SUPPLEMENTAL MATERIAL

Appendix

| Institution | Name |
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| School, Boston, USA | Coordinator);Lock JE, MD (Study |
| | Advisor); Newburger J, MD, MPH |
| | (Study Advisor); Prakash A, MD (Study |
| | PI, Site PI); Reichman J (Study |
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| | Advisor) |
| Joint Division of Pediatric Cardiology | Kutty S, MD (Study author) |
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Table S1. Office BP Classification.

| Classification | SBP | DBP |
|----------------|--|-------------------------------------|
| Normal | children: < 90th %tile | children: < 90th % tile |
| | adults: <120mm Hg | adults: and <80mHg |
| Pre-HTN | children: 90th to 95th % tile or if BP | children: 90th to 95th % tile or if |
| | exceeds 120/80mm Hg even if 90th | BP exceeds 120/80 even if 90th |
| | % tile up to 95th percentile | percentile up to 95th % tile |
| | adults: 120-139mm Hg | adults: or 80-89mm Hg |
| Stage 1 HTN | children: 95th–99th %tile plus 5mm | children: 95th–99th %tile plus 5mm |
| | Hg | Hg |
| | adults: 140-159mm Hg | adults: or 90–99mm Hg |
| Stage 2 HTN | children: 99th %tile plus 5mm Hg | children: 99th %tile plus 5mm Hg |
| | adults: ≥160mm Hg | adults: or >100mm Hg |

%tile = percentile; DBP = diastolic blood pressure; HTN = hypertension; SBP = systolic blood pressure; for children (<18yo), based on table 5 (classification of BP) and table 3 (normative values) of the National High Blood Pressure Education Program Working Group on High Blood Pressure in C, Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents;²⁵ For adults (>= 18yo), based on table 3 (classification of BP) of the 7th Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure report.²⁶

| Classification | Office BP SBP or DBP * | 24h Mean ABPM SBP or |
|-------------------------|------------------------|-------------------------|
| | | DBP † |
| No hypertension | Pediatric: <95th %tile | Pediatric: <95th %tile |
| | Adults: <140/90 mm Hg | Adults: <135/85 mm Hg |
| White Coat Hypertension | Pediatric: ≥95th %tile | Pediatric: <95th %tile |
| | Adults: >140/90 mm Hg | Adults: <135/85 mm Hg |
| Masked Hypertension | Pediatric: <95th %tile | Pediatric: >95th % tile |
| | Adults: <140/90 mm Hg | Adults: >135/85 mm Hg |
| Ambulatory Hypertension | Pediatric: >95th %tile | Pediatric: >95th %tile |
| | Adults: >140/90 mm Hg | Adults: >135/85 mm Hg |

Table S2. Classification of HTN with ABPM.

ABPM = Ambulatory blood pressure monitoring; BP = Blood Pressure; ABPM = Ambulatory Blood Pressure Monitoring; Pediatric patients have age <18yo and adult patients age ≥18yo; %tile = percentile; BP = blood pressure; DBP = diastolic blood pressure; and SBP = systolic blood pressure. *For pediatric patients, based on the normative data of the National High Blood Pressure Education Program Working Group on High BP in C, Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high BP in children and adolescents;²⁵ for adult patients, based on the 7th Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High BP report.²⁶ † For pediatric patients, based on normative pediatric ABPM values from the American Heart Association Atherosclerosis, Hypertension and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young; ²⁷ for adult patients, based on the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research report.⁶⁰

| Smallest Mean | Largest Mean | Standard | Group Sample | Total Sample |
|---------------|--------------|-----------|--------------|---------------------|
| PWV (m/s) | PWV (m/s) | Deviation | Size | Size |
| 4.0 | 4.8 | 1.0 | 30 | 90 |
| 4.0 | 4.8 | 1.1 | 36 | 108 |
| 4.0 | 4.8 | 1.2 | 43 | 129 |
| 4.4 | 5.3 | 1.0 | 24 | 72 |
| 4.4 | 5.3 | 1.1 | 29 | 87 |
| 4.4 | 5.3 | 1.2 | 34 | 102 |
| | | | | |

 Table S3. Sample Size Estimates for 80% Power.

