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CLINICAL CARDIOLOGY ALERT

A monthly update of developments in cardiovascular disease

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Late Breaking Trials From the AHA Meeting

CONFERENCE COVERAGE

Editor's Note: *The following reports from the annual scientific session of the American Heart Association held Nov. 12-15, 2000, in New Orleans, La., were obtained by handwritten notes, discussions with investigators, and news reports. No peer reviewed publications of these trials are available.*

VAL-HEFT Trial

Angiotensin receptor blockers (arb) have been available for a number of years, but their efficacy, with respect to angiotensin converting enzyme inhibitors (ACEI), remains unclear. ARBs are indicated for ACEI intolerant individuals, but direct comparisons have been few and inconclusive. VAL-HEFT, a long-awaited congestive heart failure (CHF) randomized trial was carried out in 5010 patients with class II-III CHF; 45% had coronary artery disease and 60% were NYHA class II, 55% were class III. Subjects all had increased LV dimensions; mean ejection fraction was 27%. Medications: 92% were on an ACEI, 85% diuretic, and 60% were on digoxin at baseline; 34% were on a beta-blocker. This was an international trial conducted in 300 centers in 16 countries. Patients were randomized to the ARB valsartan (VAL) or placebo (PLAC). Mean follow-up was 27 months. The primary end point was all- cause mortality and time to death, as well as a combined end point of all-cause mortality and major morbidity. The average dose of baseline ACEI was 18 mg/d for enalapril or its equivalent. The average dose of valsartan was 254 mg/d. Blood pressure decreased by 5-6 mm Hg in the VAL cohort over 30 months and by 2-3 mm Hg in the placebo (PLAC) group. The results were negative for the first end point of all-cause mortality (19.7% VAL vs 19.4% PLAC), but were positive for the combined end point of mortality and morbidity, 28.8% VAL vs. 32.1% PLAC, resulting in a relative risk reduction of 0.87 (P = 0.009). The major component of the composite end point was reduced hospitalization for CHF with VAL, which occurred in 9% of the VAL cohort patients vs. 18.5% of PLAC, a risk reduction of 37%

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INSIDE

(P = 0.00001). There was early curve separation for both end points. Mortality rate in this cohort of class II-III patients was approximately 10% per year. There were no differences in outcomes related to age, sex, ejection fractions below or above 27%, or etiology of heart failure. In patients who were on ACEI at baseline, the primary end point reduction was 12-13%, whereas there was a 45% reduction with VAL in the 7% of individuals who were not on an ACE inhibitor. All patients were stratified for beta-blocker use; at the time of randomization, 35% of patients were on a beta-blocker. In those individuals who were on beta-blockers at entry, there was no reduction in either primary end point. However, for the 65% of individuals not taking a beta-blocker, there was a 22% reduction in the composite end point, which was statistically significant. A variety of secondary end points, including NYHA class, dyspnea and fatigue, and edema, all tended to be more favorable on VAL. Major adverse events were comparable—approximately 10% in each cohort. In conclusion, combination therapy with an ACE inhibitor and VAL resulted in a decrease in mortality and morbidity by 13%; a decrease in repeat hospitalization for congestive heart failure of 27%; and a decrease in NYHA class and an increase in quality of life. Benefits of valsartan were seen across all degrees of heart failure.

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COMMENT BY JONATHAN ABRAMS, MD

