Twenty-Four-Hour Blood Pressure Monitoring to Predict and Assess Impact of Renal Denervation

The DENERHTN Study (Renal Denervation for Hypertension)

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See Editorial Commentary, pp 398–400

Abstract—The DENERHTN trial (Renal Denervation for Hypertension) confirmed the blood pressure (BP) lowering efficacy of renal denervation added to a standardized stepped-care antihypertensive treatment for resistant hypertension at 6 months. We report here the effect of denervation on 24-hour BP and its variability and look for parameters that predicted the BP response. Patients with resistant hypertension were randomly assigned to denervation plus stepped-care treatment or treatment alone (control). Average and standard deviation of 24-hour, daytime, and nighttime BP and the smoothness index were calculated on recordings performed at randomization and 6 months. Responders were defined as a 6-month 24-hour systolic BP reduction ≥20 mm Hg. Analyses were performed on the per-protocol population. The significantly greater BP reduction in the denervation group was associated with a higher smoothness index (P=0.02). Variability of 24-hour, daytime, and nighttime BP did not change significantly from baseline to 6 months in both groups. The number of responders was greater in the denervation (20/44, 44.5%) than in the control group (11/53, 20.8%; P=0.01). In the discriminant analysis, baseline average nighttime systolic BP and standard deviation were significant predictors of the systolic BP response in the denervation group only, allowing adequate responder classification of 70% of the patients. Our results show that denervation lowers ambulatory BP homogeneously over 24 hours in patients with resistant hypertension and suggest that nighttime systolic BP and variability are predictors of the BP response to denervation.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifier: NCT01570777.

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The DENERHTN[1] trial (Renal Denervation for Hypertension) showed that renal denervation (RD) with the Symplicity flex catheter added to a standardized stepped-care antihypertensive treatment (SSAHT) recommended by UK guidelines[2] significantly reduced daytime (primary end point), nighttime, and 24-hour ambulatory systolic blood pressure (SBP) by ≈6 mm Hg more than the SSAHT alone after 6-month follow-up in patients with well-defined resistant hypertension (RH) to

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4-week standardized triple therapy confirmed by ambulatory blood pressure monitoring (ABPM). We also observed a large between-patient variability in the daytime SBP response to RD, greater than that observed in the SSHAT group, suggesting that some patients could be true responders to RD. Male sex, baseline daytime ambulatory SBP, changes in daytime ambulatory heart rate (HR), low treatment score, and high adherence to study medication, but not ethnic origin, were the independent contributors to the blood pressure (BP) response.

In a PROBE trial (Prospective Randomized Open-Blind End Point), such as DENERHTN, the use of ABPM to assess the BP effect of RD has the advantage of eliminating observer bias and placebo effect.[3] Moreover, ABPM allows investigating the effects of RD on the whole 24 hours and on indices of BP variability. The aims of this predefined analysis are to report in detail the ABPM results, especially those of BP and HR variability, and to seek whether ABPM can help predicting BP response to RD.

Methods

The design of the DENERHTN trial conducted in French Hypertension Excellence Centers has been reported elsewhere[1] and will be briefly summarized. Eligible patients with confirmed essential RH, suitable renal artery anatomy, and estimated glomerular filtration rate ≥40 mL/min per 1.73 m^2 were randomly assigned in a 1:1 ratio to RD plus SSAHT or SSAHT alone. Before randomization, all eligible patients received slow-release indapamide 1.5 mg, ramipril 10 mg (or irbesartan 300 mg), and amlodipine 10 mg (or 5 mg) daily for 4 weeks to confirm treatment resistance defined by daytime ambulatory SBP ≥135 mm Hg or diastolic BP (DBP) ≥85 mm Hg. After randomization, spironolactone 25 mg, bisoprolol 10 mg, prazosin 5 mg, and rilmenidine 1 mg were sequentially added from months 2 to 5 in both groups if home BP was ≥135/85 mm Hg. We performed a median number of 11 (interquartile range, 10–12) renal nerve ablations per patient with the single electrode radiofrequency Symplicity catheter (Medtronic, Mountain View, CA) 2 to 4 weeks after randomization. The primary end point was change in daytime ambulatory SBP at 6 months. The study was approved by the Comité de Protection des Personnes Ile de France VII (ClinicalTrials.gov identifier: NCT01570777). All participants provided written informed consent to participate in the study.

