



NEWS



INTERVIEW



European Society of Cardiology consensus statement supports renal denervation for the treatment of resistant hypertension

A new consensus statement issued by the European Society of Cardiology (ESC) states that the novel catheter-based renal denervation therapy for the treatment of resistant hypertension can be considered a therapeutic option for those patients with drug-resistant hypertension who cannot achieve blood pressure goals with a combination of lifestyle and pharmacologic therapy.

The statement, published in the *European Heart Journal*, outlines the appropriate screening measures necessary, in order to select patients eligible for renal denervation therapy and the criteria which patients should comply with before renal denervation is considered. Patients are eligible for renal denervation if they meet the following criteria:

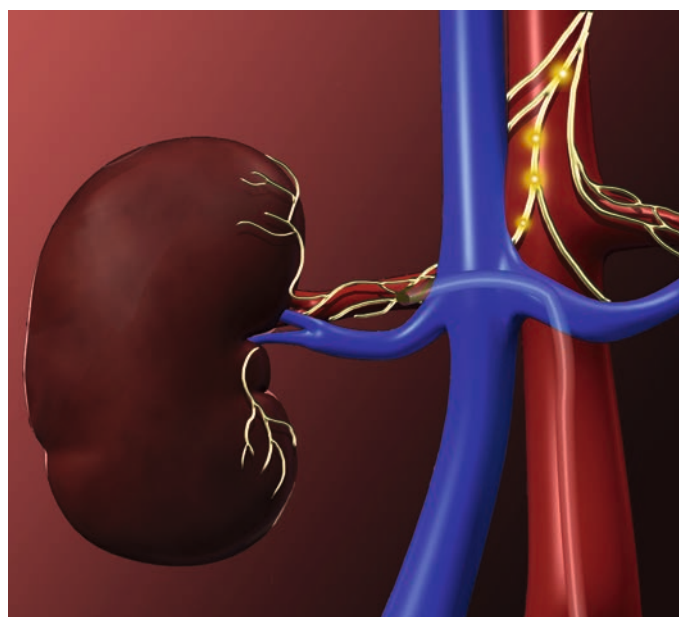
- Office-based blood pressure >160 mmHg (>150 mmHg in patients with type diabetes);
- Use of three or more antihypertensive drugs in adequate dosage and combination, including use of a diuretic;
- Have attempted to modify blood pressure with lifestyle changes;
- Secondary hypertension has been excluded;

- Pseudoresistance has been excluded with the use of ambulatory blood-pressure monitoring;
- Patients have preserved renal function (glomerular filtration rate >45 ml/min/1.73²);
- Absence of polar or accessory arteries, no renal artery stenosis, and no prior renal revascularization.

Felix Mahfoud (Saarland University, Saar, Germany), lead for the writing committee explained that the data support the concept that the radiofrequency ablation of the renal nerves reduces blood pressure and improves blood-pressure control in these difficult-to-treat patients.

In Europe, there are five renal denervation catheter systems that have received CE

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Mark approval, including the Symplicity system (Medtronic). The others include EnligHTN (St Jude Medical, MN, USA) used in the EnligHTN-1 study, Vessix V2 (Boston Scientific) used in REDUCE-HTN, OneShot (Covidien) used in the Renal Hypertension Ablation System study, and Paradise (ReCor Medical) used in the REALISE study.

The ESC reviewed the available data regarding renal denervation, which included the proof-of-concept Symplicity HTN-1 study and the multicenter, prospective, randomized Symplicity HTN-2 study. However, of note, is the remaining major challenge for the therapy, how to monitor the success of the procedure, (tests to determine whether or not denervation has been successful).

Furthermore, the ESC consensus statement acknowledges that it is not yet clear

how renal denervation works, however, the mechanism is likely the result of a reduction in peripheral resistance, reduced renin release, and favorable changes in water and salt handling. The authors state that “The fact that renal denervation also reduces whole-body sympathetic-nerve activity suggests that this therapy may also be beneficial in other clinical states characterized by sympathetic nervous system activation; this may ultimately lead to new indications.”

