a goal international normalized ratio of 2.0 to 3.0. All patients had clinical risk factors for stroke (age > 65 years, hypertension, history of transient ischemic attack or stroke, diabetes, congestive heart failure, mitral stenosis) and/or echocardiographic risk factors for stroke (left atrial enlargement or reduced left ventricular ejection fraction).

Patients were followed for a mean of 19 ± 11 months. Fifty patients had device-documented AF episodes lasting longer than 48 hours. Of these patients, 19 (38%) were asymptomatic and presented in sinus rhythm at the follow-up visit. In 51 of 110 patients (46%), AF was documented by the resting electrocardiogram (ECG) during the follow-up, with device interrogation revealing AF in 97 (88%) of patients. In 52% of the entire patient group, asymptomatic AF recurrence was detected by the implanted device in at least one follow-up interval. Device-documented AF recurrence lasted longer than 72 hours in 38% of patients, longer than 48 hours in 45% of patients, longer than 24 hours in 53% of patients, and longer than 12 hours in 64% of patients.

The results of this study imply that we overestimate the benefit of maintaining normal sinus rhythm in patients with atrial fibrillation.

Interestingly, but not surprisingly, in 40% of patients who reported AF symptoms, the ECG and device memory showed absence of AF.

Among the 55% of patients who were free of AF during the first 3 months or more of the study, 23% developed device-documented asymptomatic AF lasting longer than 48 hours during subsequent follow-up. In addition, there was no relationship between the antiarrhythmic regimen used and freedom from AF.

Unfortunately, the results of this study imply that we overestimate the benefit of maintaining normal sinus rhythm in patients with AF; many of these AF episodes were not associated with symptoms and occurred months after confirmation of NSR maintenance. In the Prevention of Atrial Fibrillation After Cardioversion trial,[1] of the 2300 daily ECG recordings that were transmitted telephonically, 75% were asymptomatic.

The implications of the results of this study are profound and suggest that large populations of patients with AF who are maintained in NSR would require lifelong anticoagulation to prevent stroke. In the Atrial Fibrillation Follow-up Investigation of Rhythm Management study,[2] the lack of a clinical benefit from rhythm-control therapy (vs rate-control therapy) was attributed to the incidence of stroke in patients from whom anticoagulation was withdrawn. In that study, 57% of strokes in the rhythm-control arm occurred in patients who stopped taking warfarin, presumably because it was felt that the likelihood of AF recurrence, and therefore stroke, was low. In an accompanying editorial, Kaufman and Waldo[3] suggest temporary anticoagulation in those patients without risk factors for stroke, particularly for whom AF is associated with a "discrete and transient precipitating event (for example, after open heart surgery or thyrotoxicosis)." They also cite data from the Stroke Prevention Oral Thrombin Inhibitor in Atrial Fibrillation III trial[4] showing ximelagatran to be at least as effective as warfarin, with less bleeding and no need for regular surveillance of prothrombin times, and suggest that lifelong anticoagulation might become much more palatable. ■

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Cardiac Arrest

Advances in Cardiopulmonary Resuscitation

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The American Heart Association estimates that 400,000–460,000 Americans die each year of cardiac causes before reaching a hospital.[1] Out-of-hospital cardiopulmonary resuscitation (CPR) has been shown to significantly reduce mortality if performed early by trained bystanders. The widespread availability of automatic external defibrillators in airports and public places has also been shown to enhance survival in patients with

sudden cardiac death. Although these efforts have made a significant impact, the statistics are still dismal: an overall survival rate of less than 3% in patients undergoing out-of-hospital CPR. Even in patients who reach the hospital, mortality is high (90%) and a significant number of patients are left with severe neurological impairment that significantly contributes to their mortality. Research in this area is particularly difficult given the logistic and consent issues, but recent advances have been made in two particular areas: the use of hypothermia and improvements in initial pharmacological support.

Therapeutic Hypothermia After Cardiac Arrest: an Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

Nolan JP, Morley PT, Vanden Hoek TL, et al.

Circulation. 2003:108:118–121.

Induced hypothermia of a moderate level (reduction in body temperature to 28°C–32°C) has been routinely used during cardiac surgery to prevent myocardial and cerebral ischemia while on heart-lung bypass. Although hypothermia has been used in the past for cardiac arrest, two perspective randomized trials have recently evaluated its use in comatose patients who survived in-hospital cardiac arrest.[2–3]

Although hypothermia has been used in the past for cardiac arrest, two perspective randomized trials have recently evaluated its use in comatose patients who survived in-hospital cardiac arrest.

All cardiac arrests were due to ventricular fibrillation. Although the studies were highly selective, both showed improved neurological outcome with hypothermia, compared to normothermia (55% vs 39% and 49% vs 26%). In-hospital mortality was also reduced in both studies by greater than 10%, with an average risk reduction of 0.75. Whereas benefit was seen even with a delay of 4-6 hours, early institution resulted in better outcome. A task force of the International Liaison Committee of Resuscitation and the American Heart Association published an advisory that recommends that "unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12–24 hours when the initial rhythm was ventricular fibrillation (VF)".[4] They also state that such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.

A Comparison of Vasopressin and Epinephrine for Out-of-Hospital Cardiopulmonary Resuscitation

Wenzel V, Krismer AC, Arntz HR, et al.

