To the editor:

Anticoagulants in portal vein thrombosis: don’t be so shy!

We read with great interest the recent article in *Blood* by Martinelli et al on rare venous thromboses.1 In the section on splanchnic vein thrombosis (SVT), it is speculated that the risk of bleeding might outweigh potential benefit from anticoagulants in patients with a high bleeding risk. We believe the definition of a “high bleeding risk” used by the authors may lead to an excessive limitation of the use of anticoagulation therapy (ACT) in these patients. Recent studies evidence a high recanalization rate with ACT in acute portal vein thrombosis (PVT) in noncirrhotic patients. Indeed, in the study of Amitrano et al,2 ACT was effective to obtain recanalization of acute SVT in 45.4% of patients. Similarly, in a recent multicentric study involving 105 patients,3 early anticoagulation allowed a 44% recanalization rate of the portal vein at 1 year. In patients with cirrhosis, in the absence of hepatocellular carcinoma, the presence of PVT should stimulate rather than limit the use of ACT. Indeed, Francoz et al have shown that in patients with chronic liver diseases awaiting liver transplantation, the incidence of PVT reached 8.4% over a 6-year follow-up period.4 The use of anticoagulants was associated with a 42% recanalization rate of the portal vein.

High risk of bleeding in the “flow diagram for treatment of portal vein thrombosis” in the article by Martinelli et al1 is defined as the presence of esophageal varices or thrombocytopenia less than 50,000/mm³. Esophageal varices are clearly a risk factor of bleeding, particularly when they are large. It is important to note that in absence of cirrhosis, esophageal varices may result from PVT itself.5 Recanalization with ACT is the best therapy for varices, whereas thrombus extension is a recognized trigger of portal pressure increase and variceal bleeds. We believe that esophageal varices are accessible to effective therapy in the majority of cases. Ineffective medical treatment should lead to variceal band ligation, which is effective in 90% of cases.6 In the exceptional situation where ligation is ineffective, transjugular intrahepatic portosystemic shunt (TIPS) can be considered. In our mind, only very few patients should temporarily be kept off anticoagulants because of uncontrollable varices. A large French cohort including 84 patients with both chronic and acute PVT who received ACT over a long follow-up period showed no increased gastrointestinal bleeding risk and a similar severity of the hemorrhagic episodes (blood units transfused, duration of hospital stay) in patients who were treated with ACT compared with those who did not receive ACT. However, large esophageal varices were predictors of bleeding, justifying the use of a prophylactic approach (beta blockers [B Bs] and endoscopic therapy). In the Francoz et al study,7 only a minor risk of gastrointestinal bleeding was associated with ACT (1 patient with a postligation ulcer).

Concerning thrombocytopenia, few data are available about a “safe” platelet count. As for varices, thrombocytopenia may be secondary to PVT alone in noncirrhotic patients. Surprisingly, a low platelet count (<70,000/mm³) was even an independent predictor of PVT.8 In our experience, hemorrhagic episodes are infrequent in patients with PVT (with or without cirrhosis) and platelet counts greater than 30,000/mm³.

As an alternative to the algorithm proposed by Martinelli et al, which limits the use of ACT in patients with esophageal varices and low platelets, we would like to propose the scheme shown in Figure 1.
that has been in use for several years in our institution for patients with PVT.

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References

Response:

Anticoagulation in splanchnic vein thrombosis

In response to Spahr et al.,1,2 we would like to point out that the “How I treat” Blood articles are meant to feature therapeutic aspects for which evidence from randomized trials is lacking. These articles are based on opinions of experts who have a large clinical experience in the specific fields.3-5 With this as preamble, we believe that the main disagreement between Spahr et al1 and us2 is on whether or not indefinite anticoagulation should be always prescribed to patients with previous splanchnic vein thrombosis (SVT), because there is no disagreement—although data stem from studies with various limits—on the indication for anticoagulants in the acute phase of SVT.6-8 In the acute phase, anticoagulants are meant to avoid the extension of thrombosis and thereby decrease the risk of portal hypertension and its related complications, mainly gastrointestinal bleeding from ruptured esophagogastric varices.

What about the use of these drugs beyond the acute phase, particularly when portal hypertension has developed despite anticoagulation? In this instance the risk of thrombosis recurrence must be carefully weighted against the risk of bleeding. Thrombosis recurrence, the prevention of which is one of the true goals of anticoagulation, is not frequent in SVT,2 being the main reason for our “shyness” to recommend this therapy in these patients at high risk of bleeding. Barring a slightly higher cutoff in platelet count, the difference between our algorithm2 and that promoted by Spahr et al1 is that we do envisage the possibility that beta blockers and endoscopic therapies fail to prevent variceal bleeding. Because the latter is life-threatening, we find it important to avoid the additional risk that anticoagulants entail. Thrombocytopenia, so frequent in these patients, is a strong risk factor for bleeding, superimposed on that carried by anticoagulants themselves.

In conclusion, we are reluctant to recommend indefinite anticoagulation in the majority of patients with SVT. But of course, as in all clinical conditions where therapeutic evidence is lacking, each SVT case must be considered in itself, with an accurate balance of the pros for anticoagulation (thrombophilia abnormalities and inflammatory conditions) against the cons (severe thrombocytopenia and large gastroesophageal varices).

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References

To the editor:

Scientific profiling

We regret to read that the editors at Blood would outright reject a review manuscript, regardless of its scientific merit, if someone employed by a pharmaceutical company had any role in the development of that manuscript.1 This stance implies that all scientists employed by a pharmaceutical company do not have the ability to be unbiased while writing or contributing to a manuscript.