Anticoagulant efficiency in case of portal vein thrombosis: Review

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Abstract: In this review, we discuss the features of PVT, pointing out reason of thrombosis and efficiency of anticoagulants in different types of PVT. We searched the PubMed, , SCOPUS, and Emabse databases through September, 2017, for studies that assessed the effect of anticoagulant therapy in patients with PVT. Portal vein occlusion is a clinically relevant disorder which needs to be diagnosed very. Particularly patients with liver cirrhosis need for special care with regard to PVT because it is related to the pathophysiology of the disease. The studies on anticoagulation use in cirrhosis with acute PVT is proving with appreciable results and no added bleeding risk, and needs to be required to patients specifically for those who are waiting for liver transplantation. But absence of enough literature on the type of anticoagulation is needed to be used, duration, keep the study on portal vein thrombosis debatable topic.

Introduction:

The term portal vein thrombosis (PVT) describes the full or partial blockage of blood circulation in the portal vein, as a result of the existence of a thrombus in the vassal lumen [1]. Although in the basic populace PVT is thought about an uncommon occasion, its occurrence amongst cirrhotic patients ranges in between 4.4%-15%, as well as is in charge of concerning 5%-10% of total instances of portal high blood pressure [2] The first case of PVT was reported in 1868 by Balfour as well as Stewart, defining a patient offering splenomegaly, ascites, and also variceal extension [3] Portal blood vessel apoplexy is a vital source of portal high blood pressure. PVT takes place in association with cirrhosis or as a

result of deadly intrusion by hepatocellular cancer and even in the lack of related liver illness. Numerous etiological reasons, either of regional or systemic beginning, may be in charge of PVT advancement, although greater than one aspect is frequently recognized. Additionally, PVT professional discussion is various in the context of acute or chronic onset as well as depends upon the advancement and also the degree of a collateral blood circulation. Intestinal tract blockage and also ischemia, with stomach discomfort, diarrhea, anal bleeding, stomach distention, nausea, throwing up, anorexia, high temperature, lactacidosis, sepsis, and also splenomegaly prevail attributes of acute PVT. In comparison, chronic PVT can be entirely asymptomatic, or identified by splenomegaly, pancytopenia, varices, as well as, seldom, ascites [3] In the existence of portal high blood pressure, PVT should constantly be explored, specifically in cirrhotic patients, even if it is thought about an unusual occasion [2]. Without a doubt, a very early medical diagnosis as well as suitable management of second portal high blood pressure could be, in many cases, life-saving for the patient

In this review, we discuss the features of PVT, pointing out reason of thrombosis and efficiency of anticoagulants in different types of PVT.

Methodology:

We searched the PubMed, , SCOPUS, and Emabse databases through September, 2017, for studies that assessed the effect of anticoagulant therapy in patients with PVT. Restrictions to English language articles applied with human subjects. more relevant studies were recruited through scanning the references list of identified articles.

Discussion:

- **Etiological Facts and Risk Factors**

In society researches, the accomplice of patients with occlusion in the portal tributary system can be split right into 3 likewise huge subcohorts of significant etiologies: i) malignant

thrombosis primarily as a result of stomach, hepatobiliary, or pancreatic cancer, ii) chronic liver conditions, particularly liver cirrhosis with portal high blood pressure, and also iii) non-malignant, non-cirrhotic PVT [4].While the underlying condition figures out the nature and also end result of patients when it comes to malignant thrombosis, both various other teams of patients are identified by a result affected by PVT [5]. In addition, non-malignant, non-cirrhotic PVT has actually frequently been referred to as an entity of its very own, causing non-cirrhotic portal high blood pressure, which stands for even more of an effect compared to a problem of an additional condition [6]. Therefore, the 3 huge etiologic classifications are explained individually in the adhering to.

Malignant Portal Vein Thrombosis

Generally, malignant PVT is related to the development of a malignant condition. A thrombosis in the portal system specifies vascular intrusion of the malignant entity and also therefore the infecting the blood system. Information are limited on this etiology relating to splanchnic thrombosis; nonetheless, main hepatobiliary cancer, metastatic cancer, and also

second malignancy of the hepatobiliary area can be identified [4]. In a big retrospective research study consisting of 23,796 successive postmortem examinations (84% of all in-hospital fatalities) in the Malmö city populace [6], most of thromboses happened because of second malignancies of the hepatobiliary area. On the other hand, in-depth data exposed that PVT existed in 14.3% of the patients with primary hepatic cancer as well as concomitant cirrhosis along with in 11.5% of the patients with pancreatic cancer. Problems of portal high blood pressure because of PVT, nonetheless, were instead reduced in cancer patients without cirrhosis in this research study, e.g. intestinal blood loss took place in just 14% as compared to 59% in cirrhotics without cancer [6].

