Prognostic Implications of Exercise Induced Hypertension in Adults with Repaired Coarctation of Aorta

Alexander C. Egbe MD, MPH; William R. Miranda, MD; C. Charles Jain, MD; Barry A. Borlaug, MD; Heidi M. Connolly, MD

From the Department of Cardiovascular Medicine, Mayo Clinic Rochester, MN 55905

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Address for correspondence:
Alexander Egbe, MD MPH, FACC
Mayo Clinic and Foundation
200 First Street SW
Rochester, MN 55905
Phone: 507-284-2520
Fax: 507-266-0103
Email: egbe.alexander@mayo.edu

Supplementary Table S1: Baseline Characteristics
|                                      | All (n=327) | Isolated rCOA (n=215, 66%) | rCOA with LVOD (n=112, 34%) | p     |
|--------------------------------------|-------------|-----------------------------|-----------------------------|-------|
| Age, years                           | 35±13       | 36±10                       | 33±9                        | 0.1   |
| Male                                 | 201 (62%)   | 131 (61%)                   | 70 (63%)                    | 0.4   |
| Age of COA repair, years             | 3 (1-6)     | 3 (2-6)                     | 1 (1-3)                     | 0.1   |
| NYHA III/IV                          | 44 (13%)    | 18 (8%)                     | 26 (23%)                    | <0.001|
| ULE SBP gradient, mmHg               | 12 (8-15)   | 13 (7-16)                   | 10 (6-15)                   | 0.6   |

**Comorbidities**

| Comorbidity                          | All (n=327) | Isolated rCOA (n=215, 66%) | rCOA with LVOD (n=112, 34%) | p     |
|--------------------------------------|-------------|-----------------------------|-----------------------------|-------|
| Coronary artery disease              | 16 (5%)     | 11 (5%)                     | 5 (5%)                      | 0.9   |
| Diabetes                             | 15 (5%)     | 12 (6%)                     | 3 (6%)                      | 0.9   |
| Atrial fibrillation                  | 28 (9%)     | 12 (6%)                     | 16 (14%)                    | 0.008 |

**Medications**

| Medication                          | All (n=327) | Isolated rCOA (n=215, 66%) | rCOA with LVOD (n=112, 34%) | p     |
|--------------------------------------|-------------|-----------------------------|-----------------------------|-------|
| ACEI/ARB                             | 192 (59%)   | 128 (60%)                   | 64 (57%)                    | 0.2   |
| Aldosterone antagonist               | 8 (2%)      | 4 (2%)                      | 4 (4%)                      | 0.8   |
| Beta blockers                        | 168 (51%)   | 97 (45%)                    | 71 (63%)                    | 0.009 |
| Calcium channel blockers             | 38 (12%)    | 24 (11%)                    | 14 (13%)                    | 0.7   |
| Thiazide diuretics                   | 33 (10%)    | 21 (10%)                    | 12 (11%)                    | 0.8   |
| Others                               | 13 (4%)     | 8 (4%)                      | 5 (3%)                      | 0.9   |

**Laboratory data**

| Laboratory parameter                 | All (n=327) | Isolated rCOA (n=215, 66%) | rCOA with LVOD (n=112, 34%) | p     |
|--------------------------------------|-------------|-----------------------------|-----------------------------|-------|
| Estimated GFR, ml/min/1.73m²         | 90±21       | 96±19                       | 84±16                       | 0.6   |

**Echocardiographic data**

| Echocardiographic parameter          | All (n=327) | Isolated rCOA (n=215, 66%) | rCOA with LVOD (n=112, 34%) | p     |
|--------------------------------------|-------------|-----------------------------|-----------------------------|-------|
| Aortic mean gradient, mmHg           | 14±8        | 11±4                        | 26±5                        | <0.001|
| ≥ Moderate Aortic regurgitation      | 19 (6%)     | 0                           | 19 (17%)                    | ---   |
| COA mean gradient, mmHg              | 13±4        | 13±4                        | 12±4                        | 0.4   |
| Septal E/e’                          | 12.1±5.7    | 11.2±3.1                    | 13.9±3.4                    | 0.005 |
| LV mass index, g/m²                  | 104±19      | 94±18                       | 122±21                      | <0.001|
| LV ejection fraction, %              | 62±8        | 64±10                       | 58±8                        | 0.6   |
| LVGLS, %                             | -21±3       | -22±3                       | -18±4                       | 0.004 |
| RVGLS, %                             | -24±4       | -25±4                       | -22±3                       | 0.09  |
| RV fractional area change, %         | 45±8        | 46±9                        | 43±7                        | 0.4   |
| RV systolic pressure, mmHg           | 34±12       | 32±10                       | 39±11                       | 0.08  |

