NEW YORK INSTITUTE OF TECHNOLOGY
College of Osteopathic Medicine

Effect of Homoarginine on Food Consumption and Cardiac Function in Mice

Neil Kaungumpillil*; Billy X. Ding, OMS-II; Anisa Raidah, OMS-II; Cindy Lin, OMS-II; Daniel Kalta, OMS-II; Bilal Shaikh, OMS-II; Mohnish Singh, MS; Olga V. Savinova, PhD

Department of Biomedical Sciences, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, USA

INTRODUCTION

- Plasma homoarginine (hArg) is a non-proteinaceous endogenous amino acid that correlates with better cardiovascular and renal disease prognosis.
- We have previously found that supplementation with hArg reduces food consumption and improves heart function in mice with chronic kidney disease (CKD).
- The effect of hArg in healthy mice is not fully understood.
- To better understand the mechanism of the supplementation of hArg in healthy mice, we compared metabolic and cardiac data following hArg supplementation in healthy mice and mice with CKD.
- We aim to study whether hArg has similar effects in healthy mice.

OBJECTIVES

- The purpose of this study was to compare the effects of the supplementation of hArg on cardiac and metabolic parameters between healthy mice and mice with CKD.
- To provide insight into the significance of hArg supplementation and potential side effects of hArg supplementation for treatment of CKD.

METHODS

- The mice of both sexes were randomly assigned into three groups receiving 14 µg/ml of hArg; 14 µg/ml arginine (Arg) – a structurally similar amino acid, or placebo treatment in drinking water.
- Data from a previous CKD ± hArg experiment were used for comparison.
- 24-hour food and water consumption, fecal and urine output, and cardiac function were measured.
- The results were compared by a one-way ANOVA.
- In a sub-analysis, the effects of health status (healthy or CKD) and treatment (placebo or hArg) were analyzed by a two-way ANOVA.

FINANCIAL DISCLOSURE

Presenter: Neil Kaungumpillil
Nothing to disclose

Authors have nothing to disclose

ACKNOWLEDGEMENTS

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We thank the Animal Care Facility of NYITCOM for providing animal care.