PWV = pulse wave velocity

| | 1-3 | 4-9 | 10-14 | ≥15 | p Value |
|---------------------------------|-----------------|---------------|---------------|---------------|---------|
| MRI proximal PWV (m/s) | 4.8 ± 2.1 | 4.2 ± 1.1 | 5.6 ± 4.4 | 4.9 ± 1.3 | 0.35 |
| AAO strain (%) | 0.48 ± 0.24 | 0.44 ± 0.16 | 0.45 ± 0.24 | 0.28 ± 0.15 | 0.02 |
| cfPWV (m/s) | 5.4 ± 1.1 | 4.8 ± 0.8 | 5.4 ± 1.1 | 5.3 ± 0.9 | 0.13 |
| AI (%) | -12 ± 14 | -14 ± 20 | -7 ±18 | -3 ± 19 | 0.21 |
| Endo-PAT index | 1.85 ± 0.55 | 1.89 ± 0.72 | 2.50 ± 0.73 | 2.34 ± 0.75 | 0.02 |
| Right arm SBP (mm Hg) | 121 ± 14 | 117 ± 12 | 124 ± 13 | 123 ± 12 | 0.34 |
| Right arm DBP (mm Hg) | 61 ± 5 | 63 ± 9 | 69 ± 11 | 68 ± 11 | 0.05 |
| 24-hour average SBP (mm Hg) | 119 ± 14 | 120 ± 11 | 124 ± 8 | 126 ± 10 | 0.20 |
| 24-hour average DBP (mm Hg) | 66 ± 8 | 64 ± 7 | 69 ± 7 | 71 ± 8 | 0.04 |
| Hypertension Classification | | | | | 0.14 |
| No HTN | 7 (58%) | 19 (70%) | 9 (53%) | 6 (35%) | |
| White coat HTN | 1 (8%) | 1 (4%) | 2 (12%) | 1 (6%) | |
| HTN/Masked HTN/Anti HTN meds | 4 (33%) | 7 (26%) | 6 (35%) | 10 (59%) | |
| Peak exercise right arm SBP (mm | 161 ± 34 | 169 ± 35 | 170 ± 27 | 180 ± 33 | 0.47 |
| Hg) | | | | | |
| hs-CRP (mg/L) | 127 (104, 146) | 127 (66, 143) | 129 (86, 149) | 128 (98, 146) | 0.67 |
| MMP-9/gelatinase B (ng/mL) | 707 (246, 4228) | 411 (91, | 515 (487, | 409 (150, | 0.15 |
| | | 2004) | 3157) | 4453) | |
| | | | | | |

Table S4. Assessment for Confounding by Age at Treatment.

Values are mean \pm standard deviation, number (percent), or median (minimum; maximum).

AAO = Ascending aorta; AI = Augmentation index; cfPWV = carotid-femoral pulse wave

velocity; DBP = Diastolic blood pressure; Endo-PAT = Endothelial pulse amplitude testing; hs-

CRP = High sensitivity C-reactive protein; HTN = Hypertension; MMP = matrix

metalloprotease; MRI = Magnetic resonance imaging; PWV = Pulse wave velocity; SBP =

Systolic blood pressure.

| | BAV | No BAV | p Value |
|-------------------------------------|----------------|----------------|---------|
| MRI proximal PWV (m/s) | 5.2 ± 3.1 | 4.2 ± 1.1 | 0.07 |
| AAO strain (%) | 0.37 ± 0.19 | 0.46 ± 0.21 | 0.07 |
| cfPWV (m/s) | 5.2 ± 0.8 | 5.1 ± 1.2 | 0.75 |
| AI (%) | -7 ± 18 | -14 ± 19 | 0.14 |
| PAT index | 2.13 ± 0.75 | 2.17 ± 0.75 | 0.79 |
| Right arm SBP (mm Hg) | 122 ± 12 | 119 ± 13 | 0.21 |
| Right arm DBP (mm Hg) | 66 ± 10 | 64 ± 9 | 0.47 |
| 24-hour average SBP (mm Hg) | 121 ± 12 | 123 ± 10 | 0.54 |
| 24-hour average DBP (mm Hg) | 68 ± 8 | 67 ± 7 | 0.68 |
| Hypertension Classification | | | 0.86 |
| No HTN | 22 (55%) | 18 (58%) | |
| White coat HTN | 3 (7%) | 1 (3%) | |
| HTN/Masked HTN/Anti HTN meds | 15 (38%) | 12 (39%) | |
| Unknown | 2 | 1 | |
| Peak exercise right arm SBP (mm Hg) | 174 ± 32 | 166 ± 34 | 0.29 |
| High sensitivity CRP (mg/L) | 128 (74, 149) | 128 (66, 146) | 0.98 |
| MMP-9/gelatinase B (ng/mL) | 488 (91, 4228) | 546 (49, 4453) | 0.45 |

