06$) and other cardiac events were significantly lower in the angioplasty group (3 vs 14; $P < 0.001$). Horie et al conclude that late angioplasty post-initial anteroseptal Q-wave MI reduces left ventricular volumes and decreases subsequent cardiac events.

COMMENT BY MICHAEL H. CRAWFORD, MD

This paper was published in *Circulation* because it is the first randomized trial of the open artery hypothesis, not because it is a great study. Remember, the first three rules of scientific publishing are priority, priority, and priority. That is not to say that this is a bad study; it is just limited in scope and underpowered to show a survival benefit alone. In order to reduce confounding variables and thereby keep the study population low, they studied patients with first anteroseptal MIs and totally occluded arteries who presented more than 24 hours after symptoms. Revascularization was accomplished 1-42 days post-MI with a higher success rate initially (93%) and at six months (94%), compared to prior observational studies of more diverse populations. In this select group, cardiac events over five years were clearly reduced beginning at about 10 months post-MI and there

was a strong trend (P = 0.06) toward reduced mortality. These data clearly support previous reports of an association between an open infarct artery and improved outcomes and fly in the face of those that would restrict post Q-wave MI catheterization based upon a lack of evidence supporting its benefit.

The mechanism of this benefit is not evident from the study, but the reduction in left ventricular volumes (systolic and diastolic) is interesting, especially since ejection fraction was not altered by angioplasty. Perhaps there is a reduction of remodeling that reduces left ventricular wall stress and prevents arrhythmias or improves diastolic function. There are no data to support the former (i.e., Holter Monitor) but most of the deaths in the medical group were due to heart failure despite an average ejection fraction of 50% in this group. Abrogation of residual peri-infarction ischemia that otherwise would have led to a heart failure death cannot be excluded since no tests for ischemia were reported. We also do not know if vessel patency was maintained after six months. Finally, the use of stents and platelet glycoprotein 11b/111a inhibitors could enhance the results in the angioplasty group. Clearly, the walls are cracking around the guards at the post-MI catheterization gates and the cracks are due to the increasing weight of evidence. ❖

A randomized trial of late post-MI reperfusion has shown:

a. reduced mortality.
b. reduced cardiac events.
c. reduced left ventricular volumes.
d. b & c.

Noncontact Endocardial Mapping in the Human Left Ventricle

ABSTRACT & COMMENTARY

Synopsis: *This system has potential use in patients undergoing mapping of complex arrhythmias since the system provides rapid analysis of real-time electrograms over the entire tachycardia circuit.*

Source: Schilling RJ, et al. *Circulation* 1998; 98:887-898.

Schilling and associates report the first clinical use of a multielectrode catheter that was developed to permit noncontact mapping of electrical activity in cardiac chambers. This study describes results obtained in 13 patients who were undergoing endocardial left ventricular mapping prior to catheter ablation of hemodynamically well-tolerated ventricular tachycardia. The system consists of a catheter containing a multielectrode array, a custom-built amplifier system, and a Silicon Graphics workstation to process and analyze the signals. The electrode catheter is a woven grid of thin wires mounted on an ellipsoidal balloon at the tip of a 9 Fr catheter. Each wire has a 0.025-inch break in insulation, making it a noncontact unipolar electrode. A ring electrode is located on the proximal shaft of the catheter in the aorta as the reference. The catheter is placed over a guide wire into the left ventricle, and the balloon is inflated with saline after it is in position. A second catheter is then used for determining chamber dimensions and ablation. A low current "locator signal" is passed between this roving catheter and the ring electrodes on the noncontact catheter. The electrode array detects and determines the locator signal angles and determines the other catheter's positions. This determines the geometry of the chamber and generates a series of coordinates for the endocardium. Electrical activity is detected by the multiple electrode array but it is of lower amplitude and frequency than the source on the endocardium. These signals must, therefore, be enhanced and resolved using a complex process involving an inverse solution to Laplace's equation by use of the boundary element method. This inverse solution of Laplace's equation allows computation of multiple endocardial electrograms from the potential sensed on the noncontact electrode. Mathematical techniques are used to minimize noise. This methodology computes the relationship between the 64 electrodes on the noncontact balloon and 3360 points on the endocardium. The signal processing for this analysis is done in real time using a Silicon Graphics workstation. This paper assesses the accuracy and timing of the

reconstructed unipolar electrograms compared with traditional contact unipolar electrograms from the same endocardial site recorded by the roving catheter.

Contact electrograms were compared at 76 points equatorial and 32 points nonequatorial to the noncontact electrode array with respect to both morphology and timing. At points distant from the equator, the correlations were lower, but acceptable recordings were still made.

Schilling et al consider this system to have potential use in patients undergoing mapping of complex arrhythmias since the system provides rapid analysis of real-time electrograms over the entire tachycardia circuit.

COMMENT BY JOHN P. DiMARCO, MD, PhD

Catheter ablation is now the preferred treatment for many cardiac arrhythmias. However, catheter ablation remains highly effective only in situations where a small critical portion of the circuit can be accurately mapped and identified. This is almost always possible in patients with accessory pathways and in patients with AV nodal reentry. It is usually possible in classic atrial flutter since the circuit in that arrhythmia passes through a known anatomic isthmus in almost all patients. Automatic rhythms usually arise from single foci and can be mapped using simple activation sequence mapping. For other arrhythmias, such as reentrant ventricular tachycardia in the setting of coronary artery disease or arrhythmogenic right ventricular dysplasia or in atrial reentrant arrhythmias, more complex mapping procedures have been necessary. Prior techniques have required catheter manipulation to reach various points within the circuit and then confirmation of participation of that site in the circuit using entrainment mapping or analysis of electrogram characteristics. This often required difficult catheter manipulation with the patient during tachycardia. This approach was severely limited in patients with unstable arrhythmias, or in those with several different arrhythmias that were difficult to sequentially map. Other techniques to map large numbers of sites simultaneously have been developed. Contact electrode arrays using various types of expandable baskets have been devised but they have been difficult to manipulate, and appropriate software for analysis of the signals has often not been available. An electroanatomic system that uses magnetic positioning has allowed accurate mapping of chamber contours and storage of signals but still requires that the catheter be moved to multiple places to generate the initial map. The system described in this paper is the first analysis recording system that permits the entire circuit of the arrhythmia to be analyzed in real time and permits positioning of an ablation catheter within that circuit guided by the electrical signals.

In this paper, no results of ablation are reported. One can anticipate that the ablation results are currently being analyzed. If the results are as good as might be expected, we should be a long way further toward the use of ablation as primary therapy for many patients with monomorphic ventricular and atrial tachycardias. ❖

Noncontact endocardial LV electrical mapping is superior to:

a. single-electrode catheter contact mapping.
b. multi-electrode catheter contact mapping.
c. contact electrode arrays.
d. All of the above

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