

# Under Pressure

The Cardio-Obstetric Implications of Hypertension in Pregnancy

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# Disclosures

I have no financial disclosures.

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# Overview

- Case Review
- Scope of the hypertensive disorders of pregnancy
- Approach to antenatal hypertension
- Preeclampsia and the heart
- Management of postpartum hypertension
- Future cardiovascular care and risk

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# Objectives

- Understand the diagnosis and management of hypertensive disorders of pregnancy
- Identify cardiac complications of preeclampsia with use of echocardiography and biomarkers
- Improve the approach to and management of postpartum hypertension

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# What is Cardio-Obstetrics?

- A village!
- Coordinated Cardio-Obstetric clinics decrease adverse cardiac complications in pregnancy
- Members of the team vary based on complexity of underlying cardiac condition
- Opportunities for discussion of:
  - Pregnancy risk
  - Optimization of cardiac health
  - Medication management
  - Surveillance needed in pregnancy & PP
  - Delivery planning
  - Contraception



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## Case Review

- 40 yo African-American P3013
- OB History:
  - 2000 SAB – D&C
  - 2002 Term PLTCS for NRFHT, FGR
  - 2010 Term RLTCs, elective
  - 2014 Term VBAC
- PMH: No known CVD, cHTN, DM, hyperlipidemia. Former smoker.
- PSH: As above
- FamHx: Mother w HTN, CHF

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## Case Review

- 2002 Pregnancy – complicated by FGR, no BP issues
- 2010 Pregnancy – uncomplicated prenatal course, elective RLTCs
  - Presented POD8 with SOB x2-3d, worsening peripheral edema
  - BP 124-168/77-86
  - TTE mild LV dysfunction, LVEF 50-55%
  - NT-proBNP 401, AST 46, ALT 49, nl Cr & CBC
  - Received IV Lasix w improvement in edema & symptoms – no HF meds given
- 2014 Pregnancy – uncomplicated, no BP issues or volume overload

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## Case Review

- Now presents to you at 23w5d with spontaneous pregnancy, new FOB
  - Referring provider notes indicate h/o peripartum cardiomyopathy
  - Denies cardiac symptoms, no limitations to activity (?mild increased SOB), no orthopnea, no edema
  - Taking low dose ASA
- Next steps as the consultant:
  - Do you agree with her presumptive diagnosis?
  - How will you stratify her pregnancy risk?
  - What will you recommend for pregnancy surveillance?

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## Hypertensive Disorders of Pregnancy



### Spectrum of disease

Preeclampsia (and related disorders)  
 Gestational hypertension  
 Chronic hypertension  
 Chronic hypertension with superimposed preeclampsia



### Other rarer disorders:

Pheochromocytoma, thyroid/parathyroid, drugs,  
 AFLP, TTP/HUS, lupus, APLAS  
 Not the scope of this talk

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## Epidemiology

- 2-8% of pregnancies worldwide are complicated by preeclampsia
  - 1% develop HDP postpartum
- 16% of maternal deaths in developed countries attributed to HDP
  - 15-20% of maternal deaths are attributed to cardiovascular disease!
- 6-7x increased risk of severe preeclampsia compared to 1980
- 2012 cost estimates in the USA: \$2.18 billion
  - Within the first 12 months of delivery
  - \$1.03 billion for mothers; \$1.15 billion for infants

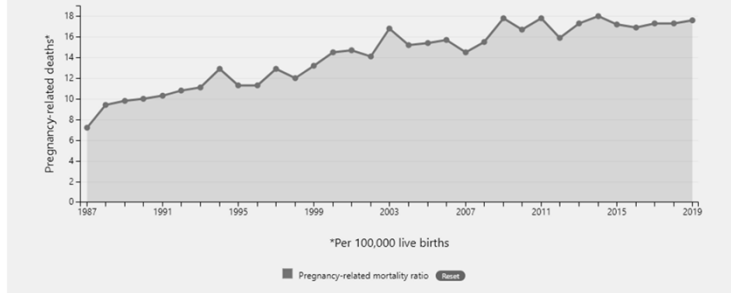
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# Why Does This Matter?

