

Sudden Cardiac Death

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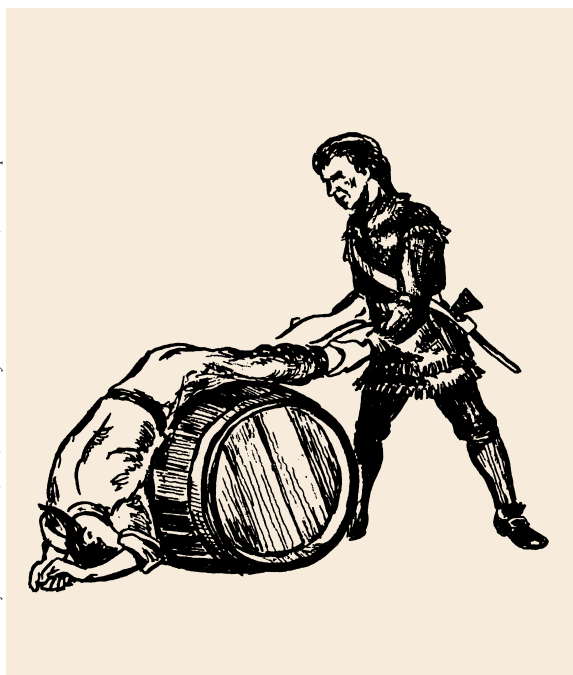


Illustration by C. Keith Wilbur, MD, *Revolutionary Medicine 1700-1800*, Globe Pequot Press.



Yorav Levy, Phototake

Pushing and pulling over a barrel was the only known way to resuscitate victims of sudden cardiac death in the 1700's. Today, even if defibrillation is performed promptly, less than one third of patients survive sudden cardiac death.

Despite a decline in age-adjusted death rates from cardiovascular causes during the past 4-5 decades, coronary artery disease still remains the most common cause of death in industrialized nations. Over half of these cardiac deaths (up to 450,000/year in the U.S.) are due to sudden cardiac death, or SCD: instantaneous or unanticipated circulatory collapse leading to death within one hour of initial symptoms. Ninety percent of these deaths are due to arrhythmias, and their causes can be delineated according to the presence or absence of structural heart disease.

Researchers have made remarkable progress in learning how to identify certain patients at high risk of sudden cardiac death, such as those with history of prior myocardial infarction, heart failure, coronary artery disease and other cardiac symptoms.

While the risk for sudden death is high among symptomatic patients, however, only a relatively small number of sudden deaths occur among patients with known risk

factors. Far more fatal events strike asymptomatic people with underlying heart disease who are unaware of their risk status. The great challenge, then, is to find ways to identify high risk patients prior to the onset of symptoms.

Determined to meet this challenge, researchers at Columbia University College of Physicians & Surgeons, Weill Medical College of Cornell University and NewYork-Presbyterian Hospital are tackling the problem from multiple fronts, including innovations in risk assessment technologies, prevention, and therapeutic avenues.

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Cardiac PET: Vast Potential

Positron emission tomography (PET scanning) can detect metabolic abnormalities in cells that precede anatomical or structural changes. Useful in a vast range of clinical and research applications, PET is heralding a new era in cardiac diagnostics.

Few physicians have the opportunity to explore the body's untapped potential in the way that Steven R. Bergmann, MD, PhD does. Using a noninvasive imaging technology known as PET, or positron emission tomography, Dr. Bergmann and colleagues are revealing unforeseen capabilities in the hearts of his patients.

Determining Myocardial Viability

One of the team's most highly publicized achievements has been its demonstration that PET testing may reveal significant amounts of previously undetected, but viable myocardium in patients with

coronary artery disease and severely depressed ejection fraction rates. Moreover, their research has shown that the life in such tissue is sufficient to sustain patients through revascularization procedures and lead to greatly improved survival rates and quality of life.

Dr. Bergmann's team studied patients with ischemic cardiomyopathy and ventricular ejection fraction rates of $\leq 22\%$ (*American Journal of Cardiology*, 2001). PET testing revealed significant amounts of viable myocardium in almost 60% of patients, where thallium scintigraphy found only scar tissue (see figure 1).

Half the patients with viable myocardium detected by PET chose to undergo coronary artery bypass grafting or angioplasty. On average, patients who chose revascularization saw their ejection fraction rates improve to 32%. Only 7% of this group experienced cardiac events and their two-year survival rate was an impressive 100%. In contrast, among patients with viable myocardium who chose medical management, 69% went on to suffer major adverse cardiac events and the two-year survival rate was 60%.

Among patients initially found to have infarcted myocardium (no viable myocardium) with PET, there was no significant advantage in survival or ejection fraction with revascularization versus medical therapy.

"PET picks up about 50% more cases of viable myocardium than conventional nuclear cardiology techniques," says Dr. Bergmann. The implications are enormous. Until recently, a finding of scar by conventional nuclear technology (which uses perfusion tracers to identify blood flow through the coronary vessels)

would rule out revascularization due to high risk. Dr. Bergmann's work demonstrates that PET can identify many patients who would clearly benefit from angioplasty or bypass surgery instead of medical management.

