1

Disclosures

- none

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2

Objectives

- Review the causes of heart failure in pregnancy
- Understand the evaluation and treatment cardiomyopathy in pregnancy
- Know the role of a multi-disciplinary team in the management of pregnant patients with cardiomyopathy

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Outline

- Why is heart failure (HF) in pregnancy important?
- Diagnosis: when to suspect HF in pregnancy
- Etiologies of HF in pregnancy
- Management of HF in pregnancy
  - Delivery considerations
  - Medical management
- Postpartum considerations: Subsequent pregnancies
- Special focus on peripartum/postpartum cardiomyopathy (PPCMP) – unique risk factors, management, and prognosis

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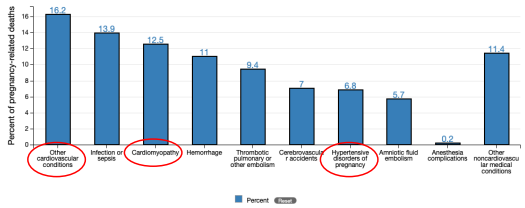
Cardiovascular disease is the leading cause of pregnancy-related death in the US

Causes of pregnancy-related death in the United States: 2016-2018



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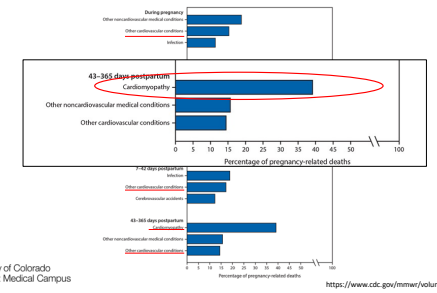
https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pmss.html

5

Timing of pregnancy-related mortality



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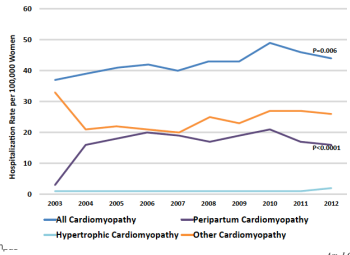
https://www.cdc.gov/mmwr/volumes/68/wr/mm6818e1.htm

6

Cardiomyopathy in pregnancy is increasing in frequency



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Am J Cardiol 2017;119:1694e1700

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Cardiomyopathy is associated with maternal morbidity

TABLE 2 Outcomes of Women With or Without Cardiomyopathy at Delivery and by Cardiomyopathy Subtype

Outcome	CDM (n = 2,078)	No CDM (n = 4,438,439)	p Value
Major adverse cardiac events*	874 (42.1%)	16,344 (0.4%)	<0.001
Mortality (maternal)	17 (0.82%)	291 (0.01%)	<0.001
Heart failure	686 (33.01%)	1,002 (0.02%)	<0.001
Cardiac arrhythmias	248 (11.93%)	13,788 (0.31%)	<0.001
Cerebrovascular events	3 (0.14%)	396 (0.01%)	<0.001
Acute myocardial infarction	26 (1.25%)	115 (0.002%)	<0.001

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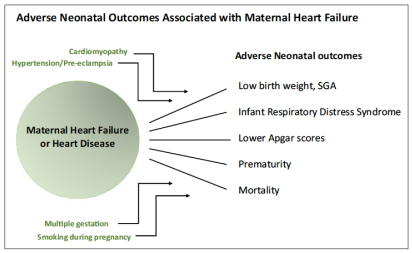
J Am Coll Cardiol HF 2015;3:257–66

8

Maternal cardiomyopathy affects neonatal outcomes



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J Am Heart Assoc. 2021;10:e021019

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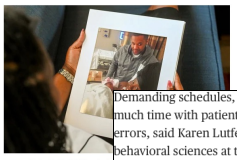
Medical mistakes are more likely in women and minorities

NBC NEWS Jan. 15, 2024, 3:30 AM MST By Liz Szabo | KFF Health News



Charity Watkins holds her daughter

Charity Watkins sensed something was deeply wrong when she experienced exhaustion after her daughter was born.

At times, Watkins, then 30, had to stop on the stairway to catch her breath. Her obstetrician said postpartum depression likely caused the weakness and fatigue. When Watkins, who is Black, complained of a cough, her doctor blamed the flu.

When a physician finally examined Watkins three days later, he [illegible] swollen, a sign that [illegible] he doctor [illegible] on in which the [illegible] en-rich blood to [illegible] eeks in intensive [illegible]

Demanding schedules, which prevent doctors from spending as much time with patients as they'd like, can contribute to diagnostic errors, said Karen Lutfey Spencer, a professor of health and behavioral sciences at the University of Colorado-Denver.

