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Timing of Aortic Valve Replacement in Aortic Stenosis

ABSTRACT & COMMENTARY

Synopsis: *Individuals with aortic stenosis without valve calcification are a low-risk subgroup and may remain event-free for many years.*

Source: Rosenhek R, et al. *N Engl J Med* 2000;343:611-617.

In 1997 otto and associates reported a prospective study of asymptomatic individuals with valvular aortic stenosis.1 They concluded that one of the most important factors predicting the need for ultimate aortic valve replacement (AVR) was a peak aortic valve velocity of more than 4 m/sec by Doppler echo. In addition, the rate of yearly progression of aortic valve narrowing was an important factor. This new study adds additional information to the sometimes difficult problem of deciding when to intervene in a patient with severe aortic stenosis who has no symptoms. This is a prospective analysis from Vienna that followed 128 asymptomatic patients with severe aortic stenosis. All had a mean aortic velocity greater than 4 m/sec; the mean baseline velocity was 5.0 ± 0.6 m/sec. Left ventricular function was preserved. Conventional echocardiographic clinical parameters were carefully noted; subjects were followed from 1994 to 1998. Two patients were lost to follow-up and 22 of the initial 128 patients underwent elective AVR within three months of enrollment in the study. The primary end point was cardiovascular death or need for AVR in the remaining106. Follow-up was 22 ± 18 months.

A total of eight deaths and 59 AVRs occurred because of development of symptoms. Kaplan-Meier curves indicated that event-free survival was poor, although the death rate was low. Of the entire group, 33% had an AVR by year one, 44% by year two, and 67% by four years. There was only one sudden death not preceeded by symptoms. Other deaths were due to aortic valve complications in symptomatic patients. Of the 59 patients who underwent AVR, the follow-up period was 28 ± 15 months. Overall acturial probability of survival was 93% at one year and 87% at four years.

Predictors of outcome included age older than 50, coronary artery

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disease, and diabetes. However, only older age affected long-term results (event-free survival for patients younger than 50 was 85% at one year and 60% at four years; for patients older than 50, (59% at 1 year and 21% at 4 years). A major predictor of outcome was the extent of aortic valve calcification. Individuals with moderate to severe calcification did poorly, and all deaths occurred in this group. Patients with no or mild calcification did well; 92% event-free at one year and 75% at four years, compared to 60% and 20% respectively, for those with significant calcification. No events occurred in 11 patients without demonstrable calcification on echocardiography with a mean follow-up of over three years. Aortic valve velocity was only slightly higher in those who had cardiac events; however, the rate of progression of velocity increase was greater in patients who had cardiac events (0.45 ± 0.38 vs 0.14 ± 0.18 m/sec/y [$P < 0.001$]). Among patients with a heavily calcified valve, the outcome was poor with an event outcome comparable to those older than 50 years. Severe aortic valve calcification and a rapid increase in aortic jet velocity identified a high-risk group. Those with an increase of 0.3 m/sec within one year and significant calcification had an 80% likelihood of need for surgery or death within two years.

Rosenhek and colleagues comment that their data and other studies show that sudden death may occur in the absence of overt symptoms in patients with severe aortic stenosis but is uncommon and is estimated to be less than 1% per year. Conversely, patients who develop symptoms required surgery within a very short time period. Factors that predict outcome in previous studies include aortic jet velocity, ejection fraction, and functional status, but not all trials reached the same conclusion. This study emphasizes the importance of extensive valve calcification. Rosenhek et al conclude that an annual echocardiogram is important in patients with asymptomatic aortic stenosis, and it is "relatively safe to delay surgery until symptoms develop." Surgical outcomes were less optimal in individuals who became symptomatic. They conclude that individuals with aortic stenosis without valve calcification are a low-risk subgroup and may remain event-free for many years. The majority of rapid progressors will require an AVR or will die within several years, and such individuals should be carefully monitored.

