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Response of elderly patients with rheumatoid arthritis to methotrexate or TNF inhibitors compared with younger patients

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Objective. To compare the efficacy of MTX and MTX+TNF inhibitors (TNFis) in elderly patients with RA with that in patients of younger age.
Methods. Data from two large, randomized, controlled, double-blind trials in patients with early RA using adalimumab or infliximab+MTX or MTX alone were obtained and pooled. Composite disease activity indices were calculated at baseline and 1 year of treatment, and compared in groups of patients classified by quartiles of age with the highest age group comprising 61–82 years using analysis of variance or Kruskal–Wallis test.
Results. Across all age quartiles, improvement on MTX was similar with respect to changes of composite disease activity indices, assessment of physical function and X-ray progression. Likewise, TNFi+MTX had similar effects across all age groups, but the effects of the combination were more profound than those of MTX monotherapy. Also in 10% of the patients with the highest age, primarily septuagenarians, improvement was seen to a similar degree as in the younger ones.
Conclusions. Responsiveness of elderly patients with RA to MTX or TNFi+MTX is similar to that observed in patients of younger age.

Key words: Rheumatoid arthritis, Methotrexate, Tumour necrosis factor, Treatment response, Elderly.

Introduction

RA is the most common chronic inflammatory joint disease in adults, affecting 0.5–1% of the population. The incidence of RA increases with age, peaking between the fourth and sixth decade [1]. Secular trends in time suggest that the mean age at diagnosis increases, as observed in a Finnish cohort, where the age of onset changed from a mean of 50 to almost 60 years during just one decade and the incidence rates declined in the younger age groups [2]. These observations, in line with the increasing life expectancy in the industrialized world, suggest that the number of elderly patients requiring DMARD therapy will increase.

The most important long-term consequence of RA is physical disability, which, however, is difficult to interpret. Disability has a component related to disease activity, which is reversible, and a component related to joint damage, which is irreversible [3]. In elderly RA patients, the reasons of physical disability are even more complex, since the decline of physical function related to ageing must be considered [4].

It has been suggested that RA in the elderly is a phenotypic variant and has an intrinsically different course compared with RA in younger individuals [5]. This concept is further supported by reports on differences in the genetics of RA in the elderly [6]. In light of these findings, it is of particular importance to understand the efficacy of DMARDs in elderly patients with established RA, since only DMARD therapy can effectively interfere with active disease, joint damage, and is able to prevent disability.

The effect of DMARDs in elderly patients with RA has not been a main research focus over the past years, although two recent reports have found good clinical effects of disease modification, including the use of TNF inhibitors (TNFis), in elderly individuals [7, 8]. However, the vast majority of these patients had longstanding disease; and in one of the studies, physical function in elderly RA patients did not improve. In contrast to studies of NSAIDs [9–11], no major clinical trials have been designed addressing this particular population. Moreover, a recent review concluded that 'data are insufficient to provide much confidence in the potential beneficial effects of DMARDs in the elderly' [11].

Therefore, older patients with RA are still less likely to receive DMARD treatment than their younger counterparts, and increasing age has been found to be an important determinant of less intensive RA care [12–14]. As a consequence of applying less effective therapies, functional impairment might progress more rapidly in the elderly compared with younger patients with RA, especially since physical function is already naturally reduced in the elderly [4]. The rapid decline in function could be further aggravated by a higher disease activity at onset. Together with an ineffective DMARD therapy, this may result in more radiographic damage as it has been observed in elderly when compared with younger patients with early RA [15]. Based on these data, RA in the elderly could be viewed as not only being more severe, but also being less responsive to DMARD therapy.

In the present study, we focused on patients with early RA to obviate potential effects of long disease duration on outcomes. We performed a subanalysis of pooled clinical trial data, and assessed the effect of age on the responsiveness of disease activity, physical function and joint damage in patients with early RA treated with MTX, or a combination of MTX with TNFi therapy.

