

EXTENDED REPORT

Early functional disability predicts both all-cause and cardiovascular mortality in people with inflammatory polyarthritis: results from the Norfolk Arthritis Register

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Ann Rheum Dis 2007;66:486–492. doi: 10.1136/ard.2006.056390

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Accepted 30 October 2006
Published Online First
7 November 2006

Objective: To investigate the predictive value of early functional disability in patients with inflammatory polyarthritis (IP), for all-cause and cardiovascular disease (CVD) mortality.

Methods: 1010 subjects with new-onset IP from the Norfolk Arthritis Register were studied. All were seen at baseline and at 1 year. Health Assessment Questionnaire (HAQ) scores were obtained at both time points. Vital status at 10 years from registration was established through central records. Mortality (all-cause and CVD) per 1000 person-years were calculated by HAQ stratum (HAQ scores <1, 1–2 and ≥2). The predictive value of HAQ (per unit increase) at the two time points, adjusted for age at onset of symptom, sex and other factors found to predict mortality, was assessed using Cox regression models. The analysis was repeated for those who satisfied the 1987 American College of Rheumatology criteria for rheumatoid arthritis (RA) by 5 years.

Results: By 10 years, 171 (16.9%) subjects had died. 89 deaths (52%) were attributed to CVD. Mortality was greatest in the highest HAQ group at both time points. Following adjustment for other predictors, HAQ score at year 1 remained a significant predictor of all-cause mortality (HR 1.46; 95% CI 1.15 to 1.85) and CVD mortality (HR 1.49; 95% CI 1.12 to 1.97). The predictive value of HAQ at year 1 was similar in the RA subgroup.

Conclusions: Our data show that at 1 year of follow-up, HAQ score is an important independent predictor of subsequent all-cause and CVD mortalities in people with IP and RA. Baseline HAQ scores are of less value.

Rheumatoid arthritis (RA) is a chronic progressive disease associated with premature mortality.^{1–3} Early deaths are more strongly associated with cumulative disease severity rather than representing a complication of treatment.^{3, 4}

Functional disability, measured using the Health Assessment Questionnaire (HAQ), has been found to predict premature mortality in RA.^{4–7} It is well recognised that the HAQ score falls during the first year or so after onset of symptoms.^{8, 9} However, it is not clear whether the initial impact of the disease, represented by baseline HAQ, or the lower HAQ score achieved after treatment has begun, is the stronger predictor of mortality.

The majority of excess deaths in RA are attributable to cardiovascular disease (CVD).^{10–13} Most of the work investigating possible explanations for the increased CVD mortality have concentrated on inflammatory markers and traditional risk factors.^{10–14–18} The role of early functional disability as an independent predictor of mortality due to CVD has not been pursued.

Using a primary care-based incidence register of patients with early inflammatory polyarthritis (IP), the main aim of our study was to investigate the predictive value of early functional disability, both at presentation and at 1 year, in relation to mortality. We particularly focused on CVD mortality, to determine whether functional disability early in the disease is a useful independent marker of increased cardiac risk.

METHODS

Subjects

The Norfolk Arthritis Register (NOAR) is a primary care-based inception cohort of patients with recent-onset IP. Further details of this register are described elsewhere.¹⁹ In brief, it covers the former Norwich Health Authority with notification

of cases through general practitioners or attendance at hospitals within the catchment area. The notification criteria are adults aged ≥16 years at onset of symptom, who had swelling of at least two joints that had persisted for at least 4 weeks and who had onset of symptom after 1 January 1990. Subjects who were subsequently diagnosed by a hospital consultant as having a diagnosis other than RA, IP, psoriatic arthritis or postviral arthritis which accounted for their joint symptoms, were excluded. Between 1990 and 1994, 1098 patients satisfied the above criteria and were referred to NOAR.

Data collection

Clinical and demographic data were collected by a research nurse using a structured interview and clinical examination shortly after registration (baseline). A further assessment was carried out annually until the 5th year, then at the 7th and 10th years. At each assessment, standardised clinical data were collected.

Demographic data included the age at onset of symptom, gender and time from symptom onset to presentation to NOAR. Clinical data included the number of swollen and tender joints derived from the clinical examination. A blood sample was taken for rheumatoid factor (RF) and C reactive protein (CRP) testing. RF was measured using a latex agglutination technique, where, for this analysis, a titre of ≥1:80 was classified as RF-positive. CRP concentration (in mg/l) was measured using an endpoint immunoturbidimetric agglutination method.