COMMENT BY JONATHAN ABRAMS, MD

This study adds to the important database of Otto et al. which did not report calcification as an independent risk factor, but this was an important observation in the Austrian study. Older age is clearly a risk factor, although it may be confounded by the ubiquity of calcification in individuals older than 50-60 years. In an accompanying editorial, Otto stresses that calcific aortic valve disease is not merely a denegerative condition of aging but "represents the end stage of active disease process." She emphasizes the depostion of lipoproteins, macrophages, and T-lymphocytes in the aortic valve, with osteopontein production in regions of macrophage concentration. She estimates that 25% of adults older than age 65 have aortic sclerosis, a small number of whom will progress to aortic stenosis. Clinically significant aortic stenosis is present in 1-2% of subjects older than 65. Any individual with a prominent systolic ejection murmur in this age group should undergo echocardiography, as it is often difficult to differentiate aortic sclerosis with aortic stenosis in the elderly. Otto also focuses on the presence or the absence of symptoms as being a primary determinate of outcome. "In contrast, adults with asymptomatic aortic stenosis have an excellent clinical prognosis." Velocity progression in the Austrian study 0.3 m/sec per year and/or a decrease in aortic valve area of $0.1 cm^2$ per year is to be expected, with wide individual variation.

In conclusion, patients with moderately severe to severe aortic stenosis without symptoms can be safely followed with serial echocardiography, but when severe calcification is present, or there is left ventricular dysfunction, consideration of preemptive surgery should be given. This study confirms that a rapid increase in the aortic valve velocity on serial echo should be a signal for

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surgery. Sudden death is rare in these individuals but may occur. For the clinician, a combination of a careful examination, history taking, and the use of high quality 2-D echocardiography should make the decision of when to intervene relatively straightforward, based on the data accumulated in these two important recent studies. ❖

Reference

1. Otto CM, et al. *Circulation* 1997;95:2262-2270.

Cardiac Tamponade During PCI

ABSTRACT & COMMENTARY

Synopsis: *Cardiac tamponade following percutancous coronary intervention occurs 0.2% of the time and often occurs later outside the catheterization laboratory. Since about half were related to temporary pacing wires, this practice needs to be reexamined.*

Source: Von Sohsten R, et al. *Am Heart J* 2000; 140:279-283.

Although cardiac tamponade is a rare complication of cardiac catheterization, many believe it is occurring more frequently in the modern percutaneous coronary intervention (PCI) era. Thus, Von Sohsten and associates prospectively analyzed their PCI complication registry for cardiac tamponade between 1994 and 1996 in 6999 patients undergoing PCI at a single university hospital. Within 36 hours of PCI, 15 patients experienced cardiac tamponade (0.2%)—six during the procedure. The median age of the patients was 72 years and 60% were women. All had received heparin, but only three received abciximab. None of the 14,927 diagnostic catheterizations during the same period resulted in tamponade. The site of perforation could be identified in 13 of the 15 cases: coronary lesion site in five; distal coronary wire perforation in three; and right ventricular perforation by a temporary pacing wire in five. The two in whom the site of perforation could not be visualized also had temporary pacing wires. The incidence of tamponade per 1000 patients was 0.3 for balloon angioplasty, 2.3 for stents, 3.2 for either DCA or TEC, and 10.8 for rotational atherectomy. Echocardiography was useful for diagnosis and surgical treatment was required in 60% of the patients. There were no in-hospital deaths. Von Sohsten et al concluded that cardiac tamponade following PCI occurs 0.2% of the time and often occurs later outside the catheterization laboratory. Since about half were related to temporary pacing wires, this practice needs to be re-examined.

COMMENT BY MICHAEL H. CRAWFORD, MD

The experience of this group suggests that cardiac tamponade complicating cardiac catheterization procedures has increased 5- or 6-fold in the multiple device coronary intervention era. Of interest, half of the cardiac tamponade complications they observed were probably due to right ventricular perforation by a temporary pacing wire. The risk of perforation by pacemaker wires and other electrodes is well known. Some reports in the early years of electrophysiology procedures suggested incidences as high as 5%! Thus, in the precoronary device era, prophylactic pacemaker use had declined; however, the advent of complex coronary device interventions has increased prophylactic pacing use again. After this study, Von Sohsten et al's group re-evaluated their use of prophylactic pacing. They are now more selective in whom they use pacing back-up and they use five or six Fr balloon tipped catheters, leaving the balloon up unless they need to pace.

