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Reperfusion Strategies in Elderly Patients with Acute MI: Angioplasty is the Winner

ABSTRACT & COMMENTARY

Synopsis: *Angioplasty patients may benefit compared to thrombolysis, but more attention needs to be focused on the early recognition of AMI and the rapid delivery of either reperfusion therapy.*

Source: Berger AK, et al. *JAMA* 1999;282:341-348.

Controversy remains whether direct angioplasty or thrombolysis is the best therapy for acute myocardial infarction (AMI). Individual clinical trial experiences and meta-analyses suggest that angioplasty may be superior to thrombolytic therapy; this is particularly true in younger patients but has not been convincingly proven in individuals older than 70. This analysis from the Medicare-based Cooperative Cardiovascular Project (CCP) assessed almost 21,000 older patients with AMI between 1994 and 1996 who were eligible for reperfusion therapy, and reported short-term (30-day) and long-term (1-year) survival as well as a variety of secondary end points. The individuals received direct angioplasty, thrombolysis, or neither reperfusion strategy. Furthermore, hospitals were assessed as to whether they are high or low volume (number of yearly AMI patients) with respect to outcome. An "ideal" subgroup of individuals who presented within six hours with ST elevation or left bundle branch block (LBBB) were separately analyzed. A wide variety of predictive variables for outcome were also assessed. The results favored angioplasty for both short- and long-term survival, although when only "ideal" patients were analyzed, the differences between the two strategies were minimal. Both reperfusion approaches resulted in considerably better survival than the majority of patients in the CCP database who did not receive either reperfusion strategy. Approximately 18,645 individuals (23%) received thrombolysis (76% TPA), and 2038 patients underwent angioplasty within the six-hour time frame from the onset of AMI.

Thus, approximately 75% of the entire database did not receive either reperfusion strategy. The overall cohort had a mean age of 73; 58% were male. The angioplasty group was more likely to

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have prior coronary revascularization and presented later to the hospital. Time to angioplasty was substantially longer than time to thrombolysis. Nevertheless, the angioplasty patients had a significantly lower 30-day mortality (8.7% vs 11.9%; P = 0.001) as well as one-year mortality (14.4% vs 17.6%; P = 0.001). There were no differences when adjusted for age and sex; the survival advantage of angioplasty over thrombolyis persisted for at least 18 months. Furthermore, angioplasty patients had substantially lower incidence of stroke and cerebral hemorrhage, as well as less postinfarction angina, but there was somewhat more bleeding in these individuals. In the thrombolytic cohort, 40% ultimately underwent cardiac catheterization and 12% received an angioplasty. After adjustments for baseline characteristics, direct angioplasty demonstrated a robust improvement in survival, with a 26% reduction in mortality at 30 days and 12% at one year. Of interest, diabetes, prior heart failure, and nonanterior infarction were not associated with benefit with angioplasty compared to thrombolysis. Among "ideal" candidates who were treated within six hours and had ST segment elevation or LBBB, angioplasty still was better than thrombolysis but the differences were less marked than in the overall cohort and were small at one year (16.2% mortality vs 17.8%; P = 0.18). Hospitals with high-volume AMI (> 150 per year) had better results than lower volume institutions, but angioplasty remained the better strategy in both. Of great importance, either reperfusion strategy resulted in a 30-day mortality of 11.8% vs. 17.2% with more (P = 0.0001). At one year, the mortality was 33% in nonreperfused subjects vs. 17.6% in the angioplasty or one-year cohort (P = 0.001).

Berger and colleagues comment that the results are concordant with a recent meta-analysis showing an advantage to primary angioplasty over thrombolysis; prior studies have shown a trend with similar outcomes in the elderly. They note the obvious limitations of a retrospective analysis, although the shear size and careful analysis of multiple-risk parameters make a distorted outcome unlikely. Lower mortality rates were associated with primary angioplasty in all subgroups except diabetics and were not directly related to catherization volume. Berger et al suggest that the higher mortality in thrombolysis patients is related to greater complication rates in these patients. The discussion emphasizes that too often, reperfusion therapy is not used at all in elderly patients (less than half of "ideal" candidates received either therapy within 6 hours of hospital arrival). While they conclude that angioplasty patients may benefit compared to thrombolysis, they stress that "more attention needs to be focused on the early recognition of AMI … and the rapid delivery of either reperfusion therapy." They suggest that triage of patients to angioplasty is less important than insisting that reperfusion be provided for all appropriate candidates.

