Pulse of CRF

The Newsletter of the Cardiovascular Research Foundation

Winter 2013 - Vol 7, TCT Issue

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Upcoming CRF Educational Events

Conference on Cell Therapy for Cardiovascular Disease
January 22-24, 2014
Vivien and Seymour Milstein Family Heart Center
New York, NY

Complex PCI
February 27-March 1, 2014
New York Marriott Marquis
New York, NY

Cutting-Edge Clinical Research Presented at TCT 2013

The annual Transcatheter Cardiovascular Therapeutics (TCT) scientific symposium is the world's preeminent forum for interventional cardiologists, cardiac surgeons, and vascular medicine specialists.

TCT celebrated a milestone 25 years at the 2013 meeting held in San Francisco, California. Attracting over 11,500 attendees, the symposium broke new ground by distributing tablet computers to attendees and producing an innovative digital app, enabling attendees to interact with sessions like never before and substantially reducing the need for printed materials. Highlights from the scientific sessions included:

New TAVR Options on the Horizon:

The pivotal CoreValve Extreme Risk trial found that transcatheter aortic valve replacement (TAVR) with the CoreValve device substantially reduced the incidence of death and major stroke at 1 year in US patients with severe aortic blockages considered too high risk to undergo surgery. An expanded study is ongoing and has enrolled nearly double the number of patients included in the current research.

Further, the REPRISE II trial tested the safety of a second-generation TAVR device internationally. The Lotus Valve System was associated with low rates of complications in symptomatic patients with severe aortic blockages who were at high risk for surgery. Successful implantation and positioning of the valve was achieved in all patients.

(See TCT 2013 page 4)

Jack Lewin, MD
President and Chief Executive Officer of CRF

CRF Selects Jack Lewin, MD, to Serve as President and CEO

The Cardiovascular Research Foundation has appointed Jack Lewin, MD, as the organization's new president and chief executive officer. Lewin, who will also serve on CRF's board of directors, comes equipped for his new role after years of experience as a practicing physician, leader and manager.

He succeeds William A. Himmelsbach, MPH, who retired in late 2012. CRF board member Colette Y. Gardner has served as president and co-chair of the Executive Leadership Council in the interim.

(See Jack Lewin, MD, page 6)

In Memoriam: Andreas Gruentzig, MD, Receives TCT Career Achievement Award

CRF was delighted to have Gruentzig's family and close associates from the early years of his career present at TCT to share in this special tribute.

The Cardiovascular Research Foundation presented Andreas Gruentzig, MD, the TCT Career Achievement Award posthumously on Tuesday, October 29, in recognition of his contribution to the development of the field of interventional cardiology.

More than 35 years ago, Dr. Gruentzig, now considered by many to be the father of interventional cardiology, performed the first balloon angioplasty of a coronary artery in Zurich, Switzerland. The procedure began a revolution in the field of cardiology, offering patients an alternative to bypass surgery and opening the door to percutaneous cardiovascular procedures including transcatheter treatment of valvular disease, hypertension and heart failure, and prevention of stroke.

Gruentzig, 46, and his wife Margaret Anne, died in a plane crash in Georgia in October 1985. CRF was delighted to have his family and close associates from the early years of his career present at TCT to share in this special tribute.

"Without Dr. Gruentzig's singular vision and determination, our subspecialty would not exist, and tens of millions of patients would not have benefited from the lesser invasive approach to coronary artery disease that is angioplasty," said TCT director Gregg W. Stone, MD.

Gruentzig had the "charisma and force of personality to stand up to doubters and persist in the face of adversity, promoting a technique that he knew in his soul could help so many," Stone said.

Birth of a Subspecialty

Gruentzig earned his medical degree in Heidelberg, Germany, in 1964 and began training in angiology. Soon after, he took an interest in techniques pioneered by vascular radiologist Charles Dotter, MD, for opening vessels in the legs using catheters. Gruentzig learned these techniques from his mentor, Eberhard Zeitler, MD, in Nuremberg, Germany.

With his interest piqued, Gruentzig began using catheters in practice but knew that in order to apply the technique to coronary arteries, a new type of device would be required. The device would have to be small enough to enter the arteries, but also would have to be able to enlarge once it was placed inside the obstruction.

