Long-term Quality of Life, Productivity Impairment, Disease Severity and Health Care Costs in Relation to Functional Impairment in Ankylosing Spondylitis Patients in the Czech Republic

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Background/Purpose

Our aim was to describe the quality-of-life (QoL), productivity impairment, clinical indicators and health care costs in relationship to functional status described by Bath Ankylosing Spondylitis Functional Index (BASFI) in ankylosing spondylitis (AS) patients in three-year follow-up. These are follow-up results; the first visit was presented in ACR 2013.

Methods

This is a prospective multicenter non-interventional observational study with AS patients in 4 specialized centers for treatment of rheumatic diseases in the Czech Republic. A two-year follow-up with 6 months period between each time point observation is ongoing. The data presented here comes from the first visit and three subsequent visits (i.e. time 0, 6, 12 and 18 months). The demographic, clinical, QoL and productivity data were directly collected from patients. Health care consumption was assessed retrospectively reviewing individual patient's medical record. Clinical data were described by ASDAS-CRP, QoL measured by EuroQol questionnaire (EQ-5D), work impairment by Work Productivity and Activity Impairment (WPAI) with respect to BASFI categories. Patients were stratified according to their BASFI into 10 categories. Within health care consumption and costs directly related to AS, we focus on medication, out-patient & in-patient care, complement and instrumental examination and out-of pocket expenditures. Health care expenditures are presented as average yearly costs per patient observed within the first year of observation. Patients were analyzed as the whole cohort and specifically by the presence of biologic treatment. We tested the differences between groups of patients with and without biological treatment.

Statistical analysis

A linear regression model was performed to identify the main factors associated with BASFI. Selection of variables for the multivariate model was based on mutual correlations, clinical judgment and findings in previous studies. The results were considered statistically significant at the significance level of p=0.05. Fixed effect model which is able to control for unobserved patient characteristics was performed with patients having 2 and 3 follow-up visits and explored the relationship between BASFI, EQ-5D and ASDAS-CRP. Statistical analyses were performed in STATA 13.1, StataCorp. Additionally, we tested for the differences in characteristics between the groups treated/not treated with biologics using Mann-Whitney test; correlation between variables was tested using Spearman's correlation coefficient.

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Table 1 - Initial visit (time 0) of AS patients

Patients on biologic drugs										
BASFI category	BASFI*	No.	Age*	Time from Dx (years)	% women*	Costs (EUR)*	% of work active	% WPAI*	ASDAS-CRP*	EQ-5D*
0-1>	0.4	52	38.0	9.8	31%	12,074	88%	6%	1.2	0.894
1-2>	1.5	42	40.8	11.9	21%	11,157	81%	21%	1.6	0.780
2-3>	2.5	35	46.2	15.3	14%	12,069	74%	27%	2.1	0.722
3-4>	3.4	29	44.6	15.1	24%	10,960	66%	27%	2.2	0.670
4-5>	4.4	23	44.5	14.9	22%	12,315	57%	40%	2.1	0.651
5-6>	5.4	20	44.8	17.9	20%	11,151	50%	41%	2.5	0.624
6-7>	6.5	7	46.4	7.1	29%	13,408	57%	23%	2.7	0.613
7-8>	7.5	2	66.5	27.0	0%	7,100	50%	70%	2.8	0.623
8-9>	8.5	6	51.0	15.5	0%	14,294	33%	40%	3.0	0.583
9-10>	9.2	2	50.5	18.5	50%	11,309	50%	95%	3.4	0.429
Mean/total	2.8	218	43.0	13.4	22%	11,740	72%	22%	1.9	0.740
Patients without biologic drugs										
BASFI category	BASFI	No.	Age	Time from Dx (years)	% women	Costs (EUR)	% of work active	% WPAI	ASDAS-CRP	EQ-5D
0-1>	0.4	15	40.6	9.5	40%	174	80%	26%	1.9	0.838
1-2>	1.6	9	45.2	8.2	44%	327	89%	37%	2.4	0.746
2-3>	2.4	8	45.8	7.6	50%	221	63%	16%	2.5	0.682
3-4>	3.6	8	49.0	16.6	63%	354	75%	36%	2.5	0.614
4-5>	4.4	8	49.9	16.6	38%	290	50%	28%	2.9	0.583
5-6>	5.4	10	54.9	18.5	20%	645	70%	53%	3.3	0.603
6-7>	6.3	3	52.7	18.7	33%	348	67%	35%	3.0	0.608
7-8>	7.4	6	52.0	20.0	17%	665	50%	51%	2.9	0.530
8-9>	8.6	6	52.5	23.0	17%	1,593	0%	n.a.	3.6	0.392
9-10>	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Mean/total	3.7	73	48.0	14.3	37%	459	64%	34%	2.7	0.653
Whole patient cohort										
BASFI category	BASFI	No.	Age	Time from Dx (years)	% women	Costs (EUR)	% of work active	% WPAI	ASDAS-CRP	EQ-5D
Mean/total	3.0	291	44.3	13.6	26%	8,910	70%	25%	2.1	0.718

