Predictors of BP Response Supplemental Material

Tables included in supplemental materials have been provided by the authors to give readers additional information about their work.
### Table S1. Baseline characteristics

| Characteristic                                      | Renal Denervation (N=64) | Sham Procedure (N=58) |
|-----------------------------------------------------|--------------------------|-----------------------|
| Age (years)                                         | 54.3±10.0                | 54.0±10.2             |
| Female sex                                          | 37.5% (24/64)            | 37.9% (22/58)         |
| Race                                                |                          |                       |
| White                                               | 82.8% (53/64)            | 72.4% (42/58)         |
| Black                                               | 14.1% (9/64)             | 17.2% (10/58)         |
| Other                                               | 3.1% (2/64)              | 10.3% (6/58)          |
| Body mass index – kg/m²                              | 29.9±6.0                 | 29.7±5.0              |
| Abdominal obesity*                                  | 55.6% (35/63)            | 65.5% (38/58)         |
| eGFR – ml/min/1.73m²                                 | 83.5±14.5                | 83.2±14.8             |
| eGFR <60 ml/min/1.73m²                               | 1.5% (1/64)              | 1.8% (1/57)           |
| Type 2 diabetes                                      | 3.1% (2/64)              | 8.6% (5/58)           |
| Sleep apnea                                         | 9.4% (6/64)              | 12.1% (7/58)          |
| Seated office blood pressure and heart rate prior to antihypertensive medication washout | | |
| SBP (mmHg)                                          | 142.6±14.8               | 145.2±15.3            |
| DBP (mmHg)                                          | 91.9±10.0                | 94.2±8.2              |
| Heart rate (bpm)*                                   | 73.2±12.0                | 71.2±11.8             |
| Number of Antihypertensive medications at screening | | |
| 0                                                   | 17.2% (11/64)            | 24.1% (14/58)         |
| 1 medication                                        | 39.1% (25/64)            | 39.7% (23/58)         |
|                                         | Renal Denervation | Sham Arm |
|-----------------------------------------|-------------------|----------|
| 2 medications in combination            | 42.2% (27/64)     | 36.2% (21/58) |
| 3 medications in combination            | 1.6% (1/64)       | 0.0% (0/58)  |

**Baseline ambulatory blood pressure following antihypertensive medication washout**

|                          | Renal Denervation | Sham Arm |
|--------------------------|-------------------|----------|
| Daytime SBP (mmHg)       | 150.5±7.3         | 149.5±9.9 |
| Daytime DBP (mmHg)       | 93.5±4.4          | 93.2±5.4  |
| Nighttime SBP (mmHg)*    | 130.6±12.3        | 131.5±13.7|
| Nighttime DBP (mmHg)*    | 78.6±8.0          | 80.0±7.4  |
| 24h SBP (mmHg)           | 142.9±7.9         | 143.2±10.6|
| 24h DBP (mmHg)           | 87.8±4.7          | 88.5±5.4  |

Data displayed as % (n/N) and mean ± standard deviation.

DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; SBP: systolic blood pressure;

* Abdominal obesity status and office heart rate prior to medication washout each had one patient with missing data in the renal denervation group. eGFR, Nighttime SBP and Nighttime DBP each had one patient with missing data in the sham arm.
### Table S2. Univariate analysis of predictors of response for change in daytime ambulatory systolic blood pressure from baseline to 2 months in the Sham group

