Evaluating the need for anticoagulant prophylaxis during pregnancy in asymptomatic heterozygous carriers of factor V Leiden

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Thrombosis during pregnancy is the leading cause of maternal death in the United States (Dizon-Townson et al., 2005). Approximately 75 to 80 percent of pregnancy-associated venous thromboembolisms (VTE) are deep vein thromboses (DVT) with the remaining 20 to 25 percent manifesting as pulmonary emboli (PE) (James, 2009).

Pulmonary embolism is responsible for about 15 percent of pregnancy-related deaths (Pomp, Lenselink, Rosendaal, & Doggen, 2008). Factor V Leiden (FVL) mutation is the most common genetic factor contributing to clot formation (Dizon-Townson et al., 2005) with an estimated five to nine percent of Caucasians with the mutation. FVL is an autosomal dominant condition. A single point mutation of the factor V gene results in a substitution of glutamine for arginine. The mutation inhibits efficient inactivation of factor V by activated protein C. Thus, the Factor V protein remains in the circulation longer leading to excessive production of thrombin and a prothrombotic state (Lockwood, 2002). Although common in white European populations, this mutation is rare in those of African and Asian descent, representing less than one percent of these populations (Preston et al., 1996).

Heterozygous carriers of FVL confer a 4-to 8-fold increased risk of thrombosis over the normal population (Kujovich, 2004). Patients with the much less common homozygous variant present an even greater risk for thrombosis and may be over 100 times more likely to experience a thrombotic episode than those without thrombophilia. The consequences of Factor V Leiden mutation may be more pronounced in the pregnant woman; however, she may not be the only person affected by the genetic trait she carries. The thrombotic tendencies of FVL can manifest as thrombotic lesions in the
uteroplacental vessels, compromising blood flow to the placenta and resulting in
deficient perfusion to the fetus. Thus, both heterozygous and homozygous carriers of
FVL may be at higher risk for vascular complications leading to adverse pregnancy
outcomes such as preeclampsia, placental abruption, intrauterine growth restriction
(IUGR), and second- and third-trimester fetal loss (Lockwood, 2002).

Pregnancy and the postpartum period are known to be a time of substantially
increased thrombotic risk, not only for those with FVL but in the general population as
well. Virchow’s triad of hypercoagulability, stasis, and endothelial injury is normally
present in pregnancy and the postpartum period. The risk for experiencing VTE is
estimated to be 0.7-1.3 per 1000 pregnant women compared to 1 per 10,000 non-
pregnant women of reproductive age (Martinelli et al., 2002). Several factors contribute
to this increased thrombotic potential, including an increase in clotting factors. Pro-
coagulants fibrinogen and factor V, VIII, IX, X, and XII levels increase while
anticoagulant protein S levels decrease and activated factor V resistance develops. The
net effect is excessive generation of thrombin (Paidas et al., 2011). Venous stasis
occurs secondary to pressure of the developing fetus on the inferior vena cava and
pelvic veins (American College of Obstetricians and Gynecologists, 2011). A surge in
pregnancy hormones increases the likelihood of thrombosis by causing hyperlipidemia
and insulin resistance. Although the exact mechanism whereby hormones cause
hyperlipidemia in pregnancy is not well-studied, elevated estrogen levels are known to
increase plasma triglycerides and lipoproteins (Louis & Platt, 2011). The intrinsic
pathway of the coagulation cascade is activated when lipoproteins contact vessel walls
triggering thrombus formation (Torshin, 2007). A decline in HDL late in the second
trimester is thought to increase insulin levels, causing insulin resistance to develop later in pregnancy (Louis & Platt, 2011). This resistance triggers adipocytes and endothelium to increase expression of plasminogen activator inhibitor-1 (PAI-1) which reduces fibrinolysis (Mills & Grant, 2002).

The antenatal period is not the only time of increased risk of thrombosis; special consideration must be given to the postpartum period. Women are 15-20 times more likely to experience a thromboembolism during the first six weeks following birth as opposed to during pregnancy (Martinelli et al., 2002). The reason for this is unknown but is hypothesized to be a selective evolutionary advantage to prevent hemorrhage and maternal death during childbirth (James, 2009). The incidence of postpartum VTE is higher in women who are non-ambulatory after giving birth (Bates, Greer, Pabinger, Sofaer, & Hirsh, 2008) and those who deliver by cesarean section. This is due to all three components of Virchow’s triad being impacted during surgical delivery: a pregnancy-associated hypercoagulable state, endothelial injury occurring during the procedure, and vascular stasis due to immobilization while under anesthesia (Queenan, Spong, & Lockwood, 2012).