Ambulatory BP Monitoring

Twenty-four-hour ABPM was performed with the Spacelabs 90207 monitor (Spacelabs Healthcare, Issaquah, WA) prior to randomization and at 6 months. BP was recorded every 15 to 20 minutes during daytime (06:00–22:00 hours) and every 15 to 30 minutes during nighttime (22:00–06:00 hours). At baseline and 6 months, patients arrived at the study center between 07:00 and 10:00 hours prior to ingestion of morning antihypertensive treatment to undergo ABPM. After the start of ABPM, patients were given their antihypertensive treatment and were asked to return to the study center the next morning without having taken their treatment. All recordings were sent to a core laboratory blind to the randomization group for data cleaning and harmonization of the daytime and nighttime periods. The minimum expected number of BP measurement was 64 over 24 hours, and recording had to be performed again if the number of available measurement was <40 and if there was a period of >2 hours without any valid measurements.

Aberrant measurements (BP or HR=0, DBP>SBP, pulse pressure <10 mm Hg) were removed as recommended.[4] For each individual valid recording, we calculated the average and standard deviation (SD) of 24-hour, daytime, and nighttime SBP, DBP, and HR using wide fixed period as for BP sampling. For BP indices of variability, we also made calculation with narrow period (day: 10:00–20:00 hours, night: 00:00–06:00 hours) to limit the influence of night–day transitions.[5] We also calculated (1) the ambulatory arterial stiffness index as 1−the slope of the regression line of DBP on SBP values from individual 24-hour recordings,[6] (2) the smoothness index as the average differences between hourly means in SBP of the baseline and 6-month recordings divided by the SD of these differences,[7] and (3) the time rate of SBP variation as previously described.[8] The proportion of patients who were dippers (decline of 10% or more in night to day SBP) or nondippers was calculated at randomization and at 6 months.

Statistical Methods

We conducted the statistical analyses on the per-protocol population in whom ABPM measurements at 6 months were available. We used the unpaired *t* test for continuous variables and the χ^2 test for categorical variables to compare (1) treatment groups at randomization and (2) responders (6-month 24-hour SBP reduction of ≥20 mm Hg) and the nonresponders. All significantly different variables between responders and nonresponders in the univariate analysis were introduced in a step-by-step discriminant analysis and for the calculation of a score (L) based on the combined selected predictors for responders in the RD group. The L score was constructed with the estimates of beta coefficients obtained by fitting a logistic regression model for the outcome of interest. We calculated Wilks's lambda (likelihood ratio criterion), and we set the *P* value to <0.05 to enter a variable and >0.10 to remove it. We then drew receiver operating characteristic curves and calculated area under curve (AUC) for each significantly discriminant variable for responders in the RD group.

Data are expressed as mean±SD or mean (95% confidence interval). We used the statistical analysis system (SAS) software version 9·4 (SAS Institute Inc, Cary, NC). A *P* value <0·05 was considered significant.

Results

Population

The distribution of the patients in the 2 groups of the DENERHTN study has been previously reported.[1] A total of 44 out of 53 patients randomized to the RD group and 53 out of 53 randomized to the control group were included in the per-protocol analysis. Nine patients randomized to the RD group were not included for the following reasons: 3 refused the procedure after inclusion, 3 had ineligible renal artery anatomy diagnosed during the procedure, 1 had a complication before RD, and 2 had missing ABPM data at 6 months. Table 1 summarizes the main characteristics of the 24-hour ABPM recordings at baseline and 6 months in the 2 groups. The average number of 24-hour BP measurements available and the ratio of done/expected measurements were high without significant differences between baseline and 6-month recordings and between groups. The interval between daytime BP measurements was set at 20′ in 25% and 15′ in 75% of the patients. For nighttime BP, the interval was set at 30′ for 65% and 20′ for 35% of the patients, without changes between baseline and 6 months recordings.

