Comorbidity affects all domains of physical function and quality of life in patients with rheumatoid arthritis

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Abstract

Objective. Comorbidities have been reported to influence physical function, but it is not clear which activities are predominantly impaired, or which other domains of health status are affected in addition to physical function. In this study, we investigated the impact of comorbidities on individual activities of daily living, and other aspects of quality of life in patients with RA.

Methods. In 380 patients with established RA, we quantified comorbidity levels according to the age-adjusted Charlson Comorbidity Index (CCI A) and functional disability by serial measures of the HAQ over 1 year. In a subset of 185 patients, we assessed quality of life using Short Form-36 (SF-36). To analyse the relationship between comorbidities, different activities of daily living and health status, we divided patients into four subgroups of CCI A and performed analysis of variance (ANOVA) and multivariable general linear regression models adjusted for gender, disease duration and disease activity.

Results. ANOVA showed significant \( P < 0.03 \) increase of disability within each domain of HAQ with increasing level of comorbidity. Similar results were observed using the physical component score \( P = 0.003 \) of the SF-36 and its domains, whereas mental component score \( P = 0.31 \) and its domains were unaffected by comorbidities. In a sub-analysis stratifying patients into different levels of disease activity, we found increase in almost all domains of HAQ within respective groups of CCI A.

Conclusions. Activities of daily living represented by HAQ are equally affected by comorbidities. More generally, health status was only affected with respect to its physical but not its mental domains.

Key words: Rheumatoid arthritis, Comorbidity, Physical function, Disability, Disease activity.

Introduction

RA is a chronic disease often associated with severe disability in patients over time. New treatment strategies and therapeutic options have allowed for more effective interference with the disease process and, hence, today a significant proportion of patients attain low disease activity or remission [1–4]. These achievements are generally expected to translate into improved functional capacity in the short and long term. Nevertheless, many RA patients are still afflicted with considerable limitations of their physical function. In patients with established disease, this is partly related to accrued structural damage which is irreversible [5–8] and, therefore, currently not amenable to drug treatment. However, there are also causes that are not related to RA, which are relevant when considering resistant functional disability [9]. Comorbidity is one of them, and we have recently reported that functional disability consistently increases with higher levels of comorbidity irrespective of disease activity or other disease characteristics [10].

In the present study, we expanded on these initial observations, which were obtained using the HAQ Disability Index (HAQ) [11], and aimed to address a number of additional questions: first, which of the domains of functional capacity (or activities of daily living, as assessed by the HAQ) are affected; and second, is the impact of comorbidity going beyond the concept of physical function, affecting other domains of health status as well. To address these questions, we studied the effects of comorbidity on the eight individual domains of the HAQ, as well as on the eight domains of the Short Form-36 (SF-36) in patients with RA.
Patients and methods

Patients

We enrolled patients fulfilling the 1987 ACR classification criteria for RA [12] from our outpatient clinic who are followed regularly, usually every 3–4 months, over the course of their disease, and whose clinical and laboratory variables are documented at each visit in a longitudinal observational database (CARAbase; Care of RA database, as previously described [13–15]). All patients gave their informed consent for anonymous analysis of their data when they were enrolled into the database and the data collection has been approved by the local ethics committee (Ethik-Kommission der Medizinischen Universität Wien und des Allgemeinen Krankenhauses der Stadt Wien AKH). From this patient population, we selected patients for our study fulfilling two criteria: (i) their most recent visit was <6 months before the beginning of the study in July 2008; and (ii) they had at least two completely documented visits during the period studied (1 June 2007 to 1 July 2008). Based on these entry criteria, we identified 380 patients. Since there were no additional inclusion or exclusion criteria, the study population showed a wide range of disease activity, disease duration and comorbidity, representative of the RA population seen at our clinic.

Study variables

HAQ Disability Index

The HAQ was recorded at every visit routinely. It comprises eight domains, each consisting of two or three questions, where every question can be answered on a 4-level scale regarding the patient’s ability to perform an activity of daily living (0 = no difficulty, 1 = some difficulty, 2 = much difficulty and 3 = unable to). The following domains, which cover the main activities of daily life, are as follows: dressing, rising, eating, walking, hygiene, reach, grip, and errands and chores. The HAQ score represents the mean of the highest values within each single domain, and therefore, is located on a scale from 0 to 3, where higher values represent worse function and vice versa. Four domains are related to dexterity (dressing, eating, reach and grip) and four to mobility (rising, walking, hygiene, and errands and chores).