Sources: Mahfoud F, Lüscher TF, Andersson B et al. Expert consensus document from the European Society of Cardiology on catheter-based renal denervation. *Eur. Heart J.* doi:10.1093/eurheart/ehz154 (2013) (Epub ahead of print); TITLE: www.theheart.org/article/1533105.do?utm_medium=email&utm_source=20130426_breaking&utm_campaign=newsletter

POSEIDON reveals that a sliding-scale hydration strategy reduces 6-month clinical events in PCI patients

Study results presented at the Society for Cardiovascular Angiography and Intervention 2013 Scientific Sessions (8–11 May 2013, Orlando, FL, USA) not only demonstrate that a new method of personalized sliding-scale hydration reduces the risk of contrast nephropathy in patients undergoing coronary angiography or PCI, the treatment was also associated with a significantly lower risk of clinical events at 6 months.

Somjot Brar (Kaiser Permanente, CA, USA), lead researcher for the POSEIDON trial reported that a hydration strategy guided by left ventricular end-diastolic pressure (LVEDP) significantly reduced the composite end point of death, MI and the need for dialysis. Brar explains “There is a bit of a black hole in the clinical-trial literature in terms of correlating the reduction in contrast nephropathy and the risk

of meaningful, hard clinical end points. A lot of the data showing an association of contrast nephropathy (with clinical outcomes) mostly come from registry studies. Part of the difficulty is that in negative trials, which are really the bulk of the literature, there is little motivation to follow up long term. But even if you look at a lot of positive, pivotal trials, even in these trials long-term follow-up is very rarely reported. The debate largely centers on whether or not the therapy is effective for contrast nephropathy.”

In POSEIDON, investigators personalized hydration strategies based on the patient’s LVEDP. In the trial, patients treated with the LVEDP-guided hydration and conventional-hydration strategies were administered 0.9% saline at a rate of 3 ml/kg over the course of 1 h. Patients in the standard arm received 1.5 ml/kg/h

during the procedure, the patients in the LVEDP-guided arm received 5 ml/kg/h if their LVEDP was less than 13 mmHg, 3 ml/kg/h if the LVEDP was between 13 and 18 mmHg, and 1.5 ml/kg/h if their pressure exceeded 18 mmHg.

The LVEDP-guided approach reduced the primary end point, a 25% or 0.5-mg/dl increase in serum creatinine levels, by 59% compared with the conventional-hydration approach. The strategy also resulted in a 10% reduction in the absolute risk of serum creatinine increases, with a number needed to treat of just 11 to prevent one case of contrast-induced nephropathy.

During follow-up at 6 months, the researchers found that the LVEDP-guided treatment significantly reduced the composite end point of death, MI, and dialysis by 68% (relative risk: 0.32; 95% CI: 0.13–0.79). The number needed to treat



to prevent one major adverse event was 16. Brar added: “For me, the 6-month data showed that the story comes together in a very consistent way.”

While clinicians will need to continue to measure LVEDP prior to intervention, which would require an extra step, Brar explained that the concept of measuring pressure is already established in other areas, with physicians consistently measuring pressure to assess fluid status in

the coronary-care or intensive-care unit to alter therapy. “It’s taking this simple concept that’s been around for decades and taking the hemodynamics that we already measure in the catheterization laboratory and marrying these together to provide a solid framework in terms of how to properly hydrate patients.”

Source: TITLE: www.theheart.org/article/1538739.do

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WATCHMAN® device superior to warfarin for mortality and primary efficacy in patients with atrial fibrillation during 4-year follow-up of PROTECT AF

4-year follow-up data from the PROTECT AF clinical trial, presented by Boston Scientific Corporation reports that the clinical trial demonstrated that the WATCHMAN® left atrial appendage (LAA) closure device was statistically superior to warfarin for preventing cardiovascular death, all-cause stroke and systemic embolization. Significant reductions in both cardiovascular and all death compared with warfarin were demonstrated within the data.

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Vivek Reddy, a principal investigator of the PROTECT AF trial, and Professor of Medicine and Director of the Cardiac Arrhythmia Services at Mount Sinai School of Medicine (NY, USA) presented the data as a late-breaking clinical trial at Heart Rhythm 2013, the Heart Rhythm Society’s 34th Annual Scientific Sessions in Denver (CO, USA).

Atrial fibrillation (AF) affects approximately 2.7 million people in the USA and 15 million people worldwide, and is the

most common cause of disabling stroke. A primary treatment goal for AF patients involves the reduction in the risk of developing blood clots which cause stroke. Patients with AF and other additional risk factors for stroke are commonly prescribed anticoagulants, such as warfarin, to prevent blood clots from forming in the heart. However, due to blood monitoring requirements, dietary restrictions, side effects and an increased risk of serious bleeding, many patients are unable or unwilling to take these medications for long periods of time. In contrast, the WATCHMAN device is designed to close off the LAA, a major source of clots in patients with AF, and reduce the risk of stroke, potentially eliminating the need for long-term use of anticoagulants.

