Pregnancy in individuals with a mechanical heart valve has been classified as very high risk because of a substantially increased risk of maternal mortality or severe morbidity. Lifelong therapeutic anticoagulation is a principal component of the medical management of mechanical heart valves to prevent valve thrombosis. Anticoagulation regimens indicated outside of pregnancy for patients with mechanical valves should be continued during pregnancy with the possibility of modifications based on the type of valve, the trimester of pregnancy, individual risk tolerance, and circumstances around the time of delivery. The purpose of this document is to provide recommendations regarding the management of anticoagulation for common cardiac conditions complicating pregnancy, including mechanical heart valves, atrial fibrillation, systolic heart failure, and congenital heart disease.

Key words: anticoagulation, congenital heart disease, mechanical heart valves

Introduction
Cardiac disease is the most common cause of maternal mortality in high-income nations. The burden of cardiovascular complications during pregnancy is expected to continue increasing because of a higher prevalence of medical diseases among reproductive-aged people (eg, obesity, diabetes mellitus, hypertension, or dyslipidemia) and because patients with complex congenital heart disease now commonly survive to childbearing age as a result of improved pediatric congenital heart disease care.

The purpose of this document is to provide recommendations regarding the management of anticoagulation for common cardiac conditions complicating pregnancy, including mechanical heart valves, atrial fibrillation (AF), systolic heart failure, and congenital heart disease. Counseling and management of anticoagulation in cardiac disease during pregnancy should be multidisciplinary and involve cardiology, cardiothoracic surgery, maternal-fetal medicine, and anesthesiology specialists.

What anticoagulation is required for pregnant individuals with a bioprosthetic heart valve?
Bioprosthetic heart valves, also known as tissue, porcine, or bovine valves, are vulnerable to thrombosis, but the risk of a hemodynamically notable thrombosis is low in the general adult population (<1%). Pregnancy outcomes in the setting of bioprosthetic valves are anticipated to be favorable with an equally low risk of thrombotic events. Bioprosthetic valves require a short period of anticoagulation with vitamin K antagonists (3–6 months) after initial placement, followed by lifelong low-dose aspirin monotherapy. The main advantage of bioprosthetic valves is that after this initial anticoagulation phase, patients require only low-dose aspirin. The main drawback of bioprosthetic valves is that the longevity of these valves is limited, and many patients will need to undergo valve replacement as soon as 5 to 10 years after placement. Anticoagulation regimens recommended outside of pregnancy for bioprosthetic heart valves should be continued during pregnancy. The use of low-dose aspirin therapy in pregnancy is well studied, although for alternative indications, and has a favorable maternal and fetal safety profile. We recommend continuing low-dose aspirin monotherapy without interruption before, during, and after pregnancy for individuals with a bioprosthetic heart valve to reduce the risk of valve thrombosis (GRADE 1C). If a bioprosthetic valve is placed during pregnancy, we suggest full-dose anticoagulation with low-molecular-weight heparin (LMWH) for the remainder of pregnancy and 6 weeks postpartum following the same principles as described below for mechanical heart valves.
What anticoagulation is required for pregnant individuals with a mechanical heart valve?

Most mechanical heart valves are bileaflet valves; tilting and caged ball mechanical valves are rarely used because of their increased risk of thrombotic complications. Because of the need for surgical replacement with bioprosthetic valves, many young individuals will opt for a mechanical valve because these valves may last a lifetime. Importantly, lifelong therapeutic anticoagulation is a principal component of the medical management of mechanical heart valves to prevent valve thrombosis. In both pregnant and nonpregnant adults, the risk of thrombosis is substantially increased in those with mechanical valves than in those with bioprosthetic valves, and thrombosis is a source of major morbidity and mortality. Additional perinatal complications are noted in pregnancies with mechanical valves, including an increased risk of perinatal loss, preterm delivery, cesarean delivery, and hemorrhage. Notably, the World Health Organization (WHO) has classified pregnancy in individuals with a mechanical heart valve to be very high risk (modified WHO risk category III) because of a substantially increased risk of maternal mortality or severe morbidity. Data from the last 20 years suggest that the mortality rate among people with mechanical heart valves is approximately 1%, with rates varying on the basis of the anticoagulation regimen used. Anticoagulation regimens indicated outside of pregnancy for patients with mechanical valves should be continued during pregnancy with the possibility of modifications based on the type of valve, the trimester of pregnancy, individual risk tolerance, and circumstances around the time of delivery. Given the higher risk of valve thrombosis and perinatal morbidity because of physiological changes associated with pregnancy, we recommend continuing therapeutic anticoagulation before, during, and after pregnancy for individuals with a mechanical heart valve (GRADE 1B).

The management options during labor and delivery are outlined separately in this document. Given the complexities of therapeutic anticoagulation management throughout pregnancy, delivery, and the postpartum period in the critical condition of a mechanical heart valve, the remainder of this document will largely focus on various management approaches, summarized in Figures 1 and 2.

How should anticoagulation for pregnant individuals with a mechanical valve be managed before a planned pregnancy and in the first trimester?

Pregnant individuals are at increased risk of valve thrombosis given the hypercoagulable state of pregnancy, with valve thrombosis occurring in approximately 5% of pregnancies. Warfarin is the preferred agent for anticoagulation in nonpregnant individuals with a mechanical heart valve. Mitral prosthetic valves are more prone to thrombosis than aortic valves because of the lower velocity of blood flow. Typically, the target international normalized ratio (INR) is 2.5 for mechanical heart valves in the aortic position and 3.0 for valves in the mitral position and right-sided valves.

