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Hypertension

Impaired Cardiac Baroreflex Sensitivity Predicts Response to Renal Sympathetic Denervation in Patients With Resistant Hypertension

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Objectives This study sought to evaluate cardiac baroreflex sensitivity (BRS) as a predictor of response to renal sympathetic denervation (RDN).

Background Catheter-based RDN is a novel treatment option for patients with resistant arterial hypertension. It is assumed that RDN reduces efferent renal and central sympathetic activity.

Methods Fifty patients (age 60.3 ± 13.8 years [mean ± SD mean systolic blood pressure (BP) on ambulatory blood pressure monitoring (ABPM) 157 ± 22 mm Hg, despite medication with 5.4 ± 1.4 antihypertensive drugs) underwent RDN. Prior to RDN, a 30-min recording of continuous arterial BP (Finapres; TNO-TPD Biomedical Instrumentation, Amsterdam, the Netherlands) and high-resolution electrocardiography (1.6 kHz in orthogonal XYZ leads) was performed in all patients under standardized conditions. Cardiac BRS was assessed by phase-rectified signal averaging (BRS_{PRSA}) according to previously published technologies. Response to RDN was defined as a reduction of mean systolic BP on ABPM by 10 mm Hg or more at 6 months after RDN.

Results Six months after RDN, mean systolic BP on ABPM was significantly reduced from 157 ± 22 mm Hg to 149 ± 20 mm Hg ($p = 0.003$). Twenty-six of the 50 patients (52%) were classified as responders. BRS_{PRSA} was significantly lower in responders than nonresponders (0.16 ± 0.75 ms/mm Hg vs. 1.54 ± 1.73 ms/mm Hg; $p < 0.001$). Receiver-operator characteristics analysis revealed an area under the curve for prediction of response to RDN by BRS_{PRSA} of 81.2% (95% confidence interval: 70.0% to 90.1%; $p < 0.001$). On multivariable logistic regression analysis, reduced BRS_{PRSA} was the strongest predictor of response to RDN, which was independent of all other variables tested.

Conclusions Impaired cardiac BRS identifies patients with resistant hypertension who respond to RDN. (J Am Coll Cardiol 2013;62:2124–30) © 2013 by the American College of Cardiology Foundation

Renal sympathetic denervation (RDN) is a novel treatment option for patients with resistant arterial hypertension. It is believed that RDN reduces efferent renal and central sympathetic activity (1). Clinical evidence comes from 1 randomized trial that showed substantial reductions of office-based blood pressures (BPs) 6 months after RDN, although effects on mean levels of 24-h ambulatory blood pressure monitoring (ABPM) were less pronounced (2).

Genesis of arterial hypertension is multifactorial, including not only sympathetic but also genetic, lifestyle, dietary, and metabolic factors. Therefore, it is unlikely that RDN is equally effective in every single patient. Furthermore, RDN is an invasive procedure with the inherent risks of side effects.

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Interference with the complex renal nervous system by RDN may cause unfavorable effects in the long-term, which are still unknown (3). Therefore, identification of patients who benefit from RDN is of great clinical importance. With exception of increased baseline BP, however, no marker predicting response to RDN has been identified so far.

It is plausible to assume that patients with pronounced sympathetic overactivity benefit the most from RDN. However, direct assessment of sympathetic activity, either by

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measuring norepinephrine spillover or by microneurographic techniques is highly impracticable in a clinical setting. Valuable information about the activity of the autonomic nervous system can also be obtained noninvasively by analyzing the interrelationship between spontaneous fluctuations of arterial BP and heart rate, which is also known as the baroreflex. The baroreflex is the most important neural mechanism in short-term control of BP. Its functional status is described by cardiac baroreflex sensitivity (BRS) relating changes of heart rate to changes of BP. Impaired cardiac BRS is a well-known phenomenon in hypertensive patients that has been linked to sympathetic overactivity (4,5).

In the present study, we hypothesized that impaired cardiac BRS identifies patients with resistant arterial hypertension who respond to RDN and patients who do not.

