HIV infection and risk of recurrent venous thromboembolism: a national cohort study

0636

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Background

- A procoagulant state may persist in people living with HIV (PLWH) despite suppressive antiretroviral therapy.
- This results in a clinically relevant elevated risk of a first venous thromboembolism.[1]
- Anticoagulant therapy duration is dependent on venous thromboembolism recurrence risk. This risk is unknown for PLWH.
- We assessed venous thromboembolism recurrence rates in PLWH compared to those in a Dutch general population cohort.

Methods

- People with a first venous thromboembolism, either a deep venous thrombosis or a pulmonary embolism, were identified between 2003 and 2015 in PLWH of the ATHENA HIV cohort. Patients with a first venous thromboembolism between 1999 and 2004 without HIV from the MEGA cohort were controls.[2]
- Provoked venous thromboembolism were those associated with cancer, surgery, oestrogen use, immobilization, or cast use.
- Primary outcome was the incidence rate of recurrent venous thromboembolism. Kaplan Meier estimates accounted for death as competing risk. Cox regression analysis was used to identify predictor variables.

References

[1]Howard JB*, Rokx C*, Smit C *et al*, Lancet HIV 2019.
[2]Timp JF, Lijfering WM, Flinterman LE *et al*. J Thromb Haem 2015.

Results

- Of 18,394 patients, including 14,389 PLWH from ATHENA, we identified patients with a first venous thromboembolism.(*Table 1)*
- Venous thromboembolism recurrence rates were higher in PLWH compared to controls after a first event, regardless of gender and whether the first venous thromboembolism was provoked or not.(*Table 2*)
- This increased risk is mainly observed in the first year after anticoagulation withdrawal.(*Figure 1*)
- Better plasma CD4+ T-cell reconstitution predicted lower recurrence risks.(*Table 3*)

***Table 1**: Baseline characteristics of included patients with a first venous thromboembolism from the ATHENA and MEGA cohorts.*

	People with HIV and a first venous thromboembolism (ATHENA, N=153)	People without HIV and a first venous thromboembolism (MEGA, N=4005)
Gender (male)	126 (82%)	1813 (45%)
Age at first event	48 (42-57)	49 (38-58)
Months of anticoagulation after first event	6 (6-7)	6 (4-7)
Unprovoked first thromboembolism	108 (71%)	1361 (34%)
Years follow up	6 (3-9)	6 (5-9)
Years since HIV diagnosis at first event	5 (1-11)	
On cART at first event	104 (68%)	
Plasma HIV-RNA copies/mL at first event	<50 (<50-767)	
CD4 T-cell count at first event	420 (270-610)	
Data are number (%) or median (IQR)		

***Table 2**: Crude incidence rates of recurrent venous thromboembolism in PLWH with a first venous thromboembolism in ATHENA and people without HIV and a first venous thromboembolism in MEGA.*

	ATHENA N=153	MEGA N=4005
Recurrent venous thromboembolism	40 (26%)	635 (16%)
Incidence rates (per 100 person years follow up)		
Overall	5.2 (3.8-7.0)	3.1 (2.9-3.4)
Male gender	5.6 (4.0-7.8)	4.8 (4.4-5.3)
Female gender	3.6 (1.5-7.5)	1.9 (1.7-2.2)
Unprovoked first event	6.0 (4.2-8.4)	5.2 (4.7-5.8)
Provoked first event	3.1 (1.4-6.1)	2.1 (1.9-2.4)
Data are number (%) or mean (95% confidence intervals)		

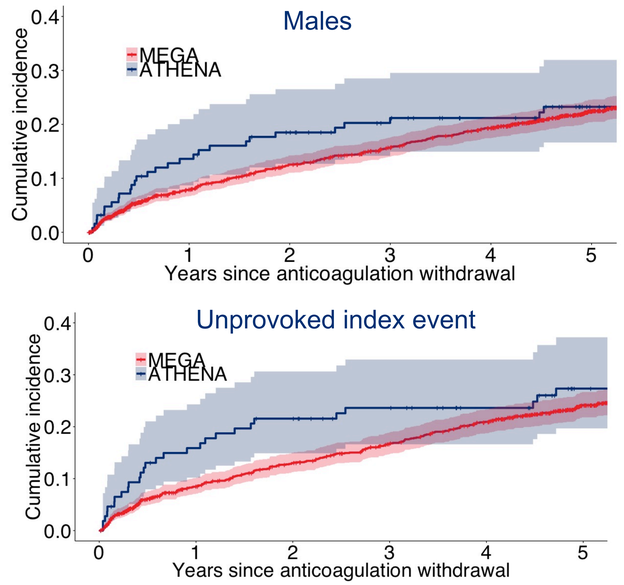

***Figure 1**: Cumulative incidence of recurrent venous thromboembolism in people with and without HIV, in strata describing only male gender and strata showing only patients with unprovoked first venous thromboembolisms. Area around the lines represent the means with 95% confidence intervals.*

***Table 3**: Results of Cox regression analysis examining hazard ratios with 95% confidence intervals, adjusting for age, gender and provoked versus unprovoked first venous thromboembolism*

Adjusted hazard ratios for predictors of recurrent thromboembolisms	ATHENA N=153	MEGA N=4005
Year 1 after anticoagulation withdrawal	1.67 (1.04-2.70)	Ref
Year 6 after anticoagulation withdrawal	1.22 (0.87-1.73)	Ref
CD4 T-cell count recovery (per 100 cells/mm^3 increase between first venous thromboembolism diagnosis and anticoagulant therapy withdrawal)	0.80 (0.68-0.95)	
Data are mean (95% confidence intervals)		

Conclusions

- The risk of recurrent venous thromboembolism seems increased in PLWH, particularly during the first year following anticoagulant therapy withdrawal for a first venous thromboembolism, and in those with reduced CD4-T cell recovery.