Atypical cardiomyopathies and implications for pregnancy

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Outline

- Physiology of pregnancy and delivery
- Hypertrophic Cardiomyopathy
- Restrictive Cardiomyopathies
  - Amyloidosis
  - Sarcoidosis
  - Hemochromatosis
  - Scleroderma
  - Endomyocardial Diseases
- Mitochondrial Disease

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Overall pregnancy related risks

- The majority of women are asymptomatic prior to pregnancy
- High risk women often unaware of risks:
  - 50% with a contra-indication to pregnancy
  - 30% at increased or high risk
- Critical importance of pre-pregnancy counseling

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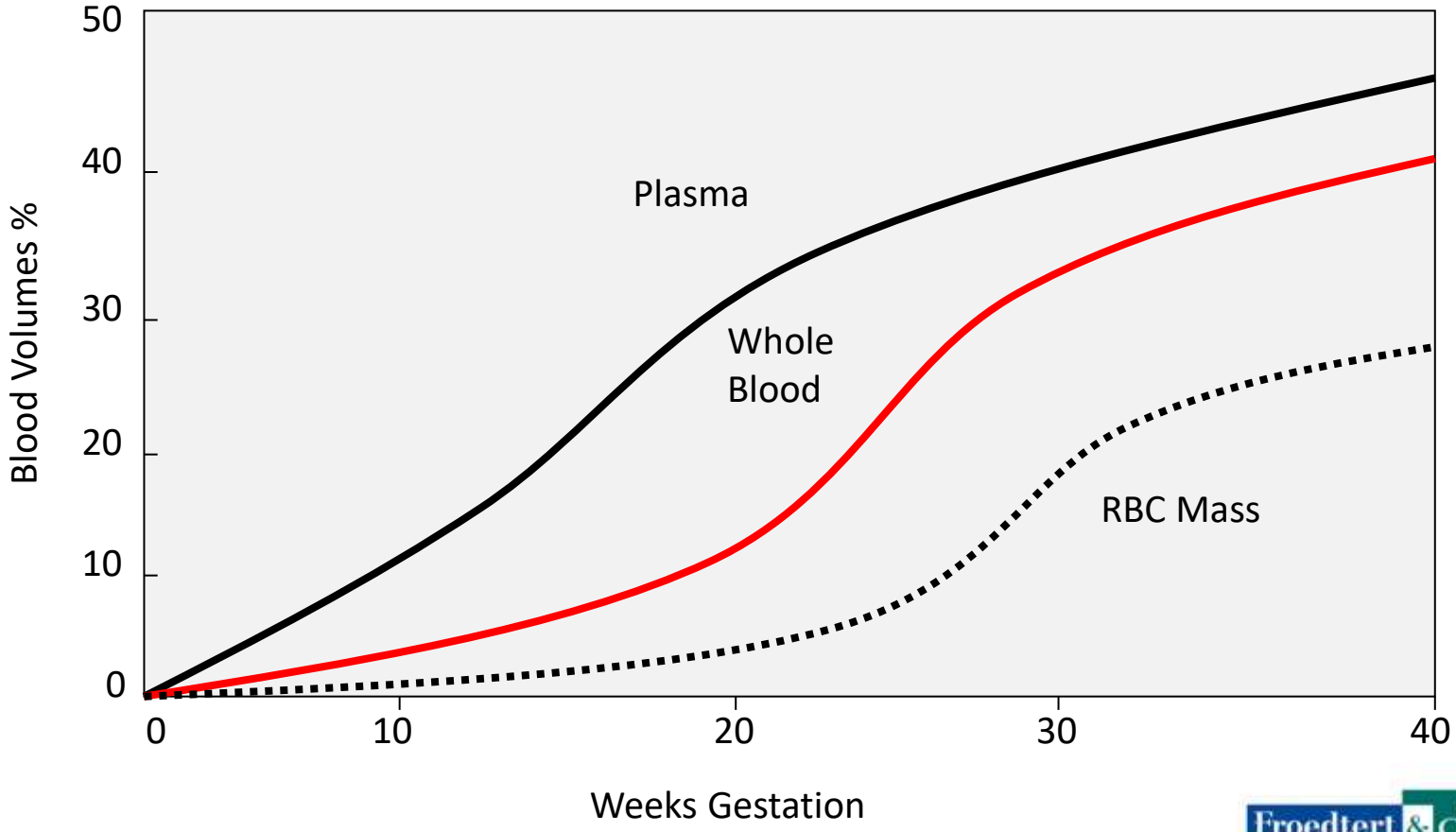
Hemodynamic Changes in Pregnancy



