Thrombosis Research 134 (2014) 251–254

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Treatment of thromboembolic events coincident with the diagnosis of myeloproliferative neoplasms: A physician survey

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ARTICLE INFO

Article history:
Received 31 January 2014
Received in revised form 26 March 2014
Accepted 28 April 2014
Available online 9 May 2014

ABSTRACT

The BCR-ABL1 negative myeloproliferative neoplasms (MPNs) are associated with an increased risk of both venous and arterial thromboembolic events. Thromboses may be the presenting clinical feature of an MPN or may occur during the course of the disease. Treatment comprises anticoagulant and antiaggregant agents as in non- MPN thromboses, and treatment of the particular MPN. The duration of anticoagulant treatment that is required for MPN thrombosis is unknown. This study was performed to survey the opinion of hematologists who treat patients with MPN regarding the duration of anticoagulation or antiaggregant therapy in patients in whom thrombosis is the presenting feature of MPN.

Five clinical scenarios in which thromboembolism (cerebral vein thrombosis, pulmonary embolism, cerebrovascular accident, splanchnic vein thrombosis, portal vein thrombosis) was a presenting feature of MPN were created using a web-based tool and were sent by email to hematologists in Israel, Italy and England and to hematologists identified as key opinion leaders in the field of MPN. Physicians were asked to recommend duration of anticoagulation and/or aspirin use choosing from 4 alternatives provided.

Seventy-three physicians responded to the survey. 42 physicians considered MPNs to be their main area of clinical interest, and 31 did not. 21 physicians saw more than 20 MPN patients per week, and 50 physicians had been in hematology practice for more than 10 years. Responses regarding the duration of anticoagulation and/or the use of aspirin varied for all of the clinical vignettes. Neither physician area-of-interest, volume of MPN patients treated nor years in practice were related to the responses obtained.

This study demonstrates that hematologists, including those specializing in MPNs, lack consensus in their approach to the long-term treatment of thromboses as the presenting feature of an MPN. Controlled clinical studies are needed to inform appropriate decision making in this area.

Introduction

The BCR-ABL1 negative myeloproliferative neoplasms (MPNs) are associated with an increased risk of both venous and arterial thromboembolic events. Thromboses may be the presenting clinical feature of an MPN or may occur during the course of the disease. Recent cohort studies have demonstrated an incidence of thrombosis of 15-20% at or prior to diagnosis in patients with polycythemia vera (PV) and 10% during the course of the disease [1], 10-12% at or prior to diagnosis in patients with essential thrombocytosis (ET) and 5-8% thereafter [2] and 7-8% at or prior to diagnosis in patients with primary myelofibrosis (PMF) and 3-4% thereafter [3]. A recent review of thrombosis in MPNs cited numerous other smaller case series which revealed similar incidences overall [4].

The role of aspirin in prevention of venous and arterial thromboses in PV was clearly demonstrated in the randomized ECLAP study [5] and more recently the CytoPV trial showed that in PV maintaining the hematocrit at 45% or less in men and 42% or less in women prevents thrombotic complications [6]. However, there has been no study performed to inform the appropriate antithrombotic and/or antiaggregant treatment in patients with MPNs who experience a thrombosis, particularly regarding the appropriate duration of anticoagulation.

In this study polled clinical hematologists who treat MPN patients and report on their opinions regarding appropriate antithrombotic treatment in five different clinical scenarios involving thrombosis as the presenting feature of a MPN.

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http://dx.doi.org/10.1016/j.thromres.2014.04.032
0049-3848/

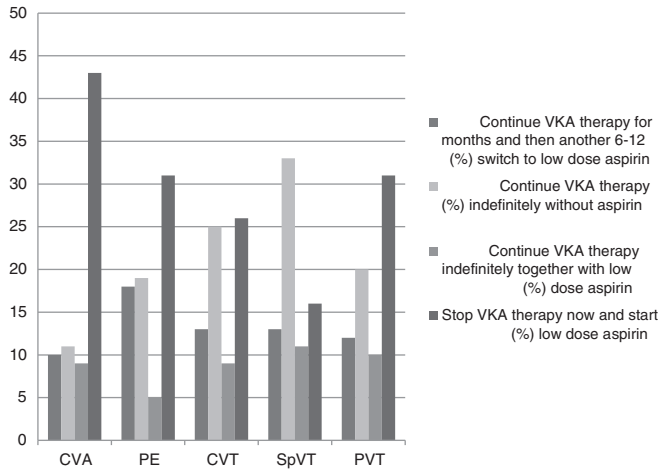

Fig. 1. Physicians' treatment decisions for each of the 5 clinical case scenarios. CVA = cerebrovascular accident, PE = pulmonary embolus, CVT = cerebral vein thrombosis, SpVT = splanchnic vein thrombosis, PVT = portal vein thrombosis.

