



## Original article

# The impact of comorbidities on the physical function in patients with rheumatoid arthritis



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## ABSTRACT

**Objectives:** To investigate the association of comorbidities with mobility limitation and functional disability in patients with rheumatoid arthritis and to identify which comorbidity indicator is the most appropriate to determine this association.

**Methods:** Sixty rheumatoid arthritis patients were enrolled in a cross-sectional study for a period of 11 months. Comorbidities were assessed using three indicators: (i) the total number of comorbidities; (ii) the Charlson comorbidity index; and (iii) the functional comorbidity index. Disease activity was assessed using the Disease Activity Score 28. Functional capacity was measured using the Health Assessment Questionnaire, and mobility was measured using Timed Up and Go Test and Five-Times-Sit-to-Stand Test. Statistical analysis was performed using a stepwise log-linear multiple regression with a significance level of 5%.

**Results:** In the final model, only comorbidity was associated with mobility limitation. The functional comorbidity index score explained 19.1% of the variability of the Five-Times-Sit-to-Stand Test (coefficient of determination  $R^2 = 0.191$ ) and 19.5% of the Timed Up and Go Test variability ( $R^2 = 0.195$ ). With regard to functional disability, the associated factors were comorbidity and disease activity, which together explained 32.9% of the variability of the Health Assessment Questionnaire score (adjusted  $R^2 = 0.329$ ).

**Conclusion:** Comorbidities were associated with mobility limitation and functional disability in rheumatoid arthritis patients. The functional comorbidity index proved to be an appropriate comorbidity indicator to determine this association.

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## Influência das comorbidades na capacidade funcional de pacientes com artrite reumatoide

### RESUMO

**Palavras-chave:**

Artrite reumatoide  
Comorbidades  
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**Objetivos:** Investigar a associação das comorbidades com a limitação da mobilidade e com a incapacidade funcional em pacientes com artrite reumatoide, bem como identificar o indicador de comorbidade mais apropriado para determinar essa associação.

**Métodos:** Em um estudo transversal foram incluídos 60 pacientes com artrite reumatoide por um período de 11 meses. Comorbidades foram avaliadas por meio de três indicadores: (i) número total de comorbidades; (ii) índice de comorbidade de Charlson; e (iii) índice de comorbidade funcional. A atividade da doença foi avaliada pelo Índice de Atividade da Doença 28. A capacidade funcional foi mensurada pelo Questionário de Avaliação da Saúde, e a mobilidade foi mensurada pelos testes senta-levanta da cadeira cinco vezes e *timed get up and go*. A análise estatística foi realizada através de regressão múltipla log-lineal Stepwise com nível de significância de 5%.

**Resultados:** No modelo final, apenas o fator comorbidades esteve associado à mobilidade. O escore no índice de comorbidade funcional explicou 19,1% da variabilidade do teste senta-levanta da cadeira cinco vezes (coeficiente de determinação  $R^2 = 0,191$ ) e 19,5% da variabilidade do *timed get up and go* ( $R^2 = 0,195$ ). Em relação à incapacidade funcional, os fatores associados foram o fator comorbidades e a atividade da doença que em conjunto explicaram 32,9% da variabilidade do escore do Questionário de Avaliação da Saúde ( $R^2$  ajustado = 0,329).

**Conclusão:** As comorbidades estão associadas com a limitação da mobilidade e a incapacidade funcional em pacientes com artrite reumatoide. O índice de comorbidade funcional demonstrou ser um indicador de comorbidade apropriado para determinar essa associação.