Moreover, PET could provide select patients on the transplantation list with the superior alternative of revascularization, improving the quality and length of life without the risks of transplantation and the burden of life-long immunosuppression. A shorter transplantation list could also reduce competition for the rare donated hearts among those patients who truly need them.

Detecting Coronary Artery Disease

In addition to detecting hibernating myocardium, PET offers the most specific and sensitive non-invasive method of detecting and delineating coronary artery disease. "While most patients can be diagnosed with conventional nuclear cardiology techniques, PET testing is a valuable alternative for patients with equivocal tests or for those who are unable or unwilling to undergo catheterization," says Dr. Bergmann. Highly accurate attenuation correction provides much greater specificity than traditional imaging, and quantitative measurement of blood flow can assess regional differences.

Evaluating angiogenesis after stem cell transplantation

PET is playing a key role in efforts to develop angiogenic therapies for coronary artery disease. In a protocol currently undergoing FDA review, researchers at Columbia University College of Physicians & Surgeons and

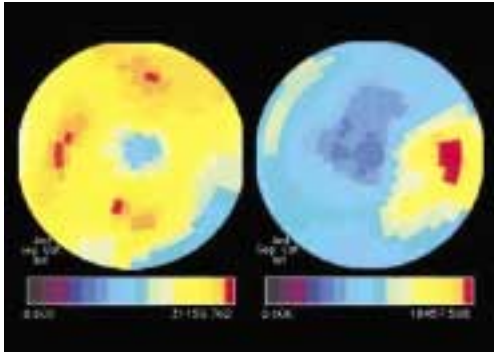


Figure 1. "Polar map" projection of the heart showing heart blood flow on the left and heart metabolism on the right. In this projection, the entire surface of the heart is displayed. Red signifies the highest amount of activity. In the blood flow map (left) there is decreased blood flow in the center (apex) and in the lateral myocardium (between 3 and 6 o'clock). However, the metabolism image (right) shows a significant hypermetabolic state in this area of decreased perfusion, which is a signature of ischemic but viable myocardium.



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NewYork-Presbyterian Hospital are using PET to study how well stem cell transplantation promotes angiogenesis in coronary blood vessels. By measuring coronary blood flow before and after stem cell transplantation, PET can detect whether blood flow has changed, and by precisely how much. At the outset, the team will inject the stem cells intravenously. Depending on the results, other delivery mechanisms to the heart may also be used. The team expects to initially treat 30 patients with CAD refractory to conventional treatment.

Evaluating cardiac nerve damage in diabetic patients

In another study with wide clinical potential, Dr. Bergmann's team is currently investigating the complex relationship between autonomic dysfunction, nerve damage in the heart, and glycemic control in diabetic patients.

"Diabetic patients who have autonomic dysfunction may have higher cardiac nerve damage than those without autonomic dysfunction, something we can measure by PET," Dr. Bergmann explains. "They have higher morbidity and mortality. Is this because their nerve damage is worse? If patients with autonomic dysfunction receive treatment, will their nerve damage improve?" Using PET to examine the effects of treatment on nerve endings in newly diagnosed diabetic patients, the team hopes to better understand and, eventually, learn to prevent cardiac nerve damage.

PET in the study of Fatty Acid Oxidation Disorders

According to yet another key study underway in Dr. Bergmann's laboratory, PET scanning offers a valuable mechanism for identifying the severity of fatty acid metabolism diseases and their

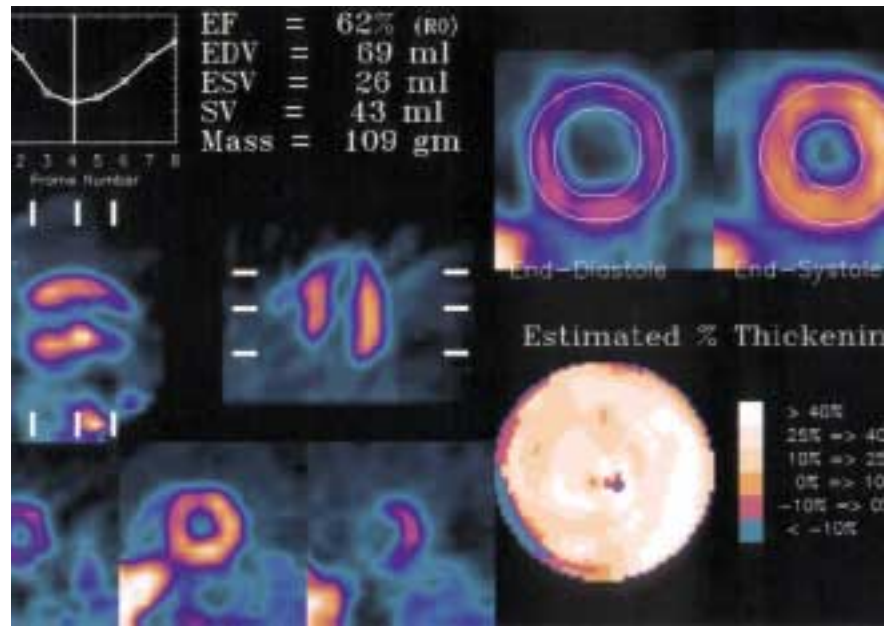


Figure 2. In addition to estimation of myocardial blood flow and metabolism, cardiac PET allows assessment of heart size and several other important indices of heart function.

effects on the heart (*Journal of Inherited Metabolic Diseases*, December 2001).