Other factors may play a role in the risk of cardiac tamponade. They noted that it was more frequent in the elderly and women. Therefore, the approach to these patients should take this risk into consideration. Increased use of anticoagulants, antithrombics and thrombolytics could explain the increased frequency, but it did not appear so in this study. Finally, two-thirds of the cases occurred after the patient left the lab, usually in the first eight hours. They recommend that tamponade be suspected if a post-procedure patient becomes hypotensive and an echocardiogram done immediately. Also, early discharge of patients after aggressive PCI procedures is probably not a good idea. ❖

New ACLS Guidelines

ABSTRACT & COMMENTARY

Synopsis: *The new AHA guidelines make appropriate changes in recommendations for acute therapy of several arrhythmias.*

Source: No authors listed. *Circulation* 2000;102:I112-I128.

The revised guidelines for advanced cardiovascular life support (ACLS) have reevaluated the role of antiarrhythmic drugs in the acute management of tachycardias.

The guidelines begin by stating that accurate electo-

cardiogram (ECG) diagnosis is the key to the appropriate pharmacologic management of patients with sustained arrhythmias; however, it should be recognized that overly complex ECG diagnostic algorithms are difficult to teach, learn, remember, and apply. Recognition of atrioventricular (AV) dissociation when possible, is very useful but a 12-lead ECG is usually required. In many emergency medical systems (EMS), a 12-lead ECG is not readily obtainable. Therefore, for those who are not cardiovascular specialists, ECG analysis should stress simplicity (e.g., rate, regularity, wide or narrow) rather than complex features. It is safer to misdiagnose supraventricular tachycardia (SVT) as ventricular tachycardia (VT) than the converse.

Lidocaine has traditionally been the first-line agent chosen for treating a patient with a wide complex tachycardia. The new guidelines cite studies showing that lidocaine is less effective than other drugs (e.g., IV procainamide, sotalol, or amiodarone) in patients with VT, and lidocaine is now relegated to second-tier therapy in the new tachyarrhythmia management algorithms.

Adenosine retains its place in the management of paroxysmal SVT, but cautions are now given concerning potential toxicity when adenosine is used in wide complex tachycardias not known to be supraventricular in origin. Rare cases of angina, hypotension, and proarrhythmia have been reported, and it is now recognized that adenosine should not be used indiscriminately for diagnostic purposes.

Amiodarone has been added to the new tachyarrhythmia management algorithms. It is particularly useful in patients with severely compromised ventricular function. Use of IV amiodarone is now recommended for patients with hemodynamically stable and unstable VT and for wide complex tachycardias of uncertain origin. Amiodarone is now also recommended in ventricular fibrillation (VF)/pulseless VT when initial attempts at electrical defibrillation have been unsuccessful.

Bretylium was formerly included in ACLS algorithms for unstable VT and VF. After review of available data on the use of bretylium, the new guidelines no longer include use of bretylium since there are limited data showing it is effective while its use is frequently associated with toxicity.

COMMENT BY JOHN P. DIMARCO, MD, PHD

The new AHA guidelines make appropriate changes in recommendations for acute therapy of several arrhythmias. Within the last 15 years, we have learned much about the electrophysiologic substrates and mechanisms responsible for arrhythmias. Clinical trial data are now available on which to base recommendations. The goal is now to use drugs with actions specific for the arrhythmia and patient being treated. For supraventricular tachyarrhythmias, adenosine and calcium channel blockers are the drugs of choice for effective manipulation of AV nodal conduction leading to either termination or effective rate control. Treatment of ventricular arrhythmias has been a more difficult topic to study since the patients are frequently unstable and/or unable to give consent. In hemodynamically tolerated patients, misdiagnosis of VT as SVT often led to the inappropriate administration of adenosine or a calcium channel blocker, occasionally with severe adverse consequences. The guidelines now appropriately caution against this practice. Since these arrhythmias most frequently arise in scarred muscle, the guidelines now recognize that use of IV procainamide, sotalol and amiodarone are likely to be more effective and these agents should be the drugs of choice.

