Peripartum Thromboprophylaxis for Homozygous and Heterozygous FVL Mutation Carriers Yields Similar Pregnancy Outcome

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ABSTRACT: **Background:** Homozygous carriers of factor V Leiden (FVL) have an up to 80-fold increased risk of venous thrombosis, but the risk of obstetric complications in FVL homozygosity is unclear.

Objectives: To compare obstetric and thromboembolic complications among factor V Leiden (FVL) homozygous and heterozygous carriers treated with prophylactic dose anticoagulation during pregnancy.

Methods: In this retrospective case-control study we performed a chart review for the years 2004–2010 of homozygous and heterozygous FVL carriers who were treated with low molecular weight heparin (LMWH) at a dose of 0.6 mg/kg/day during pregnancy. Adverse outcomes included thromboembolic and obstetric complications. A composite adverse obstetric outcome was defined as the presence of at least one of the following: late intrauterine fetal demise, severe intrauterine growth restriction (< 5th percentile), preeclampsia, and placental abruption. Pregnancy outcomes of homozygous and heterozygous FVL carriers were compared.

Results: We compared the pregnancies of 13 homozygous FVL women with those of 82 heterozygous FVL carriers. Thromboembolic events occurred only in heterozygous FVL controls. Gestational age and birth weight were similar. The composite adverse obstetric outcome rate was higher for homozygous compared with heterozygous FVL carriers (23.1% vs. 11%, respectively), although not statistically significant. A trend for prematurity among homozygous FVL patients was evident, with 2/13 women (15.3%) in the homozygous FVL group giving birth before 34 weeks gestation, compared with only 2/82 (2.3%) in the heterozygous group.

Conclusions: Pregnancy outcome was similar for homozygous and heterozygous FVL carriers on LMWH thromboprophylaxis. The overall likelihood of thromboembolic complications was low. Thromboprophylaxis may decrease the risk for placental and thromboembolic complications in homozygous FVL patients to a similar level as in heterozygotes.

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KEY WORDS: factor V Leiden (FVL), homozygous FVL carriers, thromboprophylaxis, pregnancy outcome, placental and thromboembolic complications

Pregnancy is characterized by a physiological state of hypercoagulability. Moreover, a significant portion of pregnant patients suffering from severe obstetric complications – such as stillbirth [1,2], preeclampsia [3], placental abruption and intrauterine growth restriction [4] – were found to have some form of inherited or acquired thrombophilia [5,6]. Up to 50% of gestational venous thromboembolic events are associated with heritable thrombophilias [7,8].

Congenital thrombophilias were found to be present in up to 15% in several ethnic groups [7]. The wide diversity of thrombophilias makes research in this field challenging. Although women with adverse pregnancy outcome are more likely to test positive for thrombophilia, it is unclear which specific thrombophilia is implicated in each outcome [5]. Moreover, the exact mechanisms underlying placental dysfunction in women with thrombophilia are not fully understood [9]. Since published series are rather small or combine different forms of thrombophilias [5,7], differentiating and defining a precise clinical management strategy for each type is difficult.

The most commonly recognized inherited thrombophilia is factor V Leiden mutation [10,11], an autosomal dominant trait occurring mostly in the Caucasian population (5%) with variations by regions [12]. The clinical manifestation of the FVL mutation is variable [10]. It is recognized that homozygosity carries a greater risk of venous thromboembolism than heterozygosity, with both an earlier age of onset and recurrence as well as shorter time between episodes [10]. The association between pregnancy and recurrent VTE in homozygous carriers has been emphasized [13]. Bates et al. [14] demonstrated that the risk of VTE during pregnancy in homozygous FVL carriers is high as compared with other inherited thrombophilias. Homozygous carriers of factor V Leiden have an up to 80-fold increased risk of venous thrombosis [15,16], but the risk of obstetric complications in FVL homozygosity has yet to be determined. Biron-Andreani and colleagues [17] observed that without anticoagulation, late fetal loss was more frequent in homozygotes than heterozy-

FVL = factor V Leiden
VTE = venous thromboembolism

gous patients and non-carriers. The frequency of placental abruption, preeclampsia and growth restriction did not differ between the three groups [17]. The effects of thromboprophylaxis on the incidence of thromboembolic and pregnancy complications have not been evaluated in these women.