Methods

Data sources

We obtained patient-level data from two pivotal clinical trials of early RA. In both studies, MTX-naive patients with active RA (at least 8–10 swollen and 10–12 tender joints using a 66/68 joint count) were included. Disease duration had to be $\leqslant$3 years. Patients were randomized to receive either MTX alone or in combination with TNFi: 3 or 6 mg/kg infliximab in the active controlled study of patients receiving infliximab for the treatment of rheumatoid arthritis of early onset (ASPIRE) trial; 40 mg adalimumab every other week in the prospective, multi-center, randomised, double-blind, active, comparator controlled, parallel-group study comparing the fully human monoclonal anti-TNF antibody D2E7 given every second week with MTX given weekly and the combination of D2E7 and MTX in patients with early RA

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(PREMIER) trial [16, 17]. We were provided with data on 80–90% random samples of patients from these trials. Patients had to be $\geqslant$18 years old (ASPIRE and PREMIER) and $\leqslant$75 years (ASPIRE). The mean age was 50 years for ASPIRE trial, and 52 years for PREMIER study with a range of 18–82 years. For the analyses, we pooled data of the MTX treatment arms as well as data of the combination therapy arms of the two trials. Pooling was done to increase patient numbers and power in the subgroup analysis (see below). In general, both studies had shown that a combined therapy with MTX and TNFi is more efficacious than MTX monotherapy.

Study variables

For both trials, we identified patients with complete datasets at baseline ($n=1236$) and at the 12-month visits ($n=976$). Since visits were planned at slightly different time points in the trials, visits at 52 and 54 weeks were both regarded as 12-month visits.

Based on the individual measures of disease activity, we calculated values for the following composite indices: (i) Simplified Disease Activity Index [SDAI = swollen joint count (SJC) + tender joint count (TJC) + patient global assessment (PGA) + evaluator global assessment (EGA) + CRP], where SJC and TJC each constitute 28 joint counts, respectively, PGA and EGA on a 10-cm visual analogue scale and CRP is used as milligram per decilitre; (ii) Clinical Disease Activity Index (CDAI = SJC + TJC + PGA + EGA); and (iii) Disease Activity Score 28 ($DAS28 = 0.56 \times \sqrt{[TJC28]} + 0.28 \times \sqrt{[SJC28]} + 0.70 \times \log_{nat}[ESR] + 0.014 \times$ global health) [18–20]. Other variables used for the analyses were the HAQ-disability index (HAQ-DI) and radiographic changes scored according to the modified Sharp score (PREMIER: range 0–398) or the van der Heijde modified Sharp score (ASPIRE: range 0–448). Although the two scores are not identical, they are very similar and, therefore, the data were pooled for simplicity [21].

Statistical analyses

We first analysed the association of age with the outcome variables (disease activity, physical function and radiographic damage) at baseline and their changes. To quantify the strength of correlations, scatterplots and Spearman's r or Pearson's r (if normal distribution assumption was met) were used.

For all further analyses, we grouped the study population into quartiles (Q) by the age of the complete pooled cohorts; Q1 comprised the age group of 18–41 years, and ages in Q2–Q4 encompassed patients of 42–50, 51–60 and 61–82 years of age, respectively. We initially assessed the various outcomes at baseline across these four age groups using Kruskal–Wallis (KW) test or analysis of variance (ANOVA, if normality assumption was fulfilled).

To assess the responsiveness of the different outcomes, we compared the changes in the three outcome variables between the four groups using KW or ANOVA. A *post hoc* power calculation based on the fixed sample size, the variation of the data at baseline, a targeted power of 90% ($\beta = 0.10$) and a significance level of 5% ($\alpha = 0.05$) indicated a detectable difference of 4.9 for changes in SDAI, 4.4 for changes in CDAI, 0.4 for changes in DAS28, 0.2 for changes in HAQ-DI and 6.5 for changes in radiographic scores. This *post hoc* power calculation has no purpose in study design, but is presented simply to facilitate the interpretation of results of the study. Given some differences between the four age groups at baseline, we also calculated effect sizes (ESs) for improvement for these groups to supplement the analysis. ESs were calculated as mean changes of values divided by their S.D. at baseline.

Analyses were initially performed for the pooled MTX-treated patients and then for the patients treated with TNFi+MTX. To be concise in the presentations of our results, we focused on the SDAI. However, the respective results for the two other scores, the CDAI and the DAS28, were also obtained and are partly presented. We also performed a subgroup analysis in the oldest 10% of the patients. All analyses were performed on SPSS 12.0 (SPSS, Chicago, IL, USA) and the SAS package, version 9.1.3 (SAS, Cary, NC, USA).

Results

Disease characteristics at baseline and in relation to age

Patient characteristics at baseline were comparable in both treatment arms (Table 1). The baseline characteristics of patients by quartiles of age are shown in Table 2, for the MTX-treated patients and those treated with the combination regimens.