Finally, the removal of bretylium for the ACLS guidelines is certainly appropriate and long overdue. The data supporting bretylium as an antiarrhythmic drug were old and clearly flawed. In view of the lack of evidence documenting efficacy, the high occurrence of toxicity means that bretylium should have no role in arrhythmia management. ❖

Reference

1. Kudenchuk PJ, et al. *N Engl J Med* 1999;341:871-878.

Initial Energy for Cardioversion of Atrial Fibrillation

ABSTRACT & COMMENTARY

Synopsis: *Patients with persistent atrial fibrillation an initial 360J shock for elective cardioversion is safe, much more effective than lower energy levels, and results in less cumulative energy delivery to achieve sinus rhythm.*

Source: Joglar JA, et al. *Am J Cardiol* 2000;86: 348-350.

Despite its widespread use, the initial energy setting for direct current cardioversion of atrial fibrillation is controversial. Thus, Joglar and associates studied 64 patients who had been in atrial fibrillation for more than 48 hours and were referred for elective cardioversion. Initial energy settings were randomized between 100, 200, and 360J and the electrodes were placed in an anteroposterior orientation. If the first shock

was not successful, the next level was tried or 360J with pressure to the anterior pad or 360J with an anterior-apex electrode orientation. The limit was five shocks. Immediately after cardioversion and the following day, troponin I measurements were made in 15 patients in whom the 360J level was reached. The success rate for the initial shocks were: 100J, 14%; 200J, 39%; 360J, 95% ($P < .001$). The overall conversion rate was 94%. Of the 13 patients in whom the 360J initial shock was unsuccessful, six were successful with chest pressure and another three with switch to an apical pad. Because of multiple shocks in some patients, the total energy delivered was : 615J for the 100J group; 620J for the 200J group; and 414J for the 360J group. None of the 15 high-energy shock patients had troponin I levels greater than 0.4 ng/mL and there were no serious complications observed. Joglar and colleagues concluded that in patients with persistent atrial fibrillation an initial 360J shock for elective cardioversion is safe, much more effective than lower energy levels, and results in less cumulative energy delivery to achieve sinus rhythm.

COMMENT BY MICHAEL H. CRAWFORD, MD

In the era of a more aggressive approach to atrial fibrillation, elective direct-current cardioversion is being performed more often. The American Heart Association Advanced Life Support document suggests an initial energy level of 100J. My own experience suggests that 200J is the minimally effective dose, so I was not surprised at the results of this study. This study is robust for several reasons. It is a randomized trial of different starting levels. Previous step-up trials, where all patients start at lower energy shocks first, favor the success rate of lower energy shocks because of chance, since the patients get more low-energy shocks. Such studies have suggested that 200J is a good starting energy. Also, they studied only patients in atrial fibrillation for more than 48 hours, which eliminates those that are more likely to spontaneously convert. Such patients probably convert with lower energies.

It is interesting that the editor of the *American Journal of Cardiology* must have thought this was an important paper since two editorials accompany it. Neither refutes the findings and both cautiously endorse the approach. The one caveat mentioned is that current external defibrillators use a monophasic damped sinusoidal waveform, whereas internal defibrillators use a biphasic waveform that is believed to be superior. Biphasic external defibrillators are now before the FDA for approval and may decrease the initial energy needs for atrial fibrillation conversion.