VAL-HEFT appears to answer at least one issue related to ACEI and ARB therapy: Greater angiotensin II blockade does not appear to affect survival more than therapy with ACEI alone. Hypotheses regarding breakthrough of angiotensin II and aldosterone in patients on ACEI, as well as more potent interference with the angiotensin II receptor, did not appear to make a major difference in this large, well conducted trial. Furthermore, of great interest is the observation that an ACEI and a beta-blocker eliminated the benefit of VAL on the combined end point, also suggesting that there may be a limit to the degree of neurohormonal blockade that can be beneficial. The maximum benefits seen in this trial were in patients on an ACEI and a beta-blocker or an ACEI and an ARB. Data are not available to determine which combination was more beneficial. Given that recurrent hospitalization for heart failure and need for inotrophic support represents a large economic burden in patients with chronic CHF, it is worth emphasizing that the combination of an ACE inhibitor and an ARB could be cost effective in such individuals; there was an absolute 4.6% difference in first hospitalization after randomization between the combination therapy and placebo cohort, which reflected a 37% reduction and is highly statistically significant. Such an approach needs to be balanced against the adverse responses with ACEI/ARB therapy, which appear to be equal. It is also clear that for those individuals who cannot tolerate an ACEI for any reason, an ARB provides substantial benefit, achieving 45% reduction in morbidity and mortality in the small cohort (366 patients) who were not on ACEI. Conclusion: VAL-HEFT does not provide an absolute mandate for combination ACEI and ARB therapy, but in appropriately selected patients, particularly those not taking a beta- blocker who have the characteristics of being "frequent flyers" with respect to recurrent hospitalizations, should strongly be considered for both ACE inhibition and angiotensin II receptor blockade. ❖

TACTICS (TIMI 18) and TARGET Trials

The results of TACTICS (Treat Angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy, or TIMI 18) and TARGET (Do Tirofiban and ReoPro Give Similar Efficacy Outcomes Trial), two major clinical trials evaluating the use of glycoprotein (GP) IIb/IIIa receptor antagonists, add to a rapidly accumulating body of information outlining the use of these agents in the management of patients undergoing percutaneous coronary intervention (PCI), and

patients with acute coronary syndromes (ACS). It had become quite clear that the GP IIb/IIIa antagonists, abciximab (ReoPro®, Centocor/Lilly), tirofiban (Aggrastat®, Merck), and eptifibatide (Integrilin®, Cor/Key) are effective in preventing ischemic complications in both of these clinical scenarios, particularly in the highest risk subgroups of patients. However, much remains to be learned about the use of these drugs, including optimal patient selection, choice of specific agent, dose, duration and timing of treatment, and, importantly, how these agents fit into a contemporary, cost-effective, and rapidly evolving overall strategy of management of patients with coronary artery disease. In the context of previously published literature, the results from TACTICS and TARGET help to clarify some of these issues while further confounding others.

TACTICS was designed to evaluate the efficacy of an early invasive strategy (routine catheterization and revascularization) vs. an early conservative strategy (catheterization only for spontaneous or provokable ischemia) in the management of patients with ACS treated with the short-acting GP IIb/IIIa antagonist tirofiban (Aggrastat, Merck). While this question had previously been addressed in TIMI 3B, which showed no benefit for an early invasive approach, the present study sought to revisit the question in the context of contemporary medical and revascularization therapy, namely GP IIb/IIIa inhibition and coronary stenting. The investigators hypothesized that the early invasive approach would lead to superior outcomes and chose the composite of death, myocardial infarction (MI), and need to repeat hospitalization for ACS at six months as their primary end point. They further hypothesized that the higher risk patients with elevated serum troponin T (TnT) would derive additional benefit from an early invasive approach.

A total of 2220 patients were randomized and no significant differences in baseline characteristics between the groups were noted. The patients in this study represent a reasonably high-risk ACS population: 54% demonstrated elevated TnT, 48% had ischemic ECG changes, and 66% were prior aspirin users. All patients received aspirin and unfractionated heparin. All patients received tirofiban (0.4 mcg/kg/min for 20 minutes, followed by 0.1 mcg/kg/min); the invasive group for 4-48 hours before catheterization and for 12 hours after intervention, and the conservative group for 48 hours before noninvasive testing. Of the invasively randomized patients, 97% underwent catheterization and 60% were revascularized, and of the conservative group, 51% crossed over to receive catheterization, while 36% were revascularized during the index hospitalization.