Methods

Patients. This study prospectively included 50 consecutive patients of either sex suffering from resistant arterial hypertension. Eligible patients were 18 years of age and older, had an office-based systolic BP of ≥160 mm Hg (≥150 mm Hg for patients with type 2 diabetes mellitus), and a mean systolic BP on ABPM of ≥130 mm Hg, despite being treated with at least 3 antihypertensive drugs with no changes in medication for a minimum of 2 weeks before enrollment. Patients were included if they were in sinus rhythm, which is required for estimation of cardiac BRS, and if they had an estimated glomerular filtration rate ≥45 ml/min^{-1}/1.73 m^{-2} (using the Modified Diet in Renal Disease formula). Patients were excluded if they had a known secondary cause of hypertension other than sleep apnea or chronic kidney disease. All patients underwent a complete history and physical examination, assessment of vital signs, review of medication, and blood chemistry at baseline and at 6 months after RDN. Treating physicians and patients were instructed not to change antihypertensive medications except when medically required. The study was approved by the local ethics committee. All patients gave written informed consent.

Renal denervation procedure. Patients were treated between October 2010 and September 2012. Details of RDN have been described elsewhere (2,6). Renal angiograms were performed via femoral access to confirm anatomic eligibility. The treatment catheter (Flex by Ardian/Medtronic Inc., Mountain View, California) was introduced into each renal artery using a guiding catheter. Up to 6 ablations at 8 W for 2 min each were performed in both renal arteries. Treatments were delivered from the first distal main renal artery bifurcation to the ostium proximally and were spaced longitudinally and rotationally under fluoroscopic guidance. Catheter tip impedance and temperature were constantly monitored, and delivery of radio frequency energy was regulated by a pre-determined algorithm. Visceral pain at the time energy was delivered was managed with intravenous analgetics and sedatives. Heparin was given to achieve an activated clotting time during the procedure of more than 250 s.

Ambulatory blood pressure monitoring. Twenty-four hour ABPM (oscillometric Spacelabs 90207-32 monitor; Spacelabs Healthcare, Issaqua, Washington) was performed before RDN and 6 months thereafter. Readings were taken every 20 min during the daytime and every 60 min at nighttime. Only ambulatory BP assessments that met the European Society of Cardiology and European Society of Hypertension guidelines (with more than 70% of daytime and nighttime readings) were regarded as technically sufficient for inclusion in the analysis (7). Mean systolic and diastolic BP were calculated as overall 24-h averages for every patient.

Assessment of cardiac BRS. At baseline, all patients underwent simultaneous 30-min high-resolution electrocardiographic recordings (1.6 kHz in orthogonal XYZ leads) and noninvasive continuous arterial BP monitoring using a finger photoplethysmographic device (Finapres; TNO-TPD Biomedical Instrumentation, Amsterdam, the Netherlands). The recordings were made using standardized conditions, with the patients in the supine resting position after routine morning medications were administered. An experienced technician, blinded to the clinical status of the patient, verified the raw signals and eliminated artifacts as needed. In particular, ectopic beats were carefully eliminated and calibration signals within the BP signals were removed. To analyze only normal sinus rhythm cycles, QRS classifications were carefully reviewed and manually corrected as appropriate.

Cardiac BRS was assessed from the series of RR intervals and systolic BP values by phase-rectified signal averaging (PRSA), according to previously published technologies (8-11). The exact methodology of BRS_{PRSA} assessment has been described elsewhere (10,12). Briefly, increases of systolic BP (BP↑) are identified within the BP time series. Subsequently, segments of RR intervals around BP↑ are identified and averaged. The resulting bivariate PRSA signal shows RR oscillations related to increases of systolic BP, whereas heart rate variability due to other causes is canceled out by the averaging process. The central amplitude of the bivariate PRSA signal is quantified by Haar wavelet analysis and normalized to the average systolic BP increase to obtain an estimate of BRS (10).