Abbreviations: ACR, American College of Rheumatology; CRP, C reactive protein; CVD, cardiovascular disease; DAS28, Disease Activity score 28; DMARD, disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; ICD, International Classification of Disease; IP, inflammatory polyarthritis; MTX, methotrexate; NOAR, Norfolk Arthritis Register; pyr, person-years; RA, rheumatoid arthritis; RF, rheumatoid factor

Table 1 Study population characteristics

Subjects characteristic	Entire IP cohort (n = 1098)	HAQ scores at baseline and year 1 (followed-up to first year) (n = 1010)	RA subgroup (satisfy ACR criteria by fifth year and followed-up to first year) (n = 698)
Median (IQR) age at symptom onset	54 (41–66)	54 (42–66)	56 (45–68)
Female, n (%)	715 (65.1)	665 (65.8)	460 (65.9)
Median (IQR) symptom duration at registration (months)	4 (2–10)	4 (2–10)	50 (2–10)
Median (IQR) HAQ at baseline*	0.75 (0.25–1.375)	0.75 (0.25–1.375)	1 (0.5–1.625)
Median (IQR) HAQ at year 1†	0.5 (0.125–1.25)	0.5 (0.125–1.25)	0.8 (0.25–1.5)
Mean (SD) change in HAQ from baseline to year 1	–0.12 (0.6)	–0.12 (0.6)	–0.14 (0.7)
Median (IQR) swollen and tender joint count at baseline	3 (0–8)	3 (1–8)	5 (2–11)
Median (IQR) swollen and tender joint count at year 1‡	1 (0–3)	1 (0–3)	2 (0–5)
RF-positive (RF titre ≥1:80) at baseline, n (%)§	218 (22.8)	204 (22.9)	185 (29.8)
Mean (SD) DAS28 score at baseline¶	4 (1.4)	4.03 (1.4)	4.5 (1.3)
Satisfy ACR criteria at baseline, n (%)	499 (45.5)	464 (45.9)	464 (45.9)
Satisfy ACR criteria by fifth year, n (%)	739 (67.3)	698 (69.1)	698 (100)
Treated with DMARDs by first year, n (%)	481 (43.8)	463 (45.8)	403 (57.7)
Attended hospital by first year, n (%)**	810 (75.8)	749 (74.5)	573 (82.2)

ACR, American College of Rheumatology; DAS28, Disease Activity score 28; DMARD, disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; IP, inflammatory polyarthritis; IQR, interquartile range; RA, rheumatoid arthritis; RF, rheumatoid factor.

*HAQ score at baseline obtained from 1086 subjects.

†HAQ score at year 1 obtained from 1022 subjects.

‡Joint counts at year 1 obtained on 1023 subjects.

§RF measured on 958 subjects.

¶DAS28 score obtained on 846 patients.

**Hospital attendance obtained on 1069 patients.

Using the CRP, the Disease Activity score 28 (DAS28) at baseline was calculated using the appropriate formula¹.

The American College of Rheumatology (ACR) 1987 criteria²⁰ for RA were applied both cross-sectionally at baseline and cumulatively by fifth year—that is, satisfy the ACR criteria by fifth year of assessment or by time of death, which ever was sooner.

Functional disability was assessed at each anniversary by the subject completing the Health Assessment Questionnaire (HAQ), modified for use in British patients.²¹ The questionnaire comprises 20 questions covering eight areas of daily living, where scores range from 0 (no disability) through to 3 (severe disability). The HAQ scores at each anniversary were categorised into groups as follows: 0 to <1 (none or mild disability), 1 to <2 (moderate) and 2 to 3 (severe).²²

At each assessment, information was also collected in relation to disease-modifying anti-rheumatic drug (DMARD) treatment, including oral steroids. For the purposes of this analysis, those who reported starting DMARD by their first year of assessment were categorised as having had DMARD and/or steroid treatment.

