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CLINICAL CARDIOLOGY ALERT

A monthly update of developments in cardiovascular disease

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Late-Breaking Clinical Trials: American College of Cardiology

CONFERENCE COVERAGE

Source: American College of Cardiology Scientific Sessions, March 12-15, 2000, Anaheim, CA.

The ERA Trial

The estrogen replacement and atherosclerosis (era) trial randomized 309 postmenopausal women with documented coronary artery disease (CAD) to hormone replacement therapy (HRT) or placebo for three years. Three groups of approximately 100 individuals each received conjugated equine estrogen (CEE) alone or with methylprogesterone acetate, or placebo, and underwent serial quantitative coronary angiography. The results indicated no difference in change in the coronary mean minimum diameter; there was slight progression in all groups, comparable among estrogen, estrogen plus progesterone, and placebo. There was no difference in mean minimum diameter in coronary vessels designated as mild, moderate, or more severe stenosis at baseline; there was no effect on stenosis diameter as well as new lesions.

COMMENT BY JONATHAN ABRAMS, MD

The ERA study results, while not particularly surprising, indicate that hormone replacement does not (at least for a relatively short period of several years) prevent coronary atherosclerosis progression or induce regression. In contrast, the results of many regression trials with lipid lowering have been positive with respect to rates of progression and regression. The calcium antagonist amlodopine (PREVENT trial) also failed to demonstrate an effect of the calcium antagonist on CAD progression, although older work, as well as animal studies, suggests a role for these agents in slowing atherosclerosis.

The ERA study did not address the issue of safety of HRT in postmenopausal women with CAD, which has recently received more bad news. The NIH Women's Health Initiative announced a warning that the hormone replacement component of this important trial, comprising approximately 25,000 women, was associated with a small, nonsta-

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INSIDE

tistically significant increase in vascular events, including stroke, myocardial infarction (MI), and deep venous thrombosis. The study has not been stopped. This is a primary prevention population; the data (unpublished and unavailable) indicate a slight hazard at two years, disappearing subsequently. This preliminary report mirrors the HERS trial, suggesting that there may be a true cardiovascular adverse action of HRT for several years after initiation of therapy.

None of the available data in this somewhat confusing area suggest that women who have been on HRT for longer than 24 months and are doing well, whether they have clinical vascular disease or not, should be taken off of this therapy because of the early risk associated with initiation of estrogen replacement.

Antibiotics for Restenosis?

A German trial from Munich, Roxithromycin for Prevention of Restenosis after Stenting (IRAS-3), randomized more than 1000 subjects to antibiotic or placebo to determine whether there is a role for bacterial infection in restenosis. All individuals had successful stent implantation. No laboratory tests documenting *Chlamydia pneumoniae* exposure were obtained. Treatment consisted of one month of roxithromycin, 300 mg daily, or placebo. Clinical follow-up was obtained at 30 days and one year, and angiographic follow-up was obtained at six months. The primary end point was restenosis rate at six months. Secondary end points included typical clinical events. Many of these patients had prior acute coronary syndromes; more than 80% of the lesions were complex and at least 3 mm in size. The results showed no reduction in the restenosis rates, which were approximately 30% in both groups. In addition, major coronary end points, including heart attack and death, were comparable at 30 days, at approximately 3% in each group. At eight months, the Q-wave MI rates were equivalent. Angiographic data indicated no difference between restenosis, late loss of luminal diameter, or other parameter.

COMMENT BY JONATHAN ABRAMS, MD

An infectious etiology of atherosclerosis is a fascinating and exciting concept. It is more than likely that chronic low-grade infections may contribute to an inflammatory milieu in patients who are otherwise predisposed to develop vascular disease. It makes sense that this is more of a long-term issue than related to acute infection rapidly initiating adverse coronary events, but this is speculative. A presentation from representatives of William Beaumont Hospital in Michigan reported at the American College of Cardiology (ACC) meeting indicated that seropositivity to *C. pneumoniae* was not associated with restenosis, although inflammatory markers were strongly associated with this complication. It appears unlikely that antibiotic therapy will improve outcomes in angioplasty with or without stenting.