SF-36

The SF-36 [16] as patient-reported outcome measurement constitutes a questionnaire compromising 36 items. Different sets of items are organized into eight domains whose scores are obtained via summation and transformation of item values into a scale between 0 and 100, where higher values represent better health status. Domains and the respective number of comprising items are as follows: physical function (PF; 10 items), physical role (RP; 4 items), bodily pain (BP; 2 items), general health perception (GHP; 5 items), vitality (VT; 4 items), social function (SF; 2 items), emotional role (RE; 3 items) and mental health (MH; 5 items). One single item that is not summarized is measuring the change of health status compared with the preceding year (health transition; HT). Furthermore, domains can be aggregated into two summary measures: the physical component score (PCS; including PF, RP, BP and GHP) and the mental component score (MCS; VT, SF, RE and MH).

For norm-based scoring, scores of SF-36 and its summary measures are transformed to a mean of 50 (S.D.10), achieving the same mean and S.D. across the domains and summary scores. This method enables more useful and easier interpretation of all scores. Since SF-36 is not routinely recorded a random sample of 185 patients were pleased to fill in the questionnaire.

Comorbidity

In our study, the collection of comorbidities was performed via chart review using the Charlson Comorbidity Index (CCI) [17], an established and validated instrument that also allows multidisciplinary head to head comparisons. CCI was developed for predicting 1-year mortality on a cohort of breast cancer patients and, therefore, assigns a weight to each comorbid condition according to its risk of mortality. Diseases included in this instrument and their weighting are: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatological disease, peptic ulcer disease, mild liver disease and diabetes without complications (Weight 1); diabetes with chronic complications, hemiplegia or paraplegia, renal disease, solid tumour non-metastatic, leukaemia and lymphoma (Weight 2); moderate to severe liver disease (Weight 3); metastatic solid tumour, and AIDS (Weight 6). For our analyses, we used the Charlson’s age-adjusted version (CCI_A) which, in addition to the above, considers the effect of ageing on mortality by giving one extra point for each decade above 50 [18].

Measures of disease activity

In addition, the following core set variables were collected at every visit: visual analogue scale (0–10 cm) for pain (VAS-pain), patient global assessment of disease activity (PGA) and evaluator global assessment of disease activity (EGA), as well as 28-swollen joint count (SJC = 28) and 28-tender joint count (TJC-28) and the acute-phase reactants CRP and ESR. From some of these variables, we calculated a composite index, the clinical disease activity index (CDAI) [19]. The CDAI is calculated as the sum of SJC-28, TJC-28, PGA (in centimetres) and EGA (in centimetres). The cut-off points for the major disease activity states are as follows: remission (REM) \( \leq 2.8 \); low disease activity (LDA) \( 2.8 < \text{LDA} \leq 10 \); moderate disease activity (MDA) \( 10 < \text{MDA} \leq 22 \); high disease activity (MDA) \( \geq 22 \) [20].

Statistical analyses

For statistical analyses, we initially divided our patients into four groups, according to their value of CCI_A (Group 1 = value of 0; Group 2 = value of 1 or 2; Group 3 = value of 3 or 4; Group 4 = value of 5 or more) and also calculated time-averaged HAQ values (HAQ_T) for each of the domains (HAQ_T1 to HAQ_T8). We then tested the correlation...
between the CCI_A groups and each of the functional domains HAQ_T1 to HAQ_T8 using Spearman analysis. We next assessed the differences in HAQ_T values of each domain (HAQ_T1 to HAQ_T8) across the respective groups of CCI_A employing analysis of variance (ANOVA).

To model the relationship between single domains of HAQ and CCI_A, we performed a multivariable linear regression model using HAQ_T1 to HAQ_T8 as dependent variable, and adjusted the effects of CCI_A for gender, disease duration and time-averaged disease activity (CDAI_T). To explore whether comorbidities differently affect dexterity and mobility, the model was rerun, now using dexterity or mobility as dependent variable.

