The clinical and MRI effect of TNF- α inhibitor in spondyloarthritis patients with hip involvement: a real-world prospective clinical study

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Abstract

Background: Hip involvement is an important cause of disability and poor prognostic in patients with spondyloarthritis (SpA). TNF- α inhibitor treatment had been demonstrated to be effective in SpA patients with hip arthritis, however, quantitative assessment with magnetic resonance imaging (MRI) in the long-term follow-up still needs further application.

Methods: A total of 239 patients were involved in this study, MTX and SSZ were given as basic treatment. 165 patients received TNF- α inhibitor plus basic treatment and 74 patients received basic treatment only as control. The clinical symptoms were assessed at baseline, week 12, week 24, and week 52. The MRI performances of hip arthritis including bone marrow edema (BME) and synovitis were quantitatively assessed using Hip MRI Inflammation Scoring System (HIMRISS).

Results: The clinical symptoms of ESR, CRP, BASDAI, Harris, and ASDAS-ESR of both groups got significant clinical remission at week 52 ($p < 0.001$). However, the disease activity change levels at week 52 in control group were significantly worse than TNF group. In week 52, MRI performance showed significant remission trend in TNF- α inhibitor group versus baseline of which total HIMRISS scores decreased significantly (26.49 ± 10.37 vs 20.59 ± 9.41 , $p < 0.001$), but the control group only had slight improvement trend ($p < 0.05$).

Conclusions: TNF- α inhibitor could significantly and better improve the clinical and MRI manifestation of hip involvement in SpA patients than controls. Quantitative MRI assessment combined with clinical assessment could accurately evaluate the treatment effect of TNF- α for SpA patients with hip involvement, and help to guide targeted treatment.

Trial registration: Chinese Clinical Trial Registry, ChiCTR-ONRC-11001846, Registered 28 November 2011. Retrospectively registered <http://www.chictr.org.cn/showproj.aspx?proj=7701>

Background

Hip involvement is an important cause of disability and poor prognostics in approximately 10 to 50% of spondyloarthritis (SpA) patients[1, 2], and 47%-90% with bilateral hip involvement[3]. Progressed hip involvement was reported to be associated with more severe spinal involvement[4, 5], and seriously affect joint function and life quality. In addition, nearly 8% of patients with hip involvement suffers from intractable pain and disability. Even if they are treated with total hip arthroplasty, it is likely at high risk of revision surgery and high complication rates[6].

The principal clinical manifestations of hip involvement in SpA including inflammation of the subchondral BME and synovitis effusion[7]. MRI had been widely used as a sensitive tool to detect hip arthritis. It was proved to be helpful for early diagnosis and suppression of inflammation before structural damage[8, 9]. HIMRISS was a new quantitative assessment method which was performed based on several MRI slices from one patient, and could systematically assess the synovitis and BME of femoral

head and acetabular[10]. Although the association between HIMRISS and disease activity was validated in SpA[11], the sensitivity and accuracy of HIMRISS in assessing treatment response in SpA with hip involvement need further validation.

Previous treatment strategy often focused on SpA global symptom management rather than SpA related hip lesions or other peripheral joint diseases[12, 13]. Increasing evidence had indicated that early detection and diagnosis of hip inflammation is beneficial to active treatment which was important to improve hip function and general prognosis of SpA[14]. TNF- α inhibitor had been demonstrated to be prompt and robust in improving the signs and symptoms of SpA as well as function and spinal mobility[15, 16]. In recent clinical studies, TNF- α inhibitor including etanercept, adalimumab or infliximab were also indicated to be effective for SpA patients with hip involvement in by clinical and imaging assessment[1].

However, the detailed clinical effect of TNF- α inhibitor among long-term treatment cycle need to be further observed, and previous imaging assessment were limited to radiographic assessment of BASRI-hip or ultrasound[17, 18]. More accurate imaging tools such as MRI were still not finely applied in assessing the acute and long-term followup treatment effect of TNF- α inhibitor.

Thus, the purpose of this prospective study was to quantitatively assess the detailed clinical remission and MRI changes of hip involvement under the treatment of TNF- α inhibitor versus controls. The hip inflammation was quantitatively assessed by HIMRISS based on MRI changes, as well as the systematically clinical evaluation. We aim to give a suggested assessment standard for SpA patients with hip involvement including MRI and clinical, and guide accurate and targeted treatment.