Safety of Antihypertensive Agents

ALLHAT, a major comparative antihypertensive study under way for a number of years and funded by the National Heart Lung and Blood Institute, reported immediately prior to the ACC meeting that there was a problem with the arm of the protocol that involved doxazosin. Four active drugs are being evaluated in ALLHAT: clorthalidone, doxazosin, amlodopine, and lisinopril. The doxazosin arm was discontinued because of an increased incidence of heart failure and "other cardiovascular events," compared to chlorthalidone. The investigators suggest that all patients on the alpha-antagonist talk to their physicians about continuing this antihypertension medication.

COMMENT BY JONATHAN ABRAMS, MD

The mechanism of action of an adverse outcome with doxazosin, if any, is unclear. Because there are only active treatment arms and no placebo control in ALLHAT, it may be that clorthalidone was more effective in decreasing events than the alpha blocker; both decreased

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blood pressure to a comparable degree, similar to the other two agents in the trial. Nevertheless, it appears that the use of doxazosin, and possibly other alpha adranergic antagonists, should be limited for the majority of patients undergoing hypertensive treatment. There are an ample number of other highly effective drugs available. For the individuals with benign prostatic hypertrophy (BPH), particularly when symptomatic, it remains unclear as to whether these drugs should be discontinued. There are no data to support this action and, until further analysis of the ALLHAT experience has been made public, it would appear that individuals with BPH and hypertension should continue on the drug, particularly if they have had a favorable urologic response.

Oral IIB/IIIa Platelet Inhibitors: More Bad News

The SYMPHONY trial, discussed in the last issue of *Clinical Cardiology Alert*, used the oral glycoprotein platelet inhibitor sirafiban, and indicated that there is no benefit with this drug. SYMPHONY II used aspirin in three patient groups and also used a low- and a high-dose sirafiban. The results of this trial were negative and, in fact, the high-dose group appeared to have more adverse outcomes than placebo-treated patients. Thus, in spite of millions of dollars and multiple randomized clinical trials, the oral IIb-IIIa inhibitor story does not look promising. Other oral agents with different pharmacologic antiplatelet properties are being evaluated, and it is certainly possible that this approach will pay off in the future. As of now, none of these drugs is available for clinical use.

Intravenous IIb-IIIa Inhibition

Another study of IIb-IIIa platelet inhibition, PARAGON-B, used lamifiban plus unfractionated heparin and aspirin and compared outcomes with heparin and aspirin alone in 5225 subjects with an acute coronary syndrome (chest pain duration < 12 hours and no ST elevation). The primary end point of 30-day composite of death, MI, or recurrent ischemia was no different between the two groups, and there also was no difference in the event rate at six months. There was somewhat more bleeding in the lamifiban patients. However, in a subanalysis, those individuals who were troponin positive did have a significant decrease in primary and secondary end points.

HART-2

The HART-2 trial examined whether low molecular weight heparin (LMWH) was superior to unfractionated heparin (UH) when tissue plasminogen activator (tPA) is given for acute MI. It was an angiographic study, with coronary arteriograms being performed at 90 minutes. The results indicated that enoxaparin was associated with less reocclusion and comparable bleeding rates. Early patency (90 minutes) was slightly higher (80% vs 75% TIMI 2-3 flow) with MWH. Death and the need for emergency prothrombin consumption index (PCI) were similar. Reocclusion rates at one week were lower with LMWH (3.1% vs 9.1%).

COMMENT BY JONATHAN ABRAMS, MD

The HART-2 trial is one of a number of investigations currently determining whether combination therapy with antiplatelet or antithrombin agents in addition to thrombolytics can produce higher patency rates with acceptable bleeding complications. This study does not support a change in our current use of unfractionated heparin but is encouraging. It may be that this approach will be clinically useful in the future. The PARAGON B study confirms that there is variability among the various IIb-IIIa clinical trials. However, tirafiban and eptifabatide have been positive in similar patient groups. The relationship between an elevated troponin and major efficacy of a IIb-IIIa inhibitor has been documented in several IIb-IIIa trials and is an important finding. Thus, it appears that patients with unstable angina or non-ST segment elevation MI, who have an elevated troponin, should be strongly considered to receive intravenous IIb-IIIa therapy, starting even before a planned angiography for possible PCI. A meta-analysis by Heidenreich and Hlatky, presented at the ACC meeting, confirmed that there is a substantial increased risk of death in individuals with positive troponin I or T in acute coronary syndromes, compared to normal troponin. ❖

Amiodarone to Prevent Atrial Fibrillation

ABSTRACT & COMMENTARY

Synopsis: *Amiodarone is superior to sotalol and propafenone for the prevention of recurrent atrial fibrillation.*

Source: Roy D, et al. *N Engl J Med* 2000;342:913-920.