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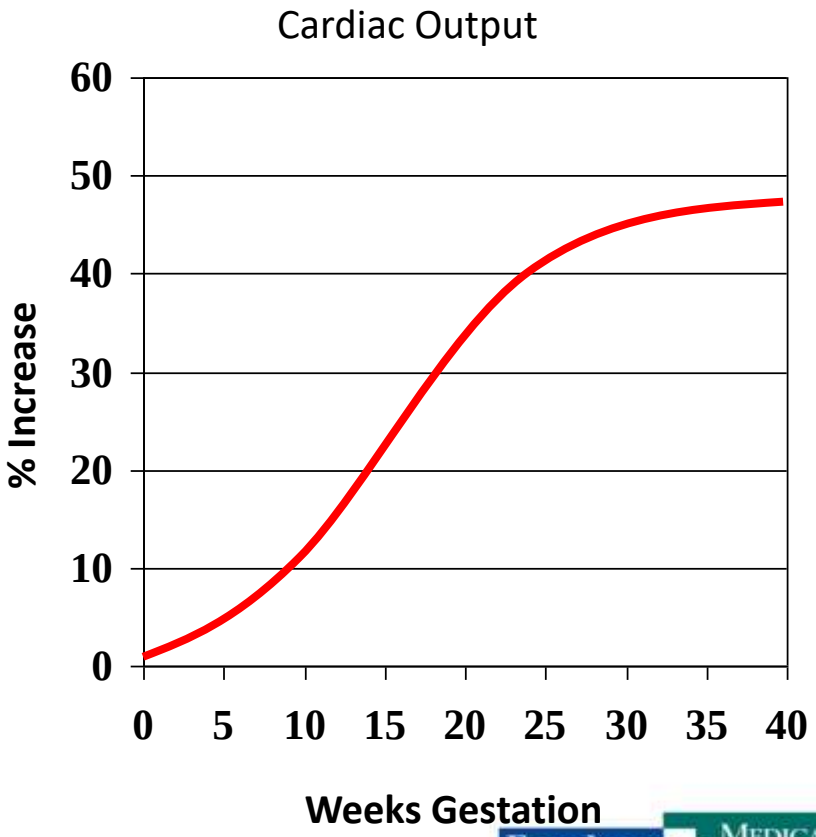
Hemodynamic Changes in Pregnancy

- HR: Increase ~ 10 bpm
- SVR and PVR both decline due to placental maturity
- Widened pulse pressure
- SBP falls though 20th week then normalizes
- Late potential reduction in preload due to caval compression



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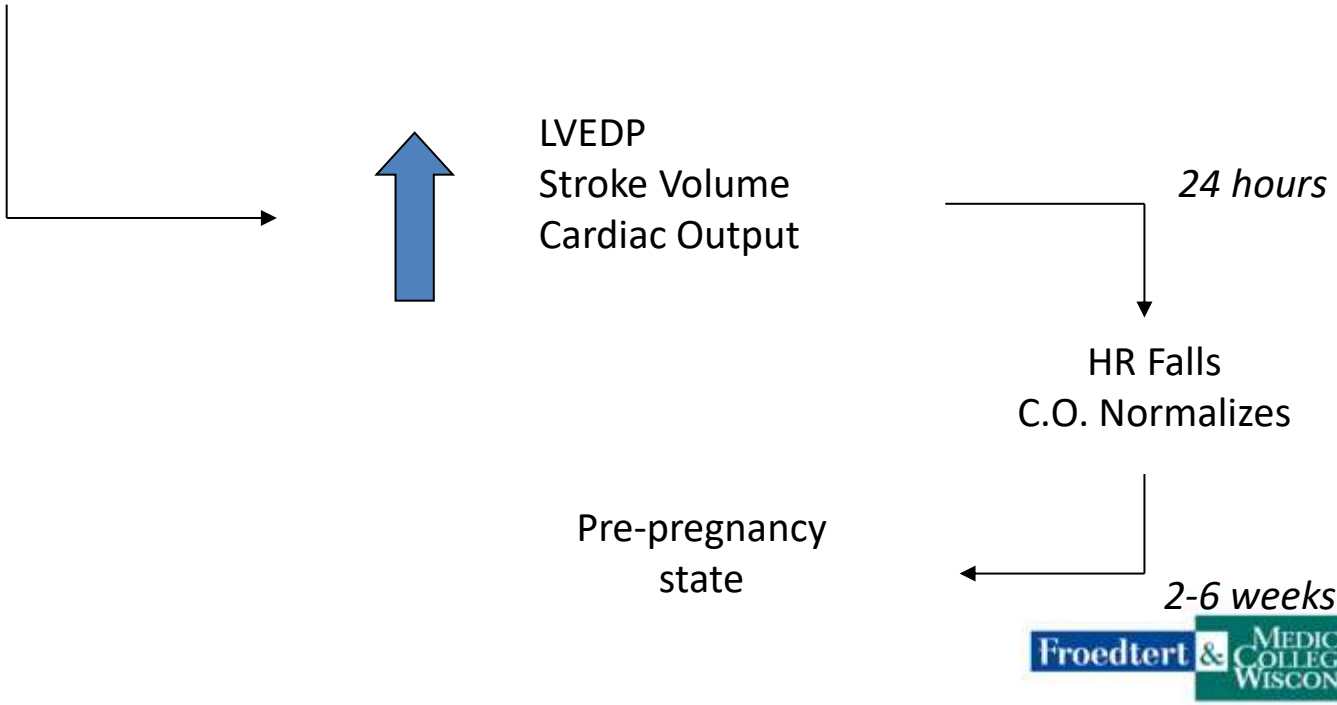
Post Partum Hemodynamic Changes