Spencer B. King III, MD, of Saint Joseph's Medical Group in Atlanta, Ga., said Dr. Gruentzig hit upon the idea of a balloon that would expand inside the artery. Working in his kitchen with colleagues, he began to experiment with materials, focused on the idea that the balloon would have to be rigid to force open the lesion.

The double lumen catheter with a polyvinyl chloride balloon they developed was tried first in leg arteries and then kidney arteries, and was finally miniaturized enough for use in coronary arteries.

Early Experiments

In 1976, Gruentzig presented the results of his animal studies involving his new device in a poster at the American Heart Association (AHA) Scientific Sessions. In the studies, a silk ligature was used as a constrictor in the canine coronary artery dilation. The balloon was expanded to break the thread and restore flow.

Although Dr. King admitted to being skeptical of the idea, the experiment caught the eye of other physicians at the meeting, including Richard Myler, MD, who would eventually invite Gruentzig to perform angioplasty on one of his sedated surgical patients in San Francisco.

Not long after in September 1977, Dr. Gruentzig performed the first coronary angioplasty on an unanesthetized patient in Zurich.

Spreading the Word

In 1977, Gruentzig was invited back to the AHA Scientific Sessions to make an oral presentation about his animal experiments. Instead, he presented his first four human angioplasty cases including one very dramatic procedure of a left main stenosis.

"The reaction from the audience was astonishment," King said. "He received a standing ovation."

As interest in learning the technique increased, Gruentzig began to televise courses from Zurich where he would demonstrate the procedure to colleagues eager to learn.

"There was a lot of collegiality at that time," said King. "People who had done 10 procedures were experts at the time and they interacted with people who were just starting out with it."

Gruentzig had a drive and determination to educate and share his knowledge with the world, but he also was concerned that the procedure not be misused.

According to Stone, Gruentzig symbolized the characteristics that exemplify current interventional cardiology including a thoughtful and evidence-based approach to procedures that always puts the patient's interests and outcomes first.

In January 1980, Gruentzig moved to the United States where he joined the faculty, including King, at Emory University in Atlanta. During the next few years, he worked with others to develop the technique. By 1984, trials comparing angioplasty with bypass surgery were initiated. Unfortunately, Gruentzig did not live to see the amazing results of those studies.

> "If he was alive today, he would be tremendously proud of this whole specialty that he started, which has gone from a kitchen table to a specialty that has grown worldwide."
>
> - Spencer B. King III, MD

"Interventional procedures not only have become the dominant procedures for coronary interventions, but also are dramatically outpacing surgery and have, more importantly, become the primary procedure for acute MI and have opened the flood gates to structural heart interventions and more," said King. ●

TCT Goes Tablet

By distributing tablets to attendees, TCT reinvents the medical conference.

For the first time in its history, the Transcatheter Cardiovascular Therapeutics conference went completely paperless and distributed tablet computers to all paid registrants for the full TCT week, a decision that reflects its 25-year history of forward thinking and innovation not only in the field of interventional cardiology but also in education.

Information at fingertips

At TCT 2013, instead of a bulky conference bag stuffed full of programs, calendars, abstracts, and agendas, each attendee received a Samsung Galaxy Tab® 3 8 tablet preloaded with all of the information needed to successfully navigate the conference.

"In addition to TCT's usual focus on the latest research breakthroughs and developments in interventional cardiology, the tablet initiative is part of CRF's overall long-term digital strategy to innovate and enhance medical education, making it more interactive, dynamic and informative. Our goal was to optimize the educational experience and enhance learning for all meeting participants." - Gregg W. Stone, MD

Johnnie White, executive director of the CRF Center for Education highlighted another benefit to the new format. "You're able to have access to the most up-to-date content for the TCT program," he said, noting that the app was updated frequently to keep pace with events during the conference.

Going paperless is not a new idea when it comes to medical conferences. Many physicians have likely attended a conference with information available online. However, these meetings rely on the attendees to have a tablet, computer, or smartphone to access that information.

Attendees were welcome to use their own mobile devices—there are downloadable Android and iOS versions of the app. Unlike program and abstract books, which are used for a few days and then typically discarded, the TCT tablet will serve as year-round educational tool that not only reduces waste but also enhances learning.

