Cardiac Challenges during Pregnancy: PPH, DVT & PE

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There are several cardiopulmonary physiologic changes with pregnancy

- Minute ventilation increases by 50% at term.
- Increases in blood volume that lead to increased stroke volume.
- Afterload is reduced
- Cardiac output is augmented
- Both the LV and the RV exhibit hypertrophic growth

At the time of delivery,

- Pain increases in heart rate, blood pressure and myocardial oxygen consumption.
- Vagal responses may also occur and lead to hypotension
- With each uterine contraction, about 500ml blood is pushed into the maternal circulation.
- After delivery, autotransfusion from the uterine circulation and increased venous return from the relief of inferior vena cave pressure cause large fluid shifts to the maternal circulation.

- **Right ventricular volume overload occurs easily**
- **Maternal death is most likely to occur in the postpartum period**

Pulmonary Hypertension in pregnancy is deadly…

- Normally, pulmonary vascular resistance (PVR) decreases to allow for these changes, an accommodation that is not possible in patients with PH.
- As afterload increases from the higher PVR, the right ventricle cannot handle the increased cardiac output and begins to fail.
- Sudden death from dysrhythmia may occur.

Pulmonary hypertension affects small number of pregnancies

However, mortality is very high…

- Recent studies indicate a decline in mortality to around 25%
- Patients in the IPAH group showing the most improvement(17%),

- As soon as a diagnosis of PH is made, patients should be followed with regular assessment of RV function with TTE.
- If dysfunction is detected, early delivery is recommended.
- Caesarean section is preferred mode of delivery
- Spinal or epidural anesthesia is preferred
- Use of oxytocin is without apparent haemodynamic consequence.
- However, oxytocin can cause systemic vasodilatation and low dose infusion has been associated with an acute rise in PVR and fall in cardiac output.

Fluid Management

- Both hypovolemia and hypervolemia can have detrimental effects.

- During delivery, hypotension may develop from the several medications includinig oxytocin, pulmonary vasodilator drugs, inotropes (dobutamine) and analgetics.

Inotropic Augmentation of RV Myocardial Function…

- Dobutamine has favorable pulmonary vascular effects at lower doses, although it leads to increased PVR, tachycardia, and systemic hypotension at higher doses
- Dopamine may increase tachyarrhythmias and is not recommended in the setting of cardiogenic shock.
- Vasopressin preferentially increases systemic vascular resistance without increasing PVR and is a viable option
- Phosphodiesterase (PDE)-3 inhibitors, Milrinone is frequently used, and nebulized milrinone has less systemic hypotension and V/Q mismatch
- Levosimendan, a calcium-sensitizing agent with inodilatory effects, holds promise

Chronic therapy is aimed at reducing PVR…

- In patients who are in WHO functional class (FC) IV or have evidence of severe right ventricular (RV) impairment, parenteral prostaglandins are recommended.
- In select patients with more preserved RV function inhaled prostaglandins iloprost may be considered.
- Oral phosphodiesterase 5 inhibitor sildenafil may be considered in patients who are in WHO FC I or II and who have normal RV function

- Parenteral prostaglandins can be combined with sildenafil

- For patients meeting strict criteria for vasodilator-response and no RV dysfunction, calcium channel blocker therapy may be continued in pregnancy, with close follow-up for deterioration (CB).

- The currently available endothelin receptor blockers and soluble guanylate cyclase stimulator are pregnancy category X and should **not** be used in pregnancy.
- If a PAH patient who is taking one or more of these medications becomes pregnant, their use should be immediately discontinued (CB).

- At the time of delivery, iv prostaglandins may be considered

- At the time of delivery, patients require close monitoring, with a central venous catheter, an arterial line

- Anticoagulation has equivocal results for IPAH
- If a PAH patient has been receiving anticoagulation therapy before pregnancy, the risks and benefits of this therapy should be reevaluated
- New oral anticoagulants are currently not recommended for PAH or chronic thromboembolic PH

VTE & PE

- 1/1000 pregnancies in women under the age of 35
- 4/1000 pregnancies in women over the age of 35
- Risk per day is actually greatest in the weeks following delivery

Concern about PE

- 13 to 24% of pregnant patients with untreated DVT experience pulmonary embolism
- Mortality of PE is 12 to 15%.

