The therapeutic landscape of cancer-associated splanchnic vein thrombosis

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ABSTRACT

Splanchnic vein thrombosis (SVT), including portal, splenic, and mesenteric vein thrombosis and the Budd–Chiari syndrome, is an uncommon manifestation of venous thromboembolism frequently associated with solid abdominal malignancies and myeloproliferative neoplasms (MPNs). The management of cancer-associated SVT is challenging due to heterogeneous clinical presentations, competing risks of thrombosis and bleeding, and the lack of high-quality clinical studies in this setting. Based on available evidence, anticoagulation is associated with higher rates of recanalization in patients with solid cancer, with no impact on the mortality rates and a non-negligible bleeding risk. Most available data derive from observational studies, with low-molecular-weight heparin (LMWH) historically representing the most frequently used anticoagulant, although direct oral anticoagulants (DOACs) are increasingly prescribed following evidence from cancer-associated thrombosis in usual sites. In MPN-associated SVT, anticoagulation is generally recommended indefinitely in combination with cytoreductive therapy. Available cohort studies suggest comparable outcomes among vitamin K antagonists (VKAs), LMWH, and DOACs, but robust comparative data are lacking. Overall, current evidence supports an individualized, risk-adapted anticoagulant approach in patients with cancer-associated SVT.

Key words: cancer-associated; splanchnic vein thrombosis.

Introduction

Splanchnic vein thrombosis (SVT) encompasses portal vein thrombosis (PVT), splenic vein thrombosis, mesenteric vein thrombosis (MVT), and the Budd-Chiari Syndrome (BCS). The estimated incidence of PVT ranges between one and four cases per 100,000 inhabitants, while the estimated incidence of BCS, the rarest of these forms, is one to two cases per million individuals.[1-3]

Solid abdominal cancer is, together with cirrhosis, one of the major risk factors associated with SVT and can be present in up to 30% of patients with PVT.[4,5] Conversely, the presence of solid abdominal cancer is infrequent in patients with BCS.[6] Several factors may contribute to the development of SVT in addition to cancer-related inflammatory and procoagulant factors, such as extrinsic mechanical compression by the tumor, abdominal surgery, chemotherapy, or immune modulatory therapy.

Myeloproliferative neoplasms (MPNs) have been reported in up to 40% of cases of BCS and 30% of patients with PVT and this association is due to a procoagulant state induced by quantitative and qualitative defects in the haematopoietic stem cells.[7] The JAK2V617F mutation is the most frequent mutation detected and can be found in the absence of other laboratory features of MPN. Since JAK2V617F mutation remains negative in a non-negligible proportion of patients with SVT, in some cases the investigation of additional mutations may be required.[8-10]

The occurrence of SVT is a possible marker of occult cancer, in particular liver, pancreatic cancer, and MPN, with a higher incidence during the first 3 months after SVT diagnosis. The overall risk remains increased after one or more years of follow-up and the occurrence of SVT in patients with liver or pancreatic cancer is a negative prognostic marker for survival.[11]

Patients with cancer-associated thrombosis (CAT) are at high risk of recurrence and bleeding complications during anticoagulant treatment. More limited evidence exists on the clinical history of cancer-associated SVT, but a recent study found no difference in event rates after cancer-associated lower limb thrombosis and pulmonary embolism and cancer-associated SVT.[12]

Low molecular weight heparin (LMWH) has represented the treatment of choice for patients with CAT thanks to its greater ef-

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ficacy when compared with the vitamin K antagonists (VKAs). The results of recent trials now support the use of direct oral anticoagulants (DOACs) also in this setting[13]. However, increased gastrointestinal bleeding rates with the DOACs have been reported in patients with unresected gastrointestinal cancers.[13]

We will here review available evidence on the treatment of SVT associated with solid cancer and MPN.

Treatment of SVT in patients with solid cancer

The incidence of SVT has increased among patients with cancer, likely due to their improved survival rates and to the greater use of imaging surveillance.[14] The association with SVT is especially stronger for gastrointestinal malignancies and is enhanced by concomitant liver disease or intra-abdominal surgery. In an international SVT registry, hepatobiliary, gastrointestinal, and pancreatic cancers accounted for 50.7%, 25%, and 8.8% of solid tumor-associated SVT, respectively.[15] All these aspects have potential impacts on therapeutic decisions.