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### Introduction

Rheumatoid arthritis (RA) is a chronic, progressive, systemic inflammatory disease which mainly affects the synovial membrane of joints, which may cause general impairment in functional status of patients.<sup>1</sup>

The study of functional disability and associated factors in RA is relevant, since the functional status is related to other clinical outcomes in this population, such as mortality,<sup>2,3</sup> loss of work capacity,<sup>4,5</sup> and use of health resources.<sup>6,7</sup>

There is increasing evidence pointing to the effect of the comorbidity factor in functional disability in patients with RA. Radner et al.<sup>8,9</sup> demonstrated the negative impact of comorbidities in all areas of functional capacity, regardless of the level of disease activity. Michaud et al.,<sup>10</sup> in a longitudinal study, showed that age over 65 years and presence of comorbidities were the main predictors of functional capacity loss in RA and that these factors not associated with the treatment of RA had the greatest effect in score progression, as measured by the Health Assessment Questionnaire (HAQ), in comparison with the effect of the treatment with biological agents.

The study of Norton et al.<sup>11</sup> showed a considerable prevalence of comorbidities at the time of diagnosis of RA and that it increases over the course of the disease. After a 15-year follow-up, 81% of RA patients presented comorbidities and, in addition, presence of comorbidities was associated with mortality and loss of functional capacity in these patients.<sup>11</sup> In an 11-year longitudinal study, Van den Hoek et al.<sup>12</sup> observed that somatic comorbidities and depression were associated with decreased functional capacity.

The published literature reveals that comorbidities are common conditions in this population, and on average each patient with RA has 1.6 comorbidities; and this number increases with age.<sup>13,14</sup> In this sense, there has been a growing interest from researchers in studying comorbidities and their impact on different clinical outcomes in RA, such as hospitalization, mortality, functional capacity and medical costs.<sup>13–15</sup>

Comorbidity is defined as a disease or medical condition that coexists with the disease of interest, identified, in this case as RA.<sup>13</sup> There are several ways to assess comorbidities.<sup>13,15</sup> The assessment of the impact of comorbidities in different clinical outcomes in patients with RA is usually performed through a simple counting of the number of existing comorbidities from a specific list established by researchers.<sup>15</sup> Using such an approach, each condition is equally scored, irrespective of its weight.<sup>15</sup>

Another way of measuring comorbidities involves the use of validated comorbidity indexes for predicting a certain clinical outcome.<sup>13</sup> Most of comorbidity indexes are designed to determine mortality, which is the case of Charlson comorbidity index (CCI)<sup>16</sup> and Kaplan–Feinstein index.<sup>17</sup> CCI has been developed by Charlson et al.,<sup>16</sup> and contains a list of 19 conditions, each of them having a weight according to its one-year risk of death. There is also a comorbidity index specifically developed to predict functionality, the functional comorbidity index (FCI).<sup>18</sup> FCI was developed by Groll et al.<sup>18</sup> using a North-American population affected mainly by orthopedic problems and that used the Quality of Life Questionnaire (SF-36) to quantify the subjects' functional capacity.

Studies pointing to an association between comorbidities and functional disability<sup>8–12</sup> evaluated the functionality

through the Health Assessment Questionnaire (HAQ) and/or by the physical domain component of the Quality of Life Questionnaire (SF-36); these tools were developed to assess the functional capacity of patients in activities of daily living. None of these studies has added mobility tests in the assessment of functionality. Thus, the mentioned studies<sup>8-12</sup> did not analyze the association of comorbidities with mobility limitation in patients with RA.

The purpose of this study was to investigate the association of comorbidities, measured by three indicators of comorbidity (total number of comorbidities, CCI and FCI) with mobility limitation and functional disability in patients with RA, as well as to identify which indicator of comorbidity is most appropriate to determine this association.

## Methods

### Study design and participants

A cross-sectional study including patients with RA was carried out to evaluate the association of comorbidities with mobility limitation and functional disability in these individuals.

Sixty patients participated in the study and were recruited from the Rheumatology Outpatient Clinic of Hospital das Clínicas, Faculdade de Medicina, Universidade Federal de Goiás (UFG) in the city of Goiânia, from September 13, 2012 to August 22, 2013.

At inclusion, all patients met the American College of Rheumatology (ACR 1987) criteria for RA.<sup>19</sup> Those subjects with hospitalization due to acute infection in the period of six months prior to the interview and with presence of some temporary disability making it impossible to carry out mobility tests (e.g., foot fracture) were excluded. The study was approved by the Research Ethics Committee of the Hospital das Clínicas (UFG) and all participants signed an informed consent form.