- **Treatment decreases the incidence of PE to 0.7 to 4.5%**
- **Reduces the mortality to 0.7%.**

To diagnose DVT…

- Compression Ultrasonography &Pulsed Doppler ultrasound
- Impedance plethysmography
- Magnetic Resonance Venography
- Venography

To diagnose PE…

- The perfusion scan is performed first, and a normal scan excludes pulmonary embolism.
- If the perfusion scan is abnormal, a ventilation scan is completed.
- **Matching ventilation perfusion defects are not suggestive of embolism.**
- Unfortunately abnormal V/Q scan results has sensitivity 98%, specificity 10%

- It can be diagnosed from a positive VQ scan and a raised D-dimer

- A normal VQ scan and D-dimer virtually exclude the diagnosis.

When clinical suspicion does not correlate with results of lung scanning…

- CT- Pulmonary angiography
- Catheterisation

- D-dimer is an unreliable test to carry out in pregnancy

- It can be elevated because of the physiological changes in the coagulation system

Right Heart Catheterisation

- RHC is required for a definite diagnosis of PAH, to determine the severity of the disease, to assess the prognosis and to select the appropriate therapy

- RHC is a safe procedure with a very low risk.

PE with shock or hypotension (high-risk)		
It is recommended to initiate intravenous anticoagulation with UFH without delay in patients with high-risk PE.	I	C
Thrombolytic therapy is recommended.	I	B
Surgical pulmonary embolectomy is recom[illegible]or patients in whom thrombolysis is contraindicat[illegible]s failed.[c]	I	C
Percutaneous catheter-dire[illegible]atment should be considered as an alternative to surgical pulmonary embolectomy for patients in whom full-dose systemic thrombolysis is contraindicated or has failed.[c]	IIa	C

Primary reperfusion

- Thrombolytic therapy with tissue plasminogen activator (rt-PA) is an approved in pregnancy
- However, there are no data from controlled randomized trials in pregnant patients.
- Thrombolysis complication rates were similar compared to non-pregnant patients for the above mentioned indications.
- rt-PA does not cross the placenta
- Hence thrombolytic therapy should not be withheld in pregnant patients in case of life-threatening or potentially debilitating thrombembolic disease.

PE without shock or hypotension (intermediate or low risk)[c]		
Reperfusion treatment		
Routine use of primary systemic thrombo… …ot recommended in patients without shock or hypoten…	III	B
Close monitoring is recom… …nts with intermediate-high-risk PE to permit early … …aemodynamic decompensation and timely initiation of re… …reperfusion therapy.	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients, if the anticipated risk of bleeding under thrombolytic treatment is high.[f]	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients, if the anticipated risk of bleeding under thrombolytic treatment is high.[f]	IIb	B

Monitoring & Rescue reperfusion

Surgical Interventions

- **Surgical embolectomy**
- **Temporary caval filter**
- **Thrombus fragmentation**

Factors that increases thrombotic risk in pregnancy

Increased maternal clotting factors
Fibrinogen and factors VII, VIII, IX, and X

Reduction in maternal levels of protein S

Impaired fibrinolysis
Placenta-derived fibrinolytic inhibitors

Venous stasis and blood pooling
Progesterone-mediated venous dilation
Compression of the inferior vena cava by the uterus in later pregnancy

Endothelial disruption of the pelvic vessels
Cesarean section

Acquired antithrombin deficiency
High-proteinuric states such as nephrotic syndrome or preeclampsia

Excessive elevation of pregnancy hormones
Ovarian hyperstimulation syndrome, multiple gestation

Other maternal risk factors
Thrombophilia
Family history of venous thromboembolism
Age > 35 years
Parity > 3
Obesity
Immobilization
Smoking
Varicose veins with phlebitis

Other maternal medical conditions
Hyperemesis gravidarum
Infection
Inflammatory bowel disease
Any condition necessitating a chronic indwelling catheter

