News & Views

Research Highlights

Highlights from the latest articles in interventional cardiology

Renal denervation: potential benefits beyond hypertension

Masataka Nakano[1], Elena R Ladich[1] & Renu Virmani*[1]

[1]CVPath Institute, Gaithersburg, MD, USA
**Author for correspondence:*
Tel.: +1 301 208 3570
Fax: +1 301 208 3745
rvirmani@cvpath.org

Evaluation of: Pokushalov E, Romanov A, Corbucci G *et al.* A randomized comparison of pulmonary vein isolation with versus without comcomitant renal artery denervation in patients with refractory symptomatic atrial fibrillation and resistant hypertension. *J. Am. Coll. Cardiol.* 60, 1163–1170 (2012).

Given that a large number of patients with hypertension are uncontrolled by multiple antihypertensive drugs, renal denervation is appealing as a new therapeutic option. The underlying mechanism of this method is based on ablation of both afferent and efferent fibers of sympathetic renal nerves, thereby regulating sympathetic nerve activity in central and peripheral autonomic systems, resulting in a decrease in systemic blood pressure (BP).

In this article, Pokushalov *et al.* presented the results from a prospective randomized clinical trial studying the impact of renal artery denervation in patients with a history of refractory atrial fibrillation (AF) and drug-resistant hypertension, who were referred for pulmonary vein isolation (PVI) [1]. Patients were randomized to PVI only (n = 13) or PVI with renal denervation by 8–10 watt radiofrequency ablations (n = 14). No complications occurred regarding either the PVI or renal ablation procedure, and no renal artery stenosis was observed on MRI evaluation at 6 months. During follow up, a reduction of systolic and diastolic blood pressure occurred by 25–30 mmHg and 10–12 mmHg, respectively, in the PVI with renal denervation group. In the PVI-only group there was minimal reduction in BP. Furthermore, in three patients in the PVI with renal denervation group, the antihypertensive drug was reduced, whereas in two patients in the PVI-only group, antihypertensive medication was increased. The most important implication of this study is that at 12 month follow-up, nine (69%) of 13 patients in the PVI with renal denervation group were AF-free, whilst only four (29%) of 14 patients in the PVI only group were AF-free on no antiarrhythmic drugs. The authors hypothesized that BP reduction via renal denervation has an impact on the suppression of AF recurrences through relaxation of the atrial wall, or that the ablation of afferent renal nervous input decreases central sympathetic output, which may attenuate autonomic triggers of AF [2].

Recently, it was reported that renal denervation may have an effect, not only on BP reduction, but also on heart rate or electrocardiographic parameters [3]. Moreover, a clinical study (REACH-Pilot study) demonstrated that renal denervation provided symptomatic improvement in all seven nonhypertensive patients with chronic systolic heart failure (mean BP: 112/65 mmHg) [4]. This suggests a potential indication of renal denervation therapy beyond controlling hypertension. Further investigation is warranted to evaluate pleiotropic effects of renal denervation therapy.

References

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FAME 2: fractional flow reserve as a mandatory device for the treatment of stable coronary disease

Evaluation of: De Bruyne B, Pijls NH, Kalesan B *et al.* Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N. Eng. J. Med.* 397, 991–1001 (2012).

Although percutaneous coronary intervention (PCI) has been established as a treatment of choice for atherosclerotic coronary disease, controversy remains concerning the selection of patients who can gain full benefits from PCI as compared with treatment with medical therapy alone. For this reason, fractional flow reserve (FFR) is gaining attention because of its potential in the detection of functionally significant coronary stenosis by physiological calculation.