The use of anticoagulation for the prevention of pregnancy complications in women with hereditary thrombophilia is controversial in the medical literature, and recommendations are largely based on data extrapolated from non-pregnant patients, case reports and case series of pregnant women [18]. Our objective was to compare obstetric and thromboembolic complications among pregnant FVL homozygous and heterozygous carriers treated with prophylactic dose anticoagulation.

PATIENTS AND METHODS

In this retrospective cohort study we reviewed the charts of all isolated homozygous and heterozygous FVL carriers who were followed at the high risk pregnancy clinic, gave birth at Sheba Medical Center, and received thromboprophylaxis during the period 2004–2010. Our interest lay in whether thromboprophylaxis offers a modification of pregnancy risk in women with the FVL mutation; therefore, we selected only women with FVL who received thromboprophylaxis. Thromboprophylaxis was initiated at the discretion of the attending physician, and the women were treated until 6 weeks postpartum. Indications for therapy varied, including previous thromboembolism, habitual abortions, prior obstetric complications, as well as the homozygous state. Thromboprophylaxis was given to some women because of additional risk factors, and to others because of their past obstetric history. Homozygous and heterozygous factor V Leiden carriers who were treated with low molecular weight heparin at a prophylactic dose of 0.6 mg/kg/day during pregnancy as previously described [19] were identified and their outcome was compared. New thromboembolic events during pregnancy were addressed by increasing the LMWH dose to the full therapeutic range of 1 mg/kg twice daily. Patients treated by prophylactic dose were not routinely monitored by anti-factor Xa activity. In order to control for possible effects of thromboprophylaxis itself we chose to evaluate only those women who received anticoagulation during pregnancy.

DATA COLLECTION

Data regarding patients' medical and obstetric history, current pregnancy complications, thromboembolic complications, thromboprophylaxis, pregnancy outcome, mode of delivery, birth weight and gender, gestational age at delivery, APGAR score, etc., were collected and entered into a computerized database. Factor V Leiden was diagnosed by polymerase chain reaction amplification of a 267 bp fragment and MNII digestion, as previously described [20] from venous blood samples.

Excluded were women with other concomitant thrombophilic abnormalities (genetic or acquired), as well as FVL carriers who did not receive thromboprophylaxis during pregnancy and the puerperium. We also excluded patients with early miscarriages as our focus was on late gestation complications which may (or may not) be influenced by therapy.

END-POINTS

Pregnancy outcome and thromboembolic events of homozygous and heterozygous FVL carriers were recorded and compared**.** Adverse outcomes included thromboembolic and obstetric complications.

Intrauterine fetal demise was diagnosed sonographically as a pulseless embryo after 20 weeks gestation. Severe intrauterine growth restriction was defined as birth weight below the 5th percentile adjusted for gestational age and gender according to locally derived tables [21]. Preeclampsia was diagnosed when repeated blood pressure measurements were higher than 140/90 with associated proteinuria (> 300 mg/24 hours). Placental abruption was diagnosed by a typical clinical presentation, and the placenta was sent for histopathological confirmation.

A composite placental complication index was composed and defined as the presence of at least one of the following: IUFD, IUGR, preeclampsia, and/or placental abruption. The thromboembolic events in pregnancy included VTE, stroke, and cerebral transient ischemic attacks. VTE was diagnosed by radiological evaluation, as was stroke. TIA was defined by a typical resolving neurological deficit. Radiological modalities included venous Doppler for deep vein thrombosis, computed tomography scan with contrast iodine for pulmonary embolism, and brain CT or magnetic resonance imaging for TIA/stroke, after receiving informed consent of the patient.

STATISTICAL ANALYSIS

Statistical analysis was performed with SigmaStat 1.0 software (Jandel Engineering Ltd, Linslade, Bedfordshire, UK). Continuous variables were compared using the *t*-test while categorical data were compared using Pearson's $\chi 2$ test as appropriate. A P value < 0.05 was considered significant. Institutional research ethics board approval was granted by the Sheba Medical Center's institutional review board.