Cardiac BRS was also assessed by the sequence method (BRS_{SEQ}) (13). Briefly, this method identifies progressive

Abbreviations and Acronyms

ABPM = ambulatory blood pressure monitoring
AIC = Akaike information criterion
AUC = area under the curve
BMI = body mass index
BP = blood pressure
BRS = baroreflex sensitivity
BRS_{PRSA} = cardiac baroreflex sensitivity assessed by phase-rectified signal averaging
BRS_{SEQ} = cardiac baroreflex sensitivity assessed by the sequence method
CI = confidence interval
IDI = integrated discrimination improvement
MSNA = muscle sympathetic nerve activity
PRSA = phase-rectified signal averaging
RDN = renal sympathetic denervation
ROC = receiver-operator characteristic

increases of systolic BP over 3 or more consecutive beats in which RR intervals simultaneously prolong. If the correlation coefficient between systolic BP and RR interval is 0.85 or more, the slope between systolic BP and RR interval is calculated for all events. BRS_{SEQ} is finally obtained by the averaging of all single slopes.

Statistical analysis. Categorical variables are presented as proportions and were analyzed using Pearson's chi-square test. Continuous variables are expressed as mean ± standard deviation, unless otherwise specified. Comparisons were performed by means of 1-way analysis of variance for nonpaired variables or Student *t* test for paired values. Spearman's rank correlation was used to test the correlation between continuous variables. Response to RDN was defined as reduction of mean systolic BP on ABPM by 10 mm Hg or more 6 months after RDN. Receiver-operator characteristic (ROC) curves for prediction of response to RDN were constructed for variables by plotting the dependency of specificity on sensitivity. ROC curves were quantified by the integrals of the curves (area under the curve [AUC]) providing a robust statistical measure of the predictive power of a variable. Confidence intervals (CIs) were estimated using bootstrapping based on 1,000 random resamples (14). Multivariable analyses were implemented by the adaptation of multinomial logistic regression models. The selection of variables was based on the Akaike information criterion (AIC) (15). Logistic regression coefficients were fully standardized using the technique described by Menard (16). The ROC curves of multivariable models were quantified by C-statistics and compared by bootstrapping. The incremental prognostic value of a model was assessed by the integrated discrimination improvement (IDI) score using the method described by Pencina et al. (17). A 2-tailed p value <0.05 was considered statistically significant. Matlab (R2011a, Mathworks Inc., Natick, Massachusetts), CRAN R (version 2.15.3) and SPSS (version 20.0; SPSS, Chicago, Illinois) were used for analyses.

Results

The left column of Table 1 shows the demographic indicators and clinical characteristics. Mean age was 60.3 ± 13.8 years. There were 22 patients (44.0%) who were female. On average, patients were taking 5.4 ± 1.4 antihypertensive drugs. RDN was performed in all patients without periprocedural complications. At 6 months after RDN, there was no significant change in the numbers and classes of antihypertensive drugs (5.3 ± 1.4; p = 0.593).

At baseline, mean systolic BP on ABPM was 157 ± 22 mm Hg, and mean diastolic BP on ABPM was 89 ± 16 mm Hg. At 6 months after RDN, mean systolic BP on ABPM was significantly reduced by 8 ± 19 mm Hg (p = 0.003), and mean diastolic BP was significantly reduced by 4 ± 12 mm Hg (p = 0.022) (Fig. 1, left panel).