Notification of deaths

NOAR subjects’ vital status was flagged through the National Health Service Central Register. The majority of patients in the UK (>95%) are registered with a National Health Service general practitioner and so are recorded on the National Health Service Central Register. The Office for National Statistics provided details of patients’ deaths including date and cause of death. The cause of death was coded using the International Classification of Disease Ninth Revision (ICD-9)²³ until the end of 2000, and the Tenth Revision (ICD-10) from 2001 onwards.²⁴ All data were converted to ICD-10 codes, and for the purposes of this analysis deaths due to CVD were all those in which CVD (ICD-10 I00-I99) was mentioned anywhere on the death certificate.

¹DAS28-3(CRP) = (0.56 * TJC28 + 0.28 * SJC28 + 0.36 * ln(CRP+1)) * 1.10 + 1.15, where TJC28 is the 28 tender joint count and SJC is the 28 swollen joint count (<http://www.das-score.nl/www.das-score.nl/index.html>)

Each subject was followed until death or 10 years from registration with NOAR, which ever was sooner. If a subject moved from England or was no longer registered with a general practitioner, the Office for National Statistics notified NOAR of the date of this “embarkation.” Follow-up for these subjects was censored at the time of embarkation.

Statistical analysis

Mortality per 1000 person-years (pyr) of follow-up, with summaries of age at onset, gender, RF and RA status at baseline, DAS28 score, DMARD treatment by first year of assessment and number of joints that were both swollen and tender (actively inflamed), were stratified by HAQ groups at both baseline and first year of assessment. As some subjects had died or were lost to follow-up before the first year visit, baseline HAQ-stratified mortality were then calculated, first, for all subjects and then restricted to those with a 1-year follow-up. The use of the latter data permits direct comparison, in subjects surviving and followed up to 1 year, between the predictive value of their baseline and 1-year HAQ on subsequent mortality.

Cox proportional hazard regression models were used to calculate the mortality hazard ratio (HR) per unit increase in HAQ score both at baseline and first year. The same models were also used to investigate which other factors were predictive of mortality—namely, change in HAQ from baseline to year 1 stratified into three groups: (1) reduction in HAQ score, (2) no change and (3) increase in HAQ score; actively inflamed joint count at baseline and year 1; RF status at baseline; RA status according to ACR criteria at baseline; DAS28 score at baseline; if treated with DMARD by the first year. The resultant HRs were adjusted for age at onset and gender. Those factors that were found to significantly predict mortality (p<0.05) were then included in multivariate Cox proportional hazard regression models with the baseline or 1 year HAQ.

All analyses were then repeated: first, restricted to patients with a cardiovascular death and, second, to those who satisfied ACR criteria for RA by fifth year of assessment or by time of death, if sooner.

All statistical analyses were conducted using Stata V.9.

Table 2 Mortality (all-cause and cardiovascular disease) per 1000 person-years, by Health Assessment Questionnaire groups at baseline and year 1

	Baseline HAQ				Year 1 HAQ			
	All (n = 1086)				All (n = 1010)			
	<1	1 to <2	2 to 3	>3	<1	1 to <2	2 to 3	>3
HAQ group, n (%)	643 (59)	328 (30)	115 (11)	590 (58)	312 (31)	108 (11)	657 (65)	99 (10)
Female, n (%)	388 (60)	234 (71)	83 (72)	361 (61)	226 (72)	78 (72)	404 (61)	77 (78)
Median (IQR) age at onset (years)	51 (39–62)	55 (43–69)	65 (53–74)	52 (39–62)	56 (43.5–69)	65 (52.5–73)	53 (40–63)	66 (51–73)
Median (IQR) swollen and tender joint count	1 (0–5)	6 (2–11.5)	11 (4–19)	2 (0–5)	6 (2–12)	10.5 (4–18.5)	2 (0–7)	4 (2–12)
RF titre ≥ 1:40 at baseline, n (%)	149 (23)	78 (24)	39 (34)	136 (23)	77 (25)	35 (32)	154 (23)	33 (33)
RF titre ≥ 1:80 at baseline, n (%)	117 (18)	67 (20)	33 (29)	108 (18)	66 (21)	30 (28)	124 (19)	28 (28)
Satisfy ACR criteria at baseline, n (%)	203 (32)	196 (60)	92 (80)	189 (32)	189 (61)	86 (80)	243 (37)	75 (76)
Mean (95% CI) DAS28 score	3.36 (3.3 to 3.5)	4.71 (4.6 to 4.8)	5.55 (5.4 to 5.8)	3.38 (3.3 to 3.5)	4.72 (4.6 to 4.9)	5.53 (5.3 to 5.7)	3.63 (3.5 to 3.7)	4.54 (4.4 to 4.7)
Treated with DMARDs by first year, n (%)	208 (32)	187 (57)	79 (69)	201 (34)	185 (59)	77 (71)	254 (39)	74 (75)
All-cause mortality per 1000 pyr over 10 years	12.1	23.5	39.7	11.5	22.1	35.8	11.9	38.9
CVD mortality per 1000 pyr over 10 years	7	12.6	23.3	6.7	11.3	20.6	6.4	21.3