COMMENT BY JONATHAN ABRAMS, MD

This is a convincing analysis of a large number of elderly patients, demonstrating that at the very least, primary angioplasty in skilled hands does not increase morbidity and mortality. Furthermore, there is support for this revascularization strategy across almost all cohorts. In patients older than 75, in diabetics, and in nonanterior infarctions, there were minimal differences in outcome between the two reperfusion approaches. Thus, in hospitals that have both thrombolytic and angioplasty capability, choice of reperfusion strategy should be driven by patient characteristics and physician choice. I agree that the failure to provide either reperfusion approach for eligible AMI patients older than the age of 65 is a significant problem, given the major survival benefits demonstrated in this database. For instance, 30-day mortality at high-volume centers was only 8.1% for primary angioplasty and 11.5% for thrombolysis. However, for all comers who did not undergo reperfusion, one-year mortality was a remarkable 33.3% compared to 17.6% for either reperfusion approach.

This analysis provides more support for proceeding

Clinical Cardiology Alert, ISSN 0741-4218, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

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Schandale Kornegay.
GST Registration Number: R128870672.
Periodical postage paid at Atlanta, GA.
POSTMASTER: Send address changes to ***Clinical Cardiology Alert,*** P.O. Box 740059, Atlanta, GA 30374.

Back issues: $17. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

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United States
$209 per year (Student/Resident rate: $100).
Multiple Copies
1-9 additional copies: $100 each. 10 or more copies: $60 each.
Canada
$243 per year including GST
(Student/Resident rate: $110 including GST).
Elsewhere
$229 per year (Student/Resident rate: $110).

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directly to the cath lab in selected older subjects with AMI. In that the elderly have a higher absolute risk of dying with AMI, the number of lives saved in such individuals is substantial. Efforts should be redoubled to provide reperfusion, either thrombolytic or direct angioplasty, in all eligible older individuals that present with ST segment elevation within six hours of MI. ❖

Importance of Performing Primary Angioplasty Early

ABSTRACT & COMMENTARY

Synopsis: *Time to treatment with PCI is a critical determinant of mortality with primary PCI therapy of AMI.*

Source: Berger PB, et al. *Circulation* 1999;100:14-20.

Although primary angioplasty has been shown to result in TIMI-3 flow more often than thrombolytic therapy, the relationship between clinical outcomes and the speed of achievement of reperfusion has not been established. Thus, Berger and colleagues evaluated data from the GUSTO-IIb trial to determine the relationship between the time required to perform primary angioplasty and early clinical outcome. The direct percutaneous intervention (PCI) substudy of GUSTO-IIb compared direct PCI to thrombolytic therapy in 57 high-volume, 24-hour-operation hospitals in nine countries. Of the 1138 patients who presented within 12 hours of myocardial infarction (MI) onset, 565 were randomized to PCI and 79% received their first balloon inflation in the culprit artery at a mean time of 76 minutes after study enrollment; the other 19% did not undergo PCI for a variety of reasons (open artery, 36; surgery, 20; early death, 5; other, 32). The primary end point of 30-day mortality was 1.0% for those whose first balloon inflation was less than 60 minutes; 3.7% for 61-75 minutes; 4.0% for 76-90 minutes; 6.4% for more than 90 minutes; and 14.1% for those assigned to PCI who did not get it ($P < 0.001$). Mean left ventricular ejection fraction was also higher in the group treated within 60 minutes (60% vs 50% for the other groups). TIMI-3 flow was achieved in 73% of all PCI patients, and their mortality was 1.5% vs. 11.7% for those achieving less than TIMI-3 flow. However, in a multivariable logistic regression analysis, time to reperfusion was a significant predictor of mortality and TIMI flow achieved did not add to this relationship. Thus, Berger et al conclude that time to treatment with PCI is a critical determinant of mortality with primary PCI therapy of acute myocardial infarction (AMI).

