PREDICTION OF PERMANENT WORK DISABILITY IN A FOLLOW-UP STUDY OF EARLY RHEUMATOID ARTHRITIS: RESULTS OF A TREE STRUCTURED ANALYSIS USING RECPAM

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SUMMARY
The objectives of this study are: (a) to determine the occurrence of permanent work disability (PWD) in early rheumatoid arthritis (RA); (b) to identify prognostic groups of patients; (c) to assess the employment rates for these groups over time. Seventy-three gainfully employed consecutive out-patients with early RA (≥ 5 ARA 1958 criteria, disease duration ≤ 12 months) at time one (T1) were re-examined at time two (T2) after a mean follow-up of 6 yr (s.d. ± 2 yr). Potential risk factors, identified at T1, for PWD at T2 were entered in a tree structured survival analysis using RECPAM (RECursive Partition and AMalgamation). Cumulative 3 yr employment rates (3-yrER ± S.E.M.) were computed from the resulting Kaplan-Meier curves. At T2, PWD occurred in 27 of the 73 patients (37%). The fastest decline in the employment rate was found within the first 3 yr of the disease onset, with a 3-yrER reduced to 73 ± 5%. The group with the poorest prognosis (n = 14; 3-yrER 14 ± 9%) was defined by age ≥ 50 yr with either ESR ≥ 60 mm/h or the combination of modified functional class (1-7) > 4 with a disease duration > 7 months. An intermediate group (n = 38; 3-yrER 79 ± 6%) was defined by (a) age ≥ 50 yr and low or moderate disease activity, (b) age < 50 yr and more strenuous job-related physical requirements, (c) age < 50 yr and less strenuous work, but joint count ≥ 15. No case of PWD occurred in 21 individuals aged <50 yr with a joint count < 15 and less physically demanding jobs. PWD occurs early in a substantial number of patients with RA. RECPAM defines risk profiles that can readily be applied in actual clinical situations and allow an estimation of the risk of PWD at different time points using the resulting Kaplan-Meier curves.

KEY WORDS: Early rheumatoid arthritis, Work disability, Follow-up study, Prognosis, Tree structured analysis.
duration ≤12 months) who were referred to the out-patient clinic between December 1982 and September 1987 were entered into a longitudinal study with prospective recording of predominantly somatic variables (T1). After a mean follow-up of 6 yr (s.d. ± 2 yr), 109 of 132 patients (83%) participated in a physical, laboratory and radiological re-examination (T2). Of the 23 patients lost to follow-up, two had died, two had moved out of the area and 19 refused further participation in the study. There were no differences in the baseline characteristics of the 19 individuals who did not participate in the re-examination, compared to those who consented. At T2, changes in the employment status and the job-related physical requirements were recorded retrospectively by means of a standardized interview. Among 36 of 109 patients who did not work at T1, four (11%) were employed at T2 and PWD occurred in six individuals (17%). These 36 persons were not considered further in this article. This report is based on all 73 of the 109 patients who were gainfully employed at T1 and re-examined at T2.

Table I shows the areas of potential risk factors for PWD obtained at T1, namely demographic and clinical variables including the patient's history, findings of the physical, laboratory and radiological examinations, employment status and job-related physical requirements.

The following dichotomous variables were recorded: sex; rheumatoid factor (latex agglutination test at least 20 IU/ml; RapiTex-RF, Behring Laboratories); definite erosive changes in at least one joint of the hands, feet or other affected joints on conventional radiographs read by a radiologist; employment status (blue- or white-collar workers); physical requirements of the job (frequent precision work and/or handwriting and/or typing, application of grip force, overhead work and strain on the lower extremities, such as standing, walking or climbing stairs).