ACR, American College of Rheumatology; CVD, cardiovascular disease; DAS28, Disease Activity score 28; DMARD, disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; IQR, interquartile range; pyr, person-year; RA, rheumatoid arthritis; RF, rheumatoid factor.

RESULTS

Characteristics of study population

Table 1 shows the characteristics of the study population. The median age at symptom onset of the 1098 patients was 54 years with two thirds being women. The median duration of symptoms at registration was 4 months. At the baseline assessment, 499 (45.5%) patients were classified as having RA, and by 5 years 739 (67%) patients had satisfied the ACR criteria when applied cumulatively.

By the first year anniversary, over 40% had been treated with a DMARD. In the year from baseline to the first year assessment, the average disease activity and functional disability of the study population fell. Thus, the median actively inflamed joint count fell from 3 at baseline to 1 by first year assessment. The mean (SD) fall in HAQ score between baseline and the first year was 0.12 (0.6) units.

The characteristics of the subjects who were followed up to 1 year were very similar to the entire IP cohort. As expected, the disease activity, functional disability and use of DMARD were greater in the subgroup that satisfied the ACR criteria by 5 years than the entire IP cohort, and in those from the IP cohort who were followed up to 1 year.

Follow-up and mortality

The median (interquartile range (IQR)) follow-up time was 10.3 (10.1–10.8) years, giving a total of 10 750 pyr of observation. During this period there were 192 deaths. The mortality was higher in those with a higher baseline or 1-year HAQ score (table 2). The mortality for those with HAQ score <1 at baseline was 12/1000 pyr compared with 38/1000 pyr for those with a score ≥2 at baseline. Those in the higher HAQ groups were older, more likely to be women, be treated with DMARD, have more actively inflamed joints, increased disease severity, be seropositive and satisfy the ACR criteria for RA.

Restricting the analysis to those who were followed-up to 1 year was based on 1010 patients with a median (IQR) follow-up time of 10.3 (10.1–10.8) years, equivalent to 9994 pyr of observation. In this group who, by definition, had survived to 1 year, there were as expected, fewer deaths—a total of 171 in the next 9 years (deaths in the first year being excluded). The crude mortality assessed by HAQ score was similar, whether based on the baseline or 1 year data. However, there were differences in the use of DMARD, the number of actively inflamed joints and disease severity and activity measures, between each HAQ strata at the two time points (table 2).

HAQ score as predictor of all-cause mortality in subjects followed up to 1 year

Table 3 shows the age-adjusted and gender-adjusted Cox proportional HRs per unit increase in HAQ score. All-cause mortality increased with increase in HAQ, whether HAQ was assessed at baseline or at 1 year. However, the association was stronger using the 1-year data. The age-adjusted and sex-adjusted mortality increased by 1.48 (95% CI 1.23 to 1.77) with every unit increase in HAQ score at year 1, whereas the adjusted mortality increased by 1.29 (95% CI 1.05 to 1.58) with every unit increase in HAQ score at baseline.

The strongest univariate predictor of all-cause mortality was baseline RF-positivity (HR 1.49; 95% CI 1.05 to 2.11) followed by HAQ score at 1 year. Other univariate significant predictors were baseline DAS28 score and early DMARD treatment. Within the model based on baseline HAQ score, RF was the only independent predictor of mortality. Within the model based on 1-year HAQ score, the HAQ score was the only significant predictor of all-cause mortality, although baseline RF status had a similar adjusted HR.

Cardiovascular mortality in subjects followed up to 1 year

Of the 171 deaths in those subjects with HAQ obtained at both anniversaries, 89 (52%) were attributed to CVD. The CVD mortality for all those with a baseline HAQ and for those who survived and were followed up to 1 year is shown in table 2. As with all-cause mortality, the CVD mortality increased sharply with increasing HAQ group at both assessments.