At six months, the composite primary end point had occurred in 15.9% of invasively managed patients vs. 19.4% of conservatively managed patients (OR = 0.78; $P = 0.05$). This was due largely to the reduction of MI in invasively treated patients (4.8% vs 6.9%; $P = 0.029$), with a marginally significant reduction in the composite of death and MI (7.3% vs 9.5%; $P < 0.05$) and a trend toward reduction in rehospitalization (11.0% vs 13.7%; $P = 0.054$) for invasively treated patients. This difference was established within the first 30 days of the follow-up period. As expected, patients with elevated TnT demonstrated a more marked reduction in the primary end point when treated using an early invasive strategy (14.3% vs 24.2%, OR=0.52; $P < 0.001$). In addition, subgroup analysis revealed that patients with ST segment depression on ECG and those with higher TIMI Risk scores also derived more benefit when treated with an early invasive approach. There was a higher incidence of major bleeding (related to vascular access sites), and a shorter initial length-of-stay in the invasively treated patients. Economic and quality-of-life analyses were not presented at this meeting but are planned for the future. Thus, TACTICS concludes that in ACS patients treated with tirofiban in addition to standard medical therapy, an early invasive strategy of catheterization and revascularization results in a significant reduction in major adverse cardiac events (largely MI) at six months of follow-up.

COMMENT BY SARAH M. VERNON, MD

While TACTICS was not designed to test the efficacy of tirofiban for the medical therapy of ACS, the previously published clinical trials PRISM and PRISM-PLUS have shown that tirofiban is beneficial when compared with placebo. The results are somewhat difficult to reconcile with those of GUSTO IV ACS, which was recently presented at the 2000 European Society of Cardiology Meeting. This study was also designed to test the role of GP IIb/IIIa inhibition in acute coronary syndromes, but differed from TACTICS somewhat in that PCI was discouraged by design, with only 5% of patients undergoing revascularization during the treatment period. In GUSTO IV, 7800 patients believed to have unstable angina and receiving conventional therapy were randomized to receive placebo, or abciximab bolus followed by a either a 24-hour or 48-hour abciximab infusion. GUSTO IV showed no reduction in the primary composite of death and MI at 30 days in either abciximab treated group (8.0% vs 8.2% vs 9.1%) when compared with placebo. In addition, patients receiving abciximab demonstrated a concerning trend toward harm, including a higher incidence of death during the first 48 hours of

treatment. Taken together, these studies suggest tirofiban may be superior to abciximab as the initial medical therapy of patients with ACS.

In contrast to the data for their use in ACS, evidence for the beneficial effects of these GP IIb/IIIa antagonists in PCI is much more robust, with durable benefit now reported out to eight years of follow-up. In addition, for this clinical indication, the superior agent to date has appeared to be abciximab. TARGET was designed to compare the efficacy of tirofiban with abciximab in patients undergoing PCI, specifically stent implantation. This study is notable in that it is the first head-to-head clinical trial comparing two GP IIb/IIIa antagonists directly, as all previous studies had been placebo controlled. TARGET was designed to include a broad range of patients undergoing stent procedures and was powered to test the hypothesis that the two agents would be equivalent.

TARGET included a broad range of patients undergoing stent implantation for both elective (non-ACS) or urgent (ACS) clinical indications. Because tirofiban is primarily renally excreted, patients with a serum creatinine of 2.5 were not enrolled in the study. Patients were randomized to receive tirofiban (10 mcg/kg, then 0.15 mcg/kg/min for up to 24 h) or abciximab (0.25 mcg/kg bolus, then 0.125 mcg/kg/min for 12 h). This is the tirofiban dose used in the RESTORE trial and is a higher dose than was used in any of the aforementioned ACS trials. All patients received unfractionated heparin and clopidogrel (Plavix®). The primary end point of TARGET was a composite of death, MI, or urgent revascularization at 30 days and each component was also assessed individually.

