Cardiovascular Topics

Changes in blood pressure after catheter-based renal denervation in South Africa

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Abstract

Background: Renal denervation (RDN) is an interventional treatment for patients with uncontrolled hypertension. The Global SYMPLICITY Registry (GSR) is a prospective, all-comer, world-wide registry designed to assess the safety and efficacy of RDN. We evaluated the outcomes in South African patients in the GSR over 12 months.

Methods: Eligible patients with hypertension had a daytime mean blood pressure (BP) > 135/85 mmHg or night-time mean BP > 120/70 mmHg. Office and 24-hour ambulatory systolic BP reduction and adverse events over 12 months were evaluated.

Results: South African patients ($n = 36$) in the GSR had a mean age of 54.4 ± 9.9 years with a median of four prescribed antihypertensive medication classes. At 12 months, mean changes in office and 24-hour ambulatory systolic BP were -16.9 ± 24.2 and -15.3 ± 18.5 mmHg, respectively, with only one adverse event recorded.

Conclusion: RDN safety and efficacy in South African patients were consistent with world-wide GSR results.

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Hypertension is a global public health concern, affecting one in three adults in the developed world, and it contributes to increased vascular and renal morbidity, as well as cardiovascular mortality.[1-3] The risk of cardiovascular death doubles for every 20 and 10 mmHg increase in systolic and diastolic blood pressures (BP), respectively, above 115/75 mmHg (systolic/diastolic BP).[4]

Multidisciplinary treatments, including dietary restrictions, lifestyle changes and pharmacological antihypertensive therapies, have proved inadequate in reducing BP to recommended levels for at least one-third of individuals with hypertension.[5,6] Non-adherence to the prescribed antihypertensive medication regimen is thought to contribute to inadequate control of BP.[7-9]

Catheter-based renal denervation (RDN) of the sympathetic nerves using radio-frequency energy has emerged as a novel, safe and effective treatment option to reduce BP in patients with uncontrolled hypertension.[10] Several randomised, sham-controlled clinical trials have demonstrated BP reduction in patients after RDN.[11-13] However, follow-up data after RDN in real-world patients is needed.[14]

The Global SYMPLICITY Registry (GSR) is an ongoing, prospective clinical study that has enrolled patients since 2012 to evaluate the impact of RDN on BP reduction in an all-comers population. In a study of more than 10 000 patients from the sub-Saharan African countries of Ghana, Kenya, Burkina Faso and South Africa, South Africa had the highest prevalence of hypertension, highlighting the need for alternative treatment options for South African patients.[15] This analysis specifically examined the safety of RDN and changes in BP up to 12 months post-RDN in GSR patients enrolled and followed up in South Africa.

Methods

The GSR is a prospective, multi-centre, open-label registry to document the safety and efficacy of RDN treatment in an all-comers population in real-world clinical settings. The design of the GSR and interim results and analyses in other subpopulations have been published previously.[16-19] National regulatory authorities, ethics committees and review boards of the participating centres approved the registry. The GSR is registered (NCT01534299) at ClinicalTrials.gov.

Enrolment eligibility for the GSR South Africa was similar to other SYMPLICITY studies.[17-19] Patients ≥ 18 years of age or as required by local regulations, with uncontrolled hypertension as described by the South African Hypertension Guidelines of 2011, with a daytime mean BP > 135/85 mmHg (systolic/

diastolic) or a night-time mean BP > 120/70 mmHg, were eligible. Exclusion criteria were pregnancy, estimated glomerular filtration rate < 30 ml/min, significant aortic stenosis, secondary causes of hypertension or complex renal vascular anatomy making RDN technically difficult.

The GSR recommended three BP measurements be taken at each office visit and 24-hour ambulatory BP measured as per published guidelines.[20] The most recent office and ambulatory BP measurements prior to the RDN procedure were used as baseline BP values. Before treatment and at each follow-up office visit, investigators interviewed patients to document changes in antihypertensive medication. All patients in the GSR were treated with the Symplicity RDN system (Medtronic, Santa Rosa, CA) using a Symplicity Flex™ or Symplicity Spyral™ catheter.