Developing fetuses are most vulnerable to warfarin at 6 to 12 weeks of gestation because of its proposed interference with crucial steps during embryonic ossification. The rate of warfarin embryopathy occurred in up to 29.6% of pregnancies exposed at some point in the first trimester of pregnancy; however, larger studies more consistently report rates ranging from 2% to 12%. The clinical features of warfarin embryopathy include nasal hypoplasia, chondrodysplasia punctata, cardiac malformations, microcephaly, optic atrophy, blindness, deafness, and central nervous system abnormalities. In addition, a miscarriage rate of up to 24% has been reported, although it is similar to the baseline rate of approximately 20%. The risk of warfarin embryopathy and other warfarin-related complications may be dose dependent, with some purporting an acceptably low risk of these complications, including warfarin embryopathy, with doses ≤ 5 mg/d. In a 2017 meta-analysis, the rate of fetal risks (defined as a composite of spontaneous abortion, fetal death, and any congenital anomaly) were similar between individuals taking warfarin ≤ 5 mg/d and those managed with LMWH (15% [95% confidence interval (CI), 7–27] vs 14% [95% CI, 4–29], respectively).

The 2020 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines regarding the management of anticoagulation in pregnant individuals with mechanical valves highlights that there is no ideal anticoagulant for pregnant individuals with a mechanical heart valve; thus, shared decision-making and prepregnancy counseling (preferred) are important to discuss the risks and benefits of each strategy. Warfarin use leads to the lowest risk of valve thrombosis; however, it is associated with the highest likelihood of congenital abnormalities (with first-trimester use) and perinatal loss, particularly with doses >5 mg/d. For patients on ≤ 5 mg/d of warfarin to maintain therapeutic INR targets, the continuation of warfarin throughout the first trimester of pregnancy is included as a reasonable approach by the ACC, the AHA, and the European Society of Cardiology (ESC). For patients who decline warfarin use during the first trimester of pregnancy, LMWH is the anticoagulant of choice given its fetal safety profile; however, the use of LMWH is associated with an increased risk of valvular thrombosis during pregnancy compared with the use of warfarin (approximately 4%–16% compared with 2%–4%, respectively). These higher rates of valve thrombosis with the use of LMWH during pregnancy initially lead to recommendations against their use in pregnant people with mechanical valves. Importantly, most of these studies did not adhere to a strict anticoagulation protocol, and many did not report whether anti-Xa levels were used to guide LMWH
It is possible that previously reported adverse outcomes are the result of inadequate anticoagulation. LMWH is preferred vs unfractionated heparin (UFH) because of better bioavailability, more predictable anticoagulation with decreased bleeding risk, and lower incidence of both osteoporosis and heparin-induced thrombocytopenia. In addition, the risk of valve thrombosis during pregnancy with the use of subcutaneous UFH is unacceptably high, and its use is not recommended.

If a patient is on warfarin and opts to switch to LMWH after counseling, the transition from 1 agent to the other should be done as early as possible (ideally before 6 weeks of gestation). The transition should take place in a setting that allows rapid evaluation and dose adjustment with close monitoring to avoid prolonged periods of suboptimal anticoagulation. It is critical to note that several studies have found that these transition periods place individuals at high risk of thrombosis, with 1 study noting that 50% of observed valve thromboses occurred during a
transition from warfarin to LMWH in the first trimester of pregnancy.9 We suggest that patients be counseled that anticoagulation transition periods during pregnancy represent a vulnerable risk time and that these rapid conversions may be best accomplished in an inpatient setting.

The recommended starting dose of the most commonly used LMWH, enoxaparin, is 1 mg/kg (actual body weight) subcutaneously every 12 hours and is adjusted to achieve therapeutic anti-Xa levels. After 3 doses have been administered, anti-Xa levels should be checked. In contrast, it is reasonable to adjust therapeutic LMWH used for maternal venous thromboembolism during pregnancy on the basis of maternal weight alone.30 For individuals with a mechanical heart valve, current guidelines recommend targeting a peak anti-Xa level of 0.8 to 1.2 U/mL.
measured 4 hours after dosing.7 Importantly, this level has been associated with subtherapeutic trough anti-Xa levels in nearly 50% of patients.38,39 The exception is that in patients with a mechanical valve in the mitral position, peak anti-Xa ideally should be between 1.0 and 1.2 U/mL.40 Recent studies have suggested the importance of monitoring not only peak but also trough anti-Xa levels.11 Trough levels are drawn immediately before the next scheduled dose of LMWH. A goal trough level of >0.6 U/mL (>0.7 U/mL for pregnant individuals at high risk of valve thrombosis) (Box) has been recommended.11 Doses >1 mg/kg subcutaneously every 12 hours are likely to be needed to achieve these recommended therapeutic ranges. Close monitoring of the patient’s symptoms to detect early hemodynamic changes suggesting valve thrombosis and monitoring both trough and peak anti-Xa levels every 1 to 2 weeks to assure patient compliance is advisable.38,39 In the unlikely event that peak levels exceed 1.5 U/mL and trough levels are low, a 3-times daily dosing schedule may be considered.

Given the fetal risks associated with the use of warfarin and the frequent dose adjustments with LMWH, many people are likely to inquire about alternative anticoagulants. The use of new oral anticoagulants, such as dabigatran, rivaroxaban, edoxaban, and apixaban, is not recommended in pregnant or nonpregnant patients with mechanical heart valves because of an excess of thromboembolic and bleeding events among patients in the dabigatan group.61 We suggest continuing warfarin in the first trimester of pregnancy after careful patient counseling in individuals requiring a warfarin dose of ≤5 mg/day to maintain a therapeutic INR, taking into account the risk of warfarin embryopathy but decreased risk of valve thrombosis (GRADE 2B). We suggest using adjusted-dose LMWH as an alternative anticoagulant during the first trimester of pregnancy in pregnant people with mechanical heart valves receiving warfarin at a dose of >5 mg/day or in those who decline warfarin, provided anti-Xa levels are monitored every 1 to 2 weeks (GRADE 2B).35,39,42,44 We recommend titrating LMWH dosing based on both trough (>0.6 U/mL) and peak (0.8–1.2 U/mL for aortic valves and 1–1.2 U/mL for mitral valves) anti-Xa levels, with more frequent anti-Xa evaluations when dosing is adjusted (GRADE 1C).38,39,43,44 We 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 (GRADE 1C). For patients declining warfarin in the first trimester of pregnancy and if anti-Xa level monitoring is not available, we recommend continuous intravenous (IV) UFH in the first trimester of pregnancy to maintain adequate anticoagulation (GRADE 1C).