For the MTX-treated patients, the correlation (r) of SDAI, HAQ-DI and radiographic scores at baseline with age are 0.16, 0.13 and 0.32, respectively (Spearman's/Pearson's correlation). While looking at the four age quartiles (Table 2) rather than the total group, the tests for statistically significant relationship of age with these three variables were $P < 0.05$ for SDAI (ANOVA), <0.05 for HAQ-DI (KW/ANOVA) and <0.0001 for X-ray scores (KW/ANOVA), respectively. The baseline correlations for the combination therapy group with SDAI, HAQ-DI and X-ray score were $r = 0.03$, 0.08 and 0.10, respectively; the statistical relationship of age quartiles with these three variables were $P =$ not significant (NS) (ANOVA), <0.05 (KW/ANOVA) and <0.0001 (KW/ANOVA), respectively.

The significant correlation between age and baseline disease activity in the MTX group indicates that the ensuing analysis of responsiveness needs to consider the differences in baseline values. This was done by using ESs (see below). On the other hand, radiographic changes and age correlated positively (r values) in both treatment groups, despite the fact that in both treatment groups mean disease duration was lowest in the highest age quartile (Table 2).

Responsiveness of clinical disease characteristics at 1 year of therapy

As expected, and demonstrated by the original reports of the ASPIRE and PREMIER trial, improvement of disease activity as measured by SDAI was significantly better in patients receiving combination treatment than under MTX monotherapy. Interestingly, this has been observed across all age quartiles ($P < 0.05$; Table 2, 'Change' columns). The same observation was made for improvement in HAQ scores ($P < 0.05$).

A similar proportion of the patients across all age quartiles completed the 1-year trial. After 1 year of therapy, the weak

TABLE 1. Patients' baseline characteristics

Variable	All patients	TNFi + MTX	MTX
Patients, *n*	1236	788	448
Female, %	72	70	75
RF positivity, %	74	73	75
Age, mean (S.D.), years	50.5 (13.3)	50.3 (13.3)	50.8 (13.2)
Disease duration, mean (S.D.), years	0.8 (0.8)	0.8 (0.8)	0.8 (0.8)
DAS28, mean (S.D.)	6.4 (1.0)	6.4 (1.1)	6.5 (1.0)
SDAI, mean (S.D.)	42.1 (13.9)	41.2 (13.9)	43.5 (13.9)
CDAI, mean (S.D.)	38.8 (12.4)	38.1 (12.5)	40.1 (12.2)
HAQ, mean (S.D.)	1.5 (0.7)	1.5 (0.7)	1.5 (0.6)
X-ray score, mean (S.D.)	14.65 (18.50)	13.36 (17.01)	16.90 (20.69)
CRP, mean (S.D.), mg/dl	3.3 (3.6)	3.2 (3.6)	3.3 (3.7)
TJC (of 28 joints), mean (S.D.)	14.9 (6.5)	14.5 (6.5)	15.7 (6.4)
SJC (of 28 joints), mean (S.D.)	11.1 (5.6)	10.7 (5.5)	11.7 (5.9)
EGA (mm on VAS), mean (S.D.)	65.6 (18.1)	65.6 (18.3)	65.5 (17.7)
PGA (mm on VAS), mean (S.D.)	62.6 (24.5)	62.7 (24.1)	62.4 (25.0)

Patients were treated with MTX or with TNFi + MTX.

TABLE 2. Baseline demographics, disease activity, function and structural damage by age quartiles at baseline and changes over 1 year for patients treated with MTX or MTX and TNFi

