Hospitalizations of Patients Treated with Anti-Tumor Necrosis Factor-α Agents — A Retrospective Cohort Analysis

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ABSTRACT. ***Objective.*** To assess the association between treatment with anti-tumor necrosis factor-α (TNF-α) agents and the occurrence of hospitalizations, their causes and complications, compared to treatment with traditional disease-modifying antirheumatic drugs in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS).

Methods. A retrospective cohort study was conducted of patients with RA, AS, and PsA treated with anti-TNF-α agents between April 2002 and December 2007. Patients were assessed during the period of anti-TNF-α treatment (Group B) and compared to an equivalent period before initiation of anti-TNF-α therapy (Group A). All hospitalization charts were reviewed and diagnoses, comorbidities, concomitant medications, and clinical course were analyzed. Statistical analysis was performed using multivariate mixed Poisson regression.

Results. In the study period of 57 months, 735 hospitalization events of 327 patients were analyzed. Statistically significant decreases were seen in the total number of hospitalization events as well as hospitalizations due to exacerbation of rheumatic diseases in Group B compared to Group A (44.4 vs 74.2 and 21.9 vs 47.5 per 100 patient-years, respectively; $p < 0.0001$). More infectious events (7.4 in Group B compared to 4.6 per 100 patient-years in Group A; $p = 0.043$) were associated with anti-TNF-α treatment, older age, and underlying disease, because patients with RA had higher rates of infections compared to patients with PsA and patients with AS.

Conclusion. The overall effect of anti-TNF-α therapy was a significant decline in total hospitalization events. The decrease was more prominent in patients with RA than in patients with AS and patients with PsA, and reflected the significant decrease in hospitalizations due to rheumatic disease exacerbation. The decrease was more pronounced than the observed increase in infectious events. (J Rheumatol First Release Oct 15 2012; doi:10.3899/jrheum.111516)

Key Indexing Terms:
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The development of biologically specific therapies has revolutionized the treatment of inflammatory arthritis. Compared with existing synthetic disease-modifying antirheumatic drugs (DMARD), these agents have increased clinical and radiological response rates, particularly when initiated early in the course of the disease[1,2,3,4,5]. The clinical efficacy of tumor necrosis factor-α (TNF-α) blockers has been demonstrated in numerous studies as monotherapy or in combination with a traditional DMARD, usually methotrexate (MTX) — the concomitant standard antirheumatic agent[1,2,3]. However, most clinical trials of these drugs were powered for efficacy and not for safety[1,2,3,5]. Data collected from surveys and registries of patients with inflammatory arthritis are now accepted worldwide as valid on the longterm safety and efficacy of the biological agents, reflecting more reliably the common practice of treating patients with complex comorbidities and of older age[6,7,8,9,10] than those participating in clinical trials.

Data regarding hospitalization, representing complications of the therapy, were included in registries but were not analyzed separately. In several reports only the admission cause was included and further clinical complications during hospitalization were not evaluated[11].

Armstrong, *et al* noted a reduction in the use of rheumatology inpatient beds in a small survey evaluating 34 patients with rheumatoid arthritis (RA) treated with anti-TNF-α agents compared to the period before the initiation of the biological agents[12]. A similar trend was noted in patients with ankylosing spondylitis (AS)[13]. The anti-TNF-α inhibitors infliximab, etanercept, and adalimumab have been included in the Israeli national list of health services for the treatment of RA since 2000 and for the treatment of psoriatic arthritis (PsA) and AS since 2002.

The objective of our study was to assess the association between treatment with anti-TNF-α agents and the occurrence of hospitalizations, their causes and complications during the course of therapy compared to treatment with traditional DMARD in patients with RA, PsA, and AS. This aspect of anti-TNF-α treatment in rheumatic diseases has not been thoroughly investigated.

