

**Influence of thrombocytopenia on bleeding and vascular events in atrial fibrillation**

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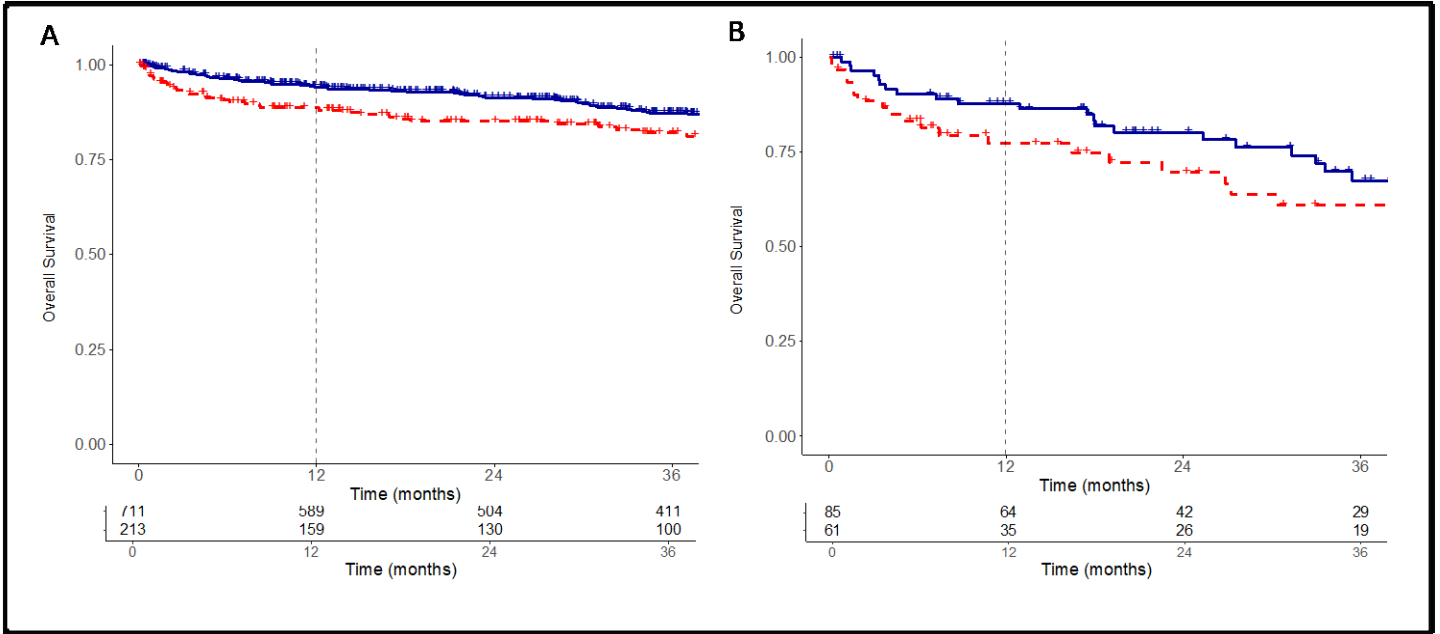
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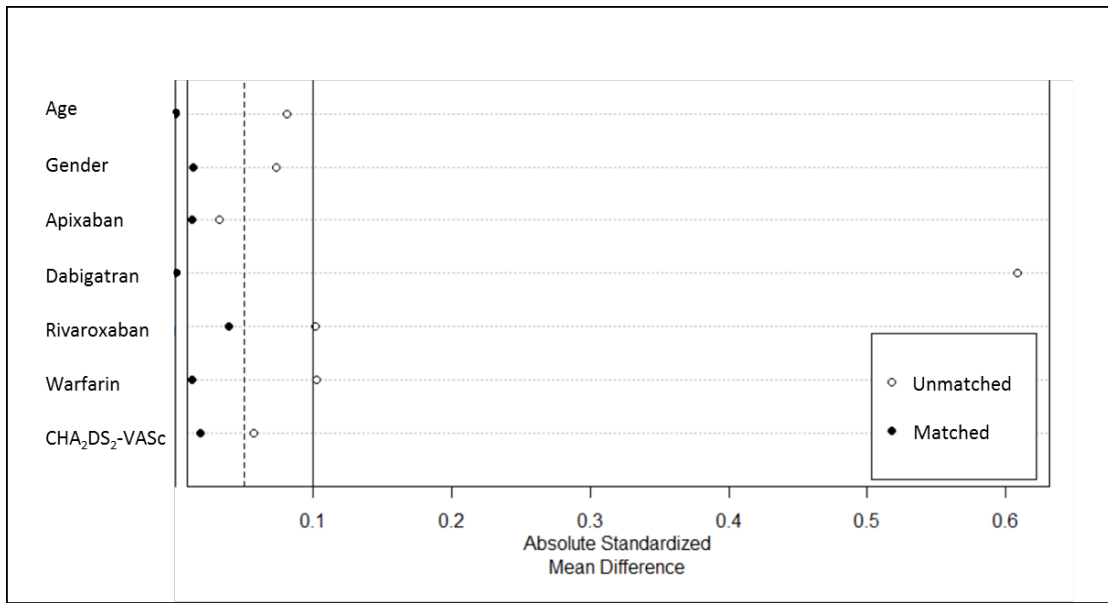
Supplementary Figure 1. All-cause mortality according to cancer status.



