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First Cardiovascular Event in Rheumatoid Arthritis: Do Patients With Venous Thromboembolism Have a Different Risk Profile Than Patients With Atherosclerotic Cardiovascular Disease?

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Program: Internal Medicine

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Objective: To assess risk factors favoring VTE over ASCVD in patients with rheumatoid arthritis (RA).

Methods: RA patients participating in FORWARD from 1998 through 2018 were assessed for incident nonfatal/fatal unprovoked VTE (no active cancer, recent surgery, hospitalization, fracture, pregnancy) and ASCVD (myocardial infarction and stroke) validated from hospital/death records. Patients with prior VTE/ASCVD and active cancer were excluded. The risk factors for VTE and ASCVD were determined separately using Cox proportional hazards compared to patients who had no history of VTE and ASCVD.

Results: Of 31,366 RA patients, we identified 539 first unprovoked VTE and 1,648 first ASCVD events during median (IQR) four (1.5-7) years of follow-up. The incidence rates per 10,000 patient-years (95% CI) were 0.34 (0.31-0.37) for VTE and 1.57 (1.51-1.63) for ASCVD. The multivariable models showed that older age, being male, having more comorbidities, prior fractures, disability, moderate/high disease activity and glucocorticoids were associated with both increased VTE and ASCVD risks (Table 1). Traditional CV risk factors, DM and HT increased only ASCVD risk. Obesity had opposite effects on VTE and ASCVD risks: increased VTE risk (HR [95% CI], 1.46 [1.13-1.87]) and decreased ASCVD risk (HR [95% CI], 0.58 [0.50-0.68]) while underweight (HR [95% CI], 1.51 [1.13-2.02]) increased ASCVD risk.

Conclusion: With different risk magnitudes, VTE and ASCVD share common risk factors representing RA disease severity including disability, high disease activity and glucocorticoid use. The main difference in risk factors for these CV events is the traditional CV risk factors; DM and HT increase ASCVD risk and obesity increases VTE risk with a paradoxical effect on ASCVD. ∎

Table 1.
Multivariable associations with VTE and ASCVD in patients with RA*

Variables	aHR (95% CI) for VTE vs. no CVD	aHR (95% CI) for ASCVD vs. no CVD
Age Groups		
<45 years	Reference	Reference
45-64 years	1.58 (1.02-2.43)	3.01 (1.87-4.86)
≥65 years	2.30 (1.43-3.69)	7.85 (4.82-12.80)
Male	1.36 (1.06-1.73)	1.76 (1.53-2.03)
Caucasian	0.94 (0.66-1.34)	1.20 (0.96-1.46)
RA duration, years	1.00 (0.99-1.01)	1.00 (0.99-1.00)
BMI in WHO categories		
Underweight	0.64 (0.26-1.58)	1.51 (1.13-2.02)
Normal weight	Reference	Reference
Overweight	1.03 (0.80-1.33)	0.74 (0.64-0.84)
Obese	1.46 (1.13-1.87)	0.58 (0.50-0.68)
Exercise	1.04 (0.92-1.17)	1.19 (1.00-1.20)
RDCI	1.21 (1.14-1.30)	1.12 (1.07-1.17)
Ever-smoked	0.90 (0.74-1.08)	1.05 (0.94-1.18)
Diabetes	0.97 (0.75-1.25)	1.35 (1.15-1.59)
Hypertension	1.18 (0.8-1.43)	1.20 (1.06-1.35)
Pulmonary disease	0.94 (0.71-1.26)	0.98 (0.81-1.19)
Prior fracture	1.59 (1.37-1.84)	1.17 (1.04-1.33)
Prior cancer	1.12 (0.86-1.45)	1.07 (0.90-1.26)
HAQ disability (0-3)	1.21 (1.03-1.42)	1.28 (1.16-1.42)
Moderate/high disease activity vs. Remission/low disease activity¶	1.29 (1.05-1.57)	1.30 (1.16-1.47)
Medication use		
Glucocorticoids	1.98 (1.64-2.38)	1.36 (1.21-1.52)
MTX	1.02 (0.85-1.22)	0.91 (0.81-1.02)
Hydroxychloroquine	0.80 (0.63-0.99)	0.80 (0.69-0.93)
TNFi	1.08 (0.88-1.33)	1.01 (0.87-1.16)
Other b/tsDMARD	0.86 (0.63-1.17)	1.09 (0.80-1.48)
NSAID	0.76(0.62-1.00)	0.94 (0.89-1.01)
Aspirin	0.80 (0.64-1.01)	1.10 (0.99-1.32)
Statin	1.02 (0.82-1.27)	1.11 (0.96-1.29)
Estrogen	0.93 (0.70-1.25)	0.88 (0.7-1.04)

* The model also included location of residence, insurance type, annual income, and calendar year.
¶ Disease activity assessed by PAS (evaluated in a separate model without individual components of PAS)