"If they were less certain, they were less likely to take action, such as ordering tests," Spencer said. "If they were less certain, they might just wait to prescribe treatment."

[illegible] ost you."

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Diagnosis – when to suspect HF?

How to tell from normal pregnancy?

- Symptoms
- Vitals/exam
- Risk factors

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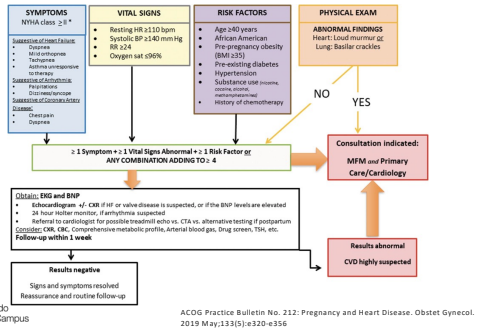

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ACOG Practice Bulletin No. 212: Pregnancy and Heart Disease. Obstet Gynecol. 2019 May;133(5):e320-e356

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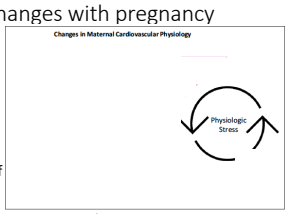
Normal cardiovascular changes with pregnancy

- CV hemodynamic changes in pregnancy
  - Systemic vascular resistance decreases by 20%
  - Heart rate increases by 15-30%
  - Plasma volume increases by 30%
  - Cardiac output increases by 30-50%
- Shifts occur early in second trimester and plateau in 3rd trimester
- During labor and delivery: augmentation of stroke volume, heart rate, and cardiac output (up to 30%)
- Rapid normalization postpartum – most changes within 1st 10 days (especially CO and SVR), normalization by 24 weeks
- Biomarkers (ie: BNP, troponin) remain within normal limits throughout pregnancy, labor/delivery, and postpartum



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Yucel et al. Curr Treat Options Cardio Med 2017;19:73
J Am Heart Assoc. 2021;10:e021019

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Common cardiac symptoms in pregnancy

- Palpitations: "rapid heart beat", "fluttering", or "pounding heart"
  - Increased visceral awareness plus hemodynamic and hormonal changes
  - Most common arrhythmias are isolated PACs and PVCs
- Mild lower extremity edema
  - Usually limited to pedal or ankle area and is dependent/positional
- Dyspnea
  - Mild hyperventilation (due to progesterone)
  - Mild in severity, plateaus or diminishes closer to term
  - Does not significantly alter exercise capacity
- Easy fatigability
  - Does not significantly alter exercise capacity

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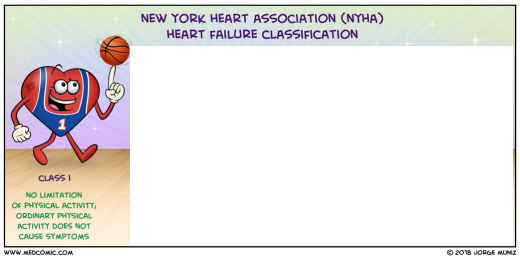
Zeldis. Clin Chest Med 1992;13:567-85

14

Functional assessment: NYHA class



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https://twitter.com/medcomic/status/1488901185062985729/photo/1

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Less common symptoms in normal pregnancy

- Orthopnea
  - Due to upward pressure of uterus on diaphragm
  - Typically worst during later stages of pregnancy and resolve postpartum
- Lightheadedness, syncope
  - Related to uterine venous occlusion or peripheral vasodilatation
- Chest pain
  - Uterine pressure on diaphragm

SYMPTOMS
NYHA class ≥ II *

Suggestive of Heart Failure:
- Dyspnea
- Mild orthopnea
- Tachypnea
- Asthma unresponsive to therapy

Suggestive of Arrhythmia:
- Palpitations
- Dizziness/syncope

Suggestive of Coronary Artery Disease:
- Chest pain
- Dyspnea

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Zeldis. Clin Chest Med 1992;13:567-85
Obstet Gynecol. 2019 May;133(5):e320-e356

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Cardiovascular exam in pregnancy