All-cause mortality in patients with baseline thrombocytopenia vs. normal platelet counts according to cancer status. (A)

Patients without cancer. (B) Patients with cancer. Thrombocytopenia in red, controls in blue.

Supplementary Figure 2. Assessment of Match.



Absolute standardized mean difference for baseline covariates before and after matching. All covariates have values smaller than 0.05, indicating that the difference in means across cohorts were relatively small after matching.

**Supplementary Table 1: Cancer diagnoses**

	<b>Thrombocytopenia <i>n</i> = 274</b>	<b>Control <i>n</i> = 801</b>
<b>Total cases, <i>n</i></b>	61	85
<b>Cancer type, <i>n</i> (%)</b>		
Brain	0 (0.0)	1 (1.2)
Breast	1 (1.6)	4 (4.7)
Gastrointestinal	10 (16.4)	9 (10.6)
Genitourinary	1 (1.6)	19 (22.4)
Gynecologic	0 (0.0)	6 (7.1)
Head and Neck	2 (3.3)	3 (3.5)
Hematologic	36 (59.0)	23 (27.1)
Lung	5 (8.2)	11 (12.9)
Skin	0 (0.0)	3 (3.5)
Other	6 (9.8)	6 (7.1)

Supplementary Table 2. Univariable analysis, major bleeding

Characteristic	All patients (n=1070)		Platelet count <75,000/ $\mu$ L (n=519)		Platelet count 75,000-100,000/ $\mu$ L (n=551)	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	<b>1.96 (1.10-3.49)</b>	<b>0.02</b>	<b>3.26 (1.15-9.21)</b>	<b>0.03</b>	1.44 (0.71-2.91)	0.31
Sex*	1 (0.64-1.56)	0.99	1.14 (0.59-2.19)	0.69	0.88 (0.48-1.63)	0.69
Hypertension	<b>2.18 (1.38-3.42)</b>	<b>0.0008</b>	1.59 (0.77-3.27)	0.21	<b>2.72 (1.51-4.92)</b>	<b>0.0009</b>
Cancer	0.78 (0.39-1.55)	0.48	0.70 (0.25-1.95)	0.49	0.88 (0.35-2.19)	0.78
Kidney disease	1.68 (0.89-3.18)	0.11	1.75 (0.68-4.48)	0.25	1.6 (0.68-3.78)	0.28
Prior Bleed	1.01 (0.24-4.26)	0.99	1.47 (0.19-11.01)	0.71	0.74 (0.10-5.66)	0.77
Thrombocytopenia	<b>2.48 (1.60-3.84)</b>	<b>&lt;0.0001</b>	<b>2.36 (1.23-4.51)</b>	<b>0.009</b>	<b>2.57 (1.42-4.65)</b>	<b>0.002</b>
Anticoagulant**	1.29 (0.83-2)	0.25	1.22 (0.64-2.32)	0.55	1.34 (0.74-2.44)	0.33
Antiplatelet	1.51 (0.88-2.61)	0.14	2.05 (0.86-4.87)	0.1	1.19 (0.59-2.4)	0.64

P < 0.05, statistically significant

\* Hazard ratios are for the female group as compared with the male group.

\*\* Hazard ratios are for the warfarin group as compared with the direct-acting oral anticoagulant group

CI, Confidence interval

Supplementary Table 3. Univariable analysis, clinically relevant non-major bleeding