The results of 4812 randomized patients were reported. Of note, 500 patients were excluded from analysis. These patients were randomized but did not receive a study drug, largely because they did not undergo intervention. No significant differences in baseline patient characteristics between the tirofiban- and abciximab-treated groups were reported, and culprit vessel distribution was balanced between the groups. There was a relative risk reduction in the primary end point of 26% for the abciximab-treated patients (6.01% vs 7.55%; P = 0.037). Thus, tirofiban appears to be inferior to abciximab for the primary end point at 30 days. This benefit for abciximab was evident by 48-72 hours suggesting that the majority of events were likely procedural in origin. While questions about adequacy of dosing and extent of platelet inhibition have been raised in previously published trials of small molecule GP IIb/IIIa antagonists, adequate platelet inhibition was confirmed in greater than 90% of the tirofiban-treated patients in this study. Minor bleeding complications were more common with abciximab as has been noted in previous clinical trials with these agents. Thrombocytopenia was more common with abciximab treatment; however, this was not associated with need for transfusion or any major bleeding complication. TARGET would, therefore, suggest that abciximab remains the gold standard GP IIb/IIIa antagonist for prevention of ischemic complications in PCI.

The results of TACTICS and TARGET support the use of tirofiban in the medical therapy of ACS with an early invasive strategy and the use of abciximab in coronary stent procedures. The difficulty now lies in knowing which agent to use in a high-risk ACS patient who will ultimately undergo coronary stenting, a scenario that is not at all uncommon in clinical practice. It is also difficult to know where eptifibatide, which is presently the only agent FDA approved for both clinical indications, fits into this overall scheme. To much fanfare, results of the ESPRIT trial were presented at the ACC meeting in March 2000, one month after randomization was stopped early due to the benefit of eptifibatide. ESPRIT compared eptifibatide to placebo in a relatively stable group of patients undergoing PCI with respect to the composite end point of death, MI, ugent target vessel revascularization, or need for "bailout" (unblinded) GP IIb/IIIa antagonist administration at 48 hours. ESPRIT showed a 37% reduction in the primary end point in the eptifibatide-treated group (6.6% vs 10.5%; P = 0.0015). Results of an analysis of the secondary 30-day composite end point have not yet been reported, and it is unclear whether follow-up at later timepoints will be performed. Therefore, unlike for abciximab, the durability of the benefit of eptifibatide is, as yet, unknown. It is also important to note that eptifibatide has not been directly compared to either abciximab or tirofiban in a randomized clinical trial. ❖

Oral Dofetilide for Atrial Fibrillation/Flutter

ABSTRACT & COMMENTARY

Synopsis: *Dofetilide is moderately effective for converting atrial fibrillation and atrial flutter to sinus rhythm and in maintaining sinus rhythm for one year.*

Source: Singh S, et al. Dofetilide atrial fibrillation investigators. *Circulation* 2000;102:2385-2390.

Singh and colleagues report a double-blind, multicenter dose ranging study on the effect of