How should anticoagulation for pregnant individuals with a mechanical valve be managed in the second and third trimesters?

As in the first trimester of pregnancy, warfarin and LMWH remain the 2 most commonly used anticoagulants in the second and third trimesters of pregnancy for pregnant individuals with a mechanical valve. The ACC and AHA recommend that warfarin be considered during the second and third trimesters of pregnancy in people with a mechanical heart valve. In a more recent meta-analysis, the estimated average risk of maternal adverse outcome (composite of maternal death, valve failure, and thrombosis) for warfarin throughout pregnancy was 5.0% (95% CI, 2.5–8.5) to 15.5% (95% CI, 7.6–25.4) for dose-adjusted LMWH throughout pregnancy and 15.9% (95% CI, 4.9–31.6) for a regimen of dose-adjusted LMWH in the first trimester of pregnancy followed by warfarin for the remainder of the pregnancy.13 Based on studies consistently demonstrating lower maternal mortality and valve complications, particularly thrombosis, with warfarin, the ACC and AHA recommend warfarin for all patients during the second and third trimesters of pregnancy.7 However, the available data suggest that regimens requiring transition from 1 type of anticoagulant to another increase the risk of thrombotic complications.7,13 These data, along with individual practice experience and comfort with dose-adjusted LMWH for pregnant individuals with mechanical heart valves, should be considered when using such regimens.

Continued warfarin exposure during the second and third trimesters of pregnancy leads to additional fetal risks because warfarin crosses the placenta and results in anticoagulation of the fetus. A meta-analysis of pregnancies with mechanical heart valves reported the following incidence of relevant fetal and neonatal adverse effects attributable to warfarin exposure throughout pregnancy: intracranial hemorrhage (2.0%), stillbirth (4.6%), and neonatal death (2.3%).15 In 1 case series examining published cases of pregnancies exposed to warfarin derivatives, the incidence of fetal hemorrhage, including live birth and stillbirth, was 4.3% (18/418).22 After counseling, pregnant individuals may choose to decline warfarin use in the second or third trimester of pregnancy in light of the associated fetal complications despite improved maternal outcomes.

In an attempt to limit warfarin dosage during pregnancy and consequently decrease the fetal risks associated with...
its use, some have proposed a “low-dose anticoagulation strategy” targeting INR values between 1.5 and 2.5 in selected patients at low risk of thrombosis.\textsuperscript{45,46} To date, the evidence is very limited, and thus, this strategy is not recommended. Instead, current guidelines during pregnancy should be followed, targeting an INR of 2.5 for aortic mechanical heart valves and 3.0 for mitral mechanical valves when using warfarin.\textsuperscript{7}

We suggest using warfarin for anticoagulation from 12 to 36 weeks of gestation, particularly for patients at high risk of thrombosis (Box), with an INR target of 2.5 for those with mechanical aortic valves and 3.0 for those with mechanical mitral valves (GRADE 2A).\textsuperscript{31} For pregnant people declining warfarin in the second and third trimesters of pregnancy after counseling, we suggest using adjusted-dose LMWH (eg, enoxaparin) as an alternative anticoagulant, provided anti-Xa levels are monitored every 1 to 2 weeks (GRADE 2B).\textsuperscript{7,9,28,42} We suggest titrating LMWH dosing based on both trough (>0.6 U/mL) and peak (0.8–1.2 U/mL for aortic valves and 1.0–1.2 U/mL for mitral valves) anti-Xa levels.\textsuperscript{38,39,43,44}

Can concomitant aspirin therapy be safely administered to pregnant individuals requiring therapeutic anticoagulation for a mechanical heart valve?

Cardiac or noncardiac indications for low-dose aspirin therapy may exist during pregnancy, such as AF, a hypercoagulable state, or for preeclampsia prevention.\textsuperscript{8} Low-dose aspirin is safe for both the mother and fetus throughout pregnancy, and its concomitant use is deemed safe by the ACC and AHA\textsuperscript{7}; however, each patient’s bleeding risk should be considered. We suggest continuing low-dose aspirin (81 mg) when indicated in pregnant individuals with a mechanical heart valve in conjunction with therapeutic anticoagulation (GRADE 2C).\textsuperscript{47}

What is the optimal timing and mode of delivery for pregnant individuals with a mechanical heart valve?

Given the complexities of anticoagulation planning around the time of delivery, attempts should be made for a coordinated, scheduled delivery. There are no studies evaluating the optimal timing of delivery in patients with mechanical heart valves, but given substantial ongoing maternal risks and favorable neonatal outcomes, it is reasonable to plan an early-term delivery. Considerations when deciding timing and mode of delivery include the patient’s current and previous obstetrical history, risks associated with interruption of anticoagulation, availability of relevant specialists, any notable fetal factors, and neonatal implications of prematurity. In general, the presence of a mechanical heart valve is not necessarily an indication for cesarean delivery, but it may be the preferred route for select patients in whom interruption of anticoagulation should be particularly minimized. Few studies have reported the mode of delivery from pregnancies with mechanical heart valves. One meta-analysis included this information and reported a high cesarean delivery rate, between 41% and 67%, in this population.\textsuperscript{5} For pregnant individuals with a mechanical heart valve and no other complication, we recommend a planned delivery between 37 0/7 and 38 0/7 weeks of gestation, taking into consideration relevant maternal and fetal factors to determine the optimal mode of delivery for each patient (Best Practice).