A number of rare, inherited fatty acid oxidation disorders (FODs) can lead to metabolic crises and, potentially, sudden death in children. Unlike genetic or enzyme assays, PET can accurately determine whether metabolic diseases are expressed in the heart before fatal cardiac events occur. "Until now, the only way we knew if such diseases were expressed in the heart was by autopsy. This way we can tell if there are heart problems while the child is alive."

Although current treatments for FOD-related cardiac disease are primarily supportive, Dr. Bergmann hopes that gene therapy will someday be able to restore metabolic activity to the heart. Nevertheless, identification of cardiac involvement at least lets physicians know the severity of the disease and can provide treatment suggestions. In addition, the ongoing study will monitor changes in metabolic expression over time, and reveal whether children develop compensatory

mechanisms as they grow older. Such observations hold tremendous research and clinical potential.

Moreover, Dr. Bergmann's laboratory is working to develop new tracers that would enable them to identify other, more common disorders in children. While current tracers can identify long-chain fatty acid metabolism disorders, different tracers are needed for imaging of other fatty acid abnormalities. Dr. Bergmann suspects that some cases of sudden infant death syndrome may prove to be caused by cardiac involvement of such disorders, conditions that could eventually be identified early enough for preventive therapy.

Accessing PET

Access to cardiac PET is typically limited to the same centers that offer cardiac transplantation surgery. Dr. Bergmann expects that the use of PET will increase, but cautions that "physicians must be quite experienced in reading the results." ■

Drug Eluting Stents

By virtually eliminating in-stent restenosis, drug-eluting stents may enable selected patients with severe coronary artery disease to undergo angioplasty rather than bypass surgery.

While the approval of stenting revolutionized coronary angioplasty during the last decade, in-stent restenosis soon emerged as the Achilles heel of this advance. About 25-30% of coronary stent recipients experience restenosis within the first six months after

It would be far better to prevent restenosis from occurring in the first place. But how?

Drug-eluting stents appear to have answered this need with great success. The evidence is so encouraging that “Elimination of restenosis is now clearly

least several years following revascularization.

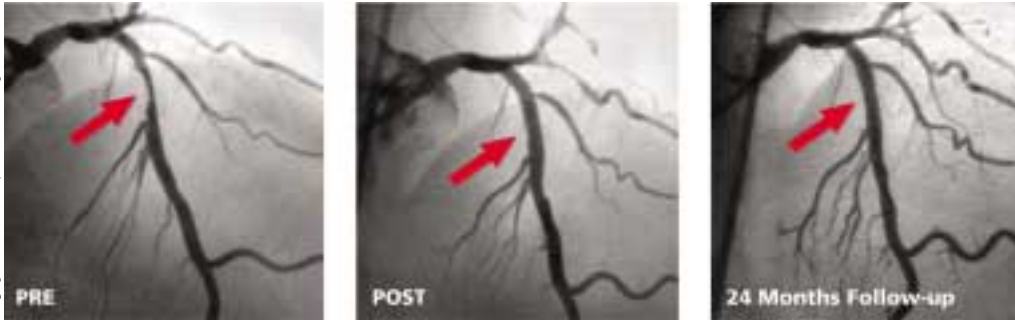
The SIRIUS trial, which randomized 1101 patients with new coronary artery stenosis, compared Bx Velocity™ (bare metal) with Cypher™ (containing rapamycin and a polymer coating). The primary endpoints investigated major adverse cardiac events (MACE) including myocardial infarction, death, and repeat revascularizations, either via angioplasty or bypass surgery, at 9 months. Efficacy of the stents and incidence of restenosis were assessed at 8 months through angiography, and primary endpoints will continue to be evaluated for 5 years.

The SIRIUS study found that in-stent restenosis was 3.2% with Cypher™, compared to 35.4% among those who received bare metal stents. Overall this represents about a 75% reduction in MACE compared to the bare metal stent group.

About 5.7% of patients did experience restenosis at the edges of the stents in the U.S. arm of the SIRIUS trial, whereas European and Canadian participants did not see this proximal edge effect. Dr. Wong speculates that the higher incidence of proximal edge restenosis in U.S. patients may have occurred because physicians in Europe and Canada use longer stents than they do in the U.S. Moreover, nearly one quarter of patients in the SIRIUS trial were diabetics, who were more likely to experience restenosis than non-diabetic patients. Nonetheless, Cypher™ demonstrated similar impact (70% restenosis reduction) in both diabetic and non-diabetic patients.

