VALVE DISEASE AND PREGNANCY

Eftihia Sbarouni, MD, FESC,FACC

OCSC, Athens

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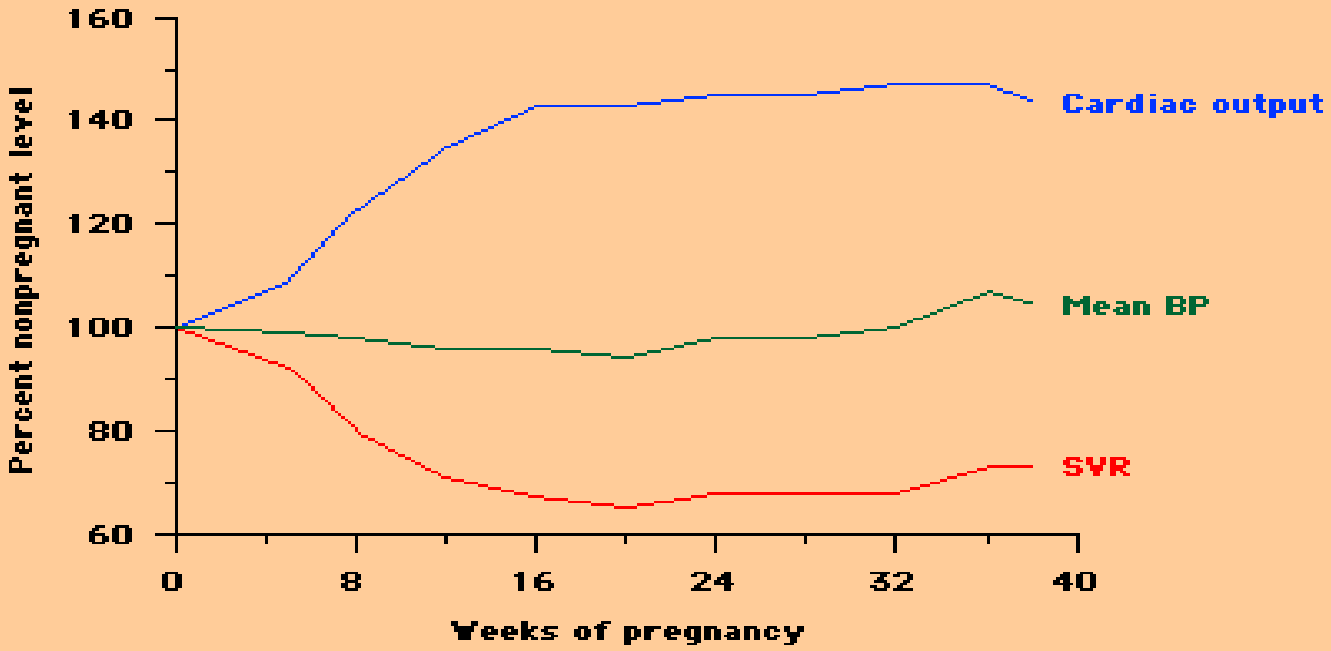
CHANGES IN PREGNANCY

- ↑CO (30-50%)
- ↑SV
- ↑HR (10-20b/min)
- ↑Blood vol (30-50%), ↑red cell mass (20-30%)
- ↓DBP,↓SVR,↓PVR
- Hypercoagulable state