| Variable                              | Estimate Parameter | Standard Error | P value |
|---------------------------------------|--------------------|----------------|---------|
| Age                                   | 0.0845             | 0.1109         | 0.4493  |
| Male                                  | -2.8058            | 2.2815         | 0.2239  |
| Black Race                            | 1.8429             | 2.9597         | 0.5360  |
| BMI                                   | 0.2305             | 0.2224         | 0.3044  |
| Abdominal Obesity                     | 4.5024             | 2.2823         | 0.0535  |
| Baseline eGFR                         | -0.0171            | 0.0775         | 0.8266  |
| Sleep Apnea                           | -2.6261            | 3.4258         | 0.4466  |
| Hemoglobin A1c                        | -0.8569            | 1.7703         | 0.6303  |
| Antihypertensive Medications at Screening (yes vs. no) | 0.1344 | 2.6216 | 0.9593 |
| Baseline Orthostatic hypertension     | 0.8521             | 2.9677         | 0.7751  |
| Baseline Office SBP                   | 0.1096             | 0.0706         | 0.1260  |
| Baseline Office DBP                   | 0.1872             | 0.1140         | 0.1061  |
| Baseline Daytime Systolic ABP         | -0.1330            | 0.1133         | 0.2456  |
| Baseline Daytime Diastolic ABP        | -0.2139            | 0.2094         | 0.3115  |
| Baseline Nighttime Systolic ABP       | -0.0690            | 0.0834         | 0.4114  |
| Baseline Nighttime Diastolic ABP      | -0.0609            | 0.1550         | 0.6959  |
| 24-hour Ambulatory Systolic Blood Pressure | -0.1170 | 0.1052 | 0.2709 |
| 24-hour Ambulatory Diastolic Blood Pressure | -0.1777 | 0.2099 | 0.4009 |
| Baseline Office Pulse Pressure        | 0.0675             | 0.0954         | 0.4822  |
| Baseline 24h ABPM Pulse Pressure      | -0.0960            | 0.1222         | 0.4352  |
| Variable                                      | Estimate Parameter | Standard Error | P value |
|------------------------------------------------|--------------------|----------------|---------|
| Baseline Office Heart Rate                    | 0.0483             | 0.0938         | 0.6088  |
| Baseline 24h Ambulatory Heart Rate           | -0.0409            | 0.1151         | 0.7237  |

ABP: ambulatory blood pressure; BMI: body mass index; eGFR: estimated glomerular filtration rate
Table S3. Characteristics of super-responders (dASBP drop ≥15mmHg)