### Assessment tools

At the time study enrollment, patients completed a standardized questionnaire, including details of: (i) demographic factors such as age, gender and self-reported race; (ii) presence of a positive rheumatoid factor (RF); (iii) disease duration; (iv) existing comorbidities; (v) history of falls in a 12-month period preceding the interview; (vi) use of walking aids; (vii) medications in use; (viii) lifestyle habits (i.e., smoking status – current or former smoker, never smoked) and physical activity practice. This questionnaire was supplemented with information from participants' medical records.

In this standardized questionnaire, comorbidities were evaluated through a list of chronic diseases, according to those covered by CCI<sup>16</sup> and FCI.<sup>18</sup> The presence of other chronic diseases not included in these indexes but reported by patients and confirmed in their medical records was also registered. From these collected data, comorbidities were measured by three indicators: (i) total number of comorbidities (NCom); (ii) CCI score; and (iii) FCI score.

CCI is composed of a list of 19 comorbidities, and each disease has a weight ranging from 1 to 6, established according

to its one-year risk of death.<sup>16</sup> The score obtained in CCI is assigned by summing all comorbidities present with their respective weights, resulting in a number which can vary from 0 to 33.<sup>16</sup>

FCI is a list of 18 comorbidities, with no difference in weight among them.<sup>18</sup> FCI score is obtained by summing all comorbidities, ranging from 0 to 18.<sup>18</sup>

In the "connective tissue diseases" item contemplated in CCI, the tool considered as "comorbid condition" the presence of systemic lupus erythematosus, polymyositis, mixed connective tissue disease and polymyalgia rheumatica, as suggested by Charlson et al.<sup>16</sup> On the other hand, in FCI, in its "arthritis" item, only presence of osteoarthritis was considered.

Disease activity was assessed by the Disease Activity Score based on 28 joints and on ESR value (DAS-28/ESR).<sup>20</sup>

To assess mobility limitation, the following tests were applied: (i) Five-Times-Sit-to-Stand Test (STS)<sup>21</sup> and (ii) Timed Up and Go Test (TUG).<sup>22</sup>

STS test is used to evaluate muscle strength of lower limbs, mobility and risk of falls.<sup>21,23,24</sup> This test, measures the fastest time to stand and sit five consecutive times with arms folded. The longer the time spent to complete the test, the worse the individual mobility.<sup>21</sup>

TUG test is used to identify patients at risk of falls and with mobility restriction.<sup>22,25</sup> To perform this test, the patient is timed while they rise from an arm chair, walk at a comfortable and safe pace to a line on the floor 3 m away, turn and walk back to the chair and sit down again. The greater the time, the worse the individual mobility.<sup>22</sup>

Functional disability was measured by the Health Assessment Questionnaire (HAQ).<sup>26,27</sup>

### Statistical analysis

Continuous data are shown as mean (standard deviation [SD]) or median (interquartile range [IQR]), where appropriate, and categorical data were shown as frequency (percentages).

A regression analysis using quasi-likelihood model,<sup>28</sup> with variance function proportional to the mean and logarithmic link function, was carried out, in order to investigate the association of indicators of comorbidity (NCom, CCI and FCI) with mobility limitation (STS and TUG) and functional disability (HAQ). To monitor the effect of confounding variables, a linear regression model using stepwise regression was constructed. The potential confounding variables chosen were: age, gender, disease duration, physical activity, positive RF test, DAS-28/ESR score.

The final model of multiple regression analysis for the dependent variables STS, TUG and HAQ was called stepwise log-linear regression.

The comparison between comorbidity indicators, with the aim to establish the most appropriate tool to determine the association of comorbidities with mobility limitation and functional disability in patients with RA, was performed by comparing the coefficients of determination ( $R^2$ ) of adjusted models against each indicator.<sup>29</sup>

The level of statistical significance was 5%. The software R version 3.0.1 was used in data analysis.