How should therapeutic anticoagulation be managed before planned delivery in pregnant people with mechanical heart valves?

The tenets of therapeutic anticoagulation in pregnant individuals with a mechanical valve around the time of delivery are 3-fold: (1) to minimally interrupt therapeutic anticoagulation and limit the risk of valve thrombosis; (2) to facilitate appropriate anesthesia, that is, neuraxial, if desired; and (3) to minimize the risk of maternal and fetal hemorrhage at the time of delivery and immediately postpartum. Various strategies may be used to achieve these goals and will likely be driven by obstetrical, anesthetic, and maternal factors. Current guidelines from the ACC, the AHA, and the ESC recommend transitioning all pregnant individuals with mechanical heart valves on warfarin to LMWH or IV UFH at 36 weeks of gestation; the latter approach necessitates inpatient care until delivery.\textsuperscript{7,11} Patients anticoagulated with LMWH in the second or third trimester of pregnancy may continue such therapy until 36 to 48 hours before their planned delivery, at which time they should be admitted for transition to IV UFH.\textsuperscript{11} The rationale for using IV UFH instead of LMWH around the time of delivery is the shorter half-life of this agent (60–90 minutes), ease of obtaining therapeutic levels, frequent titration capabilities during labor, and availability of an effective antidote (protamine sulfate) in cases of unexpected hemorrhagic complications. For pregnant individuals with a mechanical heart valve anticoagulated with warfarin during the second and third trimesters of pregnancy, we recommend transitioning to dose-adjusted LMWH at 35 to 36 weeks of gestation (with planned delivery at 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 and 1.0–1.2 U/mL for mitral valves) levels and then transitioning these patients to bridging anticoagulation with IV UFH in an inpatient setting 36 to 48 hours before planned delivery (GRADE 1C). For pregnant individuals with a mechanical heart valve anticoagulated with dose-adjusted LMWH during the second and third trimesters of pregnancy, we recommend transitioning to IV UFH in an inpatient setting 36 to 48 hours before planned delivery (GRADE 1C).

How should therapeutic anticoagulation be managed during labor and delivery in pregnant individuals with a mechanical heart valve?

IV UFH is usually started 12 hours after discontinuation of LMWH at a dose of 18 U/kg/hour, without a loading dose. Current guidelines recommend that IV UFH be titrated at...
6-hour intervals to achieve an activated partial thromboplastin time (aPTT) at least twice the baseline and maintained until 4 to 6 hours before delivery. The hypercoagulable state of pregnancy may result in shorter aPTT values rendering the test unreliable to titrate UFH during pregnancy. Studies are limited regarding the optimal target anti-Xa range, and no studies have been conducted in pregnant individuals with a mechanical heart valve. Available studies have used an anti-Xa range of 0.3 to 0.7 U/mL in nonpregnant individuals and pregnant individuals with venous thromboembolism.

Institutional protocols may involve IV UFH titration with anti-Xa monitoring; however, robust data in pregnancy, and specifically in the setting of mechanical heart valves, are currently lacking. Despite the latter, and acknowledging that anti-Xa is less affected by extraneous factors, shows less variability, and results in fewer dose adjustments to achieve therapeutic values, we suggest titrating UFH with anti-Xa levels where available, taking into consideration the catastrophic consequences of inadequate anticoagulation in pregnant individuals with a mechanical heart valve. We suggest titrating IV UFH during labor and delivery to achieve an anti-Xa level of 0.7 to 1.0 U/mL and maintaining this level until 4 to 6 hours before delivery (GRADE 2B).

Mode of delivery and anesthetic plan should be carefully discussed and planned by a multidisciplinary team, including maternal-fetal medicine subspecialists, obstetrical anesthesiologists, and cardiologists. The administration of neuraxial anesthesia in laboring people should be carefully managed in collaboration with an experienced anesthesiology team. In most cases, the route of delivery is dictated by obstetrical indications. For patients with mechanical heart valves requiring a cesarean delivery, we recommend stopping the UFH infusion 4 to 6 hours before the scheduled surgery and administering neuraxial anesthesia after documentation of a normal aPTT value (GRADE 1C). For patients with mechanical heart valves in whom vaginal delivery is expected, we recommend continuation of the UFH infusion until active labor (6-cm cervical dilation in most cases) is achieved, at which time the infusion is stopped (GRADE 1C). The goal at this point is to achieve delivery within the next 6 hours to minimize the amount of time off anticoagulation. For patients with mechanical heart valves desiring an epidural, we recommend stopping IV UFH 4 to 6 hours before planned regional anesthesia placement with documentation of a normal aPTT value (GRADE 1C). Management decisions regarding placement and removal of epidural catheters in patients receiving UFH should be based on aPTT value and not anti-Xa levels as there is a lack of evidence for the latter. Whether IV UFH should be restarted 1 hour after an uncomplicated placement of an epidural catheter and continued until active labor is achieved should be determined on a case-by-case basis taking into consideration anticipated interval until delivery, the risk of valve thrombosis, and the risk of spinal or epidural hematoma. The Society for Obstetric Anesthesia and Perinatology has not recommended the use of neuraxial anesthesia with therapeutic anticoagulation under usual circumstances; special circumstances will require careful discussion and planning by a multidisciplinary team, including maternal-fetal medicine subspecialists, obstetrical anesthesiologists, and cardiologists. If IV UFH is restarted 1 hour after uncomplicated placement of an epidural catheter, it should be discontinued once active labor is achieved until delivery. Special attention should be given to the stability of the neuraxial catheter during labor to avoid catheter displacements. After delivery, we recommend removing the indwelling neuraxial catheter 4 to 6 hours after stopping IV UFH and documentation of a normal aPTT value (GRADE 1C).