Increased preload

-Increased venous return (caval decompression)

-Auto-transfusion with uterine contraction



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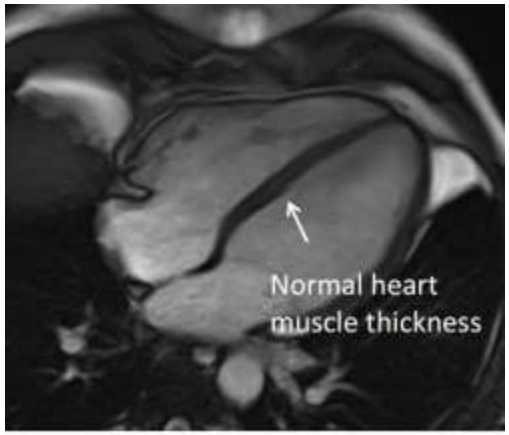
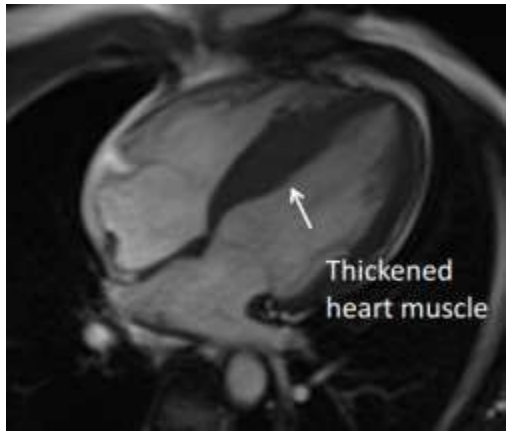
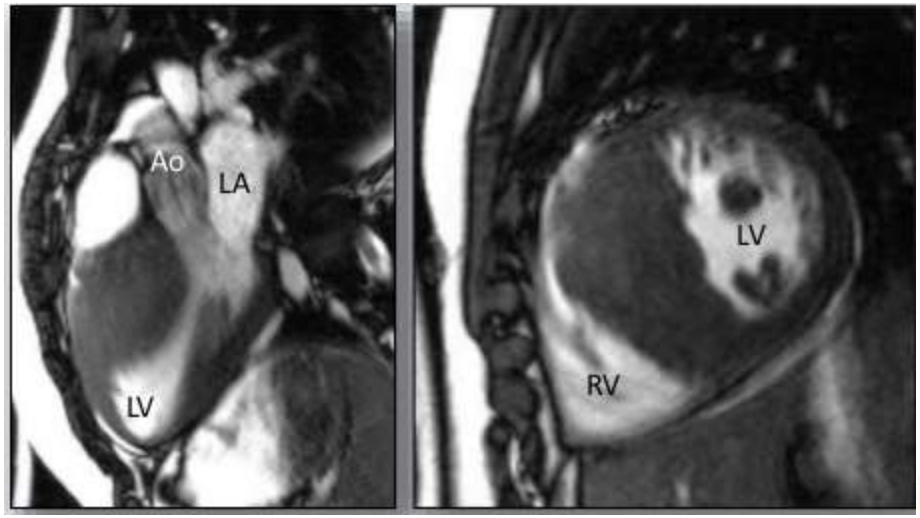
Hypertrophic Cardiomyopathy