Methods

Study population

Our study was based on data from Xijing hospital in China. All the SpA patients were enrolled with clinical diagnose, and the long-term treatment and tracking were initiated by rheumatologists in Xijing hospital. Eligible patients were 18–65 years of age and had to fullfill the recently published Assessment of SpondyloArthritis international Society (ASAS) classification criteria[19] or the Modified New York criteria for axial spondyloarthritis[20]. Both acute and chronic inflammatory changes on MRI were considered positive signs for hip involvement and coxitis. All the patients were included and under the basic treatment of MTX (10mg every week) and SSZ (2g/day given orally) from baseline to 52 weeks. Of all the eligible participants, patients in TNF- α group were allocated to three kind of TNF- α inhibitor plus basic treatment (etanercept 50 mg given once weekly subcutaneously, adalimumab treatment [40 mg s.c. every other week], infliximab [3 mg/kg iv. at baseline, week 2 and week 6 and then every 8th week]), and patients in the control group received the basic treatment only. The cost of treatment was self-funded, and the therapeutic options were determined on the consent of the doctors and patients. The study was approved by the ethics committee of Xijing Hospital of China, and all the participated patients had written the informed consent before enrollment in this study.

ESR, CRP, and human leukocyte antigen HLA-B27 was measured with standard laboratory techniques. Serum CRP and ESR were measured at baseline, 12 week, 24week and 52 week At the same time-point, evaluation of the disease activity levels (BASDAI, ASDAS-CRP and ASDAS-ESR) and hip function level (harris) were conducted by experienced rheumatologists .

Quantitative MRI assessment of changes

HIMRISS was used to assess the MRI changes between baseline and week 52. MRI was performed with coronal short-tau inversion recovery (STIR) sequence with slice thickness of 4 mm, field of view 400 × 400 mm. The baseline and at least once follow-up MRI images of both hips were recommended, and the time interval between twice MRI images should be greater than 3 months. The HIMRISS protocol was used to score the inflammatory changes in MRI images of the hip joints including BME of femoral head, BME of acetabular and synovitis[11]. The HIMRISS procedure was performed by two experienced readers (ZK and WwT) independently. The procedure was blinded to treatment arm and MRI time point, and analyzed by independent statistician. The standard HIMRISS scores were calculated based on 15 MRI image slides, therefore, in order to avoid bias, patients with MRI images of hip structure <5 slides were considered as missing samples.

Statistical analysis

The Kaplan-Meier test was used to assess the difference of clinical symptom remission(ASAS20, ASAS40, ASAS50 and ASAS70) and MRI improvement between different follow-up time points. The baseline status was taken into account and a non-parametric analysis of covariance (non-parametric ANCOVA) was used. The statistical analyses were performed using SPSS 22.0. P values <0.05 were considered as statistically significant.

Results

Demographic and clinical characteristics

Between Jan 1, 2014 to Dec 30, 2018, 239 SpA patients with coxitis were enrolled and finished the treatment follow-up. 165 patients (69.04%) received TNF- α treatment and 74 patients (30.96%) received basic treatment only as control ([Table 1](#)). In TNF- α group, 103 patients received etanercept treatment, 51 patients received adalimumab treatment and 11 patients received infliximab treatment. The SpA patients in both TNF- α inhibitor group and control group presented with 52-weeks observation period with clinical symptom and MRI evaluation. As shown in [Table 1](#), the difference of demographic and clinical characteristics including ESR, CRP, Harris, BASDAI, morning stiffness time, and ASDAS-CRP between two groups were not significant as baseline, except for ASAS-ESR ($p<0.01$) and disease duration ($p<0.001$). Patients in TNF- α inhibitor group had relative shorter disease duration and worse disease activity than control group. All patients had serious disease activity with higher BASDAI score (5.76 ± 1.20 and 5.53 ± 1.29) and ASDAS score (2.78 ± 0.62 and 2.53 ± 0.57), as well as elevated CRP and ESR values.

Table 1. Clinical characteristics including disease activity indices and hip function of both groups in baseline.

