

Mechanical Heart Valves and Anticoagulation in Pregnancy

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Mechanical Heart Valves and Anticoagulation in Pregnancy

Agreement

- Pregnancy is hypercoagulable state
- ↑ risk of thromboembolism esp valve thrombosis
- Anticoagulation required throughout pregnancy
- No ideal anticoagulant
- Risk of maternal thromboembolic complications
- Risk of maternal bleeding
- Risk of fetal risk, particularly ↑ fetal loss

Maternal Risks with Mechanical Heart Valve

- Risk of mortality for mechanical valve thrombosis ~ 20% (highest during first trimester)
- Risk of bleeding highest during delivery

Maternal deaths*

- 0.9% warfarin (2-4% TE)
- 1.8% LMWH (4-16% TE)
- higher UFH (29% TE)

* Majority due to valve thrombosis

TE- thromboembolic complications

Risk Factors for Mechanical Valve Thrombosis in Pregnancy

- prosthetic valve in mitral position
- subtherapeutic anticoagulation
- atrial fibrillation
- at time of transition for warfarin to LMWH in first trimester

Risks of VKA in pregnancy

- Warfarin embryopathy (wks 6-12)
- ↑ fetal wastage (miscarriage, still births)
 - if used throughout ~ 28%
 - (- dose \leq 5mg 19%
 - dose $>$ 5mg 64%)
- if LMWH 1st trimester, then warfarin
 - fetal loss ~ 22%

Warfarin Embryopathy

occurs ~ 2-4%* fetus when warfarin given between 6-12 wks pregnancy

- hypoplasia of nasal cartilage
- pectus carinatum
- congenital heart defects
- corpus callosum agenesis
- stippled epiphyses
- telebrachydactyly
- microcephaly

* If warfarin dose \leq 5mg/day, warfarin embryopathy ~ 0.7%

↑ Fetal loss - throughout entire pregnancy

LMWH in Pregnancy

- does not cross placenta
- cleared entirely by kidneys (therefore dose generally needs to be ↑ by ~ 50% during pregnancy)
- must be monitored by peak anti-Xa levels (weekly first trimester)

Peak levels – determined by Cr clearance
(important in 2nd & 3rd trimester)

Trough levels – determined by volume of distributions
(important in first trimester)

Monitoring of LMWH in Heparin **-Anti-Xa levels**

- measure peak levels (4-6 hrs) weekly in first trimester
- then monthly for aortic valves (two weekly for mitral valves)
- measure weekly if out of range

- target peak range 1.0-1.2 IU/ml 4-6 hrs post dose
- if trough levels performed, target trough range 0.6-0.7 IU/ml

LMWH in Pregnancy

- Continued risk of thromboembolic events even in therapeutic range
- for mitral mechanical valves, measure trough peak levels
- if low trough valves, ↑ to tds dosing
- Higher risk of post partum haemorrhage when compared to VKA
- Decrease or increase enoxaparin dose by 10mg/kg

- **Requires dedicated, multidisciplinary team for follow up – ensuring maternal compliance**

Primary Maternal and Fetal Outcomes*

Anticoagulation regime	Maternal mortality estimate %	Thromboembolic estimate %	Live births Estimate %
Vit K antagonists (INR target 2.5-3.5)	0.9	2.7	65
Sequential treatment	2.0	5.8	80
LMWH alone	2.9	8.7	92
UFH alone	NE	11.2	NE

* No randomized, controlled trials

Anticoagulant Agents & Implications in Pregnancy

Drug	Mechanism	Therapeutic Dose	Monitoring	Preg/Cat	Present in breast milk*	Crosses the placenta
Warfarin	Vit K antagonist	Variable	INR	D*	No	Yes
Unfractionated heparin	Antithrombin by potentiating antithrombin III	Variable	aPTT	C	No	No
Enoxaparin	Inhibits factor Xa + potentiates antithrombin III	1mg/kg every 12 hours	Peak anti Xa levels 4-6 hrs post dose	B	No	No
Dabigatran*	Direct thrombin inhibitor	110-150mg bd	NA	C	Unknown	Likely
Apixaban*	Selective Xa inhibitor	2.5-5.0mg twice daily	NA	β	Unknown	Yes

