

Interventional Cardiology



NEWS



RESEARCH HIGHLIGHTS



CONFERENCE SCENE



Study investigates the potential effects of circadian variation on stent thrombosis

A recently published study from researchers at the Mayo Clinic (MN, USA) concluded that coronary stent thrombosis may be more common in the early morning, due to patient circadian rhythms.

David R Holmes Jr and colleagues conducted a retrospective analysis of 124 patients who presented at the center with definite stent thrombosis between February 1995 and August 2009 in order to examine the potential effects of circadian variation, as well as weekly and seasonal changes on stent thrombosis. All 124 patients underwent repeat PCI in the previously stented coronary artery segment. Stent thrombosis was confirmed by angiographic review and the timing was derived from medical records. Patients with sudden death were excluded.

The investigators observed an association between onset of stent thrombosis and time of day, with the lowest incidence at 8 pm and the highest at 7 am ($p = 0.006$). Examining early (0–30 days), late (31–360 days) and very late (>360 days) stent thrombosis, only early cases continued to show a significant link to the time of day ($p = 0.030$). No variation was observed among different days of the week, but it was determined that stent thrombosis was more common during the summer, peaking at the end of July and beginning of August ($p = 0.036$).

The potential triggers of stent thrombosis were also explored. Overall, 96% of patients were taking aspirin at the time of occurrence, and in the early stent thrombosis group, 89% patients were receiving clopidogrel or ticlopidine, but less

than half of the patients with late or very late stent thrombosis remained on dual antiplatelet therapy.

Of the 62 patients whose activity levels were documented in their medical records, 33.9% were sleeping prior to the event, 25.8% were lying or sitting, 29% were engaged in light-to-moderate physical exertion and 11.3% were engaged in heavy physical activity. However, the link between physical exertion and coronary stent thrombosis remained circumstantial.

The researchers noted that there could potentially be a number of reasons why the risk of stent thrombosis is elevated in the early morning. For example, elevated blood pressure could cause sheer stress leading to thrombosis. In addition, high blood viscosity and coagulation in the morning could also be problematic, as may coronary spasm, and in early morning levels of antithrombotic medications are lower in the patient's system. Increased risk during summer months could be related to increased activity.

Commenting on the context of circadian rhythms Holmes said "It is clear that circadian rhythms are critical to a variety of physiologic processes, some of which occur when people first get up in the morning and others that occur when people are tired or go to bed at night. Some circadian rhythms have important signature characteristics, such as fatal heart rhythms in the middle of the night or, as is the case with this study, coronary stent thrombosis in the early morning. Identifying such characteristics and studying their pathophysiology allows physicians to then develop strategies and systems of care". Holmes added "Based on this study, practitioners might consider giving antiplatelet therapy in the evening, rather than in the morning,





so that drug levels are high enough during critical times. Moreover, once-a-day use of antiplatelet treatment may not be enough. Maybe aspirin in the morning and clopidogrel at night may be more appropriate to cover all the bases”.

Ajay Kirtane, Columbia University Medical Center (NY, USA), cautioned that the pathophysiological reasons for coronary stent thrombosis are mainly hypotheses about which “we can only speculate at this point, although all seem relatively plausible”.

“Generally, MI occurs more frequently in the morning, so it is not unreasonable for coronary stent thrombosis to be associated with similar circadian rhythms. But while the authors mentioned exertion as having a circumstantial link to early morning coronary stent thrombosis, you wouldn’t expect people to be exerting themselves at this time of day. Consequently, this

hypothesis needs further evaluation, as does the heightened risk during summer” Kirtane said.

Kirtane explained that you could argue that if you had a short-acting antiplatelet agent, you might take it at night, but these drugs can also have longer half-lives, making the issue less relevant. Overall, the literature has indicated that the majority of coronary stent thrombosis occurs early after stent placement. While the same was true in the current paper, the median time to thrombosis was 97 days after stent placement.

Kirtane requested that the results be replicated, but said, “the present study was based on a well-known database and an established group of investigators”.

Source: *Early morning circadian rhythms linked to stent thrombosis: www.tctmd.com/show.aspx?id=105045.*

Enrollment begins for new device for the treatment of refractory angina

Interventional cardiologists from the Montreal Heart Institute (Canada) have recently commenced the enrollment of patients for a new device, the Neovasc Reducer™, designed to treat patients with refractory angina. This innovative treatment, the first to be undertaken in North America, is part of the larger international study, the Coronary Sinus Reducer for Treatment of Refractory Angina (COSIRA) trial.