	Q1 (18–41 years)		Q2 (42–50 years)		Q3 (51–60 years)		Q4 (61–81 years)	
Patient baseline demographics								
	MTX	MTX + TNFi	MTX	MTX + TNFi	MTX	MTX + TNFi	MTX	MTX + TNFi
Patients, *n*	112	202	111	189	113	190	112	207
Female, %	74	77	83	68	72	70	72	67
RF positive, %	75	69	78	77	77	72	71	73
Duration of RA, mean (S.D.), years	0.9 (0.8)	1.0 (0.8)	0.8 (0.8)	0.7 (0.8)	0.9 (0.8)	0.8 (0.7)	0.7 (0.7)	0.7 (0.7)
Disease characteristics at baseline and after 1 year								
MTX	Baseline	Change	Baseline	Change	Baseline	Change	Baseline	Change
SDAI, mean (S.D.)	40.1 (12.6)	−27.0 (16.5)	42.6 (13.3)	−27.4 (14.7)	44.2 (14.0)	−26.9 (17.6)	47.0 (14.9)	−32.0 (15.8)
CDAI, mean (S.D.)	36.9 (10.9)	−25.3 (15.0)	39.9 (12.1)	−25.9 (13.6)	40.8 (12.1)	−24.8 (16.3)	42.9 (13.1)	−28.6 (13.9)
DAS28, mean (S.D.)	6.3 (1.0)	−2.6 (1.7)	6.5 (1.0)	−2.7 (1.6)	6.7 (0.9)	−2.6 (1.7)	6.7 (1.1)	−2.9 (1.3)
HAQ-DI, mean (S.D.)	1.4 (0.6)	−0.8 (0.6)	1.5 (0.6)	−0.7 (0.6)	1.5 (0.6)	−0.7 (0.7)	1.6 (0.7)	−0.9 (0.7)
X-ray score, mean (S.D.)	13.3 (22.5)	+4.7 (9.7)	12.9 (15.8)	+5.3 (11.3)	16.0 (16.0)	+3.2 (7.6)	25.4 (24.7)	+3.0 (6.4)
MTX + TNFi								
SDAI, mean (S.D.)	41.0 (13.2)	−32.5 (16.1)	40.6 (13.1)	−29.0 (15.8)	41.1 (14.2)	−28.8 (16.5)	42.2 (14.9)	−30.8 (15.2)
CDAI, mean (S.D.)	38.2 (12.2)	−30.1 (14.8)	38.0 (12.0)	−27.1 (14.3)	37.9 (12.8)	−26.2 (15.0)	38.1 (12.8)	−27.5 (12.8)
DAS28, mean (S.D.)	6.3 (1.0)	−3.4 (1.6)	6.3 (1.1)	−2.9 (1.6)	6.4 (1.1)	−2.9 (1.6)	6.4 (1.1)	−3.1 (1.4)
HAQ-DI, mean (S.D.)	1.4 (0.6)	−1.0 (0.6)	1.4 (0.6)	−0.9 (0.7)	1.6 (0.6)	−0.9 (0.7)	1.6 (0.7)	−0.9 (0.8)
X-ray score, mean (S.D.)	12.1 (16.4)	−0.1 (3.9)	10.0 (15.0)	+0.5 (3.9)	13.7 (17.0)	+1.1 (6.1)	17.4 (18.6)	+0.9 (4.4)