Notes: * the mean values of given patient characteristics on and without biol. drugs differ significantly with p<0.05 using Mann-Whitney test.

Table 2 - Follow-up observations

	1st visit (initial)			2nd visit			3rd visit			4th visit		
Mean/total	Bio	w/o Bio	Whole	Bio	w/o Bio	Whole	Bio	w/o Bio	Whole	Bio	w/o Bio	Whole
N	218	73	291	185	23	208	152	22	174	64	2	66
BASFI	2.8	3.7	3.0	2.7	4.3	2.9	2.5	4.0	2.7	2.7	n.a.	2.8
% of work active	(72%)	(64%)	(70%)	(72%)	(65%)	(71%)	(75%)	(59%)	(73%)	(70%)	n.a.	(70%)
% WPAI	22%	34%	25%	19%	26%	19%	21%	23%	21%	23%	n.a.	23%
ASDAS-CRP	2.0	3.1	2.3	1.8	2.6	1.9	1.8	2.6	1.9	1.8	n.a.	1.8
EQ-5D	0.740	0.653	0.718	0.738	0.667	0.730	0.744	0.638	0.731	0.726	n.a.	0.723

Bio – patients on biologic treatment; w/o - patients without biologic treatment; Whole – Whole cohort of patients
n.a. – not applicable due to number of observations.

Table 3 - BASFI as a function of age, sex, time from diagnoses, ASDAS, EQ-5D, costs in EUR (Ln–transformed costs): Results from multivariate linear regression analysis (n=291)

	Coefficient	P-value
Intercept	0.630	0.676
Age	0.138	0.006
Age²	-0.001	0.027
Female	-0.717	0.001
Diagnosis duration	0.019	0.111
Biological treatment	-1.052	0.069
ASDAS-CRP	0.653	0.000
EQ-5D	-6.204	0.000
Ln–transformed costs (in EUR)	0.302	0.019

Table 4 - BASFI as a function of ASDAS-CRP and EQ-5D. The results from fixed-effect model estimation using 2 follow-up visits (n=174, time=3 periods, total observation= 521)

	Coefficient	P-value
Intercept	6.820	0.000
ASDAS-CRP	0.150	0.002
EQ-5D	-6.000	0.000

Table 5 - BASFI as a function of ASDAS-CRP and EQ-5D. The results from fixed-effect model estimation using 3 follow-up visits (n=66, time =4 periods, total observation = 264)

	Coefficient	P-value
Intercept	5.471	0.000
ASDAS-CRP	0.143	0.002
EQ-5D	-4.373	0.000

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Results

291 patients with AS were registered at the first visit, 218 on biological drugs, mean age was 44.3 years, mean time from diagnoses was 13.6 years, 26.1% were female. With higher functional impairment, described by BASFI, there is a trend in age increase, increase in time from diagnosis, percentage of work impairment and also decrease in percentage of work-active patients. There is also deterioration in clinical impairment (ASDAS-CRP) and QoL observed with higher BASFI. See the results in table 1 & 2; values presented as mean. The values of all parameters in Table 1 except for time from diagnosis and % of active work differ significantly between patients treated and not-treated with biologics. That is, patients on biologic drugs have lower BASFI, lower age, have apparently higher costs, lower WPAI, lowerASDAS-CRP and higher QoL based on EQ-5D measure.