**Average resting BP**

| BP parameter                        | All (n=327) | Isolated rCOA (n=215, 66%) | rCOA with LVOD (n=112, 34%) | p     |
|--------------------------------------|-------------|-----------------------------|-----------------------------|-------|
| SBP, mmHg                            | 129±18      | 127±20                      | 132±16                      | 0.6   |
| DBP, mmHg                            | 72±12       | 71±11                       | 74±10                       | 0.8   |
| PP, mmHg                             | 57±15       | 56±12                       | 58±13                       | 0.9   |

**Doppler-derived arterial load indices**
|                          |        |        |        | 0.9 |
|--------------------------|--------|--------|--------|-----|
| EAI, mmHg/ml*m^2         | 3.3±0.6| 3.2±0.5| 3.4±0.4| 0.9 |
| TACI, mL/mmHg*m^2        | 0.8±0.4| 0.7±0.3| 0.8±0.4| 0.8 |

**Exercise data**

|                          |        |        |        | 0.3 |
|--------------------------|--------|--------|--------|-----|
| SBP at peak exercise, mmHg | 173±31 | 176±27 | 165±29 | 0.3 |
| HR at peak exercise, bpm  | 164±28 | 168±36 | 161±27 | 0.2 |
| RER                      | 1.16±0.04 | 1.15±0.05 | 1.17±0.08 | 0.3 |
| Exercise time, minutes    | 7.6±1.2 | 7.8±1.0 | 7.3±0.8 | 0.1 |
| Peak VO\(_2\), ml/kg/min | 26±6   | 28±6   | 23±5   | 0.03 |

LVOD: left ventricular outflow disease; NYHA: New York Heart Association; ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; coarctation of aorta; GFR: glomerular filtration rate; E/e’: ratio of mitral inflow pulsed wave early velocity to tissue Doppler early velocity; LV: left ventricle; RV: right ventricle; GLS: global longitudinal strain; ULE: upper to lower extremity; SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; HR: heart rate; RER: respiratory exchange ratio; VO\(_2\): oxygen consumption; EAI: Effective arterial elastance index; TACI: Total arterial compliance index
### Supplemental Table S2: Multivariable Cox Regression Models for Sensitivity Analyses

|                  | Model A          | Model B          | Model C          | Model D          | Model E          | Model F          |
|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| **HR (95% CI) for 5 mmHg increase in exercise** |                  |                  |                  |                  |                  |                  |
| **Unadjusted**   | 1.08 (1.04-1.12) | 1.07 (1.04-1.10) | 1.08 (1.05-1.11) | 1.06 (1.03-1.09) | 1.04 (1.01-1.07) | 1.07 (1.04-1.10) |
| **Adjusted**     | 1.06 (1.03-1.09) | 1.05 (1.02-1.08) | 1.06 (1.03-1.09) | 1.04 (1.01-1.07) | 1.02 (0.98-1.04) | 1.05 (1.02-1.08) |

|                  |                  |                  |                  |                  |                  |                  |
| **HR (95% CI) for EIH versus no EIH** |                  |                  |                  |                  |                  |                  |
| **Unadjusted**   | 2.74 (2.41-3.06) | 2.90 (2.53-3.45) | 2.69 (2.27-3.03) | 2.44 (1.96-2.98) | 1.83 (1.19-2.57) | 2.91 (2.37-3.41) |
| **Adjusted**     | 2.04 (1.65-2.46) | 2.14 (1.71-2.66) | 1.96 (1.61-2.37) | 2.11 (1.28-3.07) | 1.65 (0.85-2.46) | 2.52 (2.01-3.03) |

HR: hazard ratio; CI: confidence interval; Adjusted* signified HR adjusted for age and resting SBP.

Model A: Analysis restricted to males (n=201)

Model B: Analysis restricted to females (n=126)

Model C: Analysis restricted to patients isolated COA (n=215). Isolated COA was defined as the absence of concomitant LV outflow disease defined as having any of the following conditions: aortic valve prosthesis, sub-valvular, valvular, or supra-valvular aortic stenosis (mean gradient >20 mmHg) or ≥moderate aortic regurgitation.

Model D: Analysis restricted to patients with LV outflow disease (n=112)

Model E: Analysis restricted to patients that had intensification of antihypertensive therapy after exercise test (n=89)

Model F: Analysis restricted to patients without intensification of antihypertensive therapy after exercise test (n=239)
Supplementary Figure S1: A flowchart showing patient selection for the study. COA: coarctation of aortal LVID: left ventricular inflow disease.