Preventing atrial fibrillation (af) recurrences has been a challenge because they are frequent. Drug therapy has been unimpressive. Also, most of the drugs used have considerable potential toxicity. Roy and colleagues reported on the results of the Canadian Trial of

Atrial Fibrillation, which is a prospective, randomized, multicentered study designed to test the hypothesis that low-dose amiodarone is more effective than sotalol or propafenone for preventing AF recurrence. Entry criteria were at least one episode of AF within six months that lasted at least 10 minutes and was documented on electrocardiogram (ECG). Excluded were acute infarction patients, post-cardiac surgical patients, class III or IV cardiac patients, and those with an obvious reversible cause of AF and any contraindications to the study drugs. About half the patients were assigned to amiodarone (200 mg/day after loading), one-quarter to sotalol, and one-quarter to propafenone. Drugs were started before elective cardioversion when necessary and sotalol and propafenone could be substituted for each other if initial therapy was unsuccessful. Follow-up started at day 21 and the primary end point was AF recurrence. Over the 468-day mean follow-up, 35% of those assigned to amiodarone recurred vs. 63% assigned to the other drugs ($P < 0.001$). Cardiovascular events were similar in the two groups, except that stroke was less common in those treated with amiodarone (1 vs 9; $P = 0.01$). Drug discontinuation was less on amiodarone (34% vs 46%; $P = 0.01$). Drug discontinuation for lack of efficacy was less on amiodarone (8% vs 28%; $P < 0.001$). Adverse events were somewhat more common on amiodarone (18% vs 11%; $P = 0.06$). No particular clinical or echocardiographic characteristic subgroup benefited more or less from amiodarone. Roy et al concluded that amiodarone is superior to sotalol and propafenone for the prevention of recurrent AF.

COMMENT BY MICHAEL H. CRAWFORD, MD

Preventing recurrent AF after cardioversion is a major concern because of the expense and risk of cardioversion, the potential consequences of recurrent AF, and the poor performance and risk of type I antiarrhythmic drugs. Recurrence rates for type I agents have been about 60% at one year, which is what this study found with propafenone and the type III agent sotalol. The results with amiodarone were almost twice as good, with a 35% one-year recurrence rate. The relative efficacy of sotalol and propafenone was the same.

The major concern with amiodarone is long-term toxicity, which was somewhat greater than the other two drugs in this trial. However, there were no serious or life-threatening complications and, interestingly, more patients were still on amiodarone at the end of a year (72%) than the other two drugs (58%). Also, because AF was prevented more effectively by amiodarone, there were less strokes on it. Cardiac arrest due to torsade de pointes only occurred in one patient taking propafenone. Of course, the longer term potential adverse effects of amiodarone are a concern, but a larger, longer trial will be necessary to assess this issue because of the good prognosis of most patients with isolated AF.

The study was not powered for mortality, and little was observed. Also, there was no placebo group, because these were patients in whom the physician had already decided to cardiovert and try to maintain in sinus rhythm. In addition, the drug therapy was not blinded because of the differences in dosing regimens and the complexity of these agents. However, the primary end point was objectively documented recurrent AF, and unlikely influenced by the lack of blinding.

This study supports the concept that if drug therapy is deemed desirable for a patient undergoing cardioversion for AF, then low-dose amiodarone should be the first-choice agent currently, unless there are contraindications to its use. The real issue given the potential toxicity of amiodarone (and other antiarrhythmic agents) is whether prophylactic drug therapy should be given at all without a trial of no drug. Unfortunately, we do not know how many or which patients will recur on no therapy. Those who do will have to undergo cardioversion again and risk the complications of recurrent AF. There is evidence that the more AF you have, the less likely you will stay in sinus rhythm. This would argue for an aggressive approach with amiodarone for almost all. Perhaps the ongoing AF Follow-up Investigation of Rhythm Management Study by the NHLBI will answer this question. My current practice is to use amiodarone prophylaxis in higher risk patients for stroke and try no therapy first after cardioversion in lower risk patients. ❖

Amiodarone vs. ICD for Ventricular Tachyarrhythmias

ABSTRACT & COMMENTARY

Synopsis: *Amiodarone therapy results in a relative risk reduction in all-cause mortality that is similar to that reported in other studies.*

Source: Connolly SJ, et al. *Circulation* 2000;101: 1297-1302.