Cirrhotic Portal Vein Thrombosis

Liver cirrhosis is a causal aspect in about one third of all patients with PVT [7]. In patients with recompensed cirrhosis, the occurrence is around 1% [8] as well as, hence, much like the frequency reported in the complete populace [9] The frequency of PVT rises to 8-25% in patients waiting for liver transplantation [10] and also is detected in 50-70% in explanted

cirrhotic livers throughout liver transplantation [11]. Surprisingly, in a methodical evaluation of 885 patients that went through liver transplantation, the occurrence of PVT was 3.6% in primary sclerosing cholangitis, 8% in primary biliary cirrhosis, as well as 16% in alcoholic and also HBV(hepatitis B virus)-generated cirrhosis however totaled up to 36% in patients with liver cirrhosis as well as hepatocellular cancer [12].

More danger aspects for PVT have actually been recommended as well as consist of reduced platelet matter, frequent decompensation, previous blood loss episodes, as well as infections. These aspects incline as well as help with endotoxin flooding right into the portal venous system, which can triggering the coagulation cascade as well as could bring about thrombus development [13] On the other hand, acquired thrombophilias (i.e. G20210A prothrombin anomaly, variable V Leiden anomaly, TT677 MTHFR genetics anomaly) play a small pathogenic function in cirrhotic PVT [14].

Non-Malignant, Non-Cirrhotic Portal Vein Thrombosis

PVT in the lack of malignancy as well as cirrhosis is primarily as a result of systemic prothrombogenetic problems and also regional aspects [15]. Amongst these elements, myeloproliferative neoplasias look like a significant reason in 20-50% of the patients with PVT [15]. In a meta-analysis of 855 patients with PVT, myeloproliferative tumors existed in regarding 30% of the patients, as well as JAK2 V617F anomalies were discovered in 28% of the cohort [16]. First information on the function of the lately defined unique mutation in the calreticulin genetics for myeloproliferative neoplasm does not appear to play a crucial function in patients with PVT [17].

- **Anticoagulation for PVT:**

The purpose of the therapy is to reverse or avoid development of thrombosis in the portal venous system and also to treat difficulties of well-established PVT. Most of the management choices need to be individualized relying on the regional proficiency, because there is absence of randomized regulated tests. An organized evaluation reported that upto 83.3% of situations of acute PVT do not recanalise in the lack of anticoagulation as well as the staying

16.7% situations that recanalized taken place in the setup of self-restricting disease like acute pancreatitis [18]. There is a clear referral for using anticoagulation in non-cirrhotic acute PVT with excellent protection as well as efficiency information. Particular circumstances call for a strong suggestion for very early use anticoagulation like, in the setup of digestive tract ischemia advertising an infarction, decompensated liver illness waiting for liver transplant, made up liver condition, PVT providing with acute variceal bleed as well as asymptomatic patients with mesenteric venous occlusion, whereas unsuitability for liver transplant in advanced liver condition and also cavernoma development in the lack of thrombotic threat variables are circumstances where anticoagulation might not profit survival as well as results.

- **Anticoagulation in Non-cirrhotic Acute Portal Vein Thrombosis**

A current methodical overview of numerous researches on management of acute non-malignant non-cirrhotic PVT showed the irregularity in place and also level of the thrombus, approaches in starting anticoagulation whether intravenous, subcutaneous or oral [18] The recanalization rates were total in 38.3% as well as partial in 14%, total 52.3% (total plus

partial). The moment for recanalization differed from 1 to 197 days, which might have been overstated as a result of the time lag in between medical diagnosis to the efficiency of a repeat imaging. Nevertheless, the long period of time for recanalization to take place as shown in particular research studies might recommend that the anticoagulation period might really be suggested for up to 6 months period. Although a couple of authors advised long-lasting anticoagulation in case of prothrombotic condition, particular research studies provided anticoagulation for long-lasting irrespective of the etiology. Subsequent to up to 12 months in bulk, as well as growth of portal cavernoma, happened in 19.9% patients. Small complication is reported in 3 situations, retroperitoneal bleed in 1 and also gum bleed/epistaxis in 2 patients. Varices were seen in 47 patients and also variceal bleed took place in 5 patients, all 5 had actually cannot recanalize the portal blood vessel [18].