Parameters with more than two categories were disease duration and disability. Disease duration, defined as the time since the first painful joint swelling reported by the patient, was divided into four categories (1–3, 4–6, 7–9 and 10–12 months). The physician's judgement of the functional disability was determined using a modification of the ARA functional grading [24]. In this study, one class was added in between the ARA functional classes, resulting in a variable with seven categories (such as modified functional class 4 in between the ARA functional classes II and III). The continuous variables had to be categorized for the tree structured analysis: age was categorized in 5 yr age bands (from <25 yr to ≥60 yr); duration of morning stiffness until maximum improvement as no stiffness, and in 30 min time bands to 210 min and over; joint count, i.e. the number of swollen joints in five categories (<5, 5–9, 10–14, 15–19, ≥20); and erythrocyte sedimentation rate (ESR), according to Westergren's method, was categorized in 10 mm/h groups up to ≥80 mm/h.

Information was also obtained on the date of work loss or retirement and the reasons for this. In order to define the clearest group with PWD (external validity), only persons with total cessation of employment due to RA receiving a social security pension were considered as positive cases in the analyses. The complex process of the decision made by the insurance for the individual disability claimant is based on the German Social Security Law [25]. The main conditions for obtaining the PWD pension include (a) inability to work in jobs available on the labour market due to severe disability and (b) membership in the compulsory social security insurance for an individually variable period, usually 3 yr within the 5 yr preceding the PWD.

**Statistical methods**

The data were analysed using the Statistical Package of Social Sciences (SPSS) [26], BMDP [27] and RECPAM (RECursive Partition and AMalgamation) [28]. RECPAM and the Cox analysis [29] use maximum information on all members of the sample by means of censored employment rates over time: PWD due to RA was used as the main outcome variable; patients still employed at the end of the follow-up were included and individuals who had stopped working because of other reasons (such as reaching normal retirement age) were considered until the time of their dropout.

RECPAM is a new tree structured survival analysis consisting of two steps. In the recursive partition step, the entire group and, thereafter, each subgroup is divided by patient characteristics into two subgroups with the greatest differences of 'survival' curves, i.e.
Fig. 1.—Kaplan–Meier curve of continued employment in the entire sample (73 patients).

curves for continued employment. For all groups, the programme examines every allowable division on each prognostic factor and selects the best of these divisions. The most appropriate divisions for categories were selected by computing a log-rank statistic for the different employment curves. The splitting process is continued until no further subdividing is worthwhile for prognostic purposes, giving so-called terminal nodes.

By varying the significance level, different trees were generated. These trees were scanned according to the minimum Akaike Information Criterion (AIC) in order to obtain the best one [28], which was the tree with a $P$ value of 0.05. To achieve final groupings with distinct employment curves, the terminal nodes were submitted to the amalgamation algorithm. This second step of RECPAM joined terminal nodes with similar employment curves.

For the total sample and for each group identified by RECPAM, Kaplan–Meier curves [30] were calculated. The pairs of the curves at each split were compared with the log-rank test [27]. Furthermore, the proportion of the patients employed after 3 yr disease duration (cumulative 3 yr employment rate [3-yrER]) with the S.E.M. were computed from each curve.

In order to compare the results of the tree structured analysis with an established approach to censored data, all covariates analysed in RECPAM were entered with the same categories in multivariate Cox proportional hazards model analyses using BMDP [27] (significance for inclusion in the model was chosen as $P \leq 0.05$).

Fig. 2.—Results of the multivariate analysis of the employment with RECPAM. Numbers in circles, squares and rhombi indicate numbers of patients. Roman numerals I–VII designate terminal nodes of the recursive partition step. Letters A–C indicate final groups of the amalgamation algorithm. For the directions of the associations, see Fig. 3.
Both stepwise forward and backward analyses were performed.

RESULTS

After a mean disease duration of 7 yr (s.d. ± 3 yr) at T2 PWD occurred in 27 of the 73 patients (37%). Six of 73 patients (8%) had ceased work on reaching normal retirement age. In six people (8%) who reported that they had lost their work mainly due to RA, but did not receive social security pension, no information about the individual conditions for PWD (see Patients and methods) was available. Thirty-four patients (47%) were still gainfully employed.