RESULTS

We identified 12 homozygous carriers of the FVL mutation with 13 pregnancies treated by prophylactic dose LMWH, and

LMWH = low molecular weight heparin

IUFD = intrauterine fetal demise
IUGR = intrauterine growth restriction
TIA = transient ischemic attack

Table 1. Background demographic data

	Homozygous FVL carriers (n=12)	Heterozygous FVL carriers (n=63)	*P* value
No. of pregnancies	13	82	
Maternal age (yr)	36.7 ± 4.5	32.8 ± 4.5	0.005
Gravity (mean ± SD)	4.1 ± 3.7	3.8 ± 2.3	0.76
Parity (mean ± SD)	2.5 ± 1.7	2.5 ± 1.7	1
Previous VTE (%)*	5 (41.7)	14 (22.2)	0.16
Previous obstetric complications (%)**	3 (25)	25 (39.7)	0.75
S/p isolated recurrent miscarriages (%)***	1 (8.3)	6 (9.5)	1
Isolated family history of thromboembolism (%)	5 (41.7)	11 (17.5)	0.12

*Patients with a medical history that includes venous thromboembolism

**Patients with an obstetric history that includes at least one of the following placental complications: fetal demise, intrauterine growth restriction, severe preeclampsia, placental abruption

***Three or more previous miscarriages

FVL = factor V Leiden, SD = standard deviation, VTE = venous thromboembolism

Table 2. Obstetric outcome in FVL pregnancies with thromboprophylaxis

	Homozygous FVL pregnancies (n=13)	Heterozygous FVL pregnancies (n=82)	*P* value
Gestational age at delivery (wk) (mean ± SD)	36.9 ± 3	37.9 ± 2.0	0.14
Birth weight (g) (mean ± SD)	2874 ± 641	2981 ± 564	0.54
Preterm delivery < 34 wk (%)	2 (15.3)	2 (2.3)	0.087
Labor induction (%)	7 (53.8)	25 (30.4)	0.12
Vaginal delivery (%)	11 (84.6)	57 (69.5)	0.33
Urgent cesarean section (%)	0	7 (8.5)	0.58

FVL = factor V Leiden, SD = standard deviation

63 heterozygous carriers with 82 pregnancies. Women in the homozygous FVL group were significantly older than the heterozygote FVL carriers (36.7 vs. 32.8 years, $P = 0.005$), although gravidity and parity were similar. No significant differences were found regarding previous thromboembolic events or previous obstetric complications between homozygous and heterozygous FVL carriers. Patients' demographic data and medical and obstetric history are presented in Table 1. Enoxaparin prophylaxis was initiated following the diagnosis of a viable intrauterine pregnancy in 11/13 patients (84.6%) in the homozygous group and 72/86 (83.8%) in the heterozygous group. Later initiation, either during the third trimester in one patient in the homozygous cohort and four in the heterozygous group, or postpartum in one and eight pregnancies, respectively, was indicated in cases of FVL diagnosis due to family investigation without previous history of thrombotic or obstetric complications. Enoxaparin was discontinued 12–24 hours before delivery and restarted within 8–12 hours after delivery. There were no documented enoxaparin-related complications such as excessive bleeding, osteoporosis, or heparin-induced thrombocytopenia.

Gestational age and birth weight at delivery were similar in the two groups. Eleven pregnancies (84.6%) ended by vaginal delivery in the homozygous FVL group compared with 57 (69.5%) in the heterozygous group, and the rates of labor induction were also similar. We noted a trend for prematurity among homozygous FVL patients, with 2/13 women (15.3%) in the homozygous FVL group giving birth before 34 weeks gestation, compared with only 2/82 (2.3%) in the heterozygous group ($P = 0.087$). Labor and delivery outcome data are presented in Table 2.

Overall, pregnancy complication rates were quite similar for prophylactic-treated homozygous and heterozygous FVL carriers. The rates of placental abruption, IUGR, and preeclampsia were similar between the two groups. There were two cases of fetal demise among homozygous FVL women compared with only one among heterozygotes ($P = 0.047$). Nevertheless, one of the two homozygous cases was a fetus with known multiple anomalies.

The composite placental complication index (defined as at least one of the above obstetric complications) occurred twice as frequently in the homozygous FVL group compared with the heterozygotes, (23.1% vs. 11%), although this difference was not statistically significant.