Indications for anticoagulation in pregnancy by risk category

PREGNANCY RISK CATEGORY	RECOMMENDED ANTICOAGULATION
High risk	
Current arterial or venous thromboembolism (VTE)	Therapeutic low-molecular-weight heparin (LMWH) or adjusted-dose unfractionated heparin (UH)
Prior recurrent VTE, on long-term anticoagulation	Therapeutic LMWH or adjusted-dose UH
Antiphospholipid (APL) syndrome with prior VTE	Therapeutic LMWH or adjusted-dose UH ± aspirin
Mechanical heart valve	Aggressive-dose therapeutic LMWH or adjusted-dose UH ± aspirin, consider warfarin between 12 and 36 weeks of gestation
Moderate risk	
Single prior VTE with thrombophilia	Prophylactic LMWH or UH
Prior idiopathic VTE, no thrombophilia	Prophylactic LMWH or UH
Antithrombin deficiency, no VTE	Prophylactic or therapeutic LMWH or UH
Combined thrombophilias or homozygous thrombophilic mutation, no VTE	Prophylactic LMWH or UH
APL syndrome on the basis of adverse pregnancy outcomes*	Prophylactic LMWH or UH plus aspirin
Low risk	
Prior VTE with resolved temporary risk factor, no thrombophilia	Clinical surveillance or prophylactic LMWH or UH
Single thrombophilia (other than antithrombin deficiency), no VTE	Clinical surveillance, consider aspirin
Prior adverse pregnancy outcome with thrombophilia (other than APL), no VTE	Aspirin, consider prophylactic LMWH or UH

Prophylactic LMWH*	Enoxaparin, 40 mg SC once daily Dalteparin, 5,000 units SC once daily Tinzaparin, 4,500 units SC once daily
Therapeutic LMWH† (Also referred to as weight-adjusted, full-treatment dose)	Enoxaparin, 1 mg/kg every 12 hours Dalteparin, 200 units/kg once daily Tinzaparin, 175 units/kg once daily Dalteparin, 100 units/kg every 12 hours

Minidose prophylactic UFH	UFH, 5,000 units SC every 12 hours
Prophylactic UFH	UFH, 5,000–10,000 units SC every 12 hours
	UFH, 5,000–7,500 units SC every 12 hours in first trimester
	UFH, 7,500–10,000 units SC every 12 hours in the second trimester
	UFH, 10,000 units SC every 12 hours in the third trimester, unless the aPTT is elevated
Therapeutic UFH (Also referred to as weight-adjusted, full-treatment dose)	UFH, 10,000 units or more SC every 12 hours in doses adjusted to target aPTT in the therapeutic range (1.5–2.5, 6 hours after injection)

Postpartum anticoagulation	Prophylactic LMWH/UFH for 4–6 weeks or Vitamin K antagonists for 4–6 weeks with a target INR of 2.0–3.0, with initial UFH or LMWH therapy overlap until the INR is 2.0 or more for 2 days

Monitoring anticoagulation

aPTT for UFH

- The therapeutic target aPTT ratio is usually 1.5 –2.5 times the average laboratory control value(usually 60-90 secs) that corresponds to an anti-Xa level of 0.3 – 0.7 IU/mL.

aPTT may be inaccurate

- Apparent heparin resistance occurs in late pregnancy due to increased fibrinogen and factor VIII which influences aPTT

- Anti Xa levels can be a better choice in such situautions.

Anti Xa for LMWH

- Therapeutic doses of LMWH
- Renal impairment
- Extremes of body weight (<50 kgs, >90 kgs.)
- High risk of bleeding

Target Anti Xa levels

- 0.8 – 1.2 IU/ml for LMWH

(4-6 hours post dose)

- Post-dose anti-Xa level should be assessed at least weekly.

- 0.3 – 0.7 IU/ml for UFH

Heparin or Warfarin
(In the first trimester)

Fetal outcome was almost the same between the Warfarin and Heparin regimens

Maternal outcome,

the Warfarin regimen is safer than Heparin.

Class IIA recommendation

Continuation of warfarin during the first trimester is reasonable for pregnant patients with a mechanical prosthesis if the dose of warfarin to achieve a therapeutic INR is 5 mg/day or less after full discussion with the patient about risks and benefits

(Level of Evidence: B)

ACC / AHA

- Continuation of OACs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is<5 mg/day (or acenocoumarol <2 mg/day), after patient information and consent.

