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ABPM Key Points

- Allows the registration of blood pressure throughout the day and night
- High reproducibility
- Not subject to digit preference
- Identifies “white coat” hypertension
- Predicts cardiovascular outcome better than clinic blood pressure
- ABPM reductions are approximately one-third of those seen for office BP, this was confirmed for RDN in a study conducted by Mahfoud and colleagues.

What is ABPM?

Ambulatory blood pressure monitoring (ABPM) involves measuring blood pressure (BP) at regular intervals (usually every 20-30 minutes, typically less often at night) over a 24 hour period while patients undergo normal daily activities, including sleep. The portable monitor is worn on a belt connected to a standard cuff on the upper arm and uses an oscillometric technique to detect systolic, diastolic and mean BP as well as heart rate. When complete, the device is connected to a computer that prepares a report of the 24 hour, day time, night time, and sleep and awake (if recorded) average systolic and diastolic BP and heart rate.¹



¹National Heart Foundation and High Blood Pressure Research Council of Australia Ambulatory Blood Pressure Monitoring Consensus Committee - 2011

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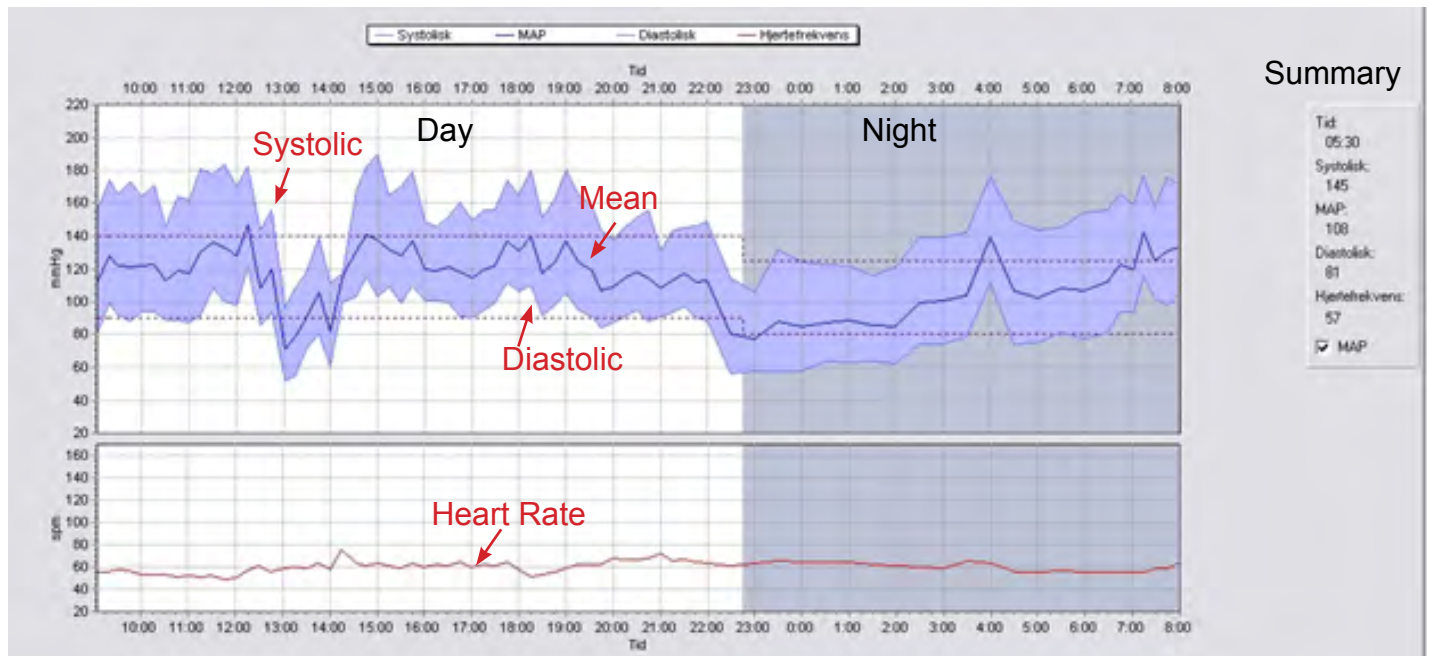


