



Center for Interventional Vascular Therapy

Winter 2006

A Structured Approach to Stroke Prevention:

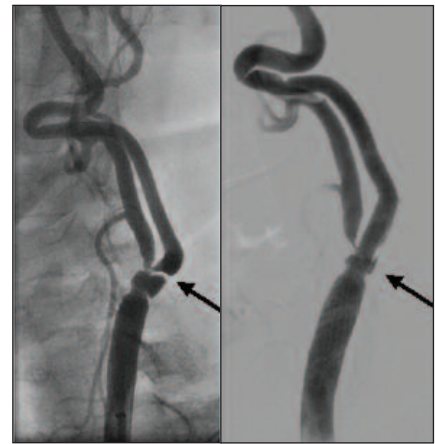
Carotid Stenting, PFO Closure, And Left Atrial Appendage Occlusion

One reason that the Center for Interventional Vascular Therapy (CIVT) has integrated interventional therapies for stroke prevention into comprehensive risk management is the relative importance of prevention. Although acute stroke is treatable, particularly with rapidly administered thrombolytics, only a small fraction of patients in the United States receive this therapy. The significant obstacles involved in the management of acute stroke include delays in patient presentation due to a lack of widespread education, the very narrow window of time in which intravenous treatment is beneficial, and the limited number of centers equipped to diagnose and treat stroke on an emergency basis with catheter-based techniques.

“There are several reasons that patients experiencing an acute stroke are not receiving the currently available therapies, but simply reaching an emergency center in time is one of the most important,” said William A. Gray, MD, Director of Endovascular Services who is working with a team at the CIVT to bring a structured interventional approach to the prevention of stroke.

“Because effective and widespread acute stroke therapy is so limited, strategies to avoid stroke in the first place become even more critical. Our initiative is the first in New York to address this systematically in at-risk patients. Although there are several major components of the program, the most important may be simply recognizing that stroke prevention needs to be more actively incorporated into the goals of a cardiovascular research and treatment center.”

The first major part of the initiative is to treat the causes of thromboemboli or



Left: Carotid artery blockage before stent; Right: Carotid artery after stent procedure.

atheroemboli in the cardiovascular or cerebrovascular systems that place patients at risk for stroke, and CIVT investigators are participating in several large clinical trials designed to identify the safest and most effective strategies to achieve this goal. The 3 primary causes that are being targeted in these investigations are carotid stenosis, atrial fibrillation, and patent foramen ovale (PFO).

One of the largest studies is the CREST (Carotid Revascularization Endarterectomy versus Stent Trial), a National Institutes of Health-sponsored study that is randomizing both symptomatic and asymptomatic patients with carotid stenosis to endovascular stent placement or routine surgery. A similar study, entitled ACT I (Asymptomatic Carotid Trial), is comparing the same 2 interventions but is enrolling only those patients with asymptomatic lesions. While

INSIDE

- 2 Overview of representative research being performed by the Center for Interventional Vascular Therapy and Columbia University Medical Center
- 3 Highlights from the 2006 Transcatheter Cardiovascular Therapeutics meeting, which included several late-breaking clinical trials on drug-eluting stent technology

For more information, visit
www.civtmd.columbia.edu



The following list, arranged by category of intervention, is a brief overview of some of the current research being performed at Columbia/CIVT. This and future issues will highlight many of these protocols and their investigators.