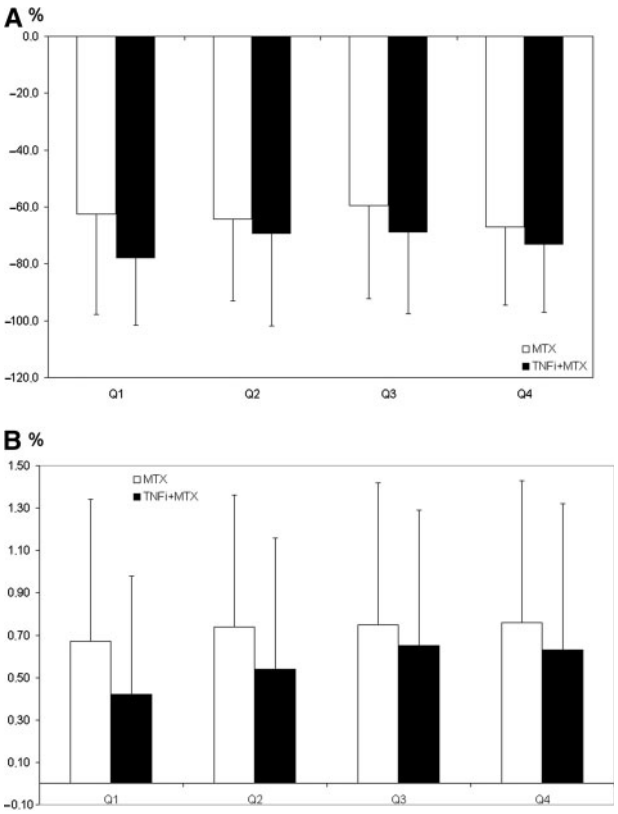

FIG. 1. (**A**) Relative change of SDAI from baseline. After 1 year of treatment, the decrease of disease activity (SDAI) was comparable between the patients in all age quartiles (Q1: 18–42 years; Q2: 43–52 years; Q3: 53–61 years; and Q4: 62–82 years), although of a significantly higher extent in those patients treated with TNFi + MTX compared with MTX monotherapy ($P < 0.05$). (**B**) HAQ-DI after at 1 year. After 1 year of treatment, HAQ-DI was comparable between all age groups, although the younger patients tended to have less impairment in their physical function, which, however, was not statistically significant. As also seen for the therapeutic effect on disease activity, patients treated with TNFi + MTX had lower HAQ-DI compared with those under MTX monotherapy ($P < 0.05$).

correlation between disease activity and age at baseline was completely lost in both treatment arms; only patients in the lowest quartile tended to have more improvement and thus less active disease (Table 2). In general, treatment efficacy reflected by the proportional decrease of disease activity after 1 year of therapy was comparable among all age groups (Fig. 1A). Similar results were seen for HAQ-DI (Fig. 1B).

No correlations of age with changes in SDAI and HAQ-DI were seen in the MTX group ($r = 0.07$ and 0.05, respectively; $P =$ NS by KW/ANOVA). The ESs for the SDAI and HAQ-DI are shown in Fig. 2. For the combination group, there was again a lacking correlation between SDAI and HAQ-DI with age ($r = 0.04$ and 0.05, respectively, $P =$ NS).

Radiographic changes

Radiographic progression was independent of age (Fig. 3): on MTX, the propensity to progress was somewhat higher in the two lower compared with the two higher age quartiles, whereas quite the reverse was observed for TNFi + MTX with no significant correlation for the MTX group by KW and $P < 0.05$ for the TNFi + MTX group with KW. Independent of age, TNFi + MTX therapy was much more effective and almost prevented radiographic progression across all age groups ($P < 0.0001$). Interestingly, only in the youngest age quartile, was mean radiographic progression fully halted, on the group level, with TNFi + MTX therapy. Overall, the mean change of the radiographic score in our cohort is comparable with that seen in the ASPIRE study [16].

Subgroup analysis in the oldest patients

We finally performed a subgroup analysis by assessing the oldest 10% of the patients, those aged 69–82 years, i.e. primarily the septuagenarians (Table 3). Regarding X-ray changes, these patients had higher scores at baseline than any other age group (compare Table 2), especially in the population randomized to receive MTX. After 1 year of therapy, the septigenerians tended to have higher HAQ-DI when compared with the younger age groups as shown in Table 3. Importantly, even in the oldest patients studied, TNFi + MTX treatment led to significantly lower disease activity and less radiographic progression after 1 year when compared with MTX monotherapy ($P < 0.01$).

Discussion

The present study demonstrates that the efficacy of DMARD therapy in elderly RA patients is comparable with that in younger patients. With MTX therapy, decrease of disease activity,

improvement of disability and reduction of radiographic progression are comparable across all age groups analysed. Moreover, similar results have been observed in the cohort of patients receiving TNFi in combination with MTX and in a subgroup analysis assessing the oldest 10% of the patients who were ~70- to 80-years old. The efficacy of treatment response in all age groups is comparable and slight numerical differences appear to be clinically meaningless. Drop-out rates or patients lost to follow-up during 1 year of treatment were low (~13%) and similar in all age groups, indicating that patients in the highest quartile were not more prone to premature discontinuation of study drugs than younger individuals. The known superiority of a combination therapy with TNFi + MTX to that of MTX monotherapy has been observed in all studied subgroups, also independent of age.

Treatment of elderly patients with RA is still difficult. In general, elderly patients suffer from comorbidities more frequently than younger ones, often giving rise to a variety of safety concerns. The fact that altered drug pharmacokinetics and pharmacodynamics may occur in patients of higher age often leads to a more cautious approach in making therapeutic decisions [11]. However, the efficacy of DMARD therapy in the elderly was also questioned, partly on the basis of presumed diversity in disease characteristics [5, 6, 15]. For all these reasons, elderly RA patients have often received less intensive treatment than younger ones [13].