- The USA is the only developed country with **INCREASING** maternal mortality
- For every maternal death, there are 84 women who suffer a severe complication

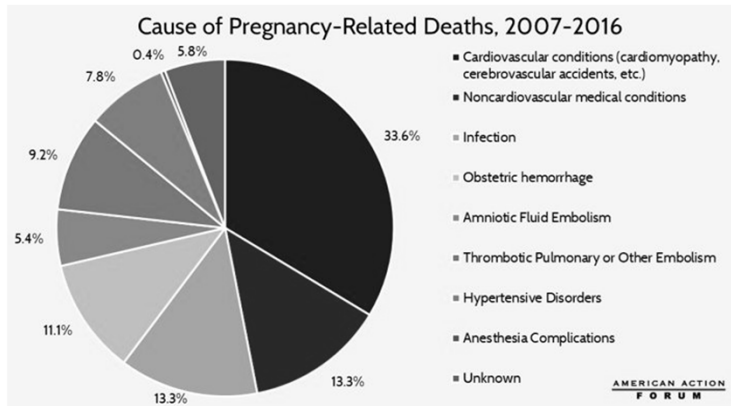
Trends in pregnancy-related mortality ratios in the United States: 1987-2019



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# Maternal Mortality

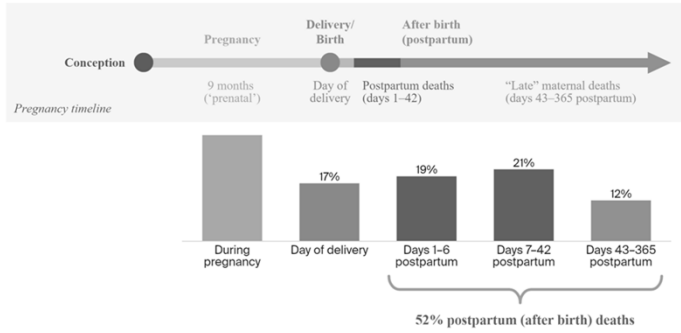
- Cardiovascular disease is the leading cause of maternal death
- Women of color are disproportionately likely to die



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# When does maternal mortality occur?

Exhibit 2  
Timing of U.S. Maternal and Pregnancy-Related Deaths, 2011–2015

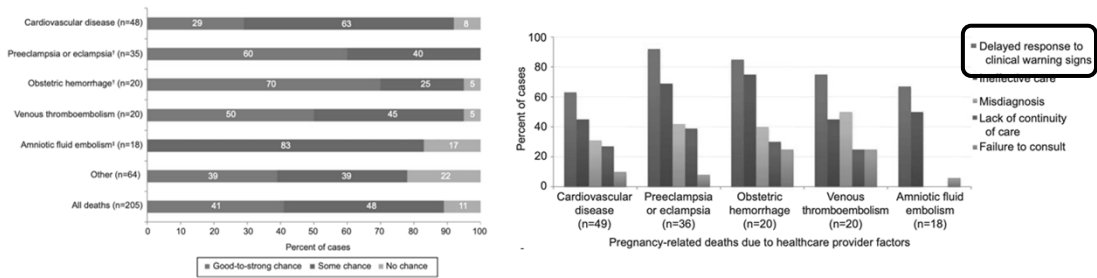


Data: Centers for Disease Control and Prevention Pregnancy-Related Mortality Surveillance data from: Emily E. Petersen et al., "Vital Signs: Pregnancy-Related Deaths, United States, 2011–2015, and Strategies for Prevention, 13 States, 2013–2017," *Morbidity and Mortality Weekly Report* 68, no. 18 (May 10, 2019): 423–29.  
Source: Roosa Tikkanen et al., *Maternal Mortality and Maternity Care in the United States Compared to 10 Other Developed Countries* (Commonwealth Fund, Nov. 2020). <https://doi.org/10.26099/411v-9255>



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# Preventable Deaths in Obstetrics



Main et al. "Pregnancy-related mortality in California." *Obstet Gynecol* 2015;125:938–47



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# Timing & Preventability of Cardiovascular-Related Maternal Death

- 2023 Publication from France
- Maternal mortality ratio 1.4/100,000 births from cardiac or vascular disease
  - >2/3 of deaths in pregnant people with no known condition before acute event
- 61% of cardiac deaths were preventable
  - Main preventability factors:
    - KNOWN cardiac disease: lack of multidisciplinary prepregnancy/prenatal care
    - UNKNOWN cardiac disease: inadequate prehospital evaluation of acute event (particularly investigation of dyspnea)
- 47% of vascular deaths were preventable
  - Main preventability factor: wrong/delayed diagnosis, mgmt of acute chest/abd pain in a pregnant person



Diguisto C, et al. Timing and preventability of cardiovascular-related maternal death. Obstet Gynecol 2023.