A current multicenter 2 year subsequent research assessed 102 patients of acute PVT unconnected to cirrhosis and also anticoagulation was given up 95 patients [19].Complying with anticoagulation 1 year portal capillary recanalization rate was 39% as well as no

recanalization took place past 6 months after initiation of anticoagulation. Splenic blood vessel and also premium mesenteric vein patency was accomplished in 80% as well as 73% specifically. Ascites and also splenic vein thrombosis are independent aspects estimating failing of recanalization [19] Table 1 sums up the professional researches on anticoagulation in acute non-cirrhotic non-malignant PVT.

Table 1.Clinical Studies on Anticoagulation in Acute Non-cirrhotic Non-malignant PVT.

Reference	No. of patients	Drug and dosage	Duration	Recanalization	Complication
Plessier et al (2010) [19]	95/102	61 LMWH, 23 UFH, 11 OA	–	39%	Portal cavernoma in 40% GIbleed-9, intestinal infarction-2
Tumes et al (2008) [20]	27	IV OR LMWH, OA	OA 6 months or lifelong in case of prothrombotic risk	44% (22% complete and 22% partial)	1 retroperitoneal hematoma, variceal bleed in 4, ascites in 5
Sogaard et al (2007) [21]	17	Not specified (16/17) anticoagulated	–	10 had improved flow	47% varices, no bleed, 47% ascites
Amitrano	21	LMWH	OA 6 months	45.5% complete	Minor gum

Reference	No. of patients	Drug and dosage	Duration	Recanalization	Complication
et al (2007) [22]		200 IU/kg/d, OA	(lifelong if bowel resection, incomplete recanalization or thrombophila)		bleed/epistaxis in 2, Rethrombosis at 22 months
Sheen et al (2000) [23]	9	IV heparin, OA	3 months OA	55.5%, at median 197 days from diagnosis	–

The period of anticoagulation is not well specified. Recanalization happens within 4-- 6 months after anticoagulation, therefore these patients ought to be continued anticoagulation for a minimum of 6 months. Long-term anticoagulation could be suggested in patients with recognized prothrombotic problems, recurring episodes of apoplexy or family history of venous thrombosis [24]. Anticoagulation needs to be launched with heparin & kept for 2 - 3 week. Later on oral Vit K antagonists need to be offered to preserve an INR of 2 - 3. There is even more conflict of its function in chronic PVT. There is insufficient proof for beginning anticoagulation in patients with portal cavernoma, although recanalization in partial PVT has actually been reported in patients with cirrhosis [25]. Anticoagulation has actually additionally

been revealed to turn around biliary irregularities because of acute portal vein thrombosis [26]. Early beginning of anticoagulation ideally within 30 days of signs is suggested because no spontaneous recanalization is reported other than in acute pancreatitis. Recanalization lowers from 69% when anticoagulation was set up within initial week to 25% when set up at 2nd week [27]. Thirty 5 percent of acute PVT program recanalization with very early anticoagulation [27].

- **Anticoagulation in Cirrhotic Portal Vein Thrombosis**

In patients with cirrhosis there are just couple of research studies on using anticoagulation for PVT. The numbers have actually been tiny in these researches and also bulk was partial PVT. The therapy programs mostly applied reduced molecular weight heparin (LMWH), one research study likewise applied oral Vitamin K antagonist. Total recanalization rates attained with anticoagulation are 42-- 75% as well as the danger of expansion of thrombosis is 5-- 7% just. The selection of anticoagulant is not plainly specific. Nonetheless the researches on cirrhosis have actually mainly made use of reduced molecular weight heparin compared to

unfractionated heparin (UFH) in the therapy of PVT with a benefit of no surveillance need, reduced blood loss danger as well as danger of thrombocytopenia with LMWH. LMWH when compared with oral anticoagulants where INR monitoring is a complex problem overall in the setup of cirrhosis once more has a benefit. The control of bleeding pertaining to oral anticoagulant usage is likewise difficult to anticipate as a result of extended fifty percent life and also anticoagulant results of oral medications. Researches on making use of anticoagulation in cirrhosis with portal vein thrombosis are restricted and also are displayed in (Table2).