It should be noted that 17.3% patients (36 out of 208) on the 2nd visit from the original non-biologic cohort initiated biological treatment. Within the 3rd and 4th visit, no other patients of the original non-biological patients initiated biological treatment.

The graphical presentation of the variables that revealed the highest correlation with the BASFI is shown in Figure 1, 2 and 3. These variables are ASDAS-CRP, EQ-5D (QoL) and natural logarithm of the costs of patients without biological treatment. The Spearman correlation coefficient is equal to 0.60, -0.69 and 0.40, respectively in ASDAS-CRP, EQ-5D and the total costs.

Within the linear regression analysis of all patients during their initial visit (n=291), BASFI was used as the dependent variable. Age, squared age (age²), gender (female), disease duration, biological treatment, ASDAS-CRP, EQ-5D and ln-transformed costs (natural logs) were used as independent variables. For the sake of interpretability, we let the BASFI score unchanged and did not apply any transformation. In the regression model were found gender, age, age², ASDAS-CRP, EQ-5D and costs as the significant predictors of BASFI. Biological treatment had borderline significance (p=0.067) and maybe remarkably disease duration was statistically insignificant. The regression model used captured 56% of variability (R^2=0.556).

The results of this regression analysis are presented in Table 3. The coefficients in Table 3 are the BASFI values for every unit of respective parameter except for ln costs in which there is a change in one natural logarithm. More specifically, an increase by one unit of ASDAS resulted in an increase in BASFI of 0.653, female sex revealed 0.717 lower BASFI compared to male sex. Within the interpretation of dependence EQ-5D to BASFI, we have to be aware to divide the coefficient by 10 because of the height of intercept of EQ-5D. For example, an increase in EQ-5D from 0.6 to 0.7 resulted in a decrease in BASFI by 0.65 points. Interestingly, age and age² are significant but age² with negative sign which means increasing BASFI with age but with decreasing rate (reverse U-shape). The maximal BASFI is then at the age of 60 years and from this point BASFI start to decrease. Because of ln-transformation of the costs, there had to be applied back transformation for the interpretation of this coefficient.

The results of fixed effect models are presented in Table 4 and 5 for two and three follow-up visits respectively (in total, three and four visits). Only ASDAS-CRP and EQ-5D were possible to examine longitudinally because other variables were not changing (were fixed) on the individual level and remained the same (age, gender or biological treatment). This type of regression can analyze only individually changing characteristics and allows for controlling the individual heterogeneity and unobserved effects. The results show similar magnitude of EQ-5D as in previous regression model but lower magnitude in ASDAS-CRP. This may be caused by smaller changes in ASDAS-CRP in the follow-up period. The model explains 52% of the variability in the data when using the data from 2 follow-up visits and 43% using 3 follow-up visits.

Conclusion

Patients with worse functional impairment revealed more significant impairment of their QoL, work productivity and revealed also worse clinical outcomes and higher costs (in non-biologic treated patients, since the costs of biologics (in biologic cohort) make almost the equal costs height without any differences based on BASFI). There is a trend of decreasing number of work active patients who are not on biologics. For patients not treated with biologics, BASFI is a relatively good cost predictor. There have not been observed substantial changes in ASDAS-CRP and EQ-5D data in the follow-up period, probably due to relatively short period (18 months) with respect to the disease natural progression rate. The findings attributed to higher BASFI impairment (BASFI > 6.0) and to patient not treated with biologics should be interpreted with caution because of lower number of patients in these categories.

We consider our findings highly helpful to decision-makers in the reimbursement process/ optimization of particular intervention. This information is important to start by adequately describing the burden of each particular health care problem with respect to QoL and other patients reported outcomes in relationship to clinical parameters, functional impairment and costs. The costs data and productivity are rather Czech specific, contrary to relationship with QoL data, functional and clinical impairment that could be transferred also into other countries.