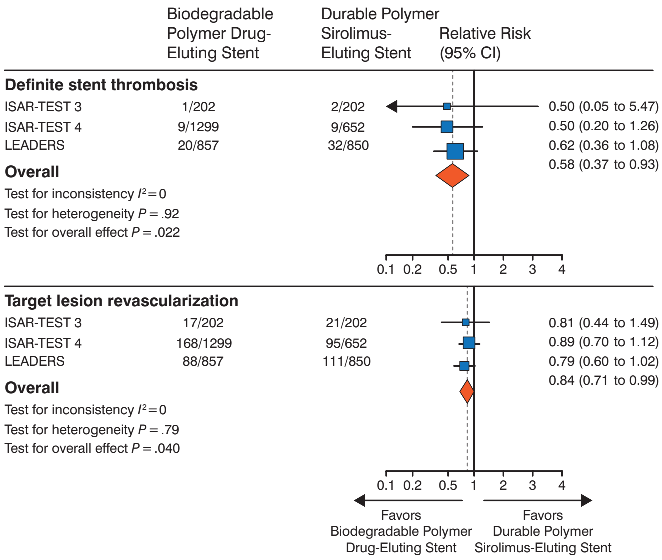
Figure 1. Biodegradable Vs Durable Polymer Drug-Eluting Stents



Adapted from *The Lancet*, 378, Stefanini GG et al. Long-term clinical outcomes of biodegradable polymer biolimus-eluting stents versus durable polymer sirolimus-eluting stents in patients with coronary artery disease (LEADERS): 4 year follow-up of a randomised non-inferiority trial. 1940–1948. Copyright © 2011, with permission from Elsevier.

contains a PVDF-HFP nonerodible fluorinated copolymer and is permanent. Patients treated with the Ultimaster stent had a 0.40% higher rate of freedom from target lesion failure (95% CI, –2.22 to 3.02; $P=.0001$) at 9 months. In the cohort of patients from Japan, the cumulative incidence of TLR events was 4.14% (95% CI, 2.52 to 6.78) and 5.67% (95% CI, 3.69 to 8.64) in the Xience arm.

A variety of other bioresorbable stents, including both polymer- and nonpolymer-based stents, and stents that elute everolimus, novolimus, and sirolimus, have undergone animal and clinical trials. To date, none of the bioresorbable stents are approved for use in the United States. In Europe, only Abbott's BVS 1.1 polymer-based stent is available for clinical use.

Prof Chevalier described clinical challenges that might arise when deploying bioresorbable stents. Bioresorbable stents are susceptible to mechanical deformation of stent strut with delivery. In addition, as the stent polymer erodes, the radial strength of the polymer decreases, which could result in late lumen loss. The ABSORB II trial [Diletti R et al. *Am Heart J.* 2012] randomized patients in a 2:1 fashion to receive the Absorb bioresorbable stent or the Xience stent. The primary end points of the study are based on changes in lumen diameter.

Prof Chevalier highlighted that the current limitations of the bioresorbable DES include a large profile (>1.4 mm), decreased radial strength over time, and limited ability to increase the diameter using postdilation inflations. The potential benefits of a bioabsorbable stent would not begin until after the PCI (eg, strut resorption, conformability, pulsatility, vasomotoricity, plaque regression, and positive remodeling). He cautioned that bioresorbable DESs have been evaluated in a relatively small number of patients and have only been used to treat simple lesions.

Current work is focused on developing thinner stent struts with a lower profile in an attempt to reduce occlusion of small side branches. Other areas of work include increasing the ability the stents to be sized further after deployment and the development new polymers and strut designs. In the meantime, Prof Chevalier pointed out that lesion preparation and appropriate sizing are important prior to deployment of a stent, particularly in bioresorbable stents, in order to prevent mechanical deformation and to achieve the best possible outcomes.

In conclusion, Prof Chevalier stated that the new, bioresorbable stents are deliverable, can be used at bifurcations, are cost-effective, and are compatible with short-term dual antiplatelet therapy. Current data suggest that bioresorbable DESs have similar short-term efficacy and safety as permanent DESs but data on long-term outcomes are needed.

RDN: Its Current Place in the Treatment of Resistant Hypertension

Written by Mary Mosley

Renal denervation (RDN) with percutaneous, catheter-based radiofrequency ablation was shown to reduce blood pressure (BP) in patients with true treatment-resistant hypertension in the initial registry of RDN [Schlaich MP et al. *Hypertension.* 2009] and in the Symplicity HTN trials [Symplicity HTN-1 Investigators. *Hypertension.* 2011; Symplicity HTN-2 Investigators. *Lancet.* 2010].

However, the promising results found in these trials of reductions in systolic blood pressure (SBP), such as –33 mm Hg at 3 years in the nonrandomized Symplicity HTN-1 trial ($P<.01$ vs baseline) and –32 mm Hg at 6 months in seated office SBP versus sham ($P<.0001$) in the randomized Symplicity HTN-2 trial, were not supported by the results of the Symplicity HTN-3 trial [Bhatt DL et al. *N Engl J Med.* 2014]. No significant difference was found for the primary efficacy end point of change in office SBP at 6 months between the denervation and sham groups (–2.39 mm Hg; 95% CI, –6.89 to 2.12; $P=.26$).

