**Risk of thrombosis and hemorrhage in patients with polycythemia vera and atrial
fibrillation treated with prophylactic oral anticoagulants**

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To the editor

Polycythemia vera (PV) is a chronic myeloproliferative neoplasm characterized by an expansion of red cell mass which leads to an increased risk of thrombotic and hemorrhagic complications (1). It is unknown if patients who suffer simultaneously from PV and atrial fibrillation (AF) present the same thrombotic and hemorrhagic risk as the ones who suffer only from AF.

In order to determine whether there were any differences, we analyzed 186 patients treated with oral anticoagulation. Sixty-two of them suffered simultaneously from PV and AF and the remaining 124 only from AF (control group). The main characteristics of both groups are shown in table 1. Thrombosis was defined according to the International Classification of Diseases. Major hemorrhage was defined as a symptomatic bleeding in a critical organ or an overt hemorrhage requiring transfusion or associated with an Hb decrease > 20 g/L without transfusion. The probability of thrombosis and bleeding was estimated according to the method of Kaplan and Meier with the log-rank test for comparisons. Risk of thrombosis and hemorrhage was estimated with the use of a Cox proportional hazards regression model. The study was approved by the Ethics Committee of the Hospital del Mar and informed consent was obtained.

Median follow-up under oral anticoagulation was 2.9 and 3.7 years for patients with PV plus AF and controls, respectively. A total of 21 thrombosis were registered while patients received oral anticoagulation (table). Rates of thrombosis were 2.75 %/year and 2.39%/year in patients with PV plus AF and controls, respectively. There were no significant differences in the probability of thrombosis among the two study groups (table). Smoking was associated with a higher probability of thrombosis (19% and 6% at 5 years in smokers and non-smokers, respectively, $p<0.001$) whereas male

patients tended to show a higher probability of thrombosis (11% in males versus 6% in females, $p=0.07$). Age, history of thrombosis prior to oral anticoagulation and other risk factors such as hypercholesterolemia, arterial hypertension or diabetes were not associated with a higher probability of thrombosis. **PV patients with leukocytosis or thrombocytosis at diagnosis experienced a similar rate of thrombosis than the remainder.** In multivariate analysis, PV patients with AF did not show a higher risk of thrombosis than controls after correction by age, sex, history of thrombosis and smoking. A total of 17 episodes of major bleeding were registered resulting in a rate of 2.75%/year and 1.75%/year in PV patients and controls, respectively. There were no significant differences in the probability of major bleeding among the study groups (table). Male sex was associated with a higher probability of major hemorrhage. There were no significant differences in the risk of major bleeding among PV patients and controls after adjusting by age, sex and concomitant use of antiplatelet therapy.

There is few data about outcomes in patients with PV receiving oral anticoagulants with no studies reporting on those with AF (2). Rate of thrombosis in clinical trials including general patients with AF receiving vitamin K antagonists ranged from 1.6%/year to 2.4%/year, whereas the corresponding incidence for major bleeding were 3.09-3.36 %/year (3-5). These figures are superimposable to the ones observed in the present study. However, it must be emphasized the small size of our cohort and the possibility of biases due to its retrospective design. With this limitations, the results from the present study suggest that patients who suffer simultaneously from PV and AF have similar thrombotic and hemorrhagic risks than the general population with AF.

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Conflict of Interest disclosure

The authors declare that they have no conflict of interest.

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Table. Main clinical characteristics and outcomes in 187 patients with atrial fibrillation receiving oral anticoagulation			
	PV + AF N = 63	Controls N = 124	p
Age at anticoagulation start, years*	73 (50-91)	77 (55-96)	0.07
Sex (Male/Female)	39/24	68/56	0.4
Vascular risk factors:			
Smoking, n (%)	10 (16%)	40 (32%)	0.02
Arterial hypertension, n (%)	47 (75%)	111 (89.5%)	0.01
Hypercholesterolemia, n (%)	13 (21%)	71 (57%)	<0.001
Diabetes Mellitus, n (%)	11 (17.5%)	41 (33%)	0.03
Thrombosis before anticoagulation, n (%)	21 (33%)	57 (46%)	0.1
Type of oral anticoagulant			0.09
Acenocoumarol, n (%)	62 (100%)	112 (90%)	
Warfarin, n (%)	-	12 (10%)	
Concomitant antiplatelet therapy	19 (30%)	24 (19%)	0.1
No. of thrombotic events, n (%)	6 (9.5%)	15 (12%)	0.8
Stroke/TIA	3 (5)	3 (2)	0.4
Coronary artery disease	1 (2)	8 (6.5)	0.3
Peripheral artery disease	1 (2)	3 (2)	0.9
DVT/PE	2 (3)	1 (1)	0.3
Probability of thrombosis at 5 years	6%	10%	0.7
No. of major hemorrhagic events, n (%)	6 (9%)	11 (9%)	0.9
Probability of major bleeding at 5 years	12%	8%	0.2

*Median (range). PV + AF: patients with polycythemia vera and atrial fibrillation. Controls: general patients with atrial fibrillation. TIA: transient ischemic attack. DVT/PE: deep vein thrombosis/pulmonary embolism.