Previous personal history of VTE is the most important factor when evaluating the likelihood a patient will experience a thrombotic event (James, 2009). Thrombotic risk may be further exacerbated by older maternal age due to increased pro-coagulant levels associated with aging (Esmon, 2009) and the presence of comorbid thrombophilias, including prothrombin and methylenetetrahydrofolate reductase (MTHFR) mutations and deficiencies in protein C and S. Each of these mutations carries a varying degree of thrombotic risk. Like FVL, the prothrombin mutation is
inherited in an autosomal-dominant fashion. A mutation in the promoter of the prothrombin gene causes increased production of prothrombin which generates excess thrombin. Patients that possess the MTHFR mutation have decreased ability to efficiently metabolize homocysteine, resulting in endothelial injury and a possible increased thrombotic risk. Deficiencies in the anticoagulants protein C and S are less common and lead to decreased degradation of specific clotting factors creating a pro-coagulant state (Kujovich, 2004).

The actual risk of VTE or adverse obstetric outcome for pregnant heterozygous carriers of FVL without comorbid thrombophilias or prior history of venous thrombosis has not yet been determined. Limited conclusive evidence exists because most of our current knowledge has been gathered from small retrospective studies with conflicting results (Said et al., 2010). The vast majority of studies have focused on women with recurrent thrombotic episodes because researchers are unable to anticipate which women will have a VTE or experience pregnancy complications secondary to FVL (Lockwood, 2002). Furthermore, a possible publication bias may exist regarding the correlation of Factor V Leiden and adverse pregnancy outcomes. Studies that report a statistically significant association between thrombophilia and pregnancy complications may be favored by journal editors and thus are more likely to be published than those studies which support the null hypothesis or are inconclusive (Said, et al., 2010).

Current recommendations for management of FVL during pregnancy proposed by the American Congress of Obstetricians and Gynecologists, formerly the American College of Obstetricians and Gynecologists (ACOG), are based only on “consensus and expert opinion” due to the low level of evidence regarding this issue. For individuals
heterozygous for FVL without previous venous thromboembolism, antepartum management includes either surveillance alone or prophylaxis with low molecular weight heparin (LMWH) or unfractionated heparin (UFH). Postpartum recommendations consist of either surveillance alone or anticoagulation therapy if the patient has other risk factors such as obesity, lack of ambulation for a prolonged period, or a first-degree relative with thrombosis before age 50. Warfarin is an option for anticoagulation in the postpartum period only as it may cross the placenta and cause bleeding in the fetus if given during pregnancy. For all patients with inherited thrombophilias, ACOG stresses the importance of individual assessment for risk factors when considering the use of pharmacologic therapy (2011).

The American College of Chest Physicians (ACCP) has put forth guidelines for pregnant patients with inherited thrombophilias and no prior history of VTE. As with the recommendations proposed by ACOG, ACCP guidelines are based on “low-quality studies”. They suggest that routine antepartum thromboprophylaxis is unnecessary in the absence of other risk factors. Patients with no family history of VTE should be closely monitored during the postpartum period but do not require anticoagulant prophylaxis. For those with history of VTE in a first-degree relative, it is recommended that patients be prescribed LMWH or a vitamin K antagonist for six weeks postpartum. These, however, are considered weak recommendations and based only on limited evidence. ACCP guidelines strongly encourage physicians to practice “clinical vigilance” and to educate their patients on the symptoms of VTE and to seek immediate medical attention should they experience these symptoms (Bates et al., 2012).
UFH and LMWH, administered through subcutaneous injections, are the agents of choice for anticoagulant prophylaxis during pregnancy because they do not cross the placenta. Because of its high molecular weight, UFH does not enter into breast milk. Some studies suggest that small amounts of LMWH may be excreted into breast milk; however, no clinical effects in nursing infants have been reported due to the low bioavailability of the drug (Bates et al., 2012). Both anticoagulants may cause adverse effects in the mother such as hemorrhage, thrombocytopenia, and local allergic reactions at the injection site. UFH therapy has been cited as a source of fractures secondary to bone loss in two percent of pregnant women using this drug. Data suggests these side effects are less common with LMWH and for this reason LMWH are preferred over UFH for the prevention of thromboembolism (Bates et al., 2012). A 2005 review of 1436 pregnancies in which a LMWH was used for thromboprophylaxis found that complications of LMWH were rare and no serious effects, such as maternal mortality, were encountered. Postpartum hemorrhage greater than 500 mL, the most common side effect, was experienced in 24 pregnancies (1.7 percent). Since nine of these patients were also receiving dextran, an anti-thrombotic agent that decreases blood viscosity, actual risk of hemorrhage may be skewed (Greer & Nelson-Piercy, 2005).

