Physical functioning in Ankylosing Spondylitis patients

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Chapter 6

Continuous improvement of physical functioning in ankylosing spondylitis patients after the start of TNF-inhibitors: a three year follow up of physical functioning and spinal mobility

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Abstract

Objectives: (i) To establish the 3-year outcome and course of physical functioning and spinal mobility impairments in patients routinely treated with TNFi and (ii) to find predictors thereof.
Methods: AS patients eligible for TNFi were followed in a 3-year prospective observational study. Prediction models were developed with linear-mixed-modelling. BASFI and BASMI were used as outcome measures for physical functioning and spinal mobility.
Results: At baseline, 257 patients were included and treated with etanercept (*n*=174) or adalimumab (*n*=83). Physical functioning improved significantly during the first 24-weeks after the start of TNFi. The BASFI-score decreased from 5.4±2.4 to 3.3±2.6 in week 24, and stabilised thereafter (BASFI year three: 3.6±2.5). The BASMI showed a stable course over time. Lower baseline BASFI and BASMI predicted a better level of physical functioning and spinal mobility after 3 years of TNFi-therapy. Other predictors for a better 3-year outcome and course of physical functioning included absence of comorbidity, physical activity, younger age, and lower BMI at baseline.
Conclusions: Physical functioning in routinely TNFi treated AS patients improved up to 24-weeks and stabilised thereafter. Spinal mobility showed a stable course over time. Predictors for the outcome and course of physical functioning after 3-years of TNFi-treatment included baseline BASFI, BASMI, comorbidity, physical activity, and BMI. The identification of these risk factors can be helpful when considering additional treatment options, such as physiotherapy or weight-reduction, to prevent further decline. In addition, these results suggest that the optimal time-point for the evaluation of treatment effects should be at 6 instead of 3 months.

Introduction

Ankylosing spondylitis (AS) is a chronic rheumatic disease characterised by inflammation, back pain, and stiffness that predominantly affects the sacroiliac joints (SI-joints) and axial skeleton. The disease can lead to reduced spinal mobility and substantial limitations in physical functioning [1, 2]. The degree of limitations in physical functioning are the main component of health-related quality of life and work disability, and the main predictor of medical costs [3, 4]. Therefore, maintaining physical functioning is the main aim of AS management, alongside controlling disease activity. Tumor necrosis factor inhibitors (TNFi), such as adalimumab and etanercept, are effective in AS [5, 6], and knowledge of predictors of a good response is accumulating. More insight into risk factors associated with limitations in physical functioning in patients receiving TNFi can provide tools to select eligible patients for and give direction to additional treatment options. However, thus far only limited information is available on the course and predictors of limitations in physical functioning and spinal mobility in AS patients receiving TNFi. Most studies hitherto concern randomised controlled trials (RCTs) instead of inception cohorts, aim to predict response to treatment instead of limitations in functioning or spinal mobility. Some other studies are based on cross-sectional or short-term (< 1 year) results.

RCTs showed a marked and sustained improvement of physical functioning after TNFi treatment [7]. However, in clinical practice the course may differ considerably between patients. In contrast to patient populations in RCTs, patients in observational studies are selected based on less strict inclusion and exclusion criteria and are therefore more heterogeneous. One of the sparse observational studies that looked at predictors of limitations in physical functioning showed a greater improvement in physical functioning after 6 months of TNFi therapy in female patients, with higher baseline Bath AS Functional Index (BASFI) and concurrent use of disease modifying anti-rheumatic drugs (DMARDs) [8].

In patients receiving treatment with non-steroidal anti-inflammatory drugs (NSAIDs), limitations in physical functioning on average increase over time, while the course of physical functioning is highly variable. Risk factors for a more marked decrease in physical functioning include male gender, age, disease activity, and peripheral joint disease. Life-style factors (e.g., smoking, lack of exercise) have also been associated with diminished physical functioning [3, 4, 9-15]. Another potential risk factor for functional decline is the presence of concomitant diseases, such as cardiovascular disease (CVD). There is accumulating evidence that AS patients have a significantly increased CVD risk, due to atherosclerotic disease as well as AS-specific cardiac manifestations [16].