- Brisk arterial pulse
- JVP more conspicuous but normal pressure
- Soft systolic ejection murmur or venous hum
- Louder heart sounds
- Wider physiologic splitting
- Physiologic S3 common
- Larger PMI and shifted to the left
- Mild pedal or ankle edema

VITAL SIGNS
- Resting HR ≥110 bpm
- Systolic BP ≥140 mm Hg
- RR ≥24
- Oxygen sat ≤96%

PHYSICAL EXAM

ABNORMAL FINDINGS
Heart: Loud murmur or
Lung: Basilar crackles

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Jugular Venous Pressure

Jugular Vein	Carotid Artery

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"Red flag" signs and symptoms

Vitals and labs
- Resting HR >120 bpm
- BP >= 160 mmHg
- Hypoxia
- Elevated BNP
- Elevated troponin

Exam
- Elevated JVP
- S4 gallop
- Loud murmurs
- Lung crackles
- Marked edema (up to or past the knees)

Symptoms
- Severe dyspnea (esp at rest)
- Chest pain (exertional)
- Syncope

- **Persistence or worsening of pregnancy signs or symptoms in the post partum period**

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ACOG Practice Bulletin No. 212: Pregnancy and Heart Disease. Obstet Gynecol. 2019 May;133(5):e320-e356

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Risk factors for CVD

RISK FACTORS
Age ≥40 years
African American
Pre-pregnancy obesity (BMI ≥35)
Pre-existing diabetes
Hypertension
Substance use *(nicotine, cocaine, alcohol, methamphetamines)*
History of chemotherapy

- Black race [1,2]
  - Higher rates of mortality (OR 1.45), MI (OR 1.23), PPCMP (OR 1.71)
  - PPCMP: more severe LV dysfunction at presentation and lower rates of LV recovery
- HTN, incl HDP [3]
  - Subclinical CVD even in otherwise normal pregnancies
  - Pre-existing CVD: 30% of patients develop HF with HDP
  - PPCMP patients are 4X more likely to have preeclampsia as compared to general population

(1) J Am Heart Assoc. 2021;10:e017832
(2) J Am Coll Cardiol 2015;66:905–14
(3) Heart 2014;100:231–238

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Initial diagnostic evaluation

- EKG
- Echocardiogram
- Labs: BNP (can consider CMP, drug screen, troponin)
- Cardiology or CardioOB and MFM referral

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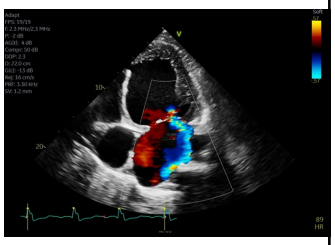
Example patient

- 32yo female G5P4004 currently at 36 weeks gestation, presenting with dyspnea
- Vitals: comfortable, afebrile, BP 100/70, HR 110, PaO2 99% RA
- Exam: JVP 15cm, tachy/regular with soft S4 gallop, systolic murmur at apex, lungs clear, gravid abdomen, 2+ LE edema to the thighs
- Echo: LVEF 25%, LVEDD 6.5 cm, normal RV, severe central MR, PASP 50-55 Hg
- Now what?



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Management of Acute Heart Failure during Pregnancy

Acute heart failure during pregnancy

- **Cardiovascular challenges during delivery**
  - Positional hypotension
  - Increased cardiac output
  - Blood loss
  - Volume administration
- **Multidisciplinary team recommended**
  - Cardiology: CardioOB, Heart Failure, Interventional,
  - CT surgery
  - MFM (or High-risk Obstetrics)
  - Anesthesia: Cardiac and Obstetric
  - Critical care
  - Neonatology

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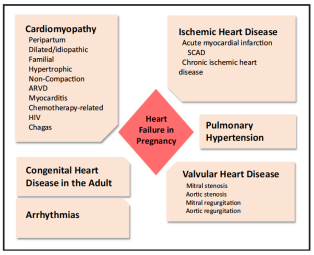
Broad DDx for Heart Failure Symptoms in Pregnancy



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J Am Heart Assoc. 2021;10:e021019

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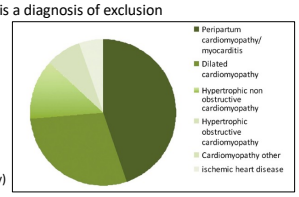
Causes of cardiomyopathy in pregnancy

PPCMP: Idiopathic LV dysfunction (LVEF <45%) with or without LV dilatation presenting in the last month of pregnancy or in the months following delivery

- Most common CMP in pregnancy, but is a diagnosis of exclusion

- Differential diagnosis:
  - Hypertensive heart disease: preeclampsia, gestational HTN
  - Ischemic heart disease: SCAD, ASCVD
  - Pre-existing cardiomyopathy: genetic/familial, idiopathic, congenital
  - Acute myocarditis
  - Stress-induced cardiomyopathy
  - Heritable systemic disease: metabolic (mitochondrial disease), muscular dystrophy carrier (dystrophinopathy, myotonic dystrophy)



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Heart 2014;100:231–238.