MATERIALS AND METHODS

Study population. A retrospective cohort analysis of patients with RA, PsA, and AS treated with anti-TNF-α agents for a minimum of 6 months and insured by Clalit Health Services in northern Israel was conducted. Clalit Health Service insurance covers over 1 million individuals in this area (about 50% of the total population) and uses a comprehensive computerized database with continuous input from pharmaceutical, medical, laboratory, and administrative computer operators. The database for biological agents included in the Israeli "health basket" contains diagnosis of the rheumatic disease as determined by a rheumatologist. These data were linked through a unique national identification number to the pharmaceutical database to retrieve information about start and stop dates of anti-TNF-α agents and DMARD. For our study, the database was searched for hospitalizations occurring between April 2002 and December 2007 of adult patients who received 1 of the following diagnostic codes: "Rheumatoid Arthritis," "Psoriatic Arthritis," or "Ankylosing Spondylitis," and were treated with anti-TNF-α agents for at least 6 months. Each patient's record was evaluated during the anti-TNF-α treatment period (Group B) and compared to an equivalent period just prior to the initiation of anti-TNF treatment (Group A). For patients in whom the anti-TNF-α treatment was discontinued, data were collected for 3 additional months after treatment discontinuation. The resulting time windows (Group A and Group B) were equivalent per patient.

Data collection. A designated database was created and included patient demographics and disease characteristics including age, sex, rheumatic disease diagnosis, and comorbidities. Laboratory investigations obtained at the beginning and the end of each period were collected, including complete blood count, kidney and liver enzymes, rheumatoid factor (RF), C-reactive protein (CRP), antinuclear antibody (ANA), anti-dsDNA, and hepatitis B and C status. Data were also recorded regarding distribution of concomitant medications including systemic steroids, nonsteroidal antiinflammatory drugs (NSAID), and synthetic DMARD (MTX, hydroxychloroquine, sulfasalazine, azathioprine, cyclosporine A, injectable gold, leflunomide, and minocycline).

Two internists reviewed all patients' hospitalization charts in parallel using a standardized protocol. A mutual crossover list review was performed to discuss discrepancies. The final review determined initial causes for admission and additional complications during hospitalization (hospitalization events) as recorded in the patients' charts. Special attention was paid to admissions due to exacerbation of the rheumatic disease, orthopedic, neurologic, and cardiologic causes. Infections were further evaluated for the site of infection and the pathogen involved as described in the discharge summary and in the computerized laboratory data.

Statistical analyses. For each subject we measured the number of hospitalization events for a specific cause, before and during treatment with anti-TNF-α agents, using these periods as a random followup period. The outcome variable of our study was the incidence of hospitalization events after the initiation of anti-TNF-α therapy compared to their incidence before initiation, with an assumed Poisson distribution. We used age, sex, and diagnosis as intersubjects explanatory (confounding) variables. To model the changes in the number of events, for a specific cause, during treatment versus before treatment, and the changes between subjects, we used the generalized estimating equations (GEE) method proposed by Liang and Zeger[14]. A Poisson distribution of the number of hospitalization events during 1 year was assumed and a log link was used. The followup period before and during the treatment was treated as a random variable. Least-squares means (LS-mean) and their differences with the corresponding 95% CI were used to estimate the effect of factors such as period, sex, and diagnosis on the number of hospitalization events for a specific cause. For all computation, the 95% CI and probability of the LS-mean to be 0 was computed. SAS GLIMIX procedure (SAS Institute Inc.) was used for computations.

RESULTS

Study population. There were 333 patients in the cohort of patients with rheumatic disease who were treated with anti-TNF-α agents between April 2002 and December 2007. Of them, complete hospitalization records were identified for 327, who were included in the study.

Mean age of the study population was 54.2 ± 15.4 years, with a female predominance of 61.8%. The study population consisted of 192 patients with RA (58.7%), 73 with PsA (22.3%), and 62 with AS (19%). Comorbidities and background diseases are listed in Table 1.

Laboratory data. The mean values of blood counts, kidney function, and liver function measures were within normal range in both groups (Group A before treatment and Group B during anti-TNF-α treatment). No statistically significant difference was noted in RF values between the groups; statistical analyses of CRP level and ferritin were not performed because of large variation of the data in Group B. Two cases of seroconversion for ANA and anti-dsDNA results and 1 case of increased titer were detected in Group B, without clinically significant associated events. A slight increase in serum lipid values was noted during anti-TNF-α treatment in all measures: total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides (197 ± 42, 117 ± 37, 53 ± 18, and 136 ± 76 mg/dl, respectively) compared to the values before treatment (190 ± 39, 115 ± 32, 50 ± 15, and 128 ± 67 mg/dl), reaching statistical significance only in triglyceride levels ($p = 0.02$).

