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Diabetes – What's Our Role?

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- No financial discloser (with manufacturers of commercial products and/or providers of commercial services)..
  - Speaker's Bureau: *none*
  - Major Stock Shareholder: *none*
  - Consultant or employee: *none*
  - Industry grant/research support: none
- Discussion of "off-label" uses of medications will be indicated by "not FDA approved"

Diabetes – What's Our Role?

- Two Case Examples
  - Early and Advanced HF
- Teaching Points and Objectives
  - Identify Heart Failure Risk Reduction Strategies
  - Outline Emerging Metabolic Treatment Options
    - Beyond Glucose Control

Case One

- 52 y/o women with mild exertional dyspnea
- No associated chest pain or past cardiac history
- Comorbidities treated hypertension, central weight gain (Wt 201 lb, BMI 31 kg/M^2); BSA 1.98 m^2
  - +FH; no past tobacco use
- Laboratory studies dyslipidemia (Tg & HDL-C)
  - Impaired fasting gluc; ALT/AST ratio > 1; Creat 1.4 mg/dL

Laboratory Data

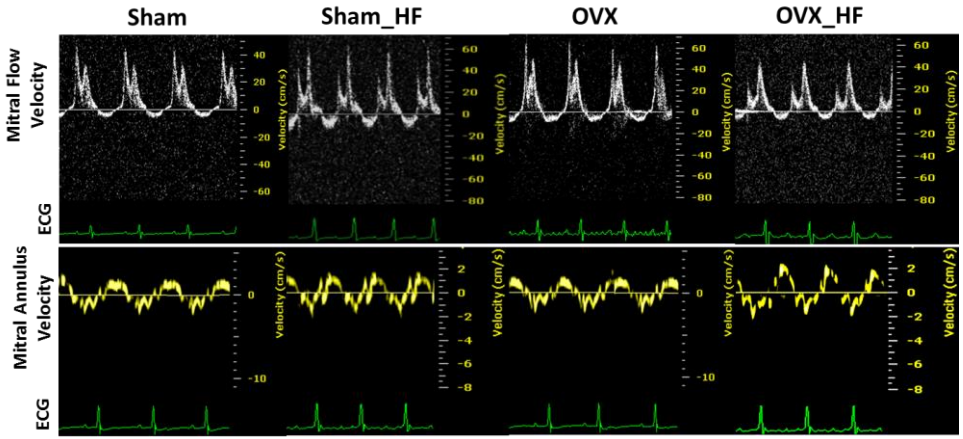
Variable	Reference Range	Result
Fasting glucose (mmol/l)	3.89 – 5.56	5.79 (104 mg/dL)
HgbA1c (%)	4.0 – 6.0	6.2
Insulin (µIU/ml)	0 – 20	13.6
HOMA-IR (index)	< 2	3.5

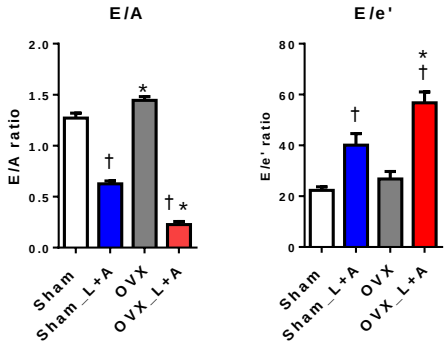
Cardiology Diagnostics

- Myocardial perfusion study– negative
  - Normal tracer distribution during stress
  - Post-stress EF 84%
- Echo findings
  - Mild LVH; EF – 55-59%; EDV 55.6 ml (reduced)
  - LAV 55 ml (difficult to assess); LAV/BSA 27.7; EDV 55.6 ml
  - E/A ratio 0.8