The fastest decline in the employment rate was found within the first 3 yr of the disease onset with a 3-yrER reduced to 73% (s.e.m. ± 5%) (Fig. 1). By means of recursive partition, a tree of demographic, clinical and laboratory variables, and job characteristics was generated (Fig. 2). The prognostic significance of the subgroups of RA patients defined by these variables was further illustrated by the corresponding Kaplan–Meier curves indicating the directions of the associations (Fig. 3). Age 50 yr or older at T1 was the primary division (P < 0.0001) of the tree shown in Fig. 2 with an unfavourable employment curve in the older age group. These patients were further divided by the ESR (P = 0.001). In all patients aged >50 yr suffering from highly active RA, as indicated by an ESR of >60 mm/h, PWD occurred within 5 yr of disease onset. A similar unfavourable employment curve was found for individuals aged >50 yr with functional disability (modified functional class 4 or more) and a disease duration between 7 and 12 months at T1, despite an ESR <60 mm/h.

In the older age group with normal or moderately elevated ESR, patients with a short disease duration (<7 months) had superior employment rates compared to longer persisting arthritis at T1 [P = 0.017, 3-yrER 80% (s.e.m. ± 10%) vs 42% (s.e.m. ± 14%)].

Patients under 50 yr of age at T1 whose work did not include frequent precision work or writing had an increased risk of PWD (P = 0.008). These jobs were characterized by more strenuous physical requirements, such as application of grip force and strain on the lower extremities, or blue-collar worker status (data not shown). The group with frequent precision work or writing was best further subdivided by joint count (P = 0.011). Even though at least 15 joints were involved in these RA patients, only a moderate decline in the employment rate was estimated [3-yrER 71% (s.e.m. ± 17%)]. The question arose whether the exclusion of gender from the tree might be explained by the function of the covariate ‘frequent precision work or writing’ as a surrogate for gender differences in this kind of job affecting employment. However, no association of these variables was found (data not shown).

When the curves of the resulting seven subgroups at each terminal node (I–VII) were plotted, three overall prognostic clusters were seen (Fig. 3). These clusters represented the final groupings A–C achieved by the amalgamation algorithm of RECPAM (Figs 2 and 3).

![Fig. 3.—Kaplan–Meier curves of continued employment of the patients in each terminal node (subgroups I–VII) and in the final groups A–C from Fig. 2. Differences between the curves of the final groups: group A vs B, P < 0.0001; group A vs C, P < 0.0001; group B vs C, P = 0.004.](image-url)
Group A, with the poorest prognosis [3-yrER 14% (S.E.M. ± 9%)], comprised 14 older individuals with either high ESR, or a combination of ESR < 60 mm/h, 7 or more months disease duration at T1, and a modified functional class 4 or more (subgroups I and II). The favourable group (group C), with no PWD during a disease duration of up to 11 yr, consisted of 21 patients aged < 50 yr with frequent precision work or writing as important job characteristics and < 15 swollen joints (subgroup VII). An intermediate group (group B) [(3-yrER 79% (S.E.M. ± 6%)] consisted of the remaining 38 patients (subgroups III–VI).

The same variables as used in RECPAM were entered in the multivariate Cox regression analysis in a stepwise forward manner. The first five steps included the prognostic factors that were also identified with RECPAM (Table II). Corresponding to the first division in RECPAM, age entered the model in step 1. In addition to the set of predictors in RECPAM, rheumatoid factor and erosive changes were included in the last two steps of the Cox model. The ESR, although related to PWD by univariate Cox analysis (P = 0.005), did not enter the multivariate model. The backward analyses yielded the same results as the Cox forward modelling.