Statistical analysis

Continuous data are reported as means (standard deviations) for normally distributed data. Categorial data are presented as percentages. Analyses were performed under the consideration of the intention-to-treat principle. All analyses were performed using the SAS statistical package (version 9.3 or higher).

Results

At the time of the analysis, 36 patients, with a mean age of 55.4 ± 9.9 years, had been enrolled in the GSR South Africa across nine centres. Seventeen of the patients were male, 10 were of African descent and four were current smokers. Baseline characteristics are presented in Table 1. At baseline, the mean office systolic and diastolic BP were 164.0 ± 20.4 and 95.0 ± 13.4 mmHg, respectively. The mean 24-hour ambulatory systolic and diastolic BP at baseline were 153.4 ± 14.5 and 87.6 ± 10.6 mmHg, respectively. Sixteen patients (45.7%) had type 2 diabetes mellitus, five (13.9%) had had a previous myocardial infarction, six (16.7%) had had a previous percutaneous coronary intervention, three (8.3%) had had a previous coronary artery bypass graft and two (5.7%) were reported to have had a previous stroke.

Patients were prescribed a median of four anti-hypertensive medications at baseline, which persisted to 12 months [interquartile range (IQR) 4–5]. Calcium channel blockers were the most common prescribed antihypertensive medication (83.3%), followed by diuretics (66.7%), beta-blockers (66.7%), angiotensin receptor blockers (63.9%), alpha-adrenergic blockers

Table 1. Baseline demographic characteristics and baseline BP readings (*n* = 36)	
Baseline characteristics	*Values*
Age (years), mean (± SD)	54.4 (9.9)
Male, *n* (%)	17 (47.2)
Current smoker, *n* (%)	4 (11.1)
Diabetes mellitus (type 2), *n* (%)	16 (45.7)
Sleep apnoea, *n* (%)	4 (12.1)
Previous MI, *n* (%)	5 (13.9)
Previous PCI, *n* (%)	6 (16.7)
Previous CABG, *n* (%)	3 (8.3)
Previous stroke, *n* (%)	2 (5.7)
Baseline BP, mean (± SD)	
Office SBP (mmHg)	164.0 (20.4)
Office DBP (mmHg)	95.0 (13.4)
24-hour SBP (mmHg)	153.4 (14.5)
24-hour DBP (mmHg)	87.6 (10.6)
MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; SBP, systolic blood pressure; DBP, diastolic blood pressure.	

Table 2. Antihypertensive medication usage at baseline (*n* = 36)	
Medication	*Values*
Median number of anti-hypertensive medication classes, *n* (IQR)	4.0 (4.0–5.0)
Antihypertensive treatment, *n* (%)	36 (100.0)
Medication, *n* (%)	
ACE inhibitors	11 (30.6)
Angiotensin receptor blockers	23 (63.9)
Calcium channel blockers	30 (83.3)
Diuretics	24 (66.7)
Aldosterone antagonists	9 (25.0)
Spironalactone	7 (19.4)
Centrally acting sympatholytics	5 (13.9)
Direct renin inhibitors	0 (0.0)
Beta-blockers	24 (66.7)
Alpha-adrenergic blocker	21 (58.3)
Direct-acting vasodilators	2 (5.6)
IQR: interquartile range, between 25th and 75th percentiles.	

(58.3%), ACE inhibitors (30.6%), aldosterone antagonists (25%), centrally acting sympatholytics (13.9%), and direct acting vasodilators (5.6%) (Table 2). The median number of prescribed medications remained constant to 12 months, despite overall reduction in office and 24-hour SBP.