dofetilide, a new antiarrhythmic drug for the conversion and maintenance of sinus rhythm in patients with atrial fibrillation and atrial flutter. The study group included 325 patients. Eighty-seven percent were male. The mean age was 67 years. Eighty-five percent of the patients had atrial fibrillation as their primary rhythm and 15% had atrial flutter. Ninety-two percent of the patients were in New York Heart Association class I or class II. Sixty-three percent had some form of structural heart disease, with hypertensive disease noted in 50%. At the time of entry, most of the patients were on digoxin for rate control with a small percentage on calcium channel blockers. All patients had a history of persistent atrial fibrillation that had lasted from two to 26 weeks. Patients with a QRS duration over 180 m/sec, a QT interval over 440 m/sec in the absence of bundle branch block (500 m/sec with a bundle branch block), RR intervals greater than 3.5 seconds, or a ventricular rate of less than 50 bpm on 12-lead ECG were excluded. Patients with a creatinine clearance of less than 20 mL/min were also excluded. Patients were admitted to the hospital and placed on continuous telemetry. Patients were assigned to receive either placebo or dofetilide in twice- daily doses of either 125 mcg, 250 mcg, or 500 mcg. Because of data from other trials indicating that doses needed to be adjusted for renal function, the prescribed dosage was cut in half if the creatinine clearance was between 40-60 mL/min and both cut in half and changed to a single-daily dose if the creatinine clearance was between 20-40 mL/min. Dosage adjustment was also permitted if the QT interval increased by greater than 15% over baseline. Patients with a QTc that exceeded 550 m/sec or increased greater than 25% over the baseline values at any time were withdrawn. Patients first received a minimum of five doses of study drug. If they failed to convert pharmacologically, electrical cardioversion was attempted. Patients in whom sinus rhythm could not be restored or maintained for 24 hours after conversion were not entered into the maintenance phase. All patients were anticoagulated according to current guidelines. During the conversion phase, only one of 84 patients who received placebo converted to sinus rhythm. In contrast, 6.1%, 9.8%, and 29.9% of the dofetilide patients treated with either 125 mcg b.i.d., 250 mcg b.i.d., or 500 mcg b.i.d. converted pharmacologically. Of the patients who converted pharmacologically, 70% did so within 24 hours and 91% within 36 hours. Pharmacologic conversion was more common in patients with atrial flutter than in those with atrial fibrillation. In the 500 mcg b.i.d. dosage group, the rates were 21.6% for atrial fibrillation and 66.7% for atrial flutter. There was a strong correlation between final dofetilide dose and the maintenance of sinus rhythm. Among the patients who converted and entered the maintenance phase, 25% of placebo patients remained in sinus rhythm whereas 40%, 37%, and 58% of the three dofetilide groups remained in sinus rhythm at 12 months. Time to recurrent episode was improved at the two higher doses. Patients with atrial flutter maintained sinus rhythm better than patients with atrial fibrillation.

Eleven patients were withdrawn from dofetilide therapy because of adverse events potentially related to treatment. Prolongation of the QT or QTc interval accounted for 10 of the withdrawals. There were seven proarrhythmic events. Singh et al considered three of these to be treatment related. There were two episodes of torsade de pointes. One episode was unwitnessed and death was presumed to be a sudden cardiac death on day eight of therapy. Four other events were noted but were thought to be due to another illness. There was no difference in all-cause mortality between the groups. By 12 months, 2.5% of dofetilide treated patients and 3.5% of placebo-treated patients had died.

Singh et al concluded that dofetilide is moderately effective for converting atrial fibrillation and atrial flutter to sinus rhythm and in maintaining sinus rhythm for one year. A careful program of in-hospital initiation and dosage adjustment based on QTc is recommended to minimize the risk of proarrhythmia.

COMMENT BY JOHN P. DiMARCO, MD, PhD

Dofetilide is an antiarrhythmic drug recently released for treatment of patients with atrial fibrillation. Previously, studies in both heart failure and post-myocardial infarction patients had shown that dofetilide did not increase overall mortality and had a favorable effect in patients with atrial fibrillation at baseline. The study by Singh et al was specifically designed to assess the effects of various doses of dofetilide in patients with persistent atrial fibrillation.

The data reported here show that dofetilide is moderately effective in atrial fibrillation. Like other antiarrhythmic drugs, it is more effective in patients who present with only atrial flutter, but currently, most patients with only classic atrial flutter would be treated with ablation rather than antiarrhythmic drug therapy. However, the drug has a narrow therapeutic range and this observation led to some unusual FDA guidelines for therapy initiation.

Physicians who wish to prescribe dofetilide must undergo a training session provided by the manufacturer. Therapy must be begun in-hospital and long-term drug supplies can only be obtained from a national center. A careful program of QT interval monitoring

during study initiation is recommended to minimize the risk of side effects. These restrictions are unique among antiarrhythmic drugs even though other drugs with a risk for producing QT prolongation and polymorphic ventricular tachycardia, such as sotalol or quinidine, would probably have enhanced safety if similar programs were followed. Even with this program, proarrhythmia may occur. In fact, this paper doesn't really give up a final estimate of incidence since Singh et al don't really define what they mean by proarrhythmia "related to other illnesses."