Despite initial concern about a possible risk of late thrombosis, data suggest that such fears are probably

First-In-Man Trial Angiograms



angioplasty, recurrences that are often more difficult to treat than original lesions.

Columbia University College of Physicians & Surgeons was the first institution to describe the use of intracoronary radiation for preventing in-stent restenosis, based on its animal studies, in the mid 1990's. Although brachytherapy was effective, placing radiation within the stent proved too cumbersome to become widely adopted.

a reachable goal,” according to S. Chiu Wong, MD, who directs the SIRIUS protocol at NewYork-Presbyterian Hospital at NewYork Weill Cornell Medical Center.

Cypher™, the first FDA-approved drug coated stent, slowly delivers rapamycin into the lining of blood vessels during the 4 weeks immediately following stent implantation. By inhibiting the activation and proliferation of smooth muscle cells and preventing growth of the intimal layer of the blood vessels, it interrupts the cellular process that normally causes dangerous regrowth of tissue.

A handful of other drugs have been tested as well, and according to Mark A. Apfelbaum, MD, the chemotherapeutic agent paclitaxel (evaluated in the TAXUS IV study) will likely gain approval in early 2004.

Several major studies have confirmed that drug-eluting stents can reduce in-stent restenosis to single-digit rates for at

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unfounded. The incidence of clot formation in the SIRIUS trial was virtually identical with that of bare metal stents (0.4% in the treatment group and 0.8% in the control group) during the first day after implantation.

Paclitaxel-eluting stents have also been tested in several trials. They failed to inhibit restenosis in the DELIVER trial, probably because the drug was impregnated into Guidant/ Cook's Achieve™ stent without any polymer coating. The European TAXUS II trial then tested paclitaxel with a polymer-coating and achieved much better results, with more than 60% reduction in in-stent neo-intimal volume as documented by intra-vascular ultrasound. The in-stent restenosis rate was reduced by 80% on 8-month angiography compared with the control group. Overall, there was a 75% reduction in target lesion revascularization rate.

The FDA-sanctioned, multicenter TAXUS IV study is continuing to monitor the safety of paclitaxel stents in the U.S. although its primary endpoints have been achieved. Over 1000 patients at about 80 centers are currently participating, and results are scheduled for publication in September.

With this first round of trials barely behind them, researchers have already begun the process of refining and improving the young technology. A wider range of drug-eluting stent sizes is now in production, and the Cardiac Catheterization Laboratory at NewYork Weill Cornell Medical Center is currently evaluating the efficacy of smaller size (2.25mm) Cypher stents in patients with blockages in small vessels. One of only two New York hospitals to participate in SIRIUS, NewYork-Presbyterian Hospital at NewYork Weill Cornell Medical Center is also participating in the 20-center SIRIUS-Direct Trial. SIRIUS-Direct will determine whether direct stenting (without pre-

dilation) may reduce trauma to the blood vessels and, consequently, restenosis, even further than stenting after balloon dilation. Eight-month angiographic evaluations of patients in SIRIUS-Direct will be performed in spring 2004.

Although safety issues demand final resolution, widespread use of drug eluting stents appears inevitable. Patients have been clamoring for the new stents for over a year, and, in an unprecedented move, the Centers for Medicaid and Medicare Services (CMS) created coding

“Physicians will become more aggressive about doing complex angioplasty and multi-vessel coronary angioplasty.”

and partial reimbursement even before the FDA granted its approval. The higher cost of drug-eluting stents (approximately \$3000, compared to \$1000 for bare metal stents) appears to be almost fully offset by the reduced need for repeat procedures.

“Physicians will become more aggressive about doing complex angioplasty and multi-vessel coronary angioplasty,” expects Dr. Apfelbaum. “While we may have hesitated to implant stents because of restenosis, patients with complex lesions and triple vessel disease may now be candidates.” Consequently, he predicts that hospitals will see a slow decline in coronary bypass surgeries.

According to Dr. Wong, “This clearly is a milestone in cardiology.” He says “There is no doubt that patient care will be markedly improved” through the use of drug-eluting stents, and predicts that “this is just the beginning,” with combinations of medicines in line to supersede single-drug coated stents as the next advance. ■

Robotic Surgery

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surgeons at Columbia Presbyterian have also performed several general thoracic procedures. Led by Dr. Joshua R. Sonett, Director of the Lung Transplantation Program at NewYork-Presbyterian Hospital, surgeons have performed robotic resection of lung and esophageal tumors. Benefits to such patients include reduced post-operative pain, reduced risk of infection, shorter hospital stay, and excellent cosmetic results.