**Table 1 – Characteristics of participants.**

Characteristics	Values
<b>Demographics</b>	
Age, mean (SD) (min–max), years	59 (9.1) (43–80)
Women, n (%)	53 (88.3%)
Self-reported race, n (%)	
Caucasian	26 (43.3%)
African	11 (18.3%)
Brown	23 (38.3%)
Positive RF, n (%)	43 (71.7%)
Disease duration, mean (SD) (min–max), years	11.5 (8.9) (0.4–30)
History of falls, n (%)	16 (26.7%)
Use of walking aids, n (%)	8 (13.3%)
Smokers or former smokers, n (%)	37 (61.7%)
Practitioners of physical activity, n (%)	10 (16.7%)
<b>Evaluation of comorbidities</b>	
NCom score, mean (SD) (min–max)	3.6 (2.1) (0–8)
CCI score, mean (SD) (min–max)	0.25 (0.51) (0–2)
FCI score, mean (SD) (min–max)	2.0 (1.5) (0–5)
<b>Disease activity assessment</b>	
ESR, median (IQR), mm/hour	22.5 (10.5–34.5)
DAS-28/ESR, mean (SD) (min–max)	3.7 (1.4) (0.5–6.8)
<b>Mobility assessment</b>	
STS, median (IQR), seconds	12.5 (10.5–20.4)
TUG, median (IQR), seconds	12.8 (10.9–16.3)
<b>Assessment of functional capacity</b>	
HAQ score, mean (SD) (min–max)	1.07 (0.76) (0–3)

SD, standard deviation; IQR, interquartile range; RF, rheumatoid factor; NCom, total number of comorbidities; CCI, Charlson comorbidity index; FCI, functional comorbidity index; ESR, erythrocyte sedimentation rate; DAS-28/ESR, Disease Activity Score based on 28 joints and on ESR value; STS, Five-Times-Sit-to-Stand Test; TUG, Timed Up and Go Test; HAQ, Health Assessment Questionnaire.

## Results

### Clinical features of participants

Sixty patients participated in the study. Patient characteristics are summarized in **Table 1**.

**Table 2** depicts the comorbidities that make up CCI and FCI, as well as the number of patients affected by each comorbidity present in these indexes. The prevalence of comorbidities given by CCI was 21.7%, i.e., 13 patients had at least one comorbidity, according to this indicator. In the other hand, the evaluation by FCI showed that 49 (81.7%) patients had at least one comorbidity.

Patients had other comorbidities, besides those shown in **Table 2**, such as fibromyalgia, anemia, epilepsy, hypothyroidism, secondary Sjögren syndrome and cardiac arrhythmias. Thus, the prevalence of comorbidities given by NCom was 90%, i.e., 54 patients had at least one comorbidity.

### Analysis of the association of comorbidities with mobility limitation and functional disability

**Table 3** summarizes log-linear regression univariate analyses of factors associated with mobility limitation (STS and TUG) and functional disability (HAQ) in patients with RA.

The independent factors that significantly explain part of the variability of STS in the univariate model were: age (coefficient of determination  $R^2 = 0.074$ ;  $p = 0.023$ ), male gender ( $R^2 = 0.058$ ;  $p = 0.049$ ), disease duration ( $R^2 = 0.056$ ;  $p = 0.042$ ), NCom score ( $R^2 = 0.121$ ;  $p = 0.005$ ) and FCI score ( $R^2 = 0.191$ ,  $p < 0.001$ ). The independent factors associated with variability of TUG in the univariate model were: age ( $R^2 = 0.063$ ;  $p = 0.052$ ), NCom score ( $R^2 = 0.144$ ,  $p = 0.005$ ) and FCI score ( $R^2 = 0.195$ ;  $p = 0.001$ ). On the other hand, the independent factors associated with variability of HAQ in the univariate model were: disease duration ( $R^2 = 0.047$ ;  $p = 0.040$ ), NCom score ( $R^2 = 0.077$ ;  $p = 0.012$ ), FCI score ( $R^2 = 0.178$ ,  $p < 0.001$ ) and DAS-28/ESR ( $R^2 = 0.244$ ,  $p < 0.001$ ) (**Table 3**).