Labour-delivery: contractions+pain→ ↑ CO

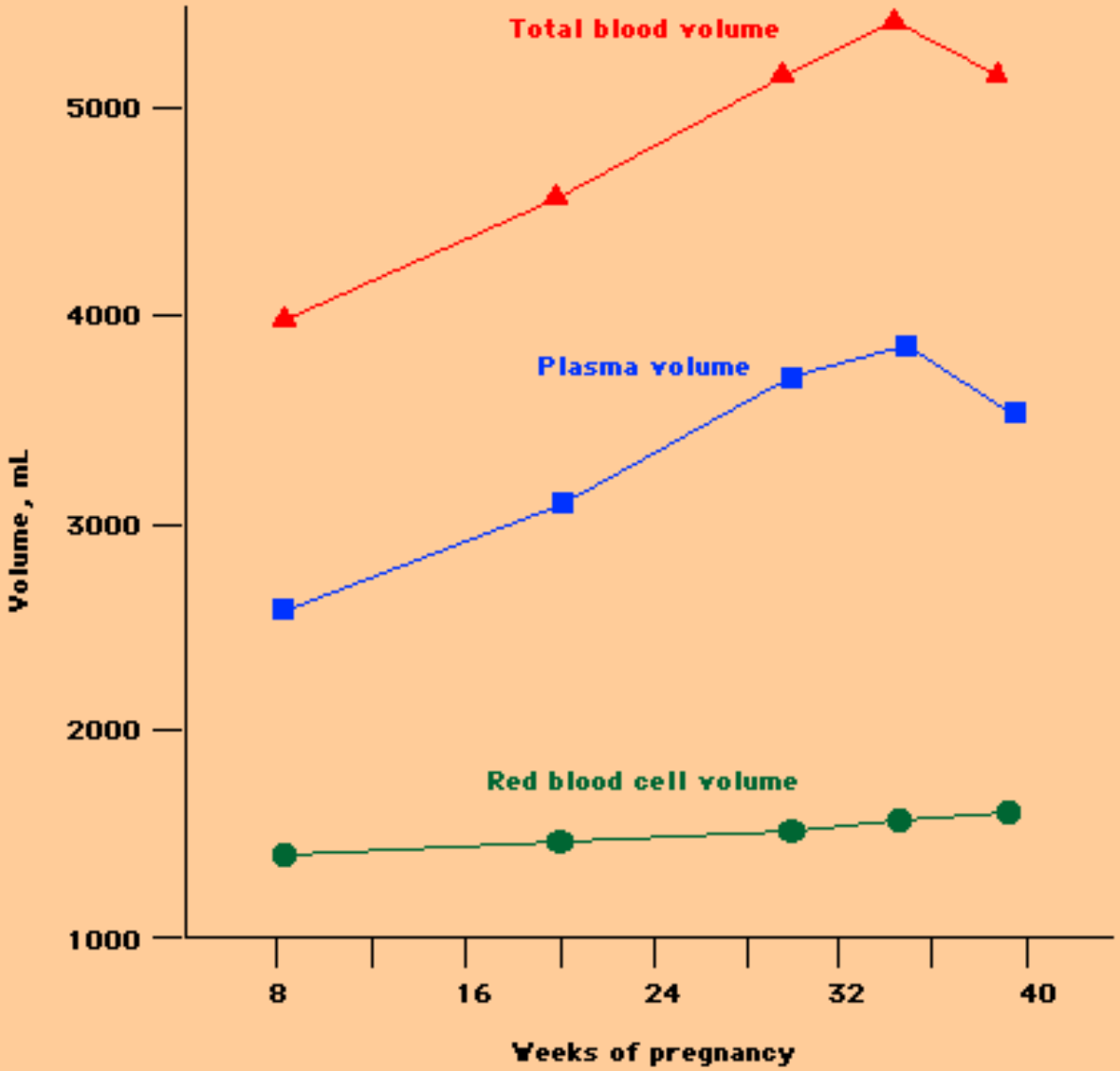
Following delivery: autotransfusion+relief of caval compression→ ↑ CO

Post partum carries risk (baseline in 1 month)



Hemodynamic changes in normal pregnancy Normal pregnancy is characterized by an increase in cardiac output, a reduction in systemic vascular resistance, and a modest decline in mean blood pressure. These changes are associated with a 10 to 15 beat/min increase in heart rate.

Total Blood Volume, Plasma Volume and Red Cell Volume in Normal Pregnancy†



†Data from Shnider, SM, Levinson, G. Anesthesia for Obstetrics, 3rd ed, Williams & Wilkins, Baltimore, p. 8.

Normal pregnancy

- Increased levels of coagulation factors (I,II,V,VII, VIII, X, XII)
- Increased levels of PAI-1 and PAI-2
- Decreased levels of protein S
- Resistance to protein C
- Decreased levels of thrombomodulin
- Lower PT and aPTT (20%)
- Increased PLT's turn-over
- Changes persist for 6-12 weeks post delivery

PATHOPHYSIOLOGY

- Pressure load
  - Myocardial ischemia
  - Ventricular failure
  - Arrythmias
- Volume load
  - ↓ SVR : ↓ MR, ↓ AR
- Myocardial dysfunction
  - ↑ CO
- Aortopathy
  - AS, CoA, Marfan (volume load, hormones)

MITRAL STENOSIS

- ↑ CO, ↑ HR → ↑ LAP → symptoms (labour: ↑ 8-10mmHg)
- AF, infection
- Safe if class I, MVA>1.5-2 cm^2, PG<5mmHg, PAP<50mmHg (mortality<1%)
- Class II, 1.0<MVA<1.5 cm^2: intermediate risk
- Class III,IV, MVA<1.0 cm^2: treat before