Table 1 Patient Characteristics

	All Patients (n = 50)	Responders (n = 26)	Nonresponders (n = 24)	p Value*
Demographics and risk factors				
Age (yrs)	60.3 ± 13.8	61.9 ± 12.3	58.5 ± 15.4	0.547
Male	28 (56.0%)	13 (50.0%)	15 (62.5%)	0.374
Body mass index (kg/m^2)	30.7 ± 5.7	32.7 ± 6.1	28.6 ± 4.6	0.013
Diabetes mellitus	18 (36.0%)	10 (38.5%)	8 (33.3%)	0.706
Coronary artery disease	15 (30.0%)	7 (26.9%)	8 (33.3%)	0.621
Creatinine (mg/dl)	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	0.616
Office-based measurements				
Systolic BP (mm Hg)	174 ± 28	178 ± 30	168 ± 26	0.162
Diastolic BP (mm Hg)	95 ± 15	99 ± 16	91 ± 13	0.067
Heart rate (beats/min)	69 ± 11	69 ± 13	69 ± 9	0.871
ABPM				
Mean systolic BP (mm Hg)	157 ± 22	166 ± 22	148 ± 18	0.001
Mean diastolic BP (mm Hg)	89 ± 16	92 ± 16	86 ± 16	0.137
Anti-hypertensive treatment				
No. of anti-hypertensive drugs	5.4 ± 1.4	5.5 ± 1.5	5.3 ± 1.4	0.505
ACE-I/ARB	47 (94.0%)	25 (96.2%)	22 (91.7%)	0.504
Renin inhibitor	22 (44.0%)	9 (34.6%)	13 (54.2%)	0.164
Beta-blockers	39 (78.0%)	19 (73.1%)	20 (83.3%)	0.382
Calcium channel blockers	44 (88.0%)	24 (92.3%)	20 (83.3%)	0.329
Diuretics	44 (88.0%)	23 (88.5%)	21 (87.5%)	0.917
Aldosterone antagonists	12 (24.0%)	7 (26.9%)	5 (20.8%)	0.614
Central sympatholytics	37 (74.0%)	19 (73.1%)	18 (75.0%)	0.877
Direct vasodilators	14 (28.0%)	8 (30.8%)	6 (25.0%)	0.650

Values are mean ± SD or n (%). *The p value for comparison between responders and nonresponders.

ABPM = ambulatory blood pressure monitoring; ACE-I = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BP = blood pressure.

Of the 50 patients studied, 26 patients (52%) had reductions of mean systolic BP on ABPM of 10 mm Hg or more. These patients were classified as responders to RDN. The middle and right columns of Table 1 show demographic indicators and clinical characteristics of responders and nonresponders, respectively. Compared to nonresponders, the responders had a higher body mass index (BMI) (32.7 ± 6.1 kg/m^2 vs. 28.6 ± 4.6 kg/m^2; $p = 0.013$) and a higher mean systolic BP on ABPM at baseline (166 ± 22 mm Hg vs. 148 ± 18 mm Hg; $p = 0.001$). All other baseline variables showed no significant difference between responders and nonresponders.

In the patients studied, BRS_{PRSA} was 0.82 ± 1.48 ms/mm Hg. BRS_{PRSA} significantly correlated with the reduction of mean systolic BP after 6 months ($r = -0.46$; $p < 0.001$). Patients with BRS_{PRSA} in the lowest tertile showed the most pronounced reductions of mean systolic BP of 17 ± 20 mm Hg at 6 months followed by patients with BRS_{PRSA} in the middle (8 ± 13 mm Hg) and highest tertile (0 ± 20 mm Hg) ($p = 0.023$ for comparison of tertiles) (Fig. 1, right panel). There was a highly significant association between BRS_{PRSA} and response to RDN, with BRS_{PRSA} being significantly lower in responders than nonresponders (0.16 ± 0.75 ms/mm Hg vs. 1.54 ± 1.73 ms/mm Hg; $p < 0.001$) (Fig. 2, left panel). This remained true in subgroups of patients, divided according to baseline mean systolic BP ≤150 mm Hg and >150 mm Hg and BMI <30 kg/m^2 and ≥30 kg/m^2 (Fig. 2, middle and right panels).

Figure 3A shows the ROC curve of BRS_{PRSA} for prediction of response to RDN. The BRS_{PRSA} yielded an AUC of 81.2% (95% CI: 70.0% to 90.1%; $p < 0.001$), which was significantly higher than the AUCs of all other variables tested ($p < 0.001$ for all). Mean systolic BP at baseline and BMI, which were the only other variables significantly associated with response to RDN, yielded AUCs of 77.1% (95% CI: 64.9% to 88.5%; $p < 0.001$) and 73.4% (95% CI: 59.7% to 84.1%; $p < 0.001$), respectively. Table 2 shows the results of the multivariable logistic regression analysis. BRS_{PRSA} was the strongest predictor of response to RDN, whereas mean systolic BP and BMI were of borderline statistical significance.