Medication distribution. The use of NSAID decreased following anti-TNF-α treatment [252 patients (77.1%) vs 220 patients (67.3%); OR 1.66, 95% CI 1.29–2.34, $p <$

Table 1. Characteristics of the study population. Data are n (%) unless otherwise indicated.

Variable	Rheumatoid Arthritis	Psoriatic Arthritis	Ankylosing Spondylitis	Total
No. patients	192 (58.72)	73 (22.52)	62 (18.96)	327
Age, yrs (SD)	57.24 (15.78)	53.54 (12.7)	45.38 (13.88)	54.17 (15.42)
Sex				
Female	142 (43.7)	38 (11.6)	21 (6.4)	202 (61.7)
Male	49 (15)	35 (10.7)	41 (12.5)	125 (38.3)
Smoking	19 (5.8)	11 (3.4)	10 (3)	40 (12.2)
Hypertension	63 (19.2)	30 (9.2)	13 (4)	106 (32.4)
Hyperlipidemia	42 (12.8)	21 (6.4)	7 (2.2)	70 (21.4)
Diabetes mellitus	19 (5.9)	14 (4.3)	3 (0.9)	36 (11.1)
IHD	34 (10.4)	10 (3)	2 (0.6)	46 (14.1)
CHF	9 (2.8)	0	1 (0.3)	10 (3.1)
COPD	5 (1.5)	1 (0.3)	1 (0.3)	7 (2.1)

IHD: ischemic heart disease; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease.

0.0001]. There was also a trend toward a decrease in the use of systemic corticosteroids [188 patients (57.5%) vs 174 patients (53.2%); OR 1.23, 95% CI 0.96–1.57, p = 0.1] and no change in MTX use [186 patients (56.9%) vs 177 patients (54.1%); OR 1.13, 95% CI 0.89–1.43, p = 0.31].

Hospitalizations. Throughout the study period of 57 months, there were 735 hospitalization events: 435 before initiation of anti-TNF-α therapy and 300 during treatment. The distribution of the hospitalization events is given in Table 2.

The frequency of hospitalization events was lower during anti-TNF-α treatment than before treatment (44.2 vs 74.2 hospitalizations per 100 patient-years; $p < 0.0001$). The decline was noted in all 3 diseases, more prominently in patients with RA than among patients with AS and PsA (183.5, 37.9, and 27.2 events/100 patient-years; $p < 0.001$, $p = 0.006$, $p = 0.03$, respectively). In a subgroup analysis, men had a higher admission rate than women ($p = 0.0003$; Tables 3 and 4).

Infections. Infectious events per 100 patient-years of followup were 7.4 in Group B compared to 4.6 in Group A. In multivariate analysis, the rate of hospitalizations was associated with anti-TNF-α treatment, age, and background rheumatic disease: patients with RA exhibited a higher rate of infections during the treatment period compared to patients with PsA and AS (Tables 3 and 4). The most common infections were respiratory, urinary, and skin infections (Table 5). The most common identified pathogens related to hospitalization in Group B were gram-negative bacteria [*Escherichia coli* (8 cases), and 1 case each of *Pseudomonas aeruginosa*, *Serratia acinetobacter*, and *Morganella morganelli*] followed by streptococcus pneumonia in 5 cases. A review of the blood, urine, synovial fluid, and skin cultures revealed 2 hospitalizations due to intercellular pathogens — *Mycobacteria fortuitum*, both of them in Group B patients. While in Group A no viral infections requiring hospitalization were identified, in Group B, during anti-TNF-α therapy, 3 cases of reactivation of hepatitis B virus were reported, 1 occurring despite prophylactic treatment with lamivudine, as well as 2 cases of herpes zoster.

Table 2. Distribution of hospitalization events before and during anti-TNF-α treatment (Group A before treatment and Group B during treatment).

Events	Group A	Group B
Total	435	300
Rheumatic disease exacerbation	271	115
Infectious diseases	41	68
Total orthopedic admissions	20	16
Due to the rheumatic disease	11	9
Other orthopedic causes	9	7
Hospitalization for surgery	23	10
Total cardiovascular admissions	32	41
Congestive heart failure	1	4
Ischemic heart disease	12	13
Cerebrovascular accident	6	6
Atypical chest pain	9	7
Other	4	11
Exacerbation of lung disease	3	0
Multiple sclerosis-like	0	2
Other neurologic causes	2	6
Hematological malignancy	0	5
Solid malignancy	2	4
Anemia	6	7
Fever of unknown origin	6	5
Elective admission	2	1
Electrolyte abnormality	3	2
Inflammatory bowel disease exacerbation	4	3
Side effects of other medications	4	0
Leg edema requiring investigation	3	0
Psoriasis skin exacerbation	4	0
Renal colic	2	1
Other	7	14
Death	0	1

TNF: tumor necrosis factor.