N Engl J Med. 2004:350:105–113.

Epinephrine has been recommended for the treatment of patients undergoing CPR for more than 100 years. However, considerable experimental work supports the superiority of vasopressin because it restores circulation with a lower myocardial oxygen demand and improved organ blood flow. This study reports the results of a multicenter randomized trial of vasopressin versus epinephrine in 1186 patients with out-of-hospital cardiac arrests.[5] Patients were immediately randomized if they were initially found to be in asystole or with pulseless electrical activity. Those in ventricular fibrillation were given three attempts at defibrillation; if defibrillation was unsuccessful, patients were randomized to drug therapy. If circulation was not restored after 3 minutes, a second injection of epinephrine was given to both groups. In patients with asystole, vasopressin use resulted in significantly more hospitalizations (29% vs 20.3%) and hospital discharges (4.7% vs 1.5%). The combined use of vasopressin and epinephrine versus two doses of epinephrine resulted in significant improvement and survival rate to hospital admission and discharge (6.2% vs 1.7%).

In the United States, we have a less uniform system for emergency medical services, and many in the population are unfamiliar with CPR.

It is this author's opinion that these two new modifications to out-of-hospital CPR could have a profound effect on survival. Although the combined effect has not been directly studied, the potential additive of effects would be an absolute 18%–20% reduction in mortality, or a decrease in risk reduction of more than 30%. Given the magnitude of the problem (450,000 deaths per year) and the very poor hospital survival rate, this could mean saving 60,000–90,000 lives per year.

Although this is an astounding improvement, caution needs to be exercised in the interpretation of these studies. In all three randomized studies, the patients were highly selected (90% of the patients were excluded) and the interventions were applied by dedicated and trained individuals. In many countries in Europe, physicians are in the ambulance and are able to administer other medications such as amiodarone or thrombolytic agents. In the United States, we have a less uniform system for

emergency medical services (EMS), and many in the population are unfamiliar with CPR. Response time for EMS in rural settings is much longer than that in metropolitan areas. In addition, vasopressin was found to be superior in patients with asystole, which represents only 20%–40% of cardiac arrests. The lack of benefit in patients presenting with ventricular fibrillation is surprising and unexplained. These results, however, are new and innovative and allow new approaches to the treatment of patients with out-of-hospital cardiac arrest. Research in this area is extremely important, and, unfortunately, extremely difficult to accomplish. There remains a considerable need for further funding and a national effort to improve the outcome for this extremely high-risk group of patients. ■

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Atherosclerosis

Computed Tomography to Evaluate Asymptomatic Coronary Plaques

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Relationship Between Stress-Induced Myocardial Ischemia and Atherosclerosis Measured by Coronary Calcium Tomography

Berman DS, Wong ND, Gransar H, et al.

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Imaging with multislice spiral computed tomography (MSCT) and electron beam computed tomography (EBCT) can demonstrate the presence of coronary calcium. In addition, the newer generation of 16- and 64-slice MSCT scanning technologies can image for both calcified and noncalcified plaque, providing the ability to detect the presence of coronary artery disease in the presymptomatic phase. However, debate continues about how to factor the information gleaned from a calcium score or non-invasive CT coronary angiography test into the Framingham risk model and results of stress testing, identify patients who may be at risk for adverse coronary events, including fatal and non-fatal myocardial infarction and the need for coronary revascularization. Berman and colleagues conducted an important study to "assess the relationship between stress-induced myocardial ischemia on myocardial perfusion single-photon emission computed tomography (MPS) and magnitude of coronary artery calcification in patients undergoing both tests."

The study included 1195 patients who were referred for MPS for clinical reasons and within 6 months underwent coronary calcium scoring with either MSCT (Volume Zoom; Siemans AG, Malvern, PA) or EBCT (Imatron C-150 or e-Speed;™ GE Healthcare Technologies, Waukesha, WI). Patients were excluded if they had previous coronary artery bypass surgery or percutaneous intervention, history of myocardial infarction, known valvular heart disease, or primary cardiomyopathy. Patients underwent MPS with either a symptom-limited Bruce protocol or with adenosine. An ischemic MPS was defined when 5% or more of the ventricle became ischemic and a moderate-to-severe ischemic response was noted when more than 10% of the ventricle was judged ischemic using a summed-difference scoring system. The calcium scanning protocol called for the acquisition of 30 to 40 3 mm (EBCT) or 2.5 mm (MSCT) slices to cover the entire heart. Foci of calcium were designated if at least 3 contiguous pixels of peak density greater than or equal to 130 Housefield units (HU) were observed within the coronary tree.

Of the 1195 patients studied, only 45 (3.8%) presented with typical angina, 380 (31.8%) with atypical angina, and 112 (9.4%) with non-anginal chest pain. Asymptomatic patients numbered 609 (51%). Seventy-six of the 1195 (6.3%) had an ischemic MPS, indicating that the population studied was at a low risk for coronary events. Among patients within the highest coronary calcium score group (> 1000), only 19.9% and 8.6% had an ischemic and moderate-to-severe MPS, respectively. In patients with a calcium score of 0, 1.6% had ischemic and 0.4% had moderate-to-severe ischemia on MPS. See Figure 1.