The canadian implantable defibrillator study (CIDS) was a randomized clinical trial looking at the relative effects of amiodarone therapy vs. implantable cardioverter defibrillator (ICD) therapy in patients with a history of known or suspected ventricular arrhythmias. Patients were eligible for the study if they had an episode

of one of the following: 1) cardiac arrest or ventricular fibrillation (VF), 2) sustained ventricular tachyarrhythmia (VT) causing syncope, 3) sustained VT at a rate of more than 150 bpm with an ejection fraction less than or equal to 35%, or 4) syncope of unknown origin with sustained VT documented at other times or induced by programmed stimulation. Patients were randomized to receive either ICD therapy or drug therapy with amiodarone. Initially, the ICD was implanted using a thoracotomy lead system but, early in the trial, improved technology permitted a switch to nonthoracotomy lead systems. Patients randomized to amiodarone were loaded with 1200 mg/day for one week or longer in the hospital. Subsequently, they received 400 mg/day for 10 weeks and then 300 mg/day. Additional antiarrhythmic drugs were permitted in both groups to control either supraventricular or nonsustained ventricular arrhythmias that were symptomatic. The primary outcome event was all-cause mortality. Arrhythmic death was a secondary event.

Between October 1990 and January 1997, 659 patients were entered into the trial. The group was predominantly (85%) male. Slightly less than half had survived an episode of VF or cardiac arrest. Slightly less than 40% had a history of sustained ventricular tachycardia and slightly more than 13% had unmonitored syncope. The mean left ventricular ejection fraction was 34%. About 80% had ischemic heart disease.

There were 328 patients who were randomly allocated to receive an ICD, but 18 patients did not receive one. The median time to ICD implant was seven days. A thoracotomy lead system was used in 33 patients. A nonthoracotomy system was used in 277 patients. There was one operative death in both groups. Among the 18 patients who did not receive an ICD, there were seven deaths in-hospital while awaiting surgery and 11 patients either decided against implant after randomization or a technical problem precluded a successful implant. During the course of the study, 16 patients had their ICD explanted because of infection, heart transplant, or patient preference. The percentage of patients randomized to an ICD who also began amiodarone therapy at one, three, and five years after randomization were 17.4%, 21.7%, and 28.1%, respectively.

Among patients randomized to receive amiodarone, all patients started therapy and at one, three, and five years, 88.7%, 80.3%, and 85.4% of surviving patients remained on therapy. The mean amiodarone dose at three years was 262 mg/day. Among the 331 patients in the amiodarone group, 52 (15.8%) also received an ICD.

Other antiarrhythmic drugs were added to both groups at hospital discharge. Beta-adrenergic blockers were prescribed in 21% of patients on amiodarone and in 34% of patients who received an ICD. Almost 20% of ICD patients were also receiving sotalol. This imbalance in concomitant drug therapy persisted throughout the trial. There was a 19.7% relative risk reduction with ICD therapy compared with amiodarone, with total mortality decreased from 10.2% per year to 8.3% per year ($P = 0.14$). There were also reductions in arrhythmic death and total cardiac death in the ICD group that did not reach statistical significance. The relative risk reduction for total mortality at one, two, and three years was 15.4%, 29.7%, and 13.7%, respectively. Net adverse effects to ICD therapy and amiodarone treatment were similar. Analysis of subgroups showed that the 95% confident intervals of hazard ratios for outcome of death from any cause overlapped for all subgroups examined.

Connolly and colleagues conclude that amiodarone therapy results in approximately a 20% relative risk reduction in all-cause mortality that is similar to that reported in other studies, particularly the Antiarrhythmics vs. Implantable Defibrillator (AVID) study.

COMMENT BY JOHN P. DiMARCO, MD, PhD

Approximately 10 years ago, three large multicenter trials were initiated to test whether ICD therapy was superior to drug therapy for patients with life-threatening ventricular arrhythmias. AVID, a study performed primarily in the United States, randomized slightly more than 1000 patients and showed that the ICD was superior to drug therapy with amiodarone or sotalol. CIDS, reported in this paper, is the second large trial to be fully reported. There were minor differences between AVID and CIDS. AVID allowed either amiodarone or sotalol to be used in the drug treatment group but most patients received the former. AVID did not allow patients with unmonitored syncope into the trial. About 13% of the patients in CIDS had this diagnosis. It is interesting to note that the point estimate for risk reduction in this group was the lowest observed. Most of the other outcome data are similar to those previously reported in AVID. There is less benefit with the ICD in patients with higher ejection fractions. The benefit of the ICD in absolute terms is modest. In this study, the absolute risk reduction at two years was a little more than 6%.