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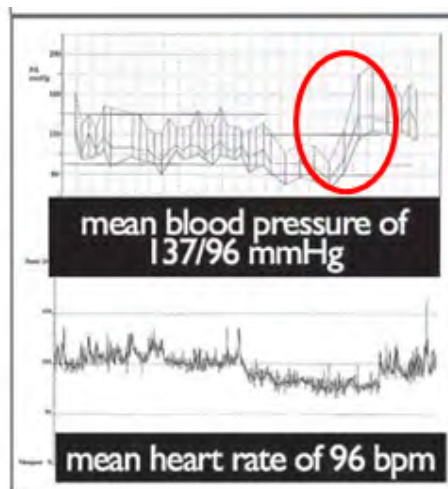


As you can see from this chart, blood pressure is dynamic. An ABPM report shows summary highlights, standard data, live SBP and DBP as well as variability, night time “dipping” and “morning surge”.

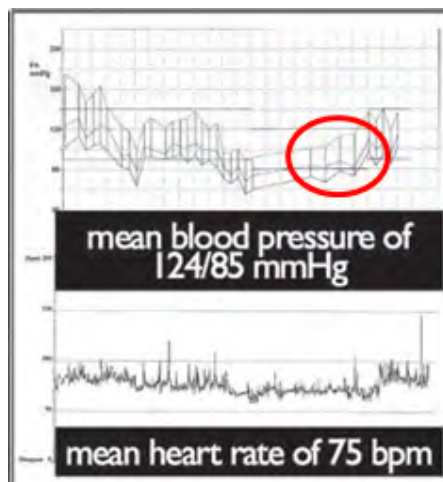


As shown in the following RDN and ABPM case report, there was a significant reduction in both mean 24-hour blood pressure as well as resting heart rate 2 weeks following treatment with renal denervation. Note that, besides the drop in 24 hr mean, there are also notable changes in variability. In particular note the presumeable “morning surge” that is present before but not after RDN. The “morning surge” has been strongly correlated with CV events. Even with smaller ABPM mean BP drops post-RDN, the morning surge spikes in BP were significantly reduced suggesting a possible reduction in CV events.

Pretreatment



2 Weeks Post Treatment





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Why is Δ ABPM lower than Δ OBP?

- ABPM reductions are approximately one-third of those seen for office BP.
- Ambulatory blood pressure takes into account nighttime readings, which are generally lower, thus you get a lower overall average.
- Lower nighttime pressures are less impacted by changes in sympathetic outflow, since sympathetic tone generally decreases at night while parasympathetic tone increases.

Table 1. Threshold clinic BP and corresponding ambulatory BP values for hypertension grades 1–3⁸

Hypertension severity	Threshold clinic BP (mm Hg)	24-h ambulatory BP (mm Hg)	Daytime BP (mm Hg)	Night-time BP (mm Hg)
Grade 1	140/90	133/84	136/87	121/76
Grade 2	160/100	148/93	152/96	139/84
Grade 3	180/110	163/101	168/105	157/93

Abbreviation: BP, blood pressure.

Schieder R et al Interpreting treatment-induced blood pressure reductions measured by ambulatory blood pressure monitoring. *J Hum Hypertens*. 2013.

What are the advantages and disadvantages of ABPM vs. office BP?

Advantages:

- Allows the registration of blood pressure throughout the day and night
- High reproducibility
- Not subject to digit preference
- Identify “white coat” and “masked” hypertension
- Highlights BP variability
- Predicts cardiovascular outcome better than clinic blood pressure

Disadvantages:

- Compliance to the monitor is at times a challenge
- Inappropriate number of readings
- Cost /reimbursement



What is White Coat HTN?

- Clinic blood pressures that are persistently elevated while out of office values are normal or significantly lower.
- Can be misinterpreted as hypertension or treatment resistant hypertension.
- Opposite of “masked HTN”. Masked HTN = normal OBP with elevated ABPM.

How is APBM tied to outcomes?

- There is growing evidence from several small studies which show that ambulatory blood pressure is a stronger predictor of outcome than office BP.
- 3 longitudinal studies^{2,3,4} conducted in patients with hypertension have shown that a diminished decline in nighttime blood pressure is a risk factor for cardiovascular mortality, independent of the overall 24 hour blood pressure.⁵
- According to the Dublin study (Hypertension. 2005;46:156-161), for every 10 mmHg increase in the mean nighttime SBP, the mortality risk is increased by 21%.



²Staessen J, Thijs L, Fagard R, O'Brien E, Clement D, deLeeuw P, Mancia G, Nachev C, Palatini P, Parati P, Tuomilehto J, Webster J for the Systolic Hypertension in Europe Trial Investigators. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. *JAMA*. 1999;282:539–546.

³Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Guerrieri M, Gatteschi C, Zampi I, Santucci A. Ambulatory blood pressure: an independent predictor of prognosis in essential hypertension. *Hypertension*. 1994;24:793–801.

⁴Kario K, Pickering TG, Matsuo T, Hoshida S, Schwartz JE, Shimada K. Stroke prognosis and abnormal nocturnal blood pressure falls in older hypertensives. *Hypertension*. 2001;38:852–857.

⁵Dolan E, Stanton A. et al. Superiority of Ambulatory Over Clinic Blood Pressure Measurement in Predicting Mortality The Dublin Outcome Study. *Hypertension*. 2005;46:156-161

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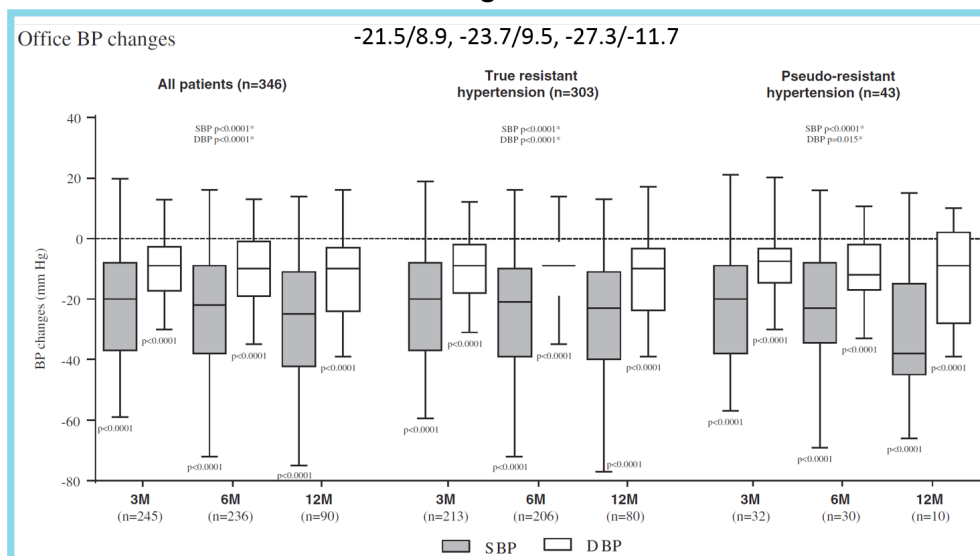
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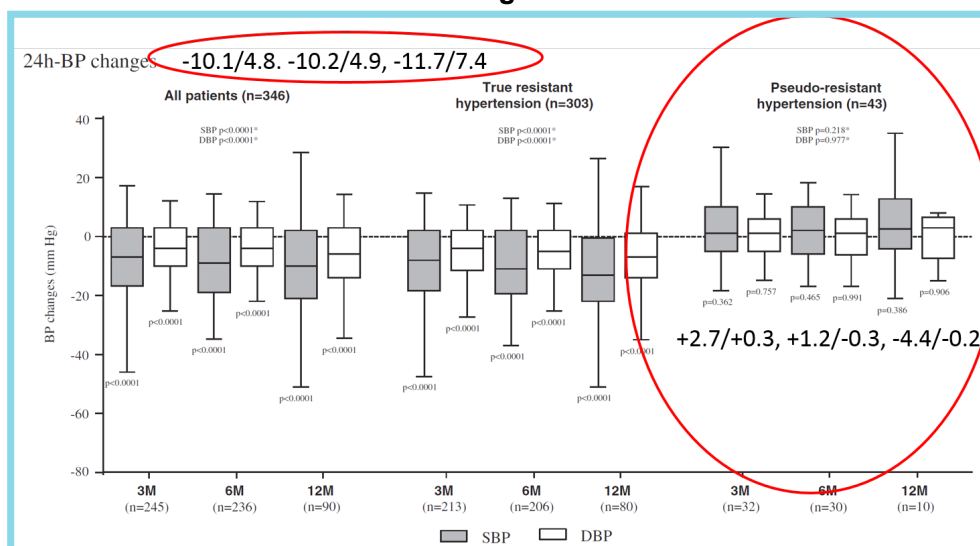
How does RDN effect ABPM?