The COSIRA trial is a multicenter, sham-controlled, randomized, double-blinded study of the Reducer, and is expected to enroll up to 124 patients examining the primary end point of efficacy in reducing angina symptoms after 6 months. The innovative treatment is promising for patients disabled by refractory angina who lack alternative treatment options. As better treatments for coronary artery disease reduce mortality, the incidence of refractory angina is set to rise, from approximately 2 million patients worldwide, as the number of patients with advanced disease increases.

The Reducer was developed in Canada by Neovasc Inc. (TSX Venture: NVC),

and is implanted in the patient’s coronary sinus vein using minimally invasive techniques, similar to the techniques used for the placement of a coronary stent. The Reducer is designed to establish a permanent and controlled narrowing of the coronary sinus, a new technique to provide relief of refractory angina symptoms, by altering blood flow in the coronary sinus, increasing the perfusion of oxygenated blood to certain areas of the heart muscle that receive an inadequate supply of oxygen.

“This new method to treat refractory angina safely, provides care for patients who cannot be helped with conventional drug, catheter or surgical therapy.”

The procedure by a multidisciplinary team from the Montreal Heart Institute composed of interventional cardiologists Drs Jolicoeur, Doucet and Tanguay and Dr Cartier, a heart surgeon. Dr Jolicoeur commented “All the initial cases have gone very well and we are optimistic that the long term results of the procedure will be

favorable. This new method to treat refractory angina safely, provides care for patients who cannot be helped with conventional drug, catheter or surgical therapy”.

Results from the initial first-in-man clinical trial of the Reducer were presented at the American College of Cardiology 2010 annual meeting. The data demonstrated that 3 years after implantation of the Reducer, the product remained safe and the majority of the 15 patients treated continued to show measurable improvement in angina symptoms.

In addition to the Montreal Heart Institute, the COSIRA trial is also enrolling patients at the University of Ottawa Heart Institute, the Antwerp Cardiovascular Institute and Ziekenhuis Oost-Linburg Hospital in Belgium; and Utrecht Medical Center in the Netherlands. Additional sites are expected to join the trial in the coming months.

Sources: *New device designed to treat patients suffering from refractory angina: www.sciencedaily.com/releases/2011/02/110224161514.htm; Trial For New Device Aimed At Treating Patients With Refractory Angina Starts Off Well: www.medicalnewstoday.com/articles/217549.php.*



US FDA approves Medtronic's first pacemaker system designed for use in the MRI environment

The US FDA has approved the Medtronic Inc. Revo MRI™ SureScan® pacing system, the first and only pacemaker in the USA specifically designed for use in an MRI environment, and was approved as MR-conditional.

Until now, MRI procedures had been contraindicated for patients with implanted pacemakers due to the potential for serious adverse events, and each year an estimated 200,000 pacemaker patients in the USA forgo MRI scans, which are critical for accurate diagnoses. The use of pacemakers will continue to rise in the coming years, due to an ever increasingly ageing population demographic. Currently, approximately 5 million patients worldwide are implanted with a pacemaker or implanted cardioverter-defibrillator and the use of MRI as a diagnostic tool also continues to rise.

J Rod Gimbel of Cardiology Associates of East Tennessee (TN, USA) commented “The new Revo MRI pacemaker is a major technological breakthrough for patients who need access to MRI. Providing pacemaker patients with access to MRI allows detection and treatment of serious medical conditions such as stroke, cancer, and a wide variety of important neurologic and orthopedic conditions”.

Pat Mackin, President of the Cardiac Rhythm Disease Management business and Senior Vice President at Medtronic added, “For the first time, patients will have access to a state-of-the-art pacemaker that is designed to work safely and effectively in an MRI environment”.

Previous to the introduction of Revo MRI, pacemaker patients could potentially face serious complications if they

were to become exposed to the powerful magnetic fields generated by MRI machines. Complications to exposure could include interference with pacemaker operation, damage to system components, or a change in pacing capture threshold. Revo MRI, when programmed into SureScan mode prior to an MRI scan, is designed to be safe for the MRI environment when used per the specified ‘MR Conditions for Use’. Revo MRI is considered MR-Conditional, a term used to indicate that a device may be used in the MRI environment under certain conditions, such as a particular type of MRI scanner and scanner settings.

Source: Medtronic receives FDA approval for first and only pacemaker system in the US designed for use in the MRI environment: www.tctmd.com/show.aspx?id=104977.

Valve-in-valve technique: a good fix following leaks after transcatheter aortic valve implantation

Data from an Italian registry has confirmed that the ‘valve-in-valve’ technique for repairing malpositioned CoreValve (MN, USA) transcatheter aortic valves is a good option for patients with significant paraprosthetic leaks without recourse to surgery.