Although safety has been assessed, there is limited data from controlled studies on the efficacy of anticoagulants in VTE prevention in pregnant women with thrombophilia, especially in those considered high-risk with multiple thrombophilias or an extensive personal or family history of thrombosis. Most of what is known about anticoagulant efficacy is extrapolated from studies performed in non-pregnant
individuals. It is controversial whether dose adjustments are required over the course of a patient’s pregnancy according to her changing weight or if the optimal therapeutic level can be maintained with no adjustments (Bates et al., 2012).

Not only is the optimal dose of anticoagulants still under investigation, their use during pregnancy may be costly for the patient. For an uninsured woman receiving a standard dose of 40 mg subcutaneous injection of enoxaparin daily, it is estimated that the average cost is approximately 7895 dollars for nine months of administration and an additional 1247 dollars if given for six weeks postpartum. Prophylaxis with a standard dose of 5000 units of UFH given subcutaneously twice daily may cost approximately 306 dollars for the duration of pregnancy and an additional 48 dollars for six weeks postpartum (Bradley, Brasel, Miller, & Pappas, 2010).

Conversely, a patient may be faced with much steeper medical bills should they forego pharmacologic therapy and experience a thrombotic event during pregnancy. According to 2009 prices in the United States, the average cost for the diagnosis and treatment of one episode of DVT is estimated to be roughly 7712 to 10,804 dollars while the diagnosis and treatment of a PE may cost between 9566 and 16,644 dollars (Dobesh, 2009).

There is no clear consensus whether clinical surveillance alone is adequate to manage the increased risk of VTE when combining the effect of pregnancy with FVL mutation or if these patients would benefit from receiving anticoagulation therapy prophylactically (Martinelli et al., 2002). The objective of this review is to evaluate the incidence of VTE (1) and adverse pregnancy outcomes (2) in untreated heterozygous
carriers of FVL with no thrombotic history and propose clear recommendations regarding management during pregnancy and the postpartum period (3).
Methods

Data Collection

A systematic review of the incidence of venous thromboembolism and adverse pregnancy outcomes of heterozygous carriers of FVL mutation with no prior history of thrombosis was carried out by searching the electronic database PubMed up to the end of August 2012. The search terms were pregnancy, Factor V Leiden, thrombophilia, heterozygous, venous thromboembolism, pregnancy outcomes, pregnancy complications, pregnancy loss, preeclampsia, placental abruption, intrauterine growth restriction, small for gestational age, asymptomatic, anticoagulants, and prophylaxis. The PubMed search was supplemented with an extensive manual search of reference lists.

Inclusion and Exclusion Criteria

All articles were acquired from peer-reviewed journals and were written in or translated into English. The quality of each report was assessed to ensure appropriateness of the research design and reproducibility of the study. Case reports, editorials, and reviews were excluded from analysis. Studies of patients with a personal history of thrombosis as well as studies where history was unspecified were also excluded. Patients with concomitant inherited or acquired thrombophilias, recurrent fetal loss, underlying medical problems that increase the likelihood of adverse pregnancy outcomes, valvular heart disease, and those using thromboprophylaxis prior to diagnosis of VTE were omitted from this review. Included in this review were prospective observational studies and case-controlled retrospective trials. All patients
had a confirmed pregnancy and underwent blood testing to confirm or rule out heterozygous carriage of Factor V Leiden.