MITRAL STENOSIS

- Symptoms or PAP>50mmHg: b-blockers (metoprolol)
- Pulmonary edema: rest, oxygen, salt, diuretics, b-blockers
- Intractable dyspnea: mitral valvuloplasty (5% acute MR)
- MVR:10-30% fetal loss

MITRAL STENOSIS

- Atrial fibrillation
  - Cardioversion
  - B-blockers, digoxin, verapamil (rate control)
  - Quinidine, procainamide: safe
  - anticoagulation

AORTIC STENOSIS

- Risk depends on severity of obstruction
- ↑ SV → ↑ LV pressure → ↑ PG → ↑ LV workload → ↑ coronary demand
- Angina, syncope, pulm edema, sudden death
- Preload dependent : avoid hypotension, blood loss, vasodilators
- Rest, b-blockers, diuretics

AORTIC STENOSIS

- Low risk
  - Class I
  - MG< 50mmHg, PG< 80mmHg (normal EF)
- Treat before
  - Symptomatic
  - Gradient> 50mmHg
  - AVA< 1cm^2
- Termination if
  - Symptoms occur before end of 1st trimester (balloon valvuloplasty, surgery)

REGURGITANT VALVE DISEASE

- ↓ SVR → ↓ RF, ↑ HR → ↓ RF
- MR (MVP)
- AR (bicuspid, SBE, Marfan)
- Safe if
  - Class I or II and normal EF
- High risk if
  - Class III or IV, EF<40%, PAP>75% SBP
- CHF (3nd trimester): diuretics, dilators (nitrates, nifedipine)

PULMONARY VALVE STENOSIS

- Mild 30-50mmHG
  moderate 50-80mmHg,
  severe > 80mmHG

Mild-moderate: well tolerated

Severe: RHF/TR/AF

valvuloplasty before pregnancy

COARCTATION

- Repair before pregnancy, if pg< 20mmHg, good prognosis
- If unoperated 3-4% maternal mortality
  - ↑risk if hypertension/associated defects
- Unrepaired normotensive allow term
- Unrepaired hypertensive consider stent
- Rupture: third trimester, labour, b-blockers
- 20% fetal loss because ↓BP

MARFAN

- Hormones → wall thinning, ↑ blood volume → ↑ wall stress
- ↑risk if
  - AR, root > 40mm (10%), history of dissection
- Risk even if
  - No AR, no MR, root< 40mm 1% risk
- B-blockers throughout
- Echo every 6-8 wks and for 6 mnts postpartum
- Root > 45mm → CS
- Root > 40mm → elective root replacement before

Thromboembolic risk

- Hypercoagulable state
- Higher risk in thrombophilias
  - Factor V (Leiden) mutation
  - G20210A prothrombin mutation
  - Antiphospholipoid antibodies (lupus anticoagulant,anticardiolipin antibodies)
  - Hyperhomocysteinemia (gene for methylenetrahydrofolate reductase)
- Reduction in bleeding
- 4-fold increase risk in DVT postpartum vs pregnancy

Indications for anticoagulation during pregnancy

- Prosthetic valves
- Severe heart failure
- Atrial fibrillation with underlying disease (ie MS, HOCM)
- DVT/PE
- Thrombophilias

PROSTHETIC VALVES

- Pregnancy: hypercoagulable state
- Effective dose of anticoagulants changes
  - ↑ Intravascular volume
  - ↑ Body weight
- Vitamin K agonists cross the placenta
  - risk of embryopathy
- Heparin does not cross the placenta
  - risk of valve thrombosis
- Maternal mortality: 1-4%

ORAL ANTICOAGULANTS

- ↑fetal loss
- embryopathy
  - 5% (4-10%)
  - dose-dependent
  - Facial and digital abnormalities, epiphyseal changes,optic atrophy, mental impairement
- CNS hemorrhage
- ↑ prematurity

HEPARIN

- Unfractionated heparin
  - ↑valve thrombosis
  - thrombocytopenia
  - osteoporosis

Table 2 Frequency of foetal and maternal complications according to the anticoagulation regimen used during pregnancy in women with mechanical heart valve prosthesis. Adapted from Chan et al.[51]

Anticoagulation regimen	Embryopathy (%)	Spontaneous abortion (%)	Thromboembolic complications (%)	Maternal death (%)
Vitamin K antagonists throughout pregnancy[a]	6.4	25	3.9	1.8
Heparin throughout pregnancy	0	24	33	15
Low dose	0	20	60	40
Adjusted dose	0	25	25	6.7
Heparin during first trimester, then vitamin K antagonists[a]	3.4	25	9.2	4.2

[a]With or without heparin prior to delivery.