All study participants received LMWH thromboprophylaxis with enoxaparin 0.6 mg/kg/day. There were no new thromboembolic events in the homozygous FVL group women compared with three cases in the heterozygous FVL group. These cases exhibited neurological manifestations: two women presented with transient neurological deficits and no evidence of lesion on radiology, and the third presented with severe headaches and brain imaging documentation of an ischemic lesion. Thromboembolic manifestations led to an increase in LMWH to intermediate doses as well as the addition of low dose aspirin. Placental and thromboembolic complications are described in Table 3.

DISCUSSION

We present thromboembolic and pregnancy complications in a cohort of pregnant homozygous and heterozygous FVL carriers receiving thromboprophylaxis. Recently published recommendations [14] regarding VTE prevention in pregnant women with inherited thrombophilias include antepartum and postpartum prophylactic dose LMWH for FVL homozygous pregnant patients with a personal or family history of VTE; in the absence of a positive history, prophylaxis is recommended for the postpartum period only. Nevertheless, clear recommendations for preventing obstetric complications are lacking. Our study is unique in that it allows an estimation of risk in the clinical setting of women on thromboprophylaxis, enabling counsel-

Table 3. Placental and thromboembolic complications in FVL pregnancies with thromboprophylaxis

	Homozygous FVL pregnancies (n=13)	Heterozygous FVL pregnancies (n=82)	*P* value
Placental complications			
IUFD (%)*	2 (15.4)	1 (1.2)	0.043
PET (%)	1 (5.9)	5 (5.9)	1.0
Abruption (%)	1 (7.7)	2 (2.4)	0.36
IUGR (%)	0	3 (3.6)	1
Composite placental complications (%)	3 (23.1)	9 (11.0)	0.2
Thromboembolic complications (%)**	0	3 (3.6)	1

*Among women with homozygous FVL: two cases of fetal demise, one at 29 weeks due to total placental abruption and the other at 31 weeks of a fetus with multiple known fetal anomalies. Among women with heterozygous FVL, one fetal demise of an IUGR fetus at 30 weeks gestation

**Two events were diagnosed as TIA according to clinical findings and in one case an ischemic lesion in the brain was demonstrated by MRI

FVL = factor V Leiden, IUFD = intrauterine fetal demise, PET = preeclampsia, abruption = placental abruption, IUGR = intrauterine growth restriction below the 5th percentile adjusted for gestational age and gender according to locally derived tables, composite placental complications = at least one placental complication as outlined above

ing of these women regarding their risk throughout pregnancy.

Overall, the outcome of homozygous factor V Leiden pregnant women in our cohort was good. All the study participants received LMWH thromboprophylaxis with enoxaparin 0.6 mg/kg/day. With this regimen, no new thromboembolic complications occurred in the homozygous FVL group, and over 75% of women gave birth to adequately grown liveborn neonates with no significant placental complications.

Martinelli et al. [16] demonstrated the prevalence of VTE among 15 FVL homozygous carriers with 19 pregnancies to be as high as 15.8% without thromboprophylaxis, most of the events occurring in the postpartum period. In contrast, in our cohort of 13 pregnancies receiving peripartum thromboprophylaxis no such events occurred. Moreover, all the women who did experience a suspected thromboembolic event in pregnancy were heterozygous FVL women. These results may augment the possible benefit of thromboprophylaxis. It should be noted that although FVL is not considered a risk factor for arterial thrombosis, there is no reliable information on the risk for these events among pregnant FVL carriers. Furthermore, the high prevalence of suspected cerebral events (stroke/TIA) in our cohort warrants attention, although whether or not this is related to FVL is not clear.

Thromboembolic events in the non-pregnant population are reported to be much more prevalent in homozygous, compared with heterozygous, FVL carriers. Factor V Leiden homozygous carriers have been shown to be at increased risk for both venous thromboembolism [10] and late fetal loss [17]. Therefore, we expected to find a higher complication rate during pregnancy in our homozygous cohort. Moreover, our homozygous FVL patients were older and had a higher rate of previous thromboembolic events than heterozygous carriers. Therefore, these women may be at an even higher risk for complications. Significantly higher rates of fetal demise were demonstrated in the homozygous group. Moreover, a trend was also evident for a higher rate of preterm deliveries among homozygous carriers, with 15% of homozygous FVL women giving birth before 34 gestational weeks, compared to only 2% of heterozygous controls. Again, this did not quite reach statistical significance ($P = 0.087$), either due to a relatively small sample size or the contributing effects of thromboprophylaxis, but the trend was the same.

