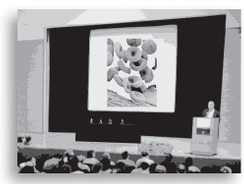
News & Views in ...

Interventional Cardiology

News & Views

News

Conference Scenes



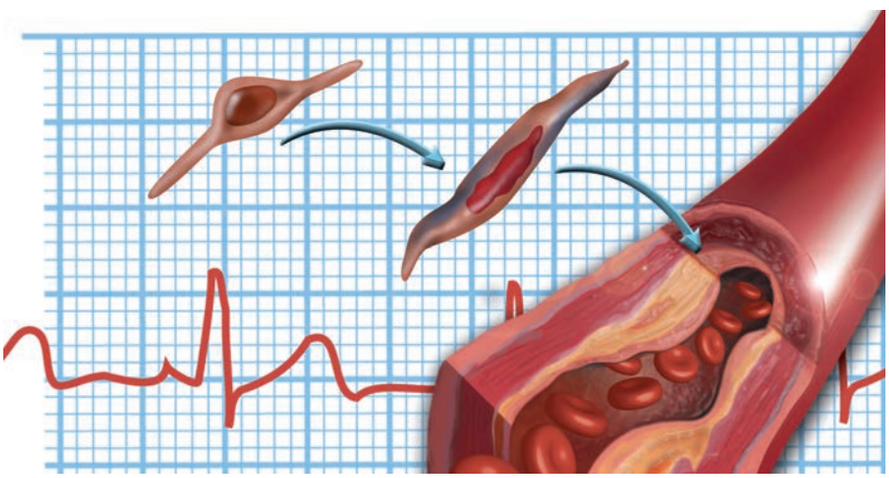
Grant awarded to study adult stem cells as an alternative to stent implantation

The NIH has awarded a 5-year US$3.3 million grant to Devendra Agrawal and his colleagues from the Creighton University School of Medicine (NE, USA) to study the possibility of using adult stem cells to repair coronary arteries following interventional procedures such as stenting and balloon angioplasty.

Agrawal explains that restenosis or re-narrowing of the arteries occurs in between 11 and 18% of patients within 4 years following intervention. Speaking to *Interventional Cardiology,* he pointed out that "Mechanical denudation of endothelial lining during coronary intervention is one of the underlying mechanisms of late stent thrombosis and neointimal hyperplasia. Although the injury may stimulate re-endothelialization, the time required for this process is too long to prevent the early critical events, leading to stent thrombosis and neointimal hyperplasia." Drug-eluting stents are used to reduce the risk of restenosis, however they carry their own risks, potentially leading to thrombosis, which when treated with antiplatelet therapy can lead to further side effects. The team's goal is therefore to ascertain whether adult stem cells, treated along with gene therapy, is superior to the use of drug-eluting stents following these procedures.

Agrawal and his team plan to inject a novel gene, along with autologous bone-marrow-derived mesenchymal stem cells that have been primed to differentiate under specific conditions, into endothelial cells to re-endothelialize the artery at the site of intervention in a porcine model. He believes that "Rapid restoration of the endothelial lining and the future ability to engineer endothelial progenitor cells to perform physiological endothelial functions might be a suitable alternative therapy for restenosis." He hopes this research will lead to the ability to eliminate the need to implant drug-eluting stents in the coronary artery.

Source: Creighton to Explore Usage of Adult Stem Cells to Improve Angioplasty Results: www.creighton.edu/publicrelations/newscenter/news/2012/january2012/january232012/agrawalgrantnr012312/index.php (Accessed March 2012).



Future Medicine part of fsg

The Resolute Integrity™ drug-eluting stent is approved by the US FDA and supported by data of the TWENTE trial

The zotarolimus-eluting Resolute Integrity™ stent (Medtronic CardioVascular, CA, USA) has received US FDA approval following studies with this device and its direct predecessor – the Resolute stent. The RESOLUTE All Comers trial was the first study to demonstrate noninferiority of the Resolute stent compared with the FDA-approved XIENCE V® stent (Abbott Vascular, IL, USA). This has now been confirmed in the TWENTE trial.