In addition, we also explored whether similar results could be observed at different levels of disease activity; therefore, we performed the same analyses in two subgroups of patients, those in remission to low disease activity (CDAI <=10) and those in moderate to high disease activity (CDAI >10), calculating estimated marginal means (EMMs) via multivariate, adjusted generalized linear models (GLMs) in respective subgroups.

We finally performed the same analyses for the various domains of health status, as assessed in the SF-36. We first correlated the values of SF-36 domains and the summary scores (physical and MH) with groups of CCI_A. Next, we performed ANOVA to identify differences in mean values of the domains of SF-36 or the two summary scores between the groups of CCI_A. Via GLM, we explored EMM of PCS as well as the four domains it consists of, using four groups of CCI_A as dependent variable, and other clinical findings as covariates for adjustment.

Data are expressed as mean (S.D.). P<0.05 was considered to be statistically significant. All analyses were performed using Statistical Package for the Social Sciences (Version 16; SPSS, Chicago, IL, USA).

### Results

#### Study population

In total, our sample contained 1605 visits of 380 patients. Baseline clinical characteristics and demographic data are shown in Table 1. Although mean values of clinical and laboratory findings like CDAI, SJC, EGA and CRP were low at group level, patients showed considerable impairment of physical function according to their HAQ values [mean of 0.94 (0.82)]. A small fraction of patients received no DMARDs (8.2%), while 61.3% were treated with traditional DMARDs, and 30.5% with biological agents.

Using CCI_A, 112 patients showed comorbid conditions (29.5% of the total). Among these patients, the most frequent comorbidities reported were chronic pulmonary diseases (20.5%), diabetes (20.5%), peripheral vascular diseases (17%), myocardial infarction (15.2%), cerebrovascular diseases (13.4%), solid non-metastatic tumours (10.7%), peptic ulcer disease (9.8%) and mild liver disease (8.9%). The CCI_A of our population ranged from 0 to 9 with mean scores of 2.12 (1.67) and 3.82 (1.61) in those who had at least one documented comorbidity.

**HAQ domains correlate significantly with the degree of comorbidity**

When correlating every HAQ domain with groups of CCI_A (Table 2), Spearman coefficients were significant, showing best correlation of time-averaged domain 5 (hygiene) (r=0.31; P<0.001), and worst correlation of time-averaged domain 7 (grip) (r=0.12; P=0.01). We also found significant correlations of HAQ upper body disability (UBD) (r=0.26; P<0.001) and lower body disability (LBD) (r=0.31; P<0.001) with groups of CCI_A.

#### TABLE 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Clinical variables of study population at baseline visit</th>
<th>Mean (S.D.)²</th>
<th>Median (quartiles)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF positive, %</td>
<td>58.4</td>
<td>–</td>
</tr>
<tr>
<td>Female, %</td>
<td>80.5</td>
<td>–</td>
</tr>
<tr>
<td>Age, years</td>
<td>60.7 (13.2)</td>
<td>61.9 (52.4–69.1)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>11.7 (10.1)</td>
<td>8.7 (3.8–16.7)</td>
</tr>
<tr>
<td>CRP, mg/dl</td>
<td>1.09 (2.23)</td>
<td>0.43 (0.18–1.07)</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>23.7 (20.5)</td>
<td>17 (9.0–28.0)</td>
</tr>
<tr>
<td>Simplified disease activity index</td>
<td>10.06 (9.47)</td>
<td>7.12 (3.64–13.62)</td>
</tr>
<tr>
<td>Clinical disease activity index</td>
<td>9.08 (8.59)</td>
<td>6.4 (3.1–12.6)</td>
</tr>
<tr>
<td>SJC-28</td>
<td>1.88 (2.62)</td>
<td>1 (0–3.0)</td>
</tr>
<tr>
<td>TJC-28</td>
<td>2.68 (4.41)</td>
<td>1 (0–3.0)</td>
</tr>
<tr>
<td>Pain (VAS², mm)</td>
<td>31.66 (23.29)</td>
<td>30.0 (11.0–49.0)</td>
</tr>
<tr>
<td>Patient global assessment of disease (VAS, mm)</td>
<td>33.28 (24.71)</td>
<td>30.0 (12.0–51.0)</td>
</tr>
<tr>
<td>Evaluator global assessment of disease (VAS, mm)</td>
<td>11.88 (14.11)</td>
<td>6.0 (2.0–16.0)</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.94 (0.82)</td>
<td>0.75 (0.25–1.38)</td>
</tr>
<tr>
<td>Time-integrated HAQ_T</td>
<td>0.94 (0.78)</td>
<td>0.79 (0.25–1.49)</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>36.71 (11.1)</td>
<td>28.4 (36.2–45.0)</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>47.04 (12.1)</td>
<td>38.3 (49.0–56.9)</td>
</tr>
</tbody>
</table>