| Study Title & Sponsor | Study Synopsis | PI |
|--|---|---|
| Acute Myocardial Infarction (AMI) | | |
| Horizons Trial Cardiovascular Research Foundation | A dual-arm, factorial randomized trial in patients with ST-segment elevation AMI to compare the results of using either anticoagulation with unfractionated heparin plus routine GP IIb/IIIa inhibition with bivalirudin and bail-out GP IIb/IIIa inhibition, and primary angioplasty with stent implantation with either the Taxus Express™ Paclitaxel-Eluting Stent or bare metal Express2™ stent | Leroy E. Rabbani, MD |
| Atrial Fibrillation & Atrial Arrhythmia Studies | | |
| Protect AF Trial Aritech, Inc | A multicenter, prospective, randomized study comparing the WATCHMAN® left atrial appendage system for embolic protection with long-term warfarin therapy in patients with atrial fibrillation | William Gray, MD |
| Carotid Studies | | |
| ACT I Abbott Vascular Devices | A randomized controlled trial evaluating carotid stenosis stenting using the Xact RX carotid stent and Emboshield cerebral protection system versus carotid endarterectomy in patients with asymptomatic extracranial carotid occlusive disease | William Gray, MD |
| Capture II Trial Guidant Corporation | A multicenter, observational, post-approval study evaluating the FDA-approved RX ACCULINK Carotid Stent Systems and RX ACCUNET Embolic Protection Systems to uncover unanticipated or rare events | Issam Moussa, MD |
| CREST Trial National Institute of Neurological Disorders and Stroke | A prospective, randomized, multicenter trial to contrast the relative efficacy of carotid artery stenting versus carotid endarterectomy in patients with symptomatic and asymptomatic extracranial carotid stenosis | William Gray, MD |
| Chronic Renal Insufficiency Studies | | |
| Cool RCN Trial Radiant Medical, Inc. | An international, multicenter, prospective, randomized study evaluating the application of endovascular cooling to prevent radiocontrast nephropathy in patients undergoing diagnostic or interventional catheterization | Gregg W. Stone, MD |
| Coronary Vessel Imaging & Measurement Studies | | |
| TopSpin Study TopSpin Medical (Israel) Limited & Medsys Inc. (USA) | A prospective, open-label study to evaluate the safety of the TopSpin intravascular magnetic resonance imaging system during coronary artery catheterization of intermediate lesions ($\leq 50\%$ DS) | Jeffrey W. Moses, MD |
| Diabetes Mellitus | | |
| Freedom National Institutes of Health | A multicenter, dual-arm, open-label prospective, randomized study evaluating the optimal management of multivessel disease with either PCI and DES placement or CABG in patients with diabetes mellitus and cardiovascular disease | George Dangas, MD |
| Gene & Stem Cell Therapy Studies | | |
| Baxter Trial Baxter Healthcare Corporation | A double-blind, prospective, randomized, placebo-controlled study to determine the tolerability, efficacy, safety, and dose range of intramyocardial injections of G-CSF mobilized Auto-CD34+ cells for reduction of angina episodes in subjects with refractory chronic myocardial ischemia (ACT34-CMI) | Warren Sherman, MD |
| High-Risk PCI | | |
| Protect I Trial Abiomed, Inc. | A prospective feasibility trial investigating the use of the Impella™ Recover® LP 2.5 system in patients undergoing high-risk PCI (elective PCI in unprotected LM or PCI in last conduit coronary conduit) | Michael Collins, MD; Susheel Kodali, MD |
| Percutaneous Valve Replacement Studies | | |
| Everest II Pivotal Study Evalve, Inc. | A prospective, multicenter, randomized study of the Evalve® cardiovascular valve repair system in the treatment of mitral valve regurgitation | William Gray, MD; Neil Goyal, MD |
| Revival Trial Edwards Lifesciences, LLC | A prospective, multicenter, nonrandomized feasibility study of the Cribier-Edwards aortic bioprosthesis valve for the treatment of critical aortic stenosis using either a transapical or transfemoral delivery approach | Jeffrey W. Moses, MD; Susheel Kodali, MD |

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; DES, drug-eluting stent; DS, diameter stenosis; G-CSF, granulocyte colony-stimulating factor; GP, glycoprotein; LM, left main; PI, principle investigator; PCI, percutaneous coronary intervention; PFO, patent foramen ovale; SFA, superficial artery

Drug-Eluting Stent Technology Focus of Attention at TCT 2006

WASHINGTON—New research on drug-eluting stent (DES) technology was presented in late-breaking clinical trials at the 18th annual Transcatheter Cardiovascular Therapeutics symposium (TCT 2006).