More insight into the course of physical functioning and spinal mobility in routinely (i.e., in daily clinical practice rather than in a RCT) TNFi treated AS patients is important for both clinicians and patients when considering treatment options. Identifying risk factors for a more marked decline in physical functioning or spinal mobility may enhance the choice of

additional treatment options to prevent further decline. More observational studies exploring the long-term course and risk factors for decline in physical functioning and spinal mobility in AS patients receiving TNFi in daily clinical care are necessary. Therefore, the aims of this study are to (i) establish the 3-year outcome and course of physical functioning and spinal mobility impairments and (ii) find predictors thereof in AS patients routinely treated with TNFi.

Patient and methods

Study population

Consecutive AS patients who were eligible for TNFi treatment were recruited from 2004-2013 at Reade, a large outpatient centre for rheumatology in Amsterdam, and included in a prospective observational cohort study. The primary aim of this study was to monitor the long-term efficacy and safety of TNFi in the treatment of AS. The inclusion criteria were age ≥18 years, diagnosis of AS (according to the modified New York criteria [17]), TNFi-naïve, eligibility for TNFi therapy according to the ASAS/EULAR guidelines [5, 18], and sufficient command of the Dutch language. Patients were treated either with etanercept (50 mg subcutaneously (SC) once weekly) or adalimumab (40 mg SC once every 2 weeks), in accordance with the clinical decision of the treating rheumatologist. Patients were assessed every 3 months during the first 2 years and every 6 months thereafter. The Institutional Review Board and medical ethical committee approved the study. All patients gave written informed consent.

Outcome measures

The BASFI was used to define limitations in physical functioning. It is a disease specific, self-reported, reliable, and responsive questionnaire consisting of 10 items regarding physical functioning in daily life. The mean of 10 item-scores completed on a numerical rating scale (NRS) is the BASFI-score (0-10). A higher score corresponds with more limitations in physical functioning [19].

The Bath AS Metrology Index (BASMI) was used to define spinal mobility. It consists of five clinical measurements that reflect axial and hip mobility (lumbar side flexion, tragus-to-wall distance, lumbar flexion (modified Schober), intermalleolar distance, and cervical rotation). Each item is graded on an 11-point answer scale and the average of the five measurements is used as outcome (0-10). A higher score corresponds with more limitations in mobility [20, 21].

Predictors

Based on literature and expert opinion [7-15], 18 baseline variables were selected: age (years); disease duration at the start of TNFi treatment (years); gender; Body Mass Index (BMI, kg/m^2); HLA-B27 status; three disease activity parameters: C-reactive protein (CRP, mg/dl), Erythrocyte Sedimentation Rate (ESR, mm/h), and Bath AS Disease Activity Index (BASDAI, 0-10) [22]; two questions on spinal pain (pain at night and pain last week, 0-10); peripheral enthesitis: Maastricht AS Enthesitis Score (MASES, 0-13) [23]; concomitant use of NSAIDs; comorbidity (i.e., objectified cerebrovascular accident (CVA), transient ischemic

attack (TIA), myocardial infarction (MI), and/or diabetes mellitus (DM)); smoking status (never, ever); self-reported peripheral arthritis (yes, no); BASFI (0-10); BASMI (0-10); and exercise behaviour (yes, no physically active). Patients were coded as being physically active if they were regularly participating in an AS exercise group and/or performing exercises or sports individually (e.g., cycling, fitness, running, soccer, swimming, etc.) (self-report).

Statistical analysis

A longitudinal analysis was used to determine the 3-year outcome, course, and predictors of physical functioning and spinal mobility after the start of TNFi therapy in AS patients in daily clinical practice. Separate models for physical functioning (0-24 weeks and 24 weeks – 3-year follow-up) and spinal mobility were developed using linear mixed models with a random intercept. Longitudinal data sets are characterised by repeated observations in the same patients with a high variability between patients and rather low variability within patients. A mixed model analysis is a regression technique that corrects for the dependency of the repeated measures on the same individual. An advantage of the analysis of longitudinal data with mixed modelling is that all longitudinal data are used and unequal numbers of repeated measurements and unequal time intervals are allowed. Furthermore, mixed modelling analysis is flexible in handling missing data and applying multilevel analysis to an incomplete dataset is even better than applying imputation methods [24]. Therefore, missing data was not imputed.