DISCUSSION

The high prevalence of PWD is compatible with the results of other studies of RA [7, 10–15]. The change in the employment status of the RA patients was not compared with a controlled group without RA since the main objectives were to identify risk profiles and thereby different employment rates over time among early cases. However, the occurrence of PWD during the follow-up in 37% of the entire sample is more than one would expect from the annual incidence of PWD in 6 cases per 1000 members of the compulsory social security insurance in Germany [31]. Furthermore, the proportion of 8% work loss without social security pension corresponds to the unemployment rate of 11% in the recruitment area (Lower Saxony) during the time of the study [31]. Although persons over the age of 50 yr may have considerable problems in finding work should they lose their job, the unemployment rate in this age group did not exceed 15% in Germany. By contrast, only 14% of the RA patients aged ≥ 50 yr with high ESR were continuously employed after 3 yr. These data indicate a highly increased risk of PWD in persons with early RA compared with average employees in the population.

An important additional finding of the present study is the particularly rapid decline of the employment rates within the first 3 yr of disease onset. This has only been reported in one 8 yr prospective study of very early cases (< 6 months duration) from Finland [13]. Although the patients’ characteristics which are compatible with other reports of early RA [21, 22, 32], are similar to the sample reported by Yelin et al. [10] with the exception of disease duration, the fast development of PWD has not been observed in the retrospective study of long-lasting RA (mean duration 9 yr) in the USA. The rapidly declining employment rate may only be recognizable in long-term follow-up studies of early cases. This finding corresponds to the fast progression of other severe outcome measures, such as functional disability, hand deformities and radiological joint destruction in the early phase of RA [33–35].

Other important findings in the present study were the prognostic factors identified in early RA by any one of the two multivariate approaches. Among the occupational characteristics, only frequent precision work or writing was significant. At first sight, it was surprising that a type of employment that did not include precision work or writing increased the risk of PWD in RA patients. However, these jobs were characterized by more strenuous physical requirements, such as application of grip force and strain on the lower extremities, or blue-collar worker status. Thus, in the analyses of the present study no, or infrequent, precision work or writing can be interpreted as the best surrogate for a physically more demanding job, which has been reported as a risk factor by other investigators [10, 11, 14, 21, 22]. Age was the most relevant single risk factor identified by both RECPAM and the Cox model. The importance of age has been reported in one 8 yr prospective study of very early cases (< 6 months duration) from Finland [13]. Although the patients’ characteristics which are compatible with other reports of early RA [21, 22, 32], are similar to the sample reported by Yelin et al. [10] with the exception of disease duration, the fast development of PWD has not been observed in the retrospective study of long-lasting RA (mean duration 9 yr) in the USA. The rapidly declining employment rate may only be recognizable in long-term follow-up studies of early cases. This finding corresponds to the fast progression of other severe outcome measures, such as functional disability, hand deformities and radiological joint destruction in the early phase of RA [33–35].

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Disease duration is associated with PWD not only in advanced RA [14]. The present study demonstrates that even within a group of patients with early RA,
the longer the disease persisted before the first examination, the less favourable the outcome in terms of employment. Although the degree of intra- and inter-observer variation of functional disability, assessed by the physician, was not determined, the identification of this parameter is in accordance with the importance of the corresponding covariate based on the well-established HAQ [14, 21, 22].

Among the other clinical, laboratory and radiological findings, a high joint count and erosive changes are risk factors identified in other studies [13, 14]. Whereas ESR and rheumatoid factor have not been mentioned previously as risk factors for PWD, the associations of these parameters with other outcome measures have been reported [2, 36-38].

Apart from the detection of single prognostic factors, the main purpose of the present study is to identify groups of patients in terms of combinations of covariates with distinct prognoses for continued employment. The risk profile described can readily be applied in actual clinical situations and allow an estimation of the risk of PWD at different time points using the resulting Kaplan–Meier curves.