Resolute Integrity may have benefits over alternative drug-eluting stents (DESs) in that it has an indication for diabetes and addresses some difficulties in deliverability. It is hypothesized that the stent is effective for the treatment of diabetic patients due to its long-term (6-month) elution of the drug, which would allow for the differences in healing and neointimal hyperplasia observed in diabetic patients. The stent is also designed to exhibit a larger range of motion and increased flexibility due to its use of sinusoidal technology and should therefore be easier to navigate.

In the RESOLUTE All Comers trial, Resolute was demonstrated to be on a par with XIENCE, with patients from each group exhibiting similar target lesion failure within 1 year. The diabetic subgroup also exhibited low target lesion failure, target lesion revascularization and definite/probable stent restenosis rates within 12 months after implantation.

The TWENTE trial is the first reported study to confirm the main findings of the RESOLUTE All Comers studies. Clemens von Birgelen, principle investigator of the trial (Thoraxcentrum Twente, Enschede, The Netherlands), explained to *Interventional Cardiology* that the controlled, head-to-head comparative DES trial randomized 1391 patients, of whom the majority presented with acute coronary syndromes, off-label characteristics and complex coronary lesions, to receive Resolute or XIENCE V. At 1 year, with complete follow-up of all patients, the groups receiving each stent were similar with regards to the primary end point of target vessel failure.

von Birgelen believes that the TWENTE study also adds its own interesting findings. "Despite the meticulous search for clinical events, the incidence of adverse clinical end points in the TWENTE trial was relatively low. For instance, in TWENTE, the incidence of definite stent thrombosis tended to be lower than in the RESOLUTE All Comers trial. In addition, TWENTE is the first randomized DES trial that revealed, in a 'real-world' population of complex patients and lesions, 0% definite stent thrombosis in a Xience study arm. TWENTE also showed no acute or sub-acute clustering of Resolute stent thromboses, as was seen in the RESOLUTE All Comers trial. This difference in events with very low incidence may be best explained by a play of chance. All this underlines the importance of performing more than just one large randomized trial to evaluate major competing medical devices."

von Birgelen and his team feel that the TWENTE trial underlines that both DES types are "excellent workhorse stents" for daily routine use in clinical practice. However, he points out that "while the relatively low adverse event rates suggest that the coatings and/or drugs used may have achieved a step forward in terms of improving biocompatibility, long-term data based on two or more years of follow-up is necessary to finally judge this issue."

Sources: Medtronic Resolute Integrity™ Drug-Eluting Stent Obtains FDA Approval for Treating Coronary Artery Disease: www.medtronic.com/Newsroom/NewsReleaseDetails.do?itemId=1329500135294 (Accessed 28 February 2012); von Birgelen C, Basalus MWZ, Tandjung K et al. *A randomized controlled trial in second-generation zotarolimus-eluting Resolute stents versus everolimus-eluting Xience V stents in real-world patients: the TWENTE trial.* J. Am. Coll. Cardiol. *doi:10.1016/j.jacc.2012.01.008 (2012) (Epub ahead of print).*

Computed tomographic angiography is effective when used as a gatekeeper prior to invasive angiography

A team from the William Beaumont Hospital (Royal Oak, MI, USA) has recently demonstrated that computed tomographic angiography (CTA) is potentially a useful method to ensure appropriate utilization of invasive angiography for suspected coronary artery disease (CAD).

Kavitha Chinnaiyan, first author of the study, explained to *Interventional Cardiology* that "The issue of over-utilization of cardiac imaging is a growing one that has resulted in multiple societies collaborating to formulate appropriate use guidelines. We know from previously published data by the National Cardiovascular Data Registry that invasive angiography across the nation results in a diagnostic yield of <40% in terms of obstructive disease, pointing once again to appropriate use and, more importantly, appropriate patient selection for the catheterization laboratory."

The group hypothesized that coronary CTA, an anatomic test, could be ideal as a 'gatekeeper' to the catheterization laboratory. Their study included data from academic centers, community hospitals, free-standing imaging centers and private physician offices, across multiple specialties. All of the 6198 patients involved had been referred for CTA within 3 months of a stress test and the team studied how well certain factors, such as stress test results and symptoms, corresponded with obstructive CAD, defined as 50% stenosis or greater. The cohort included those with symptoms suggesting ischemia (82.6%) and those with cardiac risk factors (17.4%). Of these, 58.5% had abnormal stress tests.