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# Red Flag Symptoms in CVOB

- Symptoms may overlap with pregnancy
  - "Pregnancy" should be the diagnosis of exclusion
- Red Flag Symptoms should prompt further evaluation
  - Biomarkers
  - Imaging
  - Rhythm monitoring
  - Subspecialty consultation

## Peripartum Red Flag Signs and Symptoms

Chest Pain	Tachycardia
Dyspnea	Non-Vagal Syncope
Orthopnea	Headache
Cough	Visual Changes
Edema	Hypotension/Hypertension

Patients and clinicians need to be aware of signs and symptoms that may signal cardiovascular complications during and after pregnancy.



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# Risk Stratification - mWHO

**TABLE 3 Modified WHO Risk Stratification Model**

Modified WHO Class	Conditions	Predicted Risk, %
I—No higher risk than the general population	Uncomplicated, small or mild lesions including pulmonary stenosis, VSD, PDA, and mitral valve prolapse with no more than trivial mitral regurgitation Successfully repaired simple lesions including ostium secundum ASD, VSD, PDA, and TAPVD Isolated PVCs and PACs	2.5-5
II—Small increased risk of maternal morbidity and mortality	Unoperated ASD Repaired tetralogy of Fallot Most arrhythmias Coarctation of the aorta without significant gradient or aneurysm (repaired or unrepaired) Long QT syndrome	5.7-10.5
II to III	Mild LV impairment Hypertrophic cardiomyopathy Marfan syndrome without aortic dilation Heart transplant Native or tissue valve disease not considered WHO class IV Bicuspid aortic valve without aortic dilatation	10-19

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III—Significant risk of maternal morbidity and mortality	Mechanical valve Systemic RV Post-Fontan operation Cyanotic heart disease Other complex congenital heart repair Aortic dilation without known fibrinogen disease Coarctation of the aorta with residual gradient or aneurysm (repaired or unrepaired) Marfan syndrome with aortic root dilation <45 mm or following aortic replacement Bicuspid aortic valve with aortic root dilation 45 to 50 mm	19-27
IV—Pregnancy contraindicated	Pulmonary arterial hypertension of any cause Severe left ventricular dysfunction (LVEF <30% or NYHA functional class III to IV) Previous peripartum cardiomyopathy with any residual impairment of LV function Severe left heart obstruction (AVA <1 cm <sup>2</sup> or peak gradient >50 mm Hg; MVA <1.5 cm <sup>2</sup> ) Marfan syndrome with aortic dilation >45 mm Bicuspid aortic valve with aortic dilation >50 mm	40-100

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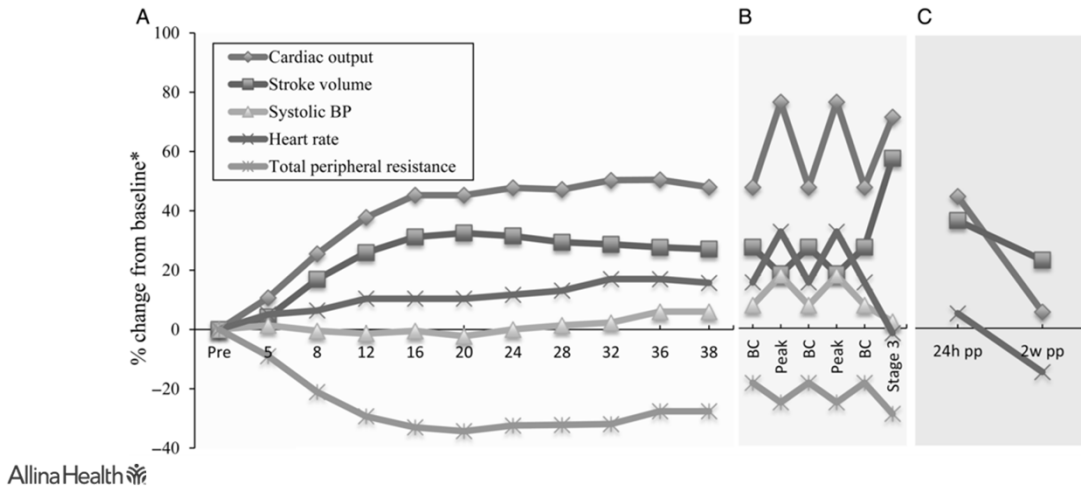
# Antenatal Hypertension