COMMENT BY MICHAEL H. CRAWFORD, MD

In centers where primary PCI is a feasible treatment for AMI, the use of thrombolytic therapy has almost disappeared. This study emphasizes that the time to achievement of an open artery is just as important with primary PCI as it is with thrombolytic therapy. In fact, if an artery cannot be opened within 90 minutes of hospital arrival, mortality may exceed what can be achieved with thrombolytic therapy. Thus, even in centers capable of performing primary PCI 24 hours a day, 7 days a week, the likely time to achieve an open artery must be considered and there may be situations when thrombolysis is preferable.

One important factor would be the time that the patient has delayed coming to the hospital. In this study, the time from symptoms to enrollment averaged 142-149 minutes for those whose enrollment to first balloon time was less than 90 minutes; those in the more than 90 minute group had a longer prehospital delay (169 minutes) and those not receiving PCI had the longest delay (201 minutes; $P < 0.02$). Why those presenting later required more time to accomplish PCI is unclear from the study. Perhaps the diagnosis was more challenging in these patients or they were less sick appearing and were treated more leisurely.

The mean time to PCI of 76 minutes in the entire group is longer than in smaller trials such as primary angioplasty in myocardial infarction (60 minutes) but shorter than the U.S. registry experience (120 minutes). Thus, the results should be applicable to many tertiary U.S. centers. Finally, this is a small study by current multicenter trial standards, with only 30 deaths. However, the results are consistent with other data and make sense clinically. Thus, before we completely abandon thrombolytic therapy in tertiary centers, we need to consider likely in-hospital time delays. ❖

Abciximab plus Thrombolysis

ABSTRACT & COMMENTARY

Synopsis: *Abciximab increases the achievement of 90-minute TIMI-3 flow without significantly increasing major hemorrhage or mortality in AMI patients.*

Source: Antman EM, et al. *Circulation* 1999;99: 2720-2732.

Thrombolysis for acute myocardial infarction (AMI) provides an important survival advantage over conservative therapy if begun early in the course of

AMI. However, initial culprit artery patency is not always achieved and reocclusion of successfully opened arteries remains a problem. Thus, Antman and colleagues tested the hypothesis that the platelet glycoprotein 11b/111a receptor blocker abciximab, in addition to reduced dose alteplase, aspirin, and two low-dose heparin regimes, would improve the achievement of TIM1-3 flow at 90 minutes after thrombolytic therapy as compared to full dose accelerated alteplase, standard weight adjusted heparin, and aspirin. During an initial dose-finding phase, 14 different reperfusion regimes were tested to maximize efficiency and minimize bleeding complications. Full dose accelerated alteplase was a bolus of 15 mg, up to 50 mg infusion over 30 minutes, and 35 mg over 60 minutes (100 mg total). Reduced dose alteplase omitted the middle infusion (50 mg total). Abciximab was given as 0.25 mg/kg bolus, followed by an infusion of 0.125 mg/kg/min over 12 hours. Full-dose heparin (given with alteplase above) was a 70 U/kg bolus followed by 15 U/kg/hr; low-dose heparin was either 60/7 or 30/4. The results are as shown in the table.

Table

Percent of Patients Achieving TIMI-3 Flow at 90 Minutes, Major Hemorrhage, and Deaths

	TIMI-3	MH	Death
Alteplase 100, full heparin	62%	6%	3%
Alteplase 50, low heparin, abciximab	77%	7%	5%
Alteplase 50, extremely low heparin, abciximab	69%	1%	0

Antman et al conclude that abciximab increases the achievement of 90-minute TIMI-3 flow without significantly increasing major hemorrhage or mortality in AMI patients and extremely low dose heparin reduces bleeding episodes.