Overall, systolic BP was reduced at three to 12 months from baseline following RDN in the South African population (Fig. 1).
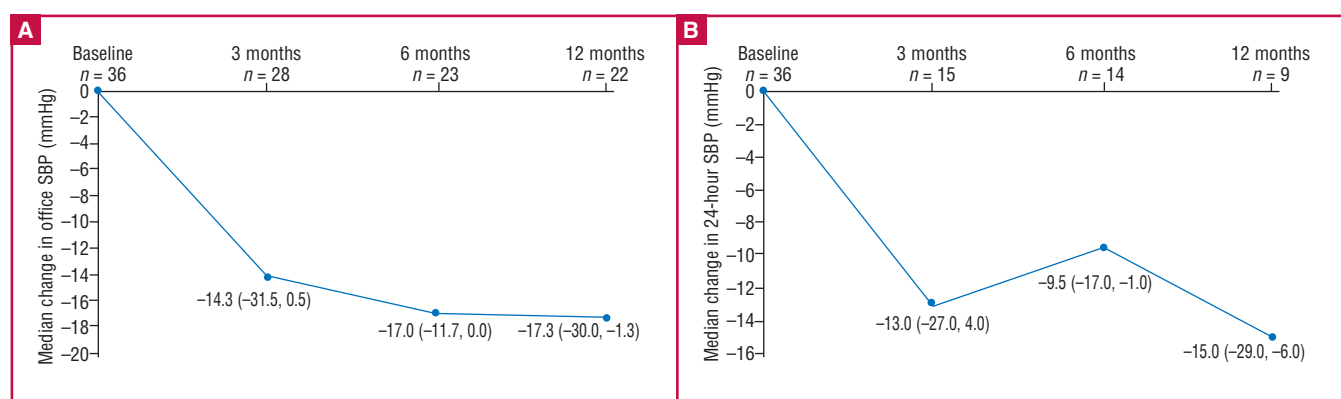

Fig. 1. Changes in (A) office and (B) 24-hour systolic BP from baseline to 12 months after RDN.

The median change in office systolic BP was –14.3 mmHg (25th to 75th percentile: –31.5 to 0.5 mmHg) at three months; –17.0 mmHg (–11.7 to 0.0 mmHg) at six months; and –17.3 mmHg (–30.0 to –1.3 mmHg) at 12 months. Among patients of African descent, there was a median change of –17.7 mmHg (–25.3 to –8.0 mmHg) in office systolic BP at 12 months. In the South Africa GSR population, the median change in 24-hour ambulatory systolic BP was –13.0 mmHg (–27.0 to 4.0 mmHg) at three months; –9.5 mmHg (–17.0 to –1.0 mmHg) at six months; and –15.0 mmHg (–29.0 to –6.0 mmHg) at 12 months.

The majority of patients receiving RDN treatment had ≥ 10 mmHg reduction in office systolic BP, with 64% achieving this goal at three months, 70% at six months and 68% at 12 months (Fig. 2). Despite the fact that the median number of antihypertensive medications remained constant throughout the follow-up period, 39% of patients receiving RDN treatment had a ≥ 20-mmHg reduction in office systolic BP at three and six months, and 45% had a reduction ≥ 20 mmHg at 12 months.

Among the South African GSR subpopulation, there were no adverse events up to 12 months, except for a single spontaneous myocardial infraction. There were no incidences of death from any cause, stroke, new-onset renal disease or cardiac-related hospitalisation in the follow-up patients.

Discussion

In the analysis presented here of South African patients enrolled in the GSR, RDN was shown to lower both office and 24-hour ambulatory systolic BP in patients with uncontrolled hypertension, with durable reductions up to 12 months, which is consistent with previously reported GSR analyses.[17-19] Since the report of the neutral efficacy results from the SYMPLICITY HTN-3 trial comparing sham and treatment groups,[21] numerous randomised, sham-controlled RDN trials have demonstrated a treatment benefit in reducing office and 24-hour ambulatory systolic BP in hypertensive patients.[11,12,22] More recent follow-up interim analyses of various high-risk groups from the GSR provide further evidence supporting the efficacy of RDN in reducing BP in a broad population with subgroups with different baseline risks and various co-morbidities.[23,24]