²When applicable.

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HAQ values in individual domains increase across groups with increasing degree of comorbidity

Categorization of CCI_A created the following subgroups for analysis: Group 1: 67 patients with CCI_A = 0; Group 2: 184 patients with CCI_A = 1 and 2; Group 3: 89 patients with CCI_A = 3 and 4; and Group 4: 40 with CCI_A = 5 or higher. ANOVA tested for linear trend showed significant ($P < 0.03$) differences of mean time-averaged HAQ values across the four groups of CCI_A for all domains. This effect was due to a consistent increase across the four groups (Fig. 1).

Relationship between domains of HAQ and CCI_A adjusting for additional variables

To adjust for additional variables, we expanded the ANOVA of CCI_A and HAQ domains to a GLM. Additional variables in that model were the CDAI (effects also introduced as time averaged), gender and disease duration. The model $R^2$ was 0.48 ($P < 0.001$).

From that model, we were also able to calculate estimated marginal means of HAQ T-domain values for each category of CCI_A. For that purpose, the covariates in the model were set to the level of the respective cohort means. This generated a comparable health status regarding the covariates across the four groups of CCI_A. As can be seen from Fig. 2A, EMMs in essentially all HAQ domains showed continuous increases from CCI_A Group 1 to Group 4. When we reran the model by upper and lower body disability, a similar increase in EMM was found within respective groups of CCI_A (UBD: 0.92 vs 0.93 vs 1.18 vs 1.43; LBD: 0.75 vs 0.82 vs 1.10 vs 1.52, respectively).

Increase of HAQ values in individual domains increase across groups of patients with increasing levels of comorbidity, independent of disease activity

For further analyses, we stratified our patients regarding their level of disease activity (as defined by CDAI) into

### Table 2: Spearman correlation of HAQ T values of individual domains and domains of SF-36 with groups of age-adjusted CCI_A (including 95% CI)

<table>
<thead>
<tr>
<th>HAQ</th>
<th>$r$ (95% CI)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAQ_1 (dressing)</td>
<td>0.30 (0.20, 0.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ_2 (rising)</td>
<td>0.28 (0.20, 0.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ_3 (eating)</td>
<td>0.20 (0.10, 0.29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ_4 (walking)</td>
<td>0.26 (0.18, 0.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ_5 (hygiene)</td>
<td>0.31 (0.23, 0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ_6 (reach)</td>
<td>0.30 (0.20, 0.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ_7 (grip)</td>
<td>0.13 (0.04, 0.23)</td>
<td>0.01</td>
</tr>
<tr>
<td>HAQ_8 (errands and chores)</td>
<td>0.29 (0.20, 0.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ UBD</td>
<td>0.26 (0.16, 0.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ LBD</td>
<td>0.31 (0.23, 0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-36 PF</td>
<td>$-0.25 (-0.38, -0.10)$</td>
<td>0.006</td>
</tr>
<tr>
<td>SF-36 RP</td>
<td>$-0.19 (-0.33, -0.05)$</td>
<td>0.01</td>
</tr>
<tr>
<td>SF-36 BP</td>
<td>$-0.16 (-0.30, -0.02)$</td>
<td>0.003</td>
</tr>
<tr>
<td>SF-36 GHP</td>
<td>$-0.23 (-0.36, -0.08)$</td>
<td>0.003</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>$-0.28 (-0.41, -0.12)$</td>
<td>0.001</td>
</tr>
<tr>
<td>SF-36 VT</td>
<td>$-0.06 (-0.20, 0.09)$</td>
<td>0.45</td>
</tr>
<tr>
<td>SF-36 SF</td>
<td>$-0.13 (-0.27, 0.01)$</td>
<td>0.07</td>
</tr>
<tr>
<td>SF-36 RE</td>
<td>$-0.07 (-0.22, -0.09)$</td>
<td>0.38</td>
</tr>
<tr>
<td>SF-36 MH</td>
<td>$-0.08 (-0.23, 0.07)$</td>
<td>0.28</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>0.01 (-0.15, 0.16)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