A particularly critical aspect is the distinction between a bland (non-tumoral) thrombosis and a tumor thrombus, the latter representing direct intravascular extension of the malignancy and occurring most frequently in pancreatic and hepatocellular cancers.[16] On tumor thrombus, anticoagulation has a minor effect, while antineoplastic treatments are the therapies of choice.[17]

A common condition in patients with CAT is represented by thrombocytopenia, which may be linked to the malignancy itself, comorbidities, or cancer-directed therapies, and can further complicate the management.[18] In patients with SVT, a low platelet count is also associated to portal hypertension, further increasing the risk for gastrointestinal bleeding. However, an observational study by Andersen *et al*. on a population of 581 patients with SVT and solid cancer reported that baseline thrombocytopenia (detected in 39.5% of patients) was not independently associated with major bleeding, as well as with progression/recurrence of SVT.[19]

Evidence regarding anticoagulation-related bleeding risk in patients with SVT is limited and mixed. Smaller retrospective studies have shown increased rates of bleeding among patients with SVT on anticoagulation.[20] In contrast, some prospective analyses have reported that anticoagulant treatment is correlated with a lower risk for bleeding due to an increased recanalization which leads to lower portal venous pressures and a reduced variceal bleeding risk, even in cancer-related SVT.[21,22] In all these studies, the most used treatments were LMWH and VKA. Although patients with solid malignancies were included in a recent systematic review and meta-analysis on anticoagulant therapy for SVT, the available data did not allow a robust assessment of anticoagulation safety and effectiveness according to cancer-related and individual risk factors.[12]

In the absence of major contraindications, guidelines generally suggest that anticoagulation should be considered in patients with acute, symptomatic SVT. An individualized clinical assessment is suggested in patients with asymptomatic and chronic SVT, where the long-term risk of thrombus extension and recurrence needs to be carefully balanced with the risk of bleeding (Table 1).

Evidence to support the acute phase treatment is mostly based on studies carried out in broader populations of patients with non-cirrhotic SVT. In a prospective study by Plessier *et al.,* early initiation of anticoagulation, with LMWH, unfractionated heparin (UFH) or VKA, in patients with recent PVT was associated with prevention of thrombus extension and a markedly lower incidence of intestinal infarction (2% *vs* 30% in patients not receiving anticoagulation). Recanalization of the thrombosed veins was achieved in approximately 30% of anticoagulated patients, occurring predominantly within the first six months of treatment.[23] Consistently, a meta-analysis conducted in the general population of SVT patients demonstrated that anticoagulant therapy was associated with higher rates of recanalization, as well as reduced mortality and bleeding risk.[21] Factors positively associated with recanalization include the anatomical site of thrombosis, particularly the involvement of the splenic or superior mesenteric veins, and early initiation of anticoagulation, defined as treatment started within 15 days from symptom onset.[24]

As regards patients with solid cancer, anticoagulation was infrequently prescribed (14.4% of patients) in a retrospective cohort study by Shang *et al.* carried out in patients with non-hepatocellular carcinoma (HCC) and bland SVT.[22] Yet, anticoagulation was associated with a significantly higher rate of recanalization (44% *vs* 15%) without increasing the incidence of major or clinically relevant non-major bleeding. Mortality rates were not affected by treatment at 6 months. Bleeding rates were relevant regardless of anticoagulation, and recurrent venous thromboembolism (VTE) often occurred shortly after treatment interruption. In patients with HCC, anticoagulation was rarely used and did not appear to influence subsequent VTE risk, while tumor thrombus was a strong marker of poor prognosis.[22]