DATA

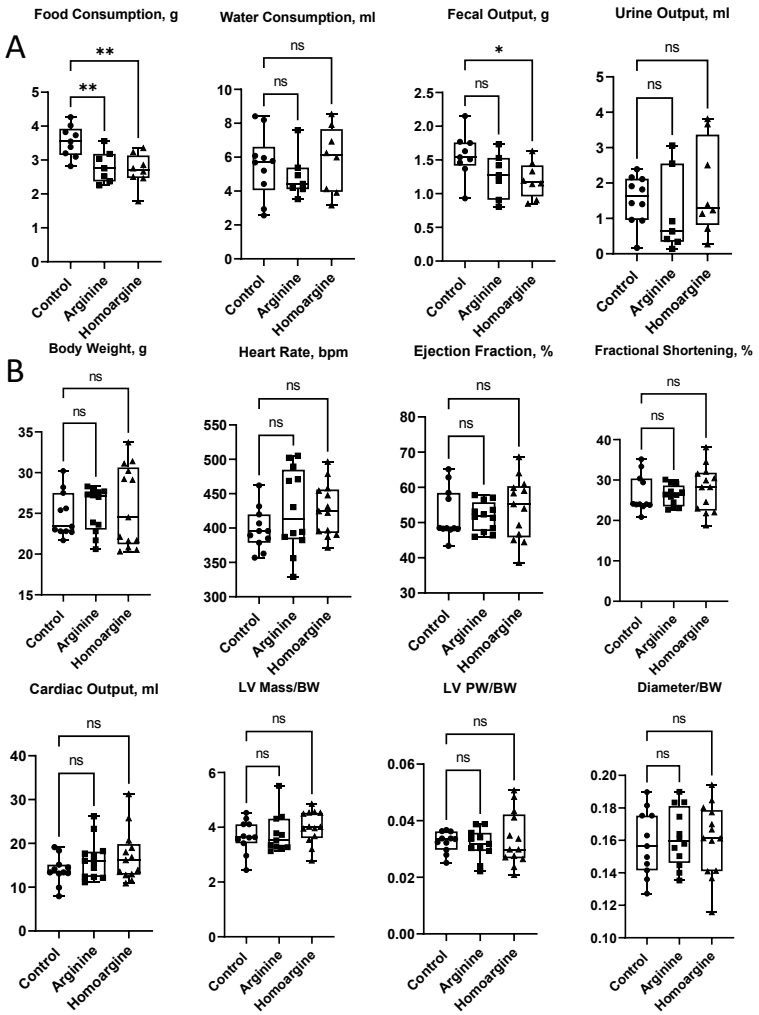

Figure 1: Metabolic and physiologic studies. A: metabolic parameters including food consumption, water consumption, fecal output, and urine output. B: echocardiogram results with cardiac parameters including bodyweight (BW), heart rate, ejection fraction, fractional shortening, cardiac output, left ventricular (LV) mass, and LV posterior diameter (LVPW). *, p<0.05, **, p<0.01, ns, not significant.

RESULTS

- hArg and Arg supplementation resulted in decreased food consumption; fecal output was reduced in hArg group; water consumption and urine output were not affected.
- There were no differences of hArg and Arg supplementation in their effect on food consumption.
- Cardiac structure and function were unaffected by hArg or Arg supplementation.

REPRESENTATIVE IMAGES

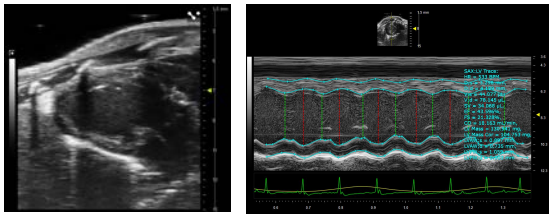

Figure 2: Echocardiography. Representative B mode image of cardiac long axis (left). Representative M mode image of cardiac short axis with tracing of wall movement and measured cardiac parameters (right).

Figure 3: Metabolic cage setup. Used for collection of metabolic data.

CONCLUSIONS

- Similar to previous CKD study, hArg supplementation reduces food consumption however, it has no effect on cardiac function in healthy mice.
- Our data suggests that the observed effect of hArg supplementation on food consumption is not unique as it also is observed in chemically similar Arg supplementation group.
- The study was limited by the small sample size and potential stress induced by solitary confinement in metabolic cages.
- Although the physiology of mice is not representative of humans, the result of the study suggests additional research into hArg supplementation in humans with CKD, is necessary.

Financial Disclosure

Presenter: Neil Kaungumpillil

Nothing to disclose

Authors have nothing to disclose

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- This work was supported by the NIH grant HL149864-01.
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- We aim to study whether hArg has similar effects in healthy mice.