COMMENT BY MICHAEL H. CRAWFORD, MD

To say that this study was complicated and the paper difficult to read is the understatement of the month. There were five different total doses of alteplase given by one to four different bolus-infusion combinations, three heparin doses, two bolus-infusion combinations of the one dose of abciximab, and four doses of streptokinase for a total of 14 combinations tested out of many more possibilities in the dose-finding phase of the trial. Based on angiographic efficiency and complication rates, the three regimes described in the table were chosen for the dose confirmation phase of the study. Streptokinase was discarded because the dosage that produced high TIMI-3 flow frequencies with abciximab caused unacceptably high major bleeding ranges even if heparin was withheld.

The theory behind this study is compelling. Arterial thrombi have variable combinations of fibrin, platelets, and thrombin. Thrombolysis attacks the fibrin mesh of the clot, but it also increases platelet activation and generates more thrombin, which produces more fibrin and also increases platelet activation. The latter procoagulant effects of thrombolysis are referred to as the "dark side." Thus, aspirin and heparin must be given to maximize the results of thrombolysis because they oppose these dark side effects on platelets and thrombin, respectively. However, aspirin is a relatively weak antiplatelet drug, which may explain why flow augmentation in the culprit artery is often suboptimal and why reocclusion can occur. Hence, the hypothesis tested in this study—that a more powerful platelet inhibitor would improve the results of thrombolysis, but with reduced doses of thrombolytics and heparin to guard against increases in major bleeding. The study proved this hypothesis suggesting that further platelet inhibition can augment the achievement of TIMI-3 flow, even with reduced doses of thrombolytics and heparin, without increasing major bleeding. Higher frequencies of TIMI-3 flow at 90 minutes post-therapy in AMI patients should translate into increased survival and higher left ventricular ejection fraction based upon other studies, but this remains to be proven in a larger trial. ❖

Ibutilide for the Conversion of Atrial Arrhythmias

ABSTRACT & COMMENTARY

Synopsis: *Ibutilide is a useful treatment alternative for the conversion of atrial arrhythmias that occur after cardiac surgery.*

Source: VanderLugt JT, et al. *Circulation* 1999;100: 369-375.

This double-blind, placebo-controlled, multicenter study was designed to assess the efficacy of ibutilide fumarate for the conversion of atrial flutter and atrial fibrillation in the early postoperative period after cardiac surgery. Patients were eligible for the study if they had atrial fibrillation or atrial flutter of longer than one hour and less than three days duration within 1-7 days of a cardiac surgical procedure for coronary or valvular heart disease. Patients were required to be hemodynamically stable and free of heart failure or angina at the time of enrollment. Patients with heart rates of less

than 60 bpm were not eligible for inclusion. Patients were randomized to receive 10-minute intravenous infusions of either placebo or 0.25, 0.5, or 1.0 mg of ibutilide. There was a downward dosage adjustment for patients who weighed less than 60 kg. Patient were observed for 10 minutes after the end of the first infusion and, if they did not convert to sinus rhythm or suffer an adverse effect, a second infusion of the original dose over 10 minutes was repeated. The infusion was discontinued at the time of arrhythmia termination if there was hypotension, an increase in the QTc to greater than 600 msec, or the appearance of new ventricular arrhythmias. Patients were then observed off other antiarrhythmic drugs for 24 hours to determine the duration of maintenance of sinus rhythm. The prespecified end point for the trial was conversion of the atrial arrhythmia for any period within 90 minutes after the start of the first infusion.