Table 2. Studies on the Use of Anticoagulation in Cirrhosis with PVT.

Reference	No. of patients	Drug and dosage	Duration	Recanalization	Complication
Amitrano et al (2010)[28]	28 uncontrolled	Enoxaparin 200 u/kg/d	6 months	Complete-21 Partial-2	None
Francoz et al (2005)[29]	19 cohort study	LMWH (Nadroparin) 5700 IU/d, followed by VKA		Complete-8	Post EVL ulcer bleed-1
Senzolo et al (2009)[30]	33 uncontrolled	LMWH antiXa 95 U/kg/bw TID		Complete-12 Partial-9	HIT-1, Non-variceal bleed-1
Pellicelli et al	9	Enoxaparin	3–4months	Complete-3	None

Reference	No. of patients	Drug and dosage	Duration	Recanalization	Complication
(2010)[31]	uncontrolled	100 U/kg/d		Partial-6	
Warmer et al (2012)[32]	28 uncontrolled	Warfarin	1 year or until recanalization	Complete-11 Partial-12	Vaginal bleed-1

- **Anticoagulation in Chronic Portal Vein Thrombosis**

Anticoagulation in chronic PVT has a debatable function. The suggestions for anticoagulation in this setup stay for those with underlying prothrombotic state. The use of anticoagulation in chronic PVT has actually been around 30% in a lot of research studies. Condat et alia [33] had actually offered some details on its usage in the setup of chronic PVT without any substantial bleeding distinctions from those without anticoagulation. Nonetheless there was a considerable decrease in brand-new thrombotic episodes. A current retrospective research study by Hoekstra et alia revealed that using anticoagulation in pregnancy with chronic PVT had positive mother's and also fetal results for the majority of maternities getting to 20 week

pregnancy, nevertheless the rate of losing the unborn baby and also preterm shipment seemed enhanced when anticoagulated on private basis [34]. Thrombocytosis was a danger aspect for undesirable maternity result. Variceal bleed happened in 3, all without ideal primary treatment. No reduced arm or leg or mesenteric capillary thrombosis happened while pregnant or blog post-partum duration [34].

- **Selection of Individuals for Anticoagulation Therapy**

Even if anticoagulation treatment is related to great rates of PV recanalization, the indicators for dealing with PVT in cirrhotic people are not well specified in the present standards as well as agreement magazines [35]. As a matter of fact, the influence of PVT on the advancement of cirrhosis is still an issue of wonderful discussion [36] as well as the medical advantages of PV recanalization have actually been shown in just couple of specific circumstances.

To this day, there is accumulating proof that cirrhotic people with PVT on the waiting listing for liver transplantation must be treated with anticoagulation treatment. Undoubtedly, Francoz

et al. have actually shown that full or partial PV recanalization was related to a much better 2-year survival rate after liver transplantation (82-83% in people with partial and also total PV recanalization as well as 50% in people with total PVT) [37]. One research revealed a 32% boost in death in people undertaking liver transplantation with PVT [38]. The various other research study revealed that the adverse effect of PVT on posttransplantation survival was limited to people with an MELD rating <15 at the time of surgical treatment [39]. The boosted death and also morbidity connected with PVT are primarily limited to the very first year after liver transplant [40]. It has actually additionally been revealed that people with PVT at the time of liver transplantation go to greater danger of recurring PVT after transplant as well as of needing retransplantation [41].

- **Conclusion:**

Portal vein occlusion is a clinically relevant disorder which needs to be diagnosed very. Particularly patients with liver cirrhosis need for special care with regard to PVT

because it is related to the pathophysiology of the disease. The study on anticoagulation use in cirrhosis with acute PVT is proving with appreciable results and no added bleeding risk, and needs to be required to patients specifically for those who are waiting for liver transplantation. But absence of enough literature on the type of anticoagulation is needed to be used, duration, keep the study on portal vein thrombosis debatable topic.