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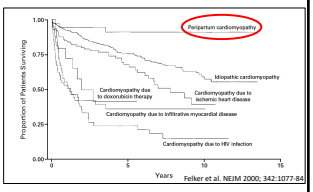
PPCMP is unique

- PPCMP with highest rates of survival compared to other forms of HF (1)
- Most recovery within 3-6 months (2)
- Delayed recovery can occur even up to 2 years – by then 83% recover (3)

Adverse predictors for recovery: (4)

- Severe LV dysfunction (LVEF <30%)
- Black or African descent



Breastfeeding has not been proven to be detrimental to recovery (2)

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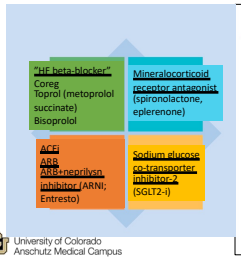
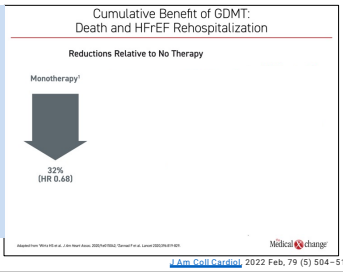
(1) Cooper. J Cardiac Fail 2012;18:28-33
(2) McNamara. J Am Coll Cardiol 2015;905-14
(3) Pillarisetti. J Am Coll Cardiol 2014;63:2831–9
(4) Davis. J Am Coll Cardiol 2020;75:207–21

26

Guideline Directed Medical Therapy (GDMT) for Cardiomyopathy: "Quad therapy"





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J Am Coll Cardiol. 2022 Feb, 79 (5) 504–510

27

Can you still use GDMT in pregnancy or lactation?

Medication[1]	During Pregnancy	During lactation
Beta-blocker - metoprolol succinate, carvedilol	Yes	Yes
ACEi/ARB	Avoid	Enalapril, captopril
ARNI (Entresto)	Avoid	No human data
Mineralocorticoid receptor antagonist	Spironolactone (not preferred)	Spironolactone
SGLT2i	No human data	No human data
Hydralazine/nitrates	Yes	Yes
Loop diuretics	Yes	Yes
Digoxin	Yes	Yes

Anticoagulation

- Treat for LVEF <40% **AND** systemic thromboembolism (LV thrombus, DVT, PE, CVA) or another indication for anticoagulation (ie: afib)
- May consider for LVEF <40% during pregnancy and up to 8 weeks postpartum
- Heparins safe in pregnancy and lactation. Coumadin safe in lactation.

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(1) Davis. J Am Coll Cardiol 2020;75:207–21
(2) Regitz-Zagrosek. Eur Heart J (2018) 39, 3165–3241

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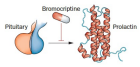
Bromocriptine: Targeted treatment for PPCMP?

- Bromocriptine: ergot derivative that inhibits prolactin secretion
- Prolactin levels are elevated in late pregnancy to promote lactation
  - May be myotoxic and contribute to cardiomyopathy
- 2018 ESC Guidelines CVD during Pregnancy[2]: Consider bromocriptine for severe PPCMP treatment (Level IIB, Evidence B)
  - Pilot/registry data and small RCT suggestive of benefit in LV recovery in PPCMP
  - Considerations: Effect of background HF GDMT; no placebo control; different population (Black participants – 1-2% in bromocriptine studies)
- Other bromocriptine risks: thromboembolic risk, lactation-suppressant
- Bromocriptine is considered experimental for PPMCP in US/Canada
- **REBIRTH** (**R**andomized **E**valuation of **Br**omocriptine **I**n Myocardial **R**ecovery **TH**erapy)
  - Inclusion criteria: new or recurrent PPCMP with EF =<40% (remote visits feasible)
  - Bromocriptine vs placebo with prophylactic anticoagulation and HF GDMT
  - Observational breastfeeding cohort



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CV risk for subsequent pregnancy