Because of the potential to improve surgical options for so many people, surgery for atrial fibrillation holds perhaps the greatest potential of all robotic cardiac procedures to date. Columbia Presbyterian's efforts at developing a minimal access procedure for AF culminated in February 2002 with the performance of the first totally closed chest surgery for AF. The patient was a 55 year old male with a 20 year history of AF refractory to medical therapy. The 2-hour procedure was performed without the use of the heart-lung machine and without opening his chest. According to Dr. Michael Argenziano, who performed the procedure, “this procedure achieves the goal we've had for five years now, which was to develop an operation for atrial fibrillation that is as minimally invasive as possible.”

Columbia Presbyterian is currently training surgeons in robotic mitral valve and ASD repair, coronary bypass surgery, and other cardiothoracic procedures. ■

MAZE Procedure

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compares quite favorably to success rates at other centers. Many of these patients have been able to completely discontinue medical therapy and anticoagulation.

Furthermore, Dr. Mack is enthusiastic about the potential for the new probe to facilitate minimally invasive cardiac procedures. He expects that as thoracoscopic and robotic procedures undergo further refinement, a completely endoscopic, closed-chest approach may facilitate treatment of “stand-alone” AF with comparable success rates as the open procedures. ■

Sudden Cardiac Death

Etiologies

Patients with structural heart disease

Seventy percent of SCD survivors have underlying coronary artery disease. However, ventricular fibrillation (VF) may be the first sign in 25% of patients, and only about 20% of SCD patients have evidence of a new ST segment elevation-myocardial infarction (MI) at the time of cardiac arrest.

In 85% of patients, ventricular arrhythmias are the primary cause of SCD. Of these, three-fourths are initially due to ventricular tachycardia (VT), while one-fourth is due to either primary VF or torsade de pointes. VT degenerating into VF, followed by asystole, is the most common sequence of events.

Ischemia can lead to SCD by creating acidosis, potassium shift from intra- to extra-cellular space, increased adrenergic

New York Heart Association functional class, with class IV patients having an annual mortality rate of 30-70%.

Arrhythmogenic right ventricular dysplasia is a process involving fibrofatty replacement of myocytes, predominantly in the right ventricle, and is an important cause of SCD in patients under 30. The mechanism of SCD is ventricular tachycardia.

In younger patients, hypertrophic cardiomyopathy, anomalous coronary arteries, and congenital heart disease are etiologies of structural heart disease which can lead to SCD. Other causes include valvular heart disease and, rarely, cardiac tumors.

Patients without structural heart disease

Only about 20% of patients with SCD have no evidence of structural heart disease. Of these, Long QT Syndrome (LQTS) is thought to be responsible for 3000-4000 deaths per year in the U.S. Among such patients, torsade de pointes degenerating into VF is the etiology of SCD.

To date, six gene loci have been identified as causes for LQTS; all affect various functions of ion channels. The most common mutation, LQT1 on chromosome 11, encodes the α -subunit of the I_{Ks} potassium channel, and occurs in about 50% of patients with LQTS. The second most common mutation, LQT2 on chromosome 7, encodes the α -subunit of I_{Kr} . LQT3, on chromosome 3, encodes the α -subunit of the sodium channel (SCN5A).

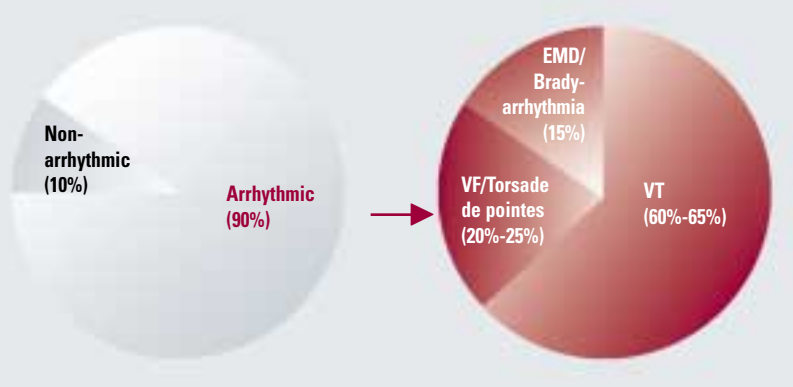
LQTS has two phenotypes, autosomal dominant (Romano-Ward) and autosomal recessive (Jervell-Lange-Nielsen), with deafness associated with the latter form. "Acquired" LQTS, with prolongation of the QT interval by exogenous factors (e.g., medications, electrolyte abnormalities), is thought to be due to a subclinical defect in one of the LQT genes, which predisposes to QT prolongation.

Brugada syndrome, another etiology of SCD, is an autosomal dominant disease which has been linked in some patients to a mutation in SCN5A gene. Diagnosis is made by EKG, which reveals right bundle branch block, downsloping ST segment elevation in leads $V_1 - V_3$ with normal QT interval and no evidence of structural heart disease. Such patients develop ventricular arrhythmias due to intrinsic heterogeneity of repolarization, which provides the milieu for onset of polymorphic VT or VF.

