Society for Maternal-Fetal Medicine

Consult Series #61

ANTICOAGULATION IN PREGNANT PATIENTS WITH CARDIAC DISEASE

cardiac disease is the most common cause of maternal mortality in high-income nations

counseling & management of anticoagulation in cardiac disease during pregnancy should be multidisciplinary & involve cardiology, cardiothoracic surgery, maternal-fetal medicine, & anesthesiology specialists

Bioprosthetic Heart Valves

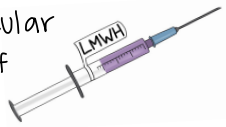
TISSUE, BOVINE, OR PORCINE

require 3-6 months of anticoagulation with vitamin K antagonist after placement, followed by lifelong low-dose aspirin monotherapy

81 continue low-dose aspirin monotherapy without interruption before, during, & after pregnancy for individuals with a bioprosthetic heart valve to reduce the risk of valve thrombosis

IF PLACED DURING PREGNANCY

Suggest full-dose anticoagulation with low molecular weight heparin (LMWH) for the remainder of pregnancy & 6 weeks postpartum



Mechanical Heart Valves

valve thrombosis occurs in approximately 5% of pregnancies

perinatal complications include:
- increased risk of thrombosis
- perinatal loss
- preterm delivery
- cesarean delivery
- hemorrhage

continue therapeutic anticoagulation before, during, & after pregnancy for individuals with a mechanical heart valve

Anticoagulants

In a meta-analysis, the estimated average risk of maternal adverse outcome → composite of maternal death, valve failure, & thrombosis throughout pregnancy for:

- warfarin was 5.0%
- dose-adjusted LMWH was 15.5%
- dose-adjusted LMWH in the 1st trimester followed by warfarin was 15.9%

Subcutaneous Unfractionated Heparin (UFH)

not recommended in pregnancy

The use of new oral anticoagulants is not recommended in pregnant patients with mechanical heart valves because of an excess of thromboembolic and bleeding events

Warfarin

lowest risk of valve thrombosis

highest likelihood of congenital abnormalities with 1st trimester use and perinatal loss, particularly with doses >5mg/day

warfarin embryopathy includes nasal hypoplasia, chondrodysplasia punctata, cardiac malformations, microcephaly, optic atrophy, blindness, deafness, & central nervous system abnormalities
- may be dose dependent
- rate in pregnancies exposed in 1st trimester 2-30%

crosses the placenta & results in anticoagulation of the fetus

compatible with breastfeeding & poses no risk to the infant

REVERSAL	prothrombin complex concentrates +/- small doses of vitamin K

Low Molecular Weight Heparin (LMWH)

preferred over UFH due to better bioavailability, more predictable anticoagulation with decreased bleeding risk, & lower incidence of both osteoporosis & heparin-induced thrombocytopenia

starting dose is 1mg/kg (actual body weight) subcutaneously every 12 hours, adjusted to achieve therapeutic anti-Xa levels

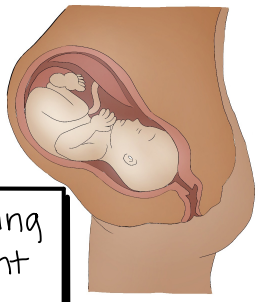
anti-Xa levels should be checked after 3 doses have been administered, 4 hours after dosing

compatible with breastfeeding

REVERSAL	protamine sulfate (only partially reverses the anticoagulant effect)

Planned Pregnancy

1st trimester



Developing fetus is most vulnerable to warfarin around 6-12 weeks of gestation

suggest continuing warfarin in the 1st trimester after counseling in individuals requiring a warfarin dose ≤ 5 mg/day to maintain a therapeutic INR, taking into account the risk of warfarin embryopathy but decreased risk of valve thrombosis

suggest using adjusted-dose LMWH as an alternative anticoagulant during the 1st trimester in pregnant people with mechanical heart valves receiving warfarin >5mg/day or in those who decline warfarin, provided anti-Xa levels are monitored every 1-2 weeks

Recommend titrating LMWH dosing based on both trough (>0.6 U/mL) & peak (0.8-1.2 U/mL for aortic valves & 1-1.2 U/mL for mitral valves) anti-Xa levels, with more frequent anti-Xa evaluations when dosing is adjusted

Recommend against subcutaneous UFH, direct thrombin inhibitors, or direct oral anti-Xa anticoagulants to achieve therapeutic anticoagulation in pregnant persons with a mechanical heart valve

in the 1st trimester For patients declining warfarin & if anti-Xa level monitoring is not available → **RECOMMEND** continuous IV UFH

2nd & 3rd trimesters

suggest using warfarin for anticoagulation from 12 weeks until 36 weeks of gestation, particularly for patients at high risk of thrombosis (BOX 1), with an INR target of 2.5 for those with mechanical aortic valves & 3.0 for mechanical mitral valves

BOX 1. Conditions at high risk for mechanical valve thrombosis.