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**Pregnancy is a stress test for the heart**

- Exacerbates underlying conditions
- Unmasks hearts predisposed to future CV disease



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**Diagnostic Criteria - Preeclampsia**

- Hypertension: BP  $\geq 140/90$  at least 4h apart after 20 weeks' GA
  - BP  $\geq 160/110$  confirmed over short interval (sustained >15 minutes)

PLUS

- Proteinuria (urine PCR >0.3, 24h urine >300mg)

OR

- Thrombocytopenia
- Renal insufficiency
- Transaminitis
- Pulmonary Edema

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## Risk Factors for Preeclampsia

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Nulliparity

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Advanced maternal age

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Assisted reproductive technology

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Multifetal gestation

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History of preeclampsia

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Chronic hypertension

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Diabetes – pre-gestational or gestational

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Renal disease

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Thrombophilia, APLAS

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Lupus

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Obesity, OSA

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## What about Chronic HTN?

- Hypertension present before pregnancy or 20 weeks' GA
  - New diagnostic criteria from the ACC & AHA – 4 categories
  - 11% will have baseline proteinuria (>300 mg/day)
- 20-50% will develop superimposed pre-eclampsia
  - Usually earlier onset, more severe, worse prognosis
  - Challenging to diagnose

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## Chronic HTN with Superimposed Preeclampsia

- Diagnostic criteria are lacking
  - Sudden increase in BP
  - Sudden increase in proteinuria
  - New thrombocytopenia or transaminitis
  - Elevated uric acid
  - Symptoms of pre-eclampsia
- When in doubt, ask for another opinion!
  - Never hurts to ask a colleague or admit for BP monitoring/close observation

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## Management of Acute Hypertension

- Medications
  - Magnesium Sulfate for seizure prophylaxis in those with severe features
- Antihypertensives in acute management of severe HTN
  - PO nifedipine
  - IV Labetalol
  - IV Hydralazine
  - Consider ICU transfer for nicardipine/esmolol drip in those with refractory severe hypertension

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# When to Deliver?

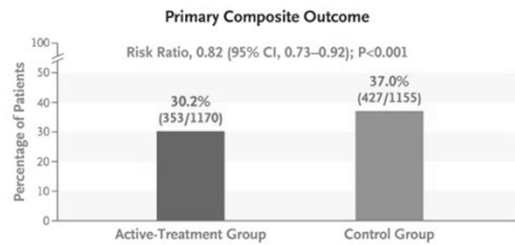
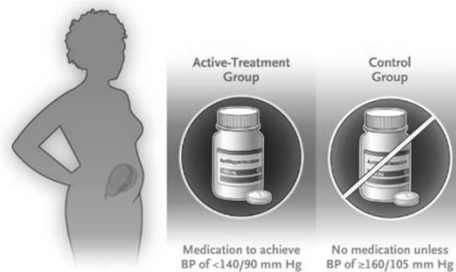
- Maternal
  - Refractory HTN
  - Persistent neurologic sx or abdominal pain non-responsive to pain medication
  - HELLP syndrome
  - Eclampsia
  - End organ damage: stroke, MI, worsening renal fxn, pulm edema
  - Placental abruption
  
- Fetal
  - NRFHT
  - IUFD
  - Reversed UA Dopplers



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# CHAP Trial

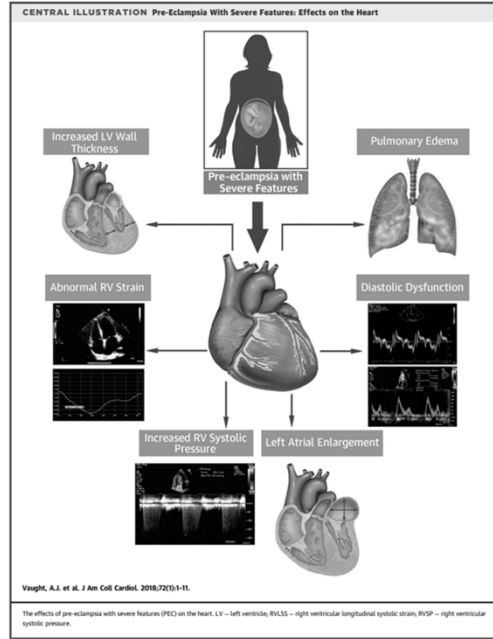
- Chronic Hypertension and Pregnancy
- 2408 women with mild cHTN were randomized
- NNT for goal BP <140/90 (instead of <160/110) = 14-15 to prevent 1 major adverse pregnancy event
  - Preeclampsia w severe features, medically indicated PTB, abruption, or fetal/neonatal death
  - No increase in SGA