A total of 302 patients were randomized. Of these, 76% were male, 201 had atrial fibrillation, and 101 had atrial flutter. The surgical procedures included coronary artery surgery alone in 69%, valvular surgery alone in 20%, and combined valve and coronary surgery in 11%. Thirty-one percent of the patients had an ejection fraction of less than 40%. By 90 minutes after the start of the first infusion, 13 of 84 (15%) placebo-treated patients and 41%, 47%, and 58% of the low, intermediate, and high-dose ibutilide groups converted to sinus rhythm. Patients with atrial flutter were more likely to convert with ibutilide compared to those with atrial fibrillation. Conversion was also more common among patients with coronary artery bypass grafting than it was among those with valvular surgery. The mean time to conversion was between 36 minutes for the 0.25-mg group and 23 minutes for the 1-mg group. Of the 104 patients successfully converted with ibutilide, 65 (63%) remained in sinus rhythm for 24 hours. Ibutilide prolonged the QT and QTc intervals, but prolongation of the QTc did not predict those who were to convert. The success rate was not statistically different between patient groups based on ejection fraction or treatment with beta adrenergic or calcium channel blocking agents. There was a trend toward increased benefit in patients treated with digoxin; 65% of digoxin-treated patients vs. 31% of patients not treated with digoxin who received 1 mg of ibutilide converted to sinus rhythm.

Noncardiovascular adverse events were uncommon with frequencies that did not differ between the placebo and ibutilide groups. Ibutilide did not have a significant effect on blood pressure. There were more ventricular arrhythmias in patients treated with ibutilide. Arrhythmias observed included ventricular premature depolarizations, nonsustained monomorphic or polymorphic ventricular tachycardia, and sustained ventricular tachycardia. Three patients who received ibutilide developed nonsustained polymorphic ventricular tachycardia and two had sustained polymorphic ventricular tachycardia, for an overall incidence of 2.3%. There was also one case of polymorphic ventricular tachycardia in the placebo group, but this occurred 27 hours after the initial infusion during treatment with procainamide. All sustained arrhythmias were successfully treated with cardioversion, magnesium, and/or pacing.

VanderLugt and associates conclude that ibutilide is a useful treatment alternative for the conversion of atrial arrhythmias that occur after cardiac surgery.

COMMENT BY JOHN P. DiMARCO, MD, PhD

Atrial fibrillation and atrial flutter are common complications of cardiac surgery, both for coronary artery disease and valvular heart disease. Although rarely life-threatening, these arrhythmias may markedly slow the process of recuperation after the procedure and can significantly prolong hospital stay. In the absence of heart failure or preprocedure atrial arrhythmias, the duration of postoperative atrial arrhythmias usually is self-limited. The peak time for occurrence is between day two and day eight after cardiac surgery, with resolution within 30 days after the surgical procedure.

Management of atrial arrhythmias after cardiac surgery is often a significant clinical problem. If the ventricular rate can be controlled and the patient is asymptomatic, it is often better just to treat with AV nodal blocking agents, anticoagulation, and time. Many of the patients will have resolved the atrial fibrillation within two or three weeks after the surgery and no specific further drug therapy will be needed. If the atrial arrhythmia is associated with persistent symptoms that delay or preclude discharge, a cardioversion strategy is usually used. Since atrial fibrillation may recur, repeated transthoracic electrical cardioversion is not a particularly attractive option. Pharmacologic conversion is therefore attractive if it can be accomplished safely. Use of ibutilide has the advantage that the drug may be used on more than one occasion if atrial fibrillation recurs over a period of several days. Pharmacologic conversion does not require anesthesia or sedation for an electrical cardioversion.

As shown in this paper, an ibutilide infusion has a reasonably high rate of efficacy, particularly for atrial flutter, which is the more difficult arrhythmia to manage, and an acceptable rate of complications. However, use of ibutilide does require careful monitoring and I would recommend it be used only in a closely monitored setting—either a procedure room or an intensive care unit, where continuous observation of changes in rhythm can be maintained.

Many cardiologists prefer a prophylactic approach to the problem of atrial arrhythmias after cardiac surgery. Beta adrenergic blockers have been shown to be effective and some recent studies have shown efficacy with oral or intravenous amiodarone. However, atrial arrhythmias still occur and cardioversion is often necessary. Either intravenous ibutilide, as used in this paper, or oral propafenone, if ventricular function is normal and revascularization was complete, is probably the drug of choice. ❖

Interactions Between Surveillance Systems and ICDs

ABSTRACT & COMMENTARY

Synopsis: *It is generally safe for a patient with an ICD to walk normally through an electronic surveillance system. However, they should not linger in a doorway where such a system is in use and should not stop completely near the gate transmitter.*

Source: Groh WJ, et al. *Circulation* 1999;100:387-392.