Another important feature of this study is that no myocardial injury was detected by troponin I in the high-dose shock group. Previous studies have suggested that troponin elevations will be occasionally detected with cumulative shocks greater than 600J. This supports the 360J start, since in this study it reduced total J delivered to an average of 400J. Another advantage of the 360J start is it allows for alternate strategies that in this study increased the success rate from 80% to 94%. One strategy was hand pressure on the sternal pad. This seems to fly in the face of the "clear!" concept, but is apparently safe for the operator since a colleague of mine routinely does this. I thought he was just trying to impress the medical students, so I was surprised to learn that this is an accepted strategy for successful cardioversion. The second strategy used was moving the pads to a sternum-apex position. I have observed that when the technician or residents place the electrodes, they often line them up in a way more conducive to ventricular defibrillation. I try to line them up so that the energy goes through the atria. Finally, only about one-third of the patients were on anti-arrhythmic drugs before cardioversion. This is consistent with clinical practice and suggests that drugs do not play a big role in conversion, but are probably more important for maintenance of sinus rhythm. In conclusion, my new approach is 360J (in a normal-sized person) and leaning on the sternal pad for initial cardioversion of chronic atrial fibrillation. ❖

The Cardiac Arrest Study Hamburg

ABSTRACT & COMMENTARY

Synopsis: *Implantable cardioverter defibrillator therapy results in a modest reduction in all-cause mortality and a larger reduction in sudden death mortality compared to the mortality rate seen in drug-treated groups. The reductions are most apparent in the first five years of therapy and become less prominent over time.*

Source: Kuck KH, et al, for the CASH investigators. *Circulation* 2000;102:748-754.

The cardiac arrest study hamburg (cash) initially randomized survivors of cardiac arrest in four treatment groups: amiodarone, metoprolol, propafenone, and implantable cardioverter defibrillators (ICD). The primary end point for the trial was all-cause mortality with sudden cardiac death and recurrent cardiac arrest being secondary end points.

A total of 349 patients were entered into the trial between 1987 and 1996. Assignment to propafenone was

discontinued in 1992 after a preliminary analysis showed a higher mortality in the treatment group. The final study included 99 ICD patients, 92 amiodarone patients, and 97 metoprolol patients. Their mean age was 58 ± 11 years, 80% were male, 73% had coronary artery disease, and 10% had no structural heart disease. The index arrhythmia was ventricular fibrillation (VF) in 84% and ventricular tachycardia (VT) in 16%. The average left ventricular ejection fraction was 46%. Both epicardial (55 patients) and endocardial (44 patients) ICD systems were used. Daily maintenance doses of amiodarone and metoprolol were 225 ± 75 and 85 ± 73 mg, respectively. During a mean follow-up of 57 ± 34 months, the crude mortality rates were 36% in the ICD group and 44% in the combined amiodarone/metoprolol group. This difference was not statistically significant (P = 0.081; hazard ratio 0.77). Although the death rate was decreased in the ICD group by more than 25% in each of the first four years of follow-up, less differences were seen at later time points. The secondary analysis of sudden death survival did show a significant advantage in the ICD group (13% vs 33%; P = 0.005). Interestingly, there was no difference between the amiodarone and metoprolol subgroups in either total or sudden death mortality.

There were five deaths associated with ICD implantation and 23% of the ICD patients experienced one or more nonfatal complications. No serious toxicity was noted in either the amiodarone or the metoprolol groups.

Kuck and associates conclude that ICD therapy results in a modest reduction in all-cause mortality and a larger reduction in sudden death mortality compared to the mortality rate seen in drug-treated groups. The reductions are most apparent in the first five years of therapy and become less prominent over time.

COMMENT BY JOHN P. DiMARCO, MD, PhD

CASH is the third of the large, randomized, clinical trials that compared ICD use to drug therapy in patients resuscitated from sustained ventricular arrhythmias. CASH differs from the two previously reported North American trials (AVID and CIDS) in that only cardiac arrest survivors could be enrolled and patients with hypotensive VT were excluded. This resulted in a study group that was younger and included more patients without structural heart disease than the group in the other trials. Unlike those studies, CASH did not show a statistically significant improvement in survival in the ICD group. However, this study was underpowered to detect a clinically meaningful difference, so its results must be considered in the context of the other trials.