A multicenter retrospective study by Garcia-Villa *et al.*[16] included 201 patients with solid cancer–associated SVT. Anticoagulation, predominantly with LMWH, was initiated in 41.3% of the patients, mostly those with involvement of multiple splanchnic venous territories. During 12-month follow-up, anticoagulation resulted in a higher rate of recanalization (p=0.005), with differences between groups emerging early (at 50 days). Nonetheless, anticoagulation was not associated with a significant reduction in thrombotic recurrence, but with higher bleeding rates (p=0.001). Of note, patients on anticoagulation had a higher prevalence of metastatic cancer, of poor performance status, and of acute compared to chronic SVT (49.3% *vs* 22.3%) compared to untreated patients. None of the cases of SVT associated with HCC received acute anticoagulant treatment. Overall survival was poor, with a mortality rate of approximately 60% at 12 months.[16] Similar results were reported in a large, single-center retrospective cohort of 581 patients with cancer-associated SVT, most of whom had solid tumors. Anticoagulant therapy, mainly LMWH, was initiated in approximately 40% of patients. The overall cumulative incidence of SVT progression or recurrence was 16.2% at 1 year. In particular, patients receiving anticoagulation had a lower incidence of progression or recurrence compared with those not receiving anticoagulation (11% *vs* 19.6%). However, anticoagulation was independently associated with a higher risk of major bleeding (adjusted risk ratio 1.74; 95% CI, 1.08-2.81) and did not confer a clear survival benefit, with a high overall mortality (46%), largely reflecting cancer-related prognosis.[19]

These observational data confirmed the previous results of a substudy of the International Registry on Splanchnic Vein Thrombosis (IRSVT), where 132 patients with solid cancer-associated SVT enrolled in the study and prospectively followed for up to two years were compared with patients with cancer with usual-

Table 1. Recommendations from guidelines and guidance documents for patients with cancer-associated SVT.

Initial anticoagulant treatment	Long-term anticoagulant treatment	Guideline or Guidance Document
LMWH or DOACs. Preference for LMWH if: • luminal gastrointestinal cancer or other active gastrointestinal mucosal diseases • genitourinary cancer at high bleeding risk • concomitant chemotherapy interfering with DOACs	At least 3 to 6 months or indefinite anticoagulant treatment duration, solid cancer and MPN being a persistent risk factor	ISTH SSC Control of Anticoagulation guidance document on SVT 2020[49] No specific recommendations on MPN-associated SVT
LMWH or DOACs or VKAs. DOACs suggested over LMWH or VKAs. Short-term treatment or observation using clinical judgment for incidental SVT	Anticoagulant treatment for secondary prophylaxis (>6 months) is suggested for active cancer. DOACs or LMWH are suggested for long-term treatment	ASH 2021: cancer-associated VTE[54] No specific recommendations on MPN-associated SVT
SVT diagnosed incidentally should be offered on a case-by-case basis, considering potential benefits and risks	LMWH, direct factor Xa inhibitors, or VKAs should be offered to select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy	ASCO 2023: cancer-associated VTE[55] No specific recommendations on MPN-associated SVT
Anticoagulation with DOACs or LMWH over VKAs in absence of contraindications. If chronic (symptoms > 8 weeks) conside anticoagulation	Continue anticoagulation as long as cancer is active, or cancer therapy is ongoing if tolerated	NCCN 2024: Clinical Practice Guidelines on cancer-associated VTE[56] No specific recommendations on MPN-associated SVT
Solid abdominal cancer LMWH or DOACs. Preference for LMWH if: • gastrointestinal cancer • concomitant chemotherapy interfering with DOACs MPN VKAs or DOACs (similar bleeding risk)	Long-term anticoagulation advised while cancer remains active or in presence of MPN	EASL 2025: Clinical Practice Guidelines on vascular diseases of the liver[57]
In patients with recent PVT, directed antithrombotic therapy should be considered to avoid intestinal ischemia and prevent the development of chronic PVT with portal hypertension	No specific recommendations.	AASL 2021: Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease[58] No specific recommendations about solid cancer associated SVT or MPN associated SVT

LMWH, low molecular weight heparin; DOACs, direct oral anticoagulants; MPN, myeloproliferative neoplasm; SVT, splanchnic vein thrombosis; VKAs, vitamin K antagonists; VTE, venous thromboembolism; PVT, portal vein thrombosis.

site VTE enrolled in a different study.[24] At 12 months, the incidence of recurrent thrombosis in patients with SVT was 4.7% (*vs* 5.5%), and major bleeding occurred in 2.3% of patients (*vs* 4.7%). All-cause mortality was high (41.7%) and comparable to that observed in patients with usual-site VTE, confirming that survival is largely driven by the underlying malignancy rather than SVT-related complications.[12]

Across the aforementioned studies, LMWH was the most frequently used anticoagulant, followed by DOACs and VKAs, without direct comparative analyses. The increasing adoption of DOACs in CAT has progressively enhanced clinicians' confidence in their use, despite the absence of strong evidence in this field.