Table S5. Assessment for Confounding by Presence of Bicuspid Aortic Valve.

Values are mean ± standard deviation, number (percent), or median (minimum; maximum). AAO = Ascending aorta; AI = Augmentation index; cfPWV = carotid-femoral pulse wave velocity; DBP = Diastolic blood pressure; Endo-PAT = Endothelial pulse amplitude testing; hs-CRP = High sensitivity C-reactive protein; HTN = Hypertension; MMP = matrix metalloprotease; MRI = Magnetic resonance imaging; PWV = Pulse wave velocity; SBP = Systolic blood pressure.

| Table S6. A | Adjustment for | · Potential | Confounders. |
|-------------|----------------|-------------|---------------------|
|-------------|----------------|-------------|---------------------|

| | Unadjusted | l Model | Adjusted Model | |
|-------------------------------------|-------------|---------|----------------|---------|
| | Coefficient | p value | Coefficient | p value |
| CMR proximal PWV (m/s) | | | | |
| Balloon dilation | -0.76 | 0.29 | -0.49 | 0.50 |
| Stent | 0.77 | 0.26 | 0.87 | 0.28 |
| AAO strain (%) | | | | |
| Balloon dilation | 0.14 | 0.02 | 0.12 | 0.04 |
| Stent | -0.02 | 0.73 | 0.03 | 0.68 |
| cfPWV (m/s) | | | | |
| Balloon dilation | 0.05 | 0.84 | 0.07 | 0.79 |
| Stent | -0.20 | 0.46 | -0.54 | 0.09 |
| AI (%) | | | | |
| Balloon dilation | 8.65 | 0.08 | 10.6 | 0.04 |
| Stent | 18.3 | 0.001 | 18.0 | 0.003 |
| Endo-PAT index | | | | |
| Balloon dilation | -0.15 | 0.48 | -0.12 | 0.59 |
| Stent | 0.11 | 0.62 | -0.12 | 0.64 |
| 24-hour average SBP (mm Hg) | | | | |
| Balloon dilation | -4.99 | 0.12 | -5.24 | 0.11 |
| Stent | 0.42 | 0.89 | -2.30 | 0.36 |
| 24-hour average DBP (mm Hg) | | | | |
| Balloon dilation | -1.15 | 0.60 | -0.26 | 0.91 |
| Stent | 0.48 | 0.83 | -2.57 | 0.29 |
| Peak exercise right arm SBP (mm Hg) | | | | |
| Balloon dilation | -20.1 | 0.03 | -19.3 | 0.04 |
| Stent | -0.28 | 0.97 | -3.28 | 0.76 |

| Log hs-CRP (mg/L) |) |
|-------------------|---|
|-------------------|---|

| Balloon dilation | -0.07 | 0.07 | -0.07 | 0.10 |
|--------------------------------|-------|------|-------|------|
| Stent | 0.02 | 0.65 | 0.03 | 0.54 |
| Log MMP-9/gelatinase B (ng/mL) | | | | |
| Balloon dilation | 0.53 | 0.02 | 0.64 | 0.01 |
| Stent | -0.27 | 0.22 | -0.29 | 0.28 |

Multivariable linear models adjusted for age at treatment and presence of bicuspid aortic valve. For each comparison, the surgical group is the reference group. AAO = ascending aorta; AI = augmentation index; CMR = cardiac magnetic resonance imaging; DBP = diastolic blood pressure; hs-CRP = high sensitivity C-reactive protein; MMP-9 = matrix metalloprotease 9; PWV = pulse wave velocity; SBP = systolic blood pressure