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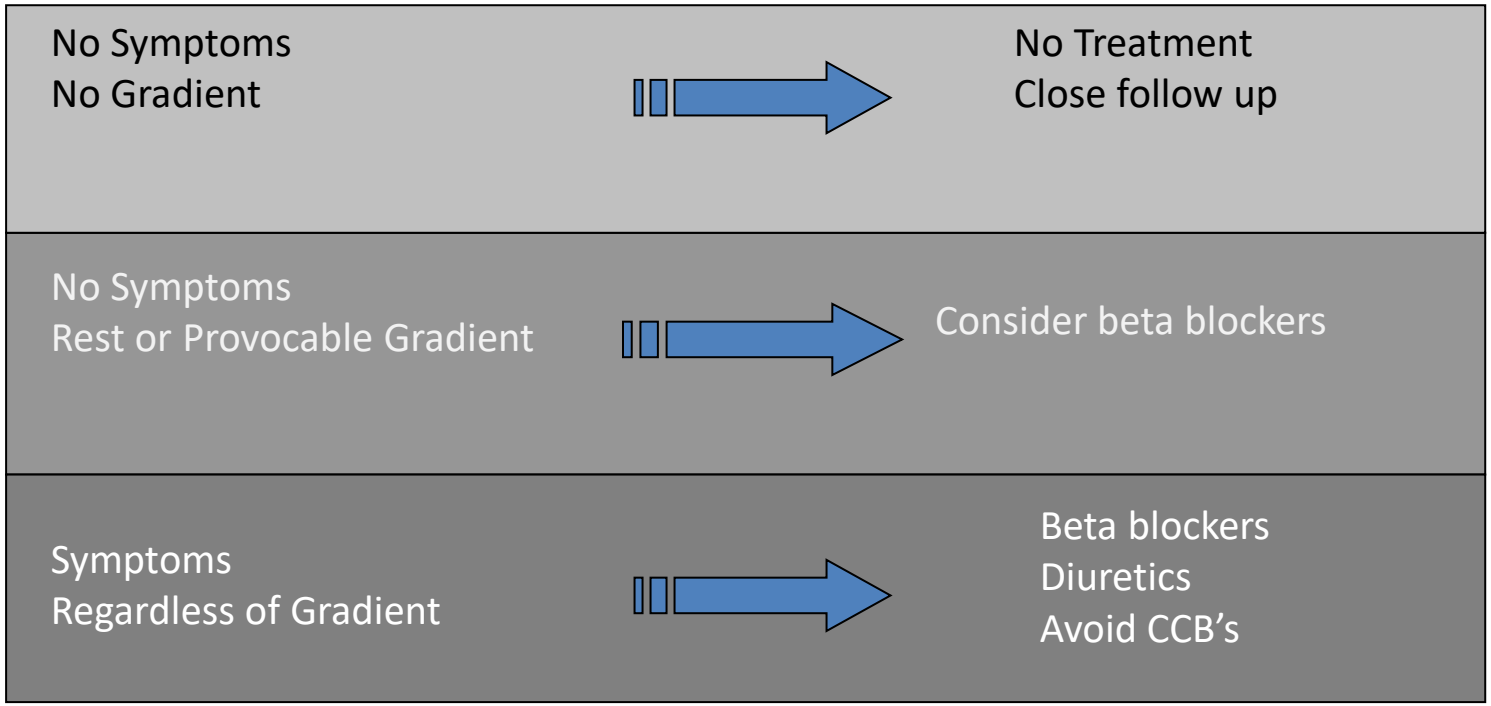
Hypertrophic Cardiomyopathy

- Autosomal Dominant Inheritance
- 1:500 prevalence
- Morphology:
  - Asymmetric hypertrophy most common
  - Non-dilated LV cavity
  - Preserved Systolic Dysfunction
  - Impaired Diastolic Function
  - Resting outflow obstruction in ~ 20%

Pregnancy Related Risks

- Likelihood of symptoms during pregnancy related to symptoms prior to pregnancy
  - Directly related to severity of LVOT gradient (esp. when > 100 mmHg)
  - Antenatal obstruction doubles risk of Sx
- SCD related to severity of LVOT obstruction
  - Highest risk with prior SCD, Sustained VT, Strong Family History
  - Incremental risk with thicker septum (> 30 mm), NSVT and BP drop with exercise

Hypertrophic Cardiomyopathy



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Hypertrophic Cardiomyopathy

- Most patients have no symptoms
- If Sx – exertional chest pain, fatigue, dyspnea, palpitations and syncope
  - DOE most common due to diastolic dysfunction and LVOT obstruction
- ~ 20 % risk or new or worsening CHF symptoms
  - While LVOT obstruction may decrease, MR may worsen and contribute to pulmonary edema
- Pregnancy not felt to alter course of HCM in women