This paper may be a closer mirror of clinical practice than was the AVID protocol. In AVID, investigators were strongly discouraged from adding an antiarrhythmic drug to patients in the ICD group. In CIDS, antiarrhythmic drugs were used in more than half of the ICD patients. Other studies have shown that addition of an antiarrhythmic drug to ICD therapy has little effect on mortality but may decrease the frequency of shocks and make ICD therapy more acceptable.

There is a third study, the Cardiac Arrest Study Ham-

burg (CASH), which has been reported in preliminary form only. This study enrolled only patients with cardiac arrest and did not include patients with ventricular tachycardia without cardiac arrest. CASH has also reported a trend toward reduction in mortality in patients treated with the ICD. These three trials have been subject to a meta-analysis. The meta-analysis confirmed the benefit of ICD therapy over drug therapy.

In the future, the ICD should be the primary option for patients with life-threatening arrhythmias, with drug therapy used as either an adjunct to the ICD or as primary therapy for patients who decline ICD therapy or are poor candidates for it. ❖

Aspirin Plus Warfarin for Mechanical Valves

ABSTRACT & COMMENTARY

Synopsis: *Aspirin plus oral anticoagulants reduce thromboembolic events but not mortality in the first year after mechanical mitral valve replacement.*

Source: Laffort P, et al. *J Am Coll Cardiol* 2000; 35:739-746.

Despite improved valve design, cardiac embolic events are still a problem with mechanical mitral valve replacement, especially in the early postoperative period. Thus, Laffort and colleagues from Pessac, France, randomized 229 patients who received St. Jude mitral valve replacements to aspirin (200 mg/day) plus oral anticoagulants (OAC) to an international normalized ratio (INR) of 2.5-3.5, or OAC alone beginning 48 hours after surgery. Transesophageal echocardiography (TEE) was performed at nine days and five months post-surgery, and all patients were followed for one year. The primary end point of the study was death, major thromboembolic event, or major hemorrhage at one year. Major thromboembolic events included stroke, acute myocardial infarction (MI) with normal coronary arteries, and valve thrombosis. Minor thromboembolic events were also assessed and included valve strands, nonobstructive valve thrombi, and transient ischemic attacks. Major hemorrhages were those requiring transfusion, cerebral hemorrhage, and those requiring surgical repair. At nine days, there was no difference in the incidence of valve strands, but minor thrombi were less frequent in the aspirin group (13% vs 5%; P = 0.03). Minor thrombi were small and located on the atrial side of the sewing ring. At five months, there was a high incidence of strands in both groups (61%), but thrombi were infrequent and less in the aspirin group (4% vs 8%; P = NS). The primary end point was higher in the aspirin group (29% vs 17%; P = NS) mainly because of more major hemorrhages (19% vs 8%; P = 0.02). Minor thromboembolic events were less in the aspirin group (8% vs 21%; P = 0.007), as were total thromboembolic events (9% vs 25%; P = 0.001).

Table

One-Year Outcomes

Event	+ Aspirin	- Aspirin	P
Death	9%	4%	NS
Major hemorrhage	19%	8%	0.02
Major TE	1%	4%	NS
Primary end point	29%	17%	NS
Minor TE	8%	21%	0.007
Total TE	9%	25%	0.001
Total events	39%	38%	NS

TE = thromboemboli

Laffort et al conclude that aspirin plus oral anticoagulants reduce thromboembolic events but not mortality in the first year after mechanical mitral valve replacement because of an increase in hemorrhagic events.

COMMENT BY MICHAEL H. CRAWFORD, MD

Although optimal anticoagulation has markedly reduced thromboembolic complications with mechanical prostheses in the mitral position, the continued occurrence of thromboembolic events (7% in this study) has prompted the search for adjuvant agents. A decade or more ago, dypyridamole plus warfarin was popular, but carefully done studies showed no overall benefit and its use declined. More recently, aspirin has been studied with mixed results. This study is unique for several reasons: it is the largest randomized trial of adjuvant aspirin; it focuses exclusively on the St. Jude valve, which is now the most commonly used; it uses the new recommended INR range of 2.5-3.5 for the newer prostheses; and TEE was included in the evaluation. Unfortunately, the overall results do not strongly endorse adjuvant aspirin use.