| Characteristics                  | Renal Denervation | Sham Procedure | p-value | Renal Denervation | Sham Procedure | p-value |
|----------------------------------|------------------|----------------|---------|------------------|----------------|---------|
|                                  | Responder (N=17) | Non-Responder (N=47) | p-value | Responder (N=3) | Non-Responder (N=55) | p-value |
| Age (years)                      | 55.1±7.9         | 54.0±10.7       | 0.702   | 56.0±8.7         | 53.9±10.3       | 0.725   |
| Male                             | 47.1% (8/17)     | 68.1% (32/47)   | 0.125   | 66.7% (2/3)      | 61.8% (34/55)   | 0.866   |
| Black Race                       | 11.8% (2/17)     | 14.9% (7/47)    | 0.750   | 0.0% (0/3)       | 18.2% (10/55)   | 0.417   |
| BMI (kg/m²)                      | 32.5±5.7         | 28.9±5.9        | 0.036   | 27.6±4.4         | 29.8±5.1        | 0.465   |
| Abdominal Obesity                | 82.4% (14/17)    | 45.7% (21/46)   | 0.009   | 66.7% (2/3)      | 65.5% (36/55)   | 0.966   |
| Baseline eGFR (ml/min/1.73m²)    | 84.2±17.6        | 83.3±13.5       | 0.830   | 81.7±22.0        | 83.3±14.6       | 0.860   |
| Sleep Apnea                      | 17.6% (3/17)     | 6.4% (3/47)     | 0.172   | 33.3% (1/3)      | 10.9% (6/55)    | 0.246   |
| HbA1c (%)                        | 5.5±0.6 (17)     | 5.5±0.6 (47)    | 0.792   | 5.8±0.9          | 5.5±0.6         | 0.580   |
| Antihypertensive Medications at Screening (yes vs. no) | 100.0% (17/17) | 76.6% (36/47) | 0.028 | 66.7% (2/3)      | 76.4% (42/55)   | 0.702   |
| Baseline Orthostatic hypertension | 41.2% (7/17)    | 12.8% (6/47)    | 0.013   | 0.0% (0/3)       | 18.2% (10/55)   | 0.417   |
| Baseline Office SBP (mmHg)       | 154.4±10.5       | 154.8±13.9      | 0.902   | 137.3±16.6       | 153.2±15.4      | 0.089   |
| Characteristics                        | Renal Denervation |                         | Sham Procedure |                         |                      | p-value |                      |                      | p-value |
|---------------------------------------|-------------------|-------------------------|----------------|-------------------------|----------------------|---------|-----------------------|-----------------------|---------|
|                                       | Responder (N=17)  | Non-Responder (N=47)   | p-value        | Responder (N=3)         | Non-Responder (N=55) |         |                       |                       |         |
| Baseline Office DBP (mmHg)            | 98.9±7.0          | 100.3±8.4               | 0.544          | 93.3±9.5                | 98.5±9.7             | 0.376   |                       |                       |         |
| Baseline Daytime Systolic ABP (mmHg)  | 150.8±7.5         | 150.4±7.3               | 0.831          | 152.1±13.9              | 149.4±9.8            | 0.645   |                       |                       |         |
| Baseline Daytime Diastolic ABP (mmHg) | 94.9±4.9          | 93.0±4.1                | 0.129          | 94.5±3.8                | 93.2±5.4             | 0.689   |                       |                       |         |
| Baseline Nighttime Systolic ABP (mmHg)| 132.8±13.3        | 129.8±11.9              | 0.388          | 141.7±23.1              | 130.9±13.2           | 0.189   |                       |                       |         |
| Baseline Nighttime Diastolic ABP (mmHg)| 81.2±9.6          | 77.6±7.3                | 0.120          | 84.3±6.6                | 79.7±7.4             | 0.302   |                       |                       |         |
| 24-hour Ambulatory Systolic Blood Pressure (mmHg) | 143.5±8.0 | 142.6±7.9 | 0.684 | 148.3±17.7 | 142.9±10.3 | 0.399 | | | |
| 24-hour Ambulatory Diastolic Blood Pressure (mmHg) | 89.4±5.7 | 87.2±4.2 | 0.100 | 90.6±5.1 | 88.4±5.4 | 0.480 | | | |
| Characteristics                              | Renal Denervation | Sham Procedure | p-value |
|---------------------------------------------|-------------------|----------------|---------|
|                                             | Responder (N=17)  | Non-Responder  (N=47) | p-value | Responder (N=3) | Non-Responder (N=55) | p-value |
| Baseline Office Pulse Pressure (mmHg)       | 55.4±10.4         | 54.5±11.0      | 0.760   | 44.0±7.5        | 54.7±11.8       | 0.127   |
| Baseline 24h ABPM Pulse Pressure (mmHg)     | 54.2±6.4          | 55.4±7.4       | 0.531   | 57.6±13.2       | 54.5±9.1        | 0.575   |
| Baseline Office Heart Rate (bpm)            | 75.2±10.9         | 71.1±13.0      | 0.252   | 68.3±4.2        | 71.0±12.3       | 0.714   |
| Baseline 24h Ambulatory Heart Rate (bpm)    | 76.6±5.6          | 71.4±10.9      | **0.017** | 75.1±10.2       | 70.5±9.8        | 0.434   |
| Total Number of Ablations                  | 5.6±0.9           | 5.4±0.9        | 0.449   |                  |                |         |
| Average Main Artery Diameter L (mm)         | 5.2±0.7           | 5.6±0.8        | 0.067   |                  |                |         |
| Average Main Artery Diameter R (mm)         | 5.0±0.6           | 5.3±0.7        | 0.068   |                  |                |         |
| Vessel Length (L Renal) (mm)                | 37.4±10.2         | 38.5±13.1      | 0.751   |                  |                |         |
| Vessel Length (R Renal) (mm)                | 46.9±10.0         | 43.9±12.5      | 0.387   |                  |                |         |
| Presence of Any Untreated Accessory         | 5.9% (1/17)       | 31.9% (15/47)  | **0.034** |                  |                |         |
| Characteristics                                      | Renal Denervation | Sham Procedure |
|-----------------------------------------------------|-------------------|----------------|
|                                                     | Responder (N=17)  | Responder (N=3) | Non-Responder (N=47) | Non-Responder (N=55) | p-value |
| Presence of Side branches Proximal to Ablations     | 29.4% (5/17)      |                | 8.5% (4/47)          |                    | 0.034   |
| Farthest Distance Bilaterally from Distal Ablation to Parenchyma | 18.9±9.6         | 18.6±9.5       |                    |                    | 0.907   |
| Operator Case #                                     | 2.1±1.7           | 2.0±1.3        |                    |                    | 0.968   |
| Contrast volume used (cc)*                          | 123.4±52.0        | 143.0±72.2     |                    |                    | 0.309   |
| Duration of procedure (min)                         | 70.6±18.3         | 69.9±24.0      |                    |                    | 0.904   |
| Fluoro time (min)*                                  | 13.1±2.4          | 13.5±7.0       |                    |                    | 0.742   |
| Paradise Catheter time (min)                        | 27.5±13.6         | 34.9±18.6      |                    |                    | 0.136   |
| Number of Different Balloon Sizes Used in Patient   | 1.8±0.8           | 1.7±0.7        |                    |                    | 0.769   |