Female mice develop diastolic dysfunction with preserved EF

OVX exacerbates DD

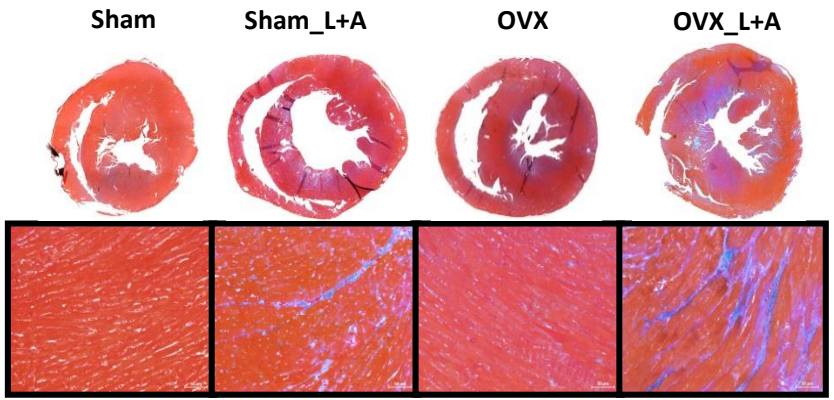


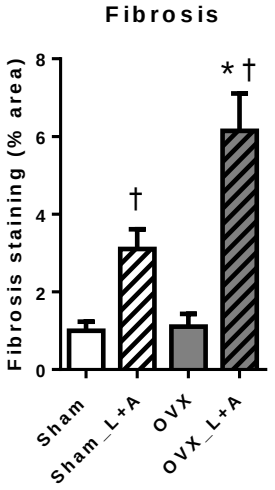


Tissue+pulse Doppler on Vevo2100

*P<0.05 vs. sham_L+A
†P<0.05 vs. sham

Mechanisms of DD in E2-deficient females?





Masson's trichrome staining for fibrosis

*P<0.05 vs. sham_L+A
†P<0.05 vs. sham

Clinical Impression

- Metabolic syndrome with moderate insulin resistance with central obesity
- Mild diastolic dysfunction, preserved EF
- Post-menopausal status (consider ERT)

Monitoring and Management Options?

Therapeutic Options

To supplement life style, weight control and estrogen

#1. Metformin

#2. DPP-IV inhibitor (‘gliptins’)

#3. GLP-1 mimetics (injectable)

#4. SGLT-2 inhibitors (oral)

#5. Combination 1 and 2

#6. Combination 1 and 3

Management and Monitoring

- Therapeutics
  - Metformin
  - Incretin-mimetic based therapy (LEADER, SUSTAIN-6)
  - SGLT-2 inhibitors (lacks diabetes diagnosis) (Empla-Reg)
- Longitudinal Monitoring
  - Clinical – weight, blood pressure, symptoms
  - Diagnostic – labs (glucose, lipids); insulin sensitivity

Case Two

- 66 y/o male with class III/IV heart failure
- Non-ischemic cardiomyopathy
- Comorbidities treated HTN, type 2 DM, obesity class 2
  - Weight 245 lbs/111 kg; Ht 5'9"; BMI 36.2 kg/m^2
- Laboratory studies
  - A1c 8.8%; CKD-3 (Cr 2.0 mg/dl; eGFR 48 mL/min/1.73 $m^{2)}$; lipids controlled

Diabetes History

- Type 2 diagnoses age 54 yrs, 12 years ago.
  - Co-morbidities: central obesity, HTN, lipids
- Initial management: nutritional and life style
  - Oral hypoglycemic agents begun in the first year
    - Meds progressively advanced for 5 years
- Microvascular complications:
  - Sensory neuropathy, microalbuminuria
- Current management: insulin, wt. adjusted dose 1.6 units/kg

Laboratory Data

Variable	Reference Range	Result
Fasting glucose (mmol/l)	3.89 – 5.56	10.0 (180 mg/dL)
HgbA1c (%)	4.0 – 6.0	8.8
Insulin (µIU/ml)	0 – 20	n/a
HOMA-IR (index)	< 2	(insulin >1.5 unit/kg) Moderate resistance

Cardiology Diagnostics

- Laboratory biomarkers for heart failure increased
  - BNP, NT-proBNP
- Abnormal EKG – cannot r/o inferior infarct
  - Age undetermined anterolateral infarct
- Echo findings
  - LV function is depressed, global hypkinesis, EF 25-29%

Clinical Summary

- Poorly controlled type 2 diabetes with micro- and microvascular complications.
- Advanced, chronic heart failure due to non-ischemic cardiomyopathy
- Insulin resistance

Therapeutic Options, plus insulin

Most oral diabetes agents not indicated (met, tzd, su)

#1. Bariatric Surgery

#2. DPP-IV inhibitor (‘gliptins’)

#3. GLP-1 mimetics (injectable)

#4. SGLT-2 inhibitors (new oral agents)

#5. Combination 2 and 3

#6. Combination 3 and 4

Management and Monitoring

- Therapeutics
  - Many oral agents are contra-indicated or lack evidence
    - Sulfonylureas, metformin, thiazolidinediones
  - Insulin basal-bolus-corrective insulin, goal A1c < 7.5%
  - Combined insulin and metabolic therapeutics
    - Incretin based therapy
    - SGLT-2 inhibitors
- Monitoring – glycemic control, cardiac functional status

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THANK YOU