The prospective single-arm cohort study by *Ageno et al*. evaluated the standard dosing regimen of rivaroxaban (i.e. 15 mg bid for 21 days followed by 20 mg od) in a population with acute non-cirrhotic SVT, but only a small proportion of patients had solid cancer (9%). At 3 months, the overall incidence of recurrent SVT and major bleeding was low, while complete vein recanalization was observed in nearly half of patients. Mortality was very low (~1%). However, the limited number of patients with cancer restricts the applicability of these results to patients with cancer-associated SVT.[25]

In conclusion, these findings suggest that physicians tend to prescribe anticoagulant drugs less frequently to patients with cancer-associated SVT than to those with cancer-associated VTE in usual sites, preferably treating the acute phase only, and considering the evolution of time of thrombosis as a factor to decide whether to initiate anticoagulation or not. A greater thrombotic burden, as well as the involvement of multiple splanchnic veins or mesenteric vein thrombosis were associated with higher prescription rates.

In this challenging setting, an even more difficult decision is to initiate anticoagulation in patients with hepatocellular carcinoma. This may be linked to the higher bleeding risk observed in this population and to the frequent presence of tumor thrombus (approximately one third of HCC), a strong predictive factor of poor prognosis with much less response to anticoagulation. Yet, tumor thrombus not uncommonly hides a coexistent bland thrombus.[17]

Overall, current evidence suggests that anticoagulation in cancer-associated SVT may increase recanalization rates, but with uncertain benefits on other major clinical outcomes (Table 2). This suggests the need for an individualized treatment approach, in which the benefit of treatment is carefully balanced against the risk of bleeding considering baseline patient characteristics, history of previous thrombosis or bleeding, type and stage of cancer, and presence and severity of bleeding risk factors.

Treatment of SVT in patients with MPN

MPNs are clonal haematopoietic stem cell disorders characterized by dysregulated and autonomous proliferation of myeloid progenitor cells within the bone marrow, resulting in increased production of mature erythroid, megakaryocytic, and granulocytic lineages in the peripheral blood. According to the revised World Health Organization (WHO) classification of myeloid neoplasms and its latest update, the classical BCR::ABL1-negative MPN subtypes include polycythaemia vera (PV), essential thrombocythaemia (ET), and primary myelofibrosis (PMF), with the recognition of a distinct prefibrotic/early-stage myelofibrosis (pre-PMF) entity, separated from the overt primary myelofibrosis.[26,27]

Patients with MPN exhibit a substantially increased risk of both arterial and venous thrombosis, estimated to be approximately up to 10-fold higher compared to the general population.[28] VTE accounts for approximately one-third of all thrombotic events in patients with MPNs, with an estimated incidence of about 0.6% per patient-year in ET and pre-PMF,[29] 0.76% per patient-year in overt PMF,[30] and approximately 1% per patient-year in PV.[31] VTE manifestations include deep vein thrombosis (DVT) of the lower extremities, pulmonary embolism (PE), SVT, and cerebral venous thrombosis. Notably, the prevalence of thrombosis in unusual sites is disproportionately high in patients with MPNs;[32] therefore, an underlying MPN should be systematically suspected.[28] With regard to SVT, MPNs represent one of the most common underlying causes of PVT and BCS, being identified in up to 40% of affected patients.[7] All MPN subtypes have been associated with the development of SVT; however, PV is the most frequently implicated entity, followed by ET, whereas PMF is only rarely involved.[33]

