PHYSIOLOGY OF CARDIAC HYPERTROPHY IN SEVERELY IRON DEFICIENT RATS USING PRESSURE-VOLUME LOOPS

BY: JACQUIE ZADRA, EMILY THOMPSON, AND ASHLEY WEGEL

FACULTY MENTOR: BUD CHEW, PH.D.
Enlargement of the heart

- Can either be adaptive or pathological
  - Adaptive hypertrophy is seen in aerobic athletes
  - Pathological hypertrophy is seen in diseases of the heart such as congestive heart failure
Adaptive hypertrophy
- Increased cardiac output
- Increased heart chamber size
- Healthy heart wall muscle

Pathological Hypertrophy
- Decreased cardiac output
- No increase in heart chamber size
- Fibrotic heart wall
  - Due to increase in collagen
PROLONGED IRON DEFICIENCY CAUSES CARDIAC HYPERTROPHY

1. Iron is at the center of Heme, to which oxygen binds
2. Iron Deficiency causes hypoxia
3. Hypoxia causes activation of the sympathetic nervous system
4. Constant stimulation of SNS results in hypertrophy
5. Hypertrophy may result in a short-term adaptation
6. Increased Cardiac Output
   - Over time, hypertrophy may result in a failing heart
   - Decreased cardiac output
CURRENT UNDERSTANDING OF CARDIAC HYPERTROPHY FROM IRON DEFICIENCY

- 12 weeks of iron deficiency
- Morphological indications of failure
- Apoptosis stimulated
- Cardiac function of this hypertrophy is poorly understood

Ref: Dong et al., 2007.
We hypothesized that four weeks of iron deficiency would result in failing cardiac function and decreased sympathetic neurotransmitter stores.
EXPERIMENTAL DESIGN

- Two groups Sprague-Dawley Rats
  - Four rats fed iron deficient diet (AIN-93G without iron)
  - Four rats fed control diet (AIN-93G)
- Four weeks of the respective dietary intervention
- Cardiac pressure-volume loop protocol
- Plasma and hearts frozen for HPLC analysis
PV LOOP PROTOCOL: SURGERY

- 2 femoral vein catheters for drug infusion
- 1 jugular vein catheter for saline calibration
- 1 carotid artery exposure for PV loop transducer
  - Inserted into the carotid artery and passed into the left ventricle
PV-LOOP PROTOCOL: DATA COLLECTION

- Aortic pressure measurements and baseline cardiac function data
- Inferior Vena Cava occlusion for measure of contractility
- Saline calibration for parallel conductance subtraction
- Dopamine infusion
- Atenolol infusion
- Second baseline data
- Heparinized rat to prevent blood clotting
- Cuvette calibration for measure of true blood volume
- Collect microhematocrit samples
- Centrifuge remaining blood for plasma
- Freeze plasma and hearts for HPLC analysis
RESULTS: IRON DEFICIENCY

Hematocrit

Body Mass

*\( p<0.05 \)
RESULTS: CARDIAC HYPERTROPHY

Iron Deficient

Control

Heart • Body Mass⁻¹ Ratio

*\( p < 0.05 \)
PRESSURE-VOLUME LOOPS

Cardiac output = (SV)(HR)

End Systolic PV relationship (ESPVR)
Isovolumic Relaxation
Ejection
End Diastolic Volume
Isovolumic Contraction
Stroke Volume
Filling
Heart Rate

LV Pressure (mmHg)
LV Volume (µL)
RESULTS: PRESSURE-VOLUME LOOPS

Control

Iron Deficient-Adaptive

Iron Deficient-Failing
RESULTS: PRESSURE-VOLUME LOOPS

Cardiac Output

CO = HR * SV

* p < 0.05
RESULTS: PRESSURE VOLUME LOOPS

Heart Rate

Stroke Volume

*p<0.05
Stroke volume is affected by three factors:

1. Preload
   - End diastolic volume

![End Diastolic Volume Graph]

\*p<0.05
RESULTS: PRESSURE-VOLUME LOOPS

(2) Contractility
- Sympathetic nervous system
- Ejection fraction
- Frank-Starling Law of The Heart

![Graph showing Ejection Fraction comparison between Control and Iron Deficient groups. The graph indicates that the Iron Deficient group has a significantly higher ejection fraction compared to the Control group, with *p<0.05.](image-url)
Control rat ejection fraction averaged 55%
Iron deficient rat ejection fraction averaged 93%
RESULTS: PRESSURE-VOLUME LOOPS

The graph shows the comparison of dp\(\cdot\)dt\(^{-1}\) Max between Control and Iron Deficient groups. The control group has a higher dp\(\cdot\)dt\(^{-1}\) Max compared to the iron deficient group.
(3) Afterload

- Aortic diastolic pressure

![Aortic Diastolic Pressure Diagram]
PROLONGED IRON DEFICIENCY CAUSES CARDIAC HYPERTROPHY

Iron is at the center of Heme, to which oxygen binds

Iron Deficiency causes hypoxia

Hypoxia causes activation of the sympathetic nervous system

Constant stimulation of SNS results in hypertrophy

Hypertrophy may result in a short term adaptation

Increased Cardiac Output

Over time, hypertrophy may result in a failing heart

Decreased cardiac output
HPLC is a technique used to separate and quantify chemical compounds in a liquid medium.

Used to determine concentration of norepinephrine in extracted plasma.
RESULTS: HPLC

Plasma Norepinephrine Concentration

NE (μg·ml⁻¹)

Control Group

Iron Deficient Group
CONCLUSION: 3 ADAPTIVE ID HEARTS, 1 FAILING ID HEART
ACKNOWLEDGMENTS

Thanks to Wyoming INBRE for funding our research