Hypertrophic Cardiomyopathy

- Aggressive screening for ventricular arrhythmias to reduce sudden death

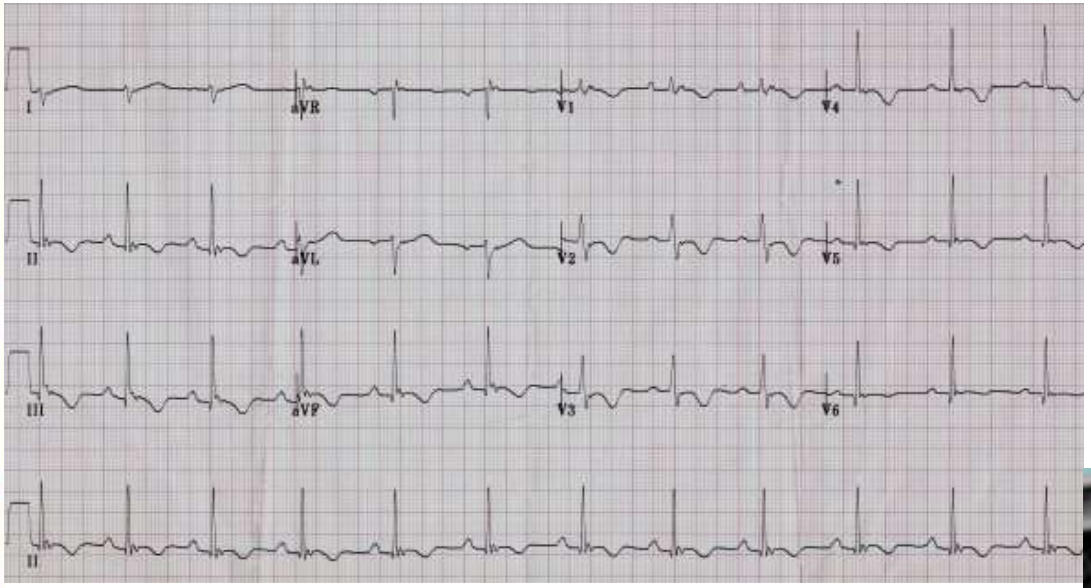
- Medical therapy:
  - Beta blockers > CCB most common (25-33% of Women)
  - Variable approach to continue / stop medical therapy without clinical sequelae

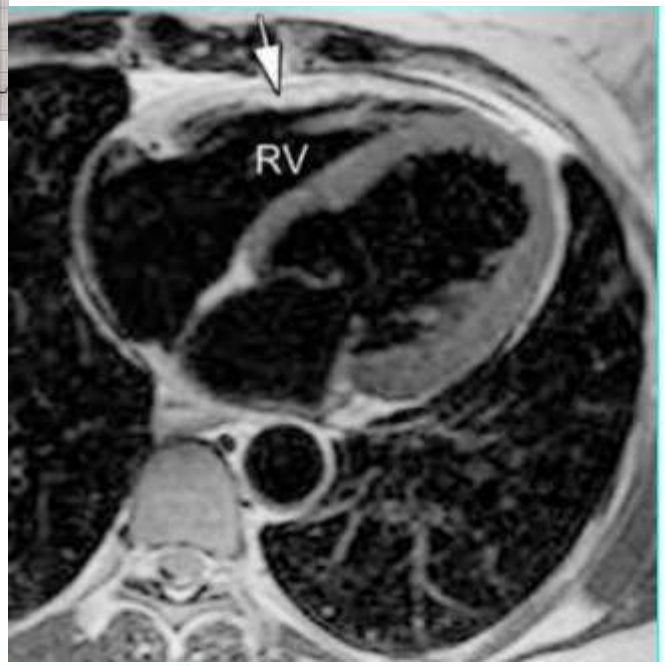
- Maternal Risks:
  - 1% mortality risk (Autore et. al., 2002)
  - 0% mortality risk and 28% risk of Sx (Thaman et. al., 2013)
  - 0% mortality risk (Probst et. al , 2002)

Hemodynamic Changes with Labor and Delivery

- Catecholamine induced tachycardia shortens diastolic filling while Valsalva reduces preload
  - Increased risk of outflow obstruction
  - Exacerbated by blood loss as well
- Delivery desirable at high risk centers
- Beta Blockers useful, caution with diuretics
- Epidural anesthesia and prostaglandins best avoided due to hypotension
- Vaginal delivery preferred, C-section in emergencies