Thrombotic complications have a significant impact on the prognosis of patients diagnosed with an MPN (as it occurs for cancer in general), representing an independent adverse prognostic factor for survival in PV[34] and ET[29] whereas in PMF, the prognostic relevance of VTE may be less apparent due to the competing risk of other complications, such as leukemic transformation and severe infections.[28]

Despite a significant proportion of patients diagnosed with MPNs remains unclassifiable from a genetic perspective,[35] the identification of MPN-associated driver mutations, JAK2 V617F, JAK2 exon 12, myeloproliferative leukaemia virus oncogene (MPL) W515L/K, and calreticulin (CALR) by highly sensitive single/multitarget panels or next generation sequencing (NGS)

Table 2. Studies including patients with solid cancer-associated SVT.

Study	Population with solid cancer and SVT	Comparator population	AC therapy	SVT recurrence	Bleeding events	SVT recanalization	Survival / mortality
RIVA-SVT 100, Ageno *et al.* (2022)	9/100 patients	NA	Rivaroxaban in all patients	Overall cohort: 2/100 (2.1%) at 3 months	Cancer SVT: NA Overall cohort: 2/100 (2.1%) MB	Overall cohort: 47.3% complete recanalization at 3 months	Overall: mortality 1/100 (1.0%)
Garcia-Villa *et al.* (2025)	201 patients	Patients with AC *vs.* patients without AC	Mainly LMWH (92.8% of treated)	AC cohort: NA Non-AC cohort: NA (no significant difference at 12 months)	AC cohort: higher bleeding incidence (exact n/% NA)	AC cohort: higher recanalization rate (exact n/% NA)	Overall: survival 39.7% at 12 months
Andersen *et al.* (2024)	581 cancer-associated SVT (38 haematologic)	Patients with AC *vs.* patients without AC	LMWH 43%, DOAC 24%, VKA 18%	Overall cohort: 94/581 (16.2%) at 12 months	Overall cohort: 62/581 (10.7%) MB	NA	Overall cohort: survival at 12 months 54.4%
Valeriani *et al.* (2021)	132 patients	132 patients with solid cancer and usual-site VTE	LMWH 46.2%, VKA 22.7%	SVT cohort: 6/132 (4.7%) at 12 months	SVT cohort: 3/132 (2.3%)	NA	SVT cohort: mortality 55/132 (41.7%)
Shang *et al.* (2024)	146 patients with HCC and 114 patients non-HCC (with and without AC)	Patients with AC *vs.* patients without AC	LMWH (70%), DOAC (24%), VKA (6%) in anticoagulated subgroup	AC cohort: 4/37 (11.1%) usual-site VTE at 6 months Non-AC cohort: 3/77 (4.0%)	AC cohort: MB 5/37 (13.9%); CRNMB 7/37 (18.9%) Non-AC cohort: MB 8/77 (10.6%); CRNMB 14/77 (18.4%)	AC cohort: 8/18 (44.4%) Non-AC cohort AC: 5/33 (15.2%)	AC cohort: 15/37 (42.1%) Non-AC cohort: 30/77 (39.2%) at 6 months

SVT, splanchnic vein thrombosis; AC, anticoagulation; NA, not available; MB, major bleeding; LMWH, low molecular weight heparin; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist; VTE, venous thromboembolism; HCC, hepatocellular carcinoma; CRNMB, clinical relevant not major bleeding.

contributed both to stratify different MPNs forms[27] and to enhance the diagnostic accuracy of MPNs in the setting of SVT; thus, the genetic pattern should be routinely incorporated into the etiological evaluation of patients presenting with SVT.[33]

In patients with MPNs and SVT, bleeding risk represents a major clinical issue, arising from the complex interplay between the intrinsic prothrombotic state of the disease and MPN-related haemostatic abnormalities. Factors such as thrombocytopenia, qualitative platelet dysfunction, acquired von Willebrand syndrome, and portal hypertension contribute to an increased susceptibility to bleeding, particularly from the gastrointestinal tract (Table 3). This aspect poses significant challenges to antithrombotic therapy, even among expert clinicians: therefore, it should be tailored and individualized, balancing patient's thrombotic and bleeding risks, within a multidisciplinary framework.[36-38]