Rheumatic disease exacerbation. After initiation of anti-TNF-α therapy, a decrease in the rate of hospitalization due

Table 3. Hospitalization events (95% CI) per 100 patient-years (Group A, before anti-TNF-α treatment, and Group B, during anti-TNF-α treatment).

	Group A	Group B	Female	Male	Ankylosing Spondylitis	Psoriatic Arthritis	Rheumatoid Arthritis
Total events	74.2 (59.7–92.5)	44.4 (35–56.2)	43.7 (35–56.2)	75.3 (58.3–97.3)	37.9 (24.6–8.4)	27.2 (17.7–41.7)	183.5 (156–215.8)
Infection	4.6 (2.8–7.5)	7.4 (4.8–11.5)	2.9 (1.7–4.9)	11.7 (7.8–17.6)	3.8 (1.6–7.9)	3.6 (1.7–7.9)	14.5 (10.7–19.6)
Exacerbation of rheumatic disease	47.5 (37.9–59.6)	21.9 (16.7–28.7)	29.8 (22.9–38.6)	34.9 (26.7–45.7)	19.5 (12.4–30.7)	18 (11.8–27.6)	95.3 (80.1–113.3)
Total orthopedic surgery	1.6 (0.6–4.3)	1 (0.3–3.1)	2.1 (0.8–5.3)	0.8 (0.2–3)	1.5 (0.3–7)	0.5 (0.6–4.2)	2.6 (1.2–5.5)
Orthopedic surgery due to rheumatic diseases	0.6 (0.1–3.2)	0.4 (0.07–2.4)	1.3 (0.4–4.2)	0.2 (0.01–2.9)	0.8 (0.1–6.3)	0.3 (0.1–4)	0.6 (0.1–3)
Total other surgery	3.2 (1.6–6.2)	2.3 (1.1–4.8)	1.1 (0.5–2.8)	6.4 (3.7–11)	4.6 (2–10.3)	1.3 (0.4–4.6)	3.1 (1.7–5.9)
IHD	0.35 (0.07–1.7)	0.38 (0.08–1.8)	0.07 (0.01–0.5)	1.9 (0.5–7.3)	0.3 (0.05–2.7)	0.08 (0.002–2.8)	1.7 (0.7–4.4)

TNF: tumor necrosis factor; IHD: ischemic heart disease.

Table 4. Comparison of hospitalization events rate per 100 patient-years.

	Total Events	Infection	Exacerbation of Rheumatic Disease	Total Orthopedic Surgery	Orthopedic Surgery Due to Rheumatic Diseases	Total Other Surgery	IHD
Mean ratio before/during	1.67	0.62	2.17	1.54	1.56	1.39	0.91
95% CI	1.4–2.01	0.39–0.98	1.7–2.76	0.6–4.02	0.34–7.18	0.62–0.62	0.35–2.32
p	< 0.0001**	0.043*	< 0.0001**	0.37	0.57	0.42	0.84
Mean ratio female/male	0.58	0.25	0.85	2.63	6.64	0.18	0.037
95% CI	0.43–0.78	0.15–0.4	0.63–1.15	0.67–10.3	0.39–112.0	0.07–0.46	0.008–0.18
p	0.0003**	< 0.0001**	0.3	0.17	0.19	0.0004**	< 0.0001**
Mean ratio RA before/during	1.58	0.51	1.99	1.37	1.37	1.22	0.82
95% CI	1.29–1.93	0.3–0.86	1.52–2.59	0.49–3.83	0.49–3.83	0.42–3.51	0.3–2.19
p	< 0.001**	0.01*	< 0.001**	0.54	0.54	0.72	0.69
Mean ratio AS before/during	2.45	8.32	3.76	1.55	1.55	1.55	3.76
95% CI	1.31–4.57	0.5–123.7	1.45–9.74	0.36–6.7	0.36–6.7	0.36–6.7	1.45–9.74
p	0.006*	0.12	0.007*	0.55	0.55	0.55	0.007*
Mean ratio PsA before/during	1.94	0.56	2.9	0.52	0.52	2.08	2.9
95% CI	1.05–3.45	0.11–2.81	1.29–6.5	0.006–42.65	0.006–42.65	0.15–28.3	1.29–6.5
p	0.03*	0.48	0.01*	0.77	0.77	0.58	0.01*