**Fig. 1** Impact of comorbidities on individual domains of HAQ. Panel depicts increase of HAQ value of individual domain of HAQ within different groups of increasing level of age-adjusted CCI_A calculated via ANOVA ($P < 0.03$).
REM/LDA (CDAI \leq 10; n = 254) or MDA/HDA (CDAI > 10; n = 126) and reran the GLM, adjusting again for disease duration and gender. In REM and LDA, we found significant differences of EMM across groups of CCI\textsubscript{A}, showing a consistent increase of HAQ values from Group 1 to Group 4 in all domains (Fig. 2B). In patients with moderate to high disease activity, values of HAQ also rose in most domains depending on values of CCI\textsubscript{A}; however, this dose–response relationship in the increase of HAQ values across groups of CCI\textsubscript{A} was not seen in three domains (eating, reach and grip), presumably due to the superimposed effect of RA disease activity (Fig. 2C).

Effects of CCI\textsubscript{A} on other domains of health status: the SF-36

SF-36 was obtained in 185 randomly chosen patients of the total cohort (48.7%). Mean values of single domains are as follows: PF = 53.2; RP = 43.1; BP = 49.5; GHP = 47.1; VT = 45.6; SF = 72.6; RE = 43.1; MH = 64.4). As displayed in Fig. 3A, mean values of all eight domains were significantly (P < 0.01) lower compared with the German general population (population means for Austria were not available). Even in comparison with German arthritis patients, or patients with cancer [21], our study population showed significant lower mean values in almost every domain (except MH, GHP and BP).

To explore which domains of health status are also affected by comorbidity of patients with RA, we again performed ANOVA and found a significant decrease of scores across the CCI\textsubscript{A} groups for the physical domains of BP, PF, GHP and SF (P < 0.05), and a trend for RP (P = 0.068). All other domains were not significantly different by CCI\textsubscript{A} group. When analysing the PCS and MCS, an almost linear decrease was seen for PCS within the four

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Fig. 2 Impact of comorbidity on individual domains of HAQ considering levels of disease activity. Plot of estimated marginal means of time-integrated values of eight HAQ domains of respective groups of CCI-age (CCI\textsubscript{A} = 0, n = 67; CCI\textsubscript{A} 1–2, n = 184; CCI\textsubscript{A} 3–4, n = 89; CCI\textsubscript{A} 5–9, n = 40). The model was adjusted for gender (set to female) and disease duration (set to cohort mean = 11.7 years). (A) Adjusted analyses of the whole sample revising the model as well for disease activity defined by CDAI (set to cohort mean = 8.7); (B and C) stratified analyses of patient with (B) REM/LDA (CDAI \leq 10; CCI\textsubscript{A} = 0, n = 49; CCI\textsubscript{A} 1–2, n = 130; CCI\textsubscript{A} 3–4, n = 47; CCI\textsubscript{A} 5–9, n = 28) and (C) MDA/HDA (CDAI > 10; CCI\textsubscript{A} = 0, n = 18; CCI\textsubscript{A} 1–2, n = 54; CCI\textsubscript{A} 3–4, n = 42; CCI\textsubscript{A} 5–9, n = 12).
groups of CCIₘ (40.8 vs 37.3 vs 32.3 vs 26.6, respectively; \(P = 0.003\)), whereas the MCS remained largely unaffected by the CCIₘ \((P = 0.31; \text{Fig. 3B})\).