Anticoagulant therapy is the cornerstone of SVT treatment in the attempt to avoid thrombus progression (and its sequelae), achieve vessel recanalization and prevent VTE recurrence[33] and, recently, several studies demonstrated that anticoagulation pursues these outcomes without significantly increasing the bleeding risk also in patients with MPNs.[38-40] Parenteral anticoagulation is usually preferred for the initial treatment of these patients and, also considered the higher incidence of heparin-induced thrombocytopenia (HIT) in patients with MPNs,[41] the use of LMWH is currently recommended over UFH. The use of fondaparinux may also be potentially interesting in these patients in order to minimize the risk of HIT; however, the available evidence regarding its use is limited to a few studies, and therefore it is not formally recommended by most scientific societies in this field.[40,42-44] Routinely, heparins are promptly replaced with VKAs in patients with stable disease and not requiring urgent surgery or invasive manoeuvres. As mentioned above, DOACs have gained progressive acceptance for the management of CAT,[45-47] however, evidence on their use in the setting of underlying MPNs remains limited, owing to the small proportion of patients enrolled in the available cohorts.[46-48] This problem also applies to patients with SVT, where the number of patients with MPN treated with DOACs reported in the studies remains limited. Indeed, the role of DOACs in this setting is important also in the light of treatment duration, being MPN a persistent risk factor generally requiring indefinite anticoagulation when not clearly contraindicated.[49]

A recent retrospective, multinational cohort study described different anticoagulant strategies for the treatment of SVT in the setting of MPNs. A total of 486 patients were included in the study, 51.2% had thrombosis in multiple vessels, 25.7% had PVT, 15.5% BCS, 1.9% MVT, and 4.3% had splenic vein thrombosis. Cytoreductive therapy was started after SVT in 58.7% of newly diagnosed MPN patients and 40.6% of those with known MPN. The most common anticoagulants were VKAs (29.2%), followed by DOACs (20.4%), and LMWH (10.5%). The median duration of anticoagulation was 23.9 months. The 1-year cumulative incidence of recurrent SVT was 5.8% (95%CI: 3.9%-8.3%). No significant difference was found among the three anticoagulant strategies either for thrombosis (VKA: 13%, DOAC: 15% and LMWH: 16%; p=0.93) or major bleeding (VKA: 5.9%, DOAC: 6.6% and LMWH: 4%; p=0.89). Finally, a trend to higher recanalization rates was observed with the use of DOACs (26.9%), compared to VKAs and heparins (21.5% and 13.6%, respectively; p=0.28).[50]

A subsequent larger cohort study aimed at evaluating the management of anticoagulation in SVT patients, regardless of the presence of an underlying MPN. The study enrolled 1197 patients diagnosed with SVT, 187 of whom had MPN. Most patients (89.5% of those with MPN and 78.0% of those without) received anticoagulant therapy for at least 6 months after the diagnosis of

Table 3. Studies including patients with MPNs and SVT.

Study	Population	Initial anticoagulant therapy	SVT recurrence	Bleeding	Recanalization	Survival / mortality
GASTRO-MPN How *et al.*[50]	486 patients with MPN and SVT	VKA: 29.2% DOAC: 20.4% LMWH: 10.5%	Overall: 5.8% (95%CI: 3.9%-8.3%) According to anticoagulant therapy: VKA: 13% DOAC: 15% LMWH: 16%	MB, overall: 5.8% (95%CI: 3.9%-8.2%) CRNMB, overall: 8.5% (95%CI: 6.1%-11%) MB, according to anticoagulant therapy: VKA: 5.9% DOAC: 6.6% LMWH: 4%	Overall: 13% (95%CI: 9.8%-16%) According to anticoagulant therapy: VKA: 21.5% DOAC: 26.9% LMWH: 13.6%	Survival, overall: 94.2% (95%CI: 91.8%-96.1%) (1 year follow-up) Survival, according to anticoagulant therapy: VKA: 96.7% DOAC: 95.6% LMWH: 89.7% (1 year follow-up)
Ko *et al.*[51]	1197 patients with SVT: 187 with MPN and 1010 without MPN	VKA: 43.9% Other anticoagulants: unknown	Patients with MPN: 3.2% Patients without MPN: 2.4%	MB in patients with MPN: 1.1% MB in patients without MPN: 3%	NA	Mortality in patients with MPN: 3.2% (6 months follow-up) Mortality in patients without MPN: 6.8% (6 months follow-up)
Sant'Antonio *et al.*[52]	518 patients with MPN and SVT	VKA: 66% LMWH: 34%	12%	MB (excluding oesophageal varices) incidence rate: 1.2 (95%CI: 0.9-1.6)	NA	Survival: 84.5% (89.9 months follow-up)