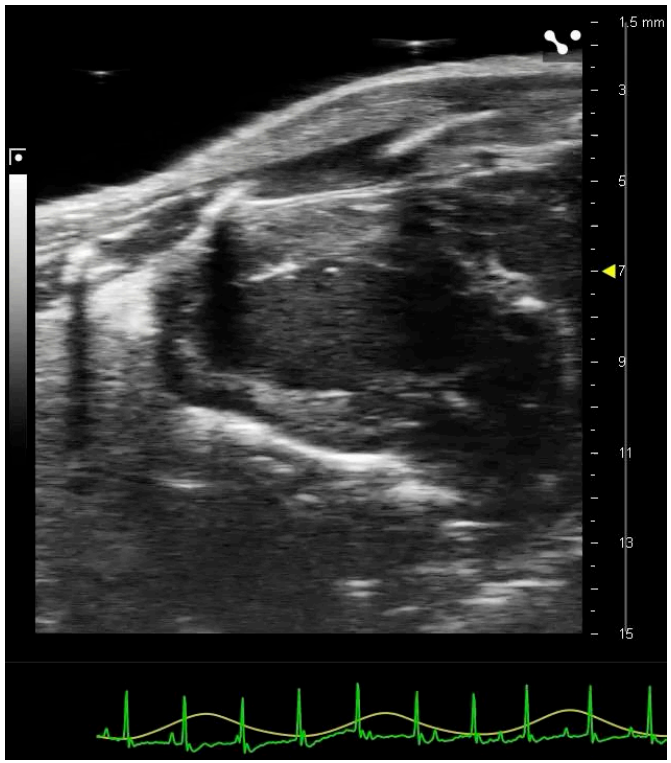
OBJECTIVE

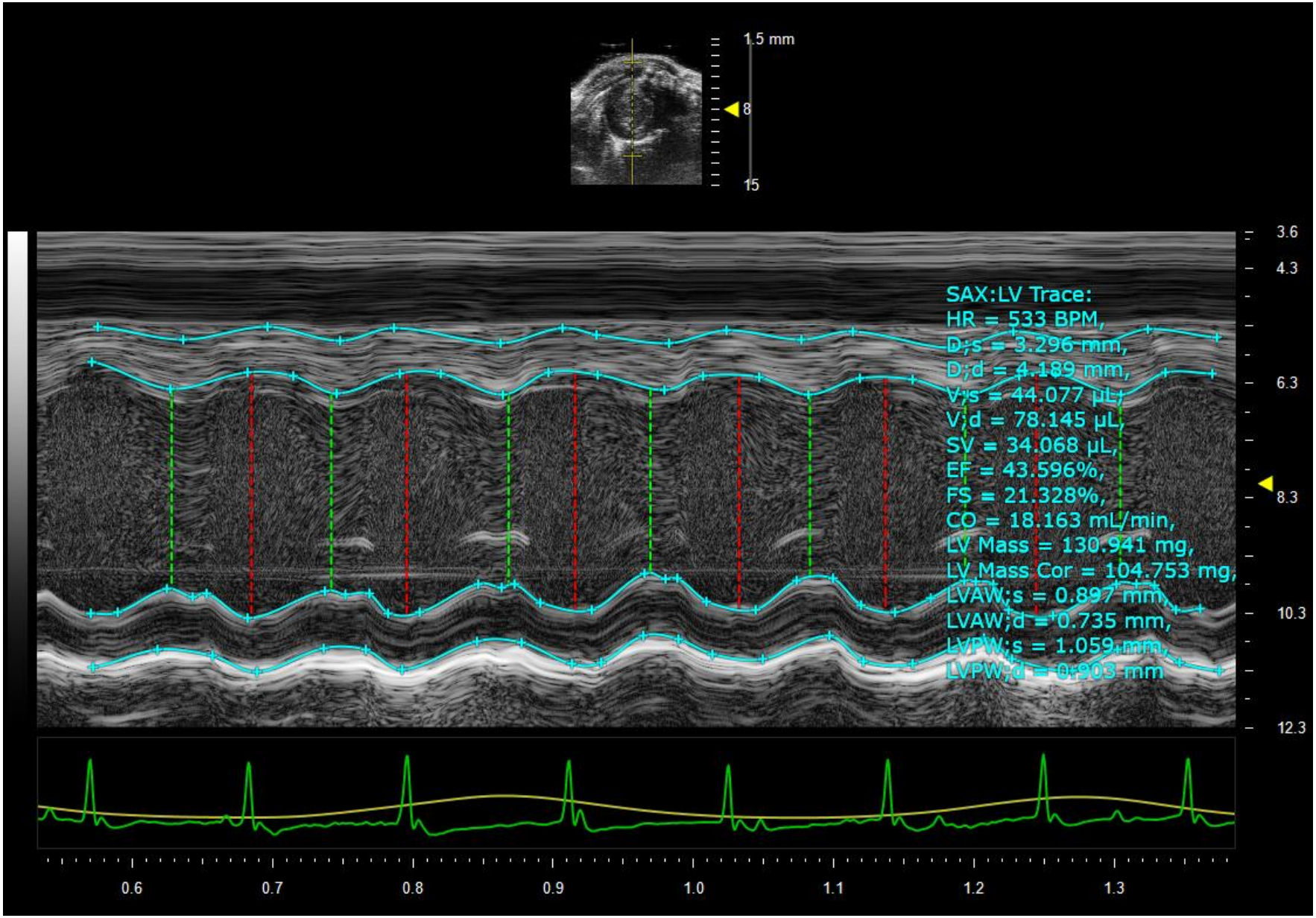
- The purpose of this study was to compare the effects of the supplementation of hArg on cardiac and metabolic parameters between healthy mice and mice with CKD.
- This could provide insight into the significance of hArg supplementation and potential side effects of hArg supplementation for treatment of CKD.
- This can serve to provide prognostic value of hArg supplementation to treat CKD in humans.