Ambulatory BP and HR Parameters

The baseline ambulatory BP and HR measurements of the 2 groups shown in Table S1 in the online-only Data Supplement were similar. The mean decreases from baseline to 6 months in daytime, nighttime, and 24-hour ambulatory SBP were significantly greater in the RD group than in the control group, with a mean baseline-adjusted difference between the 2 groups of ≈−6.0 mm Hg (Table 2). HR decreased similarly from baseline to 6 months in the 2 groups. The number of medications of the SSAHT was similar in the 2 groups. Standard deviations of SBP, DBP, and HR and time rate of SBP variation did not change significantly from baseline to 6 months (Table 2). The

Table 1. Main Characteristics of Ambulatory Blood Pressure Recordings at Baseline and 6 Months

Item	Renal Denervation (n=44)	Control (n=53)	*P* Value
Baseline			
Interval between daytime measures, min	15.80±2.63	15.47±1.47	0.45
Interval between nighttime measures, min	27.16±9.79	28,11±12.41	0.68
Number of measures done	72.61±12.88	73.42±13.13	0.76
Measures done/ expected ratio, %	88.51±9.60	88.68±11.23	0.93
6 months			
Interval between daytime measures, min	15.57±1.60	15.28±1.16	0.31
Interval between nighttime measures, min	28.41±13.32	27.17±12.84	0.64
Number of measures done	71.93±13.43	74.00±12.65	0.44
Measures done/ expected ratio, %	86.80±9.60	87.84±10.36	0.61

Data are mean±SD.

ambulatory arterial stiffness index did not change significantly from baseline to 6 months in the RD group (0.44±0.17 versus 0.42±0.17; *P*=0.19) or in the control group (0.42±0.13 versus 0.44±0.17; *P*=0.4). The smoothness index was significantly greater in the RD group (1.4±1.2) than in the control group (0.9±0.6; *P*=0.02). The proportion of nondipper patients was similar in both groups at randomization (RD 54%, control 53%) and 6 month (RD 66%, control 57%). This trend to a higher prevalence of nondippers at 6 months as compared with baseline was not significant (*P*=0.39).

Responders

The number of responders was significantly higher in the RD group (20/44, 44.5%) than in the control group (11/53, 20.8%; *P*=0.01). Table 3 summarizes the main characteristics of responders compared with nonresponders independently of the assigned group. In the univariate analysis, 5 baseline variables were significantly different between responders and nonresponders and included the treatment group, the average 24-hour, daytime, and nighttime SBP and nighttime SD_{SBP} calculated on wide or narrow periods. Because the calculation based on narrow night period did not seem to improve the discrimination between responder and nonresponder, we kept the wide period for further analyses. The number of patients with isolated systolic hypertension defined by daytime SBP≥135 mm Hg and daytime DBP<85 mm Hg did not differ significantly between responders (n=5, 25%) and nonresponders (n=9, 37%). In the stepwise discriminant analysis, baseline average nighttime SBP, nighttime SD_{SBP}, and the treatment group remained significant predictors of the daytime SBP response (Table S2). When analysis was restricted to the RD group, only average nighttime SBP and nighttime SD_{SBP} remained significantly associated to responders (*P*=0.005). In contrast, these 2 variables did not significantly discriminate between responders and nonresponders in the control group.

Figure shows the receiver operating characteristic curves to predict the responders according to baseline nighttime SBP, nighttime SD_{SBP} values, and L score in the RD group. The AUC was 0.65 (95% confidence interval, 0.486–0.816; *P*=0.07) for baseline average nighttime SBP and 0.72 (95% confidence interval, 0.565–0.874; *P*=0.005) for baseline nighttime SD_{SBP}. For baseline average nighttime SBP, a cutoff of 136 mm Hg offers the best compromise between sensitivity (75%) and specificity (54%) to predict responders. For nighttime SD_{SBP}, a cutoff of 12 mm Hg offers the best compromise between sensitivity (55%) and specificity (83%) to predict responders. When combined together, the 2 cutoff points allow adequate

Table 2. Ambulatory Blood Pressure and Heart Rate Changes From Baseline to 6 Months in the Renal Denervation and Control Groups (Per-Protocol Population)