Published data on homozygous FVL carriers in pregnancy are limited. One of the first comprehensive assessments regarding FVL homozygosity during pregnancy was published by Biron-Andreani et al. [17]. They compared 95 homozygous patients with 195 heterozygous patients and 73 non-carriers for the evaluation of early and late fetal loss. Patients receiving thromboprophylaxis were excluded. While late fetal loss was more frequent in homozygous (13.7%) compared with heterozygous patients (3.1%) and non-carriers (1.4%), the frequency of placental abruption, preeclampsia and IUGR was similar. In our study of patients on thromboprophylaxis, 23% of the homozygous cohort presented with combined adverse placental outcome compared with only 11% in the heterozygous cohort. This difference was not statistically significant, possibly due to the relatively high event rate in the control group. Possibly, heterozygous carriers referred to our tertiary care center may represent a relatively high risk control cohort compared with other heterozygous FVL women who receive community-based prenatal care.

The most apparent drawback of our study is its retrospective nature, leading to differences in background characteristics between the two groups, such as maternal age. Nevertheless, this limitation may be viewed as contributing to the strength of our findings, for although the study cohort was at increased background risk, pregnancy outcome and thromboembolic events were no worse than among controls. This may possibly be due to thromboprophylaxis lowering the rate of complications among homozygous carriers. Another possible drawback is the relatively small sample of patients. Nevertheless, although the prevalence of FVL mutation varies according to geography and ethnicity [22,23], homozygocity for factor V Leiden is relatively rare. Indeed, our group of 13 pregnancies is actually quite sizable and comparable to other reports, while information on adverse pregnancy outcomes for this patient population is scarce. Furthermore, due to the high risk for thromboembolism in untreated FVL homozygotes in pregnancy, an evaluation of the risk of obstetric complications under thromboprophylactic conditions more accurately represents real-life conditions and may contribute to prenatal counseling of these patients.

In summary, FVL homozygous carriers are at risk for thromboembolism during pregnancy as well as for major obstetric

complications. Although some studies have recommended thromprophylaxis during pregnancy [16], the arguments focus on the prevention of VTE but there are no strict guidelines or information on placenta-related complications in these patients. Our results demonstrate that with LMWH thromboprophylaxis, the occurrence of pregnancy complications is similar in FVL homozygous and heterozygous carriers. Moreover, with this regimen, antepartum and peripartum VTE episodes were less frequent than previously reported. Further studies will increase our knowledge on the effects of therapy and on the optimal dosage in this group of pregnant patients.