Reddy explained that “This is a significant development because for the first time we were able to demonstrate that the WATCHMAN device was superior to warfarin for both primary efficacy and also mortality. This has tremendous upside potential for patients. In the PROTECT AF trial, LAA closure with the WATCHMAN device demonstrated the potential for a device-based approach to reduce the risk of stroke in AF patients. As clinicians, we often feel uncomfortable with

life-long systemic anticoagulation therapy in patients because of an increased risk of falls and bleeding. The 4-year data provide additional support for LAA closure as a potential viable long term alternative to chronic warfarin therapy for patients to reduce the risk of stroke.”

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The PROTECT AF clinical trial is a multicenter, prospective randomized clinical trial designed to demonstrate the safety and effectiveness of the Boston Scientific WATCHMAN device in patients with nonvalvular AF, eligible for warfarin therapy and meet certain stroke risk factors. A total of 707 patients from 59 centers were randomized 2:1 to device or warfarin control.

In terms of the results, PROTECT AF did achieve superiority for the combined end point of all stroke, cardiovascular or unexplained death and systemic embolism. The observed primary efficacy event rate was 2.3% and 3.8% in the WATCHMAN



and control groups, respectively, demonstrating a 40% relative risk reduction in primary efficacy in the WATCHMAN group (RR = 0.60, posterior probability of superiority = 96%). Secondary analysis demonstrated a relative risk reduction and superiority to control for all-cause mortality and cardiovascular mortality.

Kenneth Stein chief medical officer, Cardiac Rhythm Management, Boston Scientific added “This is exciting news for patients with nonvalvular AF and a high risk of stroke. These data convincingly

show that the WATCHMAN device was superior to the current standard of care in these patients and demonstrated its potential to prevent stroke and save lives.”

Source: Boston Scientific press release: <http://bostonscientific.mediaroom.com/2013-05-09-New-Four-Year-Data-From-Boston-Scientific-Demonstrated-WATCHMAN-Device-Was-Superior-To-Warfarin-For-Mortality-And-Primary-Efficacy-In-Patients-With-Atrial-Fibrillation-In-Long-Term-Follow-Up-Of-The-PROTECT-AF-Trial>

FDA approves commencement of EXCELLA III clinical trial with DESyne[®] Nx Novolimus Eluting Coronary Stent System in the USA

Elixir Medical Corporation, has announced that it recently received approval from the FDA to initiate patient enrollment in the EXCELLA III clinical trial in the United States at up to 50 institutions with conditions to be addressed in parallel. Results from the EXCELLA III pivotal trial will be used to support a future premarket approval application in the US for the DESyne[®] Nx Novolimus Eluting Coronary Stent System.

The DESyne Nx Stent, is designed to treat heart vessel blockages, elutes a low dose of Elixir's proprietary drug Novolimus, an active metabolite of sirolimus, via an ultra-thin durable coating. The EXCELLA III clinical trial will be a prospective, controlled, multicenter, single-blind study comparing DESyne Nx to the Resolute Zotarolimus Eluting Coronary Stent System (Medtronic Vascular, CA, USA) as control in a 2:1 randomization of 2,051 patients recruited from US and International centers. Martin B. Leon, New York – Presbyterian Hospital and Columbia University Medical Center (NY, USA) will act as Principal Investigator for the EXCELLA III study.

The investigational device exemption approval for the EXCELLA III trial in the USA follows the successful international commercial launch of DESyne which gained CE Mark approval based on the results of the EXCELLA II trial. The EXCELLA II trial was a randomized controlled study that enrolled 210 patients at 22 clinical centers in Europe, Australia, New Zealand, and Brazil. The 3-year follow-up results were presented last October at the Transcatheter Therapeutics (TCT) Conference in Washington DC (USA)

In EXCELLA II the DESyne stent demonstrated both noninferiority and superiority to the Zotarolimus-eluting control stent for the primary endpoint of in-stent late lumen loss and achieved low clinical event rate through 3 years. The data collected from the global use of DESyne will be utilized to supplement the future premarket approval application in the US for the DESyne[®] Nx Novolimus Eluting Coronary Stent System.