Arrhythmogenic RV Cardiomyopathy





T-wave inversion in V1, V2, and V3 (> 14 y.o.) seen In 4% of healthy women and 1% of men. When present, fairly specific and considered a major diagnostic abnormality in ARVC/D

Arrhythmogenic RV Cardiomyopathy

- Autosomal Dominant, Male predominance
- Fibro-fatty replacement of myocytes in RV, LV or both
- High prevalence of arrhythmias including SCD
- Most often recognized between 2nd and 4th decade of life
- 50% of cases related to mutations in genes encoding proteins of cardiac desmosome

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Arrhythmogenic RV Cardiomyopathy

- Alteration in gap junctions promotes electrical instability
  - However, no anecdotal evidence suggests increased risk with single/multiple pregnancies
  - Estrogen may be partially protective
- ARVD generally well tolerated in pregnancy
  - Limited data historically limited to small case series and case reports

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Hopkins/Dutch Registry

- 26 women with 39 singleton pregnancies >13 weeks (1–4 per woman)
  - NO major OB complications
- Rx included β blockers (n=16), antiarrhythmics (n=6), diuretics (n=3) and implantable cardioverter defibrillators (ICDs) (n=28).
- 5 (13%) had single VA, including two ICD-terminated events.
  - Most arrhythmias occurred in absence of history of VA
- CHF developed in two pregnancies (5%)
  - All had pre-existing biventricular or isolated right ventricular disease
- 3.4 years of follow-up: No maternal cardiac mortality or transplant.
- Neither VA nor HF incidence was significantly increased during pregnancy.
- ARVD/C course (mean 6.5±5.6 years) did not differ based on pregnancy history.

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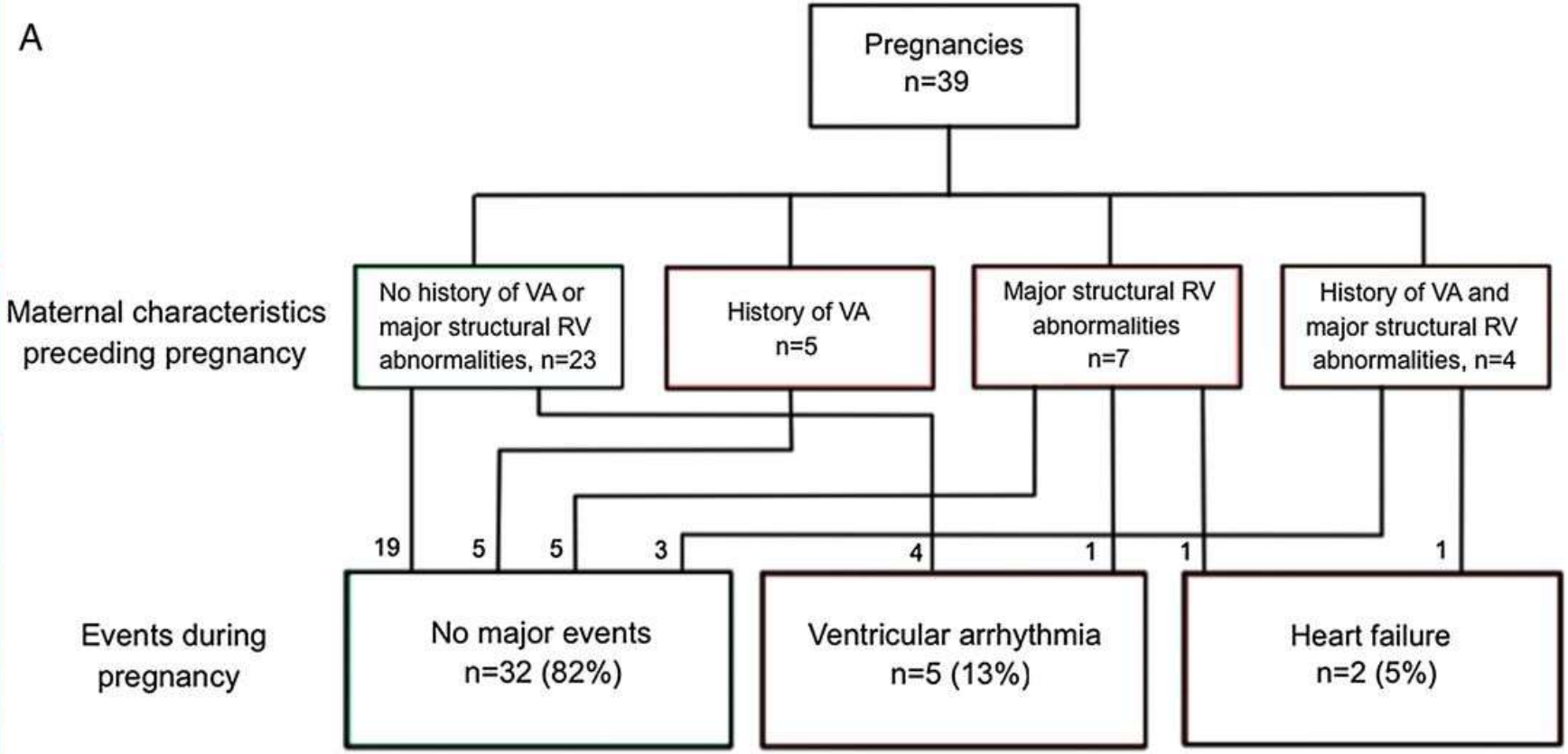
Hodes et. al., BMJ Heart, 2015