A planned cesarean delivery under general anesthesia may be an acceptable alternative in people at high risk of thrombosis (eg, mitral valve position, previous thromboembolic events, and concomitant AF) in whom the use of neuraxial anesthesia will require an unacceptably prolonged period off anticoagulation.

Cesarean delivery is preferred if a patient presents in labor while therapeutically anticoagulated with warfarin because of concerns regarding fetal anticoagulation and concomitant risk of fetal intracerebral hemorrhage during labor. Importantly, maternal INR levels may not correlate with the level of fetal anticoagulation secondary to transplacental passage of warfarin. Because of its prolonged half-life (40–60 hours), warfarin could potentially be present in the fetal circulation for days after maternal treatment was stopped. The ESC recommends that cesarean delivery be performed if warfarin has been used within the last 2 weeks. The ACC and AHA do not specify a time frame during which cesarean delivery should be performed for those who have used warfarin. For pregnant individuals with a mechanical heart valve who have been therapeutically anticoagulated with warfarin within the last 2 weeks and who require urgent delivery, we recommend proceeding with a cesarean delivery to avoid fetal complications related to therapeutic anticoagulation with warfarin (GRADE 1C).

How is anticoagulation reversed in emergent situations?

The decision to reverse anticoagulation in people with a mechanical heart valve during pregnancy is complex because the consequence of reversal may be lethal because of massive valve thrombosis, and lack of reversal may have implications for both the pregnant individual and neonate. It is unlikely that full reversal is required for either a vaginal delivery or a cesarean delivery, and any decision about anticoagulant reversal in this high-risk population should be made in conjunction with cardiology expertise. If required, the antidote of choice is prothrombin complex concentrates with or without small doses of vitamin K for warfarin and protamine sulfate for both UFH and LMWH.

As discussed earlier, if a patient presents in preterm labor while fully anticoagulated on warfarin, a cesarean delivery is
indicated to prevent potential fetal hemorrhagic complications. The decision to reverse warfarin with prothrombin complex concentrates should take into account the bleeding risk (higher with conditions, such as placental abruption, placenta previa, and multiple previous cesarean deliveries) and the potential thrombotic complications associated with anticoagulation reversal (higher in high-risk patients, such as those with mitral prosthetic valve or history of previous thromboembolic complications).

In people presenting in labor while anticoagulated with LMWH or UFH, vaginal delivery may be ideal in the absence of obstetrical contraindications. The decision to reverse LMWH or UFH with protamine sulfate should follow the same risk-benefit analysis described earlier. Notably, protamine sulfate only partially reverses the anticoagulant effect of LMWH. For individuals on IV UFH, time to normalization of anticoagulant parameters after discontinuation of the infusion is dose dependent but may be rapid enough that protamine is only needed if there is a concern for major bleeding complications. We recommend that in pregnant individuals with a mechanical heart valve, the decision for anticoagulation reversal should be made in conjunction with cardiology, hematology, and anesthesia expertise while considering the individualized maternal and fetal risks (Best Practice).

**When is it safe to restart postpartum therapeutic anticoagulation in people with mechanical heart valves?**

The ideal time to restart therapeutic anticoagulation after delivery in pregnant individuals with a mechanical heart valve is unknown; however, prolonged periods without anticoagulation should be avoided. Several factors need to be considered when making this decision, including the estimated risk of postoperative bleeding, the use of neuraxial anesthesia, and the likelihood of thrombosis of the mechanical valve. Complex surgical cases with difficulty achieving hemostasis may require a longer period without anticoagulation than straightforward cases with a low risk of postoperative bleeding. The likelihood of valve thrombosis relates to the valve position (higher risk for valves in the mitral position) and the patient’s risk factors (coexistence of AF, large left atrial size, and previous thrombotic episodes) (Box). A high likelihood of valve thrombosis may warrant restarting anticoagulation sooner rather than later. We 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 or spinal catheter (GRADE 2B).

IV UFH may be started without a bolus aiming for an anti-Xa level between 0.7 and 1.0 U/mL. Concomitant warfarin may be started when anticoagulation with IV UFH is reinitiated. IV UFH should be maintained until the INR is in the therapeutic range: 2.5 for aortic valves and 3.0 for mitral prosthetic valves. IV UFH is recommended vs LMWH during the immediate postpartum period because it is easier to manage bleeding if it occurs with UFH. Although LMWH may be desirable because it can be taken as an outpatient, transitions between anticoagulation agents should be performed on an inpatient rather than an outpatient basis to allow for faster achievement of therapeutic values and a decrease in dosage fluctuations. We suggest reinitiation of IV UFH after delivery with the concomitant transition back to warfarin in the inpatient setting for ongoing therapeutic anticoagulation (GRADE 2C).

**What is the recommended treatment for patients with a mechanical valve thrombosis?**

Thrombosis of a mechanical heart valve is a life-threatening complication requiring immediate treatment. Physical examination findings are muffled mechanical heart valve sounds (muffled closing click), new-onset murmurs, signs and symptoms of congestive heart failure (dyspnea, orthopnea, or pulmonary congestion), and signs of peripheral embolic phenomena, including myocardial infarction and stroke. Thrombosis of right-sided valves may result in right-sided heart failure with peripheral edema in the absence of pulmonary congestion. The diagnosis of valve thrombosis is usually confirmed using transthoracic or transesophageal echocardiography. Moreover, fluoroscopy may be needed and can be performed with limited risk to the fetus.

Pregnant individuals with a mechanical heart valve presenting with any symptoms concerning for valve thrombosis should undergo an echocardiogram as part of the initial urgent evaluation, with additional testing modalities ordered based on clinical parameters.