Data displayed as % (n/N) and mean ± standard deviation.
ABP: ambulatory blood pressure; BMI: body mass index; eGFR: estimated glomerular filtration rate
*Fluoro time was missing from one patient in the renal denervation responder group. Abdominal obesity status had one patient with missing data and contrast volume and fluoro time each had two patients with missing data in the renal denervation non-responder group. Baseline eGFR, Nighttime SBP and Nighttime DBP each had one patient with missing data and HbA1c had two subjects with missing data in the sham non-responder group.
Table S4. Three-way interaction model of treatment arm, sex, and age on change in daytime ABPM from baseline to 2 months

| Variable                          | p-value |
|-----------------------------------|---------|
| Treatment Arm                    | <0.001  |
| Sex                              | 0.878   |
| Treatment Arm * Sex              | 0.246   |
| Age                              | 0.081   |
| Treatment Arm*Age                | 0.335   |
| Sex*Age                          | 0.465   |
| Treatment Arm*Sex*Age            | 0.325   |

| Treatment Arm  | Sex     | Age (years) | n  | Change in Daytime SBP at 2M (Least Squares Mean) |
|----------------|---------|-------------|----|-------------------------------------------------|
| Renal Denervation | Female  | ≥55         | 13 | -5.827                                           |
| Renal Denervation | Female  | <55         | 11 | -13.418                                          |
| Renal Denervation | Male    | ≥55         | 21 | -7.048                                           |
| Renal Denervation | Male    | <55         | 19 | -8.774                                           |
| Sham Procedure    | Female  | ≥55         | 10 | 1.656                                            |
| Sham Procedure    | Female  | <55         | 12 | 0.717                                            |
| Sham Procedure    | Male    | ≥55         | 20 | -0.170                                           |
| Sham Procedure    | Male    | <55         | 16 | -1.968                                           |
Table S5. Four-way interaction model of treatment arm, sex, age, and abdominal obesity on change in daytime ABPM from baseline to 2 months

| Variable                      | p-value |
|-------------------------------|---------|
| Treatment Arm                 | 0.002   |
| Sex                           | 0.551   |
| Treatment Arm*Sex             | 0.904   |
| Age                           | 0.281   |
| Treatment Arm*Age             | 0.087   |
| Sex*Age                       | 0.733   |
| Treatment Arm*Sex*Age         | 0.120   |
| Abdominal Obesity             | 0.483   |
| Treatment Arm*Abdominal Obesity| 0.015 |
| Sex*Abdominal Obesity         | 0.696   |
| Treatment Arm*Sex*Abdominal Obesity| 0.023 |
| Age*Abdominal Obesity         | 0.504   |
| Treatment Arm*Age*Abdominal Obesity| 0.249 |
| Sex*Age*Abdominal Obesity     | 0.795   |
| Treatment Arm*Sex*Age*Abdominal Obesity| 0.927 |
| Treatment Arm | Sex    | Age (years) | Abdominal Obesity | n  | Change in Daytime SBP at 2M (Least Squares Mean) |
|---------------|--------|-------------|-------------------|----|-----------------------------------------------|
| Renal Denervation | Female | ≥55         | Yes               | 9  | -8.674                                        |
| Renal Denervation | Female | ≥55         | No                | 4  | 0.485                                         |
| Renal Denervation | Female | <55         | Yes               | 8  | -16.511                                       |
| Renal Denervation | Female | <55         | No                | 2  | -10.749                                       |
| Renal Denervation | Male   | ≥55         | Yes               | 7  | -6.938                                        |
| Renal Denervation | Male   | ≥55         | No                | 14 | -6.945                                        |
| Renal Denervation | Male   | <55         | Yes               | 11 | -8.516                                        |
| Renal Denervation | Male   | <55         | No                | 8  | -9.061                                        |
| Sham Procedure | Female | ≥55         | Yes               | 9  | 3.090                                         |
| Sham Procedure | Female | ≥55         | No                | 1  | -12.131                                       |
| Sham Procedure | Female | <55         | Yes               | 8  | 3.471                                         |
| Sham Procedure | Female | <55         | No                | 4  | -5.053                                        |
| Sham Procedure | Male   | ≥55         | Yes               | 12 | 1.937                                         |
| Sham Procedure | Male   | ≥55         | No                | 8  | -3.075                                        |
| Sham Procedure | Male   | <55         | Yes               | 9  | -3.295                                        |
| Sham Procedure | Male   | <55         | No                | 7  | -0.250                                        |
Table S6. Baseline characteristics of subjects with and without orthostatic hypertension