The log-linear regression curves of the main independent factors associated with variability of mobility (STS and TUG) and functional capacity (HAQ) are shown in **Fig. 1**.

In the final model of log-linear regression using stepwise regression with respect to factors associated with mobility limitation (STS and TUG), only the “comorbidities” factor, evaluated by FCI, was significant (**Table 4**). The exponent values of beta coefficient ( $\exp\beta$ ) for the association between FCI and STS was 1.128 (95% confidence interval [95% CI] 1.062–1.201;  $p < 0.001$ ); and for TUG was 1172 (95% CI 1.073–1.285;  $p = 0.001$ ) (**Table 4**).

As to factors associated with functional disability (HAQ) in the final model, the following variables were significant: disease activity, measured by DAS-28/ESR ( $\exp\beta = 1.279$ , 95% CI 1.132–1.451;  $p < 0.001$ ) and comorbidities as assessed by FCI ( $\exp\beta = 1.167$ , 95% CI 1.054–1.290;  $p = 0.005$ ) (**Table 4**). FCI and DAS-28/ESR factors were significant to explain, together, 32.9% of the variability of HAQ score (adjusted  $R^2 = 0.329$ ) (**Table 4**).

### Comparison among comorbidity indicators

FCI proved to be the most appropriate comorbidity indicator to determine the association of comorbidities with mobility limitation (STS and TUG) and functional disability (HAQ) in patients with RA, according to values of the coefficients of determination ( $R^2$ ) of comorbidity indicators (NCom, CCI and FCI) (**Table 3**).

The  $R^2$  value for an association between FCI and STS was 0.191; for TUG was 0.195; and for HAQ was 0.178. On the other hand,  $R^2$  between NCom and STS was 0.121; for TUG,  $R^2 = 0.144$ ; and for HAQ,  $R^2 = 0.077$ . And the  $R^2$  value between CCI and STS was 0.021; for TUG,  $R^2 = 0.000$ ; and for HAQ,  $R^2 = 0.000$  (**Table 3**).

## Discussion

This study demonstrated the association of comorbidities with mobility limitation and functional disability in patients with RA and indicated FCI as an appropriate comorbidity index in determining this association.

In this study, the multivariate analysis of factors associated with mobility limitation showed that only the factor “comorbidities”, assessed by FCI score, contributed to explain some of the variability in STS and TUG test performance. FCI explained 19.1% of the variability of STS and 19.5% of the variability of TUG. The percentage of variability of HAQ score explained by the variables used in the final model

**Table 2 – Comorbidities that compose the Charlson comorbidity index and the functional comorbidity index and number of affected patients.**

Comorbidities	n
Osteoporosis	28
Arthritis (osteoarthritis) <sup>b</sup>	27
Visual deficits (cataract, glaucoma, macular degeneration) <sup>b</sup>	17
Obesity and/or BMI >30 kg/m <sup>2</sup> <sup>b</sup>	12
Upper gastrointestinal tract disease (ulcer, hernia, reflux) <sup>a,b</sup>	11
Diabetes mellitus type 2 <sup>a,b</sup>	9
Depression <sup>b</sup>	5
Anxiety or panic syndrome <sup>b</sup>	3
Auditory deficits (difficulty hearing, even with hearing aids) <sup>b</sup>	3
Congestive heart failure <sup>a,b</sup>	1
Peripheral vascular disease <sup>a,b</sup>	1
Cerebrovascular disease <sup>a,b</sup>	1
Chronic obstructive pulmonary disease <sup>a,b</sup>	1
Asthma <sup>b</sup>	1
Neurological disease (Parkinson's disease) <sup>b</sup>	1
Connective tissue disease <sup>a</sup>	0
Liver disease (mild, moderate or severe) <sup>a</sup>	0
Angina <sup>b</sup> /myocardial infarction <sup>a,b</sup>	0
Degenerative disk disease (spinal stenosis, or severe chronic low back pain) <sup>b</sup>	0
Dementia <sup>a</sup>	0
Hemiplegia <sup>a</sup>	0
Moderate or severe kidney disease <sup>a</sup>	0
Non-metastatic solid tumor <sup>a</sup>	0
Leukemia <sup>a</sup>	0
Lymphoma <sup>a</sup>	0
Solid metastatic tumor <sup>a</sup>	0
AIDS <sup>a</sup>	0