* X in first trimester if no mechanical valve

+ C/I in non pregnant women with mechanical heart valves

↑ Breast feeding OK with VKAS, LMWH or UFH

Pre-pregnancy + Pregnancy Planning in Women with Mechanical Heart Valves

- consider bioprosthetic mitral valve in women of childbearing age (rather than mechanical MVR), despite high risk of redo heart surgery
- pre-pregnancy assessments by Cardiology, Haematology and Obstetrics
- anticoagulation plan and monitoring plan for all patients
- coordinated delivery and postpartum plan (including anticoagulation plan)

ACC/AHA & ESC Guidelines with Mechanical Heart Valves

	1 st Trimester	2 nd & 3 rd Trimester	Peripartnum
ACC/AHA 2014	Warfarin if dose <5mg (IIa) or dose adjusted LMWH (IIb) or dose adjusted IV UFH (IIb)	Warfarin + daily Aspirin	Dose adjusted IV UFH
ESC 2017	Warfarin if dose <5mg /d (IIa) or >5mg/d (IIb) Dose adjusted LMWH (IIb) or Dose adjusted IV UFH (IIb)	Warfarin	Dose adjusted LMWH or IV UFH

ESC 2017 Guidelines (Additional)

- I LMWH must be monitored by anti-Xa levels (peak \pm trough*)

- IB INR self management is recommended (weekly measurements)

- IIIB Use of NOACS is contraindicated in mechanical valves

*Trough levels

Elkayam U et al
Berreshaim M et al

RMH/RWH Recommendations for Anticoagulation for Pregnant Women with Mechanical Heart Valves

	1 st Trimester	2 nd & 3 rd Trimester
Aortic valve	LMWH 6-14 wk SC bd Peak anti-Xa levels 1.0-1.2* IU/ml	Warfarin Target INR 2.5-3.5
Mitral or Tricuspid valve	As above + low dose aspirin (100mg day) + Trough levels 0.6-0.7 IU/ml * If not adequate anti-Xa levels, particularly low trough, ↑ to tds doses	As above + low dose aspirin

- Measure anti-Xa levels weekly during first trimester
- * Trough levels subtherapeutic in 70% cases where peak anti-Xa 0.7-1.0 IU/L and in 40% where peak 1.0-1.2 IU/L

RMH/RWH Recommendations for Anticoagulation for Pregnant Women with Mechanical Heart Valves

Peri-partum Management

Aortic Valve

LMWH from 36 wks

Stop 36 hr prior to planned delivery

Start UFH IV infusion

Stop UFH when in active labour or 6 hrs prior to epidural (check APTT N prior to epidural)

Induce * at 38/40

Vaginal delivery preferred

Mitral or Tricuspid Valve

As above

Continue Aspirin**

As above

* If present in labour on full anticoagulation proceed to Caesarean section

** Start UFH with 5000 IU loading dose , then 1250 IU/hr to target APTT 2-3xN

RMH/RWH Recommendations for Anticoagulation for Pregnant Women with Mechanical Heart Valves

Postpartum

Aortic Valve

No UFH recommended post partum

Restart LMWH 24 hrs post partum if no bleeding concerns

Restart warfarin day 1 post partum (day 2 to 3 post CS)

Mitral or Tricuspid Valve

Restart UFH 4-6 hrs post partum if no bleeding concerns
(500 U/hr for 6 hrs then 1000 IU/hr then APTT 2-3 x N)

Restart LMWH 24 hrs post partum

Restart Warfarin as above

Continue LMWH until INR >2

Conclusion 1

- Pregnancy with mechanical heart valves is very high risk especially if mechanical mitral valves
- Full anticoagulation essential throughout pregnancy and post partum

Conclusion 2

- Our recommendation is sequential LMWH 6-14 weeks, VKA 14 wks-36 wks, LMWH 36-38 weeks to achieve
 - low maternal thromboembolic risk
 - avoidance of fetal embryopathy
 - decreased risk of fetal loss

References

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