Finally, we tested whether adding BRS_{PRSA} improves prediction of response to RDN by mean systolic BP and BMI. The multivariable model based on mean systolic BP and BMI yielded a C-statistic of 78.9% (95% CI: 66.8% to 88.0%). Implementing BRS_{PRSA} into the model leads to a significant increase of the C-statistic to 89.5% (95% CI: 80.3% to 95.5%; $p < 0.001$ for difference) (Fig. 3B). At the same time, the relative IDI score improved by 80% ($p < 0.001$), whereas the absolute IDI score improved by

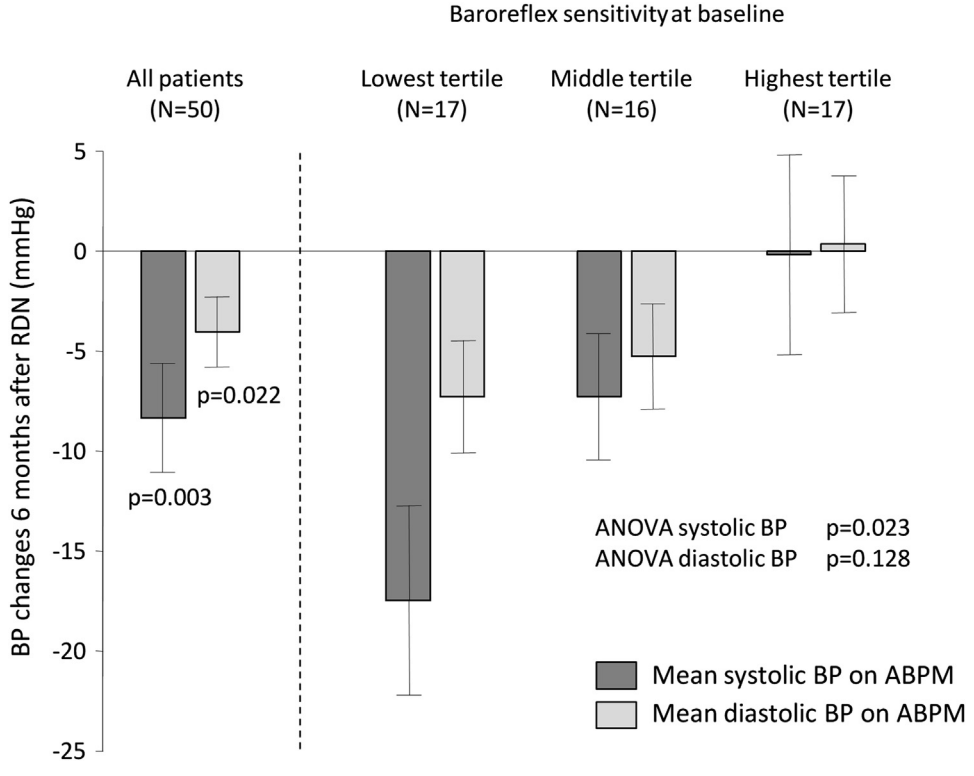

Figure 1 Effects of RDN on Mean BP Changes According to Baroreflex Sensitivity

Effects of renal sympathetic denervation (RDN) on mean systolic and diastolic blood pressure (BP) changes on ambulatory blood pressure monitoring (ABPM) after 6 months in all patients and in patients stratified by tertiles of baseline baroreflex sensitivity. Bars show standard error of the mean. ANOVA = analysis of variance.