Model building

The 3-year outcome and course of limitations of physical functioning and spinal mobility were determined by including time (in weeks) as an independent variable in a model with BASFI or BASMI as dependent outcome measures. This model showed the average change in physical functioning or spinal mobility in weeks.

First patient characteristics (i.e., predictors) associated with the 3-year outcome of physical functioning or spinal mobility were identified (e.g., do males have a higher level of physical functioning after a certain period than females?). Therefore univariate regression analyses including time and baseline variables as independent variables and BASFI or BASMI as the dependent variable were performed first. Second, after controlling for collinearity, all associated variables with a univariate *p*-value below 0.20 were simultaneously entered in a multivariate model. To assess the combined association of the variables, a backward elimination procedure was used to remove non-significant predictors from the multivariate model (p-out > 0.10).

The same analyses was performed to identify the predictors of the 3-year course of physical functioning and spinal mobility. (e.g.: is the development of the BASFI score different over time for males *vs.* females? In other words, does the gender predictor interact with time and do males and females therefore have different slopes?). However, this univariate analyses included time, potential predictor, and the interaction between time and potential predictor. All potential predictors and interaction terms were entered in a multivariate model (p-in < 0.20) and backward elimination procedures were executed (p-out > 0.10). The models provided change scores for each of the variables included in the multivariable models,

which can be interpreted as both the difference between patients (cross-sectional) and the difference within a patient (longitudinal). The longitudinal interpretation of the change score is that one unit of difference in the predictor at baseline is associated with an average of ß units lower or higher BASFI or BASMI per week over time. All analyses were performed using SPSS version 18.0 (SPSS).

Results

Study population

The 257 patients included at baseline were predominantly male (67%) and the majority were treated with etanercept (68%) and the others used adalimumab. At time of the analysis, 112 (44%) of the patients had completed a 3-year follow-up. At baseline mean age was 43 (S.D.±11) years and patients had an active disease (mean BASDAI 5.8±1.8) (Table 1). Table 2 summarises the number of observations and the mean BASFI and BASMI-score at each time point.

Table 1: Baseline characteristics of study cohort of Ankylosing Spondylitis patients, *n*=257

Age start TNF, *years*	43.3 ± 11.5
Gender, *% male (n)*	67 (173)
BMI, *kg/m²*	26.0 ± 4.4
Disease duration at start TNFi therapy, *years*	9.7 ± 9.2
Presence HLA-B27, *% positive (n)*	75 (193)
Arthritis[a], *% yes (n)*	48 (124)
Comorbidity[b], *% yes (n)*	4 (9)
Smoking, *% ever (n)*	58 (150)
Physically active[c], *% yes (n)*	51 (132)
NSAIDs, *% yes (n)*	52 (134)
CRP, *mg/dl*	16.4 ± 20.9
ESR, *mm/h*	23.5 ± 20.7
BASDAI, *(0-10)*	5.8 ± 1.8
Pain at night, *(0-10)*	4.4 ± 2.6
Pain last week, *(0-10)*	4.5 ± 2.5
MASES, *(0-13)*	1.4 ± 2.4
BASFI, *(0-10)*	5.4 ± 2.4
BASMI, *(0-10)*	3.5 ± 2.3

Values are mean ± S.D. unless stated otherwise [a] Self-reported peripheral arthritis [b] Registered cerebrovascular accident, transient ischemic attack, myocardial infarction, and/or diabetes mellitus [c] coded as being physically active if participating in AS exercises group and/or performing exercises or sports individually (e.g., cycling, fitness, running, soccer, swimming, etc.) (self-report)

Three-year outcome and course of physical functioning and spinal mobility

The course of physical functioning showed a rapid and significant improvement during the first 24 weeks after the start of TNFi therapy and then stabilised (Figure 1 and Table 2). The mean BASFI decreased from 5.4 ± 2.4 at baseline to 3.3 ± 2.6 at 24 weeks follow-up and was 3.6 ± 2.5 at 3-year follow-up. For the identification of predictors of limitations in physical functioning, these two time periods were analysed separately: from baseline up to 24 weeks and from 24 weeks up to 3-year follow-up.