**Data Analysis**

The major outcomes under investigation were incidence of VTE, pregnancy loss and stillbirth, preeclampsia, placental abruption, and intrauterine growth restriction. VTE included any objectively diagnosed DVT or PE that occurred during pregnancy or postpartum. The length of postpartum observation differed with some studies monitoring VTE occurrence for six weeks while others observed for three months. A diagnosis of pregnancy loss was defined as either fetal death occurring in utero or spontaneous expulsion of the fetus resulting in fetal death. This included early and late fetal loss and stillbirth. Preeclampsia was described as systolic blood pressure greater than 140 mmHg and/or diastolic blood pressure greater than 90 mmHg plus proteinuria, occurring on two occasions after twenty weeks gestation. This diagnosis was given only to patients previously normotensive with no proteinuria. A diagnosis of placental abruption was based on clinical symptoms of excessive vaginal bleeding, abdominal pain, and fetal distress and/or pathological examination of the placenta after delivery. Intrauterine growth restriction was defined as fetal growth in the tenth percentile or less for sex and gestation.
Results

The literature search yielded 11 studies that met the inclusion criteria. Seven of these were case-controlled retrospective studies and four were prospective studies. The methodology of each study was deemed appropriate for analysis with the overall limitations being the low number of prospective studies and the small samples of FVL patients in some studies.

VTE

Several studies assessed the incidence of VTE (Benedetto et al., 2002; Dizon-Townson et al., 2005; Kjellberg, van Rooijen, Bremme, & Hellgren, 2010; Said et al., 2010; Salomon et al., 2004; Tormene et al., 2001). Overall, heterozygous FVL carriage was not associated with venous thrombosis (Benedetto et al., 2002; Dizon-Townson et al., 2005; Said et al., 2010; Salomon et al., 2004). Two studies reported a slightly increased incidence of VTE in case patients but this difference did not reach statistical significance. Tormene et al. observed six VTE events occurring in 242 pregnancies in 94 heterozygous FVL carriers. This was compared to one VTE event occurring in 215 pregnancies of 81 non-carriers. Of these, six of the seven thrombotic events occurred during the postpartum period (2001). A prospective study by Kjellberg et al. reported three thromboembolic events in heterozygous FVL carriers, including two antenatal DVTs and one postpartum PE, which occurred out of 472 FVL carriers. This was compared to zero instances of VTE in 1030 non-carrier controls (2010).

Pregnancy Loss and Stillbirth

Six studies examined pregnancy loss and/or stillbirth in association with women heterozygous for FVL and reported conflicting results (Alfirevic et al., 2001; Dizon-
Townson et al., 2005; Kjellberg et al., 2010; Many et al., 2002; Martinelli et al., 2000; Said et al., 2010). Four studies found no significantly increased risk of pregnancy loss (Dizon-Townson et al., 2005; Kjellberg et al., 2010) or stillbirth (Alfirevic et al., 2001; Kjellberg et al., 2010; Many et al., 2002). Conversely, a case-control study by Martinelli et al. reported a 3-fold increase in late fetal loss with five of 67 case patients carrying the heterozygous FVL mutation compared to six carriers out of 232 women with normal pregnancies (2000). Said et al. observed a statistically significant association between FVL and stillbirth; however, this association must be observed with caution due to the small number of patients with this outcome (2010).

**Preeclampsia**

Eight studies reported on the incidence of preeclampsia in FVL carriers with no previous VTE (Alfirevic et al., 2001; Benedetto et al., 2002; Dizon-Townson et al., 2005; Facchinetti et al., 2003; Kjellberg et al., 2010; Kupferminc et al., 2000; Said et al., 2010; Salomon et al., 2004). Six of these did not find any statistically significant occurrence of preeclampsia in case patients (Alfirevic et al., 2001; Benedetto et al., 2002; Facchinetti et al., 2003; Kjellberg et al., 2010; Said et al., 2010; Salomon et al., 2004). A large prospective study by Dizon-Townson et al. reported a slight increase in risk for African American and Hispanic carriers of FVL, though there was no reported increase in risk for Caucasians (2005). Kupferminc et al. observed a statistically significant increased risk among FVL carriers; however, they did not report whether these patients were heterozygous or homozygous for the mutation. Their study found 15 FVL carriers out of 63 patients with preeclampsia compared to 8 FVL carriers out of 126 women with normal pregnancies (2000).
Placental Abruption