Change From Baseline	Renal Denervation (n=44)	Control (n=53)	*P* Value
24-h SBP, mm Hg	−16.16±15.76	−8.87±11.45	0.01
24-h DBP, mm Hg	−9.84±10.61	−6.43±6.93	0.07
24-h HR, bpm	−6.68±9.69	−8.04±9.45	0.49
Daytime SBP, mm Hg	−16.36±16.23	−9.26±12.59	0.02
Max daytime SBP, mm Hg	−19.00±25.33	−9.06±18.37	0.03
Daytime DBP, mm Hg	−9.82±11.04	−6.68±8.32	0.11
Max daytime DBP, mm Hg	−8.95±16.46	−7.15±14.48	0.57
Daytime HR, bpm	−7.23±10.33	−8.81±10.76	0.46
Max daytime HR, bpm	−2.55±33.72	−5.43±23.70	0.62
Nighttime SBP, mm Hg	−14.77±16.76	−6.81±12.66	0.01
Max nighttime SBP, mm Hg	−15.86±23.70	−8.13±23.29	0.11
Nighttime DBP, mm Hg	−8.91±11.58	−4.91±6.27	0.03
Max nighttime DBP, mm Hg	−8.70±16.61	−5.83±13.58	0.35
Nighttime HR, bpm	−4.89±8.61	−4.77±8.54	0.95
Max nighttime HR, bpm	−6.91±13.83	−3.91±10.91	0.24
24-h SD_{SBP}, mm Hg	−0.32±3.86	0.21±4.70	0.55
24-h TRV	−0.02±0.15	−0.14±0.25	0.95
24-h SD_{DBP}, mm Hg	−0.34±3.22	0.02±3.55	0.60
24-h SD_{HR}, bpm	−0.66±4.29	−0.85±3.67	0.81
Daytime SD_{SBP}, mm Hg	−0.14±4.31	0.49±3.99	0.46
Daytime SD_{DBP}, mm Hg	−0.50±3.59	0.23±3.12	0.29
Daytime SD_{HR}, bpm	−0.34±4.58	−0.40±3.78	0.95
Nighttime SD_{SBP}, mm Hg	−0.09±4.67	−0.62±4.92	0.59
Nighttime SD_{DBP}, mm Hg	−0.00±3.58	0.15±4.47	0.85
Nighttime SD_{HR}, bpm	−0.70±2.69	0.08±2.79	0.17
AASI	0.02±0.13	-0.02±0.14	0.12

Data are mean±SD. AASI indicates ambulatory arterial stiffness index; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; SD_{DBP}, standard deviation of DBP; SD_{HR}, standard deviation of HR; SD_{SBP}, standard deviation of SBP; and TRV, time rate of SBP variation.

Table 3. Main Characteristics of Responders and Nonresponders (Univariate Analysis)

Item	Responder (n=31)	Nonresponder (n=66)	*P* Value
Denervation (yes/no)	20/11	24/42	0.01
Sex (male/female)	21/10	38/28	0.38
White (yes/no)	26/5	49/17	0.44
Age, y	57.72±10.98	53.54±10.14	0.08
Height, cm	169.68±8.12	169.18±9.35	0.80
Weight, kg	89.44±14.22	85.52±16.32	0.25
eGFR, mL/min per 1.73 m^2	83.26±26.03	92.52±23.45	0.09
Baseline ambulatory BP and HR measurements			
24-h SBP, mm Hg	155.65±16.74	146.03±14.87	0.005
24-h DBP, mm Hg	91.77±14.55	88.38±12.20	0.23
24-h HR, bpm	74.42±11.84	75.83±8.69	0.51
24-h SD_{SBP}, mm Hg	16.19±5.11	14.79±3.44	0.11
24-h SD_{DBP}, mm Hg	11.87±3.08	11.61±2.31	0.64
24-h SD_{HR}, bpm	9.42±2.42	10.35±3.50	0.19
24-h TRV	0.67±0.25	0.60±0.22	0.19
Daytime SBP, mm Hg	159.52±17.34	150.03±15.15	0.007
Daytime DBP, mm Hg	94.68±14.32	91.47±12.33	0.26
Daytime HR, bpm	77.10±12.48	78.47±9.29	0.55
Daytime wide SD_{SBP}, mm Hg	14.77±4.67	13.38±3.29	0.09
Daytime narrow SD_{SBP}, mm Hg	13.42±4.13	12.63±3.33	0.31
Daytime SD_{DBP}, mm Hg	10.71±3.09	10.42±2.51	0.63
Daytime SD_{HR}, bpm	8.90±2.44	9.91±3.37	0.14
Nighttime SBP, mm Hg	145.13±17.42	135.33±14.81	0.005
Nighttime DBP, mm Hg	83.68±15.29	79.56±12.58	0.17
Nighttime HR, bpm	66.97±10.07	68.20±7.92	0.52
Nighttime Wide SD_{SBP}, mm Hg	13.71±4.58	11.64±3.65	0.01
Nighttime narrow SD_{SBP}, mm Hg	12.11±3.88	10.33±3.72	0.03
Nighttime SD_{DBP}, mm Hg	10.35±3.16	9.42±3.10	0.17
Nighttime SD_{HR}, bpm	6.06±2.35	6.15±2.62	0.87