Characteristic	All patients (n=1070)		Platelet count <75,000/ $\mu$ L (n=519)		Platelet count 75,000-100,000/ $\mu$ L (n=551)	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	1.2 (0.87-1.66)	0.26	1.52 (0.9-2.56)	0.11	1.02 (0.68-1.54)	0.92
Sex*	0.9 (0.67-1.2)	0.47	0.87 (0.56-1.35)	0.53	0.92 (0.62-1.34)	0.65
<b>Hypertension</b>	1.63 (1.21-2.21)	<b>0.002</b>	1.46 (0.91-2.36)	0.12	<b>1.74 (1.18-2.58)</b>	<b>0.005</b>
Kidney disease	1.44 (0.93-2.22)	0.1	1.7 (0.9-3.24)	0.1	1.24 (0.68-2.23)	0.48
Cancer	0.91 (0.6-1.39)	0.67	0.65 (0.33-1.28)	0.21	1.21 (0.71-2.04)	0.48
Prior Bleed	1.1 (0.42-2.85)	0.85	0.61 (0.08-4.65)	0.63	1.33 (0.44-4)	0.61
<b>Thrombocytopenia</b>	1.53 (1.14-2.05)	<b>0.005</b>	1.48 (0.94-2.31)	0.09	<b>1.56 (1.05-2.32)</b>	<b>0.03</b>
Anticoagulant**	1.14 (0.86-1.5)	0.37	1.23 (0.81-1.87)	0.33	1.06 (0.73-1.53)	0.77
Antiplatelet	1.32 (0.95-1.84)	0.1	1.46 (0.89-2.4)	0.14	1.2 (0.77-1.88)	0.42

P < 0.05, statistically significant

\* Hazard ratios are for the female group as compared with the male group.

\*\* Hazard ratios are for the warfarin group as compared with the direct-acting oral anticoagulant group

CI, Confidence interval

**Supplementary Table 4. Multivariable analysis, clinically relevant non-major bleeding**

Characteristic	All patients (n=1070)		Platelet count <75,000/ $\mu$ L (n=519)		Platelet count 75,000-100,000/ $\mu$ L (n=551)	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	1.19 (0.86-1.65)	0.3	1.66 (0.98-2.8)	0.06	0.95 (0.61-1.46)	0.8
Sex*	0.89 (0.66-1.19)	0.42	0.85 (0.54-1.32)	0.46	0.9 (0.6-1.35)	0.61
Hypertension	1.37 (0.97-1.94)	0.08	1.2 (0.68-2.12)	0.53	1.56 (1-2.45)	0.05
Kidney disease	1.31 (0.85-2.02)	0.23	1.63 (0.83-3.2)	0.16	1.16 (0.65-2.08)	0.62
Cancer	0.86 (0.56-1.32)	0.48	0.54 (0.26-1.11)	0.09	1.23 (0.73-2.09)	0.44
Prior Bleed	1.07 (0.41-2.79)	0.89	0.49 (0.06-3.68)	0.49	1.52 (0.5-4.68)	0.46
Thrombocytopenia	1.32 (0.94-1.85)	0.11	1.53 (0.89-2.65)	0.13	1.27 (0.82-1.95)	0.28
Anticoagulant**	1.11 (0.83-1.47)	0.49	1.26 (0.82-1.94)	0.3	1.05 (0.71-1.55)	0.79
Antiplatelet	1.2 (0.85-1.69)	0.3	1.32 (0.78-2.21)	0.3	1.08 (0.67-1.73)	0.75

P < 0.05, statistically significant

\* Hazard ratios are for the female group as compared with the male group.

\*\* Hazard ratios are for the warfarin group as compared with the direct-acting oral anticoagulant group

CI, Confidence interval

Supplementary Table 5. Univariable analysis, thrombosis

Characteristic	All patients (n=1070)		Platelet count <75,000/ $\mu$ L (n=519)		Platelet count 75,000-100,000/ $\mu$ L (n=551)	
<b>Arterial Thrombosis</b>						
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	1.37 (0.51-3.71)	0.54	1.92 (0.42-8.75)	0.4	0.97 (0.25-3.75)	0.97
Sex*	1.35 (0.59-3.13)	0.48	1.70 (0.55-5.26)	0.35	1.04 (0.29-3.67)	0.95
Diabetes	1.77 (0.6-5.22)	0.3	1.64 (0.36-7.5)	0.52	1.96 (0.43-9.06)	0.39
Heart Failure	1.01 (0.3-3.39)	0.99	1.52 (0.33-6.93)	0.59	0.62 (0.08-4.78)	0.65
Hypertension	1.74 (0.71-4.26)	0.22	3.03 (0.96-9.5)	0.06	0.86 (0.19-3.97)	0.84
Ischemic heart disease	2.02 (0.79-5.13)	0.14	3.15 (0.96-10.37)	0.06	1.19 (0.26-5.54)	0.82
Cancer	1.91 (0.7-5.16)	0.2	1.20 (0.26-5.47)	0.81	3.02 (0.78-11.62)	0.11
Thrombocytopenia	2.08 (0.89-4.88)	0.09	<b>4.38 (1.39-13.78)</b>	<b>0.01</b>	0.73 (0.16-3.45)	0.7
Anticoagulant**	2.29 (0.94-5.61)	0.07	2.24 (0.68-7.36)	0.18	2.38 (0.61-9.2)	0.21
Antiplatelet	2.32 (0.69-7.82)	0.17	1.92 (0.42-8.76)	0.4	3.18 (0.4-25.02)	0.27
<b>Venous Thrombosis</b>						
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	1.31 (0.43-4.02)	0.63	0.67 (0.2-2.29)	0.52	—	—
Sex*	2.33 (0.89-6.11)	0.09	2.99 (0.88-10.14)	0.08	1.57 (0.32-7.72)	0.58
Cancer	1.99 (0.65-6.09)	0.23	2.24 (0.6-8.4)	0.23	1.4 (0.16-12.05)	0.76
Thrombocytopenia	<b>4.31 (1.64-11.33)</b>	<b>0.003</b>	<b>8.29 (2.2-31.27)</b>	<b>0.002</b>	1.48 (0.27-8.05)	0.65
Anticoagulant**	1.21 (0.46-3.13)	0.7	0.94 (0.29-3.09)	0.92	2.04 (0.37-11.14)	0.41
Antiplatelet	0.88 (0.31-2.48)	0.8	1.03 (0.27-3.86)	0.97	0.7 (0.13-3.79)	0.68