When choosing an antiarrhythmic drug for patients with atrial fibrillation, safety is often a more significant concern than efficacy since atrial fibrillation per se is not a life-threatening arrhythmia. Dofetilide can be used as an alternative to amiodarone in patients with congestive heart failure. Unlike sotalol, the other currently available class III antiarrhythmic drug, it does not have prominent beta-blocking activity and, therefore, can be used at an antiarrhythmic dose in patients with significant heart failure without a careful up titration to avoid excess beta-blocker effect. It also is not associated with bradycardia. Since bradycardia is a predisposing factor for drug-induced polymorphic ventricular tachycardia, this is an additional safety feature. Finally, dofetilide has few extra cardiac side effects. This allows it to be an alternative to amiodarone in patients in whom years of therapy are likely to be required. ❖

Outcomes with Automated External Defibrillators

ABSTRACTS & COMMENTARY

Synopsis: *Rapid defibrillation by minimally trained nonmedical personnel using an automatic external defibrillator results in a high salvage rate for victims of cardiac arrest.*

Sources: Valenzuela TD, et al. *N Engl J Med* 2000;343:1206-1209; Page RL, et al. *N Engl J Med* 2000;343:1210-1216.

Valenzuela and colleagues performed a study of the efficacy of automatic external defibrillators (AEDs) used by security officers in the treatment of cardiac arrest victims in gambling casinos. Valenzuela et al collected data from a total of 32 casinos over a period of 32 months. Security officers in these casinos underwent training in basic cardiopulmonary resuscitation that consisted of a 5-6 hour training course that included orientation to the use of an AED. Participating casinos purchased AEDs and management of cardiac arrest with these devices became part of the security officers' routine training program. In gambling casinos, security cameras mounted in the ceiling randomly scanned public areas allowing for the rapid identification of patients who appear to be in distress. The first officer on the scene initiated manual cardiopulmonary resuscitation and a second officer brought the nearest AED to the patient. The protocol for this specific AED model used was followed and resuscitative efforts by the security officers were continued until either the return of spontaneous pulse and respiration or until the arrival of paramedics.

During the period of the study, there were 148 patients at the 32 casinos with a confirmed cardiac arrest. The mean age was 64 ± 12 years and 80% were male. Of the 148 total cardiac arrests, 90 of the patients were observed by the security cameras at the time of collapse. The start of the episode was not recorded by the security cameras in the remaining 58 cases. The initial rhythm was ventricular fibrillation in all of the witnessed arrests and in 71% of the total population. Delivery of emergency cardiac care was rapid. Among the patients with a witnessed arrest, the intervals from collapse to initiation of resuscitation was 2.9 ± 2.8 minutes, from collapse to attachment of the AED was 3.5 ± 2.9 minutes, and from collapse to first defibrillation was 4.4 ± 2.9 minutes. Paramedics arrived 9.8 ± 4.3 minutes after a witnessed collapse.

The primary outcome variable in this study was survival to discharge from the hospital. The survival rates were excellent. Among the 90 patients with a witnessed arrest, 53 (59%) survived to discharge from the hospital. In the total group of 148 patients, 38% survived to hospital discharge. If the cardiac arrest victim received their first defibrillation no more than three minutes after collapse, the survival rate to hospital discharge was 74%. Valenzuela et al concluded that rapid defibrillation by minimally trained nonmedical personnel using an automatic external defibrillator results in a high salvage rate for victims of cardiac arrest that occurs in a public area with high security.

In the second article, Page and colleagues report on the experience of a single U.S. airlines, American Airlines, with the use of AEDs aboard their aircraft. Currently, all American Airlines' flight attendants receive four hours of instruction followed annually by a 1.5-hour refresher course. This paper reports data from the use of the AEDs on 200 occasions with