Data are mean±SD. DBP indicates diastolic blood pressure, eGFR, estimated glomerular filtration rate; HR, heart rate; SBP, systolic blood pressure; SD_{DBP}, standard deviation of DBP; SD_{HR}, standard deviation of HR; SD_{SBP}, standard deviation of SBP; and TRV, time rate of SBP variation.

classification of 70% of the patients who underwent RD in responder and nonresponder groups. The AUC for the L score was 0.76 (95% confidence interval, 0.615–0.900; $P<0.001$). The AUC for the L score did not significantly differ from the AUC for baseline nighttime SBP and SD_{SBP}.

Discussion

Because ambulatory BP was the primary end point in the DENERHTN trial, we took great care to ensure the highest quality of the recordings that were performed in specialized tertiary ESH excellence centers. All recordings were sent to a core laboratory kept blind to the randomization. Average

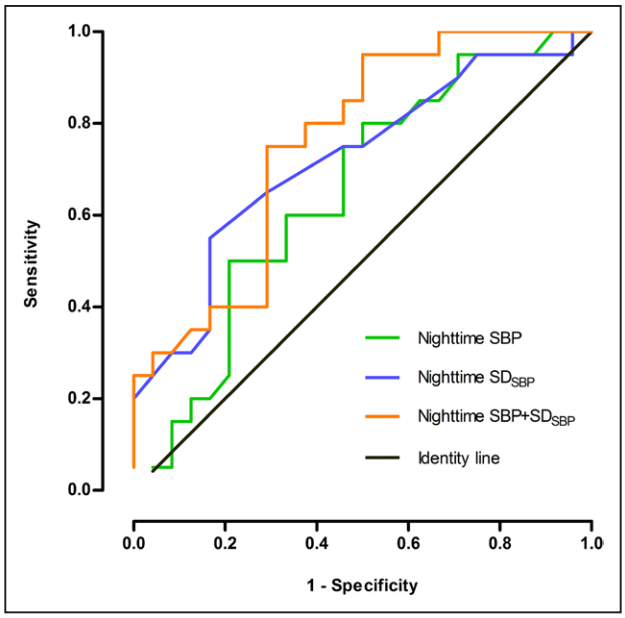

Figure. Receiver operating characteristic (ROC) curves of baseline nighttime systolic blood pressure (SBP) and its variability (SD_{SBP}) and the L score (based on the combined selected predictors for responders) to predict blood pressure response to renal denervation. SD indicates standard deviation.

24-hour, daytime, and nighttime BP were calculated from all individual valid measurements to avoid variability because of the use of different dedicated softwares.[9,10] The high number of valid measurements (≈73 on average corresponding to ≈88% of expected measurements) (1) confirms the high quality of the recordings, which was much higher than that reported in the SYMPLICITY HTN III trial[11] in which the number of expected measurements was 48 (2/hour) and the minimum required was 33, and (2) enabled more precise assessment of ambulatory BP and HR variability.

The significantly greater ambulatory SBP decrease achieved 6 months after RD was also more homogeneous over 24 hours than in the control group. Indeed, the smoothness index, which is more reproducible and better correlated to the evolution of target organ damage in hypertensive patients than the usual peak/through ratio,[12] was significantly higher in the RD than in the control group. Both the greater 24-hour ambulatory SBP decrease and the higher smoothness index after RD may, thus, impact favorably the cardiovascular prognosis if maintained on the long term.[13] The average 24-hour SBP decrease after RD was 16 mm Hg in the DENERHTN trial as compared with 7 mm Hg in the SYMPLICITY HTN III trial,[14] despite lower baseline values (152 mm Hg versus 159 mm Hg, respectively). In another randomized sham-controlled trial,[15] RD reduced 24-hour SBP significantly more than did antihypertensive treatment in patients with RH (−8.3 mm Hg versus −3.5 mm Hg in the per-protocol analysis; $P=0.04$), this smaller BP lowering effect than in our study being accounted for by lower baseline 24-hour SBP values (140 mm Hg).