In the LONG-DES II trial, patients with coronary lesions who received sirolimus (Rapamune, Wyeth)-eluting stents had a lower rate of in-segment restenosis than did patients who received paclitaxel-eluting stents. Seung-Jung Park, MD, and colleagues randomized 500 patients from 5 clinical centers in South Korea to receive sirolimus-eluting stents or paclitaxel-eluting stents. Findings revealed a rate of 3.3% in-segment restenosis in the sirolimus-eluting stent group, compared with a rate of 14.6% in the paclitaxel-eluting stent group ($P < 0.0001$). The binary restenosis rate was lower in the sirolimus group in all locations except the proximal edge.

Findings from the SORT-OUT II trial revealed no significant differences between the Taxus (Boston Scientific,

Natick, Mass) and Cypher (Cordis/Johnson & Johnson, Miami Lakes, Fla) stents with respect to primary and secondary study end points. The prospective, randomized trial included 2,100 Danish patients who underwent percutaneous coronary intervention. Patients were recruited at 5 centers throughout Denmark and followed in a “real-world setting.” The stents performed similarly; researchers were unable to detect differences between the 2 groups in major adverse cardiac events (MACE) and secondary end points.

In the ZOMAXX I trial, Bernard Chevalier, MD, and colleagues from the Centre Cardiologie du Nord, St. Denis, France, compared the ZoMaxx zotarolimus-eluting stent (Abbott Vascular, Abbott Park, Ill) with the Taxus paclitaxel-eluting stent. Researchers randomized 199 patients to ZoMaxx and 197 to Taxus. The zotarolimus-eluting stent did not compare favorably with the paclitaxel-eluting stent with respect to the non-inferiority primary end point of in-segment late loss. The result exceeded the protocol-specified noninferiority

margin by 0.02 mm. In-stent restenosis occurred in 12.9% of ZoMaxx patients versus 5.7% of Taxus patients ($P = 0.03$). Overall rates of MACE did not differ significantly between the 2 groups.

Results from the Nordic Bifurcation trial suggest that stenting the main vessel and optionally stenting the side branch may become a routine bifurcation stenting technique. Researchers enrolled 413 patients at 28 centers in 5 European countries. The rate of in-lesion stenosis of more than 50% of the luminal diameter of the main vessel and side branch occlusion was 5.3% with optional side branch stenting and 5.1% with mandatory side branch stenting.

In the single-center HAAMU (Helsinki Area Acute Myocardial Infarction Treatment Re-evaluation)-STENT trial, patients with acute myocardial infarction treated with paclitaxel-eluting stents (Taxus) had a wider luminal diameter and less late loss at follow-up than did similar patients treated with bare metal stents. “The strategy of using paclitaxel-eluting stents in STEMI-PCI appears safe and feasible in the short term, but more data are needed on its long-term effects,” said Ilkka Tierala, MD, of Helsinki University Hospital, Helsinki, Finland.

Stroke Prevention

continued from cover

those trials are being completed over the next several years, the CAPTURE (Carotid ACCULINK/ACCUNET Post-approval Trial to Uncover Rare Events) registry, in which the CIVT is participating and on whose national executive committee Dr. Gray serves, has already proved to be an important source of data for outcomes in carotid stenting. In fact, data on carotid stents from approximately 3,500 patients in the CAPTURE registry were reported at the 2006 Transcatheter Cardiovascular Therapeutics meeting. This study, the largest of its kind, demonstrated that it is possible to identify beneficial characteristics in patients undergoing the stent procedure, and Dr. Gray believes that the CAPTURE reg-

istry is likely to be an important source of data on which to base future intervention studies and determine how to improve care.

A focus on PFO is a second component of the CIVT initiative to improve interventional therapies for stroke prevention. In the absence of other risk factors, PFO is the most important risk factor for stroke in patients younger than age 50 and has generally been treated with anticoagulant medications, although preliminary evidence suggests that using a percutaneously implanted device to close a PFO may also reduce stroke risk. Two national trials are currently under way comparing the stroke outcomes of PFO patients managed with device closure and those of patients treated with anticoagulation.