Baseline RF-positivity was the strongest univariate predictor of CVD mortality (HR 2.21; 95% CI 1.41 to 3.47) followed by HAQ score at 1 year and early DMARD treatment. Within the model using baseline HAQ score, RF was the only independent predictor of CVD mortality. Within the model based on HAQ score at 1 year, RF and the HAQ score, were both independent predictors of subsequent CVD mortality.

Mortality in subgroup with RA

The mortality experience of those who satisfied the ACR criteria by 5 years was similar to that of the entire IP cohort. As expected, disease severity and activity measures were higher, compared with the entire IP cohort (table 4). The mortality (both all-cause and cardiovascular) was score, in general, slightly lower for those who satisfied the ACR criteria by fifth year or at time of death than the entire IP cohort, and were higher only in the lowest HAQ group (HAQ score <1).

The HRs were very similar in the RA subgroup compared with the entire IP cohort (table 5); although the HRs were higher for RF positivity for all-cause and CVD mortality, in both multivariate models. However, HAQ score at 1 year remained a

significant independent predictor of all-cause (1.48; 95% CI 1.13 to 1.93) and CVD mortality (1.52; 95% CI 1.09 to 2.12), following adjustment for other predictors of mortality.

DISCUSSION

In a primary care-based inception cohort of patients with recent-onset IP who survived for 1 year, we found increased 10-year mortality with increasing HAQ score, whether measured at baseline or after 1 year of follow-up. We also found that year 1 HAQ score continued to have an influence on all-cause and CVD mortality, following adjustment for other predictors. Although an association between HAQ score and mortality has been reported previously in RA,⁵⁻⁷ this analysis is the first to compare the performance of HAQ at, and between, baseline and year 1 to predict mortality in an early-onset cohort. Furthermore, we have compared the performance of the HAQ measurements with other predictors of mortality in subjects early in their disease course.

This study used a primary care-based cohort of patients with IP, and so had limited selection bias. As the sample size was high and follow-up was 10 years, we were able to produce robust estimates of the influence of physical disability, at both baseline and year 1, on mortality. It could be argued that as the study population comprised patients with IP rather than only those patients classified as RA, it includes patients with conditions other than RA and would have milder disease than seen in clinic. However, we have previously contended that it is difficult to distinguish RA among cases of early-onset IP.²⁵ Furthermore, we have previously shown that early RA status is

Table 3 HR for 10-year all-cause and cardiovascular disease mortality, by HAQ at baseline and year 1

Predictor	n	Univariate	HAQ at baseline multivariate	HAQ at year 1 multivariate
		Adjusted for age and sex HR (95%CI)	Adjusted for age and sex HR (95%CI)	Adjusted for age and sex HR (95%CI)
All deaths				
HAQ at baseline (each increase of score by 1)	1010	1.29 (1.05 to 1.58)	1.22 (0.9 to 1.66)	
HAQ at year 1 (each increase of score by 1)	1010	1.48 (1.23 to 1.77)		1.46 (1.15 to 1.85)
Change in HAQ from baseline to year 1 (adjusted for baseline HAQ)				
Reduction in HAQ score from baseline to year 1	505	1.0		
No change in HAQ score from baseline to year 1	182	1.37 (0.87 to 2.17)		
Increase in HAQ score from baseline to year 1	323	1.33 (0.95 to 1.87)		
Swollen and tender joint count at baseline (each increase in count by 1)	1010	1.00 (0.98 to 1.02)		
Swollen and tender joint count at year 1 (each increase in count by 1)	1005	0.99 (0.96 to 1.02)		
RF positive (RF titre ≥1:80) at baseline	891	1.49 (1.05 to 2.11)	1.56 (1.07 to 2.26)	1.45 (0.99 to 2.1)
Satisfy ACR criteria at baseline	1010	0.95 (0.7 to 1.29)		
DAS28 score at baseline (each increase of score by 1)	795	1.15 (1.02 to 1.3)	1.04 (0.89 to 1.22)	1.02 (0.89 to 1.17)
Treated with DMARD by first year	1010	1.41 (1.02 to 1.93)	1.37 (0.92 to 2.02)	1.37 (0.93 to 2.03)
Deaths due to CVD				
HAQ at baseline (each increase of score by 1)	928	1.22 (0.92 to 1.63)	1.12 (0.82 to 1.54)	
HAQ at year 1 (each increase of score by 1)	928	1.60 (1.24 to 2.06)		1.49 (1.12 to 1.97)
Change in HAQ from baseline to year 1 (adjusted for baseline HAQ)				
Reduction in HAQ score from baseline to year 1	466	1		
No change in HAQ score from baseline to year 1	167	1.17 (0.59 to 2.31)		
Increase in HAQ score from baseline to year 1	295	1.47 (0.93 to 2.34)		
Swollen and tender joint count at baseline (each increase in count by 1)	928	0.99 (0.96 to 1.02)		
Swollen and tender joint count at year 1 (each increase in count by 1)	923	0.98 (0.93 to 1.02)		
RF-positive (RF titre ≥1:80) at baseline	825	2.21 (1.41 to 3.47)	1.99 (1.25 to 3.17)	1.87 (1.18 to 2.98)
Satisfy ACR criteria at baseline	928	0.86 (0.56 to 1.32)		
DAS28 score at baseline (each increase of score by 1)	737	1.12 (0.95 to 1.33)		
Treated with DMARD by first year	928	1.60 (1.03 to 2.48)	1.48 (0.9 to 2.45)	1.44 (0.88 to 2.36)