Despite a large number of valid ambulatory BP measurements, we did not find a significant reduction in BP variability as estimated from 24-hour, daytime, or nighttime SD_{SBP} (whether calculated on wide or narrow periods) or time rate of

SBP variation, an index of BP variability independent of the mean. This is consistent with the results of the SYMPLICITY HTN III[11] and the EnligHTN[16] trials but contrasts with the significant reduction of SD of 24-hour SBP observed 6 months after RD reported by Ewen et al,[17] but this study had no control group. Finally, we did not find any significant variation of the ambulatory arterial stiffness index, a possible indicator of arterial stiffness, in both groups. However, this index has a poor reproducibility,[18] and its clinical significance is extensively discussed.[19]

The ambulatory BP response to RD displayed large between-patient variability illustrated by the higher SD of 24-hour SBP change at 6 months in the RD group (16 mm Hg) than in the control group (11 mm Hg), even though the 2 groups received the same SSAHT. This suggests that RD contributed to a larger ambulatory BP response in some patients considered as responders. Indeed, the number of responders displaying a 24-hour SBP decrease of ≥20 mm Hg was significantly higher in the RD group. A possible explanation is the true effectiveness of the RD procedure, but there is no practical way to check its immediate efficiency. The main challenge remains to select the right patients for RD by finding reliable, simple, and reproducible predictors of the BP response. Baseline BP,[20] younger age, higher glomerular filtration[21] were identified as possible predictors of BP response to RD. Various other potential predictors, such as slower HR,[22] use of central sympatholytic agents[23] or aldosterone antagonists,[24] indices of baseline sympathetic overdrive,[25] and different biological markers[26] have been suggested to be associated with the BP response to RD; these predictors either lack a strong pathophysiological basis or have not been confirmed in randomized controlled trials. Isolated systolic hypertension defined by office BP measurements (SBP ≥140 mm Hg and DBP <90 mm Hg) has been reported to be associated with a poor BP response to RD in an observational study.[27] We did not find such significant association when we used ambulatory BP levels to define isolated systolic hypertension, but the number of patients with isolated systolic hypertension was small.

The main result of our study is that both baseline average nighttime ambulatory SBP and its variability (SD_{SBP}) measured after 4 weeks of standardized triple combination therapy were significant and independent predictors of the 24-hour ambulatory SBP response to RD at 6 months and not to that of the SSAHT given alone. Nighttime BP levels have been shown to better predict cardiovascular morbidity and mortality than daytime BP levels,[28] and nighttime BP variability seems to bring an added predictive value.[29] Nighttime BP are less influenced by environmental factors (sleep versus activity), position of the patients (supine versus standing), and daily stresses and, thus, are more reproducible and better indicate the actual level of BP load than do daytime BP. The ability of nighttime ambulatory SBP and its variability to predict the daytime ambulatory SBP response to RD may also indicate a possible implication of the sympathetic nervous system in maintaining high BP during nighttime in some patients with RH as shown in patients with obstructive sleep apnea syndrome.[30] In our study, a cutoff point of 136 mm Hg for nighttime ambulatory SBP and 12 mm Hg for nighttime SD_{SBP} measured at baseline after 4 weeks of standardized triple combination therapy defined 70% of patients as responders 6 months after RD added to the SSAHT. Further studies with larger sample size are certainly required to confirm these results and define more precisely the cutoff points of these 2 parameters to adequately select patients for RD, depending on the expected sensitivity/specificity of prediction and the next generation of catheters that may achieve a more complete and reproducible RD.