ARVC and Pregnancy Outcomes



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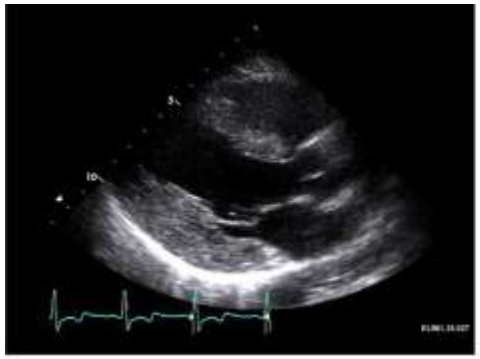
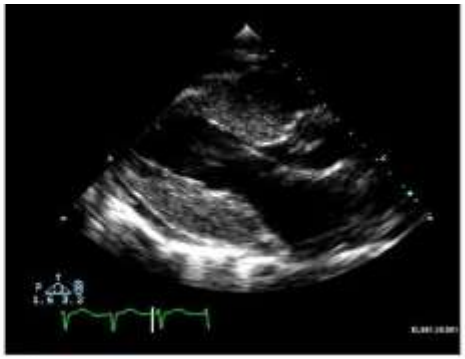
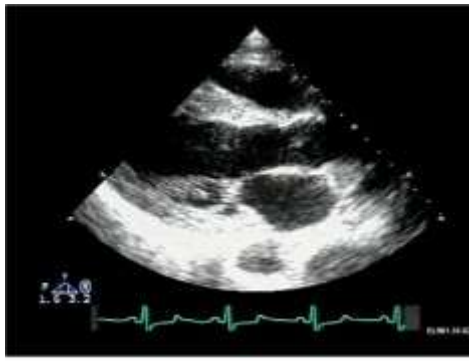
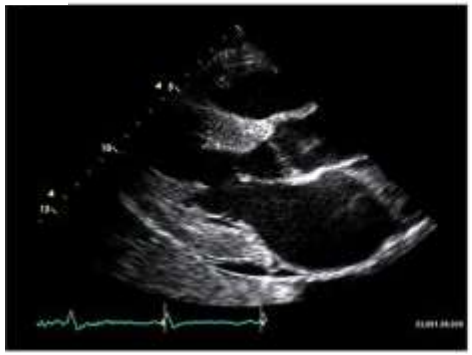
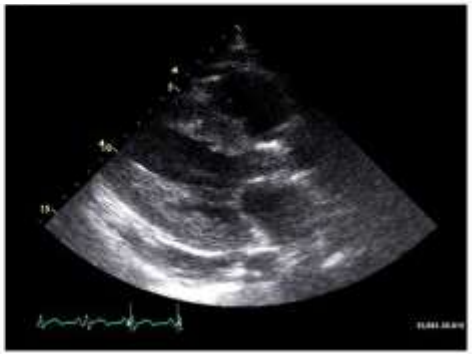
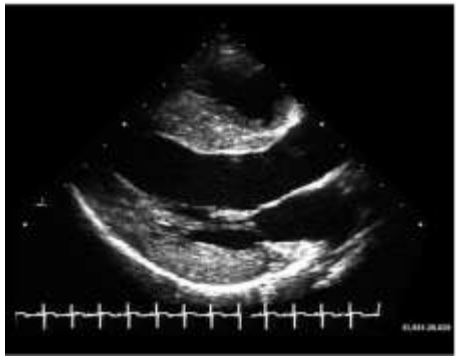
RESTRICTIVE CARDIOMYOPATHIES