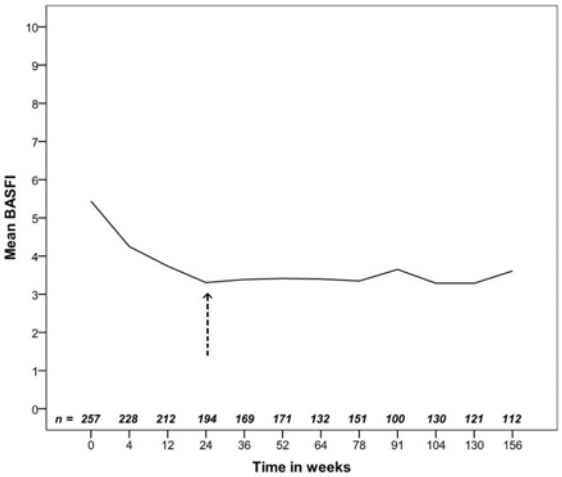

Figure 1: Course of physical functioning (BASFI) during 3-year follow-up in TNFi treated AS patients

Table 2: Number of observations and mean BASFI and BASMI-score at each time point

Time, weeks	***n***	**BASFI** Mean ± S.D.	**BASMI** Mean ± S.D.
0	257	5.4 ± 2.4	3.5 ± 2.3
4	228	4.3 ± 2.5	3.4 ± 2.1
12	212	3.7 ± 2.5	3.1 ± 2.2
24	194	3.3 ± 2.6	3.1 ± 2.2
36	169	3.4 ± 2.6	3.4 ± 2.2
52	171	3.4 ± 2.6	3.3 ± 2.2
64	132	3.4 ± 2.6	3.4 ± 2.2
78	151	3.4 ± 2.6	3.3 ± 2.3
91	100	3.7 ± 2.6	3.7 ± 2.4
104	130	3.3 ± 2.6	3.3 ± 2.4
130	121	3.3 ± 2.6	3.6 ± 2.2
156	112	3.6 ± 2.5	3.6 ± 2.3

Table 3: Results of the mixed model analysis of the longitudinal relationship between baseline predictors and physical functioning and spinal mobility

BASFI, 0 - 24 weeks	**Predictor, *unit***	**Change**	**95% CI**		**Sig.**
Model 1	Intercept	5.033	4.725	5.340	<0 .001
	Time, *weeks*	-0.074	-0.084	-0.063	<0 .001
Model 2	Intercept	-0.277	-0.964	0.410	ns
	Time, *weeks*	-0.078	-0.089	-0.067	< 0 .001
	Age start TNF, *years*	0.024	0.010	0.038	0.001
	MASES, *0-13*	0.077	0.005	0.149	0.036
	Comorbidity, *yes/no*	0.775	-0.059	1.610	0.068
	BASFI, *0-10*	0.763	0.695	0.831	<0 .001
Model 3	Intercept	0.144	-0.397	0.685	ns
	Time, *weeks*	-0.049	-0.079	-0.019	0.001
	Comorbidity, *yes/no*	0.451	-0.493	1.394	ns
	Physically active, *yes/no*	-0.005	-0.380	0.370	ns
	BASFI, *0-10*	0.876	0.787	0.964	< 0.001
	BASMI, *0-10*	0.032	-0.056	0.121	ns
	Time* comorbidity	0.092	0.032	0.151	0.003
	Time* physically active	0.023	0.001	0.045	0.038
	Time* BASFI	-0.012	-0.017	-0.007	< 0.001
	Time* BASMI	0.006	0.001	0.011	0.019
BASFI, 24 weeks - 3 years					
Model 1	Intercept	3.336	2.981	3.691	< 0.001
	Time, *weeks*	0.003	0.001	0.004	< 0.001
Model 2	Intercept	-0.198	-0.673	0.278	ns
	Time, *weeks*	0.002	0.001	0.004	0.001
	Age start TNF, *years*	0.011	-0.001	0.022	0.061
	BASFI[a], *0-10*	0.912	0.861	0.962	< 0.001
Model 3	Intercept	0.632	-0.626	1.891	ns
	Time, *weeks*	-0.025	-0.037	-0.014	< 0.001
	Age start TNF, *years*	0.003	-0.014	0.020	ns
	BMI, *kg/m²*	-0.029	-0.078	0.020	ns
	CRP [a], *mg/dl*	-0.005	-0.023	0.012	ns
	BASFI[a], *0-10*	0.984	0.909	1.058	< 0.001
	Time* Age	0.0002	0.000	0.000	0.049
	Time* BMI	0.001	0.001	0.001	< 0.001
	Time* CRP	0.0002	0.000	0.000	0.054
	Time* BASFI[a]	-0.001	-0.002	0.000	0.002