Oakley C et al. Task Force. Eur Heart J 2003;24:761-781

HEPARIN

- LMW heparin
  - anecdots on valve thrombosis

PROSTHETIC VALVES

- LMWH
- 81 pregnancies in 75 women
- 8.6% valve thrombosis
- Most cases inadequate dose, lack of monitoring, subtherapeutic anti-Xa levels

Oran b et al.Thromb Haemost 2004; 92:747

Table 2. Recommendations of the Seventh ACCP Consensus Conference on Antithrombotic Therapy for Prophylaxis in Patients With Mechanical Heart Valves

1. Aggressive adjusted-dose UFH, given every 12 h subcutaneously throughout pregnancy; mid-interval activated partial thromboplastin time maintained at ≥2 × control levels, or anti-Xa heparin level maintained at 0.35 to 0.70 IU/ml.

OR

2. LMWH throughout pregnancy, in doses adjusted according to weight or as necessary to maintain a 4-h postinjection anti-Xa heparin level of about 1.0 IU/ml.

OR

3. UFH or LMWH, as above, until the 13th week; change to warfarin until the middle of the third trimester, then restart UFH or LMWH therapy until delivery.

Reprinted, with permission, from Bates et al. (60).

ACCP = American College of Chest Physicians; LMWH = low molecular weight heparin; UFH = unfractionated heparin.

Elkayam et al. JACC 2005;46:406-410

ACC/AHA Guideline Summary: Anticoagulation regimen in pregnant women with mechanical prosthetic heart valves

Class I - There is evidence and/or general agreement that the following approaches to anticoagulation therapy are indicated in pregnant women with mechanical prosthetic heart valves

- For women who are attempting to become pregnancy, anticoagulation options during pregnancy discussed so that anticoagulation can be uninterrupted once pregnancy is achieved. Because of the risk of warfarin embryopathy between 6 and 12 weeks of gestation, pregnancy tests should be monitored.
- During pregnancy, continuous therapeutic anticoagulation with frequent monitoring.
- Women who elect to stop warfarin between 6 and 12 weeks of gestation should be treated with dose-adjusted continuous intravenous unfractionated heparin (UFH), subcutaneous UFH, or low molecular weight heparin (LMWH).
- Between 12 and 36 weeks, the patient can be treated with dose-adjusted continuous intravenous UFH, subcutaneous UFH, or LMWH, or warfarin. With warfarin compared to the different heparin regimens, the fetal risk is higher but the maternal risk appears to be lower for prosthetic valve thrombosis and systemic embolization. Heparin therapy, particularly UFH, also carries the risks of heparin-induced thrombocytopenia and osteoporosis.

1. Dose-adjusted LMWH should be given twice daily subcutaneously to maintain the anti-Xa level between 0.7 and 1.2 U/mL at four hours after dosing. LMWH should NOT be given if such monitoring cannot be performed.

2. With dose-adjusted UFH, the aPTT should be at least twice control.

3. With warfarin, the goal INR is 3.0 (range 2.5 to 3.5). Warfarin should be discontinued and continuous intravenous UFH started beginning two to three weeks before planned delivery.

Class IIa - The weight of evidence or opinion is in favor of the usefulness of the the following approaches to anticoagulation therapy in pregnant women with mechanical prosthetic heart valves

- Avoidance of warfarin between 6 and 12 weeks of gestation due to the high risk of fetal defects.
- In the absence of significant bleeding, continuous intravenous heparin should be resumed and oral warfarin should be begun four to six hours after delivery.
- In the second and third trimesters, low-dose aspirin (75 to 100 mg/day) can be given in addition to warfarin or heparin. Dipyridamole is NOT an alternative to aspirin because of its adverse effects on the fetus.

Data from Bonow, RO, Carabello, BA, Chatterjee, K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease). J Am Coll Cardiol 2006; 48:e1.

ESC guidelines

- Oral anticoagulants throughout
- Heparin (iv or sc) between 6-13 weeks and coumadin thereafter
  - Embryopathy risk 0% only if heparine before 6th week
- Heparin at 36 weeks (iv or sc) or CS
- LMWH not recommended
- ASA in high risk women (1st generation, AF, mitral position, previous stroke, multiple valves)

Table 3. Recommended Approach for Anticoagulation Prophylaxis in Women With PHV During Pregnancy