Six studies examined the incidence of placental abruption (Alfirevic et al., 2001; Benedetto et al., 2002; Dizon-Townson et al., 2005; Facchinetti et al., 2003; Kjellberg et al., 2010; Said et al., 2010). Overall, there was no observable association between heterozygous carriage of FVL and placental abruption (Alfirevic et al., 2001; Benedetto et al., 2002; Dizon-Townson et al., 2005; Kjellberg et al., 2010; Said et al., 2010). However, one small case-controlled study examined 50 cases of placental abruption and then assessed these mothers for coagulopathy. They reported 11 of the 50 women carrying the heterozygous FVL mutation compared to three carriers out of 100 patients in the healthy control group. This study reported a statistically significant association between FVL and placental abruption (Facchinetti et al., 2003).

Intrauterine Growth Restriction

Six studies reported on the association between FVL and intrauterine growth restriction. None of these studies found a statistically significant incidence of IUGR in FVL carriers when compared to populations without thrombophilia (Alfirevic et al., 2001; Benedetto et al., 2002; Dizon-Townson et al., 2005; Kjellberg et al., 2010; Said et al., 2010; Salomon et al., 2004).
Discussion

The results of this systematic review suggest that there may be only a slight association between some adverse obstetric outcomes and Factor V Leiden. It is unknown whether thrombophilia is a direct cause or if other factors may play a role in which patients experience a VTE or pregnancy complications. These results suggest only a very marginal risk of negative outcomes.

Although the relative risk for VTE during pregnancy may be slightly increased among carriers according to some studies, the overall probability for experiencing a thromboembolism or pregnancy complication is low and in our opinion does not justify use of either antepartum or postpartum pharmacologic prophylaxis; however, each patient should undergo an individualized assessment to rule out additional risk factors such as positive family history. Clinicians are encouraged to consider prophylactic LMWH during hospitalization for patients who undergo operative delivery. These recommendations agree with those discussed previously in the Ninth Edition of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

We recommend that patients with thrombophilia consider lifestyle changes to increase their chance of a successful pregnancy outcome. We suggest that patients be advised to maintain adequate hydration by drinking 8-12 eight-ounce glasses of water per day. Clinicians should counsel patients on weight control throughout pregnancy and the postpartum period. The appropriate amount of weight gain should be based on the patient’s pre-pregnancy weight and the number of fetuses she is carrying. We also recommend 30 minutes of low-impact exercise daily such as walking or swimming to improve blood flow in the lower extremities. Patients should consider compression
stockings to prevent venous stasis. Women who undergo operative delivery are advised to ambulate as soon as possible after birth to reduce the risk of developing VTE.

The above recommendations are based only on the limited data presented. A major limitation of this review is the small number of prospective studies assessing the incidence of VTE and adverse obstetric outcomes. More prospective studies could control for exposure to predisposing factors of thrombosis such as prolonged immobilization or smoking during pregnancy. Also, larger samples of FVL carriers are needed to strengthen these guidelines. These limitations may account for the conflicting results reported in several studies. The articles included in this review represent many Caucasian populations worldwide; however, these results may not be extrapolated to other races where FVL is less common. Furthermore, it cannot be assumed that the same level of risk applies to patients with more than one type of thrombophilia, since the presence of two or more thrombophilias may exert a synergistic effect (Gerhardt et al., 2000). Information is lacking on the usefulness of thromboprophylactic therapy during pregnancy. A randomized placebo-controlled study is needed to assess the efficacy of anticoagulants in prevention of pregnancy-associated VTE and placental vascular complications. It may be imprudent to support intervention until clear evidence is available showing anticoagulants improve maternal and fetal outcome, prove cost effective, and do not contribute to morbidity and mortality.

Many studies have reported on the incidence of VTE and adverse pregnancy outcomes in FVL carriers; however, the majority of these cases did not take history of VTE into account. Many studies grouped patients with previous personal thrombotic history together with patients considered low-risk with no history of VTE. It is important
to separate these two groups to stratify risk level during pregnancy. Because previous thromboembolism is the largest predictor of subsequent thrombosis, the negative effects of FVL mutation may be over-estimated in such studies when attempting to evaluate the risk for only those patients that have never experienced a thrombotic event.

The results of this review are very important to the fields of obstetrics and hematology. Carriers of the heterozygous variant of FVL with no thrombotic history can be reassured that their chances of a successful pregnancy outcome are high and prophylactic anticoagulation can be avoided in most cases.