Wolff-Parkinson-White Syndrome can also predispose to SCD. Patients at highest risk are those capable of rapid accessory pathway conduction, because this results in rapid ventricular stimulation that can degenerate into VF.

Other less common etiologies include catecholaminergic polymorphic VT, short-coupled torsade de pointes, commotio cordis, and idiopathic ventricular fibrillation. ■

Causes of Sudden Death



tone, and increased intracellular calcium. Two common scenarios are:

1. Ventricular arrhythmia triggered by acute myocardial ischemia, due either to vasospasm or unstable platelet thrombi, in patients with or without prior myocardial scar.
2. Ventricular arrhythmia related to anatomical substrate (e.g., scar from previous MI).

While treatment of acute ischemia usually results in resolution of the associated arrhythmia, revascularization rarely affects inducibility of VT in patients with myocardial scar.

In up to 10-15% of SCD survivors, dilated cardiomyopathy may be present, which may be idiopathic or due to various etiologies such as viral myocarditis, sarcoidosis, hemochromatosis, or amyloidosis. Death rates are linked to



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Non-invasive Risk Assessment

In the absence of convenient, non-invasive tests that can be administered to large numbers of people, the ability to effectively predict sudden death has eluded the best minds in cardiology. T-wave alternans testing may be the solution.

Until recently, cardiologists have relied on a variety of non-invasive tests as their first-line armamentarium in identifying people at high risk of sudden cardiac death. Based on their ability to detect depressed left ventricular function (LVF), such non-invasive testing usually begins with an echocardiogram. For heart attack survivors and others with reduced LVF, further risk stratification can be accomplished by identifying non-sustained ventricular tachycardia during Holter monitoring. Other traditional tests have included signal-averaged EKG and heart-rate variability testing, although these are now much less commonly performed.

The T-wave alternans test, approved by the FDA in 1999, can identify the risk of life-threatening arrhythmias not detectable by other noninvasive tests. Easily administered using the ECG, this highly sensitive test can detect very subtle fluctuations in T-wave morphology. Such fluctuations indicate abnormalities in repolarization that predispose to ventricular arrhythmias.

“T-wave alternans testing may be the best non-invasive tool yet for predicting and preventing sudden death,” according to Steven Markowitz, MD. Early studies found that T-wave alternans testing is more sensitive and specific than traditional non-invasive tests such as Holter monitoring or signal averaged ECG.

Moreover, these studies showed that T-wave alternans testing performed as well as invasive electrophysiology study, the gold standard of risk assessment. While EP study can effectively identify risk for serious ventricular arrhythmias, it is invasive, expensive and is not routinely performed on the patients most likely to experience SCD (those with moderate risk of ventricular arrhythmias).

To date, the efficacy of T-wave alternans testing has been demonstrated in several relatively small trials. Perhaps because of the limited nature of this evidence, or perhaps because of physician unfamiliarity, T-wave alternans testing has not yet gained widespread popularity. But a large multicenter trial is now investigating whether interventions based on such testing can positively impact patient outcomes. If results from this

trial are compelling, the test holds good promise for changing the way cardiologists treat patients.

ABCD Trial

The international, multicenter ABCD (Alternans Before Cardioverter Defibrillator) trial is evaluating whether T-wave alternans testing can predict and prevent cardiac events in patients after myocardial infarction.

Sponsored by St. Jude Medical, the ABCD trial was initiated in the spring of 2001. NewYork-Presbyterian Hospital at NewYork Weill Cornell Medical Center has enrolled more patients than any other participating center.

Eligible patients have risk factors including depressed left ventricular ejection fraction (LVEF), non-sustained left ventricular tachycardia, and prior myocardial infarction. They undergo T-wave testing on a treadmill and an EP study. Depending on the outcome of these tests, they may receive an ICD. Patients are then followed to identify whether T-wave alternans is predictive of subsequent events. One of the trial's arms will examine whether patients with normal EP data but abnormal T-wave results benefit from ICDs.

“To date no study has shown that interventions based on T-wave testing can positively impact patient outcomes,” explains Dr. Markowitz. “The real value will be if the test can lead to therapy that saves lives.” ■



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Defibrillators



Claude Beck's 1947 prototype defibrillator treated ventricular fibrillation during open-heart surgery, paving the way for resuscitation outside the operating room.

Today, the placement of AEDs in public places may markedly improve outcomes from SCD that occur outside of hospitals.



Primary Prevention

New research suggests that depressed left ventricular ejection fraction due to a previous myocardial infarction should be considered a sole marker of high risk for sudden death, and warrants ICD implantation.

The ground for secondary prevention of sudden cardiac death is well laid, with catheter ablation, medical therapy, and ICD implantation clearly indicated for high risk patients.

Three recent studies have shed new light, however, on defining just who “high-risk” patients are. They have provided important guidance about the best way to identify high-risk patients through electrophysiology testing, and have illuminated the survival benefits of ICD implantation for patients with a reduced left ventricular ejection fraction. As a result, ICDs may gain a new role as a primary method of prevention.