ACR, American College of Rheumatology; CVD, cardiovascular disease; DAS28, Disease Activity score 28; DMARD, disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; HR, hazards ratio; RF, rheumatoid factor.

a poor predictor of mortality (both all-cause and CVD).²⁶ It is interesting to note that although the IP cohort did include more patients with milder disease than those seen in clinic, the predictive value of HAQ in relation to mortality still held. Previous work has shown a similar prediction of mortality using the HAQ in patients with RA and in the general population.²⁷ Although this latter analysis only determined 2-year survival, it, along with the work presented here, indicates that people with similar levels of physical disability seem to have a similar likelihood of mortality. We did, however, repeat the analyses restricting inclusion to those patients cumulatively satisfying ACR criteria for RA by time of death or 5 years. The predictive value of HAQ at year 1 on all-cause and CVD mortality is similar in the RA cohort to that in the IP cohort.

Seropositivity was a stronger predictor of mortality in the subgroup with RA than in the whole IP cohort, which confirms our previous work.¹³ In that analysis, we found that baseline HAQ (≥ 1.5) was not a significant predictor of mortality. Here we have also found that baseline HAQ score did not predict mortality while HAQ score at year 1 did, even when adjusted for other predictors. Another study from an inception cohort of patients with RA in the UK also found that functional capacity at year 1 (measured by Steinbrocker functional grade) was associated with mortality up to 40 years later.²⁸ However, they did not adjust for other predictors and so it is not clear whether functional capacity was an independent predictor of mortality in that study.

The adjustment for treatment—that is, DMARD use by first year, did not account for time on treatment, or treatment initiated after the first year, which may have an important influence on outcome. Another possible criticism of this analysis is that we only looked at HAQ scores at baseline and year 1 rather than at later periods. However, this analysis shows that irrespective of what happens later in the disease course, the HAQ score at first year can predict early death.

As in previous reports, we have found an increased mortality with increasing HAQ score.^{5 6 29-31} The mortality in our analysis are lower than in hospital-based studies.³² For instance, Callahan *et al*⁶ found an odds ratio (OR) per unit change of HAQ for all-cause mortality of 2 in 210 patients with RA in the US, whereas we found an HR of 1.46.⁶ This difference may be explained by differences in study populations or by secular changes either in disease or treatment. Few prospective studies have concentrated on HAQ over time as an independent predictor of mortality in RA. In three cohorts of patients with established RA, change in HAQ over time was found to independently predict mortality.^{3 33 34} We did not find that change in HAQ between baseline and year 1 was a predictor of mortality.

