

EXTENDED REPORTS

Does social disadvantage contribute to the excess mortality in rheumatoid arthritis patients?

N Maiden, H A Capell, R Madhok, R Hampson, E A Thomson

Abstract

Background—Socioeconomic deprivation is associated with increased mortality from cardiovascular causes and malignancy. The influence of disadvantage in patients with rheumatoid arthritis (RA), who are known to have premature mortality, has not been ascertained.

Aim—To assess the relation between the level of patient deprivation and mortality in RA patients.

Methods—200 RA patients, enrolled in a study comparing sulfasalazine and penicillamine in 1984-85, have been followed up prospectively for 12 years. Subjects were categorised into Carstairs groups with deprivation scores ranging from 1 (most affluent) to 7 (most deprived). Information about deaths was obtained from the Registrar General in Scotland, death certificates and GP/hospital records.

Results—There were more RA patients in the deprived areas than expected compared with the West of Scotland and England and Wales. Some 47.5% of the RA patients had died by 12 years—the majority of cardiorespiratory causes or malignancy. There were no differences in the median age or disease duration in the various Carstairs groups at study entry, but the percentage of deaths was higher in the more deprived groups after 12 years (36% dead in most affluent area compared with 61% in the most deprived, that is, in groups 6 and 7).

Conclusion—In patients with RA increasing deprivation was associated with premature mortality. If confirmed elsewhere these findings have implications for rheumatological management strategies, for researchers involved in collaborative studies of patients from different socioeconomic backgrounds and for resource allocation.

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A number of studies have documented a reduction in life expectancy in patients with rheumatoid arthritis (RA).¹⁻⁴ The only exception has been a population based survey from the Mayo Clinic.⁵ It is well recognised that

patients who are treated in hospital based clinics have more severe disease and Pincus *et al* have shown a clear correlation between the number of joints involved and excess mortality in RA.⁶ Survival has also been linked to functional status.⁷ Other studies have found that markers of disease severity such as seropositivity³ and high erythrocyte sedimentation rate (ESR)⁴ predict mortality. While the excess morbidity associated with a chronic disabling condition such as RA is widely recognised, this increased mortality is not always appreciated. In some instances death can be attributed to fatal side effects from non-steroidal anti-inflammatory drugs (NSAIDs) and from glucocorticoids^{8,9} and there is an excess of deaths from infection, haematological malignancies, and renal disease, in particular amyloid. However, most patients with RA die of the cardiovascular and respiratory causes that are common in the rest of the population.⁹⁻¹² The timing of deaths may differ—Cosh studied a series of 100 patients at 10, 15 and 20 years¹⁴⁻¹⁶ and suggested that the patients whose deaths were attributable to RA or systemic complications died even more prematurely than those in whom death was unrelated to RA.

It has been noted that most chronic diseases are reported more frequently in people with fewer years of formal education¹⁷ and that differences in severity of RA are present in the early stages or develop early in patients with different levels of education.^{18,19} As most Western countries now have a statutory requirement for formal education other measures of social deprivation need to be used when assessing outcome in RA.

In the general population there is much evidence about the effect of deprivation on health and in particular the relation between social deprivation and morbidity and mortality is well established.^{20,21} The association holds not only for deaths from ischaemic heart disease and smoking related diseases but also for deaths from malignant neoplasms and all causes.²² There is some evidence that lifetime socioeconomic position is of importance²³ and that the poor cost more in terms of hospital resources.²⁴

In international terms Scotland has been shown to be one of the least healthy countries in the Western world and within the West of Scotland there is significant diversity in health

Centre for Rheumatic Diseases, Royal Infirmary, Castle Street, Glasgow G4 0SF

Correspondence to: Dr H A Capell.

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Table 1 Clinical characteristics of RA patients at study entry: medians (and ranges) are shown

	RA patients
Disease duration (y)	7 (1–30)
Duration of early morning stiffness (min)	120 (0–720)
Functional score (HAQ)	2.3 (0.38–3.0)
Haemoglobin (g/dl)	11.6 (7.7–17.3)
CRP (mg/l)	39 (4–255)
ESR (mm 1st h)	64 (2–150)

status.^{25, 26} The documentation of this diversity in social status has relied on the Carstairs index that is derived from the postcode and classifies persons from the most affluent, group 1 to deprived group 7. Of particular concern is the widening gap between the death rates of the rich and the poor in the United Kingdom²⁷ and the inadequate resources to meet the cost of social disadvantage.²⁸

In this study we set out to evaluate social disadvantage in a cohort of RA patients. Our hypothesis was that in part the higher rates of mortality in RA patients could be related to social disadvantage. The specific objectives were to divide the cohort of RA patients into groups according to their level of deprivation and assess the mortality rates and median ages at death of these groups.