* $p < 0.05$; ** $p < 0.005$. RA: rheumatoid arthritis; PsA: psoriatic arthritis; AS: ankylosing spondylitis; IHD: ischemic heart disease.

to exacerbation of the rheumatic disease was found, from 47.5 events per 100 patient-years before treatment to 21.9 per 100 patient-years after initiation of treatment ($p < 0.0001$). The decline was noted in subanalysis of all 3 diseases: RA, AS, and PsA. No sex-related or age-related differences were observed (Tables 3 and 4).

Other hospitalization events. The rate of hospitalizations due to orthopedic and surgical indications was higher before initiation of anti-TNF-α therapy compared to the period during anti-TNF-α therapy. Accordingly, a trend toward a higher rate of orthopedic procedures was found, which did not reach statistical significance, even after step regression (Table 4). The rate of hospitalizations due to ischemic heart disease was similar during the 3 periods despite older age in the anti-TNF treatment period group (Table 4). During anti-TNF-α therapy, a statistically significant decline in hospitalizations was noted in patients with spondyloarthropathies, i.e., AS and PsA. In Group B, more heart failures were reported, without further statistical processing because of the small number of events. No exacerbation of pulmonary diseases was reported. Two neurological admissions were reported for laboratory investigation of multiple sclerosis-like symptoms.

Five hospitalizations due to hematological malignancies were reported during anti-TNF-α therapy: 2 patients with non-Hodgkin's lymphoma, 1 patient with Hodgkin's lymphoma, 1 patient with myelodysplastic syndrome, and 1 patient with a myeloproliferative disorder were diagnosed 11, 23, 14, 21, and 11 months after initiation of anti-TNF-α therapy, respectively.

Solid tumors. Colon cancer was reported after 10 months, endometrial cancer after 17 months, and central nervous system tumors 5 and 50 months after the initiation of anti-TNF-α therapy. Two patients with histories of cancer (1

Table 5. Infections requiring hospitalization in both periods: Group A, before anti-TNF-α treatment, and Group B, during anti-TNF-α treatment.

Infections	Group A	Group B
Tonsillitis/sinusitis/pharyngitis	4	5
Bronchitis	3	7
Pneumonia	4	7
Sepsis	2	10
Septic arthritis	1	0
Osteomyelitis	1	0
Abscess	7	6
Cellulitis	6	4
Wound infection	1	1
Urinary tract infection	9	14
Gastroenteritis	3	6
Hepatitis	0	4
Endophthalmitis	0	1
Thrombophlebitis	0	2
Mediastinitis	0	1
Total	41	68

TNF: tumor necrosis factor.

with colon cancer and 1 with lung cancer) who were treated with anti-TNF-α agents did not experience recurrence of the malignancy during the study period.

DISCUSSION

Our study, based on data regarding hospitalizations and drug administration, laboratory measurements, and events during hospitalization, complements the assessment of treatment with anti-TNF-α agents in real-life settings. In contrast to randomized controlled trials of anti-TNF-α agents, our cohort was not limited by patients' age, comorbidities, type of rheumatic disease, or duration of treatment. We suggest that the unique focus of our study of hospitalization events in patients with different rheumatic diseases (RA, PsA, and AS) treated with anti-TNF-α agents supplements the available body of knowledge from registries of patients treated with biological agents. The results should be analyzed with caution because of the complex nature of hospitalization in patients with rheumatic diseases and therefore the findings may be attributed to reasons other than TNF therapy.

In our study, drug efficacy was addressed indirectly by assessing exacerbations of the rheumatic disease requiring hospitalization and drug administration. We found a statistically significant decrease in the dispensing of NSAID in addition to a decrease in consumption of corticosteroids, although the differences did not reach statistical significance in all 3 rheumatic diseases. Data from large-scale registries on hospitalization due to rheumatic disease exacerbation are largely unavailable, but reports of observations in small groups support our findings. Listing, *et al*[13] reported similar findings in a group of 49 patients with AS treated with anti-TNF-α agents, with a reduction in admission rate from 41% before treatment to 10% during 1 and 2 years of treatment. Reports from studies of patients with RA point to a similar decline in rheumatic disease exacerbations requiring hospitalization during treatment with anti-TNF-α compared to the same period before the initiation of the biological agents[12,15].