A number of potential explanations have emerged for the negative results in Symplicity HTN-3 and were reviewed by Oscar A. Mendiz, MD, Favaloro University, Buenos Aires, Argentina. These include technical issues such as catheter design and level of operator experience, trial conduct, Hawthorne effect, placebo effect, patient demographics, and medication changes or adherence.

In regard to catheter design, with the monopolar single-point catheter, there is energy loss into tissue and blood and nonhomogeneous injury distribution. Animal data have shown that the number of ablations is correlated with the concentration of norepinephrine and that approximately 6 to 10 ablations are required to achieve sufficient RDN [Mazor M. *J Am Coll Cardiol.* 2012]. Subanalyses of the Symplicity HTN-3 data revealed a significant reduction in SBP at 6 months in nonblack patients, which raises the question of whether this is because of racial differences or adherence to medication, said Prof Mendiz. RDN was also effective in patients taking an aldosterone antagonist at study entry.

Whether adequate maximal sympathetic blockade was achieved before RDN in Symplicity HTN-3 is questioned, because approximately 40% of the patients in the RDN and sham groups had changes in their medication between baseline and 6 months. Patients were taking about 5 drugs each, >50% had ≥1 drug change, 69% of all medication changes were "escape" changes, and about 50% were taking central-acting sympatholytics.

A subanalysis of Symplicity HTN-3 showed that the use of aldosterone antagonists at baseline, the total number of ablation attempts, and baseline office SBP ≥180 mm Hg were predictors of a change in SBP at 6 months in the RDN group [Kandzari D et al. EuroPCR. 2014]. A matched cohort analysis by these authors also showed an association between the number of ablations and change in office and ambulatory SBP, with ≥10 ablations associated with a significant reduction.

The ALSTER BP real-world registry of the Symplicity RDN system showed that there are 3 types of responders: early, late, and non [Kaiser L et al. *EuroIntervention.* 2014]. In 5 of 8 nonresponders who had a second RDN procedure, SBP was reduced at 6 months. The company-sponsored Global SYMPLICITY Registry [NCT01534299] showed that there were reductions in the mean 24-hour ambulatory SBP and in office SBP (by 11.9 to 20.2 mm Hg) in its first 1581 patients.

Prof Mendiz stated that patients with true treatment-resistant hypertension would be considered candidates for RDN after careful patient selection using a team approach with well-defined criteria in a well-trained catheterization laboratory, which should perform ≥14 ablations per patient. New RDN devices are showing promising preliminary outcomes, and new applications for different clinical settings (eg, for kidney failure, heart failure, obesity, diabetes, and sleep apnea) are being investigated.

Update on Mitral Valvotomy

Written by Mary Mosley

Mitral valvotomy is primarily used in the developing world because of the constraints in those countries, stated F. E. Smit, MD, University of the Free State, Bloemfontein, South Africa. Survival is increased, with an excellent or normal lifestyle, without the need for reintervention. A number of factors must be considered to select the type of valvotomy, including patient factors (eg, where the patient lives and the stage of the disease) as well as facility and operator factors (eg, level of training and available resources).

Several scoring systems have been developed to help optimize patient selection. The Wilkins score evaluates the extent of valvular disease and identifies patients who may be eligible for balloon valvotomy. Additional scores help predict long-term outcomes in patients with severe mitral stenosis, and a recent scoring system based on 20-year follow-up to obtain ideal results is guided by scoring systems such as the Wilkins score. Prognostic scoring systems for outcomes after balloon mitral valvotomy (BMV) include the transesophageal echocardiography (ECHO) assessment of commissure morphology [Sutaria N et al. *Heart.* 2006] and the scoring system by Zhang and colleagues that predicts late outcomes in patients with severe mitral stenosis [Zhang HP et al. *Am Heart J.* 1997]. A recent scoring system is based on the factors that predict late function as identified from the 20-year follow-up of patients who underwent percutaneous mitral commissurotomy (Table 1) [Bouleti C et al. *Circulation.* 2012].

Closed mitral commissurotomy (CMC) and open mitral commissurotomy (OMC) provided similar survival at 30 years (49.1% vs 45.9%; P=NS), but the need for another procedure was lower with OMC (5 patients vs 44 with CMC; $P<.05$), as shown by Detter and colleagues [Detter C et al. *Ann Thorac Surg.* 1999]. A series by Chen and colleagues substantiated the hemodynamic improvements achieved with valvotomy [Chen CR, Cheng TO. *Am Heart J.* 1995].

Percutaneous mitral valvotomy using the double balloon technique provided similar results as CMC and the improvement in mitral valve area (MVA) was durable at the 15-year follow-up (mean follow-up 99 months) [Rifaie O et al. *J Cardiol.* 2009]. Mitral restenosis occurred in 5 patients in each group. The durable results with BMV were also shown by Farhat and colleagues in their 7-year follow-up [Farhat MB et al. *Circulation.* 1998].

OMC provided a durable improvement in MVA in a series of 100 patients with mitral stenosis [Antunes MJ et al. *J Heart Valve Dis.* 2000]. The mean MVA was 0.99 cm^2 before surgery, increased to 2.89 cm^2 after