P < 0.05, statistically significant

\* Hazard ratios are for the female group as compared with the male group.

\*\* Hazard ratios are for the warfarin group as compared with the direct-acting oral anticoagulant group

CI, Confidence interval



Supplementary Table 6. Multivariable analysis, thrombosis

Characteristic	All patients (n=1070)		Platelet count <75,000/ $\mu$ L (n=519)		Platelet count 75,000-100,000/ $\mu$ L (n=551)	
<b>Arterial Thrombosis</b>						
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	1.27 (0.46-3.5)	0.65	1.97 (0.43-9.08)	0.38	0.85 (0.21-3.37)	0.81
Sex	1.31 (0.57-3.01)	0.52	1.73 (0.59-5.06)	0.32	0.91 (0.25-3.22)	0.88
Diabetes	1.15 (0.39-3.44)	0.8	0.65 (0.15-2.89)	0.57	<b>4.28 (1.25-14.62)</b>	<b>0.02</b>
Heart Failure	0.44 (0.12-1.55)	0.2	0.41 (0.06-2.72)	0.35	0.29 (0.02-3.93)	0.35
Hypertension	0.95 (0.35-2.62)	0.93	1.32 (0.36-4.9)	0.68	<b>0.41 (0.18-0.96)</b>	<b>0.04</b>
Ischemic heart disease	1.90 (0.8-4.55)	0.15	2.46 (0.85-7.1)	0.1	1.95 (0.5-7.61)	0.34
Cancer	2.21 (0.81-6.02)	0.12	0.86 (0.17-4.19)	0.85	<b>4.00 (1.05-15.23)</b>	<b>0.04</b>
Thrombocytopenia	1.79 (0.6-5.37)	0.3	4.23 (0.81-22.04)	0.09	0.61 (0.09-4.29)	0.62
Anticoagulant	<b>2.47 (1.03-5.93)</b>	<b>0.04</b>	2.36 (0.71-7.81)	0.16	2.99 (0.84-10.6)	0.09
Antiplatelet	2.06 (0.6-7.14)	0.25	1.66 (0.31-8.81)	0.55	2.95 (0.34-25.37)	0.32
<b>Venous Thrombosis</b>						
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age > 65	1.18 (0.38-3.63)	0.77	0.57 (0.17-1.91)	0.36	—	—
Sex*	2.28 (0.86-6.07)	0.1	3.29 (0.96-11.26)	0.06	1.54 (0.35-6.83)	0.57
Cancer	1.54 (0.42-5.69)	0.52	1.25 (0.31-5)	0.76	1.71 (0.14-20.32)	0.67
<b>Thrombocytopenia</b>	<b>4.17 (1.60-10.85)</b>	<b>0.003</b>	<b>7.76 (2.06-29.25)</b>	<b>0.002</b>	1.62 (0.3-8.79)	0.58
Anticoagulant**	1.34 (0.46-3.85)	0.59	1.00 (0.29-3.45)	0.99	2.30 (0.38-14.04)	0.37
Antiplatelet	0.84 (0.29-2.45)	0.75	1.32 (0.31-5.56)	0.71	0.59 (0.1-3.47)	0.56

P < 0.05, statistically significant

\* Hazard ratios are for the female group as compared with the male group.

\*\* Hazard ratios are for the warfarin group as compared with the direct-acting oral anticoagulant group

CI, Confidence interval