	TNF- α group	Control group	p-value
Number	165	74	
Age	28.67 $\pm$ 10.21	27.3 $\pm$ 7.11	0.362
Sex	117:48=71%:39%	43:31=58%:42%	0.067
B27	93%	87%	0.163
Disease duration (m)	25.19 $\pm$ 34.52	45.41 $\pm$ 40.48	0.000
ESR (mm)	26.91 $\pm$ 14.90	25.04 $\pm$ 14.34	0.367
CRP (mg/l)	1.42 $\pm$ 1.28	1.27 $\pm$ 1.23	0.364
Harris	67.65 $\pm$ 9.26	66.27 $\pm$ 10.85	0.313
BASDAI	5.76 $\pm$ 1.20	5.53 $\pm$ 1.29	0.199
Morning stiffness (h)	0.43 $\pm$ 0.18	0.39 $\pm$ 0.42	0.276
ASDAS-ESR	2.76 $\pm$ 0.60	2.90 $\pm$ 0.67	0.124
ASDAS-CRP	2.78 $\pm$ 0.62	2.53 $\pm$ 0.57	0.004

Quantitative magnetic resonance imaging assessment

The MRI changes of hip inflammation of those SpA patients were assessed by HIMRISS scoring system including BME and synovitis. Compared with baseline, patients in TNF- α group had significantly MRI improvement of both BME and synovitis at week 52 (all the $p < 0.001$). However, the MRI difference in control group between week 52 versus baseline was relatively less (BME of femoral head: $p < 0.05$. total BME: $p < 0.05$. synovitis: $p < 0.05$. total mean/max HIMRISS: $p < 0.05$), and the BME scores of acetabular were similar ($p > 0.01$) (Table 2).

Inter-group analysis showed that there is little difference between the total HIMRISS scores of TNF group and control group in baseline ($p > 0.05$) and week 52 ($p > 0.05$). however, the treatment group with higher total HIMRISS scores as the baseline demonstrated significant improvement at week 52, and with lower scores compared with control group (TNF- α vs control at week 52: 20.59 $\pm$ 9.41 vs 22.33 $\pm$ 7.0). Additionally, BME scores of acetabular indicated that TNF- α group were significantly more serious in baseline ($p = 0.006$), but got significantly improvement at week 52 ($p < 0.001$) (Table 2).

Table 2. The HIMRISS scores from baseline to 52 weeks of biological group and non-biological group.

	Group	Baseline	Treatment 52W	P value
BME of femoral head ^{mean} (0-65)	TNF-α group	10.53±6.78	7.74±5.77	0.000
	Control group	9.74±5.77	8.73±5.06	0.018
	P-value	0.124	0.315	
BME of acetabular ^{mean} (0-35)	TNF-α group	7.06±3.68	5.51±3.81	0.000
	Control group	6.27±2.82	5.89±2.45	0.164
	P-value	0.006	0.000	
Total BME ^{mean} (0-100)	TNF-α group	17.59±9.36	13.26±8.75	0.000
	Control group	16.05±7.11	14.61±2.44	0.019
	P-value	0.047	0.037	
synovitis-effusion score ^{mean} (0-30)	TNF-α group	8.90±3.33	7.34±2.97	0.000
	Control group	8.44±2.19	7.71±2.24	0.011
	P-value	0.002	0.088	
Total HIMRISS ^{mean} (0-130)	TNF-α group	26.49±10.37	20.59±9.41	0.000
	Control group	24.49±8.07	22.33±7.07	0.039
	P-value	0.073	0.079	
Total HIMRISS ^{max} (0-130)	TNF-α group	29.95±11.70	23.03±10.31	0.000
	Control group	27.31±9.50	24.64±8.38	0.015
	P-value	0.118	0.126	

Note: mean: the mean score of two hips; max: the max score of two hips.

Clinical outcome and hip function assessment

Both TNF-α inhibitor group and control treatment group showed a statistically significant amelioration of all clinical symptoms and hip functions at week 52 compared with baseline ([Table 3](#)). Notably, the mean BASDAI scores in TNF-α inhibitor group decreased from 5.76±1.20 to 2.16±1.90 at week 52 ($p<0.001$), ASDAS-CRP/ASDAS-ESR decreased from 2.78±0.62/2.76±0.60 to 1.06±0.46/1.42±0.60 at week 52 ($p<0.001$). CRP and ESR levels had also improved significantly compared with baseline levels ($p<0.001$ and $p<0.001$). In addition, harris score indicated a significant hip function improvement to generally normal at week 52 than baseline (67.65±9.26, 92.26±7.06, $p<0.001$).