Patients aged ≥ 50 yr with high disease activity (in terms of either highly elevated ESR or functional disability combined with longer disease duration at T1) constitute the worst prognostic group: continued employment after 3 yr disease duration is estimated for only one of seven patients in this group. Thus, this is the most important combination of predictors in terms of PWD. A moderate decrease in the employment rate, with PWD in one of five patients within 3 yr, might be expected (a) in persons aged ≥ 50 yr with low or moderate disease activity, (b) in younger individuals with more strenuous job-related physical requirements, (c) in younger patients with less strenuous work, but who suffer from extensive joint involvement (≥ 15 swollen joints). Patients with low or moderate disease activity in terms of lower joint count, and whose work is characterized by frequent precision work or writing, had the best prognosis: no case of PWD occurred during the follow-up period for this group.

One other study has sought to identify groups of RA patients in terms of PWD; this used a different tree approach in a cross-sectional study of patients with long-standing RA [14]. Corresponding to our results, functional disability, age, disease duration and employment status were identified as factors associated with PWD.

The results of the present study may guide early intervention in the individual patient to prevent, or at least postpone, PWD. In patients who have the characteristics of the poor or intermediate prognostic groups, the suppression of disease activity by early aggressive treatment may be indicated in terms of continued employment. In addition, the patients may be advised to change their work to less physically demanding jobs [7]. Whereas some evidence exists that early multidisciplinary care and aggressive therapy alter somatic outcomes [39, 40], the effectiveness of these measures remains to be demonstrated regarding PWD. The methods and prognostic groups proposed in the present study should help in the design of such intervention studies.

When the tree generated by RECPAM (with the resulting Kaplan–Meier curves) and the Cox model are compared, the association of the most important risk factors should be in the same direction. In fact, the first five steps of the Cox analysis identified all covariates included in the tree, except the ESR. The discrepancies between the two multivariate approaches can be explained by methodological differences. The established Cox proportional hazards model ascribes effects to individual covariates in the entire group, whereas the new RECPAM tree technique generates subgroups defined by combinations of covariates. For example, the highly elevated ESR is particularly relevant in the subgroup of older patients. With marginal P values, rheumatoid factor and erosiveness were significant in the total sample using the Cox model, but not in any subgroup identified by RECPAM. Thus, tree structured analyses and Cox proportional hazards modelling provide complementary information. Whereas neither of the two methods has been considered superior from the statistician’s point of view [41], RECPAM offers the advantage of readily applicable combinations of risk factors for the clinician.

Several limitations to this study are recognized. Although the work history was taken retrospectively, all patients appeared to give a very precise and spontaneous account of their daily work activities, indicating that the covariates analysed from this group of variables were unlikely to be substantially affected by recall bias.

The rapid decline in the employment rates in the first 3 yr may not be generalizable since this finding may have been influenced by (a) different systems of social security in Central and Northern Europe compared to American or other societies, (b) the current employment rate, (c) other characteristics of the labour market, such as the very limited availability of jobs suitable for disabled persons in Germany. These factors need to be addressed in more detail in separate studies.

Associations between work status and the patient’s attitude towards work and other psychological variables have been reported [19, 42, 43]. However, these possible predictors could not be ascertained in the present study because such data were not collected at T1.

The dichotomous covariate, erosiveness, is a crude measure of joint destruction. More differentiated indexes [2] may lead to the inclusion of radiological changes as significant factors in future analyses using trees.

To date, no prospective study has considered either the observation of the individual’s performance at the actual work place, or an extensive work capacity evaluation [44] as prognostic factors. Such observations are very time consuming, and a short standardized work capacity evaluation would be more practical and may add important information [45].
Finally, the cohort is not large. Therefore, the calculations of the employment curves, particularly of the poor prognosis groups, were based on only a few patients. Since one centre can hardly provide a substantially greater number of early cases within an adequate recruitment time frame, a large German multicentre study recording the relevant variables prospectively and addressing the open questions discussed in this paper is now in progress.

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REFERENCES

25. Sozialgesetzbuch VI. §44. Rente wegen Erwerbsunfähigkeit.


