Rivaroxaban for the treatment of noncirrhotic splanchnic vein thrombosis: an interventional prospective cohort study

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Background

- Splanchnic vein thrombosis (SVT) is an unusual site manifestation of venous thromboembolism (VTE).
- The complex balance between bleeding risk and the risk of thrombus extension or recurrence makes the treatment of SVT a clinical challenge.
- Anticoagulant therapy is recommended for all patients presenting with acute symptomatic SVT, starting with either low-molecular weight heparin (LMWH) or unfractionated heparin (UFH) with a transition to vitamin K antagonists (VKAs).
- A recent guidance document from the International Society on Thrombosis and Haemostasis (ISTH) suggested the possibility of prescribing DOACs in patients without cirrhosis with acute symptomatic SVT, but evidence to support this statement remains scant.

AIM of the study

- To assess the safety and efficacy rivaroxaban for the treatment of acute SVT in patients without cirrhosis.

Methods

- International, single group assignment, open-label, prospective cohort study.
- 18 centers from Italy, Canada, France, and Germany participated in the study.
- Patients aged 18 years or older with a first episode of symptomatic, objectively diagnosed PVT, mesenteric vein thrombosis, or splenic vein thrombosis were eligible for inclusion.
- All enrolled patients received rivaroxaban 15 mg twice daily for 3 weeks, followed by rivaroxaban 20 mg once daily for a total of 3 months.
- All enrolled patients were followed for a total of 6 months. During the 3-month study treatment phase, patients were scheduled for in-person visits at 3 weeks, 2 months, and 3 months. At the end of the treatment period, abdominal ultrasound or CT scan was requested to assess recanalization.
- Primary outcome was major bleeding; secondary outcomes included death, recurrent SVT, and complete vein recanalization within 3 months.