“The availability of a bailout provides a margin of safety and enhances operator confidence.”

Gian Paolo Ussia (University of Catania, Italy) and colleagues reviewed a total of 663 patients who underwent transcatheter aortic-valve implantation with the 18 F CoreValve ReValving System at 14 centers across Italy and analyzed the clinical and echocardiographic outcomes of the 24 patients who underwent a valve-in-valve intervention for severe paraprosthetic leaks. Alternatives to the valve-in-valve

technique include postdilation with balloons and repositioning of the valve using a snare catheter.

Ussia explained, “We found that a second appropriately placed device served as a good bailout method and effectively managed the hemodynamic instability. Communication and sharing of experience between implanting physicians and proctors was instrumental in understanding that this could be a very effective and safe maneuver, which then was utilized routinely”.

In the 3.6% of patients undergoing the valve-in-valve procedure to rectify a leak, the most common type of device malposition was deployment that was too low inside the left ventricular outflow tract (75% of cases). The only statistically significant baseline difference between the patients needing a second valve and those

who did not, is that the former group had a slightly larger average annulus diameter (23.6 mm vs 22.1; $p = 0.010$).

Balloon dilation was necessary in the majority of cases, to optimize the expansion of the second device. The procedural, 30-day, and 12-month outcomes of the valve-in-valve group, including survival and major adverse events, were statistically equivalent to the outcomes of those not requiring a second intervention (95.5% for the valve-in-valve patients and 86.3% for the patients who did not need a second procedure). Procedural success was obtained in 100% of the valve-in-valve patients, with no periprocedural death. No cases of valve deterioration or new onset of central or perivalvular regurgitation were observed, nor any reports of thrombotic or embolic events were reported in the valve-in-valve group.



The authors of the study explained “The valve-in-valve technique can be used readily in the catheterization laboratory as a bailout therapy for a failed implantation, resulting from a malpositioned valve with severe paraprosthetic leak, when the attempt of reposition with the snare technique fails, preventing conversion to emergency open-heart surgery. The availability of a bailout provides a margin of

safety and enhances operator confidence. This is important for a nascent technology like transcatheter aortic-valve implantation to gain widespread clinical acceptance. This margin of safety is important because which patients will develop a leak is difficult to predict prior to their initial valve-replacement procedure”.

Source: www.theheart.org/article/1188843.do.

Small randomized trial reports that a new dual-drug drug-eluting stent using cilostazol boosts paclitaxel effectiveness

The results of a small randomized trial, have demonstrated that a new drug-eluting stent (DES) that features a second drug, cilostazol, in addition to paclitaxel shows noninferiority to the standard Taxus stent, with angiographic outcomes similar to other DESs currently in clinical use.

The study by Seung-Jung Park from Asan Medical Center (Seoul, South Korea) and colleagues, examined the Cilotax stent (Seoul, South Korea) which was developed to increase the safety of paclitaxel-eluting stents, due to the addition of the antirestenotic agent cilostazol. A total of 111 patients were randomized with *de novo* coronary artery lesions less than 20 mm in length, treated at two South Korean Cardiac Centers, to receive either Cilotax (n = 55) or paclitaxel-eluting Taxus Liberté (n = 56; MA, USA) stents.

Cilostazol is an antiplatelet agent which selectively inhibits phosphodiesterase III. Most of the cilostazol incorporated in the Cilotax stent is released within 3 months, while most of the paclitaxel is released within 1 month.

At 8 month angiogenic follow up, the Cilotax stent demonstrated noninferiority for the primary end point of in-segment late loss. Both in-stent late loss and restenosis were also improved or equivalent between the two devices. Rates of clinical outcomes were also low and comparable.

The researchers concluded that “Despite the small number of patients, these findings suggest that a dual DES may improve the efficacy and safety of the paclitaxel-eluting stent”.

Although the current group of patients had relatively simple lesions, the authors noted that due to the low late loss in the Cilotax stent, there could be a potential role for its use in patients with complex stenosis, however larger studies are needed to examine clinical outcomes.

Park indicates that the angiographic outcomes of the Cilotax stent are similar to other DES in current use. “Based on the published data, angiographic efficacy values of the Cilotax stent are similar to those of the Cypher or Xience V stent. In terms of clinical outcome (safety), I think more studies are needed”.

Source: [New dual-drug DES adds cilostazol to boost effectiveness of paclitaxel: www.tctmd.com/show.aspx?id=105075](http://www.tctmd.com/show.aspx?id=105075)