- The Multicenter Automatic Defibrillator Implantation Trial (MADIT) enrolled patients considered at high risk for ventricular fibrillation based on a low ($\leq 35\%$) left ventricular ejection fraction (LVEF) due to coronary artery disease, spontaneous nonsustained ventricular tachycardia and inducible ventricular tachycardia during electrophysiologic (EP) study. Patients were randomized to receive either an ICD or antiarrhythmic therapy (primarily amiodarone). The ICD reduced mortality by 54% at 27 months.
- The Multicenter Unsustained Tachycardia Trial (MUSTT) studied patients with coronary artery disease and LVEF of $\leq 40\%$. Patients who had inducible sustained ventricular tachycardia during EP study were randomized to receive either conventional therapy or EP-guided therapy (ICD or standard antiarrhythmic medications). After 5 years, the EP-based therapy group had a 25% mortality rate compared to 32% among those receiving conventional therapy. The benefit in the EP-guided treatment group was primarily due to the use of ICDs.
- The MADIT II study was based on the hypothesis that ejection fraction alone was sufficient for identifying patients at high risk for sudden death. It tested the effect of ICD implantation on survival among patients with depressed left ventricular ejection fraction (LVEF) who were not required to undergo electrophysiologic evaluation. Enrolled patients had an ejection fraction $\leq 30\%$ and a previous myocardial



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RELATED RESEARCH: The Role of Polymorphisms

Polymorphisms in genes that regulate ion channels can predispose carriers to sudden death. Although such mutations alone are not sufficient to cause sudden death, their presence can increase the risk of lethal arrhythmias during a cardiac event such as a myocardial infarction.

SCN5A is one such case. About 13% of African Americans carry a polymorphism of SCN5A, a gene that encodes sodium channel activity in the heart and which is also implicated in the Long QT Syndrome, among other arrhythmias. While most carriers never experience arrhythmias, a study published in *Science* in August 2002 found that a polymorphism in this gene may be used as a marker of high risk in conjunction with acquired risk factors such as medications, hypokalemia, and structural heart disease.

Dr. Lerman expects that research into polymorphisms as well as other molecular approaches will elucidate the mechanisms of sudden death, in patients with and without structural heart disease. To that end, Dr. Lerman and his group at Weill Cornell are currently investigating the molecular mechanisms of ventricular tachycardia, and in particular the role of G protein regulation in the genesis of idiopathic VT. They have identified several somatic mutations in G proteins that are thought to mediate ventricular tachycardia in some of these patients.

infarction, with or without prior ventricular arrhythmias. Patients were randomized to receive either an ICD or conventional therapy. Overall, ICD implantation reduced mortality by 29% at 20 months compared to conventional therapy, with an absolute reduction in mortality of approximately 3% per year.

Implications of these studies

“MADIT I and MUSTT demonstrated that inducibility of ventricular tachycardia in patients with moderately reduced left ventricular function identifies patients at risk for sudden cardiac death,” explains Bruce B. Lerman, MD. “The results of MADIT II are important because they suggest that if patients have a markedly reduced ejection fraction ($\leq 30\%$), it is no longer necessary to obtain a Holter Monitor or perform an induction study. Instead, proceeding directly to implantation of ICD is warranted and can be expected to save lives.”

To date, the Centers for Medicaid and Medicare Services (CMS) have awarded partial coverage for MADIT II type patients. Coverage is limited to those patients whose QRS duration is >120 msec. This subset of patients showed the largest mortality benefit in the MADIT II study. ■

Cardiac Surgery Updates

Recent Developments in Robotic Cardiac Surgery

The use of surgical robots during cardiac surgery continues to develop at a rapid pace. The FDA approved the Da Vinci™ Surgical System for mitral valve and atrial septal defect repair in November 2002, and today an FDA-sanctioned, multicenter trial of robotically assisted coronary artery bypass surgery is underway.

Meanwhile, NewYork-Presbyterian Hospital surgeons at NewYork Weill Cornell and Columbia Presbyterian Medical Centers continue to develop new robotic applications and to refine currently approved procedures.

Cardiac surgeons at NewYork Weill Cornell are extremely pleased with their success in using the surgical robot during placement of left ventricular leads for cardiac resynchronization therapy.

The robotic system's superior optics permit excellent vision of key cardiac structures and landmarks without using larger incisions. "The view is better than that provided even by thoroscopic access," explains Charles A. Mack, MD. Performed through three 1-inch incisions, the robot-assisted procedure causes less pain and less blood loss than other minimal access techniques. Furthermore, the robotic technique enables surgeons to place these leads with great precision.

"The robot facilitates this procedure very nicely," says Dr. Mack. "This is one area in which the robot can impact enormously on patient care." Because of its clear advantages, the use of the surgical robot in placing left ventricular leads is now routine at NewYork Weill Cornell Medical Center.