Table 3 continues on next page

Table 3: continued

BASMI	Predictor, *unit*	Change	95% CI		Sig.
Model 1	Intercept	3.316	3.063	3.569	< 0.001
	Time, *weeks*	-0.001	-0.002	0.000	0.207
Model 2	Intercept	-0.115	-0.607	0.376	ns
	Time, *weeks*	-0.001	-0.002	0.000	0.027
	Age start TNF, *years*	0.011	0.000	0.021	0.049
	BASFI, *0-10*	0.060	0.006	0.113	0.029
	BASMI, *0-10*	0.742	0.684	0.800	< 0.001
Model 3	Intercept	0.420	0.213	0.628	< 0.001
	Time, *weeks*	0.002	0.001	0.004	0.006
	BASMI, *0-10*	0.818	0.769	0.867	< 0.001
	Time * BASMI	-0.001	-0.001	0.000	< 0.001

[a] measured at 24 weeks *Model 1:* the course over time for BASFI/BASMI. *Model 2:* predictors of the 3-year outcome of BASFI/BASMI corrected for time. *Model 3:* predictors (i.e., the interaction terms) of the 3-year course of physical functioning or spinal mobility over time.
The intercept describes the value for BASFI/BASMI if all other variables are zero. A positive change value for the interaction terms with time indicates an average of ß-points additional increase per week, and a negative change value indicates an average of ß-points additional decrease per week in the BASFI/BASMI over time.

The BASMI showed a stable course over time and varied between 3.5 ± 2.3 at baseline, 3.1 ± 2.2 at 24 weeks, and 3.6 ± 2.5 at 3-year follow-up (table 2).

Table 3 (model 1) shows the results of the longitudinal mixed model analyses describing the effect of time on the progression of the BASFI and BASMI in more detail. In the first 24 weeks after start of TNFi therapy, physical functioning improved by a 0.074 points/week decrease in BASFI ($p < 0.001$). After 24 weeks until 3 years the average change in BASFI was almost stable, with a mean increase of 0.003 units per week ($p < 0.001$). The average change in BASMI over time was even smaller with a decrease of 0.001 points per week ($p=0.207$), also indicating a stable course over time.

Predictors of the 3-year outcome of physical function and spinal mobility

Table 3 also features the results of the multivariate prediction models for the 3-year outcome of BASFI and BASMI (Model 2). Younger age, lower baseline BASFI, absence of peripheral enthesitis, and comorbidity were predictive of lower BASFI at 24-weeks, indicating better physical functioning. Younger age and lower baseline BASFI predicted a more favourable outcome of physical functioning after 3 years of treatment. Lower BASMI at 3 years, indicating better spinal mobility, was predicted by lower age, lower baseline BASMI, and lower baseline BASFI.

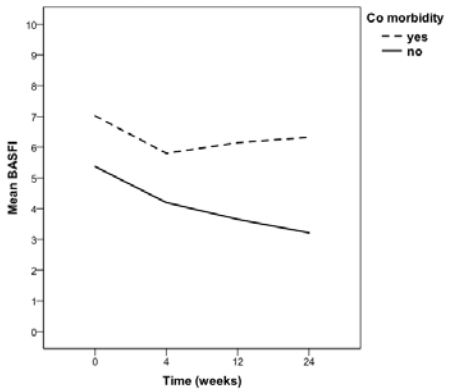

Figure 2a: The difference in course of physical functioning (BASFI) up to 24 weeks of intervention with TNFi between patients with (*n*=9) and without (*n*=248) comorbidity at baseline (i.e., registered cerebrovascular accident, transient ischemic attack, myocardial infarction, and/or diabetes mellitus).