Multidisciplinary care involving collaboration among maternal-fetal medicine, cardiology, critical care, cardiothoracic surgery, and anesthesia is necessary for determining the optimal management strategy. Urgent treatment with either low-dose slow-infusion tissue plasminogen activator (tPA) or emergent surgery is recommended for patients with symptomatic thrombosis of a left-sided prosthetic heart valve. Small clots in the mitral or aortic position (smaller than 0.8 cm²) and right-sided valve thromboses are usually managed medically with tPA. Larger clots involving the aortic or mitral valve, presence of severe symptoms, or both will usually require surgical treatment. In some instances, cardiopulmonary bypass may be needed, which carries a substantial risk of maternal and fetal mortality (approximately 10% and 30%, respectively).

Of note, tPA has a short half-life (5 minutes) and does not cross the placenta. The successful use of a low-dose slow-infusion protocol (25 mg IV over 6 hours every 24 hours, maximum 6 doses) has been described during pregnancy with favorable outcomes. When surgery is not required, a low-dose slow-infusion tPA protocol may be used when clinically indicated for the management of thrombosis of a mechanical heart valve during pregnancy. Close surveillance for bleeding complications is warranted. We recommend that the treatment of pregnant individuals presenting with mechanical valve thrombosis be guided by clinical
parameters in conjunction with a team with expertise in the management of valvular thrombosis; management options are generally similar to those in nonpregnant individuals and include thrombolytic and surgical intervention.\(^7,\text{11}\)

**Are there any considerations with breastfeeding for postpartum individuals with a mechanical heart valve?**

Counseling regarding infant feeding should occur with the usual considerations for pregnant individuals with a mechanical heart valve. Because patients will be transitioned back to warfarin after delivery, those interested in breastfeeding and poses no risk to the infant.\(^7,\text{4}\)

Warfarin is ionic, making it polar and nonlipophilic, and is heavily bound to plasma proteins.\(^7,\text{5}\) These properties result in no measurable warfarin in breast milk.\(^7,\text{6}\) Small series observing breastfeeding individuals taking 2 to 12 mg of warfarin sodium did not detect any warfarin in the breast milk of these individuals or the blood of their infants.\(^7,\text{7}\) In 1 case study, a breastfeeding individual inadvertently took 5 times the recommended dose of warfarin for 1 week and was supratherapeutic with an INR of >10, and the infant was found to have a normal INR and no clinical evidence of bleeding.\(^7,\text{9}\) We recommend warfarin for anticoagulation in all postpartum individuals with a mechanical heart valve given its superior anticoagulant properties in avoiding valve thrombosis and the safety of warfarin for the breastfed infant (GRADE 1C). LMWH and UFH are compatible with breastfeeding.\(^8,\text{0}\)

**Which birth control methods may be used in people with mechanical heart valves?**

Reproductive planning is essential for people with mechanical heart valves because of the dramatically increased risk of morbidity and mortality associated with pregnancy in this population.\(^1,\text{2}\) Patients who will be undergoing cesarean delivery should be counseled regarding the option of permanent sterilization if future fertility is not desired. Patients taking warfarin are at increased risk of hemorrhagic gynecologic complications, including heavy menstrual bleeding and hemoperitoneum from ruptured hemorrhagic cysts.\(^5,\text{1}\)

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For patients desiring contraception, the US Medical Eligibility Criteria for Contraceptive Use designates the levonorgestrel-containing intrauterine device, progesterone subcutaneous implants, and intramuscular depot medroxyprogesterone acetate as first-line therapies.\(^\text{8,1,8}\) In addition to their contraceptive effect, these methods substantially decrease the amount of menstrual bleeding; depot medroxyprogesterone acetate also prevents ovarian cyst formation and rupture. The progesterone-only pill (“minipill”) has a high failure rate (up to 9%) and should not be a first-line contraceptive agent.\(^2\)

The use of combined oral contraceptives containing estrogen may be considered on a case-by-case basis if other alternatives are not an option. The risk of thrombosis associated with the estrogen content is largely offset by the concomitant therapeutic anticoagulation with warfarin.\(^8,\text{1}\) For reproductive-aged individuals no longer desiring fertility, we recommend permanent sterilization methods for contraception; for patients who do not desire permanent sterilization, use of the levonorgestrel-containing intrauterine device, progesterone subcutaneous implants, or intramuscular depot medroxyprogesterone acetate should be first-line options (GRADE 1C).

**Which other cardiac conditions require anticoagulation during pregnancy?**

AF is rare among reproductive-aged women. However, the prevalence may increase as more people with corrected congenital heart disease survive to childbearing age. AF is a strong risk factor for cardioembolic events, and the hypercoagulable state of pregnancy may increase this risk. The decision to anticoagulate a nonpregnant patient with AF depends initially on the presence or absence of valvular disease. All patients with valvular AF, that is, coexisting with moderate or severe mitral stenosis or in the presence of a mechanical heart valve, require anticoagulation.\(^8,\text{3}\) In “nonvalvular” AF, the decision to anticoagulate depends on the CHA\(_2\)DS\(_2\)-VASc (Congestive heart failure; Hypertension; Age \(\geq75\) years; Diabetes mellitus; Stroke, transient ischemic attack, or thromboembolism history [Vascular disease]; Age 65–74 years; and Sex category [female]) score. This score considers several risk factors to identify patients with AF who will benefit from anticoagulation therapy (Table).\(^8,\text{4}\)

Because of the hypercoagulable state of pregnancy, some experts recommend therapeutic anticoagulation in all pregnant people with chronic AF regardless of the CHA\(_2\)DS\(_2\)-VASc score.\(^1,\text{3,8}\) The role of therapeutic anticoagulation in pregnant individuals with 1 self-limited episode of nonvalvular AF who are otherwise at low risk of thromboembolism is unclear.\(^8,\text{5}\) For pregnant individuals

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**TABLE**

The CHA\(_2\)DS\(_2\)-VASc scoring system for predicting stroke and thromboembolism in atrial fibrillation