Reference

1. Bayraktar Y, Harmanci O. Etiology and consequences of thrombosis in abdominal vessels. World J Gastroenterol. 2006;12:1165–1174.
2. Amitrano L, Guardascione MA, Brancaccio V, Margaglione M, Manguso F, Iannaccone L, Grandone E, Balzano A. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. J Hepatol. 2004;40:736–741.
3. Wang JT, Zhao HY, Liu YL. Portal vein thrombosis. Hepatobiliary Pancreat Dis Int. 2005;4:515–518.
4. Thatipelli MR, McBane RD, Hodge DO, Wysokinski WE. Survival and recurrence in patients with splanchnic vein thromboses. Clin Gastroenterol Hepatol. 2010;8:200–205.
5. Pieri G, Theocharidou E, Burroughs AK. Liver in haematological disorders. Best Pract Res Clin Gastroenterol. 2013;27:513–530.

6. Plessier A, Rautou PE, Valla DC. Management of hepatic vascular diseases. J Hepatol. 2012;56((suppl 1)):S25–38.
7. Tsochatzis EA, Senzolo M, Germani G, Gatt A, Burroughs AK. Systematic review: portal vein thrombosis in cirrhosis. Aliment Pharmacol Ther. 2010;31:366–374.
8. Okuda K, Ohnishi K, Kimura K, et al. Incidence of portal vein thrombosis in liver cirrhosis. An angiographic study in 708 patients. Gastroenterology. 1985;89:279–286.
9. Ageno W, Squizzato A, Togna A, Magistrali F, Mangini M, Fugazzola C, Dentali F. Incidental diagnosis of a deep vein thrombosis in consecutive patients undergoing a computed tomography scan of the abdomen: a retrospective cohort study. J Thromb Haemost. 2012;10:158–160.
10. Francoz C, Belghiti J, Vilgrain V, et al. Splanchnic vein thrombosis in candidates for liver transplantation: usefulness of screening and anticoagulation. Gut. 2005;54:691–697.
11. Primignani M. Portal vein thrombosis, revisited. Dig Liver Dis. 2010;42:163–170.
12. Francoz C, Valla D, Durand F. Portal vein thrombosis, cirrhosis, and liver transplantation. J Hepatol. 2012;57:203–212.
13. Violi F, Ferro D, Basili S, et al. Ongoing prothrombotic state in the portal circulation of cirrhotic patients. Thromb Haemost. 1997;77:44–47.
14. Tripodi A, Anstee QM, Sogaard KK, Primignani M, Valla DC. Hypercoagulability in cirrhosis: causes and consequences. J Thromb Haemost. 2011;9:1713–1723.
15. Plessier A, Darwish-Murad S, Hernandez-Guerra M, et al. Acute portal vein thrombosis unrelated to cirrhosis: a prospective multicenter follow-up study. Hepatology. 2010;51:210–218.

16. Smalberg JH, Arends LR, Valla DC, Kiladjian JJ, Janssen HL, Leebeek FW. Myeloproliferative neoplasms in Budd-Chiari syndrome and portal vein thrombosis: a meta-analysis. Blood. 2012;120:4921–4928.
17. Turon F, Cervantes F, Colomer D, Gaiges A, Hernández-Gea V, Garcia-Pagán JC. Role of calreticulin mutations in the etiological diagnosis of splanchnic vein thrombosis. J Hepatol DOI: 10.1016/j.jhep.2014.08.032. 2014.
18. Hall T.C., Garcea G., Metcalfe M., Bilku D., Dennison A.R. Management of acute non cirrhotic non malignant portal vein thrombosis: a systematic review. World J Surg. 2011;35:2510–2520.
19. Plessier A., Darwish-Murad S., Hernandez-Guerra M. Acute portal vein thrombosis unrelated to cirrhosis: a prospective multicenter follow-up study. Hepatology. 2010;51:210–218.
20. Turnes J., García-Pagán J.C., González M. Portal hypertension-related complications after acute portal vein thrombosis: impact of early anticoagulation. Clin Gastroenterol Hepatol. 2008;6:1412–1417.
21. Sogaard K.K., Astrup L.B., Vilstrup H., Gronbaek H. Portal vein thrombosis; risk factors, clinical presentation and treatment. BMC Gastroenterol. 2007;7:34
22. Amitrano L., Guardascione M.A., Scaglione M. A. Prognostic factors in noncirrhotic patients with splanchnic vein thromboses. Am J Gastroenterol. 2007;102:2464–2470.
23. Sheen C.L., Lamparelli H., Milne A., Green I., Ramage J.K. Clinical features, diagnosis and outcome of acute portal vein thrombosis. Q J Med. 2000;93:531–534.
24. Dolorich L.R., Ginsberg J.S., Douketis J.D., Holbrook A.M., Cheah G. A meta analysis comparing low molecular wt heparin with unfractionated heparin in treatment of venous thrombolism examining some unanswered questions regarding location of treatment product use and dosing frequency. Arch Int Med. 2000;160:181–188