Groh and colleagues performed a study to assess the effects of commercial electronic surveillance systems used for antitheft applications in commercial stores on the function of detection systems in implantable cardioverter defibrillators (ICDs). Three participating centers recruited 170 individuals with ICDs. The patients were left with their tachyarrhythmia detection algorithms as clinically programmed but delivery of therapy was inactivated. The patients' electrocardiograms were continuously monitored during the testing procedure to minimize risk that they might have either a device-induced or spontaneous episode of arrhythmia while the therapy function of their device was inactivated. Three types of electronic surveillance systems were tested. Three different commercial systems were studied: a pulsed acoustomagnetic system (Ultra-Max) and two different electromagnetic systems (Aislekeeper and P-Magnetic). These electronic surveillance systems are commonly used worldwide and are representative of the types of installations in common use.

Patients were exposed to the systems in three different protocols. In the routine exposure protocol, subjects were asked to walk through the middle of the gates over a 10-15 second period. This was thought to mimic typical exposure by an elderly individual entering a store. For an extreme exposure, subjects were told to stand within six inches of the gate transmitter of the surveillance system for two minutes. Subjects either turned or leaned on the gate transmitter to ensure exposure from different directions. Finally, extreme exposure format was repeated with pacing, since activation of pacing changes the sensitivity for detecting cardiac arrhythmias in many types of ICD systems.

The patients had ICDs made by five different manufacturers. They included patients with 26 different ICD models, including both abdominal and pectoral implants and several different sensing configurations (endocardial tip to ring, endocardial tip to coil, and bipolar epicardial sensing).

During routine exposure, no alteration in baseline cardiac arrhythmia was observed with gate transit. There was also no indication of ICD reprogramming. In three subjects undergoing extreme exposure, inappropriate tachyarrhythmia detection was observed. These three detections occurred with use of the pulsed acoustomagnetic system, Ultra-Max, and would have resulted in shocks if therapy had been programmed on. The extreme exposure resulted in continuous noise that was detected by the ICD as ventricular fibrillation. These inappropriate detections were observed in one Medtronic model (7219) and two Cardiac Pacemaker, Inc., model 1746 defibrillators. During extreme exposure with pacing, 19 of 126 subjects showed evidence of oversensing. No ICD reprogramming was observed. In 12 subjects, the interaction was not clinically significant, consisting of only an intermittent delay in pacing caused by noise-augmented T-wave oversensing. In seven subjects, however, the interactions were clinically relevant. Complete pacing inhibition occurred with surveillance system exposure in five patients. In two additional subjects, prolonged pacing inhibition, but not complete cessation of pacing, was observed.

Groh et al conclude that it will be generally safe for a patient with an ICD to walk normally through an electronic surveillance system. Patients should be cautioned not to linger in a doorway where such a system may be in use and certainly should not stop completely in immediate proximity to the gate transmitter.

COMMENT BY JOHN P. DiMARCO, MD, PhD

Within the last year, a number of interactions of electronic devices commmon in the environment have been reported with both pacemakers and defibrillators. Interference may occur with cellular telephones, particularly digital models, diagnostic or therapeutic medical devices, strong magnetic fields from radio transmitters, and now electronic antitheft surveillance systems. The latter interaction may be particularly significant since these devices

are ubiquitous in the environment and are often not immediately obvious to someone entering a store or business establishment. This article demonstrates that although technical problems with these devices should be rare, they can occur particularly if the patient makes an unusually close approach to the transmitter.