Furthermore, control group showed a significant clinical remission trend of ESR, BASDAI, Harris, and ASDAS-ESR/ASDAS-CRP at week 52 versus baseline ($p<0.001$) ([Table 3](#)). However, the mean BASDAI

score, ASDAS_CRP, ASDAS_ESR, and harris scores of TNF- α group were significantly better than control group at week 52 (all the p values<0.000). Especially, the degree of ASDAS_CRP indicated a real-world clinical character that, patients in TNF- α group had relatively serious disease activity in baseline, but obvious better remission at week 52.

Table 3. Clinical outcomes and hip functions from baseline to 52 weeks between TNF- α and non-biological group.

	Groups	Baseline	Treatment 52W	P value
ESR (mm)	TNF- α group	26.91 $\pm$ 14.90	11.01 $\pm$ 12.58	0.000
	Control group	25.04 $\pm$ 14.34	17.07 $\pm$ 12.23	0.000
	P-value	0.367	0.002	
CRP (mg/l)	TNF- α group	1.42 $\pm$ 1.28	0.73 $\pm$ 1.17	0.000
	Control group	1.27 $\pm$ 1.23	0.88 $\pm$ 0.91	0.047
	P-value	0.364	0.371	
Harris	TNF- α group	67.65 $\pm$ 9.26	92.26 $\pm$ 7.06	0.000
	Control group	66.27 $\pm$ 10.85	82.95 $\pm$ 7.93	0.000
	P-value	0.313	0.000	
BASDAI	TNF- α group	5.76 $\pm$ 1.20	2.16 $\pm$ 1.90	0.000
	Control group	5.53 $\pm$ 1.29	2.81 $\pm$ 1.42	0.000
	P-value	0.199	0.000	
ASDAS-CRP	TNF- α group	2.78 $\pm$ 0.62	1.06 $\pm$ 0.46	0.000
	Control group	2.53 $\pm$ 0.57	1.40 $\pm$ 0.63	0.000
	P-value	0.004	0.000	
ASDAS-ESR	TNF- α group	2.76 $\pm$ 0.60	1.42 $\pm$ 0.60	0.000
	Control group	2.90 $\pm$ 0.67	1.88 $\pm$ 0.62	0.000
	P-value	0.124	0.000	

ASAS remission rate of ASAS20, ASAS40, ASAS50, and ASAS partial were compared between TNF- α group and control group at week 52. TNF- α group had higher and better ASAS remission levels than control group (Figure 1). Moreover, the distribution of disease activity including BASDAI, ASDAS_CRP, and ASDAS-ESR between two group at week 52 was significantly different. The patients in the TNF- α inhibitor treatment group could achieve inactive disease activity (TNF- α vs control : BASDAI: 96.93% vs 74.33%, ASDAS_CRP: 80.98% vs 58.67%, ASDAS-ESR: 51.53% vs 22.67%, p<0.001). Meanwhile, a considerable

number of patients in control group were still classified as active disease activity (TNF- α vs control: BASDAI: 3.07% vs 22.67% $p < 0.001$) low disease activity (TNF- α vs control: ASDAS-CRP: 15.34% vs 24.00%, ASDAS-ESR: 35.58% vs 42.67%, $p < 0.001$) and moderate disease activity (TNF- α vs control: ASDAS-CRP: 3.07% vs 17.33%, ASDAS-ESR: 11.66% vs 32.00%, $p < 0.001$) (Figure 2).

In addition, a subgroup analysis for all patients in TNF- α group was performed to compare the treatment difference between two kinds of TNF- α inhibitors. Firstly, for all patients receiving treatment of TNF- α inhibitor, all the continuous parameters related to disease activity (i.e. CRP, ESR, BASDAI, and ASDAS) and hip joint function (i.e. harris) ameliorate significantly from week 12 (all the p values < 0.001) compared with the baseline, and persist the significant remission level until week 52 (all the p values < 0.001) (Figure 3).

Moreover, the ASAS remission rate including ASAS20 remission rate, ASAS40 remission rate, ASAS50 remission rate, and ASAS partial remission rate were compared between different TNF- α inhibitors in follow-up time. Results indicated that the difference of ASAS remission rate between different TNF- α inhibitor groups during the 52 weeks were not significant (p values > 0.01) (Figure 4).

Discussion

This study demonstrated that TNF- α inhibitor could achieve significant clinical remission and MRI manifestation changes for hip arthritis in SpA patients. In TNF- α group, the disease activity indexes including BASDAI, ASDAS, ASAS remission rate, and hip function indexes of harris scores demonstrated better improvement compared with the control group. Additionally, HIMRISS method detected the obvious better improvement of the hip inflammation based on overall MRI slices under TNF- α inhibitor treatment than control treatment. TNF- α blocking therapy were confirmed as a better treatment options for SpA patients with hip involvement.