The clinical characteristics of RA in the elderly and the changes over a 1-year period were generally similar to those observed in the younger patients. Thus, we were not able to confirm that elderly patients in a relatively early stage of RA suffer from higher disease activity [19, 22]. While there was a trend for higher activity at baseline in elderly patients randomized to treatment with MTX monotherapy, this was not observed at baseline in the treatment arms randomized to receive combination therapy. On the other hand, however, patients in the oldest quartile showed a shorter disease duration at baseline, which would have suggested lower radiographic scores, since usually (radiographic) damage is related to disease duration [3]. Therefore, caution in the interpretation of such findings is necessary, as there could be a population selection bias through entry criteria or just chance occurrence. However, baseline radiographic damage was worst among patients in the highest age quartile, and especially in the highest decile. This finding might therefore support previous observations that joint damage in patients with early RA tends to be higher with increasing age [15]. While this could be due to factors that have been described to confound the assessment of joint radiographs in elderly RA patients, especially at early phases of disease [23], it might also be an indication that similar degrees of synovitis may lead to a greater structural damage in the aged joint. More importantly, physical disability, which at baseline was clearly worst in the oldest patients, improved to almost similar levels as in younger patients in the course of therapy, suggesting that the excess functional impairment in older patients was not an age-related, 'irreversible' disability [4]. Rather, older patients may be more susceptible to develop severe disability in the presence of a certain level of disease activity, which, however, is reversible upon effective therapeutic intervention. While among patients in the highest age decile those treated with MTX had the highest residual HAQ-DI, they also had the highest radiographic damage scores,

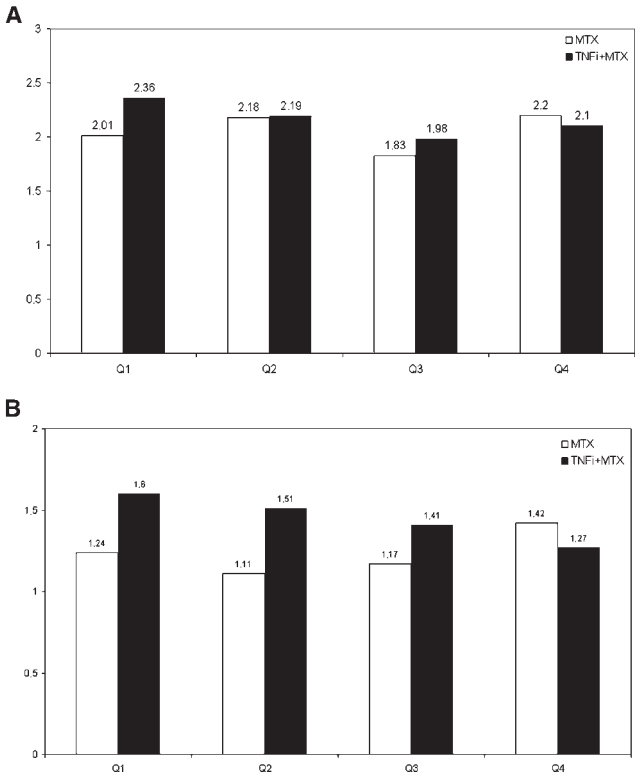

FIG. 2. ESs of SDAI (**A**) and HAQ-DI (**B**) in patients of different age quartiles (Q1–Q4) and under treatment with MTX or TNFi + MTX.

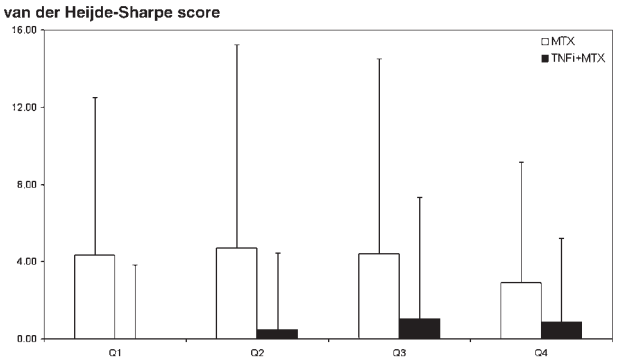

FIG. 3. Radiologic damage after 1 year of treatment: there were no statistically significant differences between younger patients and those in higher age quartiles (Q1: 18–42 years; Q2: 43–52 years; Q3: 53–61 years; and Q4: 62–82 years) within each treatment arm. Again, the progression of joint damage was almost halted in patients treated with TNFi + MTX compared with those receiving MTX monotherapy.