METHODS

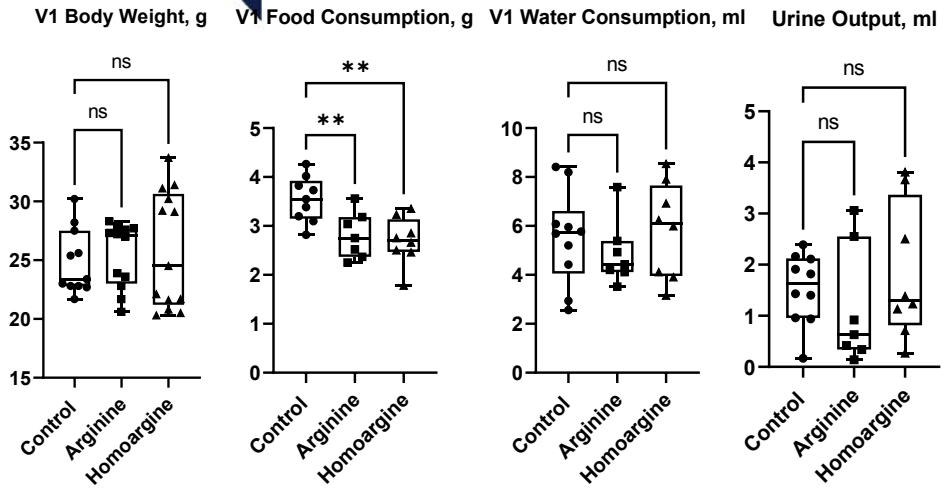
- The mice of both sexes were randomly assigned into three groups receiving 14 µg/ml of hArg; 14 µg/ml arginine (Arg) – a structurally similar amino acid, or placebo treatment in drinking water.
- Data from a previous CKD ± hArg experiment were used for comparison.
- 24-hour food and water consumption, fecal and urine output, and cardiac function were measured.
- The results were compared by a one-way ANOVA.
- In a sub-analysis, the effects of health status (healthy or CKD) and treatment (placebo or hArg) were analyzed by a two-way ANOVA.

ECHOCARDIOGRAPHY




1.5 mm
8
15
SAX:LV Trace:
HR = 533 BPM,
D;s = 3.296 mm,
D;d = 4.189 mm,
V;s = 44.077 µL,
V;d = 78.145 µL,
SV = 34.068 µL,
EF = 43.596%,
FS = 21.328%,
CO = 18.163 mL/min,
LV Mass = 130.941 mg,
LV Mass Cor = 104.753 mg,
LVAW;s = 0.897 mm,
LVAW;d = 0.735 mm,
LVPW;s = 1.059 mm,
LVPW;d = 0.903 mm
3.6
4.3
6.3
8.3
10.3
12.3
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3

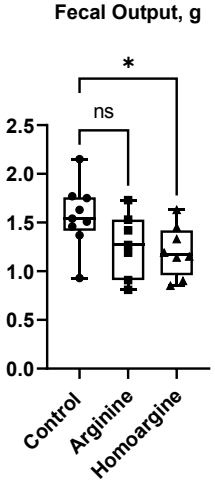
RESULT

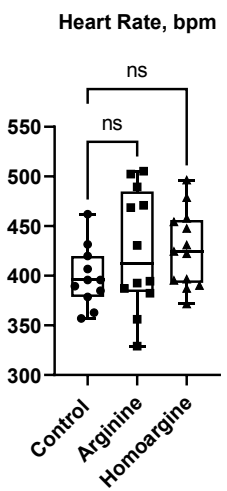

V1 Body Weight, g
ns
ns
35
30
25
20
15
Control
Arginine
Homoargine

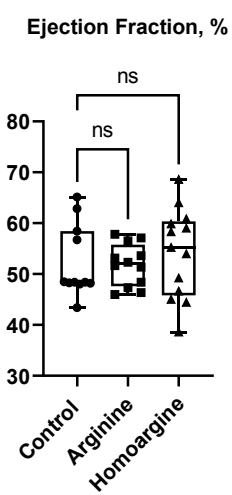
V1 Food Consumption, g
**
**
5
4
3
2
1
0
Control
Arginine
Homoargine