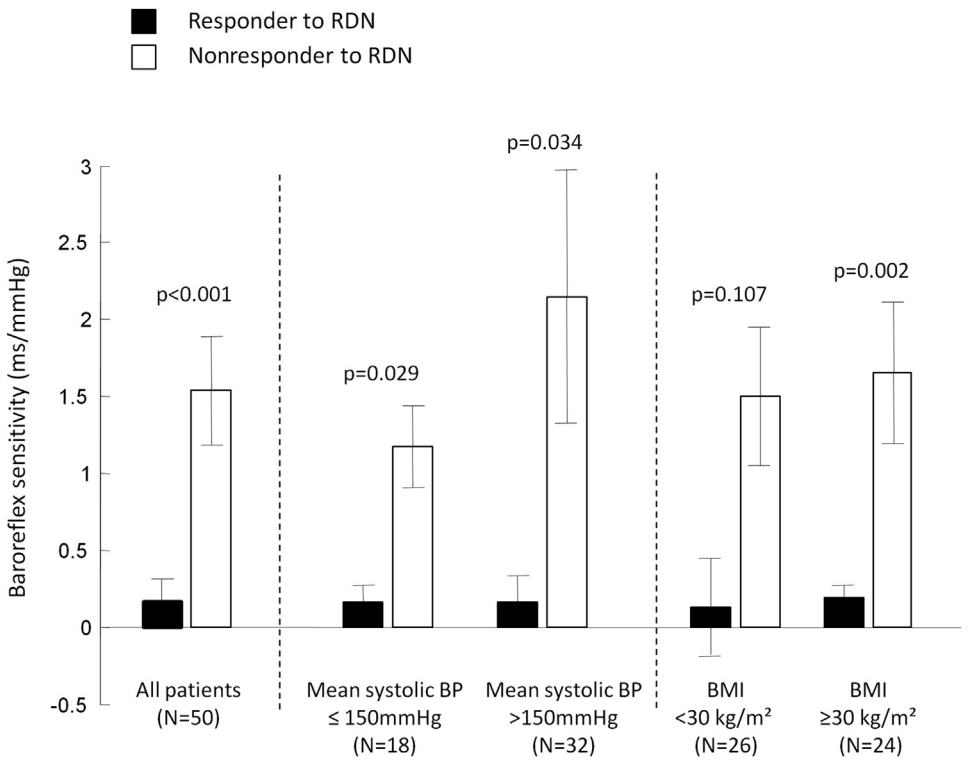

Figure 2 **Baroreflex Sensitivity in Responders and Nonresponders to RDN**

Left panel shows baroreflex sensitivity in responders and nonresponders to renal sympathetic denervation (RDN) in all patients. **Middle and right panels** show subgroups of patients with mean baseline systolic blood pressure (BP) levels ≤150 mm Hg and >150 mm Hg on ambulatory BP monitoring and body mass index (BMI) <30 kg/m^2 and ≥30 kg/m^2, respectively. Bars show standard error of the mean.

0.20 ($p < 0.001$). The combination of mean systolic BP, BMI, and BRS_{PRSA} was the model with the lowest AIC score of 49.3, indicating that the model could not be significantly improved by any other variable.

We also tested whether BRS_{SEQ} was a predictor of response to RDN. The BRS_{SEQ} could not be calculated in 7 patients (14%) for methodological reasons. Both BRS_{SEQ} and BRS_{PRSA} were significantly correlated ($r = 0.76$; $p < 0.001$). Also, BRS_{SEQ} was significantly associated with response to RDN and yielded an AUC of 73.2% (95% CI: 60.4% to 85.1%; $p < 0.001$) which was, however, significantly lower than that of BRS_{PRSA} ($p < 0.001$ for difference).

Discussion

The findings of our study indicate that cardiac BRS is a strong and independent predictor of response to RDN in patients with resistant arterial hypertension. In two-thirds of patients with BRS_{PRSA} ≤0.62 ms/mm Hg (lowest and middle tertile) RDN led to substantial reductions of mean systolic BP on ABPM of 13 ± 17 mm Hg. In contrast, in one-third of patients with BRS_{PRSA} >0.62 ms/mm Hg (upper tertile), RDN had no significant effects on mean systolic BP (change of 0 ± 20 mm Hg). The predictive value of BRS_{PRSA} was stronger than that of elevated mean systolic BP at baseline and BMI, the only other variables that were significantly associated with response to RDN. Finally, BRS_{PRSA} significantly improved prediction of response to RDN based on a combination of mean systolic BP at baseline and BMI by significantly improving the C-statistic from 78.9% to 89.5%.