Despite the fact that this study cannot stand solely on its own, CASH does provide some interesting insights. First, it is clear that a group of out-of-hospital cardiac arrest survivors is different from a group comprising patients with both cardiac arrest and sustained VT. The latter group will have more recurrent arrhythmias, a higher total mortality rate and lower ejection fractions. When planning the sample size for any study, these factors must be considered. Second, it is interesting that amiodarone and metoprolol were not different. Amiodarone is certainly more useful in sustained VT patients but the effects of beta-adrenergic blockade may be of more importance in preventing death and VF. Finally, it must be noted that the ICD group had a relatively high rate of both fatal and nonfatal device complications. Presumably, most of these occurred with the epicardial ICD systems that were used early in the trial. Without these early deaths, it seems likely that the advantages of ICD therapy would have reached statistical significance. ❖

Estrogen Replacement in Coronary Artery Disease: More Bad News

ABSTRACT & COMMENTARY

Synopsis: *Women with heart disease should not use conjugated estrogen, alone or in combination with medroxyprogesterone acetate, with an expectation of cardiovascular benefit.*

Source: Herrington DM, et al. *N Engl J Med* 2000;343: 522-529.

The heart and estrogen/progestin replacement Study (HERS) was a major disappointment for health care providers.[1] Examination of other databases as well as an early report from the Womens' Health Initiative appear to support the HERS data, suggesting a potential adverse outcome in the first year or two following hormone replacement therapy (HRT) initiation. The ERA study represents another important look at this issue. Herrington and colleagues at six centers, randomized 309 postmenopausal women with documented coronary disease to estrogen (E), progesterone (P), E plus P, or placebo. The primary end point was angiographic progression of atherosclerosis (mean minimal coronary artery diameter). Secondary end points were related to angiographic factors. In addition, clinical events were tracked. Eligible women had to have at least one greater than 30% narrowing of a major epicardial artery and be postmenopausal for five

years. Follicle-stimulating hormone (FSH) levels were used to confirm absence of estrogen activity; most subjects were older than 55 years of age. Obvious contraindications to estrogen therapy were exclusion criteria, as well as uncontrolled hypertension or diabetes. A second angiogram was available for review in 248 or 80% of the initial cohort. The mean follow-up between the first and second angiogram was 3.2 ± 0.6 years. Compliance to therapy was highest in the E ± P and placebo groups (85% compared to E alone of 75%). Subjects were followed with annual mammography and gynecological examination including measurement of uterine wall thickness. The baseline population had a mean age of 66 (range, 42-80). Hormone replacement reduced LDL cholesterol by 9.4% and 16.5 % in E ± P and E alone, respectively. HDL levels increased by 14-19% and triglcyerides rose 6-10% in both active treatment groups. Insignificant changes were noted with placebo. Primary analysis of 2317 proximal coronary segments (mean of 9.3 per patient) showed no significant differences in minimal diameter change from baseline in the active-treatment and placebo groups, nor in the increase in percent stenosis. Adjustments were made for a variety of variables, and the analysis remained the same. New lesions developed in 30% of E and 20% of E and P, vs. 33% of placebo women. Baseline segments with minimal to no angiographic disease showed no differences over time among the three groups. There was considerable uterine bleeding in the unexposed E women, who had a greater incidence of uterine hyperplasia. Cancer or fractures were not different among the groups, although there was a trend for more fractures in placebo patients. Clinical events were no different among the groups; those who underwent coronary revascularization were equally distributed. Herrington et al conclude that estrogen replacement had no effect of slowing progression of coronary atherosclerosis in these women, consistent with the HERS trial. They point out that E alone vs. E ± P made no difference in the results. This raises the possibility that estrogen may be "more effective in preventing the development of atherosclerosis than in slowing the progression of disease." In the absence of new clinical trial data, they conclude that "women with heart disease not use conjugated estrogen, alone or in combination with medroxyprogesterone acetate, with an expectation of cardiovascular benefit."

