Cardiovascular disease is the leading cause of death in the United States.

Patients with chronic kidney disease (CKD) are more likely to develop heart disease compared to the general population.

Arterial calcification is prevalent in CKD patients and leads to reduced compliance of arterial walls and hypertension.

Hyperphosphatemia promotes vascular arterial calcification and is a strong predictor of cardiovascular mortality.

In this study, we developed a mouse model of CKD with hyperphosphatemia and measured changes in heart function and vascular stiffness.

Hypothesis: Mice with CKD will present with left-ventricular hypertrophy, increased vascular stiffness, and that hyperphosphatemia will exacerbate these conditions.
Stage II Methods & Results

Echocardiography

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0.2% Adenine</th>
<th>0.2% Adenine + 1.8% Phosphate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Animals</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>LVID/BW (mm/g)</td>
<td>0.23 ± 0.02</td>
<td>0.20 ± 0.02 *</td>
</tr>
<tr>
<td>LVmass/BW (mg/g)</td>
<td>4.32 ± 0.84</td>
<td>3.82 ± 0.74</td>
</tr>
<tr>
<td>SV/BW (µl/g)</td>
<td>2.34 ± 0.49</td>
<td>2.06 ± 0.54</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>65.6 ± 8.01</td>
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</tbody>
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Vascular Ultrasound

Abdominal aorta (AA)

- AA PeakVel, m/s
- AA Elastic Modulus, kPa
- AA PPV, m/s

Conclusion

- The adenine containing diet is a can be used to induce cardiovascular abnormalities in CKD mice.
- CKD resulted in hypertensive states within both females and males, but some males developed hypotension.
- Male mice are more susceptible to cardiac compromise associated with kidney disease (reduced HR and EF and increased LVID).
- CKD mice develop aortic stiffness that can be detected in vivo by high resolution ultrasound. Dietary phosphate further exacerbates this condition.
- Surprisingly, female mice had a higher LVPW/BW and LVmass/BW at baseline, which could be cardio protective.
- Future studies on CKD induced mice can provide further correlation between CKD and cardiovascular disease.

Acknowledgements

This work was supported by the National Institutes of Health (NIH) grant number R56 HL131547-01A1 (to OVS). Acquisition of the Vevo 3100 ultrasound instrument for small animal research was made possible by NYIT College of Osteopathic Medicine (NYITCOM). We thank Jeanne Quidore-Jermann and Sandra Kahler for technical assistance.
Stage I Blood Pressure

**Dia BP, mmHg**

Compared to baseline females, females the with 0.2% adenine diet had a **significant increase** in diastolic blood pressure.

Compared to adenine females, males with the 0.2% adenine diet had a **significantly lower** diastolic blood pressure.

**Sys BP, mmHg**

Compared to baseline females, females the with 0.2% adenine diet had a **significant increase** in systolic blood pressure.

Compared to adenine females, males with the 0.2% adenine diet had a **significantly lower** systolic blood pressure.

* p < 0.05, ** p < 0.01, *** p < 0.001
**Stage I Vascular Ultrasound Results**

**AA PeakVel, m/s**

Compared to baseline males, males with the 0.2% adenine diet had a significant decrease in abdominal aorta peak velocity.

Compared to adenine females, males with the 0.2% adenine diet had a significantly lower abdominal aorta peak velocity.

**AA Elastic Modulus, kPa**

Compared to baseline, both females and males with the 0.2% adenine diet had a significantly higher abdominal aorta elasticity.

**AA PPV, m/s**

Compared to baseline females, females with the 0.2% adenine diet had a significantly higher abdominal aorta pulse propagation velocity.

* p < 0.05, ** p < 0.01, *** p < 0.001

Abdominal Aorta (AA), peak velocity (PeakVel), Pulse propagation velocity (PPV)
Stage II Vascular Ultrasound Results

**AA PeakVel, m/s**

Compared to females with only 0.2% adenine containing diet, females with 0.2% adenine and 1.8% phosphate containing diet **did not have any significant changes** in the abdominal aorta peak velocity.