WHO 2-3 depending on individual

- Mild left ventricular impairment
- Hypertrophic cardiomyopathy
- Native or tissue valvular heart disease not considered WHO 4
- Marfan syndrome without aortic dilatation
- Heart transplantation

Table 4 Conditions in which pregnancy risk is WHO 4

- Pulmonary arterial hypertension of any cause
- Severe systemic ventricular dysfunction
  - NYHA III–IV or LVEF <30%
- Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
- Severe left heart obstruction
- Marfan syndrome with aorta dilated >40 mm

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

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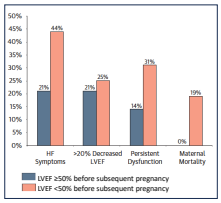
Subsequent pregnancy after PPCMP

- Pre-pregnancy LVEF is the best predictor of relapse with subsequent pregnancy
- Patients with persistent LV dysfunction (EF <50%) [1]
  - 1) Higher risk of further decline in LVEF
  - 2) Lower likelihood of recovery
  - 3) Higher rates of maternal mortality
- Normalization of LV function does **not guarantee** an uncomplicated subsequent pregnancy [2]
  - Limited HF GDMT use in pregnancy
- Long term mortality and risk of adverse cardiac outcomes high after subsequent pregnancy, regardless of LV recovery [3]
- If considering another pregnancy after PPCMP:
  - Preconception counseling with cardioOB and MFM



(1) JACC 2014;64(15):1629-36
(2) J Heart Lung Transplant 2023;42:e1–e42
(3) J Am Coll Cardiol 2023;82:16–26

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The Rise of Cardio-Obstetrics

- CU CardioOB: Multidisciplinary subspecialty dedicated to the pregnancy-related care of patients with CVD
- Clinical care: Multidisciplinary cardiac care team
  - Cardiology
    - Amber Khanna, MD: Adult Congenital Heart Disease
    - Alexis Tumolo, MD: Electrophysiology
    - Josephine Chou: General cardiology and heart failure
  - Maternal Fetal Medicine
    - Shannon Son, MD
    - Allison Faucett, MD
  - OB Anesthesia
    - Cristina Wood, MD
  - Cardiology and MFM nursing (Renee Julien, Lindsey French-Stewart)
- Education
- Research

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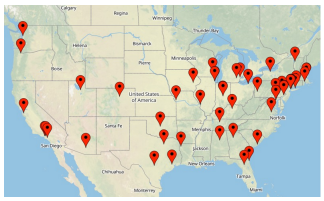
REBIRTH

- New PPCMP with EF <40%
- CU coordinator: Emanual.gebreab@cuanschutz.edu
- CU Site PI: Josephine.chou@cuanschutz.edu

National REBIRTH sites



https://peripartumcmnetwork.pitt.edu

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Conclusions

- Heart failure is a leading cause of pregnancy-related morbidity and mortality
- PPCMP is the most common form of cardiomyopathy diagnosed pregnancy
- Recognition of heart failure symptoms in pregnancy and postpartum is critical to early diagnosis and treatment
- Acute heart failure in pregnancy management is complex, and a multi-disciplinary team approach to care including Cardio-Obstetrics is highly recommended
- Ongoing education and research can hopefully help optimize treatments for pregnant patients HF and CVD

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Case 2 - JM

- 42yo Caucasian female presenting with chest pain, progressive LE edema to the upper thighs, PND, orthopnea, and dyspnea (now SOB at rest)
- PMHx: G1P0 – currently 39 weeks GA
- Vitals: afebrile, HR 110s, RR 20, BP 110/60, PaO2 97% on 2L NC
- PE: NAD, tachy but regular with loud S3 gallop, bibasilar crackles, gravid/firm, 4+ pitting edema to upper thighs
- Labs: Cr 0.8, NT-pro BNP 3,245, troponin <0.01, UA no protein
- CXR: pulmonary edema with pleural effusion
- EKG: sinus tachycardia without ST changes
- Echo: EF 30% with global hypokinesis, non-dilated LV, normal RV size/function, no valvular abnormalities, no pericardial effusion

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Case 2 - JM

- Gentle diuresis peripartum
- Underwent induction of labor with epidural, successful vacuum assisted vaginal delivery
- Transferred to CCU postpartum – continued diuresis, started on heart failure medications and bromocriptine with coumadin
- Coronary angiogram and cardiac MRI unremarkable
- Discharged on hospital day 7
- Regular heart failure cardiology follow up postpartum - last EF 48% with preserved RV function