Columbia Presbyterian Medical Center's cardiac surgeons are also using the robotic system to place leads for biventricular pacing. Moreover, surgeons in the Cardiothoracic Division have now adapted certain procedures in order to take advantage of the robotic system's benefits. The Columbia Presbyterian team, led by Dr. Michael Argenziano, has performed over 100 robotic cardiothoracic procedures (more than any other US hospital). In addition to coronary bypass, valve repair, and congenital surgery,

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MAZE Procedure: New Developments in Atrial Fibrillation

An advanced cryoablation technology has made the treatment of atrial fibrillation safe, simple, faster, and therefore available to all patients undergoing cardiac surgery.

Long used to ablate tumors and other types of arrhythmias, cryoablation is known for its safety and efficacy in treating atrial fibrillation (AF) and has been used to ablate tissue for many years. Now NewYork-Presbyterian Hospital surgeons at NewYork Weill Cornell Medical Center are using a new flexible probe (Surgifrost™ made by Cryocath) to perform a modified MAZE procedure without the use of cardiopulmonary bypass.

The probe's argon cooling source produces a far colder temperature than other cryoablation probes, -160°C, resulting in more rapid ablation. It fully maintains the tissue architecture of the ablated tissue, producing no weakening effect. It is also much less



Surgifrost™ catheter facilitates a modified MAZE procedure without the use of cardiopulmonary bypass.

likely to have a deleterious effect on adjacent structures and there is no tissue charring as seen with other devices, according to Charles A. Mack, MD, who has promoted use of the probe at NewYork Weill Cornell.

Because the probe is flexible rather than rigid, it may be used during any concomitant cardiac surgery such as mitral valve repair, coronary bypass, aortic valve replacement, atrial septal defect repair, aneurysm surgery and cardiac procedures, either with or without cardiopulmonary bypass.

"This is the most versatile, and might be the safest, device currently available," says Dr. Mack. Having routinely used the new probe since December 2002, NewYork Weill Cornell has more experience using it than any New York metropolitan hospital. At NewYork Weill Cornell, 80-85% of patients remain free from atrial fibrillation at six months after cryoablation, which

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Atrial Fibrillation Update 2003:

New Standards of Care and a Glimpse of the Future

This accredited interdisciplinary symposium on atrial fibrillation provides an exceptional medical and surgical learning experience for cardiologists, internists, PCPs, cardiac surgeons, nurses and other specialists. The program will include case presentations, interactive discussions, and video footage of innovative surgical and medical management.

October 31, 2003, New York City

Information:

http://www.columbiasurgery.org/programs/cme/cme_afib.html

Registration: **212.305.4993**

See NewYork-Presbyterian Hospital in action on the Discovery Channel's program *Second Opinion*, this fall.

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NewYork-Presbyterian Heart Institute is comprised of physicians of Columbia University College of Physicians & Surgeons and Weill Medical College of Cornell University representing medical and surgical disciplines working together with other health professionals in a collaborative process.

NewYork-Presbyterian Hospital

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Faculty Highlights



David J. Christini, PhD, Assistant Professor of Medicine at Weill Medical College of Cornell University, and Assistant Professor of Physiology and Biophysics at Weill Graduate School of Medical Sciences of Cornell University.

Dr. Christini is working on the development of arrhythmia prediction and prevention technology. Using extensive computer modeling and in vivo experimentation, together with colleagues at Weill Cornell he demonstrated that a rhythm known as alternans could be successfully sensed before its progression to lethal fibrillation. They are working on a novel control strategy, which uses 'smart' adaptive algorithms, for implantable-device arrhythmia prevention.

Dr. Christini completed his Bachelors degree at the Pennsylvania State University and earned his Masters and Doctorate degrees at Boston University. Recent publications include "Nonlinear-dynamical arrhythmia control in humans," *Proceedings of the National Academy of Science*, 98, pp. 5827-5832, 2001.

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Shunichi Homma, MD, Director, Echocardiography Laboratories, NewYork-Presbyterian Hospital at Columbia Presbyterian Medical Center, and Professor of Medicine and Associate Chief, Division of Cardiology, Columbia University College of Physicians & Surgeons.

A specialist in the use of ultrasound imaging modalities, Dr. Shunichi Homma uses transesophageal echocardiography to elucidate cardiac sources of stroke. Since he joined the faculty of Columbia University College of Physicians & Surgeons in 1988, the NIH has awarded Dr. Homma's group over \$7 million in grants. This group recently completed a large multi-center study assessing aspirin and warfarin therapy in preventing stroke recurrences among patients with Patent Foramen Ovale.

Dr. Homma serves on the board of the American Heart Association and is Vice President of the Japanese Medical Society of America. He received his undergraduate degree from Dartmouth College, medical degree from the Albert Einstein College of Medicine, and cardiology training at both Massachusetts General Hospital and Columbia Presbyterian Medical Center.

Recent publications include "Effect of medical treatment in stroke patients with patent foramen ovale: Patent Foramen Ovale in Cryptogenic Stroke Study (PICSS)" *Circulation* 2002;105:2625-31.

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