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Transmission of rheumatoid arthritis through blood transfusion: a retrospective cohort study

The long preclinical phase of rheumatoid arthritis (RA), where some factors involved in RA pathogenesis circulate peripherally, raises concern of RA transmissibility through blood transfusion.[1] Specifically, this possibility is suggested by murine RA models in which anticitrullinated peptide/protein antibodies may induce and enhance arthritis, and precursors of the RA-fibroblast-like synoviocyte cells may aggravate and spread the disease between joints.[2 3]

We used a large Danish–Swedish population-based research donations and transfusions database (SCANDAT2) with health register information on 1.5 million blood donors and 2.1 million recipients of their blood to investigate (1) RA occurrence in recipients of blood from donors who later developed RA and (2) clustering of RA among recipients of blood from individual donors, regardless of the donor's RA status.[4–6]

We used two different approaches to analyse RA transmission. First, we identified all donors who developed RA after blood donation. For each of these index donors, we identified up to 10 donors matched on age, sex, county, date of first donation, number of donations and ABO blood group, who were free of RA at the date of index donor diagnosis. We then identified all recipients of blood from the two donor populations and followed them from date of transfusion originating in said donors until date of RA diagnosis, death, emigration or end of 2012 (Sweden)/2013 (Denmark), whichever came first.

In the second approach, we investigated if RA clustered among recipients of blood from individual donors. Here, we used a modified time-dependent donor riskiness score by simply counting the RA occurrences among past recipients of each donor.

In both approaches, we only followed up recipients whose first registered transfusions occurred after 1996 and 1998 in Sweden and Denmark, respectively. We used Cox regression with age as underlying time scale, with an exposure lag of 1 year and strata defined by sex and hospital. All analyses were adjusted for calendar period and number of transfusions as restricted cubic splines with five equally spaced knots and ABO blood group. Persons with RA were identified using contemporary national International Classification of Diseases (ICD) 7, 8, 9 and 10 classifications. To reduce misclassification, we defined RA as having two registrations of RA within the course of a 2-year period. RA diagnoses were further subclassified as seropositive RA or seronegative RA.

Among a total of 938 942 blood donors, 2412 were diagnosed with RA during follow-up. We identified 13 369 patients (exposed) who received at least one unit from donors with later RA and 139 470 patients (unexposed) who received blood units from the matched donors who were free of RA at selection.

Recipient RA risk did not vary by donor RA occurrence, whether overall, by RA serotype, donor age at RA diagnosis or interval between donation and donor RA diagnosis (table 1).

Similarly, recipient RA risk did not also vary by RA occurrence in previous recipients of blood from the same donor, neither for all types of RA combined (HR per previous recipient with RA, 0.96; 95% CI 0.86 to 1.07) nor for specific RA subtypes.

The association between RA and blood transfusions has previously been explored only in two investigations, which based on self-reported transfusion history arrived at opposite conclusions.[7 8]

Table 1 Number of cases of rheumatoid arthritis (RA) overall and of seropositive RA and seronegative RA, respectively, observed among recipients whose blood donors were (exposed recipients) and were not (unexposed recipients) correspondingly diagnosed, with person-years of observation and HRs with 95% CIs for RA overall and in different strata

	Recipient outcome				
	Exposed		Unexposed		
Recipient exposed to:	Events	Person-years	Events	Person-years	HR (95% CI)
Overall RA					
Donor diagnosed with RA	63	82 551	610	756 275	1.04 (0.80 to 1.35)
Shortest latency of donor RA*					
<10 years	46	59 890	610	756 275	0.99 (0.56 to 1.72)
10+ years	17	22 661	610	756 275	1.05 (0.64 to 1.70)
Lowest age at donor RA diagnosis					
<65 years	51	69 827	610	756 275	0.80 (0.43 to 1.51)
65+ years	12	12 724	610	756 275	1.24 (0.70 to 2.20)
Seropositive RA					
Donor with seropositive RA	4	17 030	27	186 775	1.68 (0.58 to 4.84)
Seronegative RA					
Donor with seronegative RA	9	39 829	129	402 138	0.72 (0.37 to 1.43)

*Interval between donation and donor RA diagnosis.

In contrast, we exclusively analysed patients who underwent transfusion and focused on the link between donor-specific factors (eg, donor RA diagnosis) and recipient RA risk.

In conclusion, we found no evidence that RA or RA risk is transmitted through blood transfusion. In light of the study's strengths, including low likelihood of confounding and large study size ensuring meaningful statistical power, we believe the possibility of RA transmission is unlikely to be clinically relevant.

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