We further explored the PCS in an adjusted model using CDAI and disease duration as covariates (model \(R^2 = 0.36; P < 0.001\)). The estimated marginal means of PCS showed a significant \((P < 0.001)\) decrease across CCIₘ groups 1–4 (40.2 vs 36.9 vs 34.6 vs 26, respectively). This effect was seen independently in all four domains that are summarized in the PCS (PF, RP, BP and GHP). The EMMs across the four CCIₘ groups are visualized in Fig. 4.

**Discussion**

In this study, we elaborated two major findings that expand beyond our current knowledge from the literature: first, comorbidity affects any activity reflecting physical function, showing an increase of functional disability with increasing level of comorbidity in different domains. Secondly, this effect is independent of the instrument used for assessment of physical function.

We have recently shown that physical function in RA is comprised of reversible and irreversible components [7]. While treatment of RA targets disease activity and usually improves the reversible part of disability well, there remains a variable proportion of functional disability that is not amenable to treatment. Depending on the duration of RA, this irreversible component can increase considerably given increasing amounts of joint destruction. However, we also postulate that there are irreversible disability components that are not related to the index disease (in our case: RA), but to some other co-existing disease. We have in a previous study reported on the general effects of comorbidities in patients with RA [10] showing an increase of functional disability with increasing levels of comorbid condition. In the present study, we show that the impact of comorbidities is present in all activities of daily living that comprise physical function but not the mental components of health status.

These new findings support an overall impact of increasing levels of comorbidity on both dexterity and mobility, although it was slightly stronger for mobility, which according to Tuominen et al. ‘is more important than fine movements of the upper extremities’ [22]. Also, physical health status domains other than functional ability were affected by comorbidities. Importantly, there is no such effect of comorbidity on the mental components of health status.

Physical function is a central outcome in many chronic diseases, not only as a reflection of a patient’s well-being, but also given its considerable implications on work capacity, work productivity, health care resource utilization, overall cost of disease and mortality [23–26]. Given all these multifarious consequences of functional decline, an assessment of reversibility and irreversibility, and the attribution of the index disease as opposed to
comorbidities to it, are highly relevant for the patient, the physician, the payer and society.

The HAQ as a multidimensional concept comprises different activities of daily living. There have been modifications of the HAQ that aimed to improve floor and ceiling effects of the HAQ, even until very recently with attempts to introduce computerized adaptive testing approaches into functional assessment [27, 28]. However, all these attempts cannot override floor effects of function that are related to the biological construct rather than the assessment instrument. Therefore, it is essential to further identify contributors to functional disability and the magnitude of their effects to optimize restoration of physical function in our patients with arthritis. Especially, as we are now improving the disease activity more and more with new drugs and strategies, the question: ‘What is the maximum possible functional improvement/best possible functional state in a given patient?’ is very challenging.

One strength of our study is the use of a large sample of patients from daily practice rather than being based within a clinical trial setting where typically a homogeneous group of patients with high disease activity and no major comorbid conditions is enrolled. Our sample showed a wide range of disease activity, functional impairment and comorbidity as seen in everyday routine.

Several limitations need to be addressed. First, we use the CCI which is based on mortality not on functional disability. We decided to use CCI rather than some self-composed index because of its repeatedly tested validity and broad applicability, which allows comparison of different index diseases. Also, we previously showed that mortality-based rating is not decisive and calculations with CCI are acceptable [10]. Nevertheless, we could not overcome the fact that CCI only incorporates a limited number of comorbid conditions, whereas several diseases highly prevalent in RA patients, like osteoporosis or hypertension, are not assigned.

Secondly, we did not account for structural damage displayed by radiographic scores which mainly reflects the irreversible component of functional disability in RA. To overcome this limitation in our analyses, we accounted for disease duration, a surrogate variable highly correlated with radiographic damage [8, 29].

In conclusion, we expand previous observations on the important contribution of comorbid conditions to functional disability. The impact of comorbidity relates to any activity of daily living and therefore affects patients’ well-being at any point of life. Mental functioning does not seem to be affected by the level of comorbidity. This might be relevant in different health economic studies or policy decisions where functional disability is used as a therapeutic outcome [30, 31].

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References

3. Kläreskog L, van der Heijde D, de Jager JP et al. Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in