On CTA testing, it was reported that 18.7% of the patients had obstructive CAD, with a correlation between CTA and angiographic findings in the 621 patients who underwent invasive angiography. Stress test results did not independently predict obstructive CAD on CTA. The team also found that even among patients with normal stress tests, 34% had nonobstructive disease, while 15% had obstructive disease. "This suggests that these patients may not have been identified to have coronary disease without an anatomical test and that coronary CTA provides incremental information to aid in further risk stratification and optimal therapy," Chinnaiyan noted to *Interventional Cardiology*.

The researchers also report that, using CTA, they found that 23% of the studied asymptomatic patients had obstructive coronary disease. The team feel this leads to questions of whether revascularization would help in such asymptomatic patients and what the optimal revascularization approach should be.

Chinnaiyan believes that "Our results indicate that indeed, coronary CTA is well-suited to perform a gatekeeper function, particularly in patients who need adjudication of their stress test results."

The study was part of the ongoing statewide registry of coronary CTA, the Advanced Cardiovascular Imaging Consortium (ACIC). The team has several ongoing projects with the ACIC, including radiation-dose reduction and establishment of appropriate CTA use across the state.

Source: Chinnaiyan KM, Raff GL, Goraya T et al. *Coronary computed tomography angiography after stress testing: results from a multicenter, statewide registry, ACIC (Advanced Cardiovascular Imaging Consortium).* J. Am. Coll. Cardiol. *59, 688–695 (2012).*

Minimally invasive gel-based technique for heart attack-induced tissue damage on the horizon

A team from the University of California, San Diego (CA, USA) has developed a hydrogel that may be effective in treating heart attack-related tissue damage. The hydrogel can be injected via a catheter, and has been demonstrated to be safe in rats, with unpublished data also showing it to be effective in pigs.

Karen Christman, senior author of the study, explained to *Interventional Cardiology* that "Our myocardial matrix material is the first injectable material that is cardiac specific and is also the first material that has been delivered via a percutaneous transendocardial approach. The latter is particularly significant since the majority of existing injectable materials are not deliverable via a catheter over the multiple injections required in the heart, because of incompatible gelation kinetics." The team has solved this issue by producing a gel that, initially a liquid, forms the required semi-solid gel once it is injected *in vivo* and reaches body temperature.

It is intended that the hydrogel, derived from decellularized ventricular extracellular matrix, will encourage cardiomyocyte repopulation of damaged areas, promoting remodeling whilst maintaining cardiac function. The team initially injected the hydrogel into Female Sprague-Dawley rats who had experienced ischemic reperfusion 2-weeks earlier; a control group received a saline injection. The implantation response was measured using histology and immunohistochemistry, and the rats were assessed for arrhythmogenesis and underwent MRI 1 week prior to the injection and 4 weeks after the cardiac event. The gel was not rejected, nor did it trigger arrhythmia, suggesting that it may be safe in humans. Following their promising results, the team then studied a porcine myocardial infarction model, assessing the catheter delivery approach via histology, and reported improved cardiac function.

Ventrix (CA, USA), cofounded by Christman, is focusing on starting a Phase I trial in Europe using the material. Her laboratory is also hoping to explore how the material could be used as a delivery vehicle to enhance cell and growth factor therapies.

Sources: Singelyn JM, Sundaramurthy S, Johnson TD et al. *Catheter-deliverable hydrogel derived from decellularized ventricular extracellular matrix increases endogenous cardiomyocytes and preserves cardiac function postmyocardial infarction.* J. Am. Coll. Cardiol. *59, 751–763 (2012); Injectable Gel Could Repair Tissue Damaged by Heart Attack: www.jacobsschool.ucsd.edu/news/news_releases/release.sfe?id=1167 (Accessed March 2012).*

– All stories written by Francesca Lake

About the News and Views

The News and Views highlights some of the most important events and research in the field of cardiology.
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