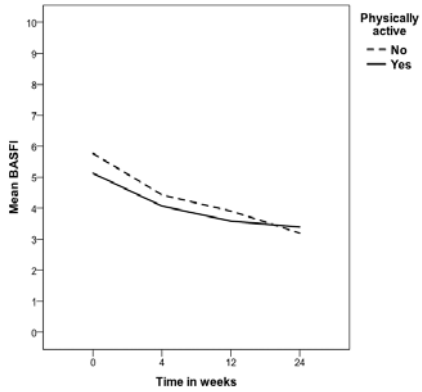

Figure 2b: The difference in course of physical functioning (BASFI) up to 24 weeks of intervention with TNFi between patients who were physically active (*n*=132) or not (*n*=125) at baseline.

Predictors of the three-year course of physical functioning and spinal mobility

Model 3 of Table 3 shows the results of the multivariate analyses of the relationship between the selected predictors and the rate of progression of the BASFI and BASMI over time.

In the first 24 weeks of TNFi therapy, a more favourable course of physical functioning was seen in physically inactive patients without comorbidity and with a higher BASFI and lower BASMI-score at baseline. Patients with comorbidity increased an additional 0.094 units/week on the BASFI compared with patients without comorbidity (Figure 2a). Patients who were physically active at baseline started with a lower mean BASFI-score but showed a mean increase of 0.023 units/week compared with non-active patients. After 24 weeks the difference in mean BASFI between active and non-active patients disappeared (Figure 2b). The BASFI had an additional increase with 0.006 units/week, with every point of increase on the BASMI-score and every point increase in baseline-BASFI resulting in a 0.012 point additional decrease in BASFI per week.

After 24 weeks up to 3 years of TNFi treatment, younger patients with a lower BMI at baseline and lower CRP and higher BASFI-score at 24 weeks showed a more favourable course of physical functioning. Results showed an additional but small increase in BASFI of 0.001 units/week compared with patients with lower BMI. Even if a stricter *p*-value of 0.05 was used, BMI remained in the model.

Only baseline BASMI was a predictor of the rate of progression in spinal mobility up to 3 years of TNFi therapy. A small but significant additional decrease in BASMI of 0.001 points/week was seen with each point increase in BASMI at baseline.

Discussion

The objective of the present study was to examine and predict the 3-year outcome and course of limitations in physical functioning (BASFI) and spinal mobility (BASMI) in daily clinical practice TNFi treated AS patients. Our results demonstrate that physical functioning showed a large, significant improvement, which continued up to 24 weeks (6 months) of TNFi therapy and stabilised thereafter. The course of spinal mobility was stable for the entire period of 3 years. Baseline BASFI, BASMI, comorbidity, physical activity, and BMI were the strongest predictors for the outcome and course of physical functioning and spinal mobility after 3 years of TNFi treatment. Younger age and lower CRP level also proved to be predictors, but contributed less strongly to the outcome and course.

Our results indicated that the improvement of physical functioning continued up to 6 months of TNFi therapy, but according to the ASAS recommendations, the time of evaluation of response is already after 3 months [6]. Therefore we would like to suggest to evaluate the efficacy of TNFi therapy after 6 months instead of 3 months, as is commonly done in daily clinical practice.

This is one of the sparse observational studies looking at the long-term outcome, course (3 years), and predictors of physical functioning and spinal mobility in TNFi treated AS patients in daily clinical practice. Most studies on this topic are RCTs or have a much shorter follow-up duration (6 months). In addition, most of these studies mainly focus on predictors of response to TNFi (disease activity) and not at functioning or mobility, and do not always include comorbidity and life-style factors as potential predictors.