It is likely that similar interactions will occur more frequently in the future. One would also like to have standards developed within the industry that might prevent further increases in the electronic output from these devices. Levels of energy that might be safe for normal individuals could increase the exposure risk in patients with implantable devices that depend on sensing small amplitude electrical events. For now, Groh et al's suggestions seem reasonable. Patients should be aware that an interaction is possible but need to eliminate only a few specific and unusual activities. ❖

DSE vs. PET for Viability

ABSTRACT & COMMENTARY

Synopsis: *PET is more sensitive for detecting viability but DSE is more specific.*

Source: Pasquet A, et al. *Am J Cardiol* 1999;84:58-64.

There are few direct comparison studies of dobutamine stress echo (DSE) to position emission tomography (PET) for the detection of myocardial viability as validated by return of left ventricular (LV) function after surgical revascularization. Thus, Pasquet and colleagues studied 94 consecutive patients with coronary artery disease (CAD) and severe LV dysfunction (ejection fraction < 35%). PET imaging was done before and after dipyridamole handgrip stress using rubidium-82 for perfusion imaging and 18-fluorordeoxyglucose to assess metabolism. DSE was done with atropine, if necessary, to achieve 85% of predicted heart rate. Both DSE and PET were done before consideration of revascularization in all patients. At about three months postsurgery, LV functional recovery was assessed at rest in 68, and at rest and stress in 29. Ischemia was defined as an induced perfusion defect on PET or wall motion abnormality on DSE. Viable myocardium was defined as perfusion-metabolism mismatch on PET or low-dose DSE wall motion augmentation. Using a 16-segment model, concordance of PET and DSE for identifying viable myocardium before surgery was 63%. Most of the discordant segments were nonviable by DSE and viable by PET; 50% of the discordant segments were in anterior or septal segments. Surgical revascularization was performed in 75 patients. Prediction of improved resting function after surgery was 83% by PET and 69% by DSE ($P < 0.001$), but the specificity of DSE was higher (78% vs 37%; $P < 0.001$), as was accuracy (75% vs 53%; $P < 0.001$). The accuracy of DSE was enhanced by consideration of the postsurgery stress images (86%), but PET was not. Pasquet et al conclude that PET is more sensitive for detecting viability, but DSE is more specific.

COMMENT BY MICHAEL H. CRAWFORD, MD

Since most centers do not have PET available, this study may seem moot. However, there are few studies of DSE using the clinical gold standard of functional recovery after revascularization. In this study, all the patients had surgical revascularization because most patients with severe LV dysfunction and CAD have multivessel disease. Of the 75 patients who had surgery, seven were dropped because of major perioperative events, so the analysis focuses on the 90% who did well with surgery. These 68 patients had 1088 myocardial segments; one-fourth were normal, half showed no improvement (non-viable), one-fourth improved (viable), and a few deteriorated (1%). Surgery seems to be a big intervention to improve the function of one-fourth of the LV. Also, the study did not report the postoperative ejection fraction values, which suggests they were unchanged. Of course, there are other reasons to do surgery. Patients may get symptom relief, experience fewer arrhythmias, and reduce remodeling after revascularization. Hence, it would have been interesting to know the long-term functional and clinical outcomes of these patients and how they related to the viability studies.

The discordance between PET and DSE is understandable since they are completely different techniques (apples/oranges) where alignment of imaging planes is likely to be inaccurate. Also, the distinction between severe hypokinesis and akinesis of a segment is difficult to determine by echocardiography. In fact, the main added value of evaluating the poststress echo images to determine recovery of segmental function was in the interpretation of hypokinetic segments. A major category of discordance was segments with PET viability but no function at rest or stress on echo. Perhaps these were stunned segments, but ordinarily stunned myocardium would augment with dobutamine. More likely, these segments had islands or peninsulas of viable myocardium large enough to affect the PET results but too small to affect segmental contractility. This would argue that DSE gives more reliable results in terms of what can be expected from surgery and this is reflected in the higher accuracy of DSE in this

study. Thus, if your center does not have PET, this application is not a good reason to buy one.