25. Francoz C., Belghiti J., Vilgrain V. Splanchnic vein thrombosis in candidates for liver transplantation: usefulness of screening and anticoagulation. Gut. 2005;54:691–697.
26. Louvet A., Texier F., Dharancy S. Anticoagulation therapy may sense biliary abnormalities due to acute portal thrombosis. Dig Dis Sci. 2006;51:11–17.
27. Turnes J., García-Pagán J.C., González M. Portal hypertension-related complications after acute portal vein thrombosis: impact of early anticoagulation. Clin Gastroenterol Hepatol. 2008;6:1412–1417.
28. Amitrano L., Guardascione M.A., Menchise A. Safety and efficacy of anticoagulation therapy with low molecular weight heparin for portal vein thrombosis in patients with liver cirrhosis. J Clin Gastroenterol. 2010;44:448–451.
29. Francoz C., Belghiti J., Vilgrain V. Splanchnic vein thrombosis in candidates for liver transplantation: usefulness of screening and anticoagulation. Gut. 2005;54:691–697.
30. Senzolo M., Ferronato C., Burra P., Sartori M.T. Anticoagulation for portal vein thrombosis in cirrhotic patients should be always considered. Intern Emerg Med. 2009;4:161–162.
31. Pellicelli A.M., Guarascio P., D'Ambrosio C. Portal vein thrombosis in cirrhotic patients: safety and efficacy of low dosage of enoxaparin. J Hepatol. 2010;52:S80.
32. Werner K.T., Sando S., Carey E.J. Portal vein thrombosis in patients with end stage liver disease awaiting liver transplantation: outcome of anticoagulation. Dig Dis Sci. 2013;58:1776–1780.
33. Condat B., Pessine T., Helene D.M., Hillaire S., Valla D. Recent portal or mesenteric venous thrombosis, increased recognition and frequent recanalisation on anticoagulant therapy. Hepatology. 2000;32:466–470.
34. Hoekstra J., Seijo S., Rautou P.E. Pregnancy in women with portal vein thrombosis: results of a multicentric European study on maternal and fetal management and outcome. J Hepatol. 2012;57:1214–1219.

35. Valla DC. Thrombosis and anticoagulation in liver disease. Hepatology. 2008;47(4):1384–1393.
36. Amitrano L, Guardascione MA, Menchise A, et al. Safety and efficacy of anticoagulation therapy with low molecular weight heparin for portal vein thrombosis in patients with liver cirrhosis. Journal of Clinical Gastroenterology. 2010;44(6):448–451.
37. Francoz C, Belghiti J, Vilgrain V, et al. Splanchnic vein thrombosis in candidates for liver transplantation: usefulness of screening and anticoagulation. Gut. 2005;54(5):691–697.
38. Englesbe MJ, Schaubel DE, Cai S, Guidinger MK, Merion RM. Portal vein thrombosis and liver transplant survival benefit. Liver Transplantation. 2010;16(8):999–1005.
39. Doenecke A, Tsui TY, Zuelke C, et al. Pre-existent portal vein thrombosis in liver transplantation: influence of pre-operative disease severity. Clinical Transplantation. 2010;24(1):48–55.
40. Amitrano L, Guardascione MA, Menchise A, et al. Safety and efficacy of anticoagulation therapy with low molecular weight heparin for portal vein thrombosis in patients with liver cirrhosis. Journal of Clinical Gastroenterology. 2010;44(6):448–451.
41. Tripodi A, Anstee QM, Sogaard KK, et al. Hypercoagulability in cirrhosis: causes and consequences. Journal of Thrombosis and Haemostasis. 2011;9(9):1715–1723.