Clinician education and knowledge regarding thrombophilia is lacking. A 2005 survey of ACOG fellows and junior fellows found that 56 percent of respondents felt their residency program did not provide them with sufficient education concerning thrombophilia. Health care providers often do not rely on the current guidelines for management, which may be due to the lack of consensus. Anticoagulation therapy may be prescribed in situations where it is not warranted. Sixty-six percent of survey respondents stated they would prescribe either low-dose aspirin, prophylactic LMWH or UFH, or a combination of low-dose aspirin and LMWH or UFH for an asymptomatic patient with FVL even though no clearly defined management guidelines exist to endorse such decisions (Clearly-Goldman, Bettes, Robinson, Norwitz, & Schulkin, 2007). Likewise, a 2002 Canadian survey of obstetricians and gynecologists found that 26 percent of respondents would recommend some form of thromboprophylactic therapy given the same clinical scenario (Rodger et al., 2002). Regarding thrombophilia management, the authors of the ACOG survey study conclude that “physicians in an
uncertain clinical situation are inclined to intervene rather than observe despite no clear
evidence to support this practice”. Alternatively, clinicians may resort to sending their
patients to high-risk specialists for management, but with the growing number of women
diagnosed with thrombophilia this is not always practical or necessary (Clearly-Goldman
et al., 2007). If health care providers do not feel adequately educated about inherited
thrombophilias they will be unable to sufficiently manage or educate their patients.

A survey of individuals diagnosed with FVL found that the majority felt they did
not fully understand the implications of thrombophilia. Forty-three percent of
respondents reported that a diagnosis of FVL increased worry about their health. Sixty-
seven percent of asymptomatic carriers overestimated their risk of VTE while 30 percent
of patients did not know that making positive lifestyle changes could alter their chances
of experiencing a thrombotic episode (Hellmann, Leslie, & Moll, 2003). Accurate
information must be provided to patients to help promote healthy outcomes and reduce
anxiety about their diagnosis.

The majority of heterozygous carriers of Factor V Leiden with no prior thrombotic
history do not require anticoagulant prophylaxis during pregnancy. If other risk factors
are present, such as positive family history of VTE, health care providers should
consider recommending postpartum prophylaxis and should counsel patients on the
benefits and risks of therapy. Further research in the area of inherited thrombophilia will
lead to more solid guidelines and a better understanding by clinicians. From this,
clinicians will be able to better educate their patients on thrombosis prevention during
pregnancy and throughout their lives.
Conclusion

There have been conflicting reports on the need for anticoagulant prophylaxis in heterozygous carriers of Factor V Leiden with no history of thrombosis. Our review supports the recommendations put forth in the Ninth Edition of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. There is a great need for large prospective studies evaluating FVL carriers. Also, more research is required regarding the efficacy of anticoagulants in VTE prevention during pregnancy. Based on the articles included in this review, the absolute risk for experiencing a VTE or adverse pregnancy outcome is low and the vast majority of untreated women with FVL will experience healthy pregnancies.
References


thrombophilia. Obstetrics and Gynecology, 99(5 Pt 1), 684-687.

doi:10.1016/S0029-7844(02)01938-5


doi:10.1056/nejm200010053431405


doi:10.1177/14746514020020011301


management of high-risk pregnancy: An evidence-based approach (6 ed.).


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Abstract

Objective: Conduct a systematic review of the incidence of venous thromboembolism and adverse pregnancy outcomes in heterozygous carriers of Factor V Leiden with no history of thrombosis and evaluate the need for anticoagulant prophylaxis in these patients. Method: A comprehensive search of the electronic database PubMed was performed up until the end of August 2012. The outcomes under investigation were incidence of venous thromboembolism, pregnancy loss and stillbirth, preeclampsia, placental abruption, and intrauterine growth restriction. Results: Eleven studies fit the inclusion criteria. Seven studies were retrospective and four were prospective observational studies. Conclusion: Although the relative risk for VTE during pregnancy may be slightly increased among heterozygous carriers of FVL according to some studies, the overall probability for experiencing a thromboembolism or pregnancy complication is low. Therefore, routine prophylactic antepartum or postpartum anticoagulation therapy is unnecessary and all patients should undergo an individualized risk assessment before receiving pharmacologic therapy.