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# Preeclampsia and Heart Failure

- State of volume overload
  - Excessive afterload --> diastolic dysfunction
- Diastolic dysfunction leads to heart failure with preserved ejection fraction (HFpEF)
  - Leads to LV remodeling
  - Increased peripheral vascular resistance
  - 10% pulmonary edema
- Preeclampsia precipitates HF in 30% of pts with preexisting cardiac dz



# The Value of Routine Echo in Severe Preeclampsia

- Study of 356 patients with severe preeclampsia – 145 had TTE
  - Excluded if high suspicion for cardiomyopathy or heart failure
  - Decision for TTE was at provider discretion
- Patients who got TTE had:
  - Increased LOS (5d vs 4d)
  - Higher rates of diuretic administration (6.2% vs 0.5%)
  - Increased antihypertensive titration (13.8% vs 2.8%)
  - Higher rate of readmission (6.2% vs 0.5%)
- 14% of TTEs were abnormal
  - LV hypertrophy
  - Pulmonary hypertension
  - Pericardial effusion
  - Enlarged atrial size
  - Did not impact antihypertensive titration or readmission but a/w diuretics and longer LOS
- Authors admit unconscious selection bias

Versus  
Peripartum  
Cardiomyopathy

Nonischemic cardiomyopathy with LVEF <45%	By definition, has no other identifiable etiology Affects 1:1000 live births
Most common complications: pulmonary edema, arrhythmia, sudden death	20% risk of recurrence in subsequent pregnancy 5-10% risk of death or transplant within 1 year of pregnancy

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## Cardiac Biomarkers in Pregnancy

- B-type Natriuretic Peptide (BNP)
  - Mildly elevated in normal pregnancy
  - Can be used longitudinally – usually stable
  - BNP ≤100 pg/mL has NPV >95% for identifying cardiac events in pregnancy
- NT-proBNP
  - Pro-peptide
  - Marker of myocardial stress
  - NOT just a marker of heart failure
- High sensitivity Troponin
  - Marker of myocardial injury

**CENTRAL ILLUSTRATION** The Utilization of Cardiac Biomarkers During Pregnancy: Suggestions for Clinical Practice

BNP and NT-proBNP	Troponins
<ul style="list-style-type: none"> <li>✗ Routinely measure</li> <li>✓ With clinical concern for heart failure</li> <li>✓ Consider at baseline and serially in patients at risk for heart failure*</li> <li>✓ Consider lower threshold in obese individuals</li> </ul>	<ul style="list-style-type: none"> <li>✗ Routinely measure</li> <li>✓ If concerns for ischemia or pulmonary embolism</li> <li>✓ At index diagnosis of peripartum cardiomyopathy</li> </ul>

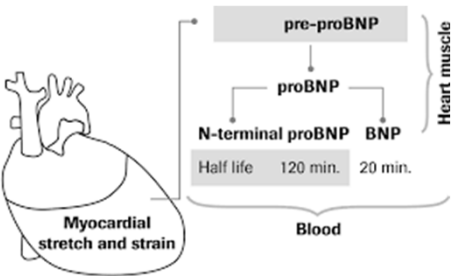
\*Inclusive of congenital heart disease, cardiomyopathy, significant valvular heart disease

Sarma AA, et al. JACC Adv. 2022;1(3):100064.


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## N-terminal pro-BNP



- NT-proBNP <128 pg/mL is normal
- NT-proBNP >200 pg/mL is seen in preeclampsia
  - Specificity 91%, NPV 95% predicting HF/preeclampsia
- NT-proBNP >300 pg/mL is associated with cardiomyopathy
- Higher levels of NT-proBNP a/w worse outcomes in PPCM
  - Particularly if >1000 pg/mL
- Should not be used as a sole marker of pathology
  - Limitation: long half life

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### Natriuretic peptides (BNP & NT-proBNP)