Methods

RA PATIENTS

The cohort of RA patients used in this study were recruited for a clinical trial in the 1980s and long term follow up data are now available. Specifically 200 patients fulfilling the ARA criteria for RA were enrolled in a prospective study comparing sulfasalazine and penicillamine in 1984–85 and have been followed up for 12 years. All were uncontrolled taking symptom relieving NSAIDs, were considered in need of a “second line” disease modifying anti-rheumatic drug (DMARD) agent, and consented to enter into the study. Patients were supervised 3–6 monthly at a specialist rheumatology clinic with general practitioner assistance with monitoring of toxicity. Patients continued to take NSAIDs as required. At the time of entry to the study no patient was receiving systemic corticosteroids and none had received this therapy or an alternative second line or cytotoxic agent in the three months before the study. Patients who were considered unlikely to cooperate with treatment were excluded as were those with a history of allergy to sulphonamides. However, in an attempt to conduct a “true to life” study patients with co-morbidity were not excluded unless the nature of their additional problem compromised safe monitoring of treatment.

All these patients were attending one of two specialised rheumatology units and were drawn from the population in the West of Scotland. The functional ability of RA patients was measured using a modified version of the Stanford Health Assessment Questionnaire (HAQ).²⁹ The intention to treat analysis of the outcome of DMARD treatment has been reported elsewhere.³⁰

Table 2 Causes of death

	RA patients	
	Number	%
Circulatory	40	42
Respiratory	14	15
Neoplasm	20*	21
Gastrointestinal	5	5
Renal/genitourinary	4	4
Sepsis	1	1.1
Musculoskeletal	5	5
Postop/drug injury/poisoning	2†	2
Other	4	4

*Details of neoplastic deaths (7 lung, 4 gastrointestinal, 3 genitourinary, 4 lymphoid/haematopoietic, 2 unknown primary).
†One methotrexate related death. Five of 15 (33%) of gastrointestinal/renal/sepsis, musculoskeletal RA deaths were taking systemic corticosteroids.

MORTALITY DATA

Notification was obtained from the General Register Office at Edinburgh with copies of death certificates in many instances. Additional information on mortality was obtained from the death certificate or hospital and/or general practitioner records. Causes of death were classified using the International Classification of Diseases 9th edition. Infection was coded according to the organ system in which it occurred (chapter 1 of ICD 9).

DEPRIVATION SCORE

Subjects were categorised into groups with deprivation scores ranging from 1 (most affluent) to 7 (most deprived). The deprivation score allocated to a patient was derived from the postcode area in which the patient lived according to Carstairs and Morris.³¹ Briefly, the Carstairs score for a postcode area depends on the level of male unemployment, overcrowding and car ownership within the area and the distribution of social class within the area's population. The West of Scotland has higher levels of deprivation and higher mortality rates than Scotland as a whole. The use of the Carstairs score as a deprivation score for our study subjects has certain limitations in that it is possible for a person living in a deprived area to be relatively affluent. However, others have shown that the excess mortality associated with residence in areas designated as deprived by census based indicators (similar to the Carstairs score) is wholly explained by the concentration in those areas of people with adverse personal or household socioeconomic factors.³²

STATISTICS

Demographic and clinical characteristics are presented as medians (and range) and were compared using Kruskal-Wallis. The predictive value of each variable (including age, sex, disease duration, baseline HAQ score, haemoglobin, ESR and Carstairs score) in relation to

Table 3 Median age (and range) in years of study patients by Carstairs group at enrolment and median disease duration of RA patients

	1 and 2	3–5	6 and 7
Number (%)	22 (12)	117 (62)	49 (26)
Age (y)	56 (33–78)	57 (22–77)	58 (25–80)
Disease duration (y)	8 (1–30)	7.5 (1–30)	5 (1–30)

Table 4 Number (%) deaths of the study patients and median age (and range) at death of RA patients according to Carstairs group

	1 and 2	3-5	6 and 7	Total
Number (%) of deaths	8 (36)	57 (49)	30 (61)	95
Age at death (y)	76 (70-84)	68 (48-86)	65 (54-88)	69 (48-88)

Totals exclude those with missing deprivation category.