In our analysis, throughout the course of anti-TNF-α therapy, fewer patients required orthopedic and general surgeries compared with the period before the treatment. However, the difference did not reach statistical significance. Similar to our results, no statistical change was observed in the number or type of orthopedic surgeries performed between 2004 (6.2%) and 2007 (5.2%) in patients treated with anti-TNF-α agents in an observational cohort database of rheumatic diseases in Japan[16]. In that report, however, the proportion of patients undergoing RA-related surgeries while treated with biologic agents was higher (9.7%) than in patients who were biologic-naive (4.7%).

An increase in the rate of infections, as we noted, has also been reported in other surveys and registries[11,13,17,18]. In contrast, in a British registry study the data were inconclusive[19]. The different design of our study may explain the findings. In our study we considered all infections either at admission or those occurring during hospitalization, as opposed to the data from a US cohort, which considered only the first hospitalization due to an infectious etiology[11]. Despite the variation in study design, most studies report an increased risk of infection. The association between the occurrence of hospitalizations and the different anti-TNF-α dosages or time following initiation of the biological agents was not assessed in our study; however, we confirmed the correlation of an increased rate of infections with older age noted by Schneeweiss, *et al*[18]. A significantly higher rate of infections in patients with RA compared to the spondyloarthropathy group was found, possibly related to the increased use of steroids and MTX in the former group[20]. The most commonly involved infection site was the respiratory tract, followed by the urinary tract, and skin infection. Others have found skin infections to be more prevalent[7,11].

Because treatment of RA with anti-TNF-α agents may predispose to a significant increase in the risk of tuberculosis (TB), all patients in our study underwent preliminary screening for TB prior to initiation of therapy[21]. In our cohort, no cases of mycobacteria tuberculosis occurred. Our study does emphasize, however, the need for continued awareness of atypical mycobacteria, because 2 cases of *Mycobacteria fortuitum* are reported here. Moreover, our data suggest that treatment with TNF-α inhibitors may be associated with increased risk of viral reactivation including herpes zoster, as reported by Strangfeld, *et al*[22], and hepatitis B virus reactivation despite antiviral therapy.

One US observational study concluded that biologic therapy is associated with an increased risk of skin cancers

but not solid tumors or lymphoma[8], in contrast to the findings of a metaanalysis of randomized control trials that noted a dose-dependent increased risk of malignancies in patients treated with anti-TNF-α agents[17]. Our study was designed to observe only hospitalization events, and therefore detection of skin cancer and other diagnoses that are usually treated in outpatient settings may have been missed.

There was no recurrence of malignancy requiring hospitalization during anti-TNF treatment and only 9 new cases of malignancy were diagnosed, numbers too small to be amenable to statistical analysis.

Rheumatic disease patients, especially patients with RA, often have an abnormal lipoprotein pattern, predominantly low levels of HDL cholesterol. We noted, in concordance with the findings reviewed by Steiner and Urowitz[23], an increase in all measurements of the lipid profile: total cholesterol, LDL cholesterol, and HDL cholesterol, reaching statistical significance only in triglyceride levels[23]. Overall, although patients treated with anti-TNF-α agents were older and had a more lipidogenic profile, they did not have an increased rate of ischemic events; and in patients with AS and PsA, a statistically significant decline was noted during treatment with biological agents. These findings are consistent with suggestions of a metaanalysis reporting that TNF-α antagonists appear to reduce the likelihood of coronary vascular disease in individuals with RA, although this was not seen as consistently as in studies of MTX[24].

Limitations of our study include the relatively small number of patients, with an unequal distribution among the rheumatic diseases treated with anti-TNF-therapy. We did not compare the influence of different anti-TNF-α agents nor did we examine economic aspects.

Our retrospective study shows that treatment with anti-TNF-α agents in patients with rheumatic disease is associated with a lower incidence of hospitalization events, especially those due to exacerbation of the basic disease. The decrease was more prominent in patients with RA than in patients with AS and PsA. Patients with rheumatic disease have an increased risk of hospitalization because of infections during treatment with anti-TNF-α agents when compared with treatment with DMARD.

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