May be elevated in many clinical scenarios

- Heart failure
- ACS
- Heart muscle disease
- Pericardial disease
- Valvular disease
- Atrial fibrillation
- Pulmonary hypertension
- Myocarditis
- Cardiac surgery
- Congenital heart disease
- Cardioversion/ablation
- Advancing age
- Anemia
- Pulmonary embolism
- Sleep apnea
- Critical illness
- Sepsis
- Burns
- Toxic/metabolic insults
- Renal failure

Adapted from Dr. James Januzzi, MHIF Grand Rounds, 2/20/23

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# Natriuretic Peptides in Pregnancy

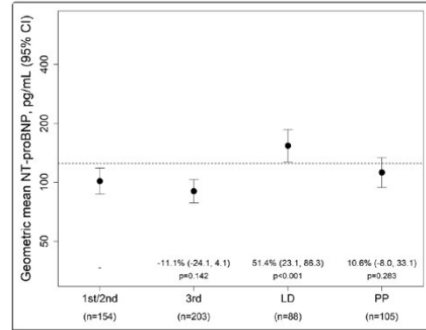


Table 2. Trimester-specific reference intervals

Biomarker	Trimester	Median (pg/mL)	Lower reference limit (pg/mL)	Upper reference limit (pg/mL)	Suggested reference interval (pg/mL)
NT-pro BNP	First	68.8	24.6 (21.5-28.2)	187.6 (182.0-200.6)	<200
	Second	68.0	20.1 (17.7-23.5)	191.9 (165.6-198.2)	
	Third	40.6	12.6 (9.6-16.2)	155.1 (142.1-171.0)	<150
BNP	First	16.5	<10	47.0 (40.8-51.8)	<50
	Second	17.1		50.9 (47.1-59.8)	
	Third	12.2		51.5 (41.9-65.7)	



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# Differentiating Heart Failure in Pregnancy

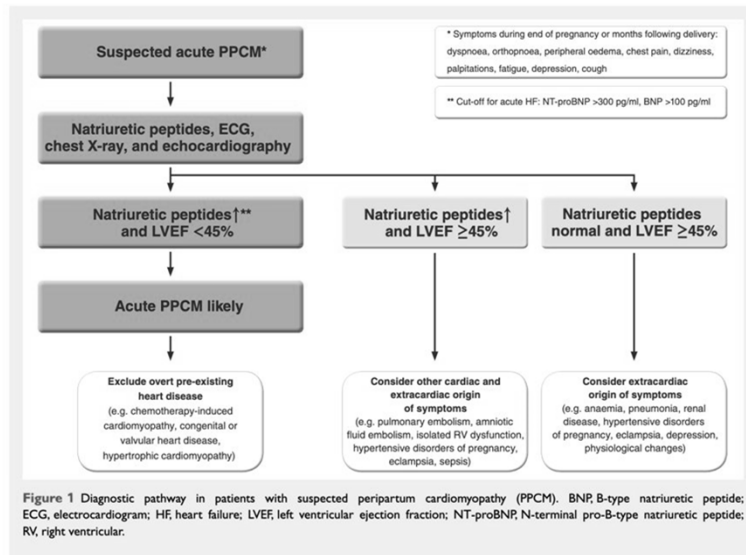


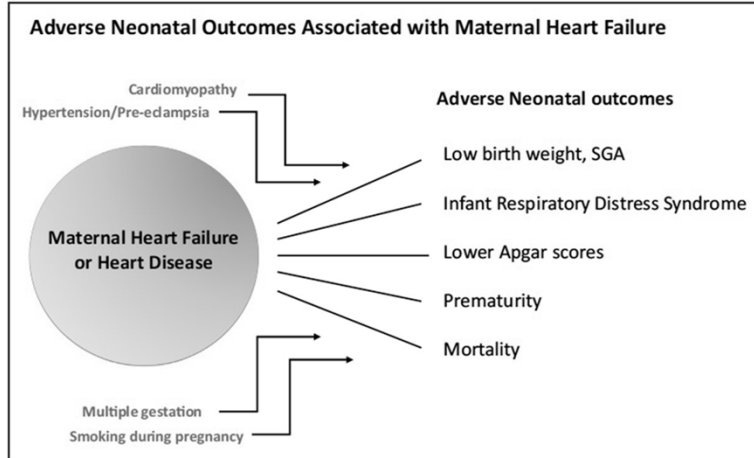
Figure 1 Diagnostic pathway in patients with suspected peripartum cardiomyopathy (PPCM). BNP, B-type natriuretic peptide; ECG, electrocardiogram; HF, heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RV, right ventricular.

