HealthManagement
Promoting Management and Leadership

Volume 13 - Issue 3, 2013 - Interventions

Interventional Radiology and Renal Denervation

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Background

Hypertension is said to be the single largest contributor to death on the global platform. Estimates are around 1 billion for the world population (World Health Organization 2011). Approximately one third are treated and controlled, another third treated but uncontrolled and the final third remain untreated (see Figure 1). As a largely asymptomatic disease the 'sting in the tail' is the long-term damaging effect it has on many of the body systems, particularly the heart (heart attacks), the brain (strokes) and the kidneys (kidney failure). Two thirds of strokes and half of all heart attacks are caused by hypertension. There is a linear relationship between blood pressure and cardiovascular death so that with every 20mm increase in systolic pressure the 10-year risks double. Although there have been huge steps forward in the pharmacological control of hypertension over the last 50 years, there are many obstacles not least patient compliance. We should not underestimate the challenges in persuading a patient with no symptoms to take lifelong medication (sometimes suffering side effects) with little if any short-term gain. Resistant hypertension is a defined sub-group:

• BP consistently >160mm (>150 mm if diabetic);

• On at least 3 different medications;

• Treatable secondary causes (e.g. adrenal disease) excluded;

• Poor compliance addressed.

The prevalence of this subgroup in the hypertensive population is difficult to accurately quantify (a figure as high as 30% has been quoted) and a more reasonable estimate after specialist work up and investigation is more likely to be 5-10%. However, with as many as one third of the population suffering from hypertension this adds up to a substantial global healthcare problem.

Sympathetic Nervous System

The cause of hypertension remains largely elusive but for several decades we have known that the sympathetic nervous system appears to be in overdrive, coined by some a 'sympathetic storm'. This complex system of nerves provides a communication pathway between many parts of the body, including the brain, heart, kidney, blood vessels, skin and muscle, to name but a few. Nerves linking the brain and the kidney are of particular interest and over activity in these pathways leads to the retention of sodium and water, vasoconstriction and activation of several neuroendocrine systems. These all summate and have a potent adverse effect on blood pressure. Early work in the 1930s involved surgeons dividing these nerve pathways and this often resulted in a potent lowering of blood pressure. The price, however, was significant post-operative morbidity and mortality, and with the advent of ever increasingly potent medications the operation fell into disuse.

Catheter-Based Renal Denervation

With the development of radiofrequency (RF) energy probes for interrupting abnormal nerve pathways in the heart and treating malignant tumours an opportunity was grasped using the same technology to destroy the sympathetic nerves running to and from the kidneys. This entails a minimally invasive ‘endovascular approach’ far safer than the surgical attempts of the 1930s.

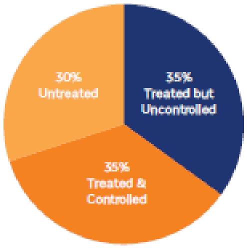
The procedure involves applying some form of energy (e.g. RF) to the inside wall of the renal artery thereby destroying the sympathetic nerves that run on the outside of the vessel (see Figure 2). Both the afferent (running from the kidney) and the efferent (running to the kidney) nerves are targeted in a non-selective manner. The renal artery is accessed using standard endovascular catheters from the femoral artery. Both kidneys are treated and the procedure takes around 30-45 minutes. The procedure is carried out under local anaesthesia and conscious sedation, and many patients can be treated on a day case basis.

The Renal Denervation Team

A multidisciplinary approach to renal denervation (RDN) is essential, and this reflects good practice and governance, to maximise patient safety and outcomes. The team should include, as an absolute minimum, a hypertension specialist and a vascular interventionalist. Careful patient selection is critical and other causes such as white coat hypertension, poor compliance and treatable secondary causes of hypertension should be excluded. The interventionalist must be familiar with renal artery catheterisation and rescue procedures should complications arise, e.g. arterial dissection, occlusion and embolisation. Interventional radiologists are in a strong position to fulfil this role, and already undertake other renal artery interventions such as stenting and embolisation.

Figure 1.
The epidemiology of hypertension (Chobanian et al. 2003)

Reference: Chobanian et al. (2003) Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension, 42(6): 1206–52.



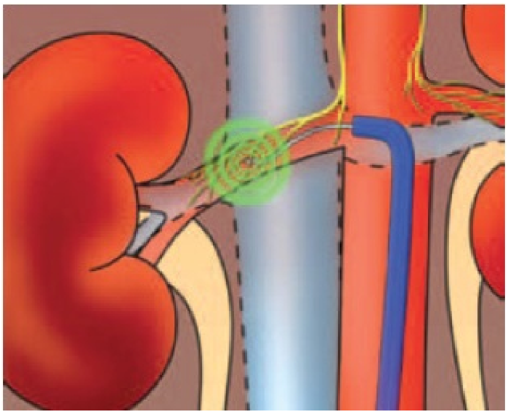


Figure 2. Diagrammatic representation of renal denervation. Image credit: Medtronic Inc. USA

The Technology

A U.S. company (Ardian) launched the first commercial product (see Figure 2), and this device remains the global leader. With so much commercial interest at stake there has been an almost unprecedented explosion in activity from the device industry. To date there are six CE marked devices with about another 50 in various stage of development. Other forms of therapy such as high intensity focused ultrasound, drug-laden nanoparticles and local drug delivery are being researched. Much of this technology is running ahead of itself, and there is very little good evidence to support the newer devices at present, although that is rapidly changing. Most of the CE marked devices need a suitable ‘landing zone’ of about 2cm within the renal artery with a minimum diameter of 4mm. This remains a significant issue for some patients with early arterial branching and multiple renal arteries which are often under 4mm diameter.

Evidence Base for RDN

Pioneering work led by Esler in Australia led to a trail blazing ‘proof of principle’ publication (Symplicity HTN-1) in the Lancet (Krum et al. 2009). This was followed by another landmark study from the same group, this time a randomised controlled trial (Symplicity HTN-2) (Symplicity HTN-2 Investigators et al. 2010). Both studies showed a convincing drop in office blood pressure in the region of 33mm Hg systolic and 11mm Hg diastolic at 6 months. In the randomised study there was no drop in BP in the control arm and the group difference was highly significant. These were small studies including fewer than 200 subjects and a third and larger trial Symplicity HTN-3 (600) is underway in the U.S.A, which includes a ‘sham arm’. The evidence base for the other CE devices is less mature and with small numbers, but larger trials are in progress. There is little long-term data with such a new technology, but 36 month results seem to demonstrate durability.

From a safety perspective there have been surprisingly few concerns. Anecdotal reports of arterial dissection and other vessel damage seem few and far between. Perhaps this is because the devices are only used when there is a normal renal artery free from atheromatous disease. Further confirmation of safety will require larger numbers followed longer term and the on-going national registries should address that concern.

Other Indications

Although the evidence base and national and international consensus statements only support the use of RDN for resistant hypertension t here m ay b e o ther i ndications. The involvement of the sympathetic nervous system in so many of the body's systems has encouraged physicians to explore new indications. Cardiac failure, diabetes mellitus, sleep apnoea, chronic kidney diseases, intractable ascites and polycystic ovarian syndrome are all currently being investigated.

The Future

RDN appears to have a solid and exciting future and we may only be on the first few pages of a very thick book. Some have likened it to angioplasty in importance to the interventional radiology community.

The ever hungry thirst for high quality evidence and cost-effectiveness at national and international level should keep RDN firmly on the rails. At a time of global financial uncertainty the pressure is on in many countries to offer clinically effective and cost effective medicine. RDN deserves to be on the medal podium.

Published on : Thu, 28 Nov 2013