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Outcomes of Splanchnic Vein Thrombosis in Patients with Myeloproliferative Neoplasms in a Single Center Experience

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To the Editor:

Myeloproliferative neoplasms (MPNs) are a group of hematologic malignancies characterized by overlapping clinical features including an increased thrombotic potential.¹ Splanchnic vein thrombosis (SVT) has a known association with MPNs, in which 8.2% of SVTs occur in the setting of an underlying MPN.² A main consequence of SVT is portal hypertension, which can lead to complications including esophageal variceal bleeding (EVB) and ascites.³ The impact of treating the underlying MPN at time of SVT on these hepatic outcomes is unknown.

We conducted a retrospective cohort study of 64 patients with MPNs who experienced an SVT between January 1995 and April 2018. Timing of SVT occurrence relative to MPN diagnosis was determined to be concurrent if SVT was diagnosed within 30 days of MPN. EVB and complications of anticoagulation were defined as International Society on Thrombosis and Haemostasis major bleeding.⁴ We used a 6-month landmark survival analysis for outcomes in order to account for immortal time bias arising from varying times to MPN diagnosis following SVT.

Table 1 details the characteristics of the cohort. SVT was diagnosed a median of 4 [1–90] months prior to diagnosis of MPN in the SVT antecedent to MPN diagnosis group while SVT was diagnosed a median of 46 [1–288] months after diagnosis of MPN in the SVT after MPN diagnosis group.

During a median follow-up of 61 months from time of SVT (1 to 279 months), EVB occurred in 13 (20%) patients, ascites in 30 patients (47%), and hepatic encephalopathy in 6 patients (9%). There was no difference between patients who were receiving MPN treatment at time of SVT diagnosis and those who did not for time to EVB ($p=0.3519$), additional SVT ($p=0.6995$), ascites ($p=0.8016$), or hepatic encephalopathy ($p=0.2642$). There was no difference in time to composite of these outcomes between those receiving MPN-direct therapy at time of SVT diagnosis versus patients who were not ($p=0.8983$) or in patients who were receiving anticoagulation and those who were not ($p=0.9222$). The median OS of the cohort was not reached. The five-year OS probability was 98% and there was no difference among patients diagnosed antecedent, concurrent, or after MPN diagnosis. Twelve patients (25% of those anticoagulated) were treated with a direct oral anticoagulant (DOAC) for median duration of 23.9 [1.7–77.6] months. Only one patient experienced a bleeding event and one patient developed recurrent thrombosis while receiving a DOAC.

Our study has a number of limitations that are important to recognize. Most importantly, our small sample size limited our ability to compare subgroups. The study period encompasses evolving diagnostic and treatment paradigms for both MPNs and SVTs. Finally, laboratory values prior to thrombosis, including gamma-glutamyl transferase, were inconsistently available, limiting our ability to confirm prior studies linking lab values to development of SVT.⁵

In conclusion, we provide new information regarding the sequencing of SVT as it relates to MPN diagnosis. In a small subgroup, DOACs appear to be safe in the treatment of MPN-associated SVT. We were not able to show dependence between treatment of the underlying MPN at time of SVT and rates of EVB, additional SVT, development of ascites, and hepatic encephalopathy. Future studies are required to further clarify the optimal therapeutic strategies for patients with an MPN-associated SVT.

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Table 1.**Patient Characteristics**

Subjects, N	64
Age at MPN diagnosis, years median (range)	43 [16–89]
Age at Thrombosis, years median (range)	45 [18–89]
Year of MPN diagnosis, median (range)	2010 [1981–2018]
Female, N (%)	46 (72%)
MPN Diagnosis, N (%)	
PMF	8 (13%)
PV	29 (45%)
ET	14 (22%)
Post ET/PV MF	5 (8%)
Pre-PMF	2 (3%)
MDS/MPN, unclassifiable	1 (2%)
MPN unclassifiable	5 (8%)
Mutational status, N (%) *	
<i>JAK2</i>	60 (95%)
<i>CALR</i>	1 (1.6%)
<i>DMNT3A</i>	1 (1.6%)
<i>EZH2</i>	1 (1.6%)
Timing of thrombosis, N (%)	
After MPN	28 (44%)
Antecedent to MPN	19 (30%)
Concurrent	17 (26%)
Multiple thromboses, N (%)	23 (36%)
Thrombosis type, N (%)	
BCS	23 (36%)
PVT	44 (69%)
Other	23 (36%)
Splenic Vein Thrombosis	13 (20%)
Superior Mesenteric Vein Thrombosis	9 (14%)
IVC	1 (2%)
Portal vein cavernous transformation, N (%)	11 (33%)
MPN treatment at thrombosis, N (%)	
Hydroxyurea	3 (5%)
Interferon-alpha	3 (5%)
Ruxolitinib	1 (2%)
Anagrelide	1 (2%)
Therapeutic Phlebotomy Only	3 (5%)

Lestaurtinib	1 (2%)
None	44 (69%)
Unknown	8 (13%)
Treatment of SVT, N (%)	
Enoxaparin	12 (19%)
Warfarin	25 (39%)
Aspirin	8 (13%)
DOAC	12 (19%)
Rivaroxaban	8 (13%)
Dabigatran	3 (5%)
Apixaban	1 (2%)
Transjugular intrahepatic portosystemic shunt	13 (20%)
None	7 (11%)
Liver Transplantation	2 (3%)
Other Surgical Procedure	1 (2%)
Unknown	2 (3%)
Fondaparinux	1 (2%)

BCS – Budd Chiari syndrome; DOAC = direct oral anti-coagulant;

ET – essential thrombocythemia; IVC = inferior vena cava;

MDS – myelodysplastic syndrome; MPN – myeloproliferative neoplasms;

PMF – primary myelofibrosis; PV – polycythemia vera;

PVT – portal vein thrombosis; SVT – splanchnic vein thrombosis

*

Non-driver mutational analysis was only performed on 9 patients (14%) at diagnosis