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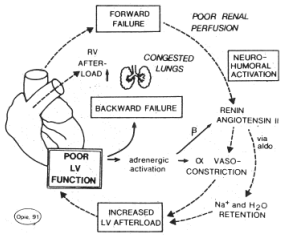
Pathophysiology of heart failure and GDMT



HF Guideline Directed Medical Therapy (GDMT) or "Quad Therapy"

- Beta-blockade
  - Carvedilol (Coreg)
  - Metoprolol succinate (Toprol-XL)
  - Bisoprolol
- Renin-angiotensin system inhibition
  - ACE-inhibitors (ACEi)
  - Angiotensin-receptor blocker (ARB)
  - ARB + neprilysin inhibitor (ARNI) - Entresto
- Aldosterone antagonism
  - Spironolactone or Eplerenone
- SGLT2i (sodium glucose transport inhibition)
  - Empagliflozin or Dapagliflozin

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HF GDMT in PPCMP: Registry data

	IMP % (n = 82)	NIMP % (n = 14)	Full recovery % (n = 45)
Beta-blockers	95 (n = 78)	50 (n = 7)	93 (n = 42)
ACE Inhib or ARB	93 (n = 76)	71 (n = 10)	91 (n = 41)
ACE Inhib	84 (n = 69)	64 (n = 9)	80 (n = 36)
ARB	11 (n = 9)	8 (n = 1)	14 (n = 6)
MRA	65 (n = 53)	57 (n = 8)	56 (n = 25)
Diuretics	76 (n = 62)	86 (n = 12)	65 (n = 29)
Digitalis	5 (n = 4)	21 (n = 3)	4 (n = 2)

Haghikia et al. Basic Res Cardiol 2013;108:366

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Patient TB

- 32yo female with history of cardiomyopathy, currently at 36 weeks gestation, presenting with dyspnea
- PMHx: 4 prior term pregnancies
  - G1 and G2: term vaginal delivery, uncomplicated
  - G3: Term SVD uncomplicated. Admitted with SOB 3 days postpartum, LVEF 45% -> recovered spontaneously without meds by 1 mo PP. Diagnosed with recovered PPCMP.
  - G4: Limited prenatal and cardiology care. LVEF 60% at 30wk GA. Term SVD (declined f/u echo). Readmitted 1 week PP with SOB, LVEF 35%. Coronary CTA and CMRI unrevealing. Started on Toprol and enalapril with recovery of LVEF to 50% by 6 mo PP. Declined birth control. Lost to follow up.
  - G5: No prenatal or cardiology care. Off all GDMT.
- Social Hx: Intermittent tobacco and EtOH use. Intermittently homeless. Domestic violence victim. All children in foster care.

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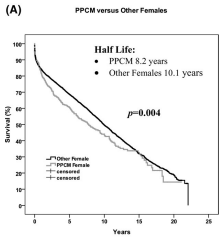
Advanced HF therapies in PPCMP

- Durable MCS in PPCMP (INTERMACS) [1]
  - Overall "good" survival: 85% at 1 year, 68% at 3 years
  - Low recovery rates (~6%)
  - 48% transplanted by 3 years
- Heart transplant after PPCMP [2]
  - Lower graft survival with PPCMP as indication for transplant

All options for recovery should be exhausted in PPCMP before undertaking advanced therapies



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Circ Heart Fail 2014;7:300-9
JHLT 2012;31:180-6

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Patient TB follow up

- Hospital course
  - Diuresed with IV Lasix with symptomatic improvement
  - Restarted Toprol
  - Deemed not a candidate for advanced HF therapies due to social factors
- Subsequent pregnancy care
  - Underwent induction of labor with early epidural with successful unassisted vaginal delivery of baby boy (immediate child protective custody)
  - Initially agreed to tubal ligation -> declined at last minute -> Nexplanon placed
  - Started Entresto; declined bromocriptine/anticoagulation
- 3mo PP: LVEF 30% with LVEDD 6.0 cm. Declined ICD.

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PPCMP basics

- Definition: Idiopathic cardiomyopathy with LV dysfunction (LVEF <45%) with or without LV dilatation presenting in the last month of pregnancy or in the months following delivery
- Incidence in the US 1:3000 (African Americans – 1:1500)
- Risk factors: multi-fetal gestation, hypertension, African or African-American race
- Etiology: multifactorial – placental and hormonal anti-angiogenic factors, pregnancy-related inflammation, and genetic factors

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