Aspirin significantly reduced thromboemboli, especially if TEE-documented thrombi are included, but a sharp increase in major hemorrhages (largely gastrointestinal) negated the overall benefit. In the aspirin group, there was only one thromboembolic event to a peripheral artery, whereas in the warfarin-alone group, there were 5:4 strokes and one prosthetic valve thrombosis. As expected, late events were related to the INR achieved. Three-quar-

ters of the thromboemboli occurred in patients with INR less than 2.5 and three-fourths of the major hemorrhages occurred in patients with INR of more than 3.5. Thus, if INR could be controlled perfectly, complications could be reduced by 75%.

There were some limitations to this study. There was no placebo aspirin arm, but it is unlikely this influenced the results since there were no subjective end points. Also, it would have been interesting to see what 81 mg of aspirin would have done, but the American College of Chest Physicians' recommendations are for 160 mg, which is closer to the 200 mg used. In addition, it would be nice to know from the reoperated patients what the strands seen on TEE were, since aspirin did not influence their incidence. With a 60% incidence at five months, clearly these strands cannot be implicated in embolic events.

Although there was no overall benefit of adjuvant aspirin, the reduction in embolic events is impressive and raises the question of whether there might be subgroups in which the risk benefit ratio was more favorable for adding aspirin. Laffort et al did not fully explore this issue, but noted that a prior history of thromboembolic events predisposed to future events. Perhaps in such patients, the benefit would outweigh the risk. Other studies have shown that patients with concomitant coronary artery disease (CAD) may benefit from adding aspirin. Finally, those with visible thrombi on TEE predischarge may be candidates for aspirin, but this requires TEE in all postoperative mechanical mitral valve replacements. Such an approach would need to be shown cost-effective to be widely adopted. At this time, most cardiologists confine adjuvant aspirin in mitral mechanical valve replacement patients with CAD and usually use 81 mg/day. Perhaps the indications should be broadened to include other high-risk patients, but this concept remains unproven. ❖

Ablation for Ventricular Tachycardia

ABSTRACT & COMMENTARY

Synopsis: *Radiofrequency linear endocardial lesions can be used to disrupt ventricular tachycardia circuits in patients with ventricular tachycardia that cannot be mapped by standard techniques.*

Source: Marchlinski FE, et al. *Circulation* 2000; 101:1288-1296.

Marchlinski and colleagues report a new technique for catheter ablation of ventricular tachycardia (VT). Sixteen patients comprised the study group. All had frequent episodes of rapid monomorphic tachycardia that had led to multiple implantable cardioverter defibrillator (ICD) shocks. All patients had failed multiple drug trials and six had failed prior ablation attempts. These 16 patients constituted one-third of the patients referred to Marchlinski et al's laboratory for catheter ablation of VT during the study period.

Nine patients had VT in the setting of prior myocardial infarction (MI) and seven had nonischemic cardiomyopathy. Patients were taken to the electrophysiology laboratory and underwent detailed voltage mapping during sinus rhythm. Only the left ventricle was mapped in patients with prior MI, but both the right and left ventricles were mapped in patients with nonischemic cardiomyopathy. Three patients had mapping and ablation performed using a standard thermistor ablation catheter. The next 13 patients underwent mapping using a magnetic mapping system (CARTO, Biosense, Inc.) that allows electroanatomic confirmation of catheter position in three dimensions. Reference values for electrogram amplitude were established for distinguishing between normal and abnormal electrograms using both systems. After determination of the area of interest, linear lesions were placed across the borders of the endocardium that demonstrated abnormal electrogram voltage, and through border zones at sites where pace mapping approximated the electrocardiographic wave (QRS) morphology of VT. Ablation was performed using sequential point lesions to create linear ablation lines. This was done using fluoroscopic guidance in the first three patients and using three-dimensional magnetic mapping in the last 13. Programmed stimulation was performed at the end of the procedure. VT recurrences during clinical follow-up were identified by device interrogation and/or report of symptoms.