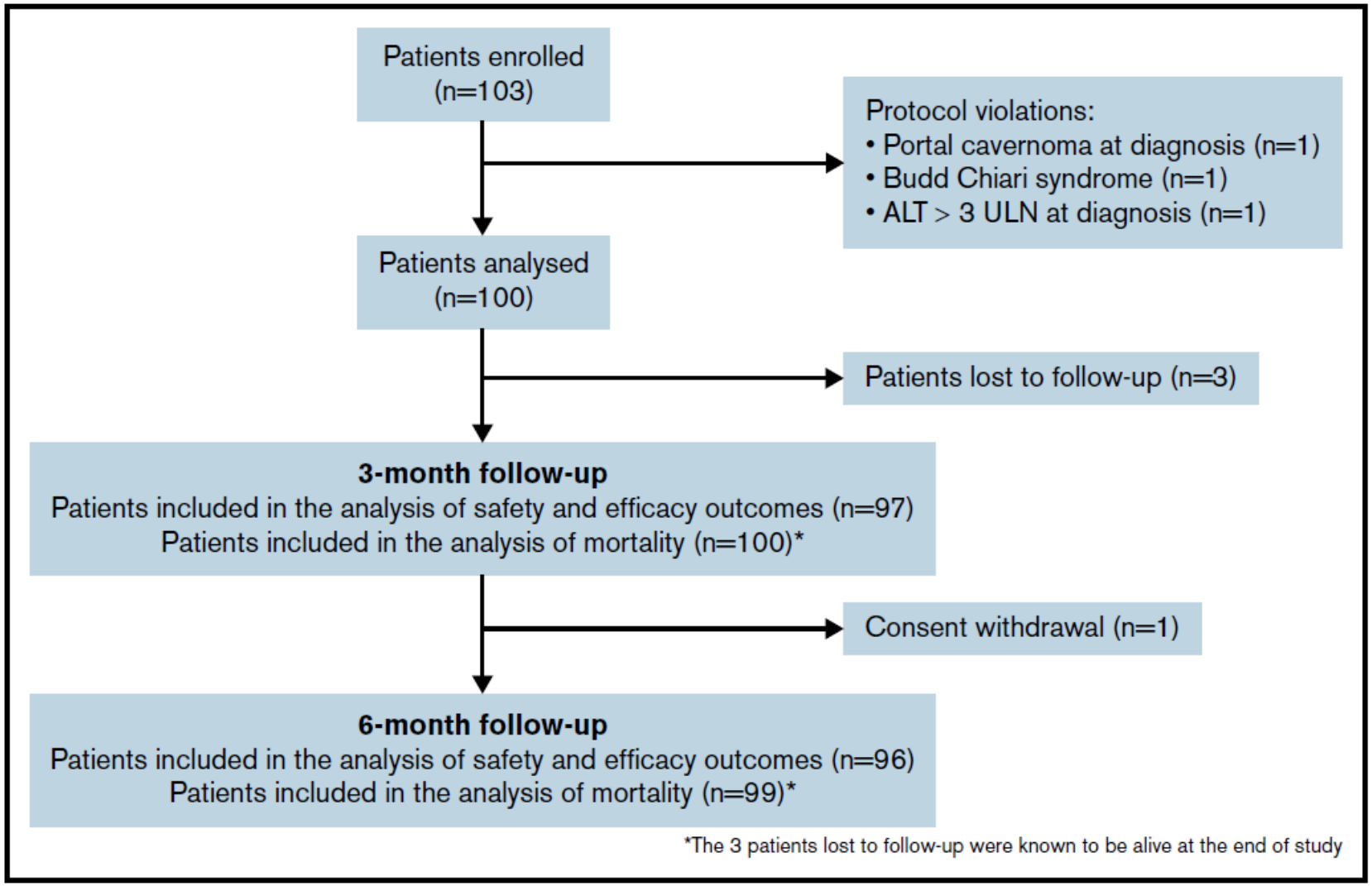


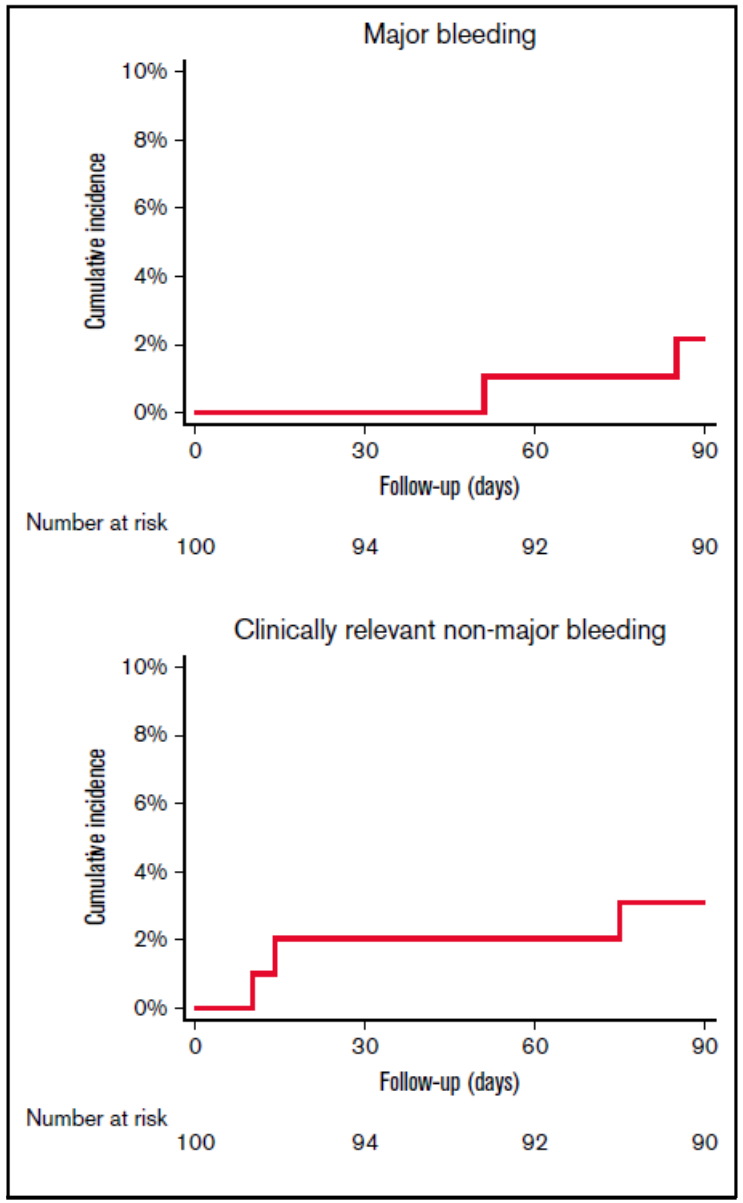
Figure 1. Flowchart of the enrolled population.