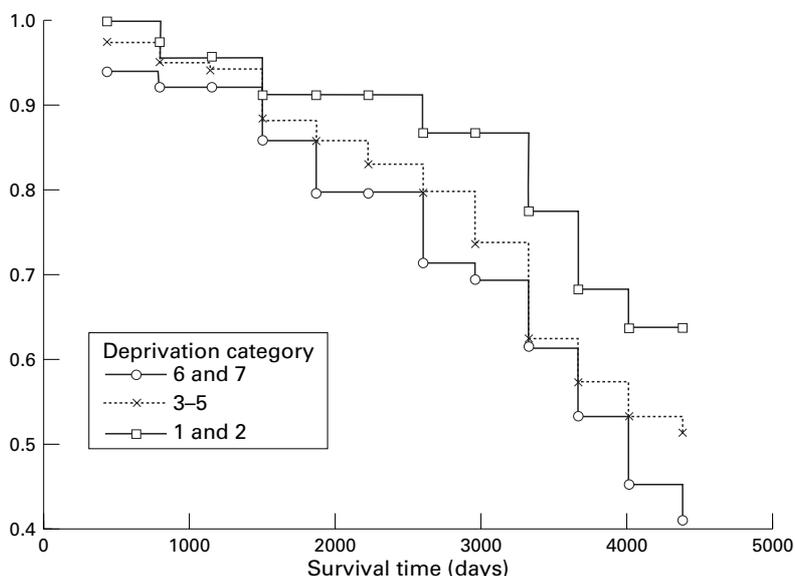


Figure 1 Twelve year survival curves by deprivation category.

time to death was examined with univariate cox proportional hazards model. Variables that were significant at the 0.05 level were studied in a multivariate stepwise cox regression that quantified the predictive value of each variable in the model when all variables are considered together.

Results

The median age of the study group was 57 years (range 22-80) 78% of the group were female. Table 1 shows the clinical characteristics of the RA patients at study entry. Overall 95 patients (47.5%) of the study group had died by 12 years of follow up. Table 2 shows the summary causes of death. Most RA patients died of cardiorespiratory causes and malignancy. There was one drug related death (methotrexate) in this cohort in a 66 year old female who despite close monitoring developed sudden pancytopenia after 18 months of methotrexate (low dose 7.5 mg/weekly). She died in the intensive care unit of pulmonary haemorrhage and infection.

Table 5 Relative rates (with 95% confidence intervals) of all cause mortality by deprivation category adjusted for age and sex

	1 and 2	3-5	6 and 7
RA patients	1	1.54 (0.73, 3.26)	1.66 (0.74, 3.69)

Table 6 Unadjusted mortality rate for each deprivation category per person years of follow up

Carstairs	1 and 2	3-5	6 and 7
Patients (n)	22	117	49
Number of person years of follow up	222	1105	446
Deaths (n)	8	57	30
Mortality rate per 1000 person years of follow up	36.0	51.6	67.2

There were more patients in the most deprived Carstairs categories in this RA cohort (6 and 7=26%) than in the general population in Scotland (6 and 7=18%) or in England and Wales (6 and 7 =5%). There were also fewer patients living in affluent areas (Carstairs 1 and 2 = 12%) compared with 18% for West of Scotland, 20% for Scotland overall and 52% for England and Wales. Table 3 shows that the age and disease duration distribution in the various Carstairs groupings at study entry were similar, as would be expected given universal access to health care in the United Kingdom. Table 4 displays the age at death and distribution of deaths by initial Carstairs score: it can be seen that the median age at death was lower and the percentage of deaths was higher in Carstairs 6 and 7. Figure 1 shows survival by deprivation category, which illustrates that category 1 and 2 (the most affluent) have better survival than those in the other Carstairs areas. Table 5 shows the relative rates of all cause mortality by deprivation category adjusted for age and sex (patients in Carstairs groups 6 and 7 (the most deprived) have 1.66 times the mortality experience of Carstairs groups 1 and 2). Median age at death for men was 63 years (range 48-76) and for women 69 years (range 53-85). Data on smoking patterns (not shown) demonstrated that smoking is more prevalent among people from the more deprived areas.

There was a variation in HAQ score (function) by Carstairs groupings at the outset: those in the most affluent areas 1 and 2 had a HAQ score of 2.25, the same as those in 3, 4 and 5, while those in the most deprived areas 6 and 7 had a HAQ score of 2.5. Kruskal-Wallis indicated a significant difference between 6 and 7 and the other groupings (p=0.04).

Some 47.5% of the RA patients in the study had died by 12 years. Sixty one per cent of the most deprived patients (Carstairs 6 and 7) had died compared with only 36% in Carstairs 1 and 2. Overall in "intention to treat" groups, 50 of 98 penicillamine (51%) and 45 of 102 (44%) of the sulfasalazine group were dead by 12 years. Table 6 shows the mortality rate per person years of follow up by deprivation category.

Cox proportional hazards regression identified age and HAQ functional score as significant predictors of mortality for the RA patients. However, entering both age and HAQ together into the model caused HAQ to lose its significance.