**AA Elastic Modulus, kPa**

Compared to females with only 0.2% adenine containing diet, females with 0.2% adenine and 1.8% phosphate containing diet **did not have any significant changes** in the abdominal aorta elasticity.

**AA PPV, m/s**

Compared to females with only 0.2% adenine containing diet, females with 0.2% adenine and 1.8% phosphate containing diet had a **significant increase** in abdominal aorta pulse propagation velocity.

* p < 0.05 vs 0.2% Adenine

Abdominal Aorta (AA) Peak velocity (PeakVel), Pulse propagation velocity (PPV)
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### Table: Comparison of Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline F</th>
<th>Baseline M</th>
<th>Adenine F</th>
<th>Adenine M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Animals</td>
<td>18</td>
<td>16</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>HR (mmHg)</td>
<td>384 ± 58 *</td>
<td>447 ± 65</td>
<td>372 ± 60</td>
<td>360 ± 67 **</td>
</tr>
<tr>
<td>SV/BW (µl/g)</td>
<td>2.13 ± 0.21 *</td>
<td>1.84 ± 0.35</td>
<td>1.91 ± 0.25</td>
<td>2.00 ± 0.34</td>
</tr>
<tr>
<td>CO/BW (ml/min*g⁻¹)</td>
<td>0.82 ± 0.14</td>
<td>0.81 ± 0.16</td>
<td>0.70 ± 0.11</td>
<td>0.71 ± 0.15</td>
</tr>
<tr>
<td>EF (%)</td>
<td>63.0 ± 12.4</td>
<td>68.8 ± 7.9</td>
<td>54.8 ± 8.6</td>
<td>57.6 ± 8.4 **</td>
</tr>
<tr>
<td>LVID/BW (mm/g)</td>
<td>0.21 ± 0.03</td>
<td>0.17 ± 0.02</td>
<td>0.21 ± 0.03</td>
<td>0.21 ± 0.02 **</td>
</tr>
<tr>
<td>LVPW/BW (mm/g)</td>
<td>0.039 ± 0.006 **</td>
<td>0.032 ± 0.005</td>
<td>0.037 ± 0.005</td>
<td>0.034 ± 0.005</td>
</tr>
<tr>
<td>LVmass/BW (mg/g)</td>
<td>4.39 ± 0.88 *</td>
<td>3.63 ± 0.66</td>
<td>4.14 ± 0.67</td>
<td>4.04 ± 0.57</td>
</tr>
<tr>
<td>LVEDV/BW (µl/g)</td>
<td>3.50 ± 0.73 *</td>
<td>2.75 ± 0.68</td>
<td>3.60 ± 0.95</td>
<td>3.53 ± 0.75 *</td>
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</table>

Compared to baseline males:
- Baseline females and males with the adenine diet had a significantly lower heart rate.
- Baseline females had a significantly higher stroke volume.
- Males with the adenine diet had a significantly lower ejection fraction.
- Males with the adenine diet had a significantly higher left ventricular internal diameter.
- Baseline females had a significantly thicker left ventricular posterior wall.
- Baseline females had a significantly greater left ventricular mass.
- Baseline females and males with the adenine diet had an increased left ventricular end diastolic volume.

* p < 0.05, ** p < 0.01, *** p < 0.001 vs Baseline Male
Heart rate (HR), Stroke volume (SV), Body weight (BW), Cardiac output (CO), Ejection fraction (EF), Left ventricular internal diameter (LVID), Left ventricular posterior wall thickness (LVPW), Left ventricular mass (LVmass), Left ventricular end diastolic volume (LVEDV)
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Compared to females with only the adenine diet, females with the adenine and phosphate diet had a significantly reduced left ventricular internal diameter.

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* p < 0.05 vs 0.2% Adenine Females

Heart rate (HR), Stroke volume (SV), Body weight (BW), Left ventricular internal diameter (LVID), Left ventricular posterior wall thickness (LVPW), Left ventricular mass (LVmass), Left ventricular end diastolic volume (LVEDV)
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Cardiac Long Axis View of the Heart in (B) Bright Mode
Cardiac Short Axis View of the Heart in Motion (M) Mode
Doppler Imaging of the Abdominal Aorta and Renal Arteries