RDN and the sympathetic nervous system. Several experimental and clinical studies investigated the effects of RDN on the sympathetic nervous system in patients with resistant arterial hypertension. First, evidence that RDN reduces efferent renal sympathetic activity came from a subgroup analysis of 10 patients enrolled in the Symplicity HTN-1 (Renal Sympathetic Denervation in Patients with Treatment-Resistant Hypertension-1) study showing that norepinephrine spillover assessed by the isotope dilution method was significantly reduced by 47% (6). A subsequent case report suggested that RDN may also reduce central sympathetic activity by demonstrating significant effects on muscle sympathetic nerve activity (MSNA) and cardiac BRS (18). This finding was questioned by a recent study that failed to demonstrate significant effects of RDN on MSNA, heart rate variability, and cardiac BRS in 11 patients (19). In this study, however, 5 of 11 patients had baseline systolic

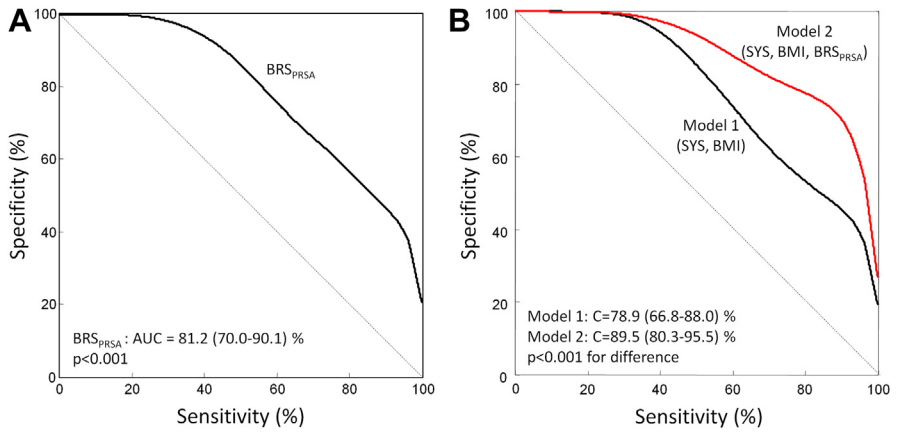

Figure 3 **Prediction of Response to RDN**

Receiver-operator characteristic (ROC) curves of risk variables for prediction of response to renal sympathetic denervation (RDN). **(A)** ROC curve of BRS assessed by phase-rectified signal averaging baroreflex sensitivity (BRS$_{PRSA}$). **(B)** ROC curves of 2 different multivariable models. Model 1 includes mean systolic blood pressure at baseline (SYS) and body mass index (BMI). Model 2 additionally includes BRS$_{PRSA}$ and is superior to Model 1 in prediction of response to RDN. AUC = area under the curve; BRS = baroflex sensitivity; BRS$_{PRSA}$ = baroreflex assessed by sensitivity phase-rectified signal averaging C = C-statistic.

office BP levels of 140 mm Hg or less and remarkably low levels of baseline MSNA (20). Therefore, lack of effects in these patients may indicate that a high baseline level of sympathetic tone is necessary to achieve a response to RDN. A more recent study in 25 patients finally demonstrated highly significant reductions of MSNA by RDN (1). The findings of our study are in line with these observations as depressed cardiac BRS might identify patients with high central sympathetic tone who respond favorably to RDN.