Previous studies of therapy in SpA mainly focused on the axial spine radiology, and to some extent, on peripheral arthritis or enthesitis[5, 21]. Hip involvement was difficult to cure, while it was often considered as an important cause of disability and poor prognostic in SpA, especially in AS[17, 22]. More attentions turned to focus on the hip arthritis in SpA, and various clinical studies including TNF- α inhibitor treatment or classical DMARDs treatment were conducted to observe the clinical and/or radiographic progress of hip joint and function. [23–25]. TNF- α inhibitor treatment had been demonstrated to be effect for SpA patients with hip involvement. However, the specific effect difference between TNF- α inhibitor and other agents need to be evaluated in long-term follow-up.

In known therapeutic studies of SpA patients with hip involvement, BASRI-h method was often adopted to study radiological changes of hip lesions[24]. However, most of the hip involvement in AS belongs to early coxitis characterized by inflammation of the subchondral bone marrow edema and synovitis[7, 26], while BASRI-h method were performed based on structural damages which may not sensitively reflect the treatment effect to those patients in early and acute inflammation stages in short-time follow-up.

Comparatively, MRI was considered as a more sensitive assessment tool for hip inflammation, and is especially helpful in early diagnosis[8, 23, 27].

Recent studies had conducted that synovial enhancement by hyperintense signals on contrast-enhanced T1 weighted images was the most frequent imaging finding in early-stage hip involvement in AS[14]. Joint effusion of femoral neck and subchondral bone marrow edema were the frequent findings by hyperintense signals on T2WI or STIR images[8, 27]. However, lesion frequency analyze or character description could not quantitatively reflect MRI changes under treatment. HIMRISS could systematically quantify the inflammatory changes including BME of femoral head, BME of acetabular, and synovitis effusion of hip based on global MRI slices of patient[10]. HIMRISS method had been previously applied in SpA patients diagnosed with hip arthritis and indicated significant correlation between MRI manifestation and harris score or disease activities[11].

In known clinical studies, the clinical manifestations assessed in SpA patients with hip involvement mostly refer to global outcome indexes including disease activity scores and inflammatory markers. Despite of the fact that the association between hip impairment and axial disease of inflammatory back pain were still argumentative[22], more evidence pointed to the fact that hip disease more frequently occur in SpA patients with severe axial disease[28]. However, the treatment efficacy changes of hip involvement in early-stage and long-term followup were still not fully understood, more detailed assessment of clinical and MRI manifestation need to be performed.

In this study, the clinical efficacy of TNF- α inhibitor for hip involvement was compared with control agents in a one-year follow-up periods. TNF- α was demonstrated to be significantly effective to improve disease activity and inflammation and the effect was significantly better than control. All the clinical indexes of TNF- α group including ESR, CRP, BASDAI, and ASDAS-CRP/ASDAS-ESR significantly ameliorated at different follow-up time compared with baseline, this result kept consistent with previous studies. Harris score was also significantly increased which reflected an outstanding improvement of hip function.

In this study, HIMRISS method was used to semi-quantify the acute and chronic inflammatory changes of hip arthritis of SpA under treatment of TNF- α inhibitor or control. HIMRISS results showed a significantly better MRI improvement of TNF- α group than control group at week 52. All HIMRISS parameters of TNF- α group including BME of femoral head, BME of acetabular, synovitis effusion and total HIMRISS scores got significant improvement with p values < 0.001.

The result indicated that, to some extent, TNF- α inhibitor could simultaneously achieve to significant long-term MRI remission and clinical remission, rather than control group could not notably achieve MRI remission. TNF- α inhibitor indicated the outstanding advantages for SpA patients with hip involvement.

An addition subgroup analyses further compared the clinical effect between different TNF- α inhibitors. Previous study had indicated that etanercept and adalimumab treatment could got similar ASDAS-CRP improvement in AS patients[16]. In this study, different ASAS remission rate were compared between etanercept/infliximab and adalimumab in different follow-up time points. The Kaplan-Meier test result

indicated that the difference of remission rate including ASAS20, ASAS40, ASAS50, and ASAS partial were not significant between different TNF- α inhibitors. TNF- α inhibitors had similar high effect on SpA patients complicated with hip involvement.