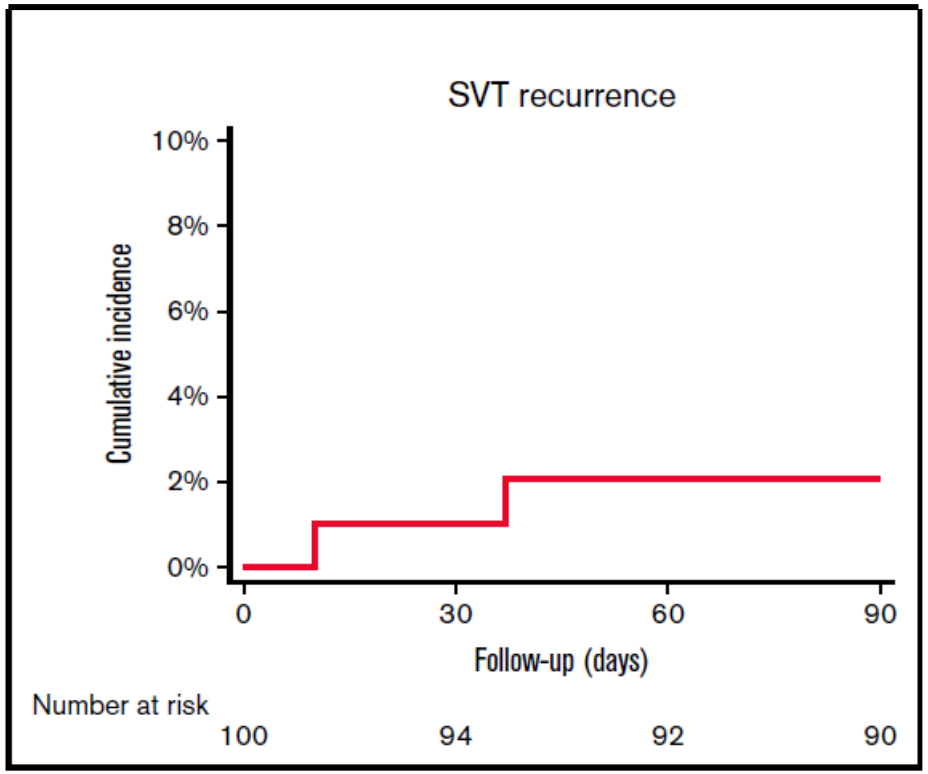
Results

- Mean age was 54.4 years; 64% were men.
- SVT risk factors included abdominal inflammation/infection (28%), solid cancer (9%), myeloproliferative neoplasms (9%), and hormonal therapy (9%); 43% of cases were unprovoked.
- JAK2 V617F mutation was detected in 26% of 50 tested patients.
- At 3 months, 2 patients (2.1%) had major bleeding events (both gastrointestinal). One (1.0%) patient died due to a non–SVT-related cause, 2 had recurrent SVT (2.1%).
- One additional major bleeding event and 1 recurrent SVT occurred at 6 months.
- Complete recanalization was documented in 47.3% of patients.

Table 2. Risk factors for SVT

	No. of patients (n = 100)
Risk factors	
Unprovoked, n (%)	43 (43.0)
Multiple risk factors, n (%)	5 (5.0)
Abdominal inflammation/infection, n (%)	28 (28.0)
Solid cancer, n (%)	9 (9.0)
Overt myeloproliferative neoplasm, n (%)	9 (9.0)
Recent abdominal surgery, n (%)	7 (7.0)
Estrogen hormonal therapy, n (%)	9 (9.0)
Thrombophilia and JAK2 V617F mutation testing	
Factor V Leiden mutation, n/N tested (%)	3/42 (7.1)
Prothrombin G20210A mutation, n/N tested (%)	9/39 (23.1)
Protein C deficiency, n/N tested (%)	2/27 (7.4)
Protein S deficiency, n/N tested (%)	1/27 (3.7)
Antithrombin deficiency, n/N tested (%)	1/26 (3.9)
Hyperhomocysteinemia, n/N tested (%)	4/25 (16.0)
Lupus anticoagulant, n/N tested (%)	2/29 (6.9)
Anti-cardiolipin antibodies, n/N tested (%)	1/34 (2.9)
Anti-β-2-glycoprotein I, n/N tested (%)	0/33 (0)
JAK2 V617F mutation, n/N tested (%)	13/50 (26.0)





Cumulative incidence of major bleeding, clinically relevant non-major bleeding, and SVT recurrent events.

Conclusions

- This is the first interventional study that specifically assessed the safety and efficacy of DOAC for the acute treatment of SVT in patients without cirrhosis.
- The results of the present study support the hypothesis that rivaroxaban can be an important alternative to VKAs, with event rates of recurrent SVT of 2.1% and of major bleeding of 2.1% at 3 months, which compare well with rates reported in studies with heparins and VKAs.
- Of note, the 2 major bleeding events were gastrointestinal bleeds, which occurred in a patient with gastrointestinal cancer and a patient with severe esophagitis: these data confirm the need for a careful assessment of patients with known gastrointestinal lesions or other predisposing factors for bleeding.
- Additional data from interventional and observational studies are needed to confirm these findings and provide information on the long-term risks (eg, after 3 months) of anticoagulation.