- Mechanical mitral valve
- Right-sided mechanical valves
- Coexistent atrial fibrillation
- Left ventricular dysfunction
- Previous prosthetic valve thromboembolic complication
- Older generation mechanical valve (eg, ball-in-cage)
- Some hypercoagulable conditions[a]

[a] In particular, personal or strong family history of thrombosis, antithrombin deficiency, and hozygosity or compound heterozygosity for the factor V Leiden and/or prothrombin gene mutations.

suggest continuing low-dose aspirin (81) when indicated in pregnant people with mechanical heart valves in conjunction with therapeutic anticoagulation

FOR PATIENTS DECLINING WARFARIN

in the 2nd & 3rd trimesters

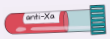
suggest using adjusted-dose LMWH, provided anti-Xa levels are monitored every 1-2 weeks

Delivery Timing & Mode of Delivery

For pregnant persons with a mechanical heart valve and no other complications, we recommend a planned delivery $37^{0/7}$ – $38^{0/7}$ weeks of gestation, taking into consideration relevant maternal & fetal factors to determine the optimal mode of delivery

For pregnant persons with a mechanical heart valve anticoagulated with warfarin during the 2nd & 3rd trimesters

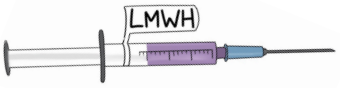
Recommend transitioning to dose-adjusted LMWH at 35 to 36 weeks of gestation (with planned delivery 37–38 weeks of gestation)



provided anti-Xa levels are monitored weekly using both trough (>0.6 U/mL) and peak (0.8-1.2 U/mL for aortic valves & 1-1.2 U/mL for mitral valves) levels

then transitioning these patients to bridging anticoagulation with IV UFH in an inpatient setting 36 to 48 hours before planned delivery

For pregnant persons with a mechanical heart valve anticoagulated with dose-adjusted LMWH in the 2nd & 3rd trimesters

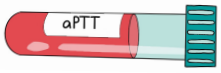
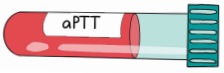


Recommend transitioning to IV UFH in an inpatient setting 36 to 48 hours before planned delivery

Labor & Delivery

IV UFH is usually started 12 hours after discontinuation of LMWH at a dose of 18 units/kg/hour, without a loading dose

suggest titrating IV UFH during labor & delivery to achieve an anti-Xa level of 0.7 to 1.0 U/mL and maintained at this level until 4 to 6 hours before delivery

For patients with a mechanical heart valve		
requiring a cesarean delivery	in whom vaginal delivery is expected	desiring an epidural
recommend stopping the UFH infusion 4 to 6 hours before the scheduled surgery & administering neuraxial anesthesia after documentation of a normal aPTT value 	recommend continuation of UFH infusion until active labor (6 cm cervical dilation in most cases), at which time the infusion is stopped The goal is to achieve delivery within the next 6 hours	recommend stopping IV UFH 4 to 6 hours before planned regional anesthesia placement with documentation of a normal aPTT value 
After Delivery	recommend removing the indwelling neuraxial catheter 4 to 6 hours after stopping IV UFH documentation of a normal aPTT value	

For patients with a mechanical heart valve who have been therapeutically anticoagulated with warfarin within the last 2 weeks & who require an urgent delivery, recommend proceeding with a cesarean delivery to avoid fetal complications related to therapeutic anticoagulation with warfarin

Reversal for emergent situations

recommend that in pregnant persons with a mechanical heart valve the decision for anticoagulant reversal should be made in conjunction with cardiology, hematology, & anesthesia expertise while considering the individualized maternal & fetal risks

Postpartum

suggest that therapeutic doses of IV UFH may be started as early as 4 to 6 hours after delivery and at least 1 hour after removal of an epidural / spinal catheter

suggest reinitiation of IV UFH after delivery with the concomitant transition back to warfarin in the inpatient setting for ongoing therapeutic anticoagulation

Breastfeeding

recommend warfarin for anticoagulation in all postpartum individuals with a mechanical heart valve given its superior anticoagulant properties in avoiding valve thrombosis & the safety of warfarin for the breastfed infant

Contraception

For individuals no longer desiring fertility, we recommend permanent sterilization

For others, 1st-line options include

levonorgestrel-containing intrauterine device	progesterone subcutaneous implants	intramuscular depot medroxyprogesterone acetate
		

Mechanical Valve Thrombosis

Physical exam findings:

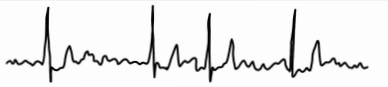
- muffled mechanical heart valve sounds
- new onset murmurs
- signs & symptoms of congestive heart failure (dyspnea, orthopnea, pulmonary congestion)
- signs of peripheral embolic phenomena (including myocardial infarction & stroke)

Diagnosis confirmed with echocardiography

Urgent treatment with tissue plasminogen (tPA) or emergent surgery

tPA has a short half-life (5 minutes) & does not cross the placenta

Atrial Fibrillation (AF)



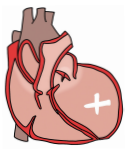
For pregnant individuals requiring therapeutic anticoagulation to decrease the risk for thromboembolic complications related to AF, recommend adjusted-dose LMWH

For postpartum individuals requiring therapeutic anticoagulation to decrease the risk for thromboembolic complications related to AF, recommend

adjusted-dose LMWH or warfarin → until 6 weeks postpartum*

*beyond 6 weeks postpartum, ongoing anticoagulation should be determined by a cardiologist

Left Ventricular Systolic Dysfunction



For pregnant individuals with left ventricular systolic dysfunction & an ejection fraction <35%, recommend adjusted-dose LMWH

For postpartum individuals with left ventricular systolic dysfunction & an ejection fraction <35%, recommend

adjusted-dose LMWH or warfarin → until 6 weeks postpartum*

*beyond 6 weeks postpartum, ongoing anticoagulation should be determined by a cardiologist

Fontan Circulation

= direct connection of the caval veins into the pulmonary arteries

For pregnant individuals with Fontan circulation who have additional risk factors for thromboembolism, recommend adjusted-dose LMWH

For postpartum individuals with Fontan circulation who have additional risk factors for thromboembolism, recommend

adjusted-dose LMWH or warfarin → until 6 weeks postpartum*

For postpartum individuals with Fontan circulation without additional risk factors for thromboembolism, recommend

prophylactic doses of LMWH during the postpartum period for 6 weeks