The efficacy results from the GSR South Africa are particularly encouraging as South Africa has the highest prevalence of hypertension among sub-Saharan African countries, with

patients of African descent having more complications from hypertension.[15,25] Ten of the enrolled patients from the GSR South Africa were of African descent. This study of the South African GSR subpopulation also demonstrates the safety of the RDN procedure up to 12 months, with no instances of renal artery re-intervention or stenosis. The safety of RDN reported here is consistent with previously reported results from a meta-analysis of RDN, which found no major procedural or clinical adverse events up to three months.[22]

Nearly half the enrolled patients from South Africa had type 2 diabetes mellitus (Table 1). A recent study of high-risk hypertensive groups in the GSR reported that patients with type 2 diabetes mellitus had a 13.4 ± 25.9-mmHg reduction in office systolic BP 12 months after RDN.[23] By comparison, the South Africa GSR cohort had a reduction of 16.9 ± 24.2 mmHg 12 months after RDN (Fig. 1). These studies underscore the potential benefit of RDN treatment in high-risk patients, such as those with type 2 diabetes mellitus.

Non-adherence to prescribed antihypertensive medication is a prevailing challenge in controlling BP in hypertensive patients.[7-9] For example, in the recent SPYRAL HTN-ON MED pilot study comparing RDN safety and efficacy between treatment and sham-control groups, patients were informed that medication adherence would be monitored at each follow up, yet by six months, nearly 40% of patients were non-adherent to their prescribed medications, based on liquid chromatography analysis of urine and plasma samples.[12]

The South Africa GSR cohort had a median of four antihypertensive medications prescribed at baseline, which was maintained throughout the 12-month follow up, although medication adherence was not evaluated in the GSR with drug or urine testing. Given the sizeable fraction of hypertensive patients world-wide that are unresponsive to traditional treatment options, including pharmacological medication, and persistent issues with non-adherence to medication, RDN may provide an attractive alternative treatment strategy to durably reduce BP in patients with uncontrolled hypertension.

Limitations

This analysis has several limitations. First, as the GSR is an all-comer registry, there was no control arm to account for potential placebo or Hawthorne effects on outcomes. Second, the GSR did not standardise follow-up procedures, therefore potentially limiting reporting of relevant events after RDN. It should be noted that the number of patients enrolled in the South African cohort was modest, and moreover, not all patients enrolled from South Africa completed 12 months of follow up at the time of this analysis. However, the office and 24-hour ambulatory systolic BP reductions over 12 months reported from this analysis of the South African cohort were consistent with previously published results from other GSR analyses.[17]

Conclusions

RDN treatment safely reduced systolic BP in hypertensive patients enrolled in the GSR from South Africa to levels similarly reported in other GSR studies. Additionally, office and 24-hour ambulatory BP reductions from RDN observed in the registry were consistent with the benefits of RDN reported in
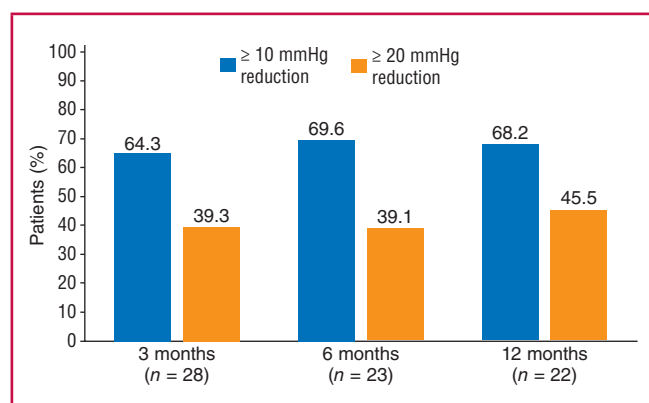
Fig. 2. Percentage of patients with reduction in office SBP by 10 and 20% from baseline.

randomised, sham-controlled clinical trials, demonstrating the potential of RDN as an alternative or complimentary strategy to traditional treatment options in lowering BP in patients with uncontrolled hypertension.

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