The observed improvement in functional disability from baseline and year 1 has been reported elsewhere with steadily increasing HAQ score from that time on.^{8 9} This initial improvement could be due to treatment effects, spontaneous improvement in disease activity or to improved coping strategies. We have previously shown that a set trajectory of declining functional ability occurs after the first year of disease,³⁵ and that 1-year HAQ is a much stronger predictor, than baseline HAQ, of the 5-year HAQ score.³⁶

As seen in previous studies, CVD was the leading underlying cause of death.^{10 11} We found that while seropositivity was a stronger predictor of deaths due to CVD compared with all-cause deaths, HAQ at year 1 was also a significant predictor of CVD mortality. Previous work on CVD mortality has looked at inflammatory markers and traditional risk factors.^{10 14-18} In our previous report, we found that baseline CRP was a predictor of subsequent cardiovascular mortality.³⁷ In this study, we have

Table 4 Mortality (all-cause and cardiovascular disease) per 1000 person-years, by Health Assessment Questionnaire groups at baseline and year 1, in rheumatic arthritis subgroup

	Baseline HAQ				Year 1 HAQ				
	All (n=728)				All (n=698)				
	<1	1 to <2	2 to 3	<1	1 to <2	2 to 3	1 to <2	2 to 3	
HAQ group, n (%)	347 (48)	276 (38)	105 (14)	331 (47)	268 (38)	99 (14)	393 (56)	213 (31)	92 (13)
Female, n (%)	200 (58)	200 (72)	76 (72)	193 (58)	195 (73)	72 (73)	227 (58)	159 (75)	74 (80)
Median (IQR) age at onset (years)	54 (43-64)	56 (44-69)	65 (53-73)	54 (43-64)	56 (44-69)	65 (52-73)	56 (44-65)	55 (45-68)	66 (51-73)
Median (IQR) swollen and tender joint count	3 (1-7)	7 (3-13)	12 (5-19)	3 (1-7)	7 (3-13)	11 (5-19)	1 (0-2)	3 (1-8)	5 (2-12)
RF titre $\geq 1:40$ at baseline, n (%)	121 (35)	75 (27)	38 (36)	113 (34)	74 (28)	35 (35)	129 (33)	60 (28)	33 (36)
RF titre $\geq 1:80$ at baseline, n (%)	98 (28)	64 (23)	32 (30)	92 (28)	63 (24)	30 (30)	106 (27)	51 (24)	28 (30)
Satisfy ACR criteria at baseline, n (%)	203 (59)	196 (71)	92 (88)	189 (57)	189 (71)	86 (87)	243 (62)	146 (69)	75 (82)
Mean (95% CI) DAS28 score	3.87 (3.7 to 4)	4.86 (4.7 to 5)	5.61 (5.4 to 5.8)	3.87 (3.7 to 4)	4.86 (4.7 to 5)	5.59 (5.4 to 5.8)	4.18 (4.1 to 4.3)	4.72 (4.6 to 4.9)	5.3 (5.1 to 5.5)
Treated with DMARD by first year, n (%)	162 (47)	174 (63)	74 (70)	158 (48)	173 (65)	72 (73)	209 (53)	124 (58)	70 (76)
All-cause mortality rate per 1000 pyr over 10 years	13.4	20.3	37.4	13.1	19.6	34.1	13.7	19.8	36.5
CVD mortality rate per 1000 pyr >10 years	8.8	9.5	20.5	8.6	8.9	18.6	7.6	10.6	19.8

ACR, American College of Rheumatology; CVD, cardiovascular disease; DAS28, Disease Activity score 28; DMARD, disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; HR, hazards ratio; pyr, person years; RF, rheumatoid factor.

Table 5 HR for 10 year all-cause and CVD mortality, by HAQ at baseline and year 1 in rheumatoid arthritis subgroup