The follow-up cycle of hip joint function and clinical characters varies from 12 weeks to 24 months in previous studies. In this study, we observed the treatment response from 12 weeks to 52 weeks. Lian et al and Huang et al [23] demonstrated that TNF- α inhibitor could maintain stable hip function by harris score and clinical remission of hip arthritis in SpA patients for 6 months. In this study, we simultaneously compared the effectiveness of TNF- α inhibitor and SSZ therapy on the clinical outcome of hip arthritis in SpA from baseline to 52 weeks. Our result further confirmed that, the clinical remission levels at week 52 of TNF- α inhibitor group were significantly better than SSZ group in all clinical parameters including ESR, CRP, harris, BASDAI, and ASDAS. TNF- α inhibitor treatment got a quick clinical remission from 12 weeks and hip function improvement, and maintained the significant improvement tendency until week 52.

Based on the fact that the economic cost of TNF- α inhibitor was relatively higher than classical DMARDs, the results indicated a real-world characteristic at baseline that patients in TNF- α group had relatively more serious disease activity and shorter disease duration than control group which was consistent with previous studies[29]. Those SpA patients with active hip arthritis were suggested to receive TNF- α inhibitor therapy to get quick pain reduction and symptom remission based on the global effectiveness of TNF- α inhibitor[30]. Similarly, the baseline result of MRI analysis also did not fulfill the criteria of no difference between two groups. Especially of the parameters about BME score of acetabular, total BME score, and effusion-synovitis. The real-world data revealed that, both disease activity and MRI features of patients under treatment of TNF- α inhibitor were relatively more serious. Those patients were suggested to TNF- α inhibitor therapy in order to quickly improve clinical outcome, relief pain and reduce adverse reactions. As a consequence of those real-world characteristics, the results must be interpreted with caution.

However, some limitations of this study should be acknowledged. Firstly, one-year treatment and observation period is short, prolonged followup need to be observed. Next, This is a single-centre study, and population bias may limit the efficiency. Moreover, although HIMRISS method was performed based on accurate MRI slices, it was not commonly used and need more application and confirmation in the future.

Conclusion

The quantitative assessment results demonstrated that TNF- α inhibitor could significantly simultaneously improve clinical outcome and MRI response of hip arthritis in SpA patients. This improvement could quickly achieve in 12 weeks treatment period and maintain in long-term follow-up, which achieved advanced curative effect than non- TNF- α agents.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of Xijing Hospital of China (Instruction number: 20110303-7).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declared that they have no conflicts of interest.

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Authors' Contributions

ZK and ZY wrote the article. HQ and LY revised the figures. WW and DJ revised the tables. ZM, ZZ and ZP revised the manuscript. All authors researched the data for the article, made substantial contributions to the content, and edited the manuscript.

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Abbreviations

SpA: spondyloarthritis; MRI: Magnetic Resonance Imaging; BME: Bone Marrow Edema; HIMRISS: Hip MRI Inflammation Scoring System; ESR: Erythrocyte Sedimentation Rate; CRP: C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASAS: Assessment of SpondyloArthritis international Society; STIR: Short-tau Inversion Recovery; DMARDs: disease Modifying Anti-rheumatic Drugs; MTX: Methotrexate; SSZ: Sulfasalazine; HLA-B27: Human Leucocyte Antigen B27; BASRI-h: Bath Ankylosing Spondylitis Radiology Index-hip score.

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Figures

Figure 1

The distribution of ASAS remission rates between TNF-α and control group at week 52.

Figure 2

The distribution of disease activity between baseline and week 52 of both groups. (Note: disease inactive: ASDAS-CRP $\leq$ 1.3, ASDAS-ESR $\leq$ 1.3 or BASDAI $\leq$ 4. low disease activity: 1.3<ASDAS-CRP/ASDAS-ESR $\leq$ 2.1. moderate disease activity: 2.1<ASDAS-CRP/ASDAS-ESR $\leq$ 3.5. high disease activity: ASDAS-CRP/ASDAS-ESR> 3.5. disease active: BASDAI>4.)

Figure 3

The clinical performance of TNF-α inhibitor group from baseline to week 52.

Figure 4

The ASAS remission rates between two kind of TNF- α inhibitor groups. (Note: ETA: etanercept. ADA: adalimumab. INF: infliximab).