Cardiac BRS. Depressed cardiac BRS is a well-known phenomenon in various diseases characterized by sympathetic overactivity including heart failure (21), myocardial infarction (22), arrhythmias (23), renal insufficiency (24), diabetes mellitus (25), and arterial hypertension (4,5). Over the last couple decades, various methods have been proposed to assess cardiac BRS. The invasive methods quantify prolongations of the RR intervals to artificial increases of BP by vasoactive drugs, whereas noninvasive methods analyze spontaneous fluctuations of RR interval and systolic BP (26). Noninvasive assessment of BRS has practical appeal, but it is challenging due to the complex nature of both signals. In particular, spectral methods are highly sensitive to artifacts and ventricular premature complexes making results unreliable (27). In the present study, we assessed BRS by the PRSA method, which overcomes these shortcomings (10,12). In a recent study, including 941 post-infarction patients, BRS$_{PRSA}$ was shown to provide significantly better prognostic accuracy than other methods of BRS assessment (11). However, in our study, BRS assessed by the sequence method was also a significant predictor of response to RDN.

Although impaired BRS$_{PRSA}$ identified responders to RDN, it did not predict the exact extent of BP reductions achieved by RDN. This could be explained by the intrinsic variability of both BRSA$_{PRSA}$ and BP, by procedural differences, as well as by RDN-induced effects on BP that are not related to reduction of central sympathetic activity.

ABPM versus office-based BP measurements. In contrast to previous studies that tested the effects of RDN on office-based BP measurements (2), we used mean systolic BP levels on ABPM to define response to therapy. Compared with office-based measurements, ABPM removes observer bias, reduces measurement error, has a greater reproducibility, minimizes the white-coat effect, and, most importantly, yields more accurate prognostic information (28,29). In our patients, we also observed highly significant reductions of systolic office-based BP of 23 ± 21 mm Hg ($p < 0.001$), which is in the range of previous reports (2,6).

The Symplicity HTN-2 study reported a responder rate to RDN of 84%, defined as a reduction of office-based systolic BP of 10 mm Hg or more (2). In our study, 39 of 50 patients (78%) fulfilled the HTN2 criteria of response ($p = 0.611$ for comparison with the responder rate of the HTN2 study). Of interest, BRS$_{PRSA}$ also predicted response to RDN defined by reductions of systolic office BP (≥10 mm Hg), yielding an AUC of 72.1% (95% CI: 54.9%

Table 2 **Multivariable Logistic Regression Analysis for Prediction of Response to Renal Sympathetic Denervation**

Variable	Standardized Coefficients (95% CI)	p Value
BRS$_{PRSA}$	−0.517 (−0.994 to −0.040)	0.035
Mean systolic BP (ABPM)	0.206 (−0.004 to 0.416)	0.056
Body mass index	0.187 (−0.02 to 0.395)	0.079

BRS = baroreflex sensitivity; CI = confidence interval; PRSA = phase-rectified signal averaging; other abbreviations as in Table 1.

to 85.8%; $p < 0.001$). As known from pharmacological trials, reductions of mean systolic BP on ABPM are generally less pronounced than office-based BP reductions (30). The numerically lower responder rate of 52% in our study compared with previous reports is explained by the mode of BP measurements (ABPM vs. office-based).

Study limitations. First, assessment of BRS is limited to patients in sinus rhythm. Second, although our study design was prospective, used cut-off values of BRS_{PRSA} needed to be prospectively validated in independent datasets. Third, noninvasive assessment of BRS requires continuous assessment of arterial BP by technologies that may not be available in all centers. Fourth, we did not obtain direct measures of sympathetic activity such as MSNA or norepinephrine spillover, which are, however, highly impracticable in a clinical setting. Fifth, it remains subject to further investigations whether RDN leads to an improvement of impaired BRS. Finally, RDN might induce additional effects on systolic BP reductions beyond 6 months, which are not covered by our analyses. However, preliminary data suggest that BRS_{PRSA} is also a significant predictor of response to RDN up to 12 months after RDN. In 29 of 50 patients with complete 12-month follow-up, BRS_{PRSA} yielded an AUC of 83.3% (95% CI: 68.1% to 93.5%; $p < 0.001$) for prediction of response 12 months after RDN.

Conclusions

BRS assessment helps to identify patients who are most likely to benefit from RDN and, of equal importance, patients who do not. Selection of candidates for RDN should take cardiac BRS into account.

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Key Words: arterial hypertension ■ baroreflex sensitivity ■ renal sympathetic denervation ■ sympathetic nervous system.