Featured Correspondence

Ischaemic heart disease in men

To the Editor: A recent study in *Heart* by Edwards and colleagues found an interesting association between rheumatoid factor (RF) and ischaemic heart disease.¹ In a forthcoming study we examined independently the related subject of the role of systemic inflammation in relation to clinical outcome.² This subsequent study reports an association between systemic inflammation, as measured by C reactive protein (CRP), and all-cause mortality (n = 22 982). We also found a weak association with heart disease, but the study was, we believe, statistically underpowered to evaluate this outcome properly. In light of the findings reported by Edwards and colleagues, here we report supplementary data from a subgroup of subjects from the CRP² study, where data were available characterising RF (n = 3588). The objective of this report was to characterise survival over a 4-year period from the first CRP observation in this subgroup of subjects where RF data were also available.

Details of the data source and the general methods have been published elsewhere.² In brief, routine data were obtained from hospital, record-linked sources in Cardiff and the Vale of Glamorgan. A Cox proportional hazards model (CPHM) was developed using SPSS for Windows v14. We evaluated a number of potential model covariates, including age, sex, prior disease (cancer, diabetes, vascular disease), general morbidity at baseline (total days in hospital in the year before the first CRP observation) and CRP itself. RF was measured in IU/ml and included in the model as a

continuous variable after logarithmic transformation.

The mean age of the 3588 evaluable subjects was 62 years and 33% were female. The CPHM of survival determined a strong association between RF and survival (hazard ratio for log RF = 1.229; p = 0.008). Furthermore, CRP (log transformed) was also included simultaneously in this statistical model (hazard ratio = 1.495; p < 0.001) in preference to other factors such as a history of diabetes and cancer. As expected, age and being male also increased risk of death in the CPHM. Figure 1 illustrates the association between RF and all-cause mortality.

Data from our study support the findings from the study by Edwards and colleagues, and show that RF not only predicts the likelihood of ischaemic heart disease but it also predicts the likelihood of all-cause mortality. Furthermore, data from this subgroup of subjects showed that CRP and RF were independent risk factors for all-cause mortality. Thus, they are likely to represent distinct inflammatory processes that increase the risk of adverse outcome.

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- 1 Edwards CJ, Syddall H, Goswami R, *et al*. The autoantibody rheumatoid factor may be an independent risk factor for ischaemic heart disease in men. *Heart* 2007;93:1263-7.
- 2 Poole CD, Conway P, Currie CJ. An evaluation of the association between the first observation and the longitudinal change in C-reactive protein, and all-cause mortality. *Heart* (in press).

To the Editor: I read with interest the original article by Edwards *et al* about the possibility of rheumatoid factor (RF) being an independent risk factor for ischaemic heart disease.¹ The contribution of inflammation to the initiation and progression of coronary atherosclerosis is well established. I agree this study adds support to the importance of inflammation in atherosclerosis. The concept of autoimmunity and the direct role of RF in the pathogenesis of the atherosclerotic disease process are fascinating and will act as a basis for future research.

The key unanswered question is whether RF is a marker of inflammation or an independent risk factor for ischaemic heart disease. As acknowledged by the authors, it may be difficult to draw a firm conclusion from this cross-sectional study. It might have been useful if the authors had correlated RF with well-established markers of inflammation such as C reactive protein.² Screening patients using RF is probably not justified at present until further research is carried out.

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References

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- 2 Blake GJ, Ridker PM. Novel clinical markers of vascular wall inflammation *Circ Res* 2001;89:763-71.

The author's reply: We read with interest the comments from Dr Currie and colleagues.

It is encouraging that their group has demonstrated that rheumatoid factor (RF) is an independent risk factor for mortality in a large cohort of patients from South Wales, supporting the importance of RF as a biomarker for poor prognosis in a number of clinical situations. Our work has shown a strong association between the presence of RF and ischaemic heart disease in men from a general population.¹ Previous groups have demonstrated an increased cardiovascular mortality associated with RF in the general population and among people with rheumatoid arthritis.²⁻³

We were also fascinated to see that the risk of all-cause mortality associated with the

Figure 1 Four-year risk of death as a function of increasing rheumatoid factor after standardisation for age, sex and C reactive protein level.