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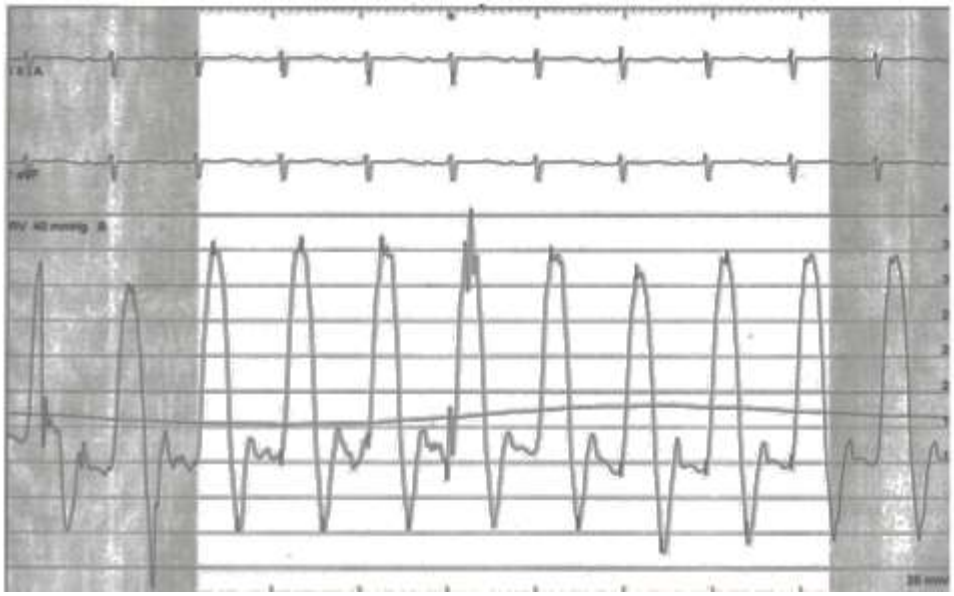
Hemodynamic Commonalities

- Impaired diastolic filling
- Generally preserved LV and RV systolic function
- Elevated diastolic filling pressures
- Intolerance to volume loading



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Restrictive Cardiomyopathies

- Infiltrative (amyloidosis, sarcoidosis)
- Storage (hemochromatosis)
- Non-infiltrative (scleroderma, idiopathic)
- Endomyocardial processes (endomyocardial fibrosis, hypereosinophilic syndrome, carcinoid, radiation, malignancy, anthracycline toxicity)
- Desmin related Cardiomyopathy

Pregnancy Outcomes in RCM

- Anecdotal case reports only:
  - One case of Sarcoid CM diagnosed post partum (uneventful) - late demise of mother with autopsy confirmation of Sarcoid
  - Case report of undiagnosed RCM with successful pregnancy
- No case reports of cardiac amyloidosis and pregnancy
  - Patients with pre-eclampsia do not have elevated levels of serum Amyloid A protein
  - Renal amyloidosis and pregnancy (including FMF) reported with renal progression linked to baseline renal disease

Mitochondrial Disease

- Mitochondria generate adenosine triphosphate (ATP) by oxidative phosphorylation – when impaired….
- Tissues with the highest energy requirement are predominantly affected
  - e.g. deafness, diabetes, proximal myopathy, external ophthalmoplegia, visual loss, gastrointestinal dysmotility, cardiomyopathy, cardiac conduction defects, epilepsy or stroke-like episodes
- Maternal inheritance of mitochondrial DNA

Mitochondrial Disease and CHF

- MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes
  - Cardiac involvement in ~ 38% of cases
- Hypertrophic remodeling early (40-56% of cases) with dilated cardiomyopathy, conduction defects and ventricular pre-excitation late
- Variable prevalence of dilated cardiomyopathy

Medical Management (MELAS)

- Coenzynme Q10 and Carnitine to improve ATP generation and scavenge free radicals
- Avoid beta blockers and statins (inhibit ATPase)
- Cardiac transplant may be an option if limited extra-cardiac manifestations
- Limited pregnancy data available
  - Complications : muscle weakness, WPW syndrome

Conclusions

- Women who often experience cardiac complications are unaware or asymptomatic
- Complications related to HCM related to severity of obstruction and pre-existing Sx
- Restrictive disease high risk due to hemodynamic loading but minimal data
  - Many women are often too ill to conceive
- ARVC generally safe, early identification critical to reduce risk of SCD
- Mitochondrial disease complications more likely theoretical –rhythm issues noted but no HF reported