Study Limitations

The strength and limitation of the DENERHTN trial have been extensively discussed.[31,32] Even though ABPM recordings were of high quality and BP measured every 15 minutes during daytime, BP was measured only every 30 minutes during nighttime in most cases to reduce sleep disturbances. In addition, we did not have a precise definition of awake and asleep time periods because all patients did not report this information on their dairy. Therefore, we could not assess precisely the day-to-night BP changes. This lower sampling frequency during nighttime may have affected the standard deviation of the baseline nighttime SD, but not its average value, which was found to be associated with daytime SBP response to RD. We suggest that ambulatory BP should preferentially be recorded every 15 minutes not only during daytime but also at night to better assess BP variability over the 24 hours.

Conclusions

This detailed analysis of ABPM data in the DENERHTN trial confirms the efficacy of RD with the Simplicity flex catheter in addition to a SSAHT in lowering BP in patients with RH, with a homogenous effect over 24 hours. Nighttime SBP and its variability in patients being treated with a renin angiotensin system blocker, a thiazide, and a calcium channel blocker seem as the best candidates that can be derived from ABPM recordings to predict responders to RD. Therefore, 24-hour ABPM should systematically precede any decision of RD as recommended by consensus guidelines.[33]

Perspectives

RD is a procedure to date limited to RH. The BP response to this procedure is linked to the ability to reduce renal sympathetic activity. The DENERHTN trial has shown a greater efficacy of RD added to standardized antihypertensive treatment as compared with the same treatment alone. However, the BP response to this method shows a high variability between patients. This may be explained by an insufficient efficacy of the procedure in some patients but may also correspond to the relative influence of the different mechanisms involved in maintaining high BP in patients and, especially, the relative influence of the sympathetic nervous system. The ability to predict a good response to this procedure is a major issue. Increased nighttime SBP and its variability are possibly linked to an abnormal persistent sympathetic activity during night and seem to be able to contribute to a better selection of potential candidates to RD. Although this is a relatively short-term study with small sample size, these results should stimulate a greater attention to night BP in future studies of RD.

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Disclosures

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Novelty and Significance

What Is New?

- This article provides a detailed report of the ambulatory blood pressure (BP) monitoring results in the DENERHTN trial (Renal Denervation for Hypertension).
- Based on good quality recordings reviewed by a corelab blind to randomization, our results show a significantly greater systolic BP reduction over 24 hours with a greater smoothness index with renal denervation (RD).
- Good responders (daytime systolic BP reduction ≥20 mm Hg) are more frequent in the RD group and baseline nighttime systolic BP, and its standard deviation predicted this good response.

What Is Relevant?

- Our findings highlight the importance of 24-hour BP monitoring to assess the BP response to RD but also to predict the daytime BP response to this procedure.

Summary

The BP response to RD shows a high variability between patients. This may be explained by an insufficient efficacy of the procedure in some patients but may also correspond to the relative influence of the different mechanisms involved in maintaining high BP and, especially, that of the sympathetic nervous system. The ability to predict a good response to this procedure is a major issue. This study is the first to show that increased nighttime systolic BP and its variability, possibly linked to an abnormal persistent sympathetic overactivity during night, seems to be able to contribute to a better selection of potential candidates to RD.

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Twenty-Four-Hour Blood Pressure Monitoring to Predict and Assess Impact of Renal Denervation: The DENERHTN Study (Renal Denervation for Hypertension)

Philippe Gosse, Antoine Cremer, Helena Pereira, Guillaume Bobrie, Gilles Chatellier, Bernard Chamontin, Pierre-Yves Courand, Pascal Delsart, Thierry Denolle, Caroline Dourmap, Emile Ferrari, Xavier Girerd, Jean Michel Halimi, Daniel Herpin, Pierre Lantelme, Matthieu Monge, Claire Mounier-Vehier, Jean-Jacques Mourad, Olivier Ormezzano, Jean Ribstein, Patrick Rossignol, Marc Sapoval, Bernard Vaïsse, Faiez Zannad and Michel Azizi

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SUPPLEMENTARY DATA

24H BLOOD PRESSURE MONITORING TO PREDICT AND ASSESS IMPACT OF RENAL DENERVATION: THE DENER-HTN study

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Short title: ABPM to predict renal denervation BP lowering