Leon explained that “EXCELLA III will be a promising trial building upon the excellent and sustained clinical outcomes of the EXCELLA II trial. I am excited about DESyne Nx's potential to validate the safety and long-term performance in this large clinical trial.”

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The primary endpoint of the EXCELLA III trial is target lesion failure, a composite measure of safety and effectiveness at 12 months defined as cardiac death, myocardial infarction related to the target vessel, and clinically-indicated target lesion revascularization. In addition, a subset of patients will be evaluated for angiographic endpoints, and all patients will be followed for 5 years.

Source: Elixir Medical Corporation news: <http://elixirmedical.com/index.php?page=ous-news-and-events>

New PCI document demotes 'high-volume', once the cornerstone of 'clinical competence'

More often than not, one of the first questions that a patient will ask a doctor when talking about a surgical procedure is "How many of these do you do?"

However, in recent years, a number of high-volume cardiologists have been reported in the media for performing more procedures than medically warranted. This has most probably caused the reflection in a new "clinical-competence" document, wherein, volume is no longer the cornerstone of the skills and attributes an operator needs to perform PCI.

The American College of Cardiology (ACC), the American Heart Association, and the Society for Cardiovascular Angiography and Interventions (SCAI) have recently released an updated document which coincided with the start of the Society for Cardiovascular Angiography and Intervention 2013 Scientific Sessions.

SCAI president and vice chair of the writing committee, Theodore A Bass from the University of Florida Shands Cardiovascular Center (FL, USA) explained that "In the past, volume was used as a surrogate for competency, and there weren't a lot of data to support that. It just made sense. If he or she wasn't good at something, they probably weren't doing a lot of them," he added. What physicians have learned, he continued, is that "how volume correlates to outcomes is a little fuzzier than we thought, and while there is some correlation, there is no breaking point to the

data that tells us what a minimum volume would be, and also, we recognize, there is so much more involved." Bass provided an overview of the new competence recommendations during a session at the Society for Cardiovascular Angiography and Intervention 2013 Scientific Sessions.

The new document provides an update to the 2007 Clinical Competence Statement on Cardiac Interventional Procedures, in which the individual and hospital 'activity level' were key components of competence assessments, and 75 procedures per year was accepted as the minimum recommended number.

In the new document, "volume" is just one of 14 line items under one of six core "competence components." Moreover, the minimum number of annual PCIs recommended to maintain competence is now 50, averaged over two years. Bass explained during the session that this number aims to take into account the fact that the range of procedures interventionalists are now performing extends beyond PCI to valve, peripheral vascular and other procedures that require many of the same skills and knowledge.

Bass further added "It's been 6 years, and the landscape of what we do has changed and our understanding of how we define physician competency has also evolved ... It was time for an update."

The six "core competence components" detailed in the update are:

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- Medical knowledge (of anatomy, pathology, stents and drugs, coagulation among others);
- Patient care and procedure skills (including volumes, patient selection, and procedural techniques);
- Practice-based learning and improvement (including monitoring personal outcomes, completing CME among others);
- Systems-based practice (including regular cath-lab conferences, awareness of risks/benefits, and cost effectiveness);
- Professionalism (practicing evidence-based, guideline-directed, and patient-centered care);
- Interpersonal skills and communication.

When asked to what extent the scrutiny high-volume interventionalists have experienced in recent years influenced the deemphasizing of ‘volume’ in the new document, Bass said “I’d like to think [the new document] is not reactive; I’d like to think that we are patient-centered and centered on outcomes. We are not just looking at hard clinical outcomes like mortality or bleeding, but we are also looking at the

appropriateness of care.”

Bass thought that it is of note that interventionalists are already performing far fewer procedures, as much as 30 or 40% fewer by some estimates, than they were back in 2007.

In summary, Bass added “I won’t say using volume [benchmarks] is a good or bad thing. I think there are minimum numbers where there is signal of a link between volume and outcomes, both institutional and individual ... But just because you are doing more doesn’t mean you are doing better. The other side of this is, of course, physicians who do very high volumes, is that a good thing? Clearly, these physicians are very skilled, but are they adhering to guidelines? Are the patients being chosen appropriately?”

Other appropriateness-criteria documents address this issue more specifically, he noted, but he also acknowledged that the “episodes of inappropriate procedures” have been on the minds of interventionalists, including writing groups such as this one.

Source: TITLE: www.theheart.org/article/1537101.do

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

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