Risk-stratification of essential thrombocythemia patients for arterial, venous thromboses and for microcirculatory disturbances

Éva Pósfai[1], Imelda Marton[1], Márta Széll,[2] Zsuzsanna László[2] , Zita Borbényi[1]

[1]*2nd Department of Medicine and Cardiology Center, Albert Szent-Györgyi Clinical Center - University of Szeged, Korányi fasor 6., Szeged H-6720, Hungary evaposfay@gmail.com*

[2]*Institute of Medical Genetics, Albert Szent-Györgyi Clinical Center - University of Szeged, Somogyi B. u. 4 Szeged H-6720*

Background: Advanced age (over 60 years) and previous thromboses are well established risk factors for thrombosis in essential thrombocythemia (ET) patients. Recently, the impact of novel risk factors, such as JAK2 V617F; MPL W515L/K mutational status or leukocytosis has been investigated.

Aim: To evaluate the cardiovascular major risk factors (hypertension, cigarette smoking, diabetes mellitus, and hyperlipidemia) JAK2 V617F, MPL W515L mutations impact on the thrombotic events of ET patients.

Methods:

Study participants: One hundred and one patients (29 males; 72 females) with median age: 61 years [range: 14–95 years] diagnosed with essential thrombocythemia between 1999 and 2011 at our Department were enrolled to the study.

Laboratory methods: DNA was isolated from EDTA-stabilized peripheral blood samples, and screened for the JAK2 V617F, MPL W515L mutations with an allele-specific PCR method.

Statistical analysis: Patients were stratified into subgroups according the presence or absence of thrombotic events which were compared by a series of variables such as age, presence of JAK2 V617F and MPL W515L mutations, measured platelet and leukocyte counts at diagnosis, cardiovascular risk factors, and thrombotic events before and after diagnosis. Mann-Whitney tests were performed to explore overall effects of these variables. Multivariate binary logistic regression was also run to estimate the probability of thrombotic events.

Results:

JAK2 V617F-positivity was proven in 61 patients. MPL W515L mutations could be detected in 16 patients. Compared to the data published so far, the incidence of thrombosis was higher in our study group. Fifty-one thrombotic events were recorded in the prior history of ET patients, (before the clinical diagnosis of ET): myocardial infarction events in 16 cases (15.8%), ischemic stroke or transient ischemic attack in 6 cases (5.9%), venous thrombotic events in 11 cases (10.9%), and microcirculatory disturbances in 26 cases (25.7%). During the follow up period, 23 new thrombotic events were recorded: myocardial infarction in 3 cases

(3%), ischemic stroke or transient ischemic attack in 10 cases (9.9%), venous thrombosis in 3 cases (3%) and microcirculatory disturbances in 13 patients (12.9%).

The univariate analysis of the individual cardiovascular risk factors, revealed that the presence of diabetes mellitus (p=0.581), high blood preassure (p=0.119), and cigarette smoking (p=0.293) were not associated with an increased risk of thrombosis. However, hyperlipidaemia (p=0.032) was associated with a significantly increased risk of thrombotic events. Multivariate binary logistic regression analysis confirmed that the probability of recurrent thrombotic events is significantly higher in patients who had prior history of thrombosis (p=0.071), especially in the view of prior myocardial infarction events (p=0.030). Nevertheless, the expected prognostic value of JAK2 V617F, MPL W515L mutations for thrombosis could not be detected in our patients.

Summary/conclusions: Despite the low number of patients, it might be seen that further risk factors also play a role in the development of thrombotic events. Therefore, we purpose that identifying and eliminating modifiable risk factors such as cardiovascular risk factors might be greatly beneficial in the complex management of ET patients.