Discussion

This study shows that in patients with RA increasing deprivation is associated with higher mortality. Study patients were assigned to deprivation categories based on an ecological index relating to the postcode area of residence. This may have led to misclassification of economically deprived patients living in affluent areas and so to an underestimation of the association between deprivation and mortality (although it is also possible for misclassification to have had the opposite effect). This RA cohort included many patients with severe disease as indicated by the high median HAQ score at outset and

the demonstration of high mortality cannot necessarily be extrapolated to patients with milder disease. Nevertheless, RA of this severity is associated with considerable morbidity and mortality, as might be expected. Patients who are socially disadvantaged in the West of Scotland are more likely to have poorer functional scores³³ and are also more likely to die prematurely. Others have shown that the discrepancy in HAQ scores are present at the outset of RA and are therefore unlikely to reflect the disadvantage that comes with a chronic disease.³⁴ While it is possible that this aspect is contributory it is clear that RA is associated with more functional impairment and greater mortality among the patients in the most disadvantaged areas. Progressive disability may worsen cardiovascular risk factors such as lack of exercise, poor diet, obesity and smoking. There has been some speculation that RA is becoming less severe³⁵ but change in disease characteristics may reflect improved resources leading to fewer patients with severe disease attending any one centre rather than a true improvement in the disease.³⁶ It is also possible that some lifestyle changes have had a beneficial effect but these remain complex and difficult to unravel.

Leigh and Fries have suggested that corticosteroid use is associated with an increased likelihood of dying prematurely,³⁷ 5 of 15 (33%) of those who died from sepsis, renal disease or gastrointestinal disease had been taking systemic corticosteroids while overall corticosteroid use in our cohort was low (8%) among survivors at 12 years.

A cross sectional analysis of mortality by country of birth has shown that mortality from all causes is higher in Scottish immigrants³⁸ and smoking has recently been shown as a risk for development of RA in men.³⁹ In this study fewer RA patients were affluent (Carstairs 1 and 2) relative to the population of the West of Scotland. The proportion of affluent patients is much smaller in Scotland compared with England and Wales.

The significant predictors of mortality in RA found in this investigation were consistent with other studies.⁴⁻⁷ A new finding, however, is the association between mortality and Carstairs score indicating that deprivation in patients with RA is associated with increased mortality rates. It remains to be shown how universal these findings are. It seems probable that there will be parallels in most Western countries. Any planned prospective study would need to be conducted in an area where there is a full spectrum of social advantage and disadvantage. This observation is particularly relevant in the context of increasing relative deprivation in Great Britain and is especially ironic given the universal free access to education and health services over the past 50 years.

What is it that leads to the association between deprivation and health in RA? The broader issue has been explored eloquently by Sir Douglas Black in his paper on deprivation and health.⁴⁰ Explanation of the association between deprivation and mortality in the general population is thought to lie in variation

in health related behaviour and lifestyle (smoking, diet, alcohol intake, efficiency in using disease prevention strategies) as well as social structure and material living conditions (education, income, housing, pollution).⁴¹ The adverse effect of deprivation on mortality may be exacerbated in patients with chronic diseases relative to the general population. A chronic illness such as RA that leads to progressive disability and reduced mobility may worsen the burden of psychosocial stress and increase the frequency of cardiovascular risk factors such as obesity, lack of exercise, poor diet and smoking all of which are already more prevalent among the deprived. It seems probable, although studies are awaited, that deprivation will lead to premature mortality among patients with most chronic, disabling diseases.

These findings have implications for rheumatologists and other chronic disease specialists, who because of the long term nature of their patient-physician relationships, are in a position to give sustained advice on health related behaviour as well as in identifying and treating medical risk factors such as hypertension, smoking, obesity and hyperlipidaemia, osteoporosis, gastrointestinal disease and dietary deficiencies. Graded exercise programmes may be difficult to achieve in patients with RA but a multidisciplinary approach should be attempted. Tackling these aspects along with a concentrated effort to change diet and social habits might have a bigger impact on the outcome of RA than combination DMARD treatments or minor refinements in available treatments—an area considered by Callaghan and Pincus.⁴² Whether this goal is achievable remains to be shown, but the complexity of managing RA will certainly escalate as these issues are investigated.

In conclusion, these findings, if confirmed elsewhere, have implications for the interpretation of cooperative studies that bridge areas of affluence and deprivation—the outcome might well be very different in discrepant areas and assumptions about severity of disease and functional impairment will require close scrutiny. Finally, there are considerable implications for resource allocation for RA patients, and training programmes for rheumatologists.

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