In addition to the traditionally preloaded apps like an Internet browser and e-mail, TCT preloaded two applications onto each tablet for the convenience of attendees:

- The TCT app: This app provided attendees the ability to view and search the TCT program, plan their schedule, claim CME credits, navigate the Moscone Center, communicate with other attendees, take notes and much more.
- TCTMD app: This app provided attendees with mobile access to slide presentations from every recent TCT as well as the library of content from the TCTMD Web site, including daily news, journal summaries, conference coverage and CME programming.

Importantly, TCT and CRF did not collect any data from the tablet, and advertisements were only visible within the preloaded apps.

Tech Savvy

The tablet also allowed attendees to tally the number of CME hours they accrued at the meeting and to have a certificate sent verifying the credits.

If attendees arrived at the conference with their own tablet, they could download the apps through iTunes and Google Play.

TCT provided technical support for the tablets on the second floor of the West building, as well as at multiple kiosks located throughout the convention center.

CRF Physician Participates in NYC Marathon

Congratulations to Philippe Généreux, MD, Director, Angiographic Core Laboratory at CRF, who ran the NYC Marathon with a time of 3:50.

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TCT 2013

High Prospects for Third-Generation DES

Safety and effectiveness of new stents were tested in two studies. The SORT-OUT VI trial compared a stent with a permanent polymer coating and a stent with a biodegradable coating that releases the drug biolimus in Scandinavian patients. Both stents were associated with low rates of major cardiovascular complications 12 months after angioplasty.

The DUTCH PEERS (TWENTE II) trial was the first to compare the safety and effectiveness of third-generation drug-eluting stents. Both the Resolute Integrity zotarolimus-eluting stent and the Promus Element everolimus-eluting stent performed well with no differences in a study of nearly 2,000 patients. The third-generation stents release the same drugs as second-generation DES, but involve novel stent platforms with more flexible designs. The trial was simultaneously published in The Lancet.

Support for Short-Term Dual Therapy

Results of two studies provided further evidence that shorter-term dual antiplatelet therapy, or DAPT, lasting 3 months after stenting may be safe, while prolonged therapy beyond 1 year may be harmful. OPTIMIZE showed the noninferiority of 3-month DAPT to standard 12-month therapy after implantation of the Endeavor stent. Importantly, short-term DAPT did not increase the risk of dangerous blood clots that can form inside the stent, known as stent thrombosis. Results of the OPITMIZE trial were also published in the Journal of the American Medical Association.

In the ARCTIC-INTERRUPTION trial, no benefit was noted and greater risk of bleeding was seen when DAPT was continued beyond 12 months. The study was the second half of the randomized ARCTIC trial, which tested adjustment of antiplatelet therapy based on platelet function testing. At 1 year after stenting, roughly half of the original randomized cohort, who were at lower risk than the overall population, were randomly assigned to either stop DAPT or continue it for up to 18 months. At follow-up, there was no difference in complication rates. However, those who discontinued DAPT experienced less bleeding

Two Stents for Bifurcation Lesions?

Treating coronary blockages that have split into two branches, also known as bifurcation lesions, has proven difficult and two studies examined the outcomes associated with using a two-stent treatment approach compared with traditional single stenting plus using an additional stent when necessary. In NORDIC-BALTIC BIFURCATION IV, rates of major complications at 6 months were comparable between treatment options.

The Tryton Bifurcation study failed to show noninferiority of the two-stent strategy compared with single-stenting plus an additional stent when necessary. However, it did find that the new technique was better than provisional stenting at widening the side branch, or the secondary branch of the lesion, at 9 months.

Angioplasty Best Practices

The CHAMPION PHOENIX trial explored the relationship between stent thrombosis that occurs during angioplasty and short-term complications. While a small percent of patients develop stent thrombosis during angioplasty, the study found that it carries serious implications for patients, as it is related to longer hospital stays. Importantly, use of the antiplatelet drug cangrelor was found to help prevent intraprocedural stent thrombosis.

Performing angioplasty via an artery in the wrist (radial) as opposed to the groin (femoral) is reasonable and may be preferable in women, according to results from the SAFE-PCI for Women study. There was a substantial reduction in complications with the radial approach, and it resulted in lower volumes of contrast dye being used. In addition, radial access was preferred by the majority of women.

A subgroup analysis from the FREEDOM trial of diabetic patients assigned to either open-heart

surgery or angioplasty with a first-generation drug-eluting stent found higher rates of major complications at 5 years among those treated with insulin. However, the differences in clinical outcomes between surgery and angioplasty were maintained regardless of the presence or absence of insulin treatment. Stroke rates were higher among patients assigned to surgery regardless of insulin use.