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References

1. Rotmensch S, Liberati M, Mittlemann M, Ben-Rafael Z. Activated protein C resistance and adverse pregnancy outcome. *Am J Obstet Gynecol* 1997; 177 (1): 170-3.
2. Rodger MA, Betancourt MT, Clark P, et al. The association of factor V leiden and prothrombin gene mutation and placenta-mediated pregnancy complications: a systematic review and meta-analysis of prospective cohort studies. *PLoS Med* 2010; 7 (6): e1000292.
3. Grandone E, Margaglione M, Colaizzo D, et al. Prothrombotic genetic risk factors and the occurrence of gestational hypertension with or without proteinuria. *Thromb Haemost* 1999; 81 (3): 349-52.
4. Grandone E, Tomaiuolo M, Colaizzo D, Ames PR, Margaglione M. Role of thrombophilia in adverse obstetric outcomes and their prevention using antithrombotic therapy. *Semin Thromb Hemost* 2009; 35 (7): 630-43.
5. Alfirevic Z, Roberts D, Martlew V. How strong is the association between maternal thrombophilia and adverse pregnancy outcome? A systematic review. *Eur J Obstet Gynecol Reprod Biol* 2002; 101 (1): 6-14.
6. Kupferminc MJ. Thrombophilia and pregnancy. *Reprod Biol Endocrinol* 2003; 1: 111.
7. Bates SM, Greer IA, Pabinger I, Sofaer S, Hirsh J; American College of Chest Physicians. Venous thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 8th edn. *Chest* 2008; 133 (6 Suppl): 844-6S.
8. Bremme KA. Haemostatic changes in pregnancy. *Best Pract Res Clin Haematol* 2003; 16 (2): 153-68.
9. Wiener Y, Frank M, Neeman O, Kurzweil Y, Bar J, Maymon R. Does low molecular weight heparin influence the triple test result in pregnant women with thrombophilia? *IMAJ* 2012; 14 (4): 247-50.
10. Procare Group. Comparison of thrombotic risk between 85 homozygotes and 481 heterozygotes carriers of the factor V Leiden mutation: retrospective analysis from the Procare Study. *Blood Coagul Fibrinolysis* 2000; 11 (6): 511-18.
11. Lockwood CJ. Inherited thrombophilias in pregnant patients: detection and treatment paradigm. *Obstet Gynecol* 2002; 99 (2): 333-41.
12. Rosendaal FR. Venous thrombosis: a multicausal disease. *Lancet* 1999; 353 (9159): 1167-73.
13. Procare Group. Is recurrent venous thromboembolism more frequent in homozygous patients for the factor V Leiden mutation than in heterozygous patients? *Blood Coagul Fibrinolysis* 2003; 14 (6): 523-9.
14. Bates SM, Greer IA, Middeldorp S, et al. VTE, thrombophilia, antithrombotic therapy, and pregnancy: Antithrombotic Therapy and Prevention of Thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141 (2 Suppl): e691-736S.
15. Lentz SR. Another lesson from the factor V Leiden mouse: thrombin generation drives arterial disease. *Circulation* 2005; 111 (14): 1733-4.
16. Martinelli I, Bauters A, Le Cam-Duchez V, et al. Risk of pregnancy-related venous thrombosis in carriers of severe inherited thrombophilia. *Thromb Haemost* 2001; 86 (3): 800-3.
17. Biron-Andreani C, Bauters A, Le Cam-Duchez V, et al. Factor v Leiden homozygous genotype and pregnancy outcomes. *Obstet Gynecol* 2009; 114 (6): 1249-53.
18. Weintraub AY, Sheiner E. Anticoagulant therapy and thromboprophylaxis in patients with thrombophilia. *Arch Gynecol Obstet* 2007; 276 (6): 567-71.
19. Shapiro NL, Kominiarek MA, Nutescu EA, Chevalier AB, Hibbard JU. Dosing and monitoring of low-molecular-weight heparin in high-risk pregnancy: single-center experience. *Pharmacotherapy* 2011; 31 (7): 678-85.
20. Dahlback B. New molecular insights into the genetics of thrombophilia. Resistance to activated protein C caused by Arg506 to Gln mutation in factor V as a pathogenic risk factor for venous thrombosis. *Thromb Haemost* 1995; 74 (1): 139-48.
21. Dollberg S, Haklai Z, Mimouni FB, Gorfein I, Gordon ES. Birth weight standards in the live-born population in Israel. *IMAJ* 2005; 7 (5): 311-14.
22. Ridker PM, Miletich JP, Hennekens CH, Buring JE. Ethnic distribution of factor V Leiden in 4047 men and women. Implications for venous thromboembolism screening. *JAMA* 1997; 277 (16): 1305-7.
23. Sottilotta G, Mammì C, Furlò G, Oriana V, Latella C, Trapani Lombardo V. High incidence of factor V Leiden and prothrombin G20210A in healthy southern Italians. *Clin Appl Thromb Hemost* 2009; 15 (3): 356-9.

Capsule

A blood-resistant surgical glue for minimally invasive repair of vessels and heart defects

Currently, there are no clinically approved surgical glues that are non-toxic, bind strongly to tissue, and work well within wet and highly dynamic environments within the body. This is especially relevant to minimally invasive surgery that is increasingly performed to reduce postoperative complications, recovery times, and patient discomfort. Lang et al. describe the engineering of a bioinspired elastic and biocompatible hydrophobic light-activated adhesive (HLAA) that achieves a strong level of adhesion to wet tissue and is not compromised by preexposure to blood. The HLAA provided an on-demand hemostatic seal, within seconds of light application, when applied to high pressure large blood vessels and cardiac wall defects in pigs. HLAA-coated patches attached to the interventricular septum in a beating porcine heart and resisted supraphysiologic pressures by remaining attached for 24 hours, which is relevant to intracardiac interventions in humans. The HLAA could be used for many cardiovascular and surgical applications, with immediate application in repair of vascular defects and surgical hemostasis.

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