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure or left ventricular dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age (\geq75) y</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke, transient ischemic attack, or thromboembolism history</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74 y</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (female)</td>
<td>1</td>
</tr>
</tbody>
</table>

Scores of 0 = low, 1 = intermediate, and \(\geq2\) = high risk. Reprinted with permission from Lip et al.\(^8,\text{1}\)

### Summary of recommendations

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>GRADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>We recommend continuing low-dose aspirin monotherapy without interruption before, during, and after pregnancy for individuals with a bioprosthetic heart valve to reduce the risk of valve thrombosis.</td>
<td>1C</td>
</tr>
<tr>
<td>2</td>
<td>We recommend continuing therapeutic anticoagulation before, during, and after pregnancy for individuals with a mechanical heart valve.</td>
<td>1B</td>
</tr>
<tr>
<td>3</td>
<td>We suggest continuing warfarin in the first trimester of pregnancy after careful patient counseling in individuals requiring a warfarin dose of $\leq 5$ mg/d to maintain a therapeutic INR, taking into account the risk of warfarin embryopathy, but decreased risk of valve thrombosis.</td>
<td>2B</td>
</tr>
<tr>
<td>4</td>
<td>We suggest using adjusted-dose LMWH as an alternative anticoagulant during the first trimester of pregnancy in pregnant people with mechanical heart valves receiving warfarin at a dose of $&gt;5$ mg/d or in those who decline warfarin, provided anti-Xa levels are monitored every 1 to 2 weeks.</td>
<td>2B</td>
</tr>
<tr>
<td>5</td>
<td>We recommend titrating LMWH dosing based on both trough ($&gt;0.6$ U/mL) and peak ($0.8$—$1.2$ U/mL for aortic valves and $1.0$—$1.2$ U/mL for mitral valves) anti-Xa levels, with more frequent anti-Xa evaluations when dosing is adjusted.</td>
<td>1C</td>
</tr>
<tr>
<td>6</td>
<td>We 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.</td>
<td>1C</td>
</tr>
<tr>
<td>7</td>
<td>For patients declining warfarin in the first trimester of pregnancy and if anti-Xa level monitoring is not available, we recommend continuous IV UFH in the first trimester of pregnancy to maintain adequate anticoagulation.</td>
<td>1C</td>
</tr>
<tr>
<td>8</td>
<td>We suggest using warfarin for anticoagulation from 12 to 36 weeks of gestation, particularly for patients at high risk of thrombosis (Box), with an INR target of 2.5 for those with mechanical aortic valves and 3.0 for mechanical mitral valves.</td>
<td>2A</td>
</tr>
<tr>
<td>9</td>
<td>For pregnant people declining warfarin in the second and third trimesters of pregnancy after counseling, we suggest using adjusted-dose LMWH (eg, enoxaparin) as an alternative anticoagulant, provided anti-Xa levels are monitored every 1 to 2 weeks.</td>
<td>2B</td>
</tr>
<tr>
<td>10</td>
<td>We suggest continuing low-dose aspirin (81 mg) when indicated in pregnant individuals with a mechanical heart valve in conjunction with therapeutic anticoagulation.</td>
<td>2C</td>
</tr>
<tr>
<td>11</td>
<td>For pregnant individuals with a mechanical heart valve and no other complication, we recommend a planned delivery between 37 0/7 and 38 0/7 wk of gestation, taking into consideration relevant maternal and fetal factors to determine the optimal mode of delivery for each individual patient.</td>
<td>Best practice</td>
</tr>
<tr>
<td>12</td>
<td>For pregnant individuals with a mechanical heart valve anticoagulated with warfarin during the second and third trimesters of pregnancy, we recommend transitioning to dose-adjusted LMWH at 35 to 36 wk of gestation provided anti-Xa levels are monitored weekly using both trough ($&gt;0.6$ U/mL) and peak ($0.8$—$1.2$ U/mL for aortic valves and $1.0$—$1.2$ U/mL for mitral valves) levels and then transitioning these patients to bridging anticoagulation with IV UFH in an inpatient setting 36 to 48 h before planned delivery.</td>
<td>1C</td>
</tr>
<tr>
<td>13</td>
<td>For pregnant individuals with a mechanical heart valve anticoagulated with dose-adjusted LMWH during the second and third trimesters of pregnancy, we recommend transitioning to IV UFH in an inpatient setting 36 to 48 hours before planned delivery.</td>
<td>1C</td>
</tr>
<tr>
<td>14</td>
<td>We suggest titrating IV UFH during labor and 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.</td>
<td>2B</td>
</tr>
<tr>
<td>15</td>
<td>For patients with mechanical heart valves requiring a cesarean delivery, we recommend stopping the UFH infusion 4 to 6 h before the scheduled surgery and administering neuraxial anesthesia after documentation of a normal aPTT value.</td>
<td>1C</td>
</tr>
<tr>
<td>16</td>
<td>For patients with mechanical heart valves in whom vaginal delivery is expected, we recommend continuation of the UFH infusion until active labor (6-cm cervical dilation in most cases) is achieved, at which time the infusion is stopped.</td>
<td>1C</td>
</tr>
<tr>
<td>17</td>
<td>For patients with mechanical heart valves desiring an epidural, we recommend stopping IV UFH 4 to 6 h before planned regional anesthesia placement with documentation of a normal aPTT value.</td>
<td>1C</td>
</tr>
<tr>
<td>18</td>
<td>After delivery, we recommend removing the indwelling neuraxial catheter 4 to 6 h after stopping IV UFH and documentation of a normal aPTT value.</td>
<td>1C</td>
</tr>
<tr>
<td>19</td>
<td>For pregnant individuals with a mechanical heart valve who have been therapeutically anticoagulated with warfarin within the last 2 weeks and who require urgent delivery, we recommend proceeding with a cesarean delivery to avoid fetal complications related to therapeutic anticoagulation with warfarin.</td>
<td>1C</td>
</tr>
<tr>
<td>20</td>
<td>We recommend that in pregnant individuals with a mechanical heart valve, the decision for anticoagulation reversal should be made in conjunction with cardiology, hematology, and anesthesia expertise while considering the individualized maternal and fetal risks.</td>
<td>Best practice</td>
</tr>
</tbody>
</table>
requiring therapeutic anticoagulation to decrease the risk of thromboembolic complications related to AF, we recommend adjusted-dose LMWH (GRADE 1C). For postpartum individuals requiring therapeutic anticoagulation to decrease the risk of thromboembolic complications related to AF, we recommend adjusted-dose LMWH or warfarin until 6 weeks postpartum (GRADE 1C). After 6 weeks postpartum, ongoing anticoagulation use should be determined by the patient’s cardiologist.