The number of endocardial sites mapped was more than 200 in all patients. Large areas with abnormal electrograms were present in both patients with coronary artery disease (CAD) (65 ± 24 cm^2) and in the right ventricle of those with nonischemic cardiomyopathy (60 ± 36 cm^2). A median of 55 radiofrequency lesions was applied per patient. These were used to create one to nine (median, 4) linear lesions. The average length of the linear lesion was 3.9 cm with a range of 1.4 to 9.4 cm. Linear ablation was effective in suppressing all inducible VT acutely in seven of 15 patients. The induced VTs in the remaining patients matched the cycle length or morphology of the clinical arrhythmia in five patients and was different in three. Procedure time ranged from six to 13.5 hours. There was no significant change in left ventricular ejection fraction in six patients who had measurements

before and after ablation. One patient experienced a cerebral vascular accident at the end of the procedure.

The minimum period of follow-up was three months. Three of the 16 patients died at three, four, and eight months after the procedure from refractory heart, pneumonia, or complications of abdominal surgery. Fifteen of 16 patients remained free of VT during the initial follow-up month and 12 of 16 patients have been free of any recurrent VT during the entire follow-up period.

Marchlinski et al conclude that radiofrequency linear endocardial lesions can be used to disrupt VT circuits in patients with VT that cannot be mapped by standard techniques. Electroanatomic mapping aids in the placement of these lines.

COMMENT BY JOHN P. DiMARCO, MD, PhD

The current standard approach for mapping and ablation of VT in patients with prior MI or ischemic cardiomyopathy involves induction of the tachycardia and subsequent entrainment mapping. Entrainment mapping requires a tachycardia that does not produce severe hypotension or hemodynamic collapse since the patient must remain in tachycardia for long periods to allow the catheter manipulation and pacing to generate an entrainment map. Only a small fraction of patients with VT can tolerate this procedure and this has limited the application of ablation therapy in patients with VT and structural heart disease. The procedure outlined by Marchlinski et al provides an alternative approach in these patients.

The concept underlying this procedure is reminiscent of the surgical approaches previously used in patients with VT and coronary artery disease (CAD). The subendocardial resection approach involved resection of all visible scar and was associated with an arrhythmia cure rate of 70-80% even if little or no intraoperative mapping was performed. However, the amount of surgery required often was extensive. This produced an adverse effect on ventricular function, and late heart failure was common. As ICD therapy has improved, the frequency of this type of surgery has declined. The encircling endocardial ventriculotomy tried to use a near full thickness excision around the area of scar to control VT. This operative approach has also largely been abandoned due to adverse effects on ventricular function. The approach described here seems to produce the same electrical results as those two surgical procedures without the expense of surgery and without producing any significant deterioration in hemodynamic function.

The electroanatomic mapping technique certainly was helpful for guiding the placement of the lesions. However, this technique still involves mapping a large number of individual points. This requires long periods of catheter manipulation and increases the risk of the procedure. Alternate approaches using either noncontact mapping or basket mapping of an entire chamber might allow the voltage maps necessary to locate the densely scarred areas to be generated more quickly. The major time requirement then would be for placement of linear lesions. Catheter designs now being tested for linear ablation of atrial fibrillation might also be helpful here. Further development of these catheters has the potential to shorten the time for these procedures.

The results reported by Marchlinski et al are impressive. It remains to be seen whether this technique can be streamlined and made applicable to larger numbers of patients. The combination of ICD therapy for disorganized arrhythmias and an ablation technique such as this for organized but previously unmappable tachycardias would be a major advance. ❖

CME Questions

25. The most effective agent for prevention of atrial fibrillation recurrence is:
a. amiodarone.
b. propafenone.
c. sotalol.
d. flecainide.

26. Recent trials suggest that life-threatening ventricular arrhythmias are best treated with:
a. sotalol.
b. amiodarone.
c. beta blockers.
d. ICD.

27. In patients with mechanical mitral valve replacement, the addition of aspirin to warfarin should be considered with:
a. visible thrombi on echo.
b. a history of prior thromboemboli.
c. coronary artery disease.
d. All of the above

28. Which approach shows promise for catheter ablation of VT?
a. Entrainment mapping during VT
b. Electroanatomic magnetic mapping
c. Fluoroscopy to detect aneurysms
d. All of the above

29. Secondary prevention of CAD progression in older women is best accomplished with:
a. estrogen.
b. lipid-lowering drugs.
c. calcium channel blockers.
d. antibiotics.

30. The strongest indication for IV platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes is:
a. left bundle branch block.
b. immediate percutaneous coronary intervention.
c. elevated troponin.
d. b and c