

Prognosis Factors for Cardiovascular Events in Patients with Rheumatoid Arthritis: Multivariate Analysis Is Indispensable

To the Editor:

I read with interest the report by Ajeganova, *et al*¹ from a longterm followup study of 105 patients with rheumatoid arthritis (RA). As well as the baseline data, RA disease measures and biomarkers of cardiovascular disease (CVD) were assessed during the followup period within 5 years. Patients experienced 17 CVD events, which included 1 acute myocardial infarction, 3 angina pectoris, 8 congestive heart failure, and 5 ischemic cerebrovascular events during followup over 15 years. Although the authors could describe some risk and protective factors for CVD events by using mainly Cox regression analysis, adjustment for age was the only possibility for their multivariate analysis. They mentioned the limited number of patients for the analysis in the discussion, and I agree that their choice of selecting a limited number of variables for adjustment was correct.

Peduzzi, *et al*^{2,3} used Monte Carlo simulation techniques to evaluate the effect of events per independent variable (EPV) in proportional hazards regression analysis. They concluded that an EPV value < 10 results in some problems in protecting the validity of the statistical model. There is another opinion, that EPV value < 10 is also acceptable in some situations in logistic regression analysis⁴, but there is no gold standard for simulation models to check the validity of the statistical outcome.

On this point, the results presented by Ajeganova, *et al*¹ require more statistical considerations for their conclusion. They adjusted only for age to determine the predictive ability of each risk factor for CVD events using Cox proportional hazard regression models, because the number of events was only 17. From the theory presented by Peduzzi, *et al*^{2,3}, adjustment for age also presents some statistical problems. If they use 9 independent variables simultaneously for multivariate analysis, the number of events needed for Cox modeling should be at least 90. Further, many more events are needed for subanalysis when stratifying the CVD events.

They selected univariate and age-adjusted Cox regression analyses, and I appreciate their decision on statistical procedures. But multivariate analysis is indispensable for patients with RA to predict CVD events. I recommend a followup study with a much larger sample size for CVD risk assessment by keeping EPV values that are satisfactory for statistical validity.

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J Rheumatol 2013;40:3; doi:10.3899/jrheum.121364