The SMART-CASE randomized trial found that in patients with intermediate coronary blockages, a conservative approach to determining appropriateness of angioplasty is safe and equivalent to an aggressive approach. At 1-year follow-up, both strategies exhibited comparable rates of adverse events

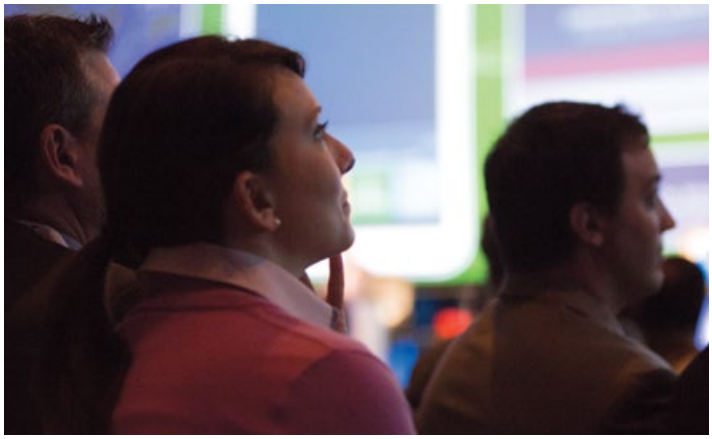
Revascularization Techniques Scrutinized

The first randomized pilot study of a new revascularization technique that combines minimally invasive bypass surgery with angioplasty is safe and feasible in select patients with multivessel heart disease, according to results from the HYBRID trial. The vast majority of patients who underwent the hybrid procedure received complete revascularization, with a small percentage requiring conversion to open surgery. Complications at 1 year did not differ between study groups, and there was no incidence of stroke in either group. Future analyses plan to address quality of life and cost-effectiveness of the hybrid procedure.

In TATORT-NSTEMI, aspiration thrombectomy, or using a device to "suck out" coronary blockages, failed to reduce the extent of microvascular obstruction or improve outcomes compared with standard coronary angioplasty alone in less severe heart attack patients. This lack of benefit was consistent across subgroups and blockage size and blood flow level. At 6 months, patients showed similar complication rates regardless of whether they did or did not receive thrombectomy with angioplasty.

Diagnostic Tools Improve Upon FFR

Two studies explored novel strategies of accurately assessing inadequate



There were over 11,500 attendees at TCT 2013. This year, 1,750 abstracts were submitted from 56 countries and 39 U.S. states. Reviewers narrowed that number down to 851—a 49% acceptance rate.

blood flow compared with a method called fractional flow reserve, or FFR. For HeartFlowNXT, FFR derived from computed CT scans (FFRCT) was compared with coronary CT angiography and invasive FFR alone. Per-patient diagnostic performance was better with FFRCT compared with the other two methods without sacrificing specificity.

ADVISE II was a global study that compared traditional FFR with instantaneous wave-free ratio (iFR), which does not require the administration of the drug adenosine. In the study, iFR performed well with regard to the percentage of coronary blockages properly classified by hemodynamic severity. A hybrid iFR/FFR approach also appropriately classified the vast majority of blockages.

Encouraging Results for Drug-Coated Balloons

Two trials showed encouraging results for drug-coated balloons in patients with diseased arteries in the legs. Six-month findings from the LEVANT 2 trial comparing an investigational paclitaxel-coated balloon with standard balloon angioplasty at 55 global sites showed advantages to the drug-coated balloon. Safety outcomes were similar between the two treatment groups.

Similarly, the multicenter, prospective, randomized RIBS V trial compared the use of DES and drug-coated balloons in treating vessel re-narrowing after stenting. Patients with bare metal stents received either the Xience Prime everolimus-eluting stent or SeQuent Please paclitaxel-coated balloon. At 1 year follow-up, the stent was slightly more effective, but both techniques yielded similarly positive outcomes.

TCT 2013 featured nine late breaking trials and 12 first report investigations. A cornerstone of every TCT, these trials are typically the initial worldwide presentation of clinical trials, impactful single-center or multicenter registries, or important follow-up data from major randomized trials and first-in-man experiences with novel devices or drugs.