SVT, splanchnic vein thrombosis; MPN, myeloproliferative neoplasm; VKA, vitamin K antagonist; DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; MB, major bleeding; CRNMB, clinically relevant not major bleeding; NA, not available.

thrombosis and VKAs were the most frequently prescribed anticoagulants (43.9%). At 6 months, no significant differences were found between patients with and without MPNs in terms of recurrent thrombosis (3.2% and 2.4%, respectively; OR 1.43 [0.86-2.45]) and major bleeding (1.1% and 3%, respectively; OR 0.77 [0.48-1.25]), suggesting the possibility to use the same anticoagulant regimens in SVT patients with or without MPN.[51]

Finally, a multicentre, multinational, retrospective study by Sant'Antonio *et al.* included a total of 518 SVT patients with known MPN, compared with 1628 unselected non-SVT MPN control patients. The study aimed at evaluating clinical and biological features of patients with MPN and SVT, focusing on thrombosis secondary prevention, with a median follow-up of 89.9 and 70.1 months for MPN-SVT cohort and control group, respectively. The majority of the included patients (91.6%) was treated with anticoagulants and/or antiplatelet agents (either aspirin, ticlopidine or clopidogrel) for the secondary prophylaxis of SVT: anticoagulant agents were administered to 84.6% of the study cohort (heparin in 34% and VKAs in 66% of cases). Site of SVT was portal in 67.4% of the patients (n=349), splenic in 29.3% (n=152), mesenteric in 24.3% (n=126) and suvra-hepatic in 24.9% (n=129). A total of 62 patients (12%) experienced SVT recurrence, with significantly higher recurrent rates when off VKAs therapy (OR 2.3 [95%CI 1.6–3.2]). Major bleedings were more frequent in MPN-SVT compared to the control group and were mainly related to oesophageal varices. The incidence rate of bleeding in other sites was 1.2 (95%CI: 0.9-1.6) among MPN-SVT and 1.0 (95%CI: 0.8-1.2) among controls.[52]

Conclusions

The management of patients with SVT and underlying malignancy still represents a clinical challenge, due to both their potential fragility and the lack of solid data from randomized cohorts. We support the (limited) available evidence and current guidelines recommending initial full-dose anticoagulation for patients with SVT and solid cancer or MPN, as for usual-site VTE, with the aim of preventing thrombus progression and VTE recurrence and achieving vessel recanalization. However, treatment decisions should be guided by reasonable diagnostic certainty, avoiding anticoagulation in patients who are unlikely to benefit or who may be harmed (e.g., patients with HCC and/or tumor thrombus).

Extended duration of anticoagulation, associated with specific cytoreductive therapy, is suggested in case of SVT and underlying MPN. Also, the duration of treatment for patients with solid cancer needs to be individually tailored, balancing the benefit of anti-thrombotic treatment with the high risk of bleeding, related to concomitant antineoplastic therapies, and the natural history of cancer itself.

So far, studies comparing different therapeutic strategies are lacking in this setting. Despite the absence of robust evidence, we consider DOACs a good choice, as they are gaining ground in this setting, following the trend of prescriptions in patients with CAT. For the long-term secondary prevention, the opportunity to prescribe reduced doses of DOACs after the first 6 months of treatment is extremely interesting, but currently not supported by any data as no patient with SVT was included in the recently published APICAT study.[53]

Therefore, it is about time to dedicate resources to the design of high-quality studies focusing on patients with cancer-associated SVT to define the optimal anticoagulant strategies by evaluating patient-centred outcomes.

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