191 uses aboard an aircraft and the remaining nine in the terminal. An AED was used in 99 patients who had transient or persistent loss of consciousness whereas, as in the 101 remaining patients, the device was placed in response to possible cardiac symptoms, usually either chest pain or dyspnea. A physician was present to assist placement and use of the AED in 139 patients. Because of memory failure, electrocardiograms were available in only 185 of the 200 cases. In 145 patients, the initial rhythm was sinus rhythm. Thirteen patients had a supraventricular rhythm; an agonal rhythm was seen in 13 patients and ventricular fibrillation was found in 14 patients. In each of the 14 patients with documented ventricular fibrillation, the arrhythmia was recognized and defibrillation was recommended. Two unconscious patients received shocks but their electrocardiograms were not stored. A shock was not delivered in one patient with a terminal illness at the request of the patient's family. Of the 15 patients who received the shocks, six (40%) were subsequently discharged home with full neurologic and functional recovery. Four of the 15 had received shocks for cardiac arrest in the terminal. None of these survived. By contrast, six of the 11 patients with documented or presumed ventricular fibrillation who received shocks aboard the aircraft survived to hospital discharge. Page et al noted that in 101 cases, the AED was placed on a patient without documented loss of consciousness, generally on the recommendation of a physician passenger. The absence of ventricular fibrillation was recognized appropriately by these devices and shock was never recommended. Statistics show that a defibrillator was used once for every 3288 flights and a death or resuscitation after cardiac arrest occurred once in every 21,654 flights. Page et al extrapolate these numbers to estimate that approximately 93 lives per year would be saved if all commercial airlines were so equipped and similar results were realized.

COMMENT BY JOHN P. DiMARCO, MD, PhD

These two papers demonstrate the value of AEDs in public settings when they are used by minimally trained personnel. The national average for survival to hospital discharge after an out-of-hospital cardiac arrest is approximately 5%. Studies have clearly shown that time to defibrillation is the most critical predictor of survival. Before the introduction of AED technology, many hours of training were required to ensure competent arrhythmia recognition and management of cardiac arrest by emergency service personnel. This effectively limited the ability of communities, organizations, and individuals to deliver early defibrillation. The casino study was performed in perhaps the ideal setting for use of an AED. In a casino, security cameras continuously monitor most public gaming areas and security personnel are immediately available to respond to emergencies. Therefore, the very high survival to hospital discharge rates in the casino study will probably not be reproduced in other settings but should serve as the goal for other trials. Cardiac arrest on an airplane is a much different situation. As shown in this study, some patients with cardiac arrest may be thought to be sleeping. The social norm among passengers and crew is often not to disturb someone in this situation; therefore, it is not surprising that the results of resuscitation on an airplane were not as good as they were in casinos. However, there is no other way to deliver emergency care once the plane has left the gate and, with that in mind, the results are excellent.

The concept of early defibrillation is so well established that the issue now is one of cost-effectiveness rather than demonstration of efficacy. The use of the AED is simple enough that even untrained individuals can often follow instructions if they know the general purpose of the device. Over time, hopefully, we will

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see more and more public places with AED's. Whether or not the concept will ever be effective in the home situation remains to be demonstrated. ❖

CME Questions

1. **The addition of an ARB to ACEI therapy for heart failure results in which of the following?**
   a. Reduced mortality
   b. Reduced morbidity
   c. Superior results vs. adding a beta blocker
   d. Increased adverse effects

2. **In acute coronary syndrome patients treated with tirofiban, an invasive strategy resulted in which of the following?**
   a. Reduced mortality
   b. Reduced re-hospitalization
   c. Reduced myocardial infarction
   d. Reduced major bleeding

3. **During percutaneous coronary interventions, abciximab compared to tirofiban showed what?**
   a. The death, MI and revascularization composite was reduced
   b. Minor bleeding was reduced
   c. Thrombocytopenia was less
   d. No reflow was reduced

4. **Oral dofetilide in atrial fibrillation patients does what?**
   a. Converts less than 30% to sinus rhythm
   b. Converts more than 60% to sinus rhythm
   c. Maintains sinus rhythm in more than 60% of those converted
   d. Is less efficacious in atrial flutter

5. **The use of automated external defibrillators by lay persons results in survival to hospital discharge in ventricular fibrillation in what percentage of patients?**
   a. 10%
   b. 25%
   c. 35%
   d. more than 50%

Readers are Invited. . .

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