Bauersachs J et al, ESC position statement on peripartum cardiomyopathy, 2019



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# Neonatal Outcomes



Bright RA, et al. Maternal heart failure. J Am Heart Assoc 2021



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# Postpartum Hypertension

Preeclampsia & hypertension are often associated with readmission

BP  $\geq 140/90$  mmHg within 24h of discharge is associated with readmission (aOR 1.98, 95% CI 1.37-2.87)

2 or more elevated BP values further increases odds (aOR 3.14, 95% CI 2.33-4.24)

Majority of women are readmitted 5-7d postpartum



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## Postpartum Hypertension – Our Approach

### Biomarkers for patients with preeclampsia and clinical signs of volume overload

- Excessive edema, SOB, palpitations, decreased UOP, early onset preeclampsia
- BNP or NT-proBNP

### Diuretic use for preeclampsia with severe features

- Agent & duration based on BNP/NT-proBNP level
- HCTZ – if BNP 50-100 or NT-proBNP 150-200
- Furosemide – if BNP >100 or NT-proBNP >200

### Evaluation for cardiomyopathy if significantly elevated biomarkers

- Maternal echo for BNP or NT-proBNP >300

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## Postpartum Hypertension – Our Approach

### Aggressive BP meds

- If >140/90 -- 1 long acting agent to target BP within 6-24h
- If >160/110 -- 2 long acting agents to target BP within 24h

### Antihypertensive agents typically used:

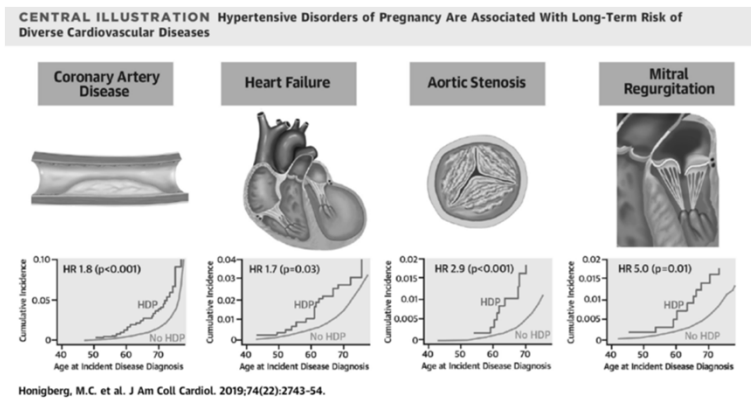
- Nifedipine ER (start 30mg QD, max 120mg/24h)
- Labetalol (start 200mg BID, max 2400mg/24h)
- Enalapril (start 5-10mg BID, max 40mg/24h)
  - Preferred for patients with known renal disease, diabetes
- Hydralazine (start 10mg Q6h, max 300mg/24h)
- Atenolol (start 50mg QD, max 100mg/24h)

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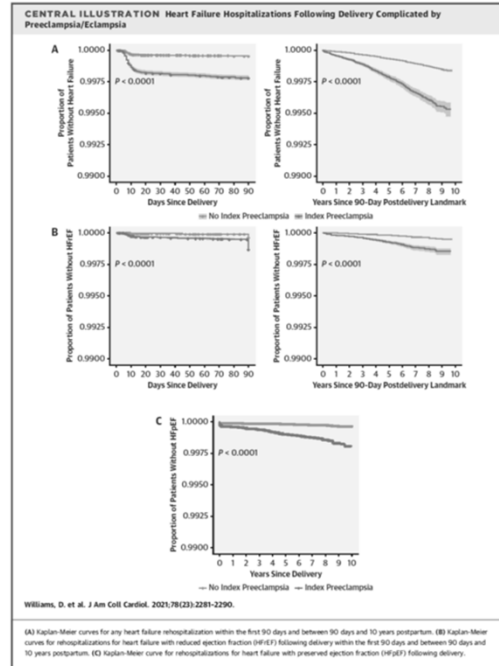
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# Future Cardiovascular Implications