The present study was conducted by De Bruyne and the FAME 2 investigators at 28 sites in Europe and North America, to assess the superiority of PCI to medical therapy alone for the treatment of patients with stable coronary artery disease. Patients with functionally significant coronary stenosis (FFR < 0.80) were randomized to FFR-guided PCI plus the best available medical therapy (PCI group) or the best available medical therapy alone (medical-therapy group). Patients without significant stenosis (FFR > 0.08) were entered into a registry and received the best available medical therapy (registry group). The study was prematurely halted at 1 year when 1220 patients were enrolled because a significant difference was detected in the percentage of patients who had a primary end point consisting of death, myocardial infarction and urgent revascularization (PCI group 4.3% vs medical-therapy group 12.7%, hazard ratio: 0.32, 95%CI: 0.19–0.53). The incidence of primary end point in the registry group was 3.0%, which was similar to the PCI group. The significant difference between the PCI and medical-therapy groups was driven predominately by a higher rate of urgent revascularization in the medical-therapy group (11.1%), compared with the PCI group (1.6%). Moreover, among the patients who underwent urgent revascularization, the procedure was triggered by either myocardial infarction or unstable angina, accompanied by evidence of ECG-ischemia in 23 patients (5.2%) in the medical-therapy group and in only four patients (0.6%) in the PCI group, suggesting that FFR-guided PCI prevents future acute coronary events in patients with stable coronary disease [1].

It seems fair to say that this, and previous studies [2,3], have collectively proven the utility of FFR as an almost mandatory device for interventionalists treating stable angina. With greater operator experience, one would expect better outcomes for this somewhat cumbersome procedure, and education of operators will facilitate expansion of the use of this device in daily clinical practice. Besides FFR, other intracoronary imaging devices also appear to be promising. Recently, high-resolution optical coherence tomography and intravascular ultrasound were used for the detection and passivation of non-flow-limiting vulnerable plaque, and showed their safety and feasibility [4]. The next step is to carefully evaluate the accumulated data obtained from these various devices, a step which should further improve patient outcomes. In addition, further data is required regarding the use of FFR in acute coronary syndromes.

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Is it truly safe to shorten dual antiplatelet therapy after drug-eluting stent implantation?

Evaluation of: Ferreira-González I, Marsal JR, Ribera A *et al.* Double antiplatelet therapy after drug-eluting stent implantation. Risk associated with discontinuation within the first year. *J. Am. Coll. Cardiol.* 60, 1333–1339 (2012).

While the advent of drug-eluting stents (DES) has achieved a dramatic reduction in restenosis rates, new concerns have emerged regarding the long-term safety of DES technology, since clinical studies pronounced an increase in late stent thrombosis. Accordingly, prolonged dual antiplatelet therapy (DAPT) is recommended for least 6–12 months or longer. However, a safe time period for antiplatelet therapy discontinuation (ATD) has not been determined to date.

Ferreira-González *et al.* studied a total of 1622 consecutive patients who underwent DES implantation from the ACDC prospective cohort study and assessed the risks associated with ATD during the first year after DES implantation. All patients were interviewed by telephone at 3, 6, 9 and 12 months, and the information about their current medical status and the approximate date of ATD were collected. For patients who died, the information was obtained from a close relative. One hundred and seventy two patients interrupted DAPT, and most (n = 111) cases of ATD were temporary (median: 7 days; interquartile range: 5–8.5 days) in this cohort. Overall, 87 cases had a major cardiac event (cardiac death or acute coronary syndrome) during follow up. Of those events, seven were associated with patients with ATD (4.1%), while the remaining 80 were observed in patients without ATD (5.5%). The unadjusted global risk (hazard ratio) of cardiac events related to ATD was 1.93 (95% CI: 0.87–4.28), and the hazard ratio was not significant even after adjusting for potential confounders (2.71 [95% CI: 0.84–8.72]). The authors concluded that discontinuation of DAPT for a few days after the first month of DES implantation may be reasonably safe in terms of major cardiac events [1].

Although the present data is likely to warrant short discontinuation of DAPT within 1 year after DES implantation, clinicians must interpret the results with caution. First, the reliability of follow up at 3-month intervals by telephone is questionable. Furthermore, 105 patients were lost to follow up, which is a sufficient number and may have resulted in conclusions based on incomplete data. In addition, the number of patients presenting with acute myocardial infarction at the time of DES placement was not shown, this is an important difference compared with other studies in which important disadvantages of ATD were documented. Importantly, interventionalists should be aware that cases do exist in which patients have died suddenly after discontinuation of DAPT, even beyond 1 year, as we have reported from our autopsy cases [2]. Therefore, it would appear that it is too early to accept the results of this study until further clinical studies reveal the optimal duration of DAPT after DES implantation.

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