CCI, Charlson comorbidity index; FCI, functional comorbidity index; BMI, body mass index; AIDS, acquired immunodeficiency syndrome.

<sup>a</sup> Comorbidity present in CCI.

<sup>b</sup> Comorbidity present in FCI.

was 32.9%; and “disease activity”, measured by DAS-28/ESR, was the main variable responsible for explaining part of this variability, followed by the factor “comorbidities”, assessed by FCI. In the final model – after FCI and DAS-28/ESR had explained part of the variability of HAQ score, and after FCI had explained part of the variability of STS and TUG – the remaining analyzed variables did not contribute significantly to explain the mobility limitation and functional disability observed, showing the importance of the factor “comorbidities” in the face of other variables, such as age, gender, disease duration, physical activity and a positive RF.

Functional disability in RA is characterized by its multidimensionality, being associated with multiple factors, aside the factor “comorbidities”,<sup>8-12</sup> such as pain,<sup>30,31</sup> reduced joint mobility,<sup>30</sup> articular cartilage destruction,<sup>32</sup> decreased muscle strength,<sup>31</sup> disease duration<sup>33</sup> and disease activity.<sup>31</sup>

The association of comorbidities with functional disability in patients with RA has been shown in some studies,<sup>8-12</sup> in which the authors assessed the functional capacity of patients through activities of daily living questionnaires (HAQ and/or SF-36).

To our knowledge, this is the first study on RA patients to determine the association of comorbidities with mobility limitation measured by timed tests (STS and TUG).

The fact that RA is responsible for a general impairment in terms of functional status of patients, causing impairment in activities of daily living, muscle strength and mobility and increasing the risk of falls, emphasizes the importance of mobility studies in this population.<sup>31,34,35</sup>

The risk of falls can be evaluated through the time spent to perform STS and TUG tests<sup>24,25,36</sup> and, in parallel, studies have shown a worse performance on these tests in patients with RA, when compared to the population without RA.<sup>37,38</sup>

Böhler et al.<sup>36</sup> showed that disease activity and functional disability (HAQ) in patients with RA correlated with worse performance in STS and TUG tests; but the authors did not evaluate the association of comorbidities with risk of falls. Jamison et al.<sup>39</sup> demonstrated that patients with RA with a history of falls exhibited a higher number of comorbidities than those without such history, drawing attention to the association between comorbidities and the occurrence of falls in this population. As occurred in the study by Böhler et al.,<sup>36</sup> Jamison et al.<sup>39</sup> have not studied the association of comorbidities with performance tests for fall risk assessment (STS and TUG).

The study of factors associated with risk of falls in patients with RA is a relevant task, since the risk of falls in these patients is increased.<sup>34-37,39,40</sup> Falls, in turn, are related to the occurrence of fractures; and this contingency has the effect of compromising the functionality, worsening the prognosis of rheumatologic diseases.<sup>35</sup> Also noteworthy is an increased prevalence of osteoporosis in patients with RA.<sup>11,13,15</sup> In our study, 28 patients (47%) had osteoporosis, and this is a comorbidity which increases fracture risk.<sup>37,41</sup>

In the present study, we evaluated the association of comorbidities with mobility limitation and functional disability in patients with RA by computing the total number of comorbidities (NCom) and through the score obtained with the use of CCI and FCI.