“Due to the increased risk of stroke

in patients with PFO, the traditional approach has been to provide chronic treatment with an anticoagulant. Now, [Robert Sommers, MD] is leading our efforts looking at a variety of methods of closure that need to be tested for their relative ability to protect against stroke,” explained Dr. Gray. He said that strategies include surgical methods with suturing or clips and “even methods like radio-frequency ablation, in which no device is implanted but the tissue is basically welded together to close the communication.” He anticipates objective evidence from current and planned trials to establish a standard of care in PFO patients.

The third component of the initiative is aimed at patients with atrial

see [Stroke Prevention](#), page 4



Stroke Prevention

continued from page 3

fibrillation, another well-recognized risk factor for stroke. The array of options to consider in reducing stroke in patients with this arrhythmia is growing. The CIVT is the first site in New York where, as part of a pivotal US trial, a dedicated device designed to trap emboli generated during atrial fibrillation is implanted in the left atrial appendage. The device is now being tested in a multicenter trial—PROTECT AF (left atrial appendage system for embolic PROTECTion in patients with Atrial Fibrillation). Although the device was initially tested in patients for whom long-term therapy with anticoagulants was inappropriate, it may prove to be a more attractive and better-tolerated approach to stroke prevention than anticoagulation, even in

patients without contraindications to drugs such as warfarin.

The majority of patients at high risk for cardiovascular events are also at high risk for cerebrovascular events. In fact, most of the risk factors for one are also risk factors for the other. Although stroke is considered a neurologic disorder, physicians who are managing patients with diseases such as atherosclerosis of the peripheral or central cardiovascular system have an opportunity to prevent stroke. Although cardiovascular specialists are generally well aware that the benefits of controlling hypertension and hyperlipidemia include protection against stroke, specialists at the CIVT are developing a complementary interventional approach to stroke prevention in patients with PFO or atrial fibrillation, which are known to place them at risk.

“There has been progress in treatments for acute stroke, but these are likely to remain problematic because there is such a short time between the event and irreversible damage. Better systems for accelerating treatment may reduce the morbidity and mortality of acute stroke, but the best approach is prevention,” Dr. Gray said. “We are putting the pieces together for a more comprehensive approach to prevention that includes identifying patients at high risk and providing safe and effective intervention, when appropriate, to reduce the rate of events.”

William A. Gray, MD, is Director of Endovascular Services at the Center for Interventional Vascular Therapy, NewYork-Presbyterian Hospital/Columbia University Medical Center, and Associate Professor of Clinical Medicine at Columbia University College of Physicians and Surgeons.

Center for Interventional Vascular Therapy

Editor:

William A. Gray, MD

Contributing Editors:

Jeffrey W. Moses, MD
Martin B. Leon, MD
Gregg W. Stone, MD

Mark A. Apfelbaum, MD
Stephane Carlier, MD, PhD
Michael B. Collins, MD
Antonio Colombo, MD
George D. Dangas, MD, PhD
Mary Egan, BSN
Michael C. Guiry, PA
Marian C. Hawkey, RN
Ajay Kirtane, MD
Susheel K. Kodali, MD
Mary A. Kral, PA-C, MSM
Edward M. Kreps, MD
Alexandra J. Lansky, MD
Roxana Mehran, MD
Issam Moussa, MD

Hilary Nierenberg, MS, ANP
Eugenia Nikolsky, MD, PhD
LeRoy E. Rabbani, MD
Warren Sherman, MD
Binoy Kumar Singh, MD
Varinder Singh, MD
Robert Sommer, MD
Paul Teirstein, MD
Giora Weisz, MD
Steven D. Wolff, MD

Administrative Contact:

Richard H. Gemming, MPH
Chief Operating Officer



COLUMBIA UNIVERSITY
MEDICAL CENTER

NewYork-Presbyterian
The University Hospital of Columbia and Cornell

161 Ft. Washington Avenue, 5th Floor
New York, NY 10032

212.305.7060 / 212.342.3660
www.CIVTMD.org

NONPROFIT ORG.
U.S. Postage PAID
Permit No. 566
Utica, NY