The real issue is when and whether to do DSE to detect viability. Patients with low ejection fraction and multivessel CAD with good targets should have revascularization surgery if feasible and DSE is unlikely to influence this decision, nor should it. DSE is accurate enough that it can be used where the clinical decision is not as obvious (i.e., if only partial revascularization is possible or the patient is at higher risk for surgery). DSE is especially useful if it shows viability (high specificity and positive predictive value). Nonviable segments on DSE may or may not recover. ❖

Is Digoxin Safe Post-MI?

ABSTRACT & COMMENTARY

Synopsis: *Digoxin is not safe in AMI patients. Beta blockers are a better alternative for the long-term treatment of supraventricular tachycardias and heart failure after AMI.*

Source: Spargias KS, et al. *Lancet* 1999;354:391-392.

Although digoxin has been proven safe in chronic heart failure patients, its safety in the acute myocardial infarction (AMI) setting is controversial. Thus, Spargias and colleagues evaluated the outcomes associated with nonrandomized digoxin treatment in the Acute Infarction Ramipril Efficacy (AIRE) study, which entered patients 3-10 days post-AMI. At entry, 12% of the 1986 AIRE patients were on digoxin. These patients were older, more likely to be female (32% vs 26%; P = 0.05), and less likely to be on beta blockers (7% vs 24%; P < 0.001). Also, they had lower ejection fractions (32% vs 40%; P < 0.001), were more likely to have anterior AMIs, and be in overt heart failure. Not surprisingly, digoxin use was associated with increased total mortality. Using a Cox's proportional hazard model to keep confounding variables to a minimum, digoxin remained a significant independent predictor of increased total mortality (hazard ratio 1.4, CI 1.07-1.86, P < 0.02). Also, digoxin was associated with an increased risk of sudden death (1.67, 1.09-2.56, P = 0.02). Spargias et al conclude that digoxin is not safe in AMI patients and suggest that beta blockers are a better alternative for the long-term treatment of supraventricular tachycardias and heart failure after AMI.

COMMENT BY MICHAEL H. CRAWFORD, MD

The profound differences in the characteristics of the patients on digoxin vs. those not is a challenge to any statistical device to eliminate confounding variables. Also, we do not know how many of these patients were on digoxin before their AMI or were started on it after their AMI but before entry into AIRE. The latter group may be at particularly high risk of mortality. Despite these difficulties with a nonrandomized retrospective analysis, there seems to be little evidence that digoxin is first-line therapy for any indication in AMI. Whether it is actually harmful would require a prospective trial, which will never be done. Thus, digoxin is a second- or third-line alternative to rate lowering calcium blockers or beta blockers for rate control in atrial fibrillation and to angiotensin converting enzyme inhibitors or beta blockers for heart failure complicating AMI. ❖

CME Questions

12. A Medicare database study of survival after AMI in patients older than age 70 concluded regarding survival that:
a. thrombolytic therapy is superior to direct angioplasty.
b. both reperfusion strategies are superior to no reperfusion therapy.
c. about three-fourths of the patients received neither therapy.
d. b and c.

13. The lowest 30-day mortality with primary angioplasty for AMI is achieved when:
a. hospital diagnosis to first balloon inflation is less than 60 minutes.
b. angioplasty is not performed.
c. TIMI-3 flow is achieved.
d. a and c.

14. TIMI-3 flow at 90 minutes post-treatment for AMI is most frequent with:
a. alteplase 100 mg, plus full-dose heparin.
b. alteplase 50 mg, reduced-dose heparin, and abciximab.
c. alteplase 50 mg, extremely low heparin, and abciximab.
d. streptokinase and abciximab.

15. Postcardiac surgery, the IV infusion of ibutilide for atrial flutter, or fibrillation results in:
a. successful cardioversion about half the time.
b. a higher conversion rate in flutter.
c. a higher conversion rate after bypass vs. valve surgery.
d. All of the above

16. Patients with ICD should be advised regarding electronic surveillance systems to:
a. walk normally through them.
b. not linger in them.
c. not get close to the transmitter.
d. All of the above