Methods

Five clinical case scenarios were constructed by one of us (M.E.). These were representative of common thrombotic events complicating MPNs namely: cerebral sinus vein thrombosis, pulmonary embolism, cerebrovascular accident (CVA), splanchnic vein thrombosis, and portal vein thrombosis. In each case the thrombotic event was the presenting feature of the MPN (PV or ET) and the MPN was subsequently controlled with medical treatment. Physicians were asked to choose between four options regarding anticoagulation and/or antiaggreagant therapy after an initial period of anticoagulation and after adequate cytoreduction. The treatment choices presented were: 1) Continue vitamin K antagonist (VKA) therapy for another 6-12 months and then switch to low dose aspirin, 2) Continue VKA therapy indefinitely without aspirin, 3) Continue VKA therapy indefinitely together with low dose aspirin, 4) Stop VKA therapy now and start low dose aspirin.

Data collected pertaining to the physicians were: whether MPN was the primary area of clinical practice, number of MPN patients treated weekly and number of years in practice. The full questionnaire appears in Appendix 1.

Physicians surveyed were members of the Israel Society of Hematology (N = 120), Italian Society of Hematology, British Clinical Research Network - MPN N(=25) or recognized experts in the field of MPN as defined by authorship of peer-reviewed articles in the field of clinical management of MPNs (N = 30). Contact was established by email and the clinical case scenarios were accessed using an online survey site (MonkeySurvey®).

Physician responses to each question were collected and tabulated. Association between the response chosen to each of the five clinical scenarios and physician area-of-interest (primarily MPN-treating physician versus non-primarily MPN-treating physician), volume of MPN patients treated weekly and years in practice was determined using the Chi square test. A p value of < 0.05 was considered significant.

Results

Seventy-three physicians responded to the survey. 42 (57.5%) physicians primarily treat MPNs, and 31 (42.5%) did not consider MPN to be their primary area of clinical practice. 21 (29%) physicians saw more than 20 and 52 (71%) physicians saw fewer than 20 MPN patients per week. 50 (68.5%) physicians had been in hematology practice for more than 10 years while 23 (31.5%) had been in hematology practice for fewer than 10 years.

Responses regarding the duration of anticoagulation and/or the use of aspirin varied for all of the clinical vignettes (Fig. 1). In the cerebral vein thrombosis case, 17.8% of physicians chose "Continue VKA therapy for another 6-12 months and then switch to low dose aspirin", 34.2% chose "Continue VKA therapy indefinitely without aspirin", 12.3% chose "Continue VKA therapy indefinitely together with low dose aspirin" and 35.6% chose "Stop VKA therapy now and start low dose aspirin".

In the case of segmental pulmonary embolus, 24.7% of physicians chose "Continue VKA therapy for another 6-12 months and then switch to low dose aspirin", 26% chose "Continue VKA therapy indefinitely without aspirin", 6.8% chose "Continue VKA therapy indefinitely together with low dose aspirin" and 42.5% chose "Stop VKA therapy now and start low dose aspirin".

For the patient with a CVA, 13.7% of physicians chose "Continue VKA therapy for another 6-12 months and then switch to low dose aspirin", 15.1% chose "Continue VKA therapy indefinitely without aspirin", 12.3% chose "Continue VKA therapy indefinitely together with low dose aspirin" and 58.9% chose "Stop VKA therapy now and start low dose aspirin".

For the patient with a splanchnic vein thrombosis, 17.8% of physicians chose "Continue VKA therapy for another 6-12 months and then switch to low dose aspirin", 45.2% chose "Continue VKA therapy indefinitely without aspirin", 15.1 % chose "Continue VKA therapy indefinitely together with low dose aspirin" and 21.9% chose "Stop VKA therapy now and start low dose aspirin".

For the patient with a portal vein thrombosis, 16.4% of physicians chose "Continue VKA therapy for another 6-12 months and then switch to low dose aspirin", 27.4% chose "Continue VKA therapy indefinitely without aspirin", 13.7% chose "Continue VKA therapy indefinitely together with low dose aspirin" and 42.5% chose "Stop VKA therapy now and start low dose aspirin".

There were no statistically significant differences between the choice of anticoagulant/antiaggregant therapy options for any of the case scenarios using the Chi squared test. Similarly, neither physician area-of-interest, volume of MPN patients treated nor number of years in hematology practice were related to the responses obtained (Tables 1–3).

Table 1
Physicians' treatment decisions for each of the 5 clinical case scenarios according to area of main clinical interest.

MPN primary clinical area	Continue VKA therapy for another 6-12 months and then switch to low dose aspirin (%)		Continue VKA therapy indefinitely without aspirin (%)		Continue VKA therapy indefinitely together with low dose aspirin (%)		Stop VKA therapy now and start low dose aspirin (%)		P value (Pearson Chi square test)
	YES	NO	YES	NO	YES	NO	YES	NO	
CVA	14.3	12.9	14.3	16.1	14.3	9.7	57.1	61.3	NS
PE	23.8	25.8	21.4	32.3	7.1	6.5	47.6	35.5	NS
CVT	16.7	19.4	38.1	29	11.9	12.9	33.3	38.7	NS
SpVT	11.9	25.8	47.6	41.9	14.3	16.1	26.2	16.1	NS
PVT	16.7	16.1	26.2	29	7.1	22.6	50	32.3	NS

CVA = cerebrovascular accident, PE = pulmonary embolus, CVT = cerebral vein thrombosis, SpVT = splanchnic vein thrombosis, PVT = portal vein thrombosis, NS = not significant.