## HDP as a Window to Cardiovascular Health



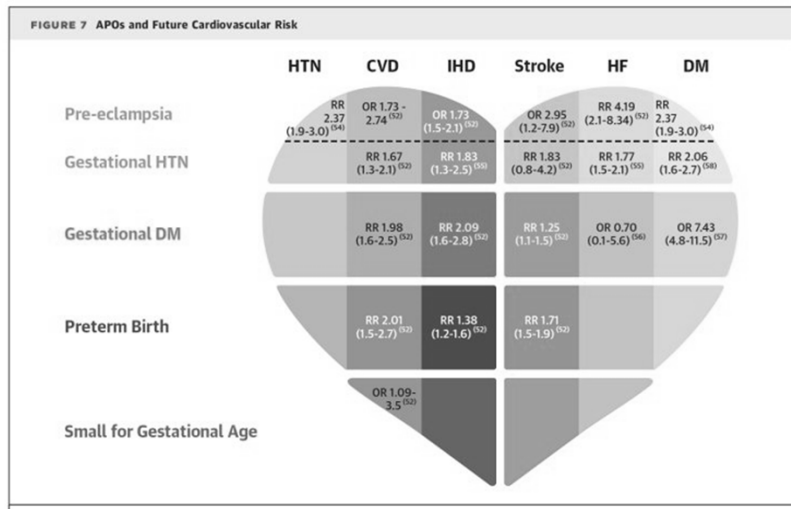
# Preeclampsia and Future Heart Failure



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# Future Cardiovascular Health



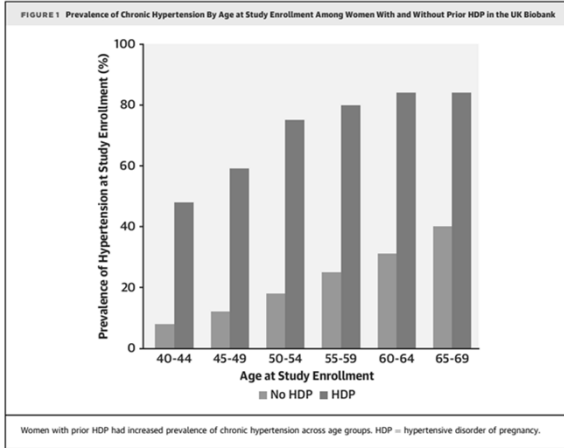
JACC Focus Seminar 2021

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## Future Cardiovascular Health

- HDPs are associated with accelerated cardiovascular aging
  - Substantially increased risk of future cHTN
- Multiple adverse perinatal outcomes have future cardiovascular ramifications
- OBs & MFMs have a critical role
  - Patients should be counseled for annual BP check, lipid screening, diabetic screening



Honigberg et al, 2019



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## Return to Our Case

- 2<sup>nd</sup> Trimester TTE:
  - LVEF 55-60%, normal LV function and size, no wall motion abnormalities. RV normal size/function.
- Baseline preeclampsia labs: Unremarkable
  - No baseline NT-proBNP indicated
- On low dose ASA with plan for routine BP checks in prenatal visits, home BP checks if >130/80
  - Growth US at 32 weeks
  - Weekly fetal testing at 32 weeks
  - Delivery at 39 weeks



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## Case Review – Delivery Recommendations

- Delivery timing: 39 weeks' gestation
- Mode of delivery: Vaginal delivery is recommended with c-section reserved for usual obstetric indications. Pt desires VBAC and will discuss further with the primary OB.
- Anesthesia: Per patient/provider preference
- IVF: No maintenance IVF in labor and recommend strict I/O to maintain euvolemia. Bolus IVF (250-500cc) only if hypotension, allow to drink to thirst during labor
- Location of delivery: Cleared for local delivery with primary OB
- Labs: proBNP if there is recurrent preeclampsia or volume overload, with Lasix or repeat TTE per usual protocol
- Postpartum BP should be <130/80 for discharge for at least 24h
- Postpartum follow up: Recommended within 1-2 weeks' of delivery for routine CVOB patients. Should have a BP check within 3-5 days of discharge for high risk of CHF.
- Annual PCP F/U for cardiovascular screening (lipids, A1c, BP). Reviewed healthy weight/diet

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## Summary

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Cardiovascular disease, including hypertensive disorders, is the leading cause of maternal morbidity and mortality

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Treatment of mild antenatal chronic hypertension improves adverse perinatal outcomes

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Biomarkers and echocardiography are the mainstay for evaluation of heart failure symptoms in pregnancy

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Aggressive management of postpartum hypertension prevents readmission and adverse outcomes

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Preeclampsia leads to cardiac remodeling and predisposes to future cardiovascular disease

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# Thank You!

Questions?

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## References/Resources

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