COMMENT BY JONATHAN ABRAMS, MD

This important study first reported at the American College of Cardiology meetings in March 2000, provides additional evidence that HRT is not beneficial for slowing coronary heart disease, in spite of the large epidemiologic and observational database, as well as a considerable basic and animal science. While the ERA trial does not suggest harm, it had a relatively short follow-up with a small cohort. For instance, only 204 patients took active hormone treatment compared to 105 placebo women. In contrast to HERS, no adverse early clinical events were noted. The side effects of vaginal bleeding and uterine hyperplasia are well known in women who take unprotected estrogen without a progestin. HERS and ERA, two major estrogen trials reported within the past 18-24 months, represent the only available randomized clinical trial database and are overwhelmingly neutral to negative with respect to benefits of HRT in women with established coronary artery disease (CAD). In both of these studies, women were well into their sixties with established vascular disease at baseline. It may be that initiation of HRT much earlier in the lifespan of coronary atherosclerosis, with dominant early lesions or no angiographic coronary atherosclerosis, might have different results, particularly over a long follow-up period of 5-10 years. Perhaps the Women's Health Initiative will be fruitful, although the results will not be available for many years. A number of ongoing trials remain, some of which are angiographic in nature, examining the benefits of HRT in women. As of now, one must agree with the conclusion of Herrington et al, as well as many other experts, that physicians should not specifically prescribe hormone replacement treatment to women with vascular disease with the hopes of slowing progression of CAD.

The angiographic data in ERA contrasts with the many lipid lowering trials using similar methodologies. These individually, and in the aggregate, have consistently shown slowing of disease progression with statins. In addition, the overall experience in these regression studies have predicted event reductions that were subsequently shown in the large, randomized, clinical trials using statins, such as 4S, CARE, LIPID, representing thousands of patients with established CAD. The mechanisms for failure of HRT to support published experimental and observational data are unknown. Recent animal and human data indicate a pro-inflammatory effect of estrogen; several studies have documented elevated c-reative protein (CRP) levels in women using estrogen that may reflect more activation of CAD. Herrington et al suggest that estrogen benefits on the vessel wall may be seen primarily in women who have a relatively healthy endothelium. Thus, initiating HRT in women with

established vascular disease, long-standing hypertension, or in the elderly, may lead to disappointment. Data in younger women with mild to no disease is unavailable. In conclusion, HRT should not be administered solely in hope of preventing or slowing coronary disease. However, the benefits of hormone therapy for women who have postmenopausal symptoms, genital/urinary problems relating to estrogen deficiency or osteoporosis, are well established. The risk of breast cancer with HRT remains controversial and at best is only a modest one. Furthermore, some evidence suggests that women who develop breast cancer who are taking estrogen may have a more benign form of the disease. Experimental data regarding dementia and HRT is of interest, but it is too preliminary to know if prevention of cognitive dysfunction will ultimately turn out to be an indication for estrogen or estrogen surrogates. ❖

Reference

1. Hulley S, et al. *JAMA* 1998;280:605-613.

CME Questions

18. Hormone replacement therapy is indicated for postmenopausal women with:
a. perimenopausal symptoms.
b. severe coronary artery disease.
c. greater than three risk factors for.
d. None of the above

19. Indicators for consideration of aortic valve replacement in aortic stenosis are:
a. symptoms consistent with aortic stenosis.
b. Doppler aortic velocity greater than 4 m/sec.
c. marked aortic valve calcification.
d. All of the above

20. The procedures most likely to result in cardiac tamponade are:
a. rotational atherectomy.
b. temporary pacing.
c. balloon angioplasty.
d. a and b

21. The best initial strategy for successful cardioversion of atrial fibrillation is:
a. 200J, anterior-apex electrodes.
b. 200J anteroposterior (A-P) electrodes.
c. 360J, A-P electrode.
d. 360J, A-P electrodes, pressure on anterior pad.

22. Which of the following new ACLS guidelines are recommended for initial therapy of wide complex tachycardia:
a. lidocaine IV.
b. procainamide IV.
c. bretyluim IV.
d. adenosine IV.