FCI proved to be the most appropriate comorbidity indicator in determining this association, when compared to NCom and CCI in our sample. The association of comorbidities evaluated by FCI was stronger versus that measured by NCom. This result was expected, since FCI has been specially developed as a tool to predict functionality.<sup>18</sup> This finding is highlighted by the fact that RA patients studied often presented with comorbidities present in FCI, these being conditions clearly associated with functional impairment.<sup>18</sup>

On the other hand, the lack of association of those comorbidities assessed by CCI in our sample, notwithstanding the demonstration of this relationship with the use of CCI in other studies,<sup>8,9,11</sup> can be explained in two ways. First, we must consider that CCI was primarily developed as an instrument to predict mortality.<sup>16</sup> And secondly, we did not find in our sample a reasonable amount of comorbidities pertaining to the calculation of ICC, and this fact may have hampered the ability of this index in predicting functionality in our patients. Perhaps this scenario would require a larger sample, as the comorbidities that make up CCI are not those most often found in outpatients with RA.<sup>8,9,11</sup>

Our study has some limitations with respect to the form of identification of comorbidities, which was based on patients

**Table 3 – Analysis of independent factors associated with mobility limitation (Five-Times-Sit-to-Stand Test and Timed Up and Go Test) and functional disability (Health Assessment Questionnaire).**

Independent variables		Dependent variables		
		STS	TUG	HAQ
Age, years	R <sup>2</sup>	0.074 <sup>a</sup>	0.063 <sup>a</sup>	0.002
Male gender	R <sup>2</sup>	0.058 <sup>a</sup>	0.010	0.000
Positive RF	R <sup>2</sup>	0.000	0.000	0.000
Disease duration, years	R <sup>2</sup>	0.056 <sup>a</sup>	0.020	0.047 <sup>a</sup>
Physical activity	R <sup>2</sup>	0.000	0.003	0.013
NCom score	R <sup>2</sup>	0.121 <sup>b</sup>	0.144 <sup>b</sup>	0.077 <sup>b</sup>
CCI score	R <sup>2</sup>	0.021	0.000	0.000
FCI score	R <sup>2</sup>	0.191 <sup>b</sup>	0.195 <sup>b</sup>	0.178 <sup>b</sup>
DAS-28/ESR	R <sup>2</sup>	0.033	0.056	0.244 <sup>b</sup>

STS, Five-Times-Sit-to-Stand Test; TUG, Timed Up and Go Test; HAQ, Health Assessment Questionnaire; R<sup>2</sup>, coefficient of determination; RF, rheumatoid factor; NCom, total number of comorbidities; CCI, Charlson comorbidity index; FCI, functional comorbidity index; DAS-28/ESR, Disease Activity Score based on 28 joints and on ESR value.

Univariate log-linear regressions.

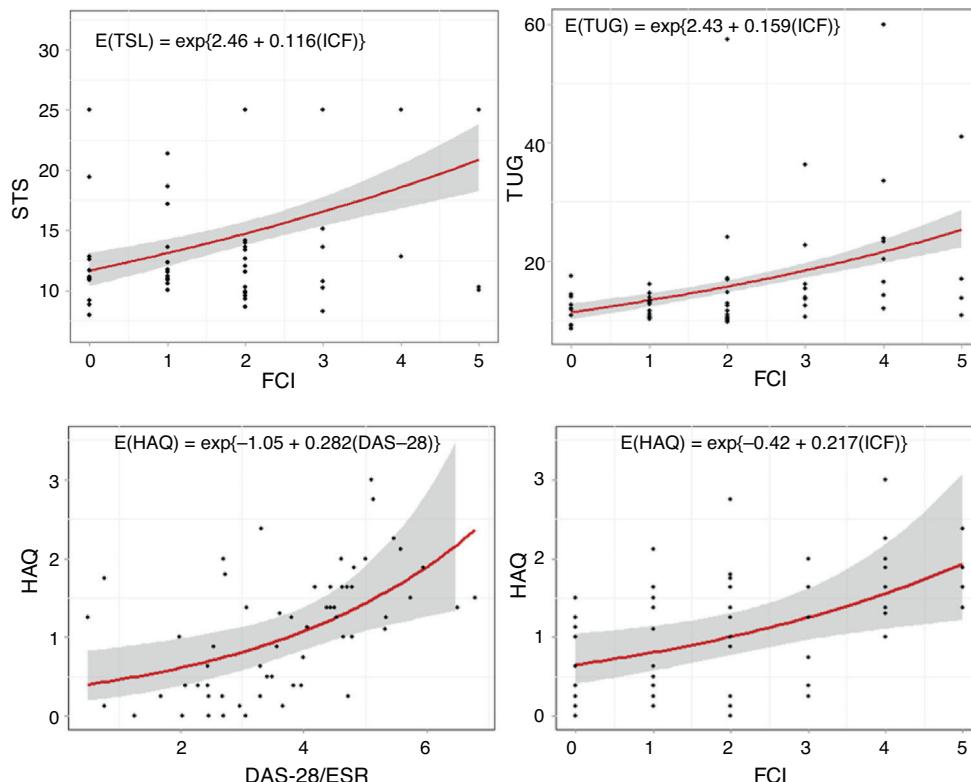
<sup>a</sup> Significant  $p \leq 0.05$ .