| Characteristics                              | With orthostatic hypertension (N=13) | Without orthostatic hypertension (N=51) | p-value |
|---------------------------------------------|--------------------------------------|----------------------------------------|---------|
| Age (years)                                 | 52.5±13.1                            | 54.8±9.2                               | 0.479   |
| Female                                      | 46.2% (6/13)                         | 35.3% (18/51)                          | 0.470   |
| Race                                        |                                      |                                        |         |
| White                                       | 69.2% (9/13)                         | 86.3% (44/51)                          | 0.016   |
| Black                                       | 15.4% (2/13)                         | 13.7% (7/51)                           |         |
| Other                                       | 15.4% (2/13)                         | 0.0% (0/51)                            |         |
| BMI (kg/m²)                                 | 32.5±7.0                             | 29.2±5.7                               | 0.084   |
| Abdominal Obesity*                          | 76.9% (10/13)                        | 50.0% (25/50)                          | 0.082   |
| eGFR (ml/min/1.73m²)                        | 90.6±18.6                            | 81.7±12.9                              | 0.046   |
| eGFR<60                                      | 100.0% (13/13)                       | 98.0% (50/51)                          | 0.611   |
| Type 2 Diabetes                             | 7.7% (1/13)                          | 2.0% (1/51)                            | 0.289   |
| Sleep apnea                                 | 0.0% (0/13)                          | 11.8% (6/51)                           | 0.194   |
| Seated office blood pressure and heart rate prior to antihypertensive medication washout |                                      |                                        |         |
| SBP (mmHg)                                  | 145.2±15.9                           | 142.0±14.6                             | 0.480   |
| DBP (mmHg)                                  | 91.0±10.4                            | 92.1±10.0                              | 0.722   |
| Heart rate (bpm)*                           | 72.3±10.0                            | 73.4±12.5                              | 0.786   |
| Number of Antihypertensive medications at screening |                                      |                                        |         |
| 0                                           | 7.7% (1/13)                          | 19.6% (10/51)                          | 0.416   |
| 1 medication                                | 30.8% (4/13)                         | 41.2% (21/51)                          |         |
| Characteristics                                                                 | With orthostatic hypertension (N=13) | Without orthostatic hypertension (N=51) | p-value |
|---------------------------------------------------------------------------------|---------------------------------------|----------------------------------------|---------|
| 2 medications in combination                                                    | 61.5% (8/13)                          | 37.3% (19/51)                          |         |
| 3 medications in combination                                                    | 0.0% (0/13)                           | 2.0% (1/51)                            |         |
| Baseline ambulatory blood pressure following antihypertensive medication washout |                                       |                                        |         |
| Daytime SBP (mmHg)                                                              | 152.8±6.6                             | 149.9±7.4                              | 0.199   |
| Daytime DBP (mmHg)                                                              | 95.0±4.2                              | 93.1±4.4                               | 0.163   |
| Nighttime SBP (mmHg)                                                            | 132.8±13.1                            | 130.1±12.1                             | 0.481   |
| Nighttime DBP (mmHg)                                                            | 79.3±7.7                              | 78.4±8.2                               | 0.727   |
| 24h SBP (mmHg)                                                                  | 144.8±8.0                             | 142.4±7.9                              | 0.321   |
| 24h DBP (mmHg)                                                                  | 88.9±4.8                              | 87.5±4.7                               | 0.355   |

Data displayed as % (n/N) and mean ± standard deviation.
BMI: body mass index; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; SBP: systolic blood pressure
*One subject in the sham arm is missing abdominal obesity status and one subject in the RDN arm is missing screening office heart rate.