Left ventricular systolic dysfunction

Left ventricular systolic dysfunction is an important risk factor for thrombosis within the left ventricle.35 Expert opinion suggests anticoagulation during pregnancy and up to 6 weeks postpartum for pregnant people with dilated cardiomyopathy and an ejection fraction of <35%.86,87 For pregnant individuals with left ventricular systolic dysfunction and an ejection fraction of <35%, we recommend adjusted-dose LMWH (GRADE 1C). For postpartum individuals with left ventricular systolic dysfunction and an ejection fraction of <35%, we recommend adjusted-dose LMWH or warfarin until 6 weeks postpartum (GRADE 1C). After 6 weeks postpartum, ongoing anticoagulation use should be determined by the patient’s cardiologist.

Fontan circulation

The Fontan circulation (direct connection of the caval veins into the pulmonary arteries) has resulted in the survival of many people born with single ventricle congenital heart disease. The passive circulation secondary to an absent right ventricle leads to stasis and a higher risk of venous thromboembolism.88,89 At the same time, chronic liver congestion leads to the abnormal synthesis of clotting factors with an increased risk of postpartum bleeding.90,91 The optimal anticoagulation regimen for Fontan patients, pregnant or nonpregnant, is currently unknown. Expert opinion suggests that anticoagulation during pregnancy should be considered in patients with a Fontan circulation and additional risk factors for thrombosis, such as atrial fibrillation.35
### Society for Maternal-Fetal Medicine grading system: GRADE recommendations

<table>
<thead>
<tr>
<th>GRADE recommendation</th>
<th>Clarity of risk and benefit</th>
<th>Quality of supporting evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A. Strong recommendation, high-quality evidence</td>
<td>Benefits outweigh risks and burdens, or vice versa.</td>
<td>Consistent evidence from well-performed, RCTs, or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.</td>
<td>Strong recommendation that can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.</td>
</tr>
<tr>
<td>1B. Strong recommendation, moderate-quality evidence</td>
<td>Benefits outweigh risks and burdens, or vice versa.</td>
<td>Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.</td>
<td>Strong recommendation that applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.</td>
</tr>
<tr>
<td>1C. Strong recommendation, low-quality evidence</td>
<td>Benefits seem to outweigh risks and burdens, or vice versa.</td>
<td>Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Any estimate of effect is uncertain.</td>
<td>Strong recommendation that applies to most patients. However, some of the evidence base supporting the recommendation are of low quality.</td>
</tr>
<tr>
<td>2A. Weak recommendation, high-quality evidence</td>
<td>Benefits closely balanced with risks and burdens.</td>
<td>Consistent evidence from well-performed RCTs or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.</td>
<td>Weak recommendation; best action may differ depending on circumstances or patients or societal values.</td>
</tr>
<tr>
<td>2B. Weak recommendation, moderate-quality evidence</td>
<td>Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens.</td>
<td>Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate.</td>
<td>Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.</td>
</tr>
<tr>
<td>2C. Weak recommendation, low-quality evidence</td>
<td>Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.</td>
<td>Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Any estimate of effect is uncertain.</td>
<td>Very weak recommendation; other alternatives may be equally reasonable.</td>
</tr>
<tr>
<td>Best practice</td>
<td>Recommendation in which either (1) there is an enormous amount of indirect evidence that justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together and carefully summarize) or (2) recommendation to the contrary would be unethical.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**GRADE**, Grading of Recommendations Assessment, Development, and Evaluation; **RCT**, randomized controlled trial.

* Adapted from Guyatt et al.33

Conclusion
The management of pregnancies complicated by maternal cardiac disease requires several considerations, including the appropriate use of anticoagulants during the antepartum, intrapartum, and postpartum periods. Patients with mechanical heart valves represent some of the highest risk pregnancies cared for by obstetricians. Adequate anticoagulation to maintain a therapeutic state is imperative in these patients and requires frequent monitoring. Other cardiac conditions in pregnancy increase the risk of thrombosis and may necessitate the need for anticoagulants during and after pregnancy. The management of these complicated cases requires an experienced multidisciplinary team, including maternal-fetal medicine subspecialists, cardiologists, anesthesiologists, and possibly cardiothoracic surgery.

REFERENCES


This document has undergone an internal peer review through a multilevel committee process within SMFM. This review involves critique and feedback from the SMFM Publications and Document Review Committees and final approval by the SMFM Executive Committee. SMFM accepts sole responsibility for the document content. SMFM publications do not undergo editorial and peer review by the American Journal of Obstetrics & Gynecology. The SMFM Publications Committee reviews publications every 18 to 24 months and issues updates as needed. Further details regarding SMFM publications can be found at www.smfm.org/publications.

SMFM recognizes that obstetrical patients have diverse gender identities and is striving to use gender-inclusive language in all of its publications. SMFM will be using the terms “pregnant person” or “pregnant individual” instead of “pregnant woman” and will use the singular pronoun “they.” When describing study populations used in research, SMFM will use the gender terminology reported by the study investigators.

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