Predictor	n	Univariate	HAQ at baseline multivariate	HAQ at year 1 multivariate
		Adjusted for age and sex HR (95% CI)	Adjusted for age and sex HR (95% CI)	Adjusted for age and sex HR (95% CI)
All deaths				
HAQ at baseline (each increase of score by 1)	698	1.29 (1.01 to 1.64)	1.27 (0.90 to 1.79)	
HAQ at year 1 (each increase of score by 1)	698	1.48 (1.19 to 1.82)		1.48 (1.13 to 1.93)
Change in HAQ from baseline to year 1 (adjusted for baseline HAQ)				
Reduction in HAQ score from baseline to year 1	365	1		
No change in HAQ score from baseline to year 1	99	1.77 (1.06 to 2.96)		
Increase in HAQ score from baseline to year 1	234	1.39 (0.93 to 2.06)		
Swollen and tender joint count at baseline (each increase in count by 1)	698	1.01 (0.99 to 1.03)		
Swollen and tender joint count at Year 1 (each increase in count by 1)	696	0.99 (0.96 to 1.03)		
RF positive (RF titre \geq 1:80) at baseline	620	1.63 (1.1 to 2.39)	1.84 (1.23 to 2.76)	1.69 (1.12 to 2.54)
Satisfy ACR criteria at baseline	698	1.13 (0.76 to 1.68)		
DAS28 score at baseline (each increase of score by 1)	552	1.22 (1.04 to 1.42)	1.13 (0.94 to 1.37)	1.12 (0.94 to 1.33)
Treated with DMARDs by first year	698	1.40 (0.95 to 2.06)		
Deaths due to CVD				
HAQ at baseline (each increase of score by 1)	636	1.1 (0.78 to 1.56)	1.15 (0.79 to 1.67)	
HAQ at year 1 (each increase of score by 1)	636	1.53 (1.14 to 2.06)		1.52 (1.09 to 2.12)
Change in HAQ from baseline to year 1 (adjusted for baseline HAQ)				
Reduction in HAQ Score from baseline to year 1	334	1		
No change in HAQ Score from baseline to year 1	86	1.39 (0.61 to 3.13)		
Increase in HAQ Score from baseline to year 1	216	1.66 (0.97 to .84)		
Swollen and tender joint count at baseline (each increase in count by 1)	636	0.99 (0.96 to 1.02)		
Swollen and tender joint count at Year 1 (each increase in count by 1)	634	0.99 (0.94 to 1.03)		
RF-positive (RF titre \geq 1:80) at baseline	570	2.46 (1.46 to 4.17)	2.45 (1.45 to 4.14)	2.30 (1.36 to 3.9)
Satisfy ACR criteria at baseline	636	1.02 (0.59 to 1.76)		
DAS28 score at baseline (each increase of score by 1)	508	1.15 (0.93 to 1.41)		
Treated with DMARDs by first year	636	1.64 (0.95 to 2.82)		

ACR, American College of Rheumatology; CVD, cardiovascular disease; DAS28, Disease Activity score 28; DMARD, disease-modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; HR, hazards ratio; RF, rheumatoid factor.

confined our analysis to subjects who survive up to 1 year. We did not have 1-year CRP measures. The 1-year HAQ score is probably a better surrogate measure of cumulative disease activity than baseline DAS28. The HAQ score will also reflect levels of physical activity, which is a recognised risk factor for CVD. This study demonstrates that RF is an independent risk factor for CVD in patients with IP and RA in addition to the 1-year HAQ score. For instance, those patients who were RF positive and had a HAQ score \geq 2 at 1 year, had a CVD mortality of 2.5 (95% CI 1.3 to 4.8) higher than subjects who were RF negative and had a HAQ score $<$ 1.

Mortality in RA does not seem to have improved in recent decades.^{38–39} However, the newer biological agents, by reducing cumulative disease activity, may have an impact. It has been shown that methotrexate (MTX) treatment may provide a significant survival benefit in patients with RA, particularly to those deaths caused by CVD.⁴⁰ This study population was recruited to NOAR in the early 1990s relatively soon after onset of symptom; and the majority were treated by the first year with sulphasalazine (283 (61%) of those treated) and/or steroids (162 (35%)), whereas only 69 (15%) were given MTX initially. Therefore, the treatment experience of this cohort will be different from those with onset of symptom since that time—that is, more use of MTX and newer treatments such as anti-TNF agents. Nevertheless, HAQ may still be a useful predictor in this era. In this study, DMARD treatment within the first 12 months was actually a predictor of subsequent mortality. This is almost certainly due to confounding by indication.

In conclusion, our data show that the 1-year HAQ score is a useful predictor of all-cause and cardiovascular mortality in people with IP and RA. These results may help guide the targeting of aggressive treatments.

ACKNOWLEDGEMENTS

We thank the rheumatologists and general practitioners within the catchment region for their continued support of NOAR. We would like to acknowledge the contribution of the NOAR metrologists in the collection of the clinical data, and database manager Stephanie Manning.

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Funding: This work was funded by the Arthritis Research Campaign, UK.

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