Our results showed a stable course over time in physical functioning after 6 months up to 3 years of TNFi treatment. This is advantageous, since patients only receiving conventional treatment with NSAIDs normally show on average a decline in functioning over a longer period of time [3, 4, 11]. The inter-individual variations in the course of physical functioning and spinal mobility were, however, large, even before the start of TNFi therapy. Therefore, the identification of patients at risk for more functional decline in future is important. The predictors found in the present study can help clinicians to identify these patients.

In all models, the baseline BASFI or BASMI-score was of major influence on the outcome of functioning and spinal mobility after 3 years and on the rate of progression. Although the decline was slower in patients with a higher BASFI and BASMI, this effect was only small and could not overhaul the difference with patients who had a lower BASFI or BASMI-score at baseline. Poor physical functioning or spinal mobility at baseline thus predicts poor functioning and spinal mobility after 3 years of TNFi treatment. This result is in line with previous observations that higher baseline BASFI favours a greater improvement in BASFI [8]. An explanation for this result could be that patients with higher scores have more opportunity for improvement than patients with lower scores (i.e., regression to the mean).

In addition to baseline BASFI and BASMI, physical activity and comorbidity were important contributors to the rate of progression of physical functioning in the first 24 weeks of TNFi treatment. Although the number of patients with comorbidity at baseline was small (n=9), our results support the evidence that comorbid conditions, like CVD, increase the burden of disease

and have an unfavourable impact on physical functioning [16]. By contrast, it was remarkable that physically active patients had a lower baseline BASFI, but showed a more unfavourable course of physical functioning during treatment. This difference in functioning in relation to physical activity disappeared after 24 weeks of treatment. This result can be explained by the fact that physically inactive patients at baseline become more active after the start of TNFi therapy, and thereby reduce the difference between them and their active counterparts. Pain, stiffness, and fatigue are important barriers for performing physical activities [25-27], but decrease with TNFi treatment and thus might motivate patients to become physically active. This is in line with previous studies that showed that AS patients treated with TNFi are more motivated to exercise, spend more time on exercise, and exercise with higher intensity [28]. The positive influence of exercising on physical functioning has not been studied yet in long-term TNFi cohorts. In addition, the ideal exercise treatment parameters are not known. More research into this elementary component of the treatment of AS patients should be done in the near future.

After 24 weeks of TNFi treatment, physical functioning showed a stable course up to 3 years. However, patients with lower BMI at baseline had a more favourable course of physical functioning over 3 years of treatment than patients with higher BMI. To our knowledge, BMI has not previously been described as a predictor of physical functioning in AS patients on TNFi. Recent research showed that overweight AS patients had a greater burden of symptoms [29]. Furthermore, high BMI negatively influences the clinical response to infliximab in AS patients [30]. An explanation for this result could be that fatty cel tissue produce TNF alpha, which increases the TNF alpha level in the blood. Consequently, the response to TNFi might decrease and more medication would be necessary. Recent studies confirm this association [31], but more research into this topic should be done.

A limitation of this study is that data on structural damage was not available, and therefore not included in the analyses, but might be interesting for future research. Furthermore, it is important that more research is done to find predictors for long-term physical functioning and spinal mobility in routinely TNFi treated AS patients. Awareness of these factors might influence treatment strategy and potentially identify patients at risk of more rapid functional decline.

In conclusion, physical functioning in routinely TNFi treated AS patients improved up to 24 weeks and stabilised thereafter. Spinal mobility showed a stable course over time. The strongest predictors for a more favourable outcome and course of physical functioning and spinal mobility after 3 years of TNFi treatment included lower baseline BASFI, BASMI scores, absence of comorbidity, physical activity and low BMI. The identification of these risk factors can be helpful when considering additional treatment options to prevent further decline, such as physiotherapy or weight loss. In addition, these results suggest that the optimal time point for the evaluation of treatment effects should be at 6 instead of 3 months.

Key messages

- Physical functioning in routinely TNFi treated AS patients improved up to 24-weeks and stabilised thereafter.
- Evaluation of TNFi treatment effects should be at 6 instead of 3 months.
- BASFI, BASMI, comorbidity, physical activity, and BMI predict outcome and course after TNFi treatment.

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