(Level of Evidence: C)

ESC

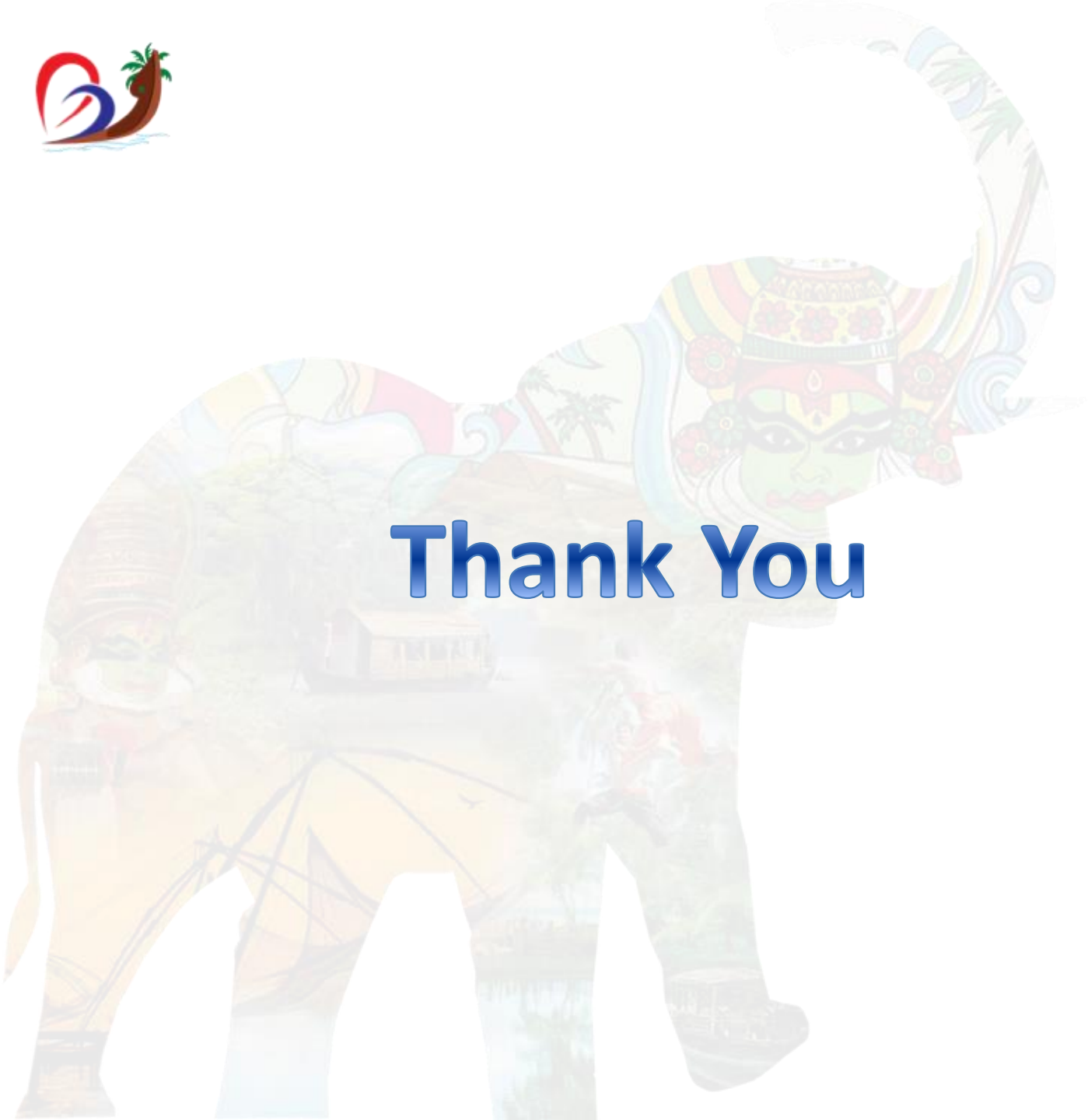
3rd Trimester and Delivery

- OAC should be discontinued and dose-adjusted UFH /LMWH started at the 36th week
- LMWH should be switched to i.v. UFH at least 36 h before the induction of labour or caesarean delivery.
- UFH should be discontinued 4 – 6 h before anticipated delivery, and restarted 6 h after delivery if there are no bleeding complications.
- Neither UFH nor LWMH is found in breast milk in any significant amount and they do not represent a contraindication to breastfeeding.
- Warfarin can be restarted 5–7 days after delivery. Warfarin is safe in breastfeeding.

CONCLUSION

- PPH, DVT & PE are dreaded complications in pregnancy
- Diagnostic options are often limited & misleading
- Both acute and chronic management strategies are essential
- With proper treatment mortality & morbidity can be substantially reduced
- Warfarin can be continued in 1st Trimester

  at <5mg /day



Thank You