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The DENERHTN investigators

The following investigators (with the number of patients enrolled and randomized at each centre given in parentheses) and committees participated in the DENERHTN trial: Hôpital Européen Georges Pompidou, Paris (31/28)—Laurence Amar, Guillaume Bobrie, Aurélien Lorthioir, Matthieu Monge, Jean-Yves Pagny, Pierre-François Plouin, Marc Sapoval; Hôpital Cardiologique, Lille (20/15)—Gonzague Claisse, Pascal Delsart, Marco Midulla, Edouard Herriot, Lyon (14/13)—Pierre-Yves Courand, Raphaël Dauphin, Jean-Pierre Fauvel, Pierre Lantelme, Olivier Rouvière; Hôpital Saint André and Hôpital Pellegrin, Bordeaux (14/13)—Antoine Cremer, Philippe Gosse, Nicolas Grenier, Yann Lebras, Hervé Trillaud; Hôpital Arthur

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Table S1 : Ambulatory blood pressure and heart rate parameters in the renal denervation and control groups at randomization.

Item	*Renal denervation (n=44)*	*Control (n=53)*	*P value*
BMI (kg/m^2)	30.80±5.09	29.73±4.54	0.28
24h SBP (mmHg)	151.89±16.81	146.79±15.17	0.12
24h DBP (mmHg)	90.32±15.53	88.75±10.60	0.56
24h HR (bpm)	74018±10.98	76.38±8.61	0.27
24h SD_{SBP} (mmHg)	14.89±4.49	15.53±3.71	0.44
24h SD_{DBP} (mmHg)	11.43±2.75	11.91±2.40	0.37
24h SD_{HR} (bpm)	9.41±3.36	10.58±3.09	0.08
24h TRV	0.61±0.23	0.63±0.24	0.61
Daytime SBP (mmHg)	155.57±16.66	150.98±16.04	0.17
Max Daytime SBP (mmHg)	190.64±22.86	184.21±18.71	0.14
Daytime DBP (mmHg)	93.05±15.32	92.04±10.84	0.71
Max Daytime DBP (mmHg)	118.34±16.89	117.62±14.05	0.82
Daytime HR (bpm)	76.27±11.43	79.49±9.27	0.13
Max Daytime HR (bpm)	101.98±20.94	104.30±12.53	0.50
Daytime wide SD_{SBP} (mmHg)	13.75±4.52	13.89±3.17	0.86
Daytime narrow SD_{SBP} (mmHg)	12.52±3.91	13.18±3.33	0.38
Daytime SD_{DBP} (mmHg)	10.48±3.00	10.55±2.43	0.90
Daytime SD_{HR} (bpm)	9.23±3.32	9.89±2.95	0.31
Nightime SBP (mmHg)	142.09±17.82	135.45±14.33	0.13
Max Nightime SBP (mmHg)	167.02±20.36	161.32±22.05	0.19
Nightime DBP (mmHg)	82.66±16.47	79.40±10.51	0.24
Max Nightime DBP (mmHg)	102.55±21.01	99.64±16.70	0.45
Nightime HR (bpm)	68.23±9.70	67.45±7.70	0.66
Max Nightime HR (bpm)	82.34±14.14	80.15±9.87	0.37
Nightime wide SD_{SBP} (mmHg)	11.84±4.27	12.58±3.91	0.38
Nightime narrow SD_{SBP} (mmHg)	10.44±3.99	11.27±3.72	0.29
Nightime SD_{DBP} (mmHg)	9.68±3.56	9.75±2.77	0.92

Nightime SD_{HR} (bpm)	6.30±2.89	5.98±2.19	0.55

Data are mean±SD. SBP : systolic blood pressure, DBP : diastolic blood pressure, HR: heart rate, SD_{SBP} : standard deviation of SBP, $SD_{DBP:}$ standard deviation of DBP, $SD_{HR:}$ standard deviation of HR. TRV: Time rate of SBP Variation

Table S2: Stepwise discriminant analysis of responders

Step	*Tolerance*	*P to remove*	*Wilks's lambda*
1: Nightime SBP	1	0.006	0.922
2: Nightime SBP	0.998	0.006	
Nightime SD_{SBP}	0.998	0.01	0.864
3: Nightime SBP	0.981	0.02	
Nightime SD_{SBP}	0.972	0.006	
Treatment group	0.955	0.01	0.81

Tolerance is the proportion of a variable's variance not accounted for by other independent variables in the equation.