Higher Risk	Lower Risk
First generation PHV (e.g., Starr-Edwards, Bjork Shiley) in the mitral position, atrial fibrillation, history of TE on anticoagulation	Second generation PHV (e.g., St. Jude Medical, Medtronic-Hall) and any mechanical PHV in the aortic postion
Warfarin (INR 2.5–3.5) for 35 weeks, followed by UFH (mid-interval aPTT >2.5) or LMWH (pre-dose anti-Xa ~0.7) + ASA 80–100 mg q.d. OR UFH (aPTT 2.5–3.5) or LMWH (pre-dose anti-Xa ~0.7) for 12 weeks, followed by warfarin (INR 2.5–3.5) to 35th week, then UFH (aPTT >2.5) or LMWH (pre-dose anti-Xa ~0.7) + ASA 80–100 mg q.d.	SC UFH (mid-interval aPTT 2.0–3.0) or LMWH (pre-dose anti-Xa ~0.6) for 12 weeks, followed by warfarin (INR 2.5–3.0) for 35 weeks, then SC UFH (mid-interval aPTT 2.0–3.0) or LMWH (pre-dose anti-Xa level ~0.6) OR SC UFH (mid-interval aPTT 2.0–3.0) or LMWH (pre-dose anti-Xa ~0.6) throughout pregnancy

Reprinted, with permission, from Elkayam et al. (61).

aPTT = activated partial thromboplastin time; ASA = acetylsalicylic acid; INR = international normalized ratio; PHV = prosthetic heart valve; SC = subcutaneous; TE = thromboembolism; other abbreviations as in Table 2.

Elkayam et al. JACC 2005;46:406-410

Anticoagulation in pregnancy Conclusions

- Pregnancy is a hypercoagulable state
- Oral antiocoagulants :
  - safe for the mother
  - risk for embryopathy
- Heparin :
  - Safer for the baby
  - Risk for valve thrombosis
- Controversy
- Discuss with the parents
- Close monitoring

DCM

- Advise against pregancy (deterioration)
- Terminate pregnany if EF< 45-50% or LVEDD> 55mm
- High risk pregnancy
- Echo pre in women with history of familial DCM or PPCM

HOCM

- If class I good prognosis
- Fatalities have been reported
- AF: DC, LMWH
- Pulmonary edema: bed rest, b-blocker
- Blood loss
- Genetic risk

PPCM

- Definition :
  - Last month or first 5 months post delivery
  - No other cause of heart failure (DCM 2nd trimester)
- HF, thromboembolism, arrythmias
- Conventional treatment+anticoagulation
- Considerable mortality
- LVEF may recover (↑ possibility ↑EF)
- Advise against other pregnacy (recurrence)
- Pregnancy-CM early similar

ARRHYTHMIAS

- DC safe
- SVT: adenosine, vagal manoeuvres
- VT : DC if hemodynamic instability

PRE-PREGNANCY EVALUATION-F/UP

- Full non-invasive assessment
- Stop teratogenic drugs (ACE-inhibitors, statins)
- Discuss risks for mother and fetus
- Specify possible risks for CHD
- Valvuloplasty for PS, MS, AS/ repair for MVP
- Each trimester and when change symptoms

DRUGS

- Antihypertensives: methyldopa, b-blockers
- Vasodilators: nitrates, calcium blockers
- Antiarrythmics: adenosine, digoxin, verapamil, quinidine, procainamide
- Antibiotics (SBE): ampicillin, vancomycin, gentamycin

CARDIAC SURGERY

- SBE
- Acute MR complicating valvuloplasty
- Thrombosis of a prosthetic valve (thrombolysis for right-sided valves)
- Aortic dissection
- Elective surgery 16-20 weeks

DELIVERY

- Vaginal delivery
- CS for
  - Marfan with dilated root
  - Oral anticoagulants last 2 wks
  - IUGR
- Left lateral (avoid IVC compression)
- Short second stage
- SBE prophylaxis (ruptured membranes, laceration, bladder catheter)
- Heparin may start 6hrs post vaginal delivery or 12 hrs post CS

THERAPEUTIC ABORTION

- Less risk than continuing pregnancy
- Safer 1st trimester
- Hospital admission
- Contraception: barrier methods, tubal ligation, progestin-only

HIGH RISK

- Cyanosis
- Fragile aorta
- Mechanical valves
- Class III-IV
- EF< 40%
- Previous TIA or stroke
- Previous CHF

LOW RISK

- Class I-II
- L to R shunt
- Valvular regurgitation
- Modest LV outflow obstruction
  - MVA> 2.0 cm^2
  - AVA> 1.5 cm^2
  - LVOT< 30 mmHg
- Right ventricular outflow obstruction

ABSOLUTE CONTRAINDICATIONS

- Pulmonary hypertension
- Marfan with aortic root dilation
- Left sided severe obstruction
- EF< 20%