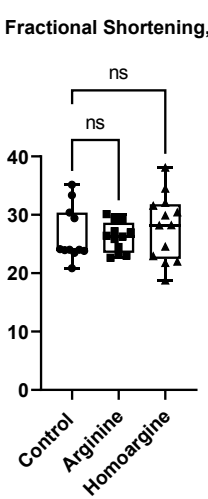
V1 Water Consumption, ml
ns
ns
10
8
6
4
2
0
Control
Arginine
Homoargine

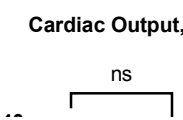
Urine Output, ml
ns
ns
5
4
3
2
1
0
Control
Arginine
Homoargine

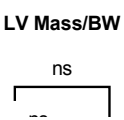

Fecal Output, g
*
ns
2.5
2.0
1.5
1.0
0.5
0.0
Control
Arginine
Homoargine

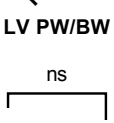

Heart Rate, bpm
ns
ns
550
500
450
400
350
300
Control
Arginine
Homoargine

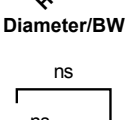

Ejection Fraction, %
ns
ns
80
70
60
50
40
30
Control
Arginine
Homoargine


Fractional Shortening, %
ns
ns
40
30
20
10
0
Control
Arginine
Homoargine

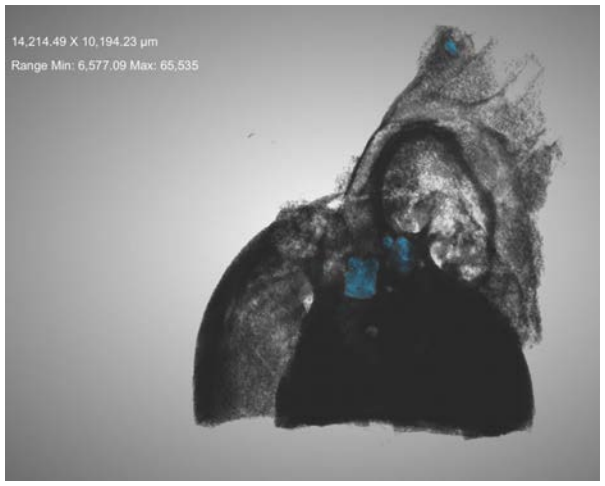

Cardiac Output, ml
ns


LV Mass/BW
ns

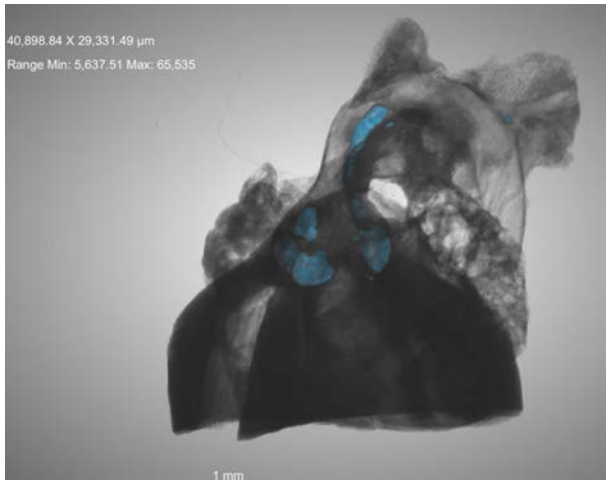

LV PW/BW
ns

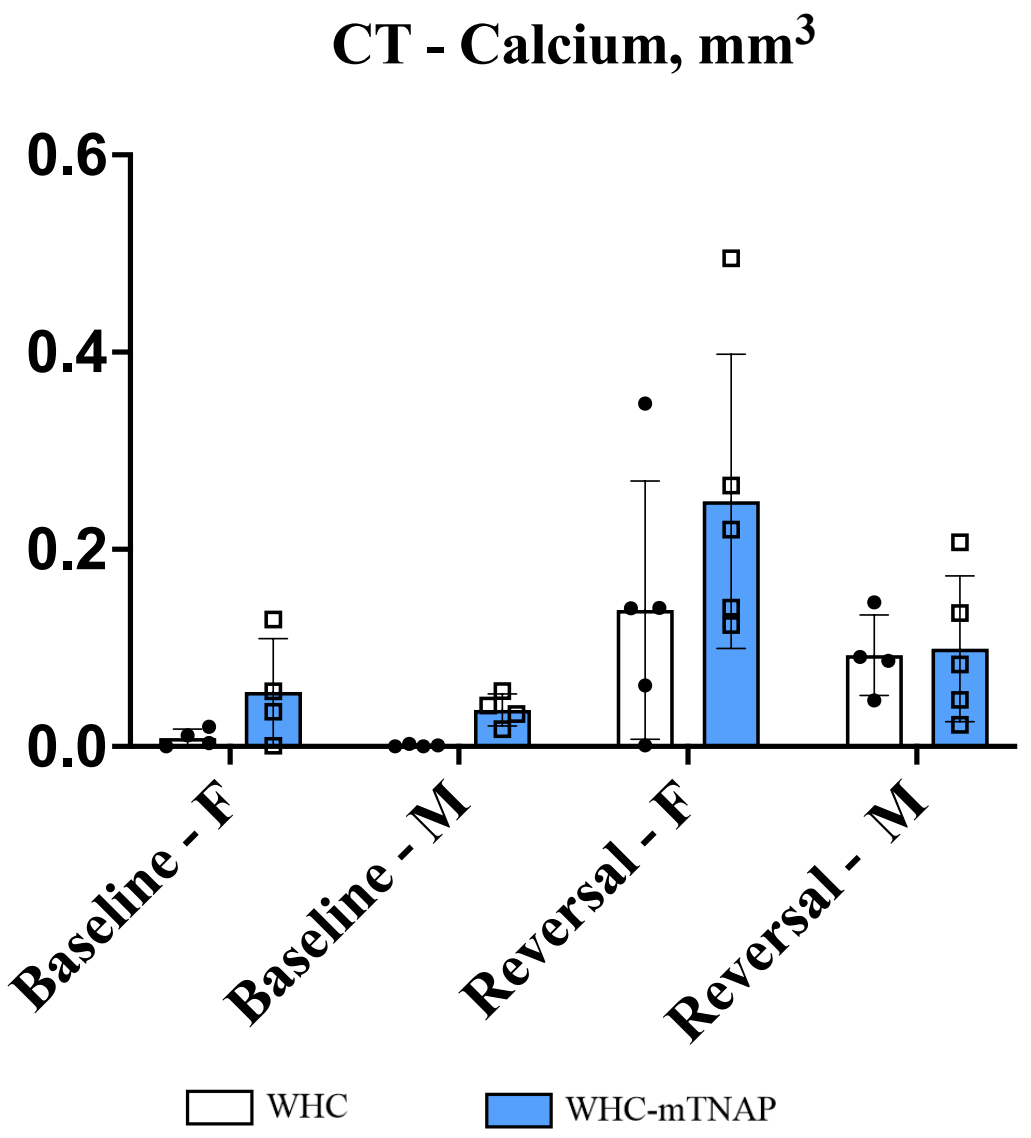

Diameter/BW
ns

WHC



WHC-mTNAP





RESULTS

- Neither hArg nor Arg supplementation affected metabolic or cardiac parameters in healthy mice.
- CKD status had no effects on food consumption and fecal output but was associated with increased water consumption and urine output ($p < 0.0001$).
- CKD mice were smaller compared with healthy controls ($p < 0.0001$).
- Cardiac function and left ventricular dimensions adjusted to body size were increased in CKD mice independent of treatment ($p < 0.05$).

CONCLUSION

- Our data suggest that that hArg supplementation has a differential effect in healthy and CKD mice..
- The study was limited by the small number of animals analyzed for each group, normal cardiac structure for all mice was assumed, study can be repeated using a blind methodology, metabolic cages could have stressed mice, influencing metabolic data.
- With a larger sample size, the study would be provided with greater accuracy and statistical power. The mice could have been analyzed for their cardiac structure and be acclimated to living in metabolic cages to eliminate extraneous variables.
- Although the physiology of mice is not representative of humans, the result of the study suggests additional research into hArg supplementation in patients with CKD, is necessary.