TABLE 3. Disease activity, physical function and progression of joint damage at baseline and after 1 year of the indicated treatment in the oldest 10% of the patients (age 69–82 years)

Treatment	Visit	*n*	Duration, years	SDAI	CDAI	DAS28	HAQ	X-ray score	Change in X-ray score
TNFi + MTX	Baseline	71	0.8 (0.7)	43.3 (15.4)	38.8 (13.5)	6.4 (1.1)	1.6 (0.7)	20.5 (20.5)	
	1 year	52		9.8 (9.4)	9.0 (9.3)	3.1 (1.3)	0.7 (0.7)	21.8 (21.9)	0.7 (4.3)
MTX	Baseline	45	0.6 (0.7)	47.0 (14.0)	43.1 (12.9)	6.7 (0.9)	1.6 (0.7)	34.6 (29.2)	
	1 year	38		17.4 (13.4)	16.4 (13.0)	4.2 (1.4)	0.9 (0.7)	39.4 (36.2)	4.4 (7.2)

Values are given as mean S.D.

consistent with the recently described reduced reversibility of functional impairment with increasing joint damage [3]. Radiographic progression in our cohort is comparable with that seen in the ASPIRE study. Nevertheless, over the 1-year period the progression of joint damage in the MTX group is also not very high in the two older quartiles (mean of ~3), and was reduced to ~1 by combination therapy. However, if extrapolated to a 5-year period, the difference between the groups would amount to 10 Sharp score units, corresponding to an increase in irreversible disability of ~0.1 HAQ units that may affect elderly patients who already have impairment of physical function due to age more than the young. Therefore, a clinically significant advantage of TNFi + MTX therapy can be expected under extended treatment with TNFi even in elderly patients.

In the present study, a large number of early RA patients (more than 1300) was analysed, and the results were robust across the two standard therapeutic approaches, MTX treatment and combination therapy of TNFi + MTX. In particular, we did not find a correlation between age and treatment response in patients with early RA. Thus, the data suggest a generalizable efficacy of DMARDs in elderly patients. This is further supported by recent observations on etanercept mono- and combination therapy [7]. While a limitation of our study is that we did not have safety data available for analysis and, therefore, did not address safety aspects in this investigation, the proportion of patients who completed the trials was similar across all age quartiles. This means that discontinuations were not different among the age groups. Moreover, in the context of clinical trials, entry criteria usually exclude patients with significant comorbidities. Therefore, additional safety information should be better obtained from large registries with patient populations that are not restricted by stringent study criteria [24–26].

Our data are at variance with a very recent publication by Radovits *et al*. [27], who concluded that elderly patients with RA have a reduced response to treatment with TNFis. However, this study came from an observational cohort of patients, whereas our data are pooled from randomized controlled clinical trials. By nature of our data source, we had results from control treatment arms employing MTX available and could complement the clinical data with radiographic outcome. Even more importantly, in the observational study by Radovits *et al*. [27], elderly patients with RA had much higher disease activity at baseline than younger age groups and the change in disease activity was similar among the age groups [27]. In contrast, in our study, baseline disease activity was similar among the age groups. Indeed, we have recently shown that baseline disease activity is a determinant of subsequent treatment response [28]. Moreover, our study population suffered from early RA with a disease duration <3 years; in the study cohort of Radovits *et al*., disease duration among patients of highest age was much longer than in the younger groups (10 *vs* 6 and 4 years, respectively). Their results suggest that disease duration rather than age may be an important factor for outcome.

In summary, the data shown here demonstrate that (i) patients with RA respond to DMARD therapy, including anti-TNF agents, irrespective of their age and (ii) like in younger individuals, the efficacy of a TNFi + MTX regimen is superior to MTX monotherapy in older patients. This information is of particular importance, since impaired physical function as well as the systemic effects of inflammation on the cardiovascular system and bone may affect elderly patients to a much more relevant degree than the young and lead to rapid deterioration of their general health [29, 30]. Therefore, after ensuring that no severe comorbidities pose as potential contraindications for intensive therapies, physicians should not use age to limit their therapeutic options.

Rheumatology key messages

- The response of elderly patients with active RA to DMARD therapy is comparable with that of younger patients.
- Both MTX and its combination with TNFis are effective in elderly patients.
- Physicians should not use patients' age to limit their therapeutic options.

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