<sup>b</sup> Significant  $p \leq 0.01$ .

reports and on medical records; thus, this identification was subject to underdiagnosis, when compared to a systematic search of associated diseases. In addition, in NCom indicator all comorbidities reported by patients and present in their medical records were considered, without establishing specific criteria on which diseases would be, or not, taken into

account. This method may have hampered the ability of NCom indicator in determining the association with functional disability in our sample, whereas other studies have stressed this association.<sup>10–12</sup>

Thus, it becomes apparent the importance of knowing what are the main comorbidities that ultimately influence the



**Fig. 1 – Log-linear regression curves of the main predictors of mobility variability (Five-Times-Sit-to-Stand Test and Timed Up and Go Test) and functional capacity (Health Assessment Questionnaire). Scatter plots with log-linear regression curves.** STS, Five-Times-Sit-to-Stand Test; TUG, Timed Up and Go Test; HAQ, Health Assessment Questionnaire; FCI, functional comorbidity index; DAS-28/ESR, Disease Activity Score based on 28 joints and on ESR result.

**Table 4 – Impact of comorbidity (functional comorbidity index) and disease activity (Disease Activity Score based on 28 joints and on ESR value) in mobility (Five-Times-Sit-to-Stand Test and Timed Up and Go Test) and functional capacity (Health Assessment Questionnaire).**

Dependent variables	Independent variables	$\exp(\beta)$	95% CI	p	Adjusted R <sup>2</sup>
STS	FCI	1.128	1.062–1.201	<0.001	0.191
TUG	FCI	1.172	1.073–1.285	0.001	0.195
HAQ	FCI	1.167	1.054–1.290	0.005	0.329
	DAS-28/ESR	1.279	1.132–1.451	<0.001	

STS, Five-Times-Sit-to-Stand Test; TUG, Timed Up and Go Test; HAQ, Health Assessment Questionnaire;  $\exp(\beta)$ , exponential of beta coefficient; 95% CI, confidence interval of 95%; R<sup>2</sup>, coefficient of determination; FCI, functional comorbidity index; DAS-28/ESR, Disease Activity Score based on 28 joints and on ESR value.

Multivariate log-linear regression model using stepwise regression.

functionality in patients with RA; with this, we can obtain more suitable criteria, when establishing the comorbidities associated with functional status of this population.

This study has relevance for pointing out the effect of comorbidities on limiting the mobility and, hence, on increasing the risk of falls in patients with RA; it must be taken into account that the tests used (STS and TUG) are recommended in the fall risk assessment. In addition, the study also draws attention to the use of FCI as an alternative tool to evaluate the impact of comorbidities on functionality of patients with RA.

In conclusion, the comorbidities in patients with RA are associated with mobility limitation and functional disability; and the indicator FCI is an appropriate comorbidity index in the determination of this association.

## Conflicts of interest

The authors declare no conflicts of interest.

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