- In the Symplicity HTN-2 trial, in patients with paired ABPM measurements (n=20), there was a significant -11/-7 mmHg reduction following RDN at 12 months.
- A recent study published in *Circulation*⁶ (Felix Mahfoud and colleagues) showed that in over 300 patients, treatment with the Symplicity™ renal denervation system showed a significant reduction in both office and ambulatory blood pressure at 6 and 12 months.
 - Consistent with previous results, ABPM reductions were approximately one-third of those seen for office BP reductions.

BP changes Post RDN⁶



ABPM changes Post RDN⁶



⁶Mahfoud F et al. Ambulatory blood pressure changes after renal sympathetic denervation in patients with resistant hypertension. *Circulation*. 2013; 12 & 132-140.

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What does the RDN ABPM data tell us?

- The ABPM data collected to date tells us that RDN is an effective treatment option to lower both office and ambulatory blood pressure with the expected drop achieved in ambulatory BP relative to office BP seen in prior studies.
- The reductions seen are in line with what you would expect from pharmaceutical trials – there is a 30:10 mmHg correlation between office BP reduction and ABPM reduction especially when the baseline BP levels are high (see graphs below). With lower starting BP, the correlation is closer to a 1:1 match.
- The ABPM results are some of the strongest arguments in favor of RDN.
- RDN's strong impact on mean ABPM, day and night ABPM, variability and potentially dipping patterns are some of the strongest data in favor of RDN efficacy and sympathetic mechanism.

Table 2. Summary of therapeutic studies reporting office versus ambulatory BP reduction

Citation	Study type	Patient no.	Follow-up period	Baseline office BP (mm Hg)	Baseline 24-h BP (mm Hg)	Reduction in office BP (mm Hg)	Reduction in 24-h BP (mm Hg)	SBP, 24-h reduction/office reduction (%)	DBP, 24-h reduction/office reduction (%)
Mancia and Parati ²³	Meta-analysis	5842 SBP; 5764 DBP	1–144 weeks	161.9/100.2	151.5/94.5	– 19.1/ – 10.3	– 12.5/ – 8.3	65.4	80.6
Cheng et al. ²⁴	Meta-analysis	126	8 weeks	152.6/102.6	142.7/94.4	– 13.7/ – 9.9	– 10/ – 6.7	73.0	67.7
Ishikawa et al. ²⁵	Meta-analysis	1246	5 weeks–1 year	N/R	N/R	– 15.2/ – 10.2	– 11.9/ – 8.5	78.3	83
Staessen et al. ²⁶	Randomized controlled trial	419	26 weeks	CBP group: 164.4/104.0 ABP group: 164.9/102.9	CBP group: 143.9/89.7 ^a ABP group: 142.5/88.5 ^a	CBP group: – 24.1/ – 14.4 ABP group: – 20.8/ – 13.0	CBP group: – 15.9/ – 10.6 ^a ABP group: – 13.1/ – 9.0 ^a	CBP group: 66.0 ^a ABP group: 63.0 ^a	CBP group: 73.6 ^a ABP group: 69.2 ^a
Bakris et al. ²⁷	Randomized controlled trial	364 (darusentan group)	14 weeks	151/88	134/78	– 15/ – 10	– 10/ – 8	66.7	80.0
Esler et al. ²⁹	Randomized controlled trial	20 ABPM; 49 office BP (renal denervation group)	6 months	178/96	N/R	– 32/ – 12	– 11/ – 7	34.4	58.3

Abbreviations: ABP group, treatment adjusted based on daytime ambulatory BP measurement; ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CBP group, treatment adjusted based on clinic BP measurement; DBP, diastolic BP; N/R, not reported; SBP, systolic BP. ^aDaytime ambulatory BP.

Schieder R et al Interpreting treatment-induced blood pressure reductions measured by ambulatory blood pressure monitoring. *J Hum Hypertens.* 2013.



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How is ABPM used in Symplicity HTN-3?

- SYMPLICITY HTN-3 utilizes ABPM as both a screening entry criteria as well as a powered secondary endpoint.
- In SYMPLICITY HTN-3, ABPM will reduce the possibility of white-coat hypertensives being enrolled in the study.
- SYMPLICITY HTN-3 will represent the largest body of randomized evidence on post-RDN ABPM to date.

“On the basis of prospective follow-up studies of treated hypertensive patients with a pretreatment baseline SBP of 180 mmHg, in order to achieve the same reduction in CV event rates, the fall in 24-hour ambulatory BP needs to be approximately one-third to one-half the reduction in office BP.”

—Schmieder R. *J Hum Hypertens*, 2013.



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