Treatment Additions for STEMI Patients Explored

Results from CHILL-MI indicate that in patients who have suffered the most serious form of a heart attack known as STEMI, rapid cooling prior to restoring blood flow is safe and feasible. Patients were randomly assigned to standard of care or hypothermia induced by cold saline and endovascular cooling. Cooling did not reduce infarct size in relation to heart tissue at risk in the allotted time. No patient died, but the incidence of clinical heart failure was lower in the hypothermia group.

Administering the antithrombin agent bivalirudin to STEMI patients during transport to the hospital reduces the risk of short-term death and major bleeding better than heparin plus optional use of a glycoprotein IIb/IIIa inhibitor, or GPI, according to results from the EUROMAX trial. No difference was seen between the two strategies for all-cause or heart-related death, although the trial was underpowered for these endpoints. Findings of the trial were also published in the New England Journal ofvcine

Inconsistent Results with Platelet Function Testing

TRANSLATE-POPS showed that routine blood platelet function testing with the VerifyNow P2Y12 test had only a modest impact on the amount of adjustment to antiplatelet therapy of patients with STEMI and non-STEMI heart attacks. Incidence of therapy adjustment before hospital discharge in the patients who received routine platelet function testing was higher than in those not undergoing such testing. The majority of adjustments manifested as drug switches, rather than adjustments in dose, and primarily involved switching from the standard blood-thinner clopidogrel to the newer agent prasugrel.

But in the GIANT trial, platelet function testing was helpful for optimizing antiplatelet therapy for individual patients tested within 48 hours of an acute heart attack and treated with a first-time angioplasty with stenting. Among slow responders to clopidogrel who were adjusted to optimal therapy based on platelet function testing, the occurrence of death, heart attack, and stent thrombosis at 1 year was similar to normal or high responders. ●

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Jack Lewin, MD

Shaping the future of interventional cardiology

According to Lewin, as soon as he was approached about the new role, he was eager to hear more. "There's not a cardiologist in the interventional space worldwide who doesn't know what TCT is or hasn't looked at the TCTMD Web site," he said. "CRF itself is a fantastic institution that runs not only conferences but also pursues clinical and preclinical research. Putting that all together to advance science and translate those findings to clinical practice is really exciting."

During his time as CEO of the American College of Cardiology (ACC) between 2006 and 2012, the ACC and CRF began discussing ways to collaborate. In 2008, CRF began to help select interventional content for the Innovations in Interventions (i2) Summit at ACC's Annual Scientific Session, and in 2011 ACC became an official co-sponsor of TCT.

One of the most pressing concerns in the United States, Lewin noted, is how to curb costs while providing the best possible care for patients.

"There is an enormous amount of change going on in terms of economics that will radically influence where research, education, and clinical practice go," he explained. "The American health care system, for all of its fantastic achievements, is not always fantastic at the point of care. There's a lot of unevenness in quality. But the key issue is that it's unaffordable and unsustainable, and there are many people not included in coverage today."

CRF, Lewin predicted, could be the chief advocate in the cardiovascular space. "I look forward to bringing information back to CRF about where health care is going, and I would like to bring our experience here back to the national discussion," he said. "Cardiovascular medicine constitutes almost 40% of the Medicare budget, so to the extent that we can figure out better ways to make people healthier using technology and lifestyle and whatever else we learn, CRF's work is going to be important for the nation's economic future."

Bringing proven leadership and expertise on board

According to Gregg W. Stone, co-director of the Medical Research and Education Division of CRF, Lewin will be a good fit. "Jack Lewin is a true visionary with exceptional experience in health care delivery, and in leading cardiology systems in new and exciting directions," Stone commented.

Prior to joining the ACC, Lewin was CEO of the California Medical Association and director of health of Hawaii. As a commissioned officer in the U.S. Public Health Service, he founded and directed the Navajo Nation Department of Health, serving the needs of America's largest American Indian tribe. Lewin received his BA in Biological Sciences from the University of California, Irvine, and his MD from the University of Southern California. He and his wife Sandra have three children.

Pulse of CRF

President and Chief Executive Officer
Jack Lewin, MD

External Relations
Irma J. Damhuis

Managing Editor
Jason Kahn

Associate Editors
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Program Manager
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Project Manager
Juan Iturriza

Designer
Diana Sanchez

CARDIOVASCULAR RESEARCH FOUNDATION
At the